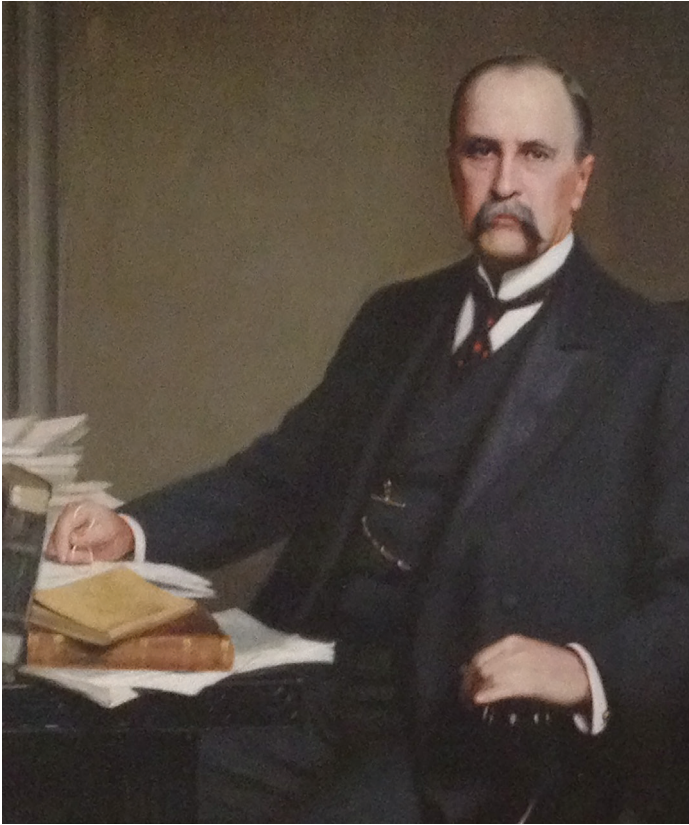


The Interurban Clinical Club (1905–2015)

*A Record of Achievement in
Clinical and Biomedical Science*

John N. Forrest, Jr.



Sir William Osler

Image in public domain (PD-1923)

THE INTERURBAN
CLINICAL CLUB
(1905–2015)

*A RECORD OF ACHIEVEMENT
IN CLINICAL AND BIOMEDICAL SCIENCE*



John N. Forrest, Jr

ACKNOWLEDGMENTS



The following are gratefully acknowledged for contributing financial support for the book.

Department chairs:

Mark Zeidel
Department of Medicine
Beth Israel Deaconess Medical Center
Harvard Medical School

Gary Desir
Department of Medicine
Yale School of Medicine

Donald Landry
Department of Medicine
Columbia College of Physicians and Surgeons

Richard Shannon
Former Chair, Department of Medicine
Perelman School of Medicine
University of Pennsylvania

Michael Parmacek
Department of Medicine
Perelman School of Medicine
University of Pennsylvania

Myron Weisfeldt
Former Chair, Department of Medicine
Johns Hopkins School of Medicine

Joseph Loscalzo
Chair, Department of Medicine
Brigham and Women's Hospital
Harvard Medical School

Individuals who contributed to the MD-PhD fund:

Jonathan Epstein
Executive Vice Dean and Chief Scientific Officer Perelman School
of Medicine University of Pennsylvania

Barbara Kazmierczak
MSTP Director
Yale School of Medicine

Copyright 2016 The Interurban Clinical Club.
Published by the New York Academy of Sciences

DEDICATION



for Catherine Lee Kiene Forrest

GREETINGS FROM THE OSLER FAMILY



The descendants of the Osler family sincerely wish to thank the editor and the active and emeritus members of the Interurban Clinical Club (ICC) for this book that keeps alive the ongoing celebration of the legacy of Sir William Osler as the founder of the club. Medicine is ever changing, but the concept of getting together to hear diverse scientific papers of new findings from the best creative physician-scientists of five east coast cities (Boston, New Haven, New York City, Philadelphia and Baltimore) will never be out of date. We were pleased that Eve Osler Hampson, the grand niece of Sir William, was invited to participate in the 200th meeting of the club in Baltimore, MD. We urge members of the ICC to visit the Osler libraries and museums at McGill Medical School, Johns Hopkins Medical School, and The Osler Club of London.

PREFACE



In 2010, I was asked to bring the history of the Interurban Clinical Club up to date in a fourth volume. The early history of the club, founded by William Osler in 1905, was published in 1937.¹ The first volume was prepared by a committee of the Club, composed of David Riesman of Philadelphia (editor), S. W. Lambert of New York, T. B. Fitcher of Baltimore, W.D. Stroud of Philadelphia, and H. A. Christian of Boston. Two additional volumes, published in 1976 and 1994, were edited by Mac Harvey of Johns Hopkins.

In the first volume, there was no reference to the original research done by the members of the Club. As Mac Harvey examined the programs of the meetings, it became clear that the activities of the Club and the careers of its members represented an important record of the development of clinical science and academic medicine in the United States. Thus, the scientific accomplishments of each member were included in their biographies, a practice continued in this volume.

The objects of the Club, as stated by Osler, were “to promote the scientific investigation of disease and stimulate the study of internal medicine; by mutual intercourse and discussion to improve our methods of work and teaching; and to increase our knowledge of the methods of work in other clinics than our own.” When the Club began, clinical science was in its infancy, and the cities in which the members resided (Boston, New York, Philadelphia, Baltimore, and later New Haven) and the universities and medical schools in which they worked were the major centers of activity in academic medicine.

Thus, the scientific programs represent a unique picture of the progress of American medicine in the last 110 years, and the members, as well as the non-members who participated in the programs, provide a composite of the men and women who were primarily responsible for the rapid progress of medicine by applying the methods of science to the study of disease in man.

The influence of the Interurban Clinical Club has been great. At its inception, it furnished a much needed, intimate meeting ground for the leaders in academic medicine who were responsible for areas of research, for training programs for young individuals, and for innovations in medical practice. In 1910, soon after the Club began its activities, the Flexner Report appeared and newly organized and reorganized Schools of Medicine were looking for leadership in their research programs. The meetings of the Interurban Club provided a forum where young people wishing to engage in a career in clinical science, could present their work for evaluation and could become known to the leaders of medicine whose counsel was sought regarding the recruitment of faculty members. For example, it was through the Interurban Club meetings that E.A. Locke met and learned of the unusual qualities of David Edsall. This led to Edsall's appointment as Jackson Professor of Medicine and director of one of the medical services at the Massachusetts General Hospital- an event considered a critical turning point in the development of clinical science in Boston.

This contribution of William Osler's did not stop with the original Interurban Clinical Club. Similar clubs were organized when the activities of the original group became known in various parts of the country. This development provided a forum for the rapid exchange of ideas among the various schools and hospitals in relation to advances taking place in basic and clinical research, clinical practice, and medical education. As an example of the importance of these satellite groups, the Central Society for Clinical Research was born out of the activities of the Central Interurban Club.

In agreement with Mac Harvey, I did not attempt to set the activities of the Club into the background of historical events. The book is a record of the activities of a group of physician scientists over the decades in the growth of clinical science in the United States. It is hoped that the volume will not only be of interest to the members of the Interurban Club, but will also serve historians as a source of information about the vital contributions that these leaders made to clinical science.

To present a sequential picture of the development of research and clinical science, the biographies of living members are presented in alphabetical order by each city in the club, listing active members first and then emeritus members. A section on recent scientific programs has been included (Chapter 9).

Chapters have been added by members to this volume on The Legacy of Sir William Osler and the Interurban Clinical Club (Chapter 4 by Thomas Duffy), The Blood Vessel and its Disorders: A Brief, Early History of Vascular Physiology and Medicine in Boston (Chapter 5 by Joseph Loscalzo), Why Junior and Senior Physician-Scientists and All Members of the Interurban Clinical Club Should Embrace Club Meetings (Chapter 6 by Cynthia Sears), on the development of our website (Chapter 7 by Wafik El-Deiry) and on the Osler Young Investigator Awards given at each meeting (Chapter 8 by William Chin).

The after dinner speakers at recent dinners of the club and their topics are included in the programs. No attempt has been made to summarize the lively discussions that followed the speakers.

Information for the biographical sketches was furnished by the living club members. Each member was asked to give an account of his or her career, including early education, medical education, and the genesis of interest in research, research training, and accomplishments in investigation. Important honors and memberships are listed. Great importance was placed on the research contributions of each member. All original source material will be offered to the National Library of Medicine, along with the programs of the scientific meetings of the Club.

I deeply appreciate the cooperation of the members of the Club in supplying biographical material and to the councilors in each city and the officers of the club, particularly Dr. Mone Zaidi of New York City, the current secretary-treasurer, and Dr. Jon Epstein, of Philadelphia, the current President of the Club. Dr. Epstein suggested having MD-PhD students present at the meetings and wrote about this in Chapter 10. Dr. Wafik El-Deiry, a previous secretary-treasurer and president, was instrumental in making sure this book was published.

I also gratefully acknowledge the excellent assistance in the preparation of this volume by my secretaries at Yale, Ms. Donna Carranzo, Ms. Mae Geter, and Ms. Kelly-Jo Carlson, and Dr. Zaidi's secretary Ms. Nanette Fraticelli of New York City.

The publication of this volume and the opportunity to present it to the members of the Club, to the libraries of the schools of medicine and departments of internal medicine has been made possible by contributions from the department chairs of medicine in the cities of the Club.

I am grateful to Dr. Douglas Braaten, Senior Vice President - Science Publications at the New York Academy of Sciences, who kindly agreed to publish this history of the ICC and devoted his staff to this effort.

John N. Forrest, Jr., MD, Sc.D (Hon.)
Professor of Medicine, Yale University School of Medicine, Editor

¹ Riesman, D. (Ed): History of the Interurban Club (1905-1937). Philadelphia, The John C. Winston Company, 1937.

William Osler and the Interurban Clinical Club. Bull. No. IX, International Association of Medical Museums. Sir William Osler Memorial Number. Privately issued, Montreal , 1926, p. 333

CONTENTS



Acknowledgments

Dedication

Greetings from the Osler family

Preface

- Chapter 1.** *The Organization of the Interurban Clinical Club
and Its First Meeting*
- Chapter 2.** *The Founding Members Biographies*
- Chapter 3.** *Recent History of the Interurban Clinical Club*
- Chapter 4.** *The Legacy of Sir William Osler and the
Interurban Clinical Club*
- Chapter 5.** *The Blood Vessel and its Disorders: A Brief, Early History of
Vascular Physiology and Medicine in Boston*
- Chapter 6.** *Why Junior and Senior Physician-Scientists and All Members of
the Interurban Clinical Club Should Embrace Club Meetings*
- Chapter 7.** *The Interurban Clinical Club Website*
- Chapter 8.** *The Sir William Osler Young Investigator Award*
- Chapter 9.** *Programs of Recent Interurban Clinical Club Scientific Meetings*
- Chapter 10.** *Broadening the Mission of the Interurban Clinical Club*
- Chapter 11.** *The Interurban Clinical Club Constitution and Officers*
- Chapter 12.** *Biographies of Living Members from Baltimore*
- Chapter 13.** *Biographies of Living Members from Boston*
- Chapter 14.** *Biographies of Living Members from New Haven*
- Chapter 15.** *Biographies of Living Members from NYC*
- Chapter 16.** *Biographies of Living Members from Philadelphia*

Index

Chapter 1

ORGANIZATION OF THE INTERURBAN CLINICAL CLUB AND ITS FIRST MEETING



The American Society of Clinical Surgery

Late one pleasant August afternoon in 1900, three distinguished American surgeons, Alton J. Ochsner, William J. Mayo, and Harvey Cushing, sat in a relaxed mood on a stone balustrade of the Pont d'Alexandre overlooking the River Seine.¹ The 13th International Medical Congress was underway in Paris, with an attendance of over 6,000 people, and the city was filled with physicians and surgeons. In addition, people were arriving from all over the world to attend the great Paris Exposition. The three men were completely exhausted and bored from listening to the many papers presented at the Congress, most of which were presented in languages they could ill understand. What had proved to be the chief attraction during that week for the visiting surgeons was not a part of the program of the Congress. It was instead an operative clinic given each morning by an ambidextrous genius and showman, Eugène-Louis Doyen, and held in his recently completed private hospital on the Avenue du Bois de Boulogne. (The building in later years served as the home of the American Red Cross Military Hospital No. 2.) Though these distinguished surgeons from the United States shuddered at Doyen's complete disregard for hemostasis and his emphasis on speed (for example, performing a mammary resection for cancer in seven minutes), they visited his operating room every day. However they might have disapproved of Doyen and his surgical techniques, his demonstrations were preferable to the boredom of listening for hours on end to presentations at the International Congress, whose value they were unable to gauge.

As the three men sat on that Paris bridge discussing this surgical exhibition, Cushing suggested that opportunities of this sort were important, if only to see other surgeons display their true colors. His friends replied that this was exactly what they had done with regularity for a number of years — paid visits to other clinics in order to see the nature and quality of work performed by their peers. The three lamented that some surgeons did not have close friends practicing surgery in other cities whom they could visit, nor a surgical colleague in their own city to whom they could entrust the

care of their patients while on such a tour. The idea was put forth that it might be possible to observe much more in less time if a small group of surgeons made these visits together and the host clinic prepared a specific program for them. All three agreed that this proposal had great merit.

Some 18 months later, after Cushing had completed his studies with Hugo Kronecker in Berne and with Masso in Turin and returned to Baltimore, he attended a meeting of the Biological Societies in Cleveland. During this visit he presented to George Crile the idea of organizing a small travel club of clinical surgeons who had an interest in “physiological pathology,” as the recent work in laboratory investigation was referred to.

Cushing made a significant contribution to the medical community by being the first to introduce into the United States the Riva-Rocci blood pressure apparatus that he had seen demonstrated in Pavia.² While Cushing was describing the device to Crile, their conversation was overheard by William T. Councilman, professor of pathology in Boston and president of the newly organized Suffolk District Medical Society. This new apparatus for measuring blood pressure seemed an ideal topic for discussion at one of the early meetings of the society. On October 24, 1902, Councilman wrote to Cushing and Crile, asking them to attend a meeting designed “to give a practical demonstration on the subject of [the] apparatus for measuring blood pressure, and speak of the advantages of knowing just what the heart is doing in surgical operations generally.” Both Crile and Cushing accepted, and a special meeting titled “Consideration of Blood Pressure” was held at the Boston Medical Library on January 19, 1903. Crile spoke first on “Some Observations on the Method of Control in the Blood Pressure,” followed by Cushing’s report on “The Clinical Value of Blood Pressure Observation.” The subsequent publications of these speeches were discussed by such notables as William T. Porter, professor of physiology, and Richard C. Cabot, professor of medicine. As a result of Cushing’s paper, a printed circular was distributed in February 1903 to all members of the department of surgery at the Harvard Medical School, requesting that a committee be formed to consider the “importance of blood pressure observations in surgical diagnosis and treatment.” This committee deliberated at length and eventually concluded that the skilled use of the finger was of much greater value clinically for determining the state of the circulation than any pneumatic instrument. In telling this story, Cushing always recited the following verse from Oliver Wendell Holmes’s “Stethoscope Song”:

*Now such as hate new-fashioned toys
Began to look extremely glum;
They said that rattles were made for boys,
And vowed that his buzzing was all a hum.*

This whole event strengthened the feeling of Cushing and his friends that the time was ripe to bring together for mutual benefit a group of young surgeons interested in studying surgical problems through experimentation. At that time, plans for an experimental laboratory of medicine and surgery, which were being pressed by Cushing, were underway in Baltimore, and in Cleveland an endowment had been secured for a laboratory of experimental medicine that became known as the Cushing Laboratory in honor of Cushing's father.³ Similar facilities were also under consideration in other cities, and so it appeared to be an ideal time for interested surgeons to join together and periodically pay visits to their colleagues' home institutions. There was a further exchange of letters in regard to this idea, and finally a meeting was held in New York at the home of George Brewer on July 11, 1903. Cushing could not attend, as his wife had just given birth to their first child, and Mayo had other commitments, but Brewer, Crile, Monroe, Frazier, and Munford met, drew up a tentative list of charter members, nominated themselves to office, and designated Baltimore as the place of their first meeting.

It was a very distinguished and congenial group that met in the house of officers' assembly room in the Johns Hopkins Hospital on Friday morning, November 13, 1903, to conduct the first meeting of the American Society of Clinical Surgery. The program for that first day began with attendance by invitation at Professor Halsted's customary Friday morning exercise for third-year students, held in the basement of old Ward G. Because the Johns Hopkins Hospital had as yet no surgical amphitheater, the members then moved to Howard Kelly's operating room, where J. M. T. Finney demonstrated his newly devised pyloroplasty for ulcer. A demonstration of the teaching of operative surgery on animals to third-year students, which Cushing had organized, was held in the Hunterian Laboratory for Experimental Surgery. Joseph Bloodgood explained his course in surgical pathology, and at the end of the day there was a demonstration of Hugh Young's new operation, perineal prostatectomy. All of the members felt they had started something that had the air of outstanding success.

As Cushing pointed out, William Osler obviously noticed this air of enthusiasm. By inviting the assembled surgeons to dine with him at the Mary-

land Club, Osler got himself invited to the first dinner of the American Society of Clinical Surgeons. This indicated to the surgical group that they had taken hold of an idea that was certain to spread, and that Osler would personally ensure that physicians created a similar society. Charles N. Camac commented on the origination of the idea for the Interurban Clinical Club in his essay entitled “Osler and Medical Gatherings” as follows:

In the summer of 1903 I was stopping with the Oslers at Caribou Lodge, Murray Bay. One day, on the golf course, as we walked between strokes, Dr. Osler said, “Don’t you think the meeting of a few of you fellows at each other’s laboratories and clinics, where you could see the work in progress and hear the teaching being given, would be worthwhile? We could get four or five fellows from New York, another group from Boston, another from Philadelphia, another from Baltimore.” Here, indeed, was the inception of an idea — but the period of gestation was nearly two years.⁴

Thus, the idea was in Osler’s mind before the first meeting of the American Society of Clinical Surgery. Elliot Joslin also mentioned that Richard Cabot had a similar idea and had talked it over with Osler. Osler probably had discussed this matter with Cushing long before the first meeting of the surgical group.

The Birth of the Interurban Clinical Club

With this unequalled knowledge of what the younger American clinicians were doing, Osler recognized that such a club organized for internists would be a way to advance medicine in America in a unique way. In early 1905, he called together a group of men — six from each of the four large cities of the East (Boston, New York, Philadelphia, and Baltimore) — to form the Interurban Clinical Club patterned after the Society of Clinical Surgery, which had been organized in July 1903. The invitees received a note as follows:

It is proposed to start among a few of the younger men in the Eastern cities an Interurban Club on lines somewhat similar to the Society of Clinical Surgery. The number of members will be limited. The objects of the Club will be: (1) to stimulate the study of internal medicine, (2) by mutual intercourse and discussion to improve our methods of work and teaching, (3) to promote the scientific investigation of disease, (4) to increase our knowledge of the methods of work in other clinics than our own. It is

proposed to meet twice a year to have demonstrations and discussions but not set papers. The program of each meeting is to be supplied by the men in the city in which the meeting is being held. It is proposed to hold the first meeting at the Johns Hopkins Hospital on April 28 and 29. The rules to govern the Club will then be discussed and adopted. You're invited to become a member and to be present on that date.

On the evening of April 28, the assembled group met for dinner at the Maryland Club and, with Osler as temporary chairman, officially organized the Interurban Clinical Club and elected Cabot as president and Thomas McCrae as secretary. Osler was elected the first honorary member. The charter members of the Interurban Clinical Club, all but one of whom (Barker) were present at this inaugural meeting, were Richard Clarke Cabot, Elliott Proctor Joslin, Edwin Allen Locke, Frederick Taylor Lord, Joseph Hersey Pratt, and Wilder Tileston of Boston; Charles N. Camac, Lewis Atterbury Conner, Walter Belknap James, Theodore Caldwell Janeway, Samuel Waldron Lambert, and Frank Sherman Meara of New York; David Linn Edsall, Aloysius Oliver Joseph Kelly, Warfield Theobald Longcope, David Riesman, Joseph Sailer, and Alfred Stengel of Philadelphia; Lewellys Barker, Rufus Cole, Charles P. Emerson, Thomas Futcher, Thomas McCrae, and William Sydney Thayer of Baltimore.

As one looks back over the past 110 years, the organization of the Interurban Clinical Club has perhaps had a more continuing influence than any other contribution which Osler made. Most of Osler's contributions were not truly original, whether one considers his clinical descriptions of disease, his relatively minor contributions in the laboratory, the origin of the basic concepts behind his "innovative" approaches to education, or the implementation of effective mechanisms for the exchange of ideas about education, research, and practice. But he often astutely picked up the ideas of others and was responsible for making them work. He had an intuitive sense of what was important as well as the personality and character to promote successfully those ideas which appeared to him worthwhile. His ability to clearly see a need and to provide an impetus is well illustrated by the founding of the Interurban Clinical Club.

INTER-URBAN CLINICAL CLUB MEETING FOR ORGANIZATION
AT THE JOHNS HOPKINS HOSPITAL BALTIMORE
April 28th and 29th, 1905

PROGRAM

Friday, April 28

12 noon.	Out-door Clinic	Dr. Osler
1 p.m.	Lunch at the Johns Hopkins Hospital	
2:30 p.m.	Demonstration of Cases of Stokes-Adams Disease; Experimental Demonstration of Heart-Block	Dr. Erlanger (by invitation)
	Influenza Infection	Dr. Boggs (by invitation)
	Demonstration of Cases of Gout	Dr. Futcher
7 p.m.	Dinner at the Maryland Club, after which the meeting for organization will be held	

Saturday, April 29

9 a.m.	Ward Visit	Dr. Osler
10 a.m.	Discussion of the Method of Keeping Hospital Records	Dr. Bloodgood (by invitation) Dr. Cullen (by invitation) Dr. McCrae
	Description of the Methods Used in the Clinical Laboratory	Dr. Emerson
12 noon.	Clinical Lecture	Dr. Osler

The Program of the First Meeting

The program of the first meeting was dominated by Osler. Fifty years later, Joseph Pratt recalled vividly the presentation by Joseph Erlanger of his work on “Experimental Heart Block in the Dog.” All of those in attendance leaned forward in the little amphitheater, trying to see the bundle of His encompassed by the special clamp he had devised. The situation reminded Pratt of Rembrandt’s group of surgeons at Dr. Tulp’s anatomy lesson. Following this demonstration, Osler presented a patient with heart block. Characteristic of Osler’s usual manner, he combined laboratory and clinical approaches in a clinical setting by tracing the patient’s cardiac apex beat with the Marey Cardiograph and the venous pulsations with an air-filled tambour. The first electrocardiograms were not taken in this country until 1909.

Joslin, who of course was famous for the obsessive zeal with which he followed all of his diabetic patients after he began practice in 1897, demonstrated this obsession by providing at the 100th meeting a follow-up on the patient with heart block who Osler had presented at that first meeting. The patient, Donald McCormick, had left the hospital shortly after his appearance before the Interurban Clinical Club. In 1942, some 37 years later, he was found by Joslin to be president of the Dauphin Deposit and Trust Company in Harrisburg, Pennsylvania. At that time he was without symptoms, but his blood pressure was 210/100. His chest X-ray was normal, and his electrocardiogram was normal except for the evidence of left ventricular preponderance and a slight delay in conduction time. The patient worked regularly until the day of his death on May 1945, at the age of 77. His demise was sudden and occurred 50 years after complete heart block had been diagnosed. There are a number of interesting accounts of that memorable initial meeting of the Interurban Clinical Club. One is that of Alan W. Freeman, a medical student of the class of 1905:

One spring morning when the student came on ward F to see if a new case had been assigned to him overnight, he found the ward in an unmistakable flutter. Miss Nutting, the supervising nurse, and the head nurse of the ward were standing together in the center of the ward, looking severely efficient. The pupil nurses were straightening the corners of the bed coverings and patting the pillows. The ward maids were mopping the last suspicion of dust from the floors. The intern stood at the door in a stiff, clean uniform. Even the patients looked expectant. From a classmate the student learned the reason

for the unusual bustle. The Interurban Clinical Club was meeting in Baltimore and was going to accompany Osler when he made rounds on the wards at 10 o'clock...

Promptly at 10 Osler came on the wards surrounded by the dozen or so members of the club and with even more casual followers than usual. They came down the center aisle of the ward, Osler nodding or speaking to the patients as he passed their beds. He stopped in front of one of the student's cases.

"Whose case is this?" he asked. The student stepped forward. "It's mine, sir," he said. Osler looked at his eyeglass case which he carried in his hand and where he had pasted a printed list of the students on medicine. "Well, Mr. Freeman, this is your case," he said. "What is the first thing we want to do to him?" The student thought he knew the answer to that. "We want to read his history, sir." "No, we've already read his history. We want to examine him. What's the first thing to do?" Surely, thought the student, there can be only one reply. I've heard him say it a dozen times. "We want to look at him, sir." "No, we're not ready to look at him yet. What should we do first?" There was certainly only one thing to say. "I'm sorry, sir, I don't know what you have in mind." "Well," said Osler dryly. "The first thing to do is to ask Dr. Lambert to stand out of the light." After that the student never tried to look at a patient without first being sure that the light was as good as he could make it.⁵

Osler's Out-door Clinic at the Saturday session was described by Riesman:

No one privileged to be present will ever forget the great teacher's clinic on the occasion of the first meeting — the amphitheatre crowded with students and physicians; the members of the newly formed club on the front benches, and in the pit the patient with Osler on one side and a perspiring student on the other. The case was that of a young colored girl who had had lobar pneumonia sometime before but who had not yet fully recovered. Tuberculosis had been suggested but numerous sputum examinations had been negative. Osler asked the student whether he had any suggestions or ideas about the case. In great earnestness with a contracted brow, the embarrassed student bent over and scrutinized the patient long and profoundly, but saw no light. Finally, Osler, patient and sympathetic, said to him: "Will you please walk around?" The student passed to

the other side of the patient and then in the neck he beheld a mass of cheesy glands. The incident was a valuable lesson. It illustrated a point often dealt with by Osler in his writings; namely that most of our mistakes in diagnosis arise from errors of omission rather than from those of commission.⁶

Osler had planned to sail for England on May 19, and on the Saturday before his departure he held his last clinic in the Johns Hopkins Hospital. Some of the members of the Interurban Clinical Club returned to attend. The third- and fourth-year students had come in early and occupied the front row seats which were theirs by right. In the remaining seats and standing in every possible place were the students of the first and second years, the house staff, most of the visiting staff, and as many nurses, hospital employees, and physicians from the city as could squeeze in. The space in the front of the room was empty except for the patient whose case was to be discussed. He lay on his bed and looked with curiosity about the crowded room. Only one ceremony had been arranged. The students of the third and fourth years had each contributed a few dollars for the purchase of a gift to the chief — a loving cup, nearly a foot in height and mounted on a tall ebony pedestal. It was ornamented in the florid style of the times and, as the jeweler had assured the committee, “made a most handsome appearance.” Much care had been devoted to the composition of the inscription, which was meant to convey as much of the feeling of the students toward Osler as they could express in words. Alan Freeman, the student chosen to present the gift to Osler, sat in the front row of seats, clutching his short manuscript in his sweating hands and reading the words over and over. Freeman’s brother Douglas, a PhD candidate in history at that time, described the event in a letter to his father:

May 13, 1905. The whole interest of the day of course centered on the affair up at the University Medical School where the presentation was to come off. I went up, of course, to see the whole affair.... The chief came in when the house was as packed as it could be, every seat taken and then standing everywhere. He didn’t hesitate, putting his beaver down on the table, went at it immediately. The clinic was delightful, one of those brilliant clinics which made the name of Osler and the “Saturday clinic” famous.... One, two, three cases were wheeled in, discussed and discoursed upon and then when he had gone over several specimens and demonstrated them to the class, the moment came. The old man perched himself up on a chair.... I can’t tell you exactly what happened then, that is, what he said, for my

eyes were following a tall fellow who got up from somewhere walked across the room behind the chief and returned presently with a man following him carrying an immense covered cup.... I felt for him, my heart beat with his, for it was old Nal. He waited with perfect ease.... I won't tell you what he said because you will see it in all the papers which I will send you. But he did it finely.... It was easy, graceful and to the point, not strained in the least, and breathing, good sense and good taste along with excellent language and fine humor to relieve the situation.... He concluded with a graceful little line, and revealed the cup.... When the speaker took his seat, such a round of applause you never heard in your life.... Then the chief responded, in the same strain and with the same mood, reflecting exactly the sentiments Nal had expressed. He left then, in university fashion.

After the clinic, when Nal and I went in to have Osler sign his portrait for them, the Chief took him by the hand, grasped it cordially and said "That was beautifully expressed Freeman," and then he repeated, "beautifully expressed..."⁷

The Interurban Clinical Club has flourished, and it served an important role during the developmental period of the "new medicine." Osler's appreciation of a need and the drive to meet it led to a chain of events that provided a helpful forum for teachers and investigators in the field of internal medicine during its logarithmic phase of growth.

Notes

1. Cushing, H. The Society of Clinical Surgery in Retrospect. *Am J Surg* 169 (1969): 1.
2. Fulton, J.F. *Harvey Cushing: A Biography*. Springfield, IL: Charles C. Thomas, 1946. p. 212–216.
3. Harvey, A. McGehee. Harvey Williams Cushing: The Baltimore Period 1896–1912. *Johns Hopkins Med J* 138 (1976): 196.
4. Camac, CNB. Osler and Medical Gatherings: The Origin of Interurban Societies. *Sir William Osler Memorial Number*. Bulletin No. 9 of the International Association of Medical Museums. Montreal: private issue, 1926. p. 328.
5. Freeman, A.W. *Five Million Patients*. New York: Scribner and Sons, 1946. p. 23.
6. Riesman, D. William Osler and the Interurban Clinical Club. *Sir William Osler Memorial Number*. Bulletin No. 9 of the International Association of Medical Museums. Montreal: private issue, 1926. p. 333.
7. From the Freeman papers. Archives of the Johns Hopkins University.

Chapter 2

THE FOUNDING MEMBERS BIOGRAPHIES



Edited from Volume 2, The Interurban Clinical Club, 1905-1976, by A. McG Harvey

There is little doubt of Osler's sound appraisal of the young men active in internal medicine in 1905 when one looks at the careers of those he chose as charter members of the Interurban Clinical Club. All proved to be outstanding physicians; many made fundamental contributions to medicine's scientific base, and to the application of scientific developments in the practice of medicine.

Today we recognize a blight on this record, which is that none of the founding members were women. At the time when Osler, Halstead, Welch, and Kelley in 1893 founded Johns Hopkins Hospital and medical school, forward looking women from Baltimore gave large sums of money to allow the new school to be built. These women had sufficient influence to request that women be admitted to the new school on equal terms as men.

Richard Clark Cabot, MD (1868-1939)

Richard Clarke Cabot, the son of James Elliott and Elizabeth Dwight Cabot, was born in Brookline, Massachusetts, on May 21, 1868. His father, a philosopher, was an overseer of Harvard College and a friend and biographer of Ralph Waldo Emerson. Both of Richard's parents came from old Boston families, prominent in social and financial ways but also distinguished for independent thought and action, qualities which Cabot was himself to display in his distinguished career. He graduated summa cum laude from Harvard in 1889 and received his M.D. degree in 1892. His paper before the Boylston Medical Society, the student medical society dating back to 1811, concerned a study of "The Medical Bearing of Mind-care." Christian Science was a quarter of a century old at the time. In what was to prove his characteristic approach to clinical investigation, the author accumulated a vast amount of knowledge by direct mail questionnaires to 150 prominent

Christian Scientists.

Cabot's ability and drive were already evident during his 18 months of internship served at the Massachusetts General Hospital (MGH). During this period he published the results of his first clinical research project on "Leukocytosis as an Element in the Prognosis of Pneumonia." The following year (1894-1895), while he was a Dalton Research Fellow at the MGH, he was the first to note that the white blood cell count increases during pyogenic infections and that a leukocytosis is additional laboratory evidence to support the diagnosis of appendicitis. Cabot introduced clinical hematology to the MGH and his studies on the blood were put into book form in 1896 when he was just four years out of medical school. The volume was entitled *A Guide to the Clinical Examination of the Blood*; the first book of its kind in English, it went through five editions. As a reflection of his interest in diseases of the blood, his name is given to the remains of a nuclear membrane sometimes seen within the red cells in severe anemia-Cabot's ring.

After serving in the Spanish-American War, Cabot returned to Boston where he entered private practice and continued his interest in research. In 1899 a small monograph on the "Serum Diagnosis of Disease" appeared, relating mainly to the Widal reaction in typhoid fever. In 1901 he finished the first edition of his *Physical Diagnosis of Diseases of the Chest* and over the next few years expanded it to a complete textbook of physical diagnosis which went through 12 editions up to the time of his death in 1939.

Cabot's method of conducting clinical investigation was to gather data from large numbers of cases and to arrive at conclusions statistically. Beginning in 1830 a group of famous Boston physicians, including Henry I. Bowditch, Oliver Wendell Holmes and James Jackson, Jr., studied in Paris under Louis, who was the first to apply statistical methods to the analysis of clinical disease (the "numerical method"). These physicians popularized clinical study in the United States. Using this method, Cabot conducted a study which led to what has been considered his most important contribution to medical science: his paper on "The Four Common Types of Heart Disease." In this paper he classified heart disease according to its causes, finding that 93% of all cardiac disease was rheumatic, arteriosclerotic, syphilitic, or nephritic. Paul Dudley White, in appraising this work, wrote as follows: "For the first time proper emphasis was laid on the etiological diagnosis of heart disease. The paper is a landmark in medical history which places him as the greatest contributor to cardiology in our generation."

Another important contribution made by Cabot was the introduction of the case method of teaching. The idea of using summaries of cases to teach medicine systematically was first introduced by Walter B. Cannon. In about 1898, while he was still a medical student, Cannon made this suggestion to Cabot, as well as to other members of the clinical faculty, and in 1900 published several articles concerning it. He first got the idea from a roommate, a student in the Harvard Law School, who described to him the new case teaching method used in the law school. Cabot realized the potential of the idea and in 1902 published a small book of 43 case summaries called *Exercises in Differential Diagnosis*. By 1906 he had enlarged the book, which was then entitled *Case Teaching in Medicine*. He soon became impressed with the usefulness of having a definite final answer in the form of a pathological lesion found at operation or at autopsy. This added great value to the teaching session by making it possible to relate the clinical picture to the pathological one. As early as 1905 he was calling such sessions *Clinical Pathological Exercises*. He soon developed the fully organized *Clinical-Pathological Conference (CPC)* for which he deserves full credit as the originator. The CFC, as it came to be known, received the praise of Alan Gregg when he said: "It is the wonder and admiration of many of our foreign visitors, who see in it a candor and fearlessness all together to the credit of American medicine."

As pointed out by Williams, Cabot was a master of the "constructive and inspirational speech or essay," both of which were popular in his day. His essays are characterized by their graceful use of the language, their clarity of expression, and the persuasiveness of their logic. One of the things which Cabot often spoke and wrote about was the sorely neglected hospital outpatient department. He was concerned about the difficulty in getting proper treatment for patients and tried to remedy this situation by establishing a "medical social service." In October 1905, a small force of social workers were organized to attend to any cases which the outpatient physicians might see fit to send to them. Cabot was well aware of the other efforts that had been made in this direction, particularly the one begun in July 1905 when Joseph H. Pratt organized classes designed to improve the treatment of tuberculous patients in their homes. An important part of Pratt's plan was the "friendly visitor"-a paid female worker who went into the home regularly to instruct, advise, and report on conditions and progress. The organization of social service at the MGH is an example of Cabot's ability to recognize valuable ideas and his drive to put them into action by the creation of a new institution. Miss Ida M. Cannon, sister of Professor Walter B. Cannon, became head social worker at the MGH in

1907 and deserves equal credit with Cabot for developing this new field. Cabot wrote profusely about this new organization, his best work on the subject being *Social Service and the Art of Healing* published in 1909.

Cabot was one of the earliest American physicians to recognize the importance of Freud's work, an indication of his familiarity with the literature and his open-mindedness about new ideas. As early as 1906 Cabot indicated that remarkable therapeutic successes had been obtained through the use of Freud's methods and conceptions: "It is now a solid science, and we have been verifying its results at the MGH." This was some three years before Freud came to America on a visit which he called "The Introduction of Psychoanalysis into North America." Cabot thought religion to be the central driving force in human beings and that psychotherapy would have to acknowledge and use this force if it were to be as useful and efficient as possible.

He was also interested in postgraduate teaching. In 1902 he initiated at the MGH a summer course in internal medicine which was attended by physicians from all parts of the country. This pioneer development in postgraduate education was conducted annually until 1929.

Cabot came to the conclusion from his own experience that group medicine in the teaching hospital gave better medical care than could the private practitioner. He expressed this view in public addresses and in articles, the most controversial of which appeared in May 1916 in the *American Magazine* entitled "Better Doctoring for Less Money." Here he strongly advocated some system of health insurance centered around the hospital as a better way to give medical care for less money — even at the expense of the doctor-patient relationship if that were necessary.

In 1916 he set out on a lecture tour to the Midwest to convince people that the U.S. should enter the war immediately. When America did become involved in the conflict, Cabot served as Chief of Medicine with Base Hospital #6 formed at the MGH; here he created desperate problems for military-minded people such as Frederic Washburn, the hospital director, because he never learned to salute or keep his shoes shined.

Not content with his position in the Base Hospital, Cabot obtained leave and with Dr. Wright ran a dispensary for refugees and repatriots in Paris from November 1917 to March 1918. He lectured at the Sorbonne in French on medical social work; these lectures were published in 1919 in

Paris under the title of “Essais de Medecine Sociale.”

Cabot’s interest in the social aspects of medicine and in ethics led in 1919 to his becoming professor and director of the department of social ethics at Harvard at the same time that he held a full professorship of medicine. The major part of his later years was spent delving into social and ethical problems. In 1927 he published “The Goal of Social Work,” in 1933 the “Meaning of Right and Wrong,” in 1936 “The Art of Ministering to the Sick,” and in 1937 “Christianity and Sex.”

Cabot had many other interests. He was editor of the *Archives of Internal Medicine* and of the *Case Records of the Massachusetts General Hospital*. He was a member of the Association of American Physicians. He was also the choral director who always led the MGH Glee Club on the steps of the Bulfinch Building on such occasions as the dedication of the new Outpatient Building in 1903, or led Christmas carolers over Beacon Hill and through the wards of the hospital; events which he himself originated.

Cabot was clearly the heir apparent to Frederick C. Shattuck as chief of the Medical Services at the Massachusetts General Hospital. In a conversation with Cabot in which Edwin A. Locke (a founding member) was discussing with him the important qualifications which David Linn Edsall (another founding member) had for the position, Cabot replied “I’ve always expected to succeed Shattuck . . . Edsall is a better man than I am . . . I will do anything and everything in my power to help him.” When Edsall became chief of the East Medical Service and Jackson Professor of Medicine (1912), Cabot was as good as his word.

Cabot always espoused the telling of truth to patients on ethical grounds, even when it was disagreeable, and in his own final illness he practiced what he preached. He demanded to know the truth and did not flinch from pain or from the realization of the grave prognosis given. Uncomplaining, he followed with professional interest the course of his own heart failure, which developed after he had been plagued for 20 years by peptic ulcer and angina pectoris. This man who made extraordinary contributions to medicine, social service, and ethics died on May 8, 1939.

References

Cabot, R.C.: The four common types of heart disease. *JAMA*, 63:1461, 1914.

Willims, T.F.: Cabot, Peabody and the care of the patient. *Bull. Hist. Med.*, 24:462, 1950.

Cannon, W.B.: The case system in medicine. *Boston Med. Surg. J.*, 142:563, 1900.

Elliot Proctor Joslin, MD (1869-1962)

Elliott Proctor Joslin was born in Oxford, Massachusetts, on June 6, 1869. After receiving his AB at Yale, he studied chemistry for a year in the Sheffield Scientific School under Professor R. H. Chittenden. He then entered Harvard Medical School, graduating in 1895. His first paper on diabetes was given before the student Boylston Medical Society in 1893 under the title "Pathology of Diabetes Mellitus." After his graduation from medical school, Joslin studied abroad. From the clinic of Professor Ewald in Berlin, in association with Kuttner and Rost, he published the results of a study of metabolism in a case of gastric ulcer with resection and a gastroenterostomized case with feedings of eucasein and peptone.

When he returned to the United States in 1897, he spent a year as medical house pupil at the MGH. During this year he reviewed the records of the diabetic patients admitted over the preceding three quarters of a century, a study that was published in collaboration with Reginald Heber Fitz. In 1898 he again spent time in Europe visiting the clinics of Naunyn, Minkowski, Magnus-Levy and Gerhardt.

Although he was known particularly as a diabetologist, his early years in practice were characterized by a general interest and he actually started as an assistant to James J. Putnam, a neurologist. Up until World War I, he saw patients with a wide variety of illnesses, and despite his primary concentration on diabetes, his medical interests were always broad. When he began the practice of medicine, he was associated with the Boston City Hospital where he remained as a consultant in medicine until his death. His first academic position at Harvard was as an assistant in physiological chemistry from 1898 to 1900. He then became an assistant in the theory and practice of physic and was promoted through the various academic grades to clinical professor of medicine in 1925.

In 1916 he published the first edition of his famous *Treatment of Diabetes Mellitus*. This book went through many editions as did the smaller companion volume, *A Diabetic Manual for the Mutual Use of Doctor and Patient*. From Joslin's long association with Francis G. Benedict, then director of the nutrition laboratory at the Carnegie Institution (in Boston), three monographs resulted—*Metabolism in Diabetes Mellitus*, *A Study of the Metabolism in Severe Diabetes*, and *Diabetic Metabolism with High and Low Diet*. Joslin early recognized the value of the work of Frederick M. Allen, who, in the pre-insulin days, carried on studies first at Harvard Medical School, then at the Hospital of The Rockefeller Institute. He adopted the concept of undernutrition in the treatment of diabetes during the years 1914–23, thereby keeping many patients alive and in reasonable physical condition.

Joslin was one of a small group of physicians who in 1922 were invited to Toronto to discuss the use of insulin in patients and to learn of the latest laboratory findings. As a result of this meeting, it was possible on August 7, 1922, to initiate treatment with insulin in a diabetic patient at the New England Deaconess Hospital.

Joslin was instrumental in establishing the Ellen Osborne Proctor Fund for the study of chronic disease at Harvard Medical School. In 1932 Joslin was awarded the Kober Medal of the Association of American Physicians. In addition he received many honorary degrees and awards for his work in diabetes. He held membership in the American Society for Clinical Investigation, the Association of American Physicians, the American Philosophical Society, and was a Fellow of the American Academy of Arts and Sciences. He died on January 28, 1962.

References

Marble, A.: Elliott Proctor Joslin (1868-1962). *Trans. Assoc. Am. Physicians*, 75:25, 1962.

Woodyatt, R.T.: Presentation of the Kober Medal to E. P. Joslin. *Trans. Assoc. Am. Physicians*, 47:8, 1932.

Edwin Allen Locke, MD (1874-1971)

Edwin Allen Locke was born in Halifax, Massachusetts, on October 15, 1874. He earned the PhB and MA degrees at Brown University, where he became a lifelong friend of John D. Rockefeller, Jr.

He graduated from Harvard Medical School in 1901 and served as a medical house pupil at the MGH. He then entered the private practice of medicine and joined the staff of the Boston City Hospital, where he taught clinical medicine and served as a visiting physician. He devoted a good deal of his time and effort to the care of patients with tuberculosis at the Boston Consumptives Hospital — later called the Boston Sanatorium — of which he became physician-in-chief. His interest in tuberculosis extended beyond the medical care of patients with this disease to the psychological, economic, and social problems associated with it. He played an important role in shaping the educational and research policies of the National Association for the Study and Prevention of Tuberculosis. At Harvard he advanced to the rank of clinical professor of medicine and at the Boston City Hospital became physician-in-chief of the Fourth Medical Service.

During the influenza pandemic of 1918, Locke established a ward for the study and treatment of influenza at the Boston City Hospital. Among his associates in this undertaking was Henry M. Thomas, Jr. Bacteriological and clinical investigations of pneumonias and observations on the serum treatment of Type I pneumococcal pneumonia were carried out on that ward for several years.

In 1924 Locke invited Gerald Blake and George R. Minot to join him in a partnership and to share his office building and practice; thus he organized the first group practice in Boston. William P. Murphy was one of many other members later taken into this “firm.”

As one of the founding members of the Interurban Clinical Club, Locke became a close friend of David L. Edsall, then at the University of Pennsylvania, and his brother-in-law, Wilder Tileston of Boston. Locke soon became aware of Edsall’s great talents as a physician, clinical investigator and innovator. Locke, though not a regular member of the staff there, persuaded the trustees at the MGH and Henry Christian, then dean of Harvard Medical School, to invite Edsall to succeed Frederick Shattuck as Jackson Professor of Clinical Medicine and chief of service at the hospital, positions which he accepted. Locke later played an important role in Edsall’s appointment as

the first full-time dean of the Harvard Medical School. The appointment of James H. Means to succeed Edsall at the MGH was also one in which Locke had an important influence.

And it was Locke who initiated the establishment of separate teaching services for the medical schools of Harvard and Tufts at the Boston City Hospital and later persuaded the trustees of that hospital to join the Harvard Medical School in supporting the first full-time academic department of medicine for teaching, clinical investigation and the care of patients in a municipal hospital. The trustees appropriated a substantial sum of public money to supplement a private gift to build the Thorndike Memorial Laboratory. Francis W. Peabody, whose medical career Locke helped to shape from the time Peabody completed his service as house officer at the MGH, was chosen as the first director of the Thorndike Memorial Laboratory and also as director of Harvard's Clinical Service, of which Locke was physician-in-chief. Peabody brought to the Boston City Hospital a staff of brilliant young physicians and investigators, including Joseph T. Wearn, Herrman Blumgart, William B. Castle, Soma Weiss and Henry Jackson, Jr., the forerunners of a long line of physicians who were to become leaders in academic medicine in the United States and who helped set high standards for the care of patients and for clinical investigation.

When Peabody died, Locke persuaded George R. Minot, a member of his "firm," to move from the Huntington Memorial Laboratory and the Peter Bent Brigham Hospital to the Thorndike to succeed him.

Most of Locke's medical publications, some 40 in number, dealt with tuberculosis and other diseases of the chest, but they also included case studies and reviews of a wide variety of clinical subjects such as iodine reactions of the blood (1903); various infectious diseases including scarlet fever (1905), Haverhill fever (1933) and epidemic pleurodynia (1936); chronic diseases of bones and joints; and several dealing with the economic, public health and social implications of tuberculosis and other chronic diseases. He was sole author of most of his medical contributions, but he had a number of distinguished co-authors including Richard C. Cabot, Wilder Tileston, S. Burt Wolbach, Henry Jackson, Jr., Henry M. Thomas, Jr., and George R. Minot. His greatest contributions to American medicine, however, were made quietly and tactfully behind the scenes, using his deep and perceptive understanding of people, his total unselfishness and generosity, his great power of persuasion and his vast influence in medical circles, all of which he used in the best interest of improving medical education and

clinical research at Harvard.

Among the many societies in which Locke was active were the American Academy of Arts and Sciences, the American Clinical and Climatological Association, the International Tuberculosis Association, and the American Society for the Advancement of Clinical Research.

In September 1935, Locke became director of health and athletics, with full professorial rank, at Williams College; he held this position until 1942. He died on March 6, 1971, at the age of 96.

References

Stetson, R.P.: Edwin A. Locke, M.D. *Trans. Am Clin. Climatol. Assoc.*, 83:xli, 1971.

Finland, M.: Edwin A. Locke, 1874-1971. *Trans. Assoc. Am Physicians*, 85:27, 1972.

Frederick Taylor Lord, MD (1875-1941)

Frederick Taylor Lord was born in Bangor, Maine, on January 16, 1875. In 1897, he obtained a B.A. from Harvard and three years later graduated from the Harvard Medical School. His first knowledge of clinical medicine was acquired in the MGH during his internship, for at that time there were no clinical clerkships at Harvard and fourth-year students were not allowed in the wards. From the time he became a house officer until he retired as a visiting physician in 1935, his life was intimately connected with the MGH.

On finishing his internship, Lord entered private practice, but at the same time began research in bacteriology at the MGH under the personal direction of J. Homer Wright, who was as skilled in bacteriologic technic as he was in pathology. At the outset, he received help and inspiration from William H. Smith, but Wright and Reginald Fitz were the two men who influenced him most. His first study published from the laboratory dealt with the influenza bacillus, which he cultivated from 11 cases of acute and 18 cases of chronic infection of the upper respiratory tract (1902). Additional studies of the influenza bacillus appeared in 1905. This work made a favorable impression on Osler who asked Lord to prepare the section on

influenza for Osler's System of Medicine. He also contributed, with Walter Jones, the chapter "Diseases of the Pleura" to Osler's System (1907).

Later, Lord and Robert N. Nye carried out valuable studies on the biology of the pneumococcus. Pneumonia and tuberculosis were his major subjects of study in later years and Lord was one of the first to investigate the anti-pneumococcus serums. In collaboration with Roderick Heffron and Elliott Robinson, he wrote two books on the treatment of pneumonia, the second of which dealt with chemotherapy as well as serum therapy.

In 1915, his valuable book *Diseases of the Bronchi, Lungs and Pleura* appeared; ten years later a second edition, which was thoroughly revised and included a section on pulmonary tuberculosis, was published. This work was primarily based on Lord's experience at the MGH and in his private practice.

Lord was a remarkably successful teacher. Year after year, he gave a course for practitioners which was attended by as many as a hundred physicians at one time. His consulting practice was one of the largest in Boston, and he made good use of this abundant material. In the birthday volume presented to Sir William Osler in 1919, Lord reported an analysis of 100 cases of pulmonary abscess. By 1925 he was able to add 127 cases.

In 1930 Lord was made professor of clinical medicine at Harvard, becoming emeritus in 1935. In 1932 he was president of the American Society for Thoracic Surgery. He was a member of the American Society for Clinical Investigation, the Association of American Physicians and the American Clinical and Climatological Association.

In 1917 he went to Serbia as a member of the American Red Cross Commission and in recognition of the services of the Commission was decorated by the Crown Prince. He died in 1941.

References

Pratt, J.H.: Frederick Taylor Lord, 1875-1941. *N. Engl. J. Med.*, 226:869, 1942.

King, D.S.: Frederick Taylor Lord, M.D. *Trans. Am. Clin. Climatol. Assoc*, 58:1xxi, 1946.

Means, J.H.: Frederick Taylor Lord 1875-1941. *Trans. Assoc. Am. Physicians*, 5726, 1942.

Joseph Hersey Pratt, MD (1872-1956)

Joseph H. Pratt was a rugged New Englander, born in Middleboro, Massachusetts, on December 5, 1872. At the age of 18 he entered the Sheffield Scientific School of Yale where he met Russell H. Chittenden, who first introduced him to investigation. In the autumn of 1894 he entered Harvard Medical School. Physiology was then a flowering experimental science at Harvard. William T. Porter was working with nerve-muscle preparations, Charles S. Minot was studying the development of the guinea pig embryo, and Walter B. Cannon was contributing to our knowledge of the digestive process. Pratt learned from each of them.

After his first year at Harvard, he transferred to Johns Hopkins. Here he recognized that the study of pathology was the key to the understanding of disease. He was tremendously influenced by Osler, and in 1949, at the age of 77, Pratt published his student notes taken in Osier's clinic in a small volume entitled *A Year with Osler, 1896-97*. After graduation in 1898, Pratt returned to Harvard to work under William T. Councilman in pathology for four years. During that period he took a leave of absence to work in Strasbourg for a few months with Professor Ludolf Krehl, who was then writing his *Principles of Clinical Pathology*, a book which Osler said filled the gap between empirical and scientific medicine.

From 1900 to 1917, Pratt was on the staff of the Harvard Medical School. In 1902 he began the private practice of medicine but he managed to combine this with laboratory investigations into diseases of the blood, the pancreas, pneumonia, the psychoneuroses, and tuberculosis. In 1906 Pratt offered a course in clinical research as an elective for fourth year students; one of his students was Francis W. Peabody, who later became a distinguished professor of medicine at Harvard. This course was significant because at that time a great barrier of prejudice and misunderstanding existed between scientists and clinicians. Pratt tried at every chance to unite the "old humanities and the new sciences".

Pratt was responsible for the reintroduction of pneumothorax as a therapeutic procedure in this country; he was the first to emphasize the importance of prolonged bedrest without exercise in the treatment of pulmonary tuberculosis; and he was the originator of group psychotherapy for these patients. Because he was not able to meet every patient in the clinic individually, he organized a class so that he could supervise his patients each week in a group. His interest in the cardiac arrhythmias was stimulated

by contact with James MacKenzie who in 1908 showed him how to use the polygraph. Pratt was a leader in introducing the modern methods of analysis of the heartbeat to this country.

The importance of pancreatic juice for the absorption of fat was first shown experimentally by Claude Bernard, who observed large amounts of fat in the feces after destruction of the pancreas by the injection of oil into the ducts. Pratt demonstrated the paramount importance of the pancreatic juices, using a method devised by F.T. Murphy which completely isolated the pancreas from the intestine. In all of his animal experiments, Pratt found a marked impairment of fat absorption, 67 percent of the intake being recovered from the feces. The fat-splitting was normal and the amount of soap in the feces inconstant. As in human beings with a like condition, the stools were massive, and fat visible to the naked eye was present.

In the summer of 1930 Mr. William Bingham, II, needed a doctor during convalescence in Maine. Pratt stayed with him for six weeks and convinced Bingham to help improve medical care in New England. Pratt recognized that family doctors needed help in diagnosing and planning management for their patients. If something could be done in this regard, the knowledge as well as the prestige of the local physician would improve. The idea appealed to Bingham and a unit was set up in the old Boston Dispensary. The plan succeeded and on Pratt's birthday in 1937 the cornerstone of the new Joseph H. Pratt Diagnostic Hospital, with its 65 beds and its complete laboratory and X-ray equipment, was laid. Other buildings followed, including one for surgical care and one for medical research. The New England Medical Center of Tufts University School of Medicine and Dental Medicine thus came into being.

Pratt enunciated his philosophy of medicine in 1928 in his presidential address before the American Clinical and Climatological Association: "We need physiological clinicians and not clinical physiologists. Without a firm foundation of physiology or pathological anatomy clinical experience can with justice be compared to a house built on sand . . . But a scientific foundation without clinical knowledge and experience is no house at all." As Dr. Samuel Proger wrote: "Dr. Pratt appeared on the medical scene when scientific medicine in America was in its infancy. He left the medical scene when scientific medicine in this country had made such great strides as to place it in a position of world leadership. His driving energy, relentless probing, insatiable curiosity, and boundless enthusiasm added much to the ferment that made American medicine bloom."

Pratt held membership in the American Society for Clinical Investigation, the Association of American Physicians, the American Clinical and Climatological Association, the American Physiological Society, the American Society for Experimental Pathology, and was a Fellow of the American Academy of Arts and Sciences.

Pratt died on March 3, 1956, at the age of 83.

References

Spector, B.: Joseph Hersey Pratt, M.D., Sc.D. *Bull. Hist Med.*, 30:473, 1956

Rackemann, F.M.: Joseph Hersey Pratt, M.D. *Trans. Am. Clin. Climatol. Assoc.*, 68:xlvi, 1956.

Proger, S.: Dr. Joseph Hersey Pratt. *N. Engl. J. Med.*, 254:920, 1956.

Wilder Tileston, MD (1875-1969)

Wilder Tileston was born in Concord, Massachusetts, on January 22, 1875. He received his AB (1895) and his MD (1899) degrees from Harvard. His internship was served at the MGH in 1899-1900. At the Harvard Medical School he was assistant in chemistry (1902-1903); assistant in clinical medicine (1906-1908); instructor in pathology (1908-1909); and director of the medical summer school in 1909. In 1908-1909 he was Dalton Fellow at the MGH. It was during this period that he developed his interest in diseases of the pancreas and studied cases in which there was complete absence of pancreatic secretion from the intestine. During these studies he had the constant help of Otto Folin. He presented his results before the Association of American Physicians in 1911.

In 1909 Tileston went to New Haven as assistant professor of medicine at the Yale University School of Medicine. In 1919 he was made professor of clinical medicine and chief of staff at the Grace Hospital and served in this position until 1920. Tileston was a charter member of the American Society for Clinical Investigation, of which he was secretary from 1909 to 1912 and vice-president in 1913. He was secretary of the Section on Internal Medicine of the American Medical Association from 1907 to 1910. He was a member of the Association of American Physicians. During World War I he worked as a volunteer at the military heart hospital in Hamp-

stead, London, under Sir Thomas Lewis. In 1914, with C. W. Comfort, Jr., he published a paper entitled "Total Nonprotein Nitrogen and Urea of the Blood in Health and Disease as Estimated by Folin's Method." This very extensive study, which was published in the *Archives of Internal Medicine*, represented observations on 5 healthy subjects and 142 cases.

Tileston and Frank Underhill reported their studies on three cases of secondary tetany with special reference to alkalosis and calcium metabolism at the annual meeting of the American Society for Clinical Investigation, May 1, 1917. An increase of the bicarbonate of the blood was demonstrated in these cases of tetany, one of which followed the administration of sodium bicarbonate. A low serum calcium was found in one case, and another showed a normal calcium concentration during the period of latent tetany. In 1937 Tileston reported a case of Pelger's nuclear anomaly of the leukocytes with a familial "shift to the left" of the leukocytes.

Tileston was recognized at Yale as an outstanding clinician and teacher. He was a master of physical diagnosis which he taught for many years. His association with medical teaching spanned the period during which the full-time system was developing. He adjusted gracefully to this system and demonstrated that a fine practitioner has a place on the medical faculty even though he cannot devote his full time to academic pursuits. He died on May 2, 1969.

Samuel Waldron Lambert, MD (1859-1942)

Samuel Waldron Lambert was born in New York City, on June 18, 1859. He received the AB degree from Yale in 1880, and the degree of PhB from the Sheffield Scientific School of Yale in 1882. He received his MD degree from the College of Physicians and Surgeons of Columbia University in 1885.

After serving as intern at the Bellevue Hospital (1885-86), he was clinical assistant in the Vanderbilt Clinic, Columbia University (1888-95); attending physician to New York Hospital (1898-1909), and to St. Luke's Hospital (1908-1929). He was professor of applied therapeutics and of clinical medicine at the College of Physicians and Surgeons of Columbia University (1903-1919), and dean of the same college (1904-1919). While he was dean, amalgamation between this school and the Presbyterian Hospital took place, which later culminated in the development of the present great

medical center. He was also consulting physician to the New York Hospital, the Presbyterian Hospital and St. Luke's Hospital.

Lambert was primarily a clinician. In the earlier years of his practice he was very active in the field of obstetrics and from this base developed a successful practice in general internal medicine. During the years of his interest in obstetrics he was attending surgeon at the New York Lying-in Hospital (1892-1904) and attending physician at the Midwifery Dispensary (1890-1892).

Lambert's major educational interest was in the extension of bedside teaching, and the "Sunday school class" for students and interns which he conducted weekly at St. Luke's Hospital became famous. This format was well adapted to Lambert's unusual abilities as a clinical teacher and his keen interest in and understanding of younger men.

He was a trustee of the New York Academy of Medicine for many years and also served a term as president of that institution. He was especially interested in the library of the Academy and he was largely responsible for the development of the Rare Book Room through the acquisition of the famous Streeter Collection. He was a member of many societies, including the Association of American Physicians, the New York Academy of Science, and the American Gastroenterological Association. He received an honorary MA degree from Yale in 1905 and an honorary ScD from Columbia in 1922.

His literary work consisted of many articles on obstetrical subjects, hospital construction, medical education, internal medicine, and a history of medicine entitled "Medical Leaders from Hippocrates to Osler" with Goodwin as co-author. He was the uncle of Dickinson W. Richards, Jr., who was also a consummate bibliophile interested in the history of medicine. Lambert died on February 9, 1942.

References

Miller, J.A.: Samuel Waldron Lambert, 1859-1942. *Trans. Assoc. Am Physicians*, 5724, 1942.

Walter Belknap James, MD (1858-1927)

Walter Belknap James was born in Baltimore, Maryland, on May 11, 1858. He graduated from Yale in 1879. After spending a year in the biological laboratory of Professor Henry Newell Martin at Johns Hopkins, James entered the College of Physicians and Surgeons in New York, receiving his MD in 1883. He served as an intern in medicine at the Roosevelt Hospital after which he worked in various European clinics for two years. After his return James became one of the clinical assistants in the service of Professor Delafield at the Vanderbilt Clinic.

His active professional career as a teacher began with the change of the college from a proprietary to a university medical school connected with Columbia University. His duties as visiting physician in Bellevue, Roosevelt and Presbyterian Hospitals were closely linked with the chair of the theory and practice of medicine to which James succeeded on the retirement of Professor Francis Delafield in 1902. During his early medical career James had served for two years as an assistant pathologist at the New York Hospital under Professor George L. Peabody and from then on took an interest in the relation of pathology to clinical medicine. He was the only founding member of the Interurban Club who was a full professor at the time of its organization. He eagerly studied the teaching methods as the Club visited the centers in Philadelphia, Boston and Baltimore and incorporated the best that he saw in the various hospitals which were under his supervision in New York. Of particular interest in the New York setting at that time were the clinical therapeutic classes. When he retired from the Bard Professorship in 1909, he handed over to his successors, Theodore Janeway and Warfield Longcope, a superbly organized service in the Presbyterian Hospital and Vanderbilt Clinic.

James had a clinical interest in diseases of the heart and published a lengthy paper in the *Transactions of the Association of American Physicians* in 1908 entitled "A Clinical Study of Some Arrhythmias of the Heart." In this study he used the techniques of sphygmographic and tambour recording as electrocardiography had not yet been introduced in the United States. In fact it was James himself who published the first paper on electrocardiography in this country. He worked with Horatio B. Williams, an accomplished electrophysiologist who was professor of physiology at Columbia. James secured an instrument from Europe and he and Williams published their first paper in 1910 entitled "The Electrocardiogram in Clinical Medicine."

James retired from active teaching at the age of 60, but continued as a member of the executive committee of the combined Presbyterian Hospital and College of Physicians and Surgeons during the amalgamation of those medical institutions into the present medical center at 168th Street and Broadway. His activities were recognized by several universities with the award of an honorary degree: Yale in 1896, Columbia in 1904 and Harvard in 1932. He was a member of the Association of American Physicians. Early in his career he came under the influence of three great physicians: the first a master of the science of medicine, Francis Delafield; the second of the art, William Draper; and the third of the amenities, Edward Trudeau. He died on April 10, 1927.

References

Warthin, A.S.: Presidential Address. *Trans. Assoc. Am. Physicians*, 42:3, 1927.

James, W.B., and Williams, H.B.: The electrocardiogram in clinical medicine. *Am. J. Med. Sci.*, 140:644, 1910.

Charles N. B. Camac, MD (1868-1940)

Charles N. B. Camac was born in Philadelphia, Pennsylvania, on August 6, 1868. He received an AB degree from the University of Pennsylvania in 1892 and the MD degree in 1895 from the same school. In 1892-93 he was a medical student at Guy's Hospital and at Columbia. He did graduate study in physiology at Oxford under Burdon-Sanderson and in medicine at the Johns Hopkins University in Baltimore. In 1894-95 he served as an instructor in physiology at the University of Pennsylvania.

In 1895 he was an intern at the Johns Hopkins Hospital and the following year an assistant resident physician. It was during this period that he formed a friendship with William Osler which had a major influence in his subsequent career. In 1898 Camac moved to New York to become physician to the Heart and Lung Clinic of the Bellevue Hospital's outpatient department. At the end of that year he was appointed visiting physician to the City Hospital of New York, a position he retained until 1916. From 1899-1905 he served as director of the laboratory of clinical pathology in the Cornell Medical School. This was the first laboratory of clinical pathology in New York and its organization was primarily the work of Camac.

From 1900-1905 he was chief of the outpatient department of the medical clinic of Cornell, which was the first outpatient department clinic organized in New York City in which each patient had a complete history, a disease index system was maintained, and an annual scientific report was published. It was also the first clinic to be run in conjunction with a clinical pathology laboratory. From 1905-1909 he was an instructor at the Cornell Medical School and in 1910 was made professor of clinical medicine. In 1937 he was appointed emeritus professor of internal medicine at the New York Polyclinic Medical School and Hospital.

Camac's major contributions were in the field of medical history. He was the author of a book entitled *Epoch Making Contributions to Medicine, Surgery and the Allied Sciences* published in 1909. In 1905 he published *Counsels and Ideals from the writings of Sir William Osler*. He was a member of the History of Science Society and the Association of American Physicians.

During World War I he had a distinguished career. In 1915 he volunteered for overseas service as a medical officer seeing duty first at Paignton, England, and later in Flanders. He was in charge of the Officers' Training Camp and School for Medical Officers at Fort McPherson, Georgia, and later was medical chief at the U.S. Army General Hospital No. 38 at White Plains, New York. In April 1917 he was commissioned as first lieutenant in the medical reserve corps of the U.S. Army and at the time of his discharge in July 1919 he held the rank of lieutenant colonel in the medical corps. After his retirement he lived for a number of years in California where he died on September 27, 1940.

References

Conner, L.A.: Charles Nicoll Bancker Camac, 1868-1940. *Trans. Assoc Am. Physicians*, 56:13, 1941.

Lewis Atterbury Conner, MD (1867-1950)

Lewis Atterbury Conner was born in New Albany, Indiana, on January 17, 1867. He graduated from the Sheffield Scientific School of Yale University with a PhD in 1887. He received his MD degree from Columbia University College of Physicians and Surgeons in 1890. After graduation in medicine, Conner served as a house officer at the New York Hospital, thus commenc-

ing an association which was to extend over more than half a century. He was assistant pathologist at the same hospital from 1895-1900; attending physician at the Hudson Street Hospital 1894-1906, and at the New York Hospital 1905-1931. His exceptional ability was almost immediately recognized and from the time he completed his internship he was sought for positions of responsibility. In 1898 he was selected as a member of the original faculty of Cornell University Medical College. Two years later, at the age of 34, he was appointed professor of clinical medicine. He held this position until 1916 when he was succeeded by W. Gilman Thompson.

Conner was one of the founders of the American Heart Association and served as its president in 1924 and 1925. He was the first editor of the *American Heart Journal*, and to his leadership from 1925 to 1937 may be attributed its early growth and rapidly expanding influence.

Conner was a preeminent teacher. He was educated at a time when the unaided senses still represented the only resource in the clinical study and recognition of many diseases. He became a master of physical diagnosis and this invaluable asset, for that period, he combined with qualities of scholarship and perception which enabled him to appreciate and evaluate scientific knowledge as it emerged and to share the enthusiasm and aspirations of his younger colleagues. His learning, his clinical judgment and his integrity made him the idol of the students at Cornell as well as the house staff at the New York Hospital.

He never engaged in experimental medicine but wrote a number of papers on various aspects of clinical medicine especially relating to the circulatory system. He became a member of the Association of American Physicians in 1908. He served with distinction in the Army during World War I, first in charge of heart examinations in the Office of the Surgeon General and later as chief of the Division of Internal Medicine. In 1920 he was awarded the Distinguished Service Medal.

In 1933, Columbia University awarded him the University Medal. He died on December 4, 1950, at the age of 84.

References

Barr, D.P.: Lewis Atterbury Conner, 1866-1950. *Trans. Assoc. Am. Physicians*, 64:8, 1951.

Frank Sherman Meara, MD (1866-1927)

Frank Sherman Meara was born at Salem, Massachusetts, on May 6 1866. He graduated with an AB degree from Yale University in 1880 and a PhD from the same institution in 1892. From 1890 to 1892, he was an assistant in physiological chemistry under Chittenden. He received his medical degree at the College of Physicians and Surgeons of Columbia University in 1895. From 1903 to 1904 he was instructor in *Materia Medica* and from 1904 to 1909 instructor in pediatrics at the College of Physicians and Surgeons and attending physician in charge of the Children's Medical Service. From 1909 to 1920 he was assistant attending physician and attending physician at Bellevue Hospital. He was made professor of therapeutics at Cornell Medical College in 1909, a position he held until 1920 when he was made professor of clinical medicine.

In 1916 Meara published the first edition of his textbook entitled *The Treatment of Acute Infectious Diseases*. A second edition appeared in 1921. He also contributed to Hare's *Modern Medicine* and to Forcheimer's *Therapeutics of Internal Diseases*. In his later years he was interested in the history of medicine.

Frank Meara was a superb physician and a sound writer on clinical subjects. Like most men who develop a strong personality, he was influenced during his educational period by other strong personalities; at Yale by Chittenden and in New York by Emmett Holt.

It was as a teacher that Meara excelled. He had a faculty for classifying and systematizing what he knew and of presenting it in a vivid and interesting form. He had the wit to see that the science and art of medicine are not antagonistic but complementary. It was, however, the art of medicine which interested him and he was sharply critical of those full-time faculty members at Cornell whom he thought lacking in the art, especially if they regarded themselves as teachers of internal medicine.

He died on October 9, 1927, at the age of 61 after a protracted illness with myocardial insufficiency and septicemia.

Theodore Caldwell Janeway, MD (1872-1917)

Theodore C. Janeway was born in New York City, on November 2, 1872, the son of Edward G. Janeway, one of the foremost physicians of his day. Through the influence of his father Theodore Janeway was inspired to become a thorough physician, clearly imbued with ideals of service to humanity and the advancement of medical education and medical science.

Janeway was graduated from the Sheffield Scientific School of Yale in 1892 where he came under the influence of Chittenden. Three years later he received the doctorate in medicine from Columbia's College of Physicians and Surgeons and then took up the duties of intern at St. Luke's Hospital in New York City. From 1898 to 1905 he was instructor and lecturer in medical diagnosis at the New York University and Bellevue Hospital Medical College and from 1902 to 1911 visiting physician to the Hospital of New York City.

Early in his career Janeway began to stress the rational interpretation of symptoms and the value of pathological physiology to his students. He was the first to introduce in New York teaching clinics which made use of autopsy material, a method of teaching used earlier in Boston by Richard Cabot. His expertise in teaching and his work with hypertension lead to his being appointed to the Bard Professorship at the College of Physicians and Surgeons of Columbia University in 1909 upon the retirement of Walter Belknap James. As an organizer and clinician Janeway became one of the leaders of a young group of "physiological clinicians" who quietly but surely transformed American medicine.

Janeway's most important contribution to clinical science was his work on blood pressure. His treatise on this subject was published in 1904 when he was 32 years of age. He also ventured into the field of experimental hypertension and with the assistance of Alexis Carrel studied the increase in blood pressure following reduction in kidney substance (1909). After 1909, when he became professor of medicine at Columbia, Janeway found little time to carry on experimental work in hypertension. He made one more attempt in collaboration with Edwards A. Park in 1911, when they examined the role of epinephrine in the circulation and its relation to blood pressure. His best paper on hypertension, which appeared in December 1913, described a nine-year study of 870 cases of essential hypertension in which he emphasized that the height of the systolic pressure was a minor factor in determining life expectancy.

Janeway's early success attracted the attention of Mrs. Russell Sage and led in 1907 to her endowment of the Russell Sage Institute of Pathology.

In 1914 Janeway became the first full-time professor of medicine at the Johns Hopkins University. Janeway organized the department along the lines Lewellys Barker had already established. He brought Herman O. Mosenthal from New York to direct the chemical division, and Leonard G. Rowntree transferred from Abel's department of pharmacology to medicine. Paul W. Clough joined the full-time department in September 1916 as a member of the biological division. As time passed it was clear that Janeway was not happy in his transformation from a very active New York consultant and teacher to a full-time university professor. In 1917 he resigned his professorship with the idea of returning to New York, partly because his restrictions from practice created a financial hardship and partly because he was no longer entirely in sympathy with full-time plan. During his short period as professor of medicine, however, the medical department and medical divisions of the hospital with the wards, laboratories, dispensaries, and classrooms were efficiently organized, the spirit of research was constantly fostered and teaching was on a high plane. Janeway did feel that the experiment of full-time medicine had justified itself and that he had been able to bring about more adequate teaching, research, and better administration than had been possible under the "part-time" system. With America's entry into World War I, Janeway was called to a position in the Office of the Surgeon General. In December 1917 he died prematurely of pneumococcal pneumonia.

References

Mosenthal, H.O.: Theodore Caldwell Janeway, A.M, M.D. *Johns Hopkins Alumni Magazine*, 6:264, 1918.

Barker, L.F.: Theodore Caldwell Janeway. *Science*, 47:273, 1918.

Flaxman, N.: Janeway on hypertension: Theodore Caldwell Janeway (1872-1917). *Bull. Hist. Med.*, 9: 505, 1941.

Alfred Stengel, MD (1868-1939)

Alfred Stengel was born in Pittsburgh, Pennsylvania, on November 3, 1868. He began the study of medicine at the University of Pennsylvania in 1886. The course was then but three years in length and no college level pre-medical work was required. During his senior year Stengel was one of the students elected to be included in Eakins' celebrated painting of the Agnew Clinic. He is pictured as a youthful, smooth-shaven lad in those days of bearded students. His head rests on the shoulder of a fellow student, Clarence A. Butler, whose head rests on the top of Stengel's. They do not appear to be sleeping but merely trying to see, with apparently little success, the operation being performed by Agnew. After graduation, Stengel spent 15 months of internship at the Philadelphia General Hospital. Dr. Allen J. Smith helped him obtain a subordinate position in the pathological department of the University of Pennsylvania and offered to share his small home and office with him. However, Smith soon left to accept the chair of pathology at the University of Texas. Before he departed he nominated Stengel as his successor as a pathologist in the medical institution, and a quizmaster in pathology. Stengel gained excellent experience in this position, and in 1893 he was appointed pathologist to the German Hospital. In the spring of 1892 he became office assistant to William Pepper, then professor of medicine and provost of the University.

With the opening of the William Pepper Laboratory of Clinical Medicine, the first of its type in the country, Stengel became assistant director. A few years later the first director, John Shaw Billins, left for a position in New York. William Pepper assumed directorship of the Laboratory, with Stengel, continuing as assistant during the year 1896. Early that year, following Roentgen's announcement of the discovery of X-rays, Charles Lester Leonard purchased an X-ray tube and assembled Billins electrical equipment in a small room in the Pepper Laboratory. This was the beginning of unique laboratory investigations under the guidance of Stengel who was in all practical aspects leader of the laboratory personnel. On Pepper's death in 1898, Stengel became full director and the work of the laboratory continued to prosper. In 1903 William G. Spiller was appointed to a special professorship in neuropathology. He spent many productive years in the Pepper Laboratory and during this period perfected the operation for relief of trigeminal neuralgia. A division of physiological chemistry was organized under Casper Miller, David Edsall, George Woodward and Alonzo Taylor; a division of bacteriology under Dr. Samuel S. Kneass; a division of serology in 1905 by Ravenel and others; and a division of clinical microscopy by

Dr. C. Y. White. In 1906 Herbert Fox became pathologist to the laboratory of comparative pathology and eventually assumed the position of director.

Stengel, who had been professor of clinical medicine since 1897, was elected professor of medicine in 1911. In 1931 he became vice-president in charge of medical affairs of the University of Pennsylvania. The Martin Maloney Memorial Clinic at the University, which stood on the site of the old Pepper Laboratory, was a monument to Stengel's foresight and planning.

Stengel was a prolific writer. His earlier articles were chiefly on hematological or pathological topics. In 1898 he published a successful *Textbook of Pathology*, which went through eight editions. He accepted the editorship of the *American Journal of Medical Sciences* in 1898, and from 1902 to 1904 he was editor of the American edition of *Nothnagel's Encyclopedia of Practical Medicine*.

Stengel was a member of the Association of American Physicians, and the American Philosophical Society. He was a president of the American College of Physicians as well as of the College of Physicians of Philadelphia. He died on April 10, 1939.

References

Pepper, W.: Memoir of Alfred Stengel. *Trans. Stud. Coll. Physicians Phila.*, 8:242, 1940.

Miller, T.G.: Alfred Stengel, 1868-1939. *Trans. Assoc Am. Physicians*, 54:15, 1939.

David Linn Edsall, MD (1869-1945)

David Linn Edsall was born in Hamburg, New Jersey, on July 6, 1869. He began his career in medicine in the early decades of this century when medical knowledge was undergoing careful scientific reexploration. Research laboratories were being organized in several institutions, and Edsall found an opportunity available to him at the University of Pennsylvania. Edsall's interest in medical research was concerned principally with the chemical aspects of disease. The gross inadequacy of scientific training for medicine in America at that time is illustrated by his experience when he tried to further his knowledge of chemistry while in college; a step which

would have improved his training for the investigative approach he later adopted: “I had a strong desire to know about the subject and a rather vague but insistent idea that it might help me understand medicine better and perhaps aid me if I wished to attempt investigation in the vast area of the unknown in medicine. With the consent of the Dean I took the then radical step of asking the Professor of Chemistry of the School of Science to allow me to take the elementary laboratory course. He asked me what I was headed for and I said medicine. He replied with entire disapproval. “A doctor does not need to know any chemistry. You would be wasting your time. I left with the feeling that I had been stupid and impractical.”

When Joe Aub returned home at the end of World War I, he wanted to spend part time in the physiological laboratory under Walter Cannon. He sought the advice of two physicians who he thought might advise him better than most: Richard Cabot, who had done a good deal of work in hematology, and Sir James Mackenzie, a pioneer in the study of cardiac arrhythmias. When asked what would happen if he studied physiology for two years instead of continuing immediately with clinical medicine, both indicated that it would ruin his life: “I would lose touch with people, would not know how to handle them well. These two men were the best I could consult I thought; they both gave me the same advice, they both told me not to do it. I did it anyhow and frankly I could not see then nor later that it did me anything but good.” David Edsall’s firm desire to improve his background in the fundamental sciences was unique for the times, and his protégé, Aub, found that times had not changed.

Edsall received his AB degree from Princeton in 1890 and his MD degree from the University of Pennsylvania in 1893. He chose to intern at the Mercy Hospital in Pittsburgh rather than at either of the two well-known hospitals in Philadelphia. He saw in Pittsburgh his first case of heat cramp, not at that time differentiated from heat stroke, heat prostration and the like, but which came in later years to bear his name — Edsall’s disease. Here he became aware for the first time of the close relationship between occupation and disease and the groundwork was laid for his later contributions to industrial medicine. In 1894 he went abroad for a year, studying in London, Vienna, and Graz, an experience he thought was the single most important factor in his development. Edsall returned to Pittsburgh and entered private practice but after six months he became so dissatisfied that he moved to Philadelphia.

Edsall became an associate in clinical medicine attached to the William

Pepper Laboratory before the end of 1895. Among his close friends was Alfred Stengel, whom he had admired as a young instructor. It was probably Stengel's stimulating teaching which ultimately led Edsall to institute the tutorial system at Harvard. Another of the excellent group in the laboratory was Alonzo E. Taylor. He and Edsall had a common enthusiasm for studying urine, analyzing every unusual sample they could obtain. One day Edsall brought him a clear yellow specimen that he said deserved study. Taylor spent two days investigating it and finally came back to Edsall completely confused. "I can't make head or tail of this specimen," he said. "It isn't like anything I have ever gone over before." Taylor replied in response to Edsall's question that he had run many, many tests on it. Finally, Edsall asked: "Have you tasted it?" Taylor replied: "Naturally not." Sticking his finger into it Edsall licked a drop and said: "Try it. Maybe that will help you find out what it is." The answer, of course, was beer.

In 1907 Edsall succeeded H. C. Wood as professor of therapeutics and pharmacology at Pennsylvania. He arranged his work in such a way that he was functioning as a full-time academic medical professor a number of years before the first official full-time chairs in clinical departments were inaugurated at Johns Hopkins. As a result of his intense interest in research, Edsall played a role in the foundation of a number of early research societies in addition to the Interurban Clinical Club. He was an early member of the Society for Experimental Biology and Medicine which was founded in 1903 by Graham Lusk and S. J. Meltzer. Edsall was elected to membership in 1905 finding himself in a group which included Walter B. Cannon, Otto Folin, Reid Hunt, and Ernest Tyzzer from Harvard, in addition to important people from Pennsylvania such as Richard M. Pearce, A.N. Richards, and Alonzo Taylor. Neither the Interurban Club, the older Association of American Physicians nor the newly founded Society of Biology and Medicine gave the young clinicians interested in the application of the methods of science to the study of disease the format that they needed. Thus, in 1907, at a meeting of the American Medical Association, Meltzer selected Warfield Longcope, Joseph Pratt, and David Edsall to talk about the formation of a society of their own. Edsall was made temporary chairman of the group, and H.A. Christian temporary secretary; thus was born the American Society for Clinical Investigation. That same year at the meeting of the American Medical Association, interest was expressed in having the Association publish a journal to bridge the gulf between purely scientific research and its application to practical medicine. This led to the creation of the *Archives of Internal Medicine*, and Edsall served on the founding committee along with George Dock, William S. Thayer, Joseph L. Miller,

Theodore Janeway, and Richard Cabot.

Edsall's early research was characterized by his tenacity in applying chemical determinations to the study of disease problems; the resulting papers were all good, but contained no earthshaking discoveries. A good example was "A Brief Report of the Clinical Periodic Paralysis," co-authored with John K. Mitchell and Simon Flexner. This paper focused attention on the metabolism of potassium, the attacks having been definitely shortened by the taking of large quantities of potassium; it was a remarkable feat to describe so early the relation of this disease to an abnormality in potassium metabolism. In 1903, he and Casper Miller published "A Contribution to the Chemical Pathology of Acromegaly." In this study they demonstrated a striking retention of phosphorus and nitrogen which led them to conclude "that there is in acromegaly a growth of abnormal bone rather than a mere abnormal growth of bone in that there are very marked abnormalities in the soft tissues as well as in bone. A chemical study of the bone, as well as chemical studies of the disease in general may demonstrate definitely that the alterations in the bone are the result of metabolic abnormalities." This was a rather astute conclusion for that period (1903). It is easy to understand why Edsall's work dealt mainly with urinary analyses since satisfactory techniques of blood analysis were yet to be developed by Folin and Benedict. As result of his metabolic studies, Edsall delivered the Harvey Lecture in November 1907 on "The Bearing of Metabolism Studies on Clinical Medicine." Edsall was one of the first to appreciate the important effects of X-rays on body function, and that a single exposure could have profound influence on metabolism for days afterwards.

Edsall's first paper in the field of industrial medicine, which appeared in the *American Journal of Medical Sciences* in 1904, was entitled "Two Cases of Violent but Transitory Myokymia and Myotonia Apparently Due to Excessive Hot Weather" — what are now called "heat cramps." By 1908 he was able to delineate more clearly this newly described disorder in a report to the American Medical Association entitled "A Disorder Due to Exposure to Intense Heat Characterized Chiefly by Violent Muscular Spasms and Excessive Irritability of the Muscles - Preliminary Note." Edsall recognized that it was a separate disorder from heat stroke and heat prostration. In 1908 he again discussed the subject before the Association of American Physicians. Still searching for the cause of the disease, he demonstrated in two cases an absence of chloride excretion in the urine. The clue was in his hands but it took some decades to unravel it. It was not until the 1920's in Great Britain that J. B. S. Haldane ascribed the cramps to salt depletion and

prevented them by giving salt solution orally. By 1910 Edsall had acquired such a reputation in the field of industrial medicine that Professor Henry W. Farnam of Yale president of the American Association for Labor Legislation, appointed him to a five man committee which was to acquaint the President of the United States with these problems.

Edsall had his early medical experiences with the Harvard Medical School between 1904 and 1909 when he was sent by Pennsylvania to review the new method of medical education which was in its experimental stage in Boston. As a result of these contacts, and friendships gained through Interurban Club with Locke and other Boston members, the idea began to emerge that Edsall would be an excellent successor for Frederick Shattuck, the distinguished clinician who was professor of clinical medicine at the Harvard Medical School and head of the East Service at the MGH. While this idea was germinating Musser at Pennsylvania heard of it and advised Edsall that his opportunities would be greater in Philadelphia. At almost the same time, however, Edsall unexpectedly received an offer from Washington University in St. Louis to help reorganize the school of medicine there. Edsall emphasized that in order to make Washington University the "Johns Hopkins of the southwest" it would be necessary to fill the important chairs with first-class men and to make suitable provisions for laboratories, equipment, and a budget for research. When it was clear that Edsall might leave, Pepper offered him the professorship of medicine at Pennsylvania with the opportunity to reorganize the whole department as well as name new heads in some other departments, and undertook to change the age limit for retirement. This resulted in severe frictions within the school but a petition from five hundred doctors was enough to bring about support for a complete reorganization at Pennsylvania along the lines that Edsall wished. Important appointments resulted, including Howard Taylor Ricketts of Chicago, who was named to the chair of pathology, and Richard Pearce of the Bellevue Medical College, who came to fill the chair of experimental medicine. Tyson, who retired from the chair of medicine to make way for Edsall, obviously had some outdated ideas; but it should not be forgotten that it was Tyson who in 1874 introduced for the first time the only methods of laboratory work then used in internal medicine, those of pathological histology, into American medical education. However, to these "new men" he was now hopelessly old-fashioned; the only research he was known to have carried out was the fermentation method of determining the urea in the urine.

Soon, however, the conservatives won out over Edsall's demands for reor-

ganization. As early as November 21, 1910, Edsall had made up his mind against Philadelphia. During the Interurban Club meeting in Philadelphia on December 2 and 3, John Howland was a house guest of Edsall's. Howland was quick to pursue the chance that Edsall might finally accept the position in St. Louis. Edsall's needs were met at this time and he accepted the professorship of preventive medicine at Washington University.

Edsall was granted a year's leave of absence for study and research, for which he went to the Carnegie Nutrition Laboratory in Boston. Here he started some promising experiments on the problems of respiration. His salary in St. Louis was to be \$8,000, his department having a budget of \$15,500, and he was promised approximately 30 beds in the hospital. Difficulties arose at Washington University which resembled in many respects those that Edsall had encountered in Philadelphia, the old fighting the advent of the new. Thus, he was officially professor at Washington University for only one year when he was called to Harvard University as Jackson Professor of Clinical Medicine and chief of the East Medical Service of the Massachusetts General Hospital. The Harvard professors of clinical subjects who held positions at the Massachusetts General Hospital had been Bostonians since the Harvard Medical School was founded and Edsall's appointment in 1912 was the first to break this tradition.

When Edsall assumed his position in Boston, his greatest desire was to stimulate study of the mechanisms of disease. One of his first steps, was to select promising young men and send them away for postgraduate research training in order to build research competence in the various fields. Many of the young men Edsall chose at that time later became distinguished clinical investigators and the first three listed here became members of the Interurban Clinical Club: George Minot, James Gamble, Stanley Cobb, J. H. Means, Cecil Drinker, Paul Dudley White, Harry Newburgh, Francis Rackemann, Oswald Robertson, and Carl Binger.

The MGH already had some tradition of laboratory investigation. It began when J. Homer Wright came to Boston as pathologist at the hospital. There were 16 benches for staff members in Wright's laboratory in the pathology building when it was completed in 1896. Each staff member who wanted to do some research had to pay \$25 a year for the privilege of using a bench. By the time Edsall left the hospital in 1923, he had only \$13,000 to support the research that was being done. By contrast the MGH in the mid-60's spent some \$10 million in medical research and there were 840 investigators and clinical and research fellows.

The organization of a laboratory for clinical investigation was made possible in the spring of 1918 when the old administrative offices on the ground floor of the Bulfinch Building were vacated. Six rooms became, available which could accommodate about 12 workers. The chief idea underlying the establishment of the medical laboratory was that it should be primarily a place for original work in the field of clinical investigation. Routine work was not done there except in the case of some highly technical tests. Some of the more important investigations conducted in this laboratory included: studies of blood gases by Arlie Bock and Professor L. J. Henderson; of the blood by Minot and his colleagues; of metabolism of bile pigments by Chester Jones; of thyroid disease involving members of the medical, surgical services, and radiology with measurements of metabolic rate by Means and Aub; of clinical calorimetry of infants by Fritz Talbot; of the bacteriology of pneumonia by Lord; of blood and urinary chemistry in diabetes and nephritis by Reginald Fitz; and laboratory work for Dr. Rackemann's anaphylaxis clinic. As Rackemann said: "There is no doubt that it was Edsall who did more than any other man to promote clinical research at the Massachusetts General Hospital. He can be credited with introducing clinical investigation at the hospital in a professional sense. The historian of the future will credit him with giving the hospital a new and broader conception of its functions."

One of Edsall's most important contributions was the establishment of an Industrial Disease Clinic at the MGH. It was first directed by Harry Linenthal and then by Wade Wright. The hospital's method of record keeping was changed to include information on each patient's occupation. Cases of poisoning from benzine, brass, naphtha, turpentine and benzol were uncovered which had been wrongly diagnosed as anything from "apprehension" to "appendicitis." Among the most important were the cases of lead poisoning and the uncovering of the basal ganglia changes seen in chronic manganese poisoning.

In 1918 Edsall became dean of the Harvard Medical School without giving up his position at the Massachusetts General Hospital or the professorship of medicine. In 1921 he was also appointed dean of the Harvard School of Public Health. Two years later he resigned his chair of medicine and from active work at the MGH to become full-time dean of the Faculty of Medicine and School of Public Health of Harvard University, positions he held until his retirement in 1935.

Thus, Edsall made many significant contributions, and, as Cecil K. Drink-

er said, he was responsible for making industrial hygiene and medicine subjects of true graduate school importance in this country. Of equal importance was his role in putting clinical investigation at the MGH and in Boston on a sound basis. Pioneer of “scientific medicine” as he was, he frequently had to combat fear and misunderstanding of the new methods. “Nothing would more rapidly degrade the medical course than to fear making it scientific in the true sense,” Edsall stated in his first Dean’s Report. “It demands a nice adjustment to make a background of facts and methods sufficient, to give some skill in their use and to bring out clearly fundamental principles of thought and action, while at the same time avoiding such a multiplication of minutiae as actually to obscure the view of principles and confuse the student’s judgment as to the essentials.” Edsall’s experiences in curriculum reform at Harvard were presented in a paper, which he gave before the Interurban Clinical Club in 1924 entitled “The Question of Correlation and Opportunity of the Superior Student with Comments on the Comprehensive Examination and the Tutorial Methods.” In this paper he discussed all the newer features of the course in medicine given to bridge the gap between physiology and medicine.

Edsall held membership in the Association of American Physicians, the American Academy of Arts and Sciences and the American Philosophical Society. He died on August 12, 1945, at the age of 76.

References

- Aub, J.C. and Hapgood, R.K.: Pioneer in Modern Medicine: David Linn Edsall of Harvard. Boston, *Harvard Medical Alumni Assoc.*, 1970, pp. 9, 181.
- Edsall, D.L., and Miller, C.: A contribution to the chemical pathology of acromegaly. *Univ. Penn. Med. Bull.*, 16:143, 1903.

Aloysius Oliver Joseph Kelly, MD (1870-1911)

Aloysius Oliver Joseph Kelly was born in Philadelphia, Pennsylvania, in 1870. He received the AB degree from LaSalle College in 1888 and an MA from the same institution in 1891 — the same year of his graduation from the medical department of the University of Pennsylvania. He spent the next three years in Vienna studying pathology and internal medicine. Most of his professional career was spent in Philadelphia, but for a time

he was professor of medicine at the University of Vermont. Through his efforts the medical department there was reorganized and raised to a high plane of efficiency. For a number of years he was professor of pathology in the Women's Medical College in Philadelphia, visiting physician to St. Agnes and University Hospitals, and pathologist to the German Hospital in Philadelphia where he had charge of the clinical laboratory.

In association with John H. Musser, he edited an extensive system of therapeutics. He was also author of a notable chapter on "Diseases of the Liver and Biliary Passages" in Osler's *Modern Medicine*. He was an editor of the *International Clinics* and later was editor of the *American Journal of Medical Sciences*, one of the oldest and most important medical periodicals. As assistant professor of medicine in the University of Pennsylvania, his lectures were considered to be excellent.

He was an active member of the College of Physicians of Philadelphia and the Association of American Physicians. He died on February 23, 1911.

David Riesman, MD (1867-1940)

David Riesman was born on March 25, 1867, near Eisenach, in Thuringia, Germany. He was educated in the United States, finishing high school in Portsmouth, Ohio. After attending the University of Michigan Medical School for one year, he entered the University of Pennsylvania Medical School, receiving his MD in 1892. In June 1937 he received the honorary degree of doctor of laws from the University of Wisconsin and in 1928 was made a Chevalier of the Order of the Crown of Italy. In 1931 he received the Strittmatter Medal of the Philadelphia County Medical Society.

He was active as a teacher and physician in a number of hospitals in Philadelphia. At the University of Pennsylvania Medical School Riesman was demonstrator of pathology from 1896-1901; instructor in clinical medicine from 1901-1905; assistant professor of clinical medicine from 1905-1912; and professor of clinical medicine from 1912-1933. He was also professor of clinical medicine at the Polyclinic Hospital and College for Graduates in Medicine from 1901-1918. He remained active long after he became professor emeritus at the University of Pennsylvania in 1933. He had a continuing interest in medical history and was made professor of the history of medicine in the graduate school in 1933. For the academic year 1937-38

he was Vanuxem Lecturer at Princeton. In 1927 he was physician-in-chief pro tempore of the Peter Bent Brigham Hospital.

Riesman participated in many medical societies. He was a Fellow of the College of Physicians of Philadelphia and chairman of its library committee, and was a member of them Association of American Physicians, the American College of Physicians, and the American Association for the History of Medicine.

The more than 250 articles which Riesman contributed to the medical literature are a tribute to his amazing vigor. His writings dealt chiefly with diseases of the heart and gall bladder, and the chronic forms of nontuberculous bronchopneumonia. However, he published clinical papers on a wide variety of subjects ranging from the soft eyeball in diabetic coma to the hemorrhagic diathesis in Bright's disease. He edited a *Textbook of Pathology* with Ludwig Hektoen, and published a "Life of Thomas Sydenham" and many other articles on the history of medicine. For many years he was associate editor of the *Annals of Medical History*. Riesman wrote the first history of the Interurban Club from its inception to 1937.

Reisman was primarily a practitioner and consultant. A sophisticated senior resident once remarked: "Dr. Riesman gets as big a kick out of 'making a diagnosis' as a third year student." This remained true to the end of his life. He never became bored with the practice of medicine, was never blind to the diagnostic data of disease, never unmindful of the patient as a person, and always alert and ready for discovery. He died in 1940.

References

Fitz-Hugh, T., Jr.: David Riesman, 1867-1940. *Trans. Assoc. Am. Physicians*, 56:24, 1941.

Joseph Sailer, MD (1867-1928)

Joseph Sailer was born in Philadelphia, Pennsylvania, on October 1, 1867. He received his AB degree from the University of Pennsylvania and graduated from the medical school of that institution in 1891. After an internship in the Presbyterian and Philadelphia General Hospitals, he studied pathology, internal medicine, and neurology in Zurich, Vienna, and Paris. His period under Charcot determined his lifelong interest in neurology.

When Simon Flexner succeeded John Guiteras as professor of pathology at Pennsylvania, he made Sailer a demonstrator of morbid anatomy. Although he never lost his interest in scientific medicine, Sailer was not destined to pursue his career in that direction as his close association with John H. Musser soon kindled his love for internal medicine. He was made an instructor in clinical medicine and ultimately in 1912 professor of clinical medicine. He taught in the Philadelphia General Hospital and most of his investigative work was done there, although for a time he worked in the William Pepper Laboratory in Philadelphia. He was interested in diseases of the gastrointestinal tract and became professor of that branch of medicine at the Philadelphia Polyclinic.

After World War I he devoted a great deal of effort to the field of cardiology and was one of the first in Philadelphia to have an electrocardiograph machine in his office. He organized and was the first president of the Philadelphia Heart Association, and was also an organizer and a president of the American Heart Association. He was a member of the Association of American Physicians.

Sailer's work in medicine covered a wide field as is shown in his bibliography of over 100 medical contributions. He was especially interested in the unusual diseases; and on that account was able at times to make brilliant diagnoses where other able men had failed. He had a large and select private practice and was in great demand as a consultant. Sailer died in Philadelphia on December 31, 1928.

References

Howard, C.P.: President's Address. *Trans. Assoc. Am. Physicians*, 44:4, 1929.

Warfield Theobald Longcope, MG (1877-1953)

Warfield Theobald Longcope was born in Baltimore, Maryland, on March 29, 1877. He came from a distinguished line of physicians. His great-great-grandfather was Nathan Smith of Dartmouth and Yale. His mother's brother was Samuel Theobald, the first professor of ophthalmology at the Johns Hopkins University School of Medicine. Longcope received his undergraduate education at the Johns Hopkins University, graduating with the AB degree in the class of 1897. He received his MD degree from the

same institution in 1901.

Although he had no way of anticipating such an appointment, Longcope's training prepared him admirably for the full-time chair of medicine that was later to be his at the Johns Hopkins University. It is informative to follow Longcope's career after graduation from medical school since his growth reflects what was taking place in relation to medical education and the preparation for academic medicine during that period.

At Johns Hopkins he had close contacts with Welch, Halsted, Osler, Mall, Howell, and Kelly. Mall, in particular, opened a door that let him see both the rewards and difficulties of medical research. By the time he graduated he had published three papers, and when he left Baltimore at the age of 24 he took with him the best that this country had to offer in medical education at that time. From Johns Hopkins he went to the Pennsylvania Hospital in Philadelphia as resident pathologist. It seems paradoxical that this great clinician had no medical internship.

At the time Longcope went to Philadelphia, experimentation in clinical medicine was in its infancy. Observations made at the bedside with simple forms of apparatus, inquiries into the etiology of disease carried out by rather crude bacteriological techniques, and pathological examinations of material obtained at autopsy formed the basis for clinical studies. Venipuncture for bacteriological culture was such an innovation that Longcope once stated: "As a daring novice trembling with apprehension I made the first blood cultures ever performed at the Pennsylvania Hospital." While working under the direction of Simon Flexner in the Ayer Laboratory of the Pennsylvania Hospital, Longcope began his studies in immunology. Later, with David Edsall, he learned the importance of employing chemical methods in clinical research. Longcope's experience in the Ayer Laboratory is particularly important because through it he developed the combination of clinical activity and laboratory study that serves as a model of the full-time academic medical scientists who populate university departments of medicine at the present time. Longcope's activities in the Ayer Laboratory included work in pathology, biochemistry, bacteriology and serology. He was looked upon at that time by his colleagues as somewhat "wacky" for spending so much time in the laboratory when he might have been practicing clinical medicine. However, he also visited the wards frequently and gave valuable advice about diagnosis and treatment of patients. In 1909 he received an additional appointment as assistant professor of applied clinical medicine at the University of Pennsylvania. When he finished his term

of service at Pennsylvania, he emerged as a uniquely trained academician who set a new standard of learning in several different scientific disciplines, all merging in a broader approach to the problems of disease and an understanding of the nature of disease both etiologically and pathologically.

In 1911 he was appointed associate professor of medicine at Columbia's College of Physicians and Surgeons, and at the age of 37 became Bard Professor of Medicine at this institution and director of the medical service of the Presbyterian Hospital in New York City. His career was interrupted by duty in Washington during World War I, and he later served overseas. After the war he returned to Columbia, but in 1922 he made his final change of position when he became professor of medicine at the Johns Hopkins University School of Medicine. Longcope was a Fellow of the American Academy of Arts and Sciences and a member of the National Academy of Sciences, the American Society for Clinical Investigation, and the Association of American Physicians. He was a president of the Association of American Physicians and the American Association for the Advancement of Science. He was one of the founding members of the American Academy of Allergy.

Longcope's most important investigative work was on glomerulonephritis and its pathogenesis. He made many other contributions, including significant studies in the field of allergy and immunology. During World War II he performed excellent studies of the use of BAL (British anti-Lewisite) in the treatment of metallic poisoning by such substances as arsenic and mercury. These reports were models of clinical investigation. His first important article on the kidney, "The Production of Experimental Nephritis by Repeated Protein Injections," was published in 1913. His interest later shifted to the problem of acute hemorrhagic nephritis and its relationship to hemolytic streptococci. Among his clinical contributions were the recognition of the contracted kidney due to pyelonephritis, the modern description of sarcoidosis, and the early recognition of viral pneumonia.

In his remarks upon being awarded the George M. Kober Medal of the Association of American Physicians, Longcope said: "But all of us who have spent much time in the wards of a hospital are subject to the irresistible temptation of describing rare forms of disease, or of recounting the clinical features presented by a group of patients suffering from a malady that has not previously been clearly defined. Though information gained from this type of simple observation, in which I must confess to have indulged, still has some place in clinical medicine, we all know that the most fertile field

of work lies in the investigation of the fundamental processes that form the basis of disease in man.”

Longcope was a pioneer in applying the methods of laboratory research to the problems of clinical medicine. At the same time he was the “Dean” of American clinicians, who by his keen observation at the bedside and his broad knowledge of medicine made several important new descriptions of disease. He died on April 25, 1953.

References

Mackenzie, G.M.: Presentation of the Kober Medal to Dr. Warfield T. Longcope. *Trans. Assoc. Am. Physicians*, 61:22, 1948. 1975.

Bordley, J., Ill Warfield Theobald Longcope, 1877-1953. *Trans. Assoc. Am. Physicians*, 669, 1953.

Tillett, W.S.: Warfield Theobald Longcope Mar 29, 1877 - Apr. 25, 1953. *Biog. Mem. Natl. Acad. Sci.*, 33:205 1959.

Longcope, W.T.: Acceptance of the Kober Medal Award. *Trans. Assoc. Am. Physicians*, 61:25, 1948.

William Sydney Thayer, MD (1864-1932)

William Sydney Thayer was born in Milton, Massachusetts, on June 23, 1864. He graduated from Harvard College in 1885, and four years later received his medical degree from Harvard. He was then a house officer at the MGH. In November 1890 he went to Johns Hopkins as Osler's second assistant on the resident medical staff. In September 1891 he was appointed resident physician, a post he held for seven years. He then served as Osler's first assistant, with the rank of associate professor, until the time of Osler's resignation in 1905. Thayer was appointed professor of clinical medicine in that year and in 1918 became chairman of the department of medicine at the Johns Hopkins University and physician-in-chief to the Johns Hopkins Hospital. He held both positions until 1921 when he voluntarily withdrew, believing that he should make way for a younger man.

During World War I Thayer was appointed chief medical consultant of the United States Expeditionary Forces in France, with the rank of Brigadier General. In 1927 he was elected president of the American Medical Associ-

ation. For many years he was a member of the Harvard Board of Overseers, and he received many honors including an honorary degree of doctor of laws from Edinburgh University (1927), and honorary membership in the Therapeutical Society in Moscow (1897), the Royal Society of Medicine of Budapest (1909), the Academy of Medicine of Paris (1918), the Royal Society of Medical and Natural Sciences in Brussels (1919), the Royal Society of Medicine, London (1923), and the Association of Physicians of Great Britain and Ireland (1925). He was also a member of the American Philosophical Society (1924) and a Fellow of the American Academy of Arts and Sciences (1921).

In the year preceding his arrival in Baltimore, Thayer had studied in Germany, particularly with Virchow, but also with Ehrlich from whom he learned new blood staining techniques. At that time two infectious diseases were rampant in Baltimore — malaria and typhoid fever. Thayer's studies in the clinical laboratory were directed toward malaria for which his knowledge of Ehrlich's techniques especially qualified him. His investigations with Hewetson enlarged this expanding subject, and Thayer's Lectures on "Malarial Fevers", superbly illustrated and published in 1897, carried the new knowledge about this disease throughout the English-speaking world.

Thayer's early studies of the physiological third heart sound, an auscultatory event which he discovered independently, were exemplary. Thayer was also impressed with the accentuated third sound of mitral regurgitation which he thought was caused by "the sudden tensing of the mitral leaflet and perhaps the tricuspid valve at the time of the first and most rapid phase of diastole." Thayer also introduced the term "opening snap" for the characteristic sound heard in mitral stenosis and he was the first to describe an epigastric venous hum with hepatic cirrhosis. With his pathologist colleague, William G. MacCallum, he bled dogs and studied the effects of the anemia on the auscultatory findings in the heart, noting the development of an aortic diastolic murmur. Thayer was one of the early clinicians to employ blood cultures in the study of patients with fever and heart murmurs. His studies on bacterial endocarditis were extensive and in 1896 he reported the first case of gonococcal endocarditis. In 1930 he gave the prestigious Gibson Lectures in Edinburgh, which were entitled "Bacterial or Infective Endocarditis."

Thayer rapidly became a vital force in medicine in the United States. In his delightful essay on "The Medical Education of Jones", he stated: "Twenty-five years have passed by. Great changes have taken place in medicine.

Through the introduction of procedures, diagnostic and therapeutic, based on the application of the fundamental sciences remarkable advances have been made in the art and science of medicine. Researches in no way inferior to those carried on in the laboratories of the fundamental sciences are being pursued by members of the clinical staff." However, Thayer detected a regrettable tendency, against which he warned: "that a sound basis in the fundamental sciences, however desirable and necessary for him who would be a scholarly physician, was in no way a shortcut to that experience, practical and human, which always has been and always will be necessary to make a good diagnostician, a good doctor and a good clinical teacher." He deplored, therefore, that so large a proportion of American and foreign physicians were sadly lacking in the essential foundations of a training in clinical diagnostic methods, and he warned against a growing tendency to substitute laboratory reports for clinical observations.

Thayer died on December 10, 1932.

References

Thayer, W.S.: "The Medical Education of Jones". From: *Osler and Other Papers*. Baltimore, The Johns Hopkins Press, 1931, p. 51.

Harlan, H.D., et al.: The Thayer Memorial Exercises held in the Hurd Memorial Amphitheatre, February 24, 1934. *Johns Hopkins Hosp. Bull.*, 55 :201, 1934.

Reid, E.G.: *The Life and Convictions of William Sydney Thayer, Physician* London, Oxford University Press, 1956.

Carter, E.P.: William Sydney Thayer, June 23, 1864-Dec. 10, 1932. *Johns Hopkins Hosp. Bull.*, 52:1, 1933.

Thomas Barnes Futcher, MD (1871-1938)

Thomas Barnes Futcher was born at St. Thomas, Ontario, Canada, on New Year's Day, 1871. He graduated from the University of Toronto Medical School in 1893 and then served a year as house officer in the Toronto General Hospital. He first went to Baltimore in 1894 to serve as resident physician at a convalescent home for children at Mount Wilson. During that year he attracted the attention of William Osler, who selected him as an assistant resident physician at the Johns Hopkins Hospital. Thus Futcher

served with Osler in those intimate years before the opening of the Johns Hopkins School of Medicine in 1893. From 1896 to 1898 he studied abroad, first at Graz and then at Strasbourg.

Upon his return to Baltimore in 1898, Futcher assumed the position of chief resident in medicine which had become vacant through the resignation of William S. Thayer. The position of resident, of course, was a very responsible one which included the care of all patients on the medical service as well as the organization of the teaching of the medical students. Futcher, in addition to his student rounds and practical work with the clinical clerks, organized an excellent course in clinical microscopy, a course which Osler had initiated for the first time in Baltimore as part of the clinical instruction in medicine.

Futcher's ability as a physician and teacher was promptly recognized and he was appointed associate in medicine in 1898, associate professor in medicine in 1901 and associate professor of clinical medicine in 1914 at which time he became one of the visiting physicians of the Johns Hopkins Hospital. After relinquishing his post as resident physician in 1901, Futcher lived with a group of friends, among whom were Henry Barton Jacobs and Harvey Cushing, in a house on Franklin Street next to the Oslers' home. At this time he entered private practice, but continued his teaching duties at the medical school.

During World War I Futcher joined the Canadian Armed Forces and was placed in charge of the medical division of the 16th Canadian General Hospital at Orpington, Kent, England.

Throughout Futcher's 44 years of association with the Johns Hopkins, he never ceased to teach and practice medicine. His medical interests were wide, and while he did not participate in active clinical investigation he was an acknowledged authority on diabetes, gout and other diseases of the endocrine glands. He was president of the Association of American Physicians in 1932. Dr. Futcher died suddenly on February 25, 1938.

References

Longcope, W.T.: Thomas Barnes Futcher, 1871-1938. *Trans. Assoc. Am. Physicians*, 53:10, 1938.

Longcope, W.T.: Thomas Barnes Futcher, Jan. 1, 1871-Feb. 25, 1938. *Bull Johns Hopkins Hosp.*, 63:129, 1938.

Rufus Cole, MD (1872-1966)

Rufus Cole was born in Rowsburg, Ohio, on April 30, 1872. He received his undergraduate education at the University of Michigan and attended the University of Michigan Medical School for one year. Then, having been impressed by an exhibit of the then newly opened Johns Hopkins School of Medicine which he chanced to see at the World's Columbian Exposition in Chicago, he transferred to the Baltimore school. After graduation from the Johns Hopkins School of Medicine in 1899, Cole became a resident physician on William Osler's medical service. He had the opportunity to see at first hand the great skill of Osler as a clinical observer and diagnostician as well as the importance of the graded system of residency training which Osler had established at Johns Hopkins. After Osler's departure for Oxford in 1905, Cole became the resident physician for the new chief of medicine, Lewellys Barker. From Barker, Cole learned of the German emphasis on the investigation of disease as a major obligation of a department of medicine.

When Barker returned to Baltimore from his professorship of anatomy at the University of Chicago to assume the position of professor of medicine as Osler's successor, he took the important step of organizing research divisions within the department of medicine to provide opportunities for investigation into the nature of various disease processes. Under Barker's chairmanship of the department of medicine, there were three research divisions: chemical, physiological and biological. The biological division was placed under the direction of Rufus Cole. It was in this position that Cole had his first opportunity to do systematic clinical research and he soon demonstrated his talents as an investigator. He did a thorough study of the bacteriological aspects of typhoid fever, showing the bacteremia which occurred in this disease, and also became interested in the study of pneumococcal pneumonia.

Soon he was offered the professorship of medicine at the University of Michigan, but when given the opportunity he decided to stake his future career on the proposed clinical research hospital in New York which was to be associated with the Rockefeller Institute for Medical Research. On October 10, 1908, Cole was elected a member of the Rockefeller Institute in charge of the scientific and medical conduct of the hospital, and on November 28 was named director of the Rockefeller Hospital. Cole visualized in the activities of this hospital an opportunity to develop a program of medical investigation in an environment pervaded by the research spirit,

free from the ordinary routine of practice and of the teaching of medical students. Here, he thought, young men and women could be trained who would later carry the new methods and the new scientific approach to clinical medicine to other medical schools and teaching hospitals. This multiplier effect proved successful, and had a tremendous influence in providing the scientific base for medical practice as we know it today.

Although the Institute already housed laboratories in which distinguished scientists were engaged in research problems of ultimate importance to clinical medicine, Cole insisted that the hospital be provided with its own laboratories so that the clinicians could pursue their investigations close to the patient wards.

For his own research, Cole studied the highly important problem in those days of pneumococcal lobar pneumonia. He assembled a small team of assistants, including Alphonse Dochez, and developed an immune serum for the treatment of Type I pneumococcal pneumonia. He knew that further efforts to control the disease depended on detailed knowledge of the slight chemical differences that gave each strain of pneumococcus the ability to elicit its own particular antibody. Recognizing the need for an investigator with a thorough knowledge of bacteriology and a background in chemistry, he recruited Oswald T. Avery. This was perhaps one of the outstanding moves of Cole's career.

When Cole retired as director of the Rockefeller Hospital in 1937, Avery was still involved in the investigation of the chemistry of the pneumococcus which he had begun long ago at Cole's suggestion. Avery's later years were marked by his great discovery of pneumococcal transformation and its relationship to DNA. Thus, not only did Cole create a clinical investigation unit which was to exert a major influence on the future of medical education, research, and practice in the United States, but the persistence of this group in the study of a single outstanding problem in medicine — the nature of pneumococcal pneumonia — led to one of the most fundamental discoveries in medicine. The story of Rufus Cole and the Hospital of the Rockefeller Institute is replete with valuable lessons. It traces one of the most important facets in the evolution of clinical science.

Cole held membership in the National Academy of Sciences, the American Association for the History of Medicine, the American Society for Clinical Investigation, the American Society for Experimental Pathology, the Society of American Bacteriologists, the American Association of Immunologists, the American Society of Pharmacology and Experimental Therapeu-

tics, and was a Fellow of the American Academy of Arts and Sciences. He was awarded the Kovelenco Medal of the National Academy (1966). Cole died on April 20, 1966.

References

Corner, G.: *A History of the Rockefeller Institute (1901-1953)*. New York Rockefeller Institute Press, 1964.

Harvey, A. McG.: Creators of clinical medicine's scientific base: Franklin Paine Mall, Lewellys Franklin Barker and Rufus Cole. In *Adventures in Medical Research. A Century of Discovery at Johns Hopkins, Baltimore*, Johns Hopkins University Press, 1976, p. 124.

Tillett, W.S.: Rufus Cole, 1872-1966. *Trans. Assoc Am. Physicians*, 80:9, 1967.

Charles Phillips Emerson, MD (1872-1938)

Charles Phillips Emerson was born at Methuen, Massachusetts, on September 4, 1872. He graduated from Amherst College in 1894 and received his medical degree from the Johns Hopkins University in 1899. He became an intern at the Johns Hopkins Hospital and then served as assistant resident physician in charge of the clinical laboratory. Later he became resident physician and associate in medicine. During this period he spent a part of each of three years in study at Strasbourg, Basel, and Paris. By 1908 he possessed an almost encyclopedic knowledge about internal medicine and had acquired the ability to present his knowledge in a clear and orderly fashion. When he left Baltimore he became superintendent of the Clifton Springs Sanitarium and Clinic where he remained for three years. During part of this time he carried on some teaching in medicine at Cornell University in Ithaca.

The clinical laboratory which Emerson had charge of for several years in Baltimore was the first of its kind in the country. In 1896 a special clinical laboratory was built for the students of the Johns Hopkins School of Medicine which was enlarged in 1904 when the new clinical building was erected. On each of the two floors about 50 students were accommodated and there were adjacent rooms for special workers and for assistants. Jesse Lazear, of yellow fever fame, was the first physician-in-charge and

under Thayer's direction the well-known researches of Maccallum, Opie and Lazear on malaria were carried out. In 1900, after Lazear died in Cuba, Emerson was placed in charge of the laboratory which he reorganized in a thorough and scientific manner. Concurrently with the systematic instruction in the outpatient department, which formed a large part of the work of third year medical students, a course on microscopical and chemical methods was given, each student having his own place in the laboratory at which he could work throughout the year. Based on several years of experience in this laboratory, Emerson wrote the first comprehensive textbook on clinical pathology published in this country—*Clinical Laboratory Medicine*. As Osler pointed out in the introduction of this book, by its use the student could work out for himself, as the patients came under observation, every detail in the application of scientific methods to clinical study.

In 1911 Emerson was appointed professor of medicine and dean of the Indiana University School of Medicine. He held these positions for 21 years until he retired from the deanship in 1932 to become research director of medicine. The extraordinary development of that medical school, the improvement in its standards, the introduction of modern scientific methods, and the great extension of clinical facilities occurred during the period of Emerson's leadership.

Emerson was a pioneer in developing organized hospital social services, having begun work in this field while he was still in Baltimore. Although his most outstanding contributions were in the fields of education and social service, he did contribute information to a number of clinical conditions and methods of treatment, such as pneumothorax and the management of chronic arthritis. He also engaged in writing for textbooks on medicine, clinical diagnosis and physical diagnosis.

Emerson was a member of the Association of American Physicians, and in 1922 was president of the Association of American Medical Colleges. In 1934 he was awarded the degree of Doctor of Science by Amherst. He died on September 26, 1938.

References

Cole, R.: Charles Phillips Emerson, 1872-1938. *Trans. Assoc. Am. Physicians*, 54:11, 1939.

Thomas McCrae, MD (1870-1935)

Thomas McCrae was born in Guelph, Ontario, Canada, on December 16, 1870. He received his AB (1891), MB (1895) and MD (1903) degrees from the University of Toronto. He was awarded the honorary degree of ScD from the same university in 1927, and had received the Starr Gold Medal for his MD thesis. He was a member of the Royal College of Physicians of London beginning in 1901 and a Fellow after 1907. After serving his house officer ship at the Toronto General Hospital in 1895-96, he studied for a period at the University of Gottingen. He then joined the staff of the Johns Hopkins Hospital, where he was an assistant resident physician from 1896 to 1901 chief resident from 1901 to 1904; and associate professor of medicine and therapeutics from 1905 to 1908. In 1912 he was appointed professor of medicine at the Jefferson Medical College of Philadelphia and became physician to the Jefferson Hospital and to the Pennsylvania Hospital. He was a member of the American Philosophical Society, and served as president of the Association of American Physicians in 1930.

Although McCrae was not an investigator, his contributions to the medical literature were excellent. Particularly noteworthy were his works concerning typhoid fever, lobar pneumonia, arthritis deformans, carcinoma of the stomach, and acute leukemia. Perhaps his most important contribution was his publication, in association with Osler, of a seven-volume *System of Medicine*. He was co-editor with Osler of the later abridged edition entitled *Modern Medicine*, and continued to edit this volume after Osler's death. McCrae was also the editor of the 11th and 12th editions of *The Principles and Practice of Medicine*, familiarly known as "Osler's Medicine." He contributed widely to the history of medicine and was an associate editor of the *Annals of Medical History*.

McCrae delivered the Lumleian Lectures at the Royal College of Physicians of London and was made an honorary foreign member of the Association of Physicians of Great Britain and Ireland.

His friend of many years, Dr. Thomas Barnes Futcher, wrote of him as follows: "McCrae was one of the best house officers the Johns Hopkins ever had. He was an excellent bedside teacher and instructor of students in physical diagnosis. He organized a course in medical anatomy in which the students were taken to the autopsy room for instruction in topographical anatomy of interest in connection with their clinical work: pleural reflections, lung fissures, where to do a paracentesis thoracis, paracentesis

pericardii, etc.”

McCrae died on June 30, 1935.

References

Woodyatt, R.T.: President’s Address. *Trans. Assoc. Am. Physicians*, 51:1, 1936.

Lewellys Franklin Barker, MD (1867-1943)

Lewellys Franklin Barker assumed the post of professor of medicine at Johns Hopkins when Osler left Baltimore in 1905 to become the Regius Professor of Medicine at Oxford. Born at Milldale, Ontario, on September 16, 1867, he was a graduate of the University of Toronto. He interned for one year in Canada and went to Baltimore for the first time in 1891 to work in the newly opened Johns Hopkins Hospital. After spending a year in Osler’s clinic, Barker was made a fellow in pathology under Welch. After this year he joined Mall in the anatomical laboratory and for the first time felt the thrill of discovery by demonstrating the presence of iron in eosinophil cells. Barker advanced to the position of associate professor of anatomy, and in 1899 was also appointed associate professor of pathology. Thus, over a period of 8 years, he worked in close association with Osler, Mall, and Welch.

In 1895 he spent six months in Leipzig under von Frey. While there he carried out a detailed study of the localization of the sensory points in the skin of the arm, using for his purpose his own arm in which sensation was disturbed owing to the presence of a cervical rib. When Barker returned from Germany he wrote a large illustrated book entitled *The Nervous System and Its Constituent Neurons* which was a pioneer effort in this field. In 1899, Barker and Simon Flexner led a commission to study the diseases of the Philippine Islands. Shortly after his return to the United States he accepted the position of professor of anatomy at the University of Chicago, although he had “always hoped and expected to work in internal medicine.” During his period in Chicago he translated and edited Spalteholz’s *Anatomy*.

In 1902 Barker delivered an address entitled “Medicine and the Universities,” in which he made a plea for the reorganization of the clinical de-

partments in medical schools. He believed that they should rank with the other departments of a university and should emphasize research into the problems of human disease as well as teaching. To do this, he stressed, professors would have to be relieved of the necessity of carrying on private practice. Mall had already pointed out that such a change was necessary, an idea which he apparently got from his mentor, the great German physiologist Ludwig. Such a step followed logically from the changes which had already been made in the preclinical departments with such brilliant results. Mall clearly understood that clinical medicine had to change, had to add to the art of healing all that science could contribute toward greater skill in diagnosis and treatment. During his early years in Baltimore, Mall discussed this goal with his staff and students among whom was Lewellyn Barker, who was responsible for the course in neuroanatomy. Thus, Barker was a spokesman for Mall's ideas in relation to full-time medicine.

In 1903 Barker was given a leave of absence to work in Munich with the famous German clinician Fredrich von Müller, and in the equally famous chemical laboratory of Emil Fischer. There he witnessed the vigorous pursuit of research both in the laboratory and in the clinic, a joint endeavor characteristic of German medicine.

When Barker assumed the post of professor of medicine in Baltimore in 1905, he wanted it to be on a full-time basis, but the university did not have sufficient endowment to put such a plan into effect. Nevertheless, Barker took the important step of organizing full-time research divisions within the department to provide opportunities for investigation into the nature of various disease processes. Of course, scientific investigations in departments of medicine did not begin with the opening of these laboratories, but the institution of laboratories for this specific purpose started a movement which not only greatly influenced the character of university clinics but also started a chain reaction in the evolution of clinical investigation that was to play a major role in creating the scientific base of modern medical practice. His appointments to the directorship of the research divisions in his department were spectacular in the beginning, with Rufus Cole, another founding member of the Interurban Club, as head of the biological laboratory; Arthur D. Hirschfelder as head of the physiological laboratory; and Carl Voegtlin as head of the chemical laboratory. However, Barker's subsequent appointments did not match these in terms of productivity and since several of the incumbents had no MD degree, their work did not have the influence that was to come with the work of Rufus Cole's staff at the Hospital of the Rockefeller Institute.

By the time an endowment had been provided by the Rockefeller Foundation for the institution of full-time professorships in medicine, surgery, pediatrics and obstetrics at Johns Hopkins (1913), Barker's private practice had become so large that he felt compelled to turn down the opportunity to assume the full-time position.

Barker served as president of the National Committee for Mental Hygiene (1909-18), the Association of American Physicians (1913), the American Neurological Association (1916) and the Association for the Study of Internal Secretions (1919).

Barker died on July 13, 1943.

References

Barker, L.F.: Time and the Physician: *The Autobiography of Lewellys F. Barker*. New York, G.P. Putnam's Sons, 1942.

*Sir William Osler, MD (1849-1919)**

William Osler was the founder of the Interurban Clinical Club and we, its members, have this, among other things to thank him for. The Surgical Interurban Club had been formed a short time before and he heard enthusiastic accounts of its meetings, especially from Harvey Cushing. Dr. Osler suggested to some of us on his staff that we should follow their example and establish a similar group in medicine. Considerable thought was given to the choice of men in the other cities who should be invited to join and I think that Dr. Osler wrote to some of the older men asking opinions as to the best men in each city. He chose the members himself and I fancy that everyone of the original group felt that he had chosen well.

The program of the first meeting was a simple affair with a good deal of attention given to teaching and the keeping of records. The personality of William Osler was through it all and, as my memory serves, we dined at the Maryland Club as his guests. He delegated to me the drawing up of some sort of constitution for submission to the members at the first meeting.

He was always deeply interested in the meetings and the program. As long as I was secretary, a copy of each program was sent to him and subse-

quently some account of the meetings. He was greatly delighted with our discussions on terminology which went on for several meetings. He always felt that, apart from the medical interest in such a gathering, the opportunity it gave the men from various cities to learn to know each other was an important element. We will all agree that time has proven the correctness of this view.

It hardly seems necessary to detail the various stages of Sir William Osler's career as these have been given so often. Some phases of his influence will be discussed. Medical societies were always a great interest in his life. Wherever he was, the medical societies were helped and stimulated by him. He was sometimes much in the background as shown perhaps especially in the formation of the Association of American Physicians and in the Royal Society of Medicine. In Baltimore the various societies at the Johns Hopkins Hospital owed much to him. He was a regular attendant at the meetings.

He often carried out William Harvey's precept as to the wisdom of dining together but very often the lunch or dinner was supplied by William Osler.

His relations to the profession were very close and he had high ideals as to what the practice of medicine should be. Naturally he was consulted by many physicians either for themselves or members of their family. This grew to be a heavy burden but any "complaint" from him was really not a complaint but a wish that they would be a little more considerate. Doctors had a habit of descending on a consultant without warning and expecting him to drop everything else and attend to them. One afternoon when he had got through a heavy day there were four physicians waiting to consult him about themselves. He saw them all and when the last one had gone, threw himself in a chair absolutely fagged and said, "Truly, virtue has gone out of me." Probably each of these men went away feeling that it had been a great pleasure and privilege for William, Osler to have the opportunity of examining him.

He had a hatred of controversy and wrangling, but when the need existed he could take hold of a situation very vigorously and "talk out in the meeting." But he would not listen to gossip about or criticism of another practitioner. No one could utter a mean thing in his hearing without rebuke, rarely in words as such but by his manner or silence. Even when he had good cause for complaint he said very little. In the editing of his "System of Medicine" there were some trials. One contributor from whom he had

expected much sent in an article which fell so far short of what was anticipated that it was almost laughable. But he did not feel much like laughing as it put us in a sad predicament. All that Sir William said was, "Oh well, we must not blame X too much. He carries too much sail for the lead in his keel and he is not altogether to blame for that." One of the men who influenced his life in a striking way was Father Johnson, one of his early teachers. For him he had a deep affection but in him the boy had had an example of the evils of controversy. Father Johnson was always in hot water, principally over quarrels relating to church and theological matters. He scented the battle from afar and entered into strife with joy. The papers of those times are full of the accounts of bitter conflicts. It would seem that this example must have influenced William Osler in his hatred of strife and his determination to have none of it when it could be avoided.

He was always keenly interested in morbid anatomy and no one who heard him in the autopsy room can ever forget his demonstrations. In fact some of them stand out in my mind more clearly than clinics at the bedside. No one could do an autopsy more deftly than he did and with a slow pathologist — and there was a very slow one who did some of the autopsies at that time — he often elbowed him aside in a gentle way and did the work himself. He always insisted on respect being shown to the body and if it had not been done already, he would put a towel over the face of the dead. The specimens in which he had the greatest interest were some which he had brought from Montreal and which were examples of animal pathology. They were stored away in a dark corner in a basement but at intervals he would have them out and go over them. He had a remarkable memory as to the history connected with pathological specimens.

As to his interest in disease and its manifestations, one might describe it as particularly in the natural history of disease. The variations in a disease such as typhoid fever or tuberculosis were of absorbing interest. He had a remarkable memory for patients and their histories. I have seen a patient come into the dispensary whom he had not seen for months or perhaps years. If there had been something of interest in the past condition he could usually give the important points without referring to the history. He never forgot and constantly emphasized to others, the need of not forgetting that the patient was a human being and that consideration of this should never be forgotten. The importance of the psychical side was always kept forward. His memory for other cases like the one under consideration was remarkable. I have told elsewhere the story of the patient whom I saw in consultation in Canada when the diagnosis was evident although even

then it was an atypical case. Over a period of many years he had seen men in Canada, the United States, Great Britain, France, Germany, and Austria. He had a collection of opinions which was valuable for the signatures alone. Sir William had seen him many years before and was the only one to suggest the diagnosis long before it could be made with fair certainty. He said to the patient's physician, "I do not know what your patient has but the only patient like him whom I have ever seen proved later to have paralysis agitans." Such it was.

Of his propensity to joking much has been told. The Egerton Y. Davis habit must have given him many chuckles and perhaps no more than when he wrote regarding him in the form of an apparently solemn statement which he put away in a book where it might not be discovered for years. I found it by chance after his death and Cushing has quoted it in the biography, volume 1, page 240. No doubt he said to himself, that will add to the puzzle after I am gone. The exchanges between William Osler and William Halsted were always interesting and honors were usually about even.

He did not wear his heart on his sleeve. Few men have been so difficult to know thoroughly. There can't have been but few personalities whom so many men thought they knew well. At once on meeting him a stranger was put at his ease and his charm of manner was irresistible. But few were admitted to a deep intimacy with him. It was very difficult to read what went on behind that of ten inscrutable countenance. It was perhaps part of his gospel of equanimity. After the death of his son no one meeting him in the ordinary way could have any suspicion of the sorrow in his heart. I saw him during those days and one could only marvel at his spartan courage.

His life was full of work and play. We must wonder at what he accomplished in so many fields of endeavor. He warmed both hands at the fire of life. When the end came in sight he warned Lady Osler not to be encouraged too much by the cheering views of consultants. He cast his own horoscope accurately.

We of this Interurban Club revere his memory, as our founder, as our teacher, and above all as our friend.

**Thomas McCrae, M.D. (This biography was written by McCrae for History of the Interurban Club, 1905-1937.)*

Chapter 3

RECENT HISTORY OF THE INTERURBAN CLINICAL CLUB



The Interurban Clinical Club continued to meet twice each year through the 1990s, hosted in Boston, New Haven, New York, Philadelphia, or Baltimore. Meetings began on a Friday with all-day scientific sessions followed by a black-tie dinner with keynote speaker and a Saturday morning scientific session that ended around noon. I made many trips by train to New Haven as a young physician-scientist, returning home late Saturday afternoon. In the mid-1990s, the ICC, perhaps recognizing the proliferation of sub-specialty meetings, decided to limit the scientific sessions to Friday only. This tradition has continued, with the exception of the 200th meeting in Baltimore, at which a Saturday morning session was held during Johns Hopkins Medical Grand Rounds.

The 200th meeting was a special and lively celebration planned by an organizing committee, with Eve Osler Hampson, a grandniece of William Osler, serving as honorary chairperson. Members of the organizing committee were Frank Austen, Ed Benz, Frank Bunn, Jeff Drazen, Kurt Isselbacher, John Potts, Tom Stossel, Megan Sykes, and Mark Zeidel from Boston; Jeffrey Bender, Arthur Broadus, Lloyd Cantley, Thomas Duffy, Jack Elias, Bernie Forget, John Forrest, Steve Malawista, and John Wysolmerski from New Haven; Craig Basson, Leonard Chess, Edward Fisher, Rochelle Hirschhorn, Richard Kitsis, Paul Marks, Aaron Marcus, David Shafritz, and Babette Weksler from New York; Barry Blumberg, Robert Coleman, Wafik El-Deiry, Stephen Emerson, Jon Epstein, William Kelley, Richard Shannon, Koneti Rao, and Scott Waldman from Philadelphia; and Mark Donowitz, Diane Griffin, Tom Hendrix, Richard Johns, Gerald Lazarus, Guy McKhann, Antony Rosen, Richard Ross, Cynthia Sears, and Mike Weisfeldt from Baltimore.

Concerning women elected to the group, the ICC did not have an excellent early record. For 80 years there were no women members. In 1985 Rochelle Hirschhorn, a physician-scientist from New York University and distinguished alumna of Barnard College, was the first woman elected to membership. She served as president of the ICC in 1987.

The inclusion of women in the ICC has improved in recent years. Many distinguished women have been elected to membership since 1985, in-

cluding Babette Wexler, Cynthia Sears, Laurie Glimcher, Nancy Andrews, Michelle Barry, Nancy Berliner, Linda Bockenstedt, Anne Cappola, Lynda Chin, Mary Crow, Betty Diamond, Elizabeth Engle, Linda Fried, Diane Griffin, Barbara Hempstead, Elizabeth Henske, Catherine High, Elizabeth Jonas, Barbara Kazmierczak, Judy Lieberman, Susan MacDonald, Barbara Murphy, Maria New, Thersa Shapiro, Megan Sykes, Carol Tacket, Chloe Thio, and Rachel Werner.

In the 1990s and early 2000s, the scientific sessions of the ICC were often focused on discoveries of novel intracellular molecular pathways and the identification and location of cellular proteins, but there was uncertainty whether these discoveries would ever have clinical relevance. After sequencing and annotation of the human genome was declared complete in 2003, papers began to indicate a return to clinical medicine and diseases, but with a new molecular slant. This new slant has included genotyping of specific viruses to aid in appropriate treatment, identification of mutations linked to different forms of cancer, and design of medications and more accurate prediction of their effects. Many papers presented before the ICC have described the genetic predisposition to illnesses such as breast cancer, colon cancer, hemostasis disorders, cystic fibrosis, liver diseases, and Alzheimer's disease.

It is clear that a deeper understanding of the etiologies of Alzheimer's disease, many cancers, and other areas of clinical medicine will benefit from additional genome information, and such knowledge may eventually lead to significant advances in disease management.

In the two most recent ICC meetings, president Jon Epstein proposed — and the council approved — inviting MD-PhD students from the host city to present their research and attend the Friday night dinner. (See Chapter 10, in which Epstein explains the rationale for this new venture.) This approach added great value to ICC meetings but will require the support of the MD-PhD program director to continue.

As subspecialty meetings in internal medicine continue to expand, so do the many opportunities for physician-scientists to present their latest findings to their own colleagues. However, the ICC meetings provide a chance for members and guests to learn of research outside of their particular subspecialty, and the value of this is unmistakable. The ICC scientific sessions are often the only opportunity for members to learn of the remarkable breakthroughs occurring in areas outside of their own specialties. Twice each year we hear “the best science” of the host city, presented by the

people responsible for the discoveries. This was the original intent of our founder, William Osler — “exchanging ideas,” as he called it, and it continues to serve a vital purpose.

May the Interurban Clinical Club continue to flourish for at least another hundred years!



Members of the ICC Club and spouses gather before the black tie dinner at the 200th Anniversary meeting of the club in Baltimore, November 6, 2009.



Members of the ICC Council at dinner in Baltimore, November 5, 2009. From left to right: Wafik El-Deiry, Eve Osler Hampson, Craig Basson, Anthony Rosen, Rick Shannon, John Wysolmerski, Aaron Marcus, Richard Blumberg, Cindy Sears, John Forrest, Megan Sykes.



Eve Osler Hampson, grand niece of Sir William Osler, extending greetings from the Osler family at the 200th meeting of the ICC in Baltimore, November 6, 2009.

Chapter 4

THE LEGACY OF SIR WILLIAM OSLER
AND THE INTERURBAN CLINICAL
CLUB



Presented at the 200th anniversary meeting of the ICC

Thomas Duffy

Member, New Haven

Sir William Osler, his life and his way of life, has continued to inspire many subsequent generations of physicians for almost a century after his death. His biographies, authored by Harvey Cushing¹ and, more recently, Michael Bliss,² are panegyrics that document a near-seamless life and devotion to medicine.

But not all viewers of his life share the sentiments regarding the god-like stature of Osler. Philip Bondy, a member of the Interurban Clinical Club and chair of the Department of Medicine at Yale from 1965 to 1972, questioned his legendary greatness and described his puzzlement surrounding Osler's longstanding, near-cultish hold on the profession of medicine.³ Bondy wondered what the fuss was all about. He believed that Osler's greatness was much exaggerated. His former chief of medicine at Peter Bent Brigham Hospital, Soma Weiss, was thought worthy of an equal eminence, although Bondy acknowledged that Weiss's premature death had limited his impact and hold upon the profession.

Bondy was not the only naysayer regarding Osler's near canonization by the profession. Another member of the ICC, Gerald Weissman, professor emeritus of medicine at New York University, decried Osler's fabled *aequanimitas* and portrayed him as the father of cool detachment, an enemy of empathic caring.⁴ He tried to tumble Osler from his precious throne by accusing him of possessing the public tone of the academic snob. Weissman claimed that although Osler wore the title of the great clinician, he appeared more interested in autopsies than in living patients. In support of Weissman's contentions, it is known that one of the major reasons for Osler's eager acceptance of the Regius Professorship at Oxford was the too-great burden of caring for patients in his busy and very profitable consult-

ing practice in Baltimore.⁵

Bondy and Weissman were not the only critics of the infatuation surrounding Osler. There are other candidates that some believe were as worthy of the same veneration. Disciples of Paul Beeson consider Beeson to be Yale's modern counterpart to Osler; he elicited a comparable degree of devotion in his immediate circle and maintains an ongoing aura among his trainees.⁶ However, the intensity of his radiance and adulation may already be waning, and it has never possessed the magnitude of Osler's halo. Beeson's portrait, commissioned by his last group of interns, occupies a front wall of the Fitkin Medical Amphitheater at Yale, while John Singer Sargent's famous portrait of Osler with Halsted, Kelly, and Welch occupies a prominent place in the center of the Johns Hopkins University Welch Library Reading Room. Each has medical services named after him, at Yale and Hopkins, respectively. The portrait of the "Great Doctors" has a luster that transcends the medical world; this may be secondary to the fame and reputation of Sargent as much as the esteem surrounding its famous subjects.

Still, most others have been kinder, more respectful and adoring of the man, and the adulation for him has continued up to the present. Annual meetings of the Osler Society are held with pilgrimages to his shrine at the Osler Library in Montreal; an Osler Newsletter keeps his image alive for modern physicians. A room in the Hopkins Hospital dome where he completed his magnum opus, *The Principles and Practice of Medicine*, has been re-furbished with the furniture and assorted memorabilia that originally occupied the room. Up until his death, Victor McKusick led frequent jaunts to this "sanctum sanctorum," demonstrating his devotion to the man and his ideals for the next generation of physicians. Osler's spirit still hovers over the ICC meetings, which have taken place almost continuously since the club's founding by Osler in 1905.

The establishment of the ICC was one of Osler's last contributions to American medicine; he sailed to England one month after its first meeting to assume the Regius Professorship at Oxford. There is no record that he attended any subsequent meetings, and yet he has remained an influential presence throughout the club's history. His departure from America occurred over 100 years ago, his death almost nine decades ago, and still the sobriquet of Osler conveys the master clinician, the doctor's doctor, the model to which many physicians aspire. It must be asked why there has been no figure to replace him. What characteristics and qualities explain his charismatic hold on his many followers? Is the establishment of the ICC

a window into understanding his lasting legacy in medicine?

The historian Bernard Spector sought to identify the source of Osler's greatness by comparing his accomplishments with those of the recognized greats of medicine who preceded him and who were, in kind, venerated by Osler.⁷ In order to explore the source, Spector capitalized upon a birthday gift that Grace Revere Osler had given to her husband. It was a copy of a triptych of portraits originally viewed by Osler when he visited the home of Sir Henry Acland, the reigning Regius Professor at Oxford, while Osler was attending a meeting of the British Medical Association. The triptych is composed of the portraits of Thomas Sydenham, Thomas Linacre, and William Harvey — the three individuals who epitomized *praxis*, *litterae*, and *scientia* for Osler. This triad constituted the trinocular vision that Osler believed physicians should strive to possess, a forerunner of the triple threat of teacher, clinician, and researcher that many in the ICC command today.

Sydenham was the first real clinician of modern times. Osler's reputation rests in major part upon his skill as a clinician, and his clinics provided occasion to demonstrate his legendary skills at the bedside. There is a description of his entertaining the diagnosis of *situs inversus* after viewing an upright male and noting that his right testicle sat lower than the left — remarkable not only for observing this minor detail but for examining a standing patient. Like Sydenham, Osler's name remains in the eponymic designation of the several disease entities he described, including Osler-Weber-Rendu syndrome (also known as hereditary hemorrhagic telangiectasia) and Vasquez-Osler disease (polycythemia rubra vera). Terms such as "Osler nodes," "Osler's triad," and "Osler's maneuver" all keep current his presence in clinical medicine. Both men excelled at *praxis* — it was an end in itself for Sydenham, but only a means to an end for Osler, who was a clinical teacher and consultant more than he was a practitioner. He rarely assumed primary care responsibilities. His patients constituted his teaching materials, and the hospital wards were his classrooms. His innovative admission of students to the medical wards where patients could serve as textbooks to learn medicine was considered by Osler as his greatest accomplishment. *Doctrina*, the teaching of students and fellow physicians, took precedence over *praxis* throughout Osler's life, and it was as a teacher of medicine that his enduring mark was made.

The second member of the triptych was Linacre, the father of English medicine and the founder of the Royal College of Physicians. Linacre was

more involved in literature, both of medicine and in general. He transmitted what had been described in medicine but never had original, creative ideas of his own. There was much of Linacre in Osler, as *litterae* was a major passion throughout Osler's life, the classics and medical history being his particular focus. His bedside library contained the likes of Ovid and Marcus Aurelius but no modern authors.⁸ Osler was elected president of the British Classical Association and the British Philosophical Association and amassed a vast collection of historical books that constitute the Osler Library at McGill University. He disregarded his own counsel that, whereas it might be well for a physician to have pursuits outside his profession, it was dangerous for them to be too absorbing. Osler's *litterae* was his avocation, and it resonated nicely with his vocation. His industry for writing and his talent for doing so resulted in a medical text that he revised at three-year intervals for almost thirty years. This book has contributed to his lasting fame, aided by the subsequent reworking of the book by A. McGehee Harvey and Victor McKusick starting in the 1960s.⁹ *Litterae* certainly enhanced Osler's reputation, but it hardly explains the aura that continues to surround him.

The last portrait in the triptych, that of William Harvey, represents *scientiae*, the area in which Osler has been found most wanting. Osler's major scientific contribution in the description of blood platelets fades to insignificance in the face of Harvey's investigation of the circulation of the blood. Osler used his extensive observations of autopsies to introduce new classifications into clinical medicine, but he never derived any central insights from the material. His work was descriptive and never experimental. He made no claim to originality or creativity, relegating himself to the category of transmitter of information and transmutor of the fashion in which medicine was taught. In the final analysis, *praxis*, *litterae*, *scientiae* do not individually constitute Osler's greatness, but all contributed to his talents as a teacher of clinical medicine. The crowning of the triad with *doctrina*, or teacher, highlights Osler's belief that teaching was his major talent and the achievement of which he was the most proud.

Examination of the ICC founding objectives attests to the centrality of medical teaching in Osler's life and his efforts to engage others in this pursuit.¹⁰ The original objectives of the club were to stimulate the study of internal medicine, improve the methods of work and teaching medicine, promote the scientific investigation of disease, and increase knowledge of the methods of work in one another's clinics. The program for the initial meeting, held in Baltimore in 1905, demonstrated how Osler and his col-

leagues were committed to achieving those objectives. There was a medical clinic in which Osler displayed his vaunted skills of observation and inspection of patients; he diagnosed a case of scrofula on the basis of his detection of unilateral cervical adenopathy on physical examination. There was also a display of basophilic stippling of red blood cells on a peripheral smear as a manifestation of lead poisoning. A major portion of the meeting was an exercise that has remained a central tradition of the ICC: an anatomical dissection and manipulation of an animal's Bundle of His to create heart block. Osler, in a bench-to-bedside presentation, then discussed a patient with Stokes Adams attacks and the role of heart block in its genesis. Internal medicine, its study, teaching, and investigation formed the make-up of the initial meeting, and this constellation has remained the focus of each meeting throughout the history of the ICC. This is a major part of the lasting legacy of Osler and the ICC, which became the provenance of the physician-scientist as the vital link between the practicing physician and the basic scientist. The ICC was strongly influential in the development of the scientific basis of medicine throughout the 20th century, and this has continued up to the present.

This legacy is a major one, but it obviously does not explain medicine's continuing involvement in matters Oslerian. There are many great teachers who have been members of the ICC who have since become anonymous and little known for their accomplishments. What was a distinguishing feature of Osler was his uninterrupted attention to the body politic of the profession. There have been few others who have consistently and repeatedly tended to the medical enterprise in the manner of Osler. He took literally the words of the Hippocratic Oath, which identifies the duty of physicians to hand on the craft of medicine to individuals who take the Oath and to treat as family those who were one's teachers. Osler remained indebted throughout his life to the three individuals responsible for nurturing his scientific interests and his medical career; he dedicated his medical textbook to James Bovell and "Father" William Johnson, his preparatory school teachers, and Palmer Howard, his medical teacher. He personally underwrote the medical education of his nephew, Billy Francis, and the education of the children of a deceased colleague. His Saturday meetings were occasions where medical students dined on his kitchen, library, and intellectual victuals; a favored few were latchkeyers with total access to the richness of his home. After becoming the Regius Professor at Oxford, his house at 13 Norham Gardens became the home-away-from-home for large numbers of visiting Americans and Rhodes Scholars; during the war, parents of wounded soldiers found some solace in the house that was aptly

christened “Open Arms”. Osler acknowledged any publications or promotions of colleagues and his mentees with a brief congratulatory note. Unprofessional behavior unbecoming of a physician did not escape his critical message and gentle discipline.¹¹

Osler also demonstrated fealty to his forebears in medicine. During a medical congress in Paris in 1905, he participated in a graveside ceremony at the Montparnasse tomb of Pierre Louis, the great clinical teacher with whom many American physicians had studied and who was responsible for the clinical methods they had learned. Osler’s attention to the creation and participation in clubs and societies makes it difficult to accept that he ever dined at home. The Cushing biography lists 42 clubs or societies of which he was a member, and in all of these he was a very active participant. He was a founding member and president of the Association of American Physicians; the founding member and president of the Historical Section of the Royal Society of Medicine; president of the American Medical Association, the American Pediatric Society, and the Canadian Medical Association; fellow of the Royal College of Physicians and the Royal Society; and president of the Ashmolean Natural History Society. All of these involvements were in addition to his serial professorships in Montreal, Philadelphia, Baltimore, and Oxford. Everywhere he lived and taught, he created occasions and venues where physicians could gather to share their ideas and methods with one another. He was the centerpiece of these gatherings, which cemented further his hold on the profession. He participated in this way in the covenant of medicine, and it is the power of the covenant that most convincingly explains his continuing hold on the profession and its persistence to the present.

The covenantal portion of the Hippocratic Oath precedes the codal portion; the covenant identifies our familial obligations to one another in the profession, including our predecessors and those who are our students. The code of the oath spells out our responsibilities to our patients.¹² Many have questioned this prioritization of our responsibilities in the oath, with covenant preceding the code.¹³ Commentators have used this ordering to ask whether the bond that exists between members of the profession deserves preeminence over physicians’ commitment to the common ideal of service to their patients. The bond was originally sanctified by swearing to the god of medicine, Asclepius, an oath-taking that is now often omitted but without any loss of commitment to the original resolve. This covenant serves to float medicine on a higher moral level, with the individual behavior of each physician reflecting upon others in the profession. There is a

collective empowering of individual physicians as each member strives to achieve medicine's articulated ideals.

Osler was dedicated to the creation of organizations that brought physicians together to share their knowledge, experience, and ideas. The many societies that he established permitted the spirit of the covenant to be better realized. Medical and scientific knowledge was the primary text at ICC meetings, but friendships were also renewed and maintained. The original dinners of the ICC were followed not by formal presentations but by lengthy discussions and conversations, some of which were contentious and many laced by plenteous spirits. Osler guaranteed that the covenant remained strong by establishing numerous venues and occasions for fellowship, where the links between physicians were forged and strengthened.

These organizations remain active up to the present, and Osler's memory remains burnished as a result. This helps explain his lasting hold on the imagination of the profession — its duration — but still not all of its magnitude. A possible explanation of his greatness, a clue to its source, may be manifest in all of our medical institutions as physicians attend the ceremony of Grand Rounds each week. The clinical discussion of a patient now encompasses not only classical pathophysiology and diagnostic reasoning but often a particular emphasis upon molecular pathways.

Osler's original bench-to-bedside exposition at the first meeting of the ICC remains in place, but with a molecular flavor added to the mix. There is always a wide range of attentiveness among the members of the audience as discussants move fluently and rapidly through the territory of "gene-speak," the degree of attentiveness likely determined by how comfortable the members of the audience are with gene-speak and the complicated pathways of molecular biology. This variation in the degree of attentiveness always disappears when a patient is introduced and the details of his life, his person, and his illness are revealed. Everyone in the hall usually sits up, leans forward, and hangs on every word of the patient's story. Whatever each individual's degree of knowledge of the vast vertical hierarchy of reasoning in medicine, wherever he is perched on the whole bio-psycho-social-spiritual gamut of medicine, the patient remains the center of the physician's life in medicine. Every patient represents the "Ark of the Covenant" of medicine and helps explain Osler's lasting greatness in medicine. From his very evident and influential positions at four major institutions and his role as the ultimate medical organization man on three continents, he, in his care of patients and his handing on of medical knowledge, paid testi-

mony to the lives of all other members of the profession, the members of the covenant. They responded in kind with devotion to the man who was the keeper of the ark, the centerpiece of their lives in medicine. Their devotion to him is a shared devotion to all of their colleagues in medicine and is testimony to the noble enterprise in which they are mutually engaged.

Osler's legacy remains alive in venues such as the ICC and will continue to be so as all of his sons and daughters in medicine continue their participation in the covenant of medicine. Osler links all physicians with their forebears and their successors — his legacy in the ICC remains alive. The club that he established over a century ago, in its intent and realization, is an important key to unlocking the lasting mystique and greatness of Sir William Osler.

Notes

1. Cushing, Harvey. *The Life of Sir William Osler*. London: Oxford University Press, 1925.
2. Bliss, Michael. *William Osler: A Life in Medicine*. New York: Oxford University Press, 1999.
3. Bondy, Philip. What's So Special About Osler? *Yale J Biol Med* 53 (1980): 213–217.
4. Weissmann, Gerald. Against Aequanimitas. *Hosp Pract* 19 (1984): 159–169.
5. Fye, W.B. William Osler's Departure from North America. The Price of Success. *N Engl J Med* 320 (May 25, 1989): 1425–1431.
6. Rapport, Richard. *Physician: The Life of Paul Beeson*. Fort Lee, NJ: Barricade Books, 2001.
7. Spector, Bernard. Osler: An Example of Litterae, Scientiae, Praxis and Doctrina. *Bull Hist Med* 23 (1949): 378–386.
8. LaCombe, Michael and Elpern, David, eds. *Osler's Bedside Library: Great Writers Who Inspired a Great Physician*. Philadelphia: ACP Press, 2010.
9. Harvey, A McGehee and McKusick, Victor. *Osler's Textbook Revisited*. New York: Appleton-Century-Crofts, 1997.
10. Harvey, A. McGehee. *The Interurban Clinical Club (1905–1976): A Record of Achievement in Clinical Science*. Philadelphia: Saunders, 1978.
11. Duffy, Thomas. The Osler-Cushing Covenant. *Perspect Biol Med* 48, no. 4 (2005): 592–602.
12. Edelstein, Ludwig. *The Hippocratic Oath: Text, Translation and Interpretation*. Baltimore: Johns Hopkins University Press, 1943.
13. May, William. *The Physician's Covenant: Images of the Healer in Medical Ethics*. Lexington, KY: John Knox Press, 2000.

Chapter 5

THE BLOOD VESSEL AND
ITS DISORDERS: A BRIEF,
EARLY HISTORY OF
VASCULAR PHYSIOLOGY
AND MEDICINE IN BOSTON



*Presented at the 212th meeting of the
Interurban Clinical Club*

Joseph Loscalzo

Member, Boston

Let me begin with a warning and an apology. The warning, to the younger members of the Interurban Clinical Club, is to beware: if you are asked to discuss some aspect of medical history, you have likely become history! The apology is to members alive and dead of the greater Boston vascular community whose contributions I will not mention here. In the interests of time and space, I will focus my remarks only on contributions to the field of vascular physiology (not vascular biology) made only by individuals who are deceased.

Research in vascular physiology and medicine has a rich tradition in Boston medicine that dates to the early part of the 20th century. Tinsley Harrison, who ultimately became the founding editor of *Harrison's Principles of Internal Medicine*, trained as a resident at the Peter Bent Brigham Hospital under its first chief of medicine, Henry Christian. (Christian, of course, was a trainee of Sir William Osler at Johns Hopkins University, thus loosely linking this vascular tradition to the founder of the Interurban Clinical Club.) As a resident (1922–1924), Harrison studied blood flow quantitation using the Fick method and demonstrated the effect of arteriovenous fistulae on cardiac output. These efforts to quantitate blood flow, cardiac output, and blood oxygen saturation represent a theme that evolved over the subsequent 20 years through the efforts of several important leaders of academic medicine in Boston, as discussed later.

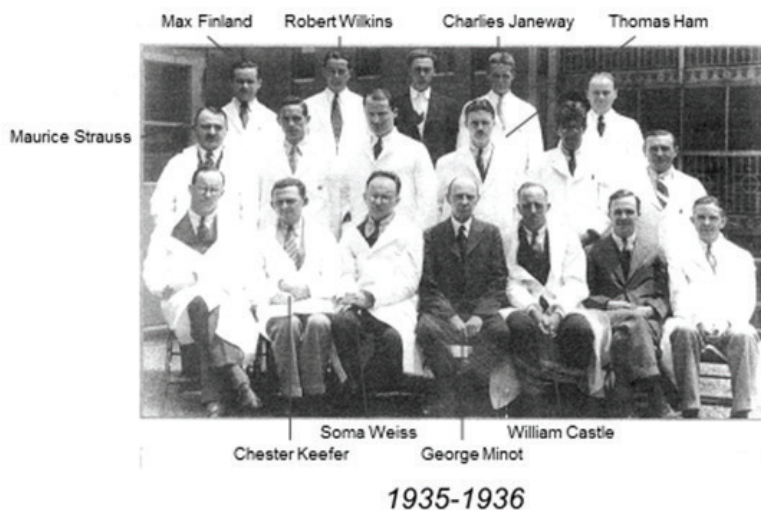


Fig. 1. Staff members of the Thorndike Memorial Laboratory, 1935–1936.

To appreciate the richness of the academic medical environment in Boston in that era, it is useful to reflect on the members of the Thorndike Memorial Laboratory at Boston City Hospital. As shown in Figure 1, a photo taken in 1936, members of the research staff included the nephrologist Maurice Strauss, infectious disease specialists Maxwell Finland and Chester Keefer, hematologists William Castle, Thomas Ham, and George Minot (who shared the Nobel Prize in Physiology or Medicine in 1934 with William Murphy and George Whipple, for their discovery of the treatment of pernicious anemia with liver extract), immunologist and pediatrician Charles Alderson Janeway, and cardiologists Soma Weiss and Robert Wilkins. This incredible pantheon of medical luminaries helped establish and maintain a level of research rigor that set the stage for the advances in vascular physiology and medicine soon to follow.

Weiss, Hersey Professor of the Theory and Practice of Physics at Harvard Medical School and second chief of medicine at the Peter Bent Brigham Hospital, first described carotid sinus hypersensitivity, and together with Mallory first described Mallory-Weiss syndrome. In addition, working with Hermann Blumgart at the Beth Israel Hospital, Weiss first applied radioactive tracers to human studies *in vivo*. Unfortunately for the academic community, Weiss died an untimely death in 1942 at the age of 39 owing to a ruptured cerebral aneurysm.

Blumgart, arguably the father of diagnostic nuclear medicine, developed the first radionuclide detector for clinical application (a cloud chamber) with Otto C. Yens. In its first human application, he injected the radium decay products $_{82}\text{Pb}^{214}$ and $_{88}\text{Be}^{214}$ into himself and measured the circulation time.¹ This self-experiment was one of many in the history of modern medicine.² The notion of a physician-scientist serving as his own research subject (self-experimentation) may seem foreign to us now, as well as ethically unsound, but was commonplace among biomedical investigators until the first half of the 20th century.

Yet another notable member of the vascular research community of this era was Sidney Burwell, dean of Harvard Medical School, who trained with Henry Christian and Paul Dudley White and served as the Samuel A. Levine Professor of Medicine at Peter Bent Brigham Hospital. With Eugene Eppinger, a cardiologist at Peter Bent Brigham Hospital and director of its internal medicine residency program for many years, Burwell prevailed upon the pioneering pediatric cardiac surgeon Robert Gross, of Boston Children's Hospital, to sample blood in patients with vascular shunts in order to quantitate shunt flow by measuring blood oxygen content and using the Fick principle. Gross was the first surgeon to ligate a patent ductus arteriosus and, thereby, had ready access to patients with shunts amenable to this analysis. This early work on intra-operative determination of shunt flow would influence the catheter-based methods later developed by Lewis Dexter.



Fig. 2. Portrait of Lewis Dexter (1910–1995)
(Brigham and Women's Hospital)

Dexter (Figure 2) first worked as a fellow with Weiss, studying the physiology and pathophysiology of preeclampsia and eclampsia. In fact, he and Weiss published a monograph on the topic in 1941,³ which served as the basis for his growing research interests in the neurohumoral factors that regulate vascular tone. After Weiss's death, Dexter spent time in Argentina with Nobel laureate Bernardo Houssay, studying renin biology and physiology. He returned from that experience to Weiss's laboratory, now run by Florence Haynes following Weiss's death, with a plan to develop a renin

assay in Boston and to apply it to preeclamptic and eclamptic patients in an effort to determine the role of renin in these hypertensive disorders. Doing so required catheterization of the renal vein as a blood sampling site, a technique Dexter had learned from Stanley Bradley at Boston University, in order to optimize the detectable concentration of renin in the vasculature.

Dexter next decided to turn his attention to renal vein renin measurements in hypertensive subjects. At the time, there were limited treatments available for severe hypertension, and these were largely surgical; thus, understanding the biochemical and molecular correlates or etiologies of hypertension was a field in its infancy. In the course of catheterizing one such hypertensive patient's renal veins, Dexter described an eventful procedure that established his pre-eminence in cardiac catheterization and congenital heart disease, here described in his own words:

I got to the renal vein, got some venous blood, and had time left over; I decided to wander around the heart which I understood to be above the diaphragm somewhere. Suddenly, this catheter came clear out in the lung field and I was sure I had perforated the heart. I didn't have any idea of what to do and, so I turned on the overhead lights and said, "Mr. _____, how are you?" He said, "I feel a hell of a lot better than you look." Then I was pretty sure that the catheter had perforated the heart and I wondered what would happen when I pulled it back. I hoped that it would seal itself off and so I closed my eyes and pulled the catheter back and nothing happened. And then it was all over and I put a little band-aid on his wound and went and looked up the anatomy of the chest and figured that I had gone into the pulmonary artery.⁴

Indeed, this is precisely where he had gone, and after consulting with Sidney Burwell, Dexter recognized the potential impact this innocent foray into anatomy north of the diaphragm would have on the minimally invasive assessment of cardiac hemodynamics and its application to understanding the pathophysiology of congenital heart disease. In addition to this important application of his initial serendipitous catheterization of the pulmonary artery, Dexter also recognized that he could obtain oxygenated blood from the "wedge" position in the pulmonary artery. This observation was also serendipitously made when he recognized that blood drawn back through the pulmonary catheter in one patient was bright red, leading to his exploring the more distal placement of the catheter in the

pulmonary capillary wedge position, pressures from which location he was also able to show were equivalent to left atrial pressure.

Yet another chapter in the illustrious history of Lewis Dexter's contributions is that of his fellow, Richard Gorlin. Gorlin trained in Dexter's cardiac catheterization laboratory in the 1950s, during which time he developed with his engineer father a hydraulic formula that could be used to estimate the cross-sectional area of a stenotic valve. This so-called Gorlin formula was published in a highly cited paper written by the Gorlins; notably absent as a coauthor of the paper was Dexter, who removed his name because he wished to ensure that this important contribution would be attributed to the Gorlins alone. Such overt academic generosity was another remarkable quality of this extraordinary member of our academic community.

By the early 1950s, biomedical research involving human subjects was becoming more formally institutionalized, particularly with the advent of clinical research centers. George Thorn, Weiss's successor as chief of medicine at Brigham, established a metabolic research unit on the F2 wing of the old hospital. Patients, most of whom had adrenal or hypertensive disorders, were admitted for weeks at a time to this clinical research unit. While the Nuremberg Code of research ethics had recently been established (1947), the metabolic group's investigators adhered to the code of ethics of the medical professions generally, and satisfied "democratic morality, ethics, and law."⁵ At this time, Renée Fox, a founder of the discipline of medical sociology, was conducting her first major study of academic medical social structures by observing the interactions among physician-scientists, among patients, and between physicians and patients on the metabolic unit between 1951 and 1954. Her observations culminated in the publication of her first book, *Experiment Perilous: Physicians and Patients Facing the Unknown*, in 1959.⁵ At this time in the history of "modern" experimental medicine, there were no formal guidelines for clinical trial design, institutional review boards as we now know them did not exist, and randomized controlled trials were not yet enshrined as the most acceptable standard. Patients with diseases of interest were selected for experimental treatments that were designed based on an educated review of the relevant literature, limited published experience of individual practitioners, and/or a logical extension of other pre-clinical experiments. Importantly, when the book was first released, Fox anonymized the institution at which she made these observations, especially given the frank and poignant dialogue that she reported among those she observed. Many years later, when the book was re-released in 1997, Fox revealed that this important study was

conducted at the Brigham.

Among the therapies that attracted Fox's observant eye was the treatment of refractory hypertension with bilateral adrenalectomy. As one might imagine, rendering a patient an-adrenal would certainly reduce blood pressure, and the expectation was that, with the rapidly evolving but nascent adrenal hormone pharmaceutical industry, adequate replacement of corticosteroids would minimize Addisonian risk. Importantly, however, mineralocorticoids were not discovered until 1955, and the quality control for the commercial synthesis of glucocorticoids was suboptimal. Outcomes were therefore abysmal. To quote Fox:

And one after another, the patients with severe advanced hypertensive vascular disease ... on whom total adrenalectomies were carried out died enigmatic deaths that seemed to be related to [the surgery] as well as their grave illnesses. The added suffering and risk to which these path-making clinical trials often subjected patient-subjects, and their dismal, death-ridden results triggered dismayed comments and vociferous criticism throughout the hospital. Eventually, a quietly declared clinical moratorium was called on the performance [of this procedure].⁶

Meanwhile, across town at Boston University, Robert Wilkins, another member of the 1936–1937 Thorndike Memorial Laboratory staff, was developing pharmacotherapeutic strategies for the treatment of hypertension. As early as 1952, he pointed out that “no case of hypertension with normal renal function is accepted as impossible to treat medically until proven so.” At the time, physicians widely believed that reduction of blood pressure in hypertensives might impair tissue perfusion. Wilkins felt otherwise, and first demonstrated the effectiveness of reserpine (derived from the Indian plant *Rauwolfia serpentina*) and thiazide diuretics (chlorothiazide) as antihypertensive drugs.⁷ Furthermore, he established step-care therapy for hypertension, in which different classes of antihypertensive agents are added to the regimen of a given patient until blood pressure control is achieved. Wilkins was awarded the Lasker Award in 1958 for these important contributions.

Jay Coffman, an early proponent of the field of vascular medicine in the US, was a trainee of Wilkins. On the faculty of Boston University for many years until his death in 2004, Coffman studied blood flow in reactive hyperemia, was the first to compare skin circulation in normal subjects and

in patients with Raynaud's disease, and studied blood flow in normal exercising and ischemic limb musculature. In addition, Coffman trained many disciples who have espoused the importance and uniqueness of the field of vascular medicine, included among whom is Mark Creager, current president of the American Heart Association.

Lastly, I would like to recognize Joseph Vita as a more recent contributor to the field. Vita helped establish the concept of endothelial function and dysfunction and its assessment *in vivo*. After training with Andrew Selwyn and Peter Ganz at Brigham and Women's Hospital, Vita studied perturbations in coronary and peripheral endothelial and vasomotor function in atherothrombosis, first at West Roxbury VA Medical Center, and then at Boston University, where he worked for over 20 years until his untimely death in 2014.

Clearly the pantheon of Boston vascular physiology and medicine is an extraordinary one filled with many important contributions. As the pedigree in Figure 3 demonstrates, excellence in academic medicine "breeds true," each generation improving the discipline over the preceding generation and each benefiting from heterosis, or hybrid vigor, as result of the contributions of others who enter the arena from different academic backgrounds. Importantly, this tradition of excellence continues to this day in the field of vascular biology and medicine in Boston, about which we members of that community can be proud and which we all aspire to maintain.

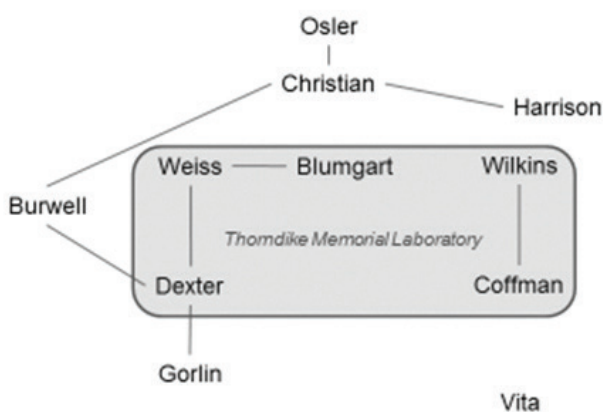


Fig. 3. Boston vascular pedigree.

Acknowledgement

I would like to thank Scott Podolsky for his helpful comments and recommendations in dissecting this brief history.

Notes

1. Blumgart, H. and Yens, O.C.: Studies on the Velocity of Blood Flow. I. The Method Utilized. *J Clin Invest* 4 (1926): 1–13.
2. Fiks, A.P. and Buelow, P.A.: *Self-Experimenters: Sources for Study*. Santa Barbara, CA: ABC-CLIO, 2003. p. 26.
3. Dexter, L. and Weiss, S.: *Preeclamptic and Eclamptic Toxemia of Pregnancy*. Baltimore: Williams and Wilkins, 1941.
4. Dalen, J.E., Dexter, L., Ockene, I.S., Paraskos, J.A., Rapaport, E., Smith, T.W., Stein, P.D., and Alpert, J.S.: Faculty of Medicine Memorial Minute: Lewis Dexter. *The Harvard University Gazette*, September 24, 1998, <http://news.harvard.edu/gazette/1998/09.24/FacultyofMedici.html>.
5. Fox, R.C.: *Experiment Perilous: Physicians and Patients Facing the Unknown*. New York: The Free Press, 1959. p. 46–47.
6. *Ibid.*, p. 267–268.
7. Greene, J.A. Releasing the flood waters: Diuril and the reshaping of hypertension. *Bull Hist Med* 79 (2005): 749–794.

Chapter 6

WHY JUNIOR AND SENIOR PHYSICIAN-SCIENTISTS AND ALL MEMBERS OF THE INTERURBAN CLINICAL CLUB SHOULD EMBRACE CLUB MEETINGS

Cynthia L. Sears

President, 2007–2008

For students, residents, fellows, and faculty alike at medical schools in the cities of Boston, New Haven, New York City, Philadelphia, and Baltimore, the Interurban Clinical Club provides access to a unique academic experience, one in which more individuals beyond the ICC members should choose to participate.

My experience with the ICC began when, as a junior faculty member, I was asked to present our work to this august group of physician-scientists. It was a terrific experience. I was struck by, and so clearly remember, the keen interest expressed by the diverse audience through their insightful, probing questions as well as their collegiality and warmth when they spoke with me after my talk. To my surprise, Carol Johns urged me to attend the dinner that evening as her guest, a suggestion which other members around her chimed in to support. Any sense of academic hierarchy dissipated at dinner as I met and spoke with senior and notable members of the Johns Hopkins University faculty, including Richard Johns and Victor McKusick. My first experience with the ICC was truly delightful.

Some years later, in 2005, I joined the ICC as a member, and I served as president in 2007–2008. Over the years I have further experienced the inspiring science presented at meetings in each city. For a single day twice a year, the ICC allows us to be immersed in outstanding, thought-provoking science that is wide-ranging in topic but always impactful, as well as a renewed spirit of collegiality. These talks broaden each participant's scientific outlook and spur cross-disciplinary thinking, which is increasingly key to advancing the translation of science to our patients. These meetings simply represent the best medical science occurring in each city.

For our junior colleagues — students, residents, and fellows — I believe these meetings provide not only a day of stimulating science but also a chance to hear about medical advances in the making and to meet those likely to play a role in bringing these discoveries to the bedside. The club's history makes for apt reading, as it reveals a lineage of physician-investigators since Sir William Osler who have played critical roles in the evolution and practice of medical science. Thus, the ICC represents medical history in the making. Only a few medical schools in a handful of cities on the Eastern Seaboard are fortunate enough to constitute the ICC. Every physician-scientist in these cities should attend and participate in these rich scientific and collegial meetings.

Chapter 7

THE INTERURBAN CLINICAL CLUB WEBSITE



Wafik S. El-Deiry

President, 2013–2014

When I became an active member of the Interurban Clinical Club in 2005, my division chief from the University of Pennsylvania, Steve Emerson, was then secretary-treasurer and Koneti Rao, at Temple University, was president. At my first meeting, which was held at Yale University, I sat in the auditorium next to Alan Gewirtz, a colleague from the University of Pennsylvania, and was impressed by the engagement Alan showed by asking insightful questions. Alan, who is also a pilot, was interested in the field of antisense therapeutics for leukemia and had moved to Penn in the early 1990s from Thomas Jefferson University to pursue clinical translation. At that meeting I was also impressed by the incredible quality of the science presented, especially in the field of immunology (which is not my field), and the fact that the dean at Yale gave a scientific talk on circadian rhythms. Over the last few years, deans from Hopkins, Penn, Jefferson, Mount Sinai, and Harvard have spoken at ICC meetings, but usually these presentations have focused more on the state of academic medicine or the management of complex healthcare systems. Another thing that made an impression on me at my first meeting was overhearing Rao express doubt about whether the ICC would survive. From my perspective at the time, it was a great honor to have just become a member of this society, and I honestly could not relate to his concerns. Who wouldn't want to be a member of such a club — to spend a day twice each year listening to an eclectic collection of science that is arguably among the best in the world and is presented by such luminaries? In our busy, highly specialized lives, we often don't have a chance to learn about the latest and most exciting research from other disciplines, in molecular medicine and beyond. In this way, the content of these meetings for me is very reminiscent of meetings at Howard Hughes Medical Institute that I was fortunate to participate in from 1995 to 2004.

In 2005, having just joined the ICC, I immediately noticed that there was no web presence. I thought it was curious that the programs had maintained a specific format with lots of useful content over the years that was

handed down. I thought, who was I to go against the traditions of such an established and historic society, to even suggest that an online presence might in some way help the ICC gain more visibility? Such a resource might also serve as a repository of information for members or others. Certainly other societies such as the American Society for Clinical Investigation, which I joined in 1999 (the same year I was promoted to associate professor with tenure at Penn), had websites at the time. However, my first meeting experience left me with the sense that this would be a radical idea for a historic society and that there would be some risk in broaching the topic. I had previously attempted to approach historic organizations with new ideas and been told “that’s just not something we do” or “we haven’t done that in the past.” Such attempts in and of themselves are worthwhile, because if we are motivated and creative we will find ways of accomplishing our goals, and often the results are much better in the end. I mentioned the idea of an ICC website to Rao and Emerson after the meeting, because I thought they would not immediately dismiss it as something that could not be done. They were receptive to the idea and gave their permission for me to research and start developing a website. There was no discussion of financial or administrative resources to support the endeavor, but I was eager to work on the project, which I felt would provide a chance to learn about Osler and to be involved in creating a framework for what I thought was an exciting project.

I had started the biotech company Oncoceutics in 2004 to develop anticancer drugs, and this situation was similar in terms of needing visibility yet having no resources. I had created a very simple website on my own for that company and so had some knowledge that I could apply. I purchased the domain names of *interurbanclinicalclub.com* and *interurbanclinicalclub.org* and started drafting the website. I determined that the two domain names could be linked to each other and began developing content for each site. The constraint was that each page was limited as to the number of components (including links) that could be added, but it was possible to include a photo of Sir William Osler. I decided to include links to information about Osler’s life while he was in Toronto and other freely available online resources that addressed his life, accomplishments, and impact on the medical field. Some introduction to the club’s history was needed, and for this I found Harvey’s 3rd volume on the ICC particularly useful.

The color scheme for the website is dark and renders a sense of mystery, as does the ICC to those who know nothing about it. Because the ICC was founded in 1905, I thought a black and white color scheme made the

most sense. The original site included a description of the ICC, followed by names of the different categories of members and information needed to nominate new members. It also included names of all Osler Award recipients. This award had been first presented only 15 years previously, so I was able to locate information on all recipients; however, I had to decide which information to include about the awardees that would be useful to future visitors to the site. Years later, at the 202nd meeting in Boston on November 5, 2010, I met Bill Chin, who had first suggested the idea for the award, and showed him where the information about the awardees has since been archived. Finally, the website included dates and locations of upcoming meetings. This information is generally available 3–4 years in advance, as the meetings occur on a rotating cycle among the five member cities.

I was still developing the website when I became the councilor for the Philadelphia chapter in March 2007. For the 197th meeting, in April 2008, I put together a handout to update meeting attendees on the status of the website project.

There was some discussion in 2007–2008 about whether the website should be based at one of the participating institutions, for example at Johns Hopkins University, where Osler was when he started the club. I argued that the site should remain autonomous of any one institution and volunteered to continue to maintain and develop it to the best of my abilities. This was acceptable to the ICC membership, but there was some discussion that I should not have to pay my own money for the website. I agreed to be reimbursed by the ICC for any fees pertaining to renewal of the website domain name.

When I organized the 199th meeting of the ICC (held April 3, 2009, in Philadelphia), I decided to include the scientific program on the website. I also chose to include programs from a few previous meetings. I was able to track down electronic versions of a few meetings that had been held at New York and Boston, by working with city councilors Craig Basson and Megan Sykes. I added programs from the meetings they had organized to an archive page on the website.

The format of the website has remained stable over the last several years, although a number of issues have surfaced that the ICC will need to address in the future. I agreed to continue to archive data and maintain the website, especially after completing my term as secretary-treasurer in 2013. The role of secretary-treasurer was a full plate as it was, but I think that

maintaining the site will be helpful to the ICC.

I also discussed with John Forrest plans to renovate and modernize the website to be more consistent with that of other societies. For this project it is obvious what needs to be done. Our goals are ambitious, and reality presents limitations in terms of time, money, expertise, personal commitment, and long-term direction.

Upgrading the website into a more modern configuration will provide an opportunity to add content, including individual pages for active and emeritus members. As the initiator of the website, I of course wish this could have been done by now, but it is not so simple. It is possible to make a career out of developing and maintaining content for websites, and the ICC is a slim organization that has survived for nearly 110 years with little administrative or bureaucratic structure. It is a meeting organized by physicians and physician-scientists for physicians and physician-scientists. In this regard, as a nonprofit organization it remains highly focused on its core purpose. I believe it is possible to move forward within this framework and to update and modernize the website while maintaining autonomy from the host institutions and minimizing cost and administrative burden. As I write this chapter in 2013, I am serving a term as president of the ICC (2013–2014) and will follow through on the above-stated goals.

Interurban Clinical Club



Founder: Sir William Osler

Web Site:
<http://interurbanclinicalclub.org/>

Interurban Clinical Club

FOUNDER - SIR WILLIAM OSLER



Sir William Osler

Excerpt from "The Interurban Clinical Club 1900-1904: A Record of Achievement" by G. MacGee Harvey, M.D., M.D., F.R.C.

...vision Osler described the Interurban Clinical Club in 1903 for the purpose of exchanging ideas and information among medical teachers in some of the leading English medical schools. Since then, before a year had elapsed, there had been a number of meetings in London, New York, Boston and Providence, a few more after the organization of the Club. ...

"Osler recognized that such a club organized in America would be a way to advance medicine in America in a unique way. ...

Ward (1875); EC Janssen (1878); B. Abrahams (1878); J. Borden; H. C. B. ...

FOUNDER - SIR WILLIAM OSLER
ECCA (1870); G. J. ...

MEMBER STATES
THE SIR WILLIAM OSLER YOUNG INVESTIGATOR AWARD

NEW YORK - Drs. Craig T. ...

MEMBER STATES
THE SIR WILLIAM OSLER YOUNG INVESTIGATOR AWARD

Interurban Clinical Club

FOUNDER - Sir William Osler

OFFICERS OF THE INTERURBAN CLINICAL CLUB (April 2008)

President:
Cynthia L. Sears
Secretary/Treasurer:
Richard W. Mitsis

Councillors:
Craig Basson
Lloyd Castley
Wafik S. El-Deiry
Nyam I. Levitsky
Megan Sykes

OFFICERS OF THE INTERURBAN CLINICAL CLUB (November 2007)

President:
Cynthia L. Sears
Secretary/Treasurer:
Richard W. Mitsis

Councillors:
Craig Basson
Lloyd Castley
Wafik S. El-Deiry
Nyam I. Levitsky
David V. Scadden

OFFICERS OF THE INTERURBAN CLINICAL CLUB (March 2007)

President:
Stephen G. Emerson
Secretary/Treasurer:
Richard W. Mitsis

Councillors:
Craig Basson
Lloyd Castley
Wafik S. El-Deiry
Nyam I. Levitsky
David V. Scadden

OFFICERS OF THE INTERURBAN CLINICAL CLUB (November 2004)

President:
Stephen G. Emerson
Secretary/Treasurer:
Richard W. Mitsis

Councillors:
Craig Basson
Lloyd Castley
Barry Goldstein
Nyam I. Levitsky
David V. Scadden

OFFICERS OF THE INTERURBAN CLINICAL CLUB (April 2004)

President:
Jeffrey Bender
Secretary/Treasurer:
Stephen G. Emerson

Councillors:
Barry Goldstein
Richard Mitsis
Nyam I. Levitsky
Paul W. Mobil
David V. Scadden

OFFICERS OF THE INTERURBAN CLINICAL CLUB (November 2005)

President:
Jeffrey Bender
Secretary/Treasurer:
Stephen G. Emerson

Councillors:
Barry Goldstein
Richard Mitsis
Nyam I. Levitsky
Paul W. Mobil
David V. Scadden

OFFICERS OF THE INTERURBAN CLINICAL CLUB (April 2005)

President:
A. Koneti Rao
Secretary/Treasurer:
Stephen G. Emerson

Councillors:
Barry Goldstein
Susan McMichael
Paul W. Mobil
David V. Scadden
Edward T. Skolnik

THE SIR WILLIAM OSLER YOUNG INVESTIGATOR AWARD

- Scott Armstrong, M.D., Ph.D., Dana-Farber Cancer Institute, Harvard University (first recipient at 1978 ICC Meeting, Boston 4-4-88) "Genetic and Epigenetic Programs in Leukemia Stem Cells"
 - Arya Mook, M.D., Yale University (25th recipient at 1988 ICC Meeting, New Haven 11-3-87) "Metabolic Phenotype Linked by a Single Gene Mutation"
 - Lynn Bevan, M.D., Ph.D., West Coast Medical College (19th recipient at 1988 ICC Meeting, New York 3-30-87) "Mating Faces: How Males Meet in Drosophila Males of Conflicting Faces"
 - Volker H. Haese, M.D., University of Pennsylvania School of Medicine (28th recipient at 1988 ICC Meeting, Philadelphia 11-3-88) "The VHL/HPH Oxygen Sensing Pathway in Cancer"
 - Vitor Veloso, M.D., Ph.D., Johns Hopkins University (17th recipient at 1988 ICC Meeting, Baltimore 4-7-88) "Genetic Analysis of Signaling Pathways in Human Cancer"
 - Hanna Mook, M.D., Ph.D., Massachusetts General Hospital (16th recipient at 1988 ICC Meeting, Boston 11-3-88) "The Transcriptional Regulation of Neuroepithelial Stem Cells and Leukemia"
 - Polly J. Lee, M.D., Yale University School of Medicine (20th recipient at 1988 ICC Meeting, New Haven 4-4-88) "The Heme Oxygenase-1 System: A Cytoprotective Response to Acute Lung Injury"
 - Steven Marx, M.D., Columbia University (14th recipient at 1988 ICC Meeting, New York 11-3-84) "Regulation of the Calcium-dependent 8k Channel by a Macromolecular Complex: Implications for Cardiovascular Disease"
 - J Eric Rouss, M.D., University of Pennsylvania School of Medicine (15th recipient at 1988 ICC Meeting, Philadelphia 4-6-88) "Therapeutic Potential of Embryonic Genes in Human Hemoglobinopathies and Thalassemias"
- MEMBERS**
- BALTIMORE**
 - BOSTON**
 - NEW HAVEN**
 - NEW YORK**
 - PHILADELPHIA**
- John Lynch, M.D., Johns Hopkins University (17th recipient at 1988 ICC Meeting, Baltimore 11-3-88) "New Tricks for Old Dogs: Sites, Codes, Regulation of Development & Physiology by Parathyroid Hormone-Related Protein"
 - Stanley Falk, M.D., West Medical College of Cornell University (26th recipient at 1988 ICC Meeting, New York 4-5-87) "Recruitment of Stem Cells for Tissue Vasculature and Organogenesis"
 - Jonathan Epstein, M.D., University of Pennsylvania (28th recipient at 1988 ICC Meeting, Philadelphia 11-3-87) "Resolving a Dream Team: Mouse Models of Complicated Heart Disease"
 - Greg Carlson, M.D., The Johns Hopkins University (7th recipient at 1988 ICC Meeting, Baltimore 4-4-88) "Myocardial Pericytes"
 - Rayford R. Lowell, M.D., Ph.D., Harvard Medical School/BWHMC (26th recipient at 1988 ICC Meeting, Boston 11-3-88) "Mitochondrial Uncoupling Proteins 1 and 2: Regulation of Mitochondrial Energy Metabolism in Health and Disease"
 - Linda N. Rosenblatt, M.D., Yale University School of Medicine (25th recipient at 1988 ICC Meeting, New Haven 4-1-88) "Of Mice and Men: The Pathogenesis of Lister Disease"
 - Laurie Rowlett, M.D., Albert Einstein College of Medicine (23rd recipient at 1988 ICC Meeting, New York 11-3-87) "Nutrient Sensing and Insulin Action"

- And K. Rowley, M.D., University of Pennsylvania (2nd recipient at 1978 ICC Meeting, Philadelphia 4-3-78) "Circadian Rhythms: Epithelial Cell Biology and Genetics"
- Anthony Rosen, M.D., Johns Hopkins University (2nd recipient at 1978 ICC Meeting, Baltimore 11-4-78) "Apoptosis and Autophagy"
- Michael J. Mendicino, M.D., Tufts University (1st recipient at 1978 ICC Meeting, Boston 4-3-78) "Cyclic GMP Signaling in Vascular Biology"

INTERURBAN CLINICAL CLUB MEETINGS:

- April 2, 2010 (201st meeting) New Haven
- November 6, 2009 (200th meeting) Baltimore
- April 3, 2009 (199th meeting) Philadelphia
- November 7, 2008 (198th meeting) New York
- April 4, 2008 (197th meeting) Boston
- November 2, 2007 (196th meeting) New Haven
- March 30, 2007 (195th meeting) New York
- November 3, 2006 (194th meeting) Philadelphia
- April 7, 2006 (193rd meeting) Baltimore
- November 4, 2005 (192nd meeting) Boston
- April 1, 2005 (191st meeting) Yale University School of Medicine, 100th Anniversary of the ICC
- November 5, 2004 (190th meeting) New York University School of Medicine

- ABOUT SIR WILLIAM OSLER (1849-1919)**
- OSLER IN THE CANADIAN MEDICAL HALL OF FAME**
- OSLER - VOYAGES IN MEDICAL HISTORY**
- OSLER - JOURNALS FROM HIS BEQUEST TEACHINGS AND WRITINGS**
- ABOUT THE INTERURBAN CLINICAL CLUB**

Chapter 8

THE SIR
WILLIAM OSLER YOUNG
INVESTIGATOR AWARD



William W. Chin

President, 1997–1998

In 1998 the Interurban Clinical Club initiated the Sir William Osler Young Investigator Award to recognize “outstanding research achievement by a young clinician-scientist in the tradition of Sir William Osler” and to honor the founder of the ICC. As president of the ICC, I had the privilege of proposing the award, which the council approved, in keeping with the mission of the ICC and the spirit embodied by the work of Osler, who noted, “He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all.”

This award is bestowed upon a physician-scientist under of the age of 45, often a junior faculty member at an institution in one of the five ICC cities who has performed outstanding basic and/or clinical investigation in the tradition of Osler. It is awarded at each meeting by the host city, the recipient chosen by its members in rotation. Each award recipient is asked to give a presentation and participate in the meeting and dinner and is provided with a stipend and award certificate. This opportunity provides increased visibility of ICC among young investigators, and vice versa.

The award was first bestowed upon Michael E. Mendelsohn at the 177th meeting in Boston. Over the ensuing 17 years, 36 Sir William Osler Young Investigator Awards have been presented. Many of the awardees have gone on to develop illustrious careers in investigative medicine, and several have become active ICC members.

*Sir William Osler Young Investigator
Award Recipients, 1998–2015*

177th meeting, Boston (April 3, 1998)

Michael E. Mendelsohn, MD, Tufts University School of Medicine:
“Cyclic GMP Signaling in Vascular Biology”

178th meeting, Baltimore (November 6, 1998)

Antony Rosen, MD, Johns Hopkins University School of Medicine:
“Apoptosis and Autoimmunity”

179th meeting, Philadelphia (April 9, 1999)

Anil K. Rustgi, MD, University of Pennsylvania School of Medicine:
“Oral-Esophageal Epithelial Cell Biology and Genetics”

180th meeting, New York (November 5, 1999)

Luciano Rossetti, MD, Albert Einstein College of Medicine:
“Nutrient Sensing and Insulin Action”

181st meeting, New Haven (April 7, 2000)

Linda K. Bockenstedt, MD, Yale University School of Medicine:
“Of Mice and Men: The Pathogenesis of Lyme Disease”

182nd meeting, Boston (November 3, 2000)

Bradford B. Lowell, MD, PhD, Harvard Medical School, Beth Israel
Deaconess Medical Center: “Mitochondrial Uncoupling Proteins 2 and 3:
Regulators of Intercellular Energy Metabolism in Health and Disease”

183rd meeting, Baltimore (April 6, 2001)

Greg Germino, MD, Johns Hopkins University School of Medicine:
“Polyfunctional Polycystin-1”

184th meeting, Philadelphia (November 2, 2001)

Jonathan Epstein, MD, University of Pennsylvania School of Medicine:
“Fashioning a Broken Heart: Mouse Models of Congenital Heart Disease”

185th meeting, New York (April 5, 2002)

Shahin Rafii, MD, Weill Medical College, Cornell University:
“Recruitment of Stem Cells for Tissue Vascularization and Organogenesis”

186th meeting, New Haven (November 1, 2002)

John Wysolmerski, MD, Yale University School of Medicine:
“Regulation of Mammary Gland Development and Physiology by
Parathyroid Hormone-Related Protein”

187th meeting, Boston (April 4, 2003)

Lloyd Paul Aiello, MD, PhD, Harvard Medical School:
“VEGF and Diabetic Retinopathy”

188th meeting, Baltimore (November 7, 2003)

Charles J. Lowenstein, MD, Johns Hopkins University School of
Medicine: “New Tricks for Old Dogs: Nitric Oxide Regulation of
Exocytosis”

189th meeting, Philadelphia (April 2, 2004)

J. Eric Russell, MD, University of Pennsylvania School of Medicine:
“Therapeutic Potential of Embryonic Globins in Human
Hemoglobinopathies and Thalassemias”

190th meeting, New York (November 2, 2004)

Steven Marx, MD, Columbia University School of Medicine:
“Regulation of the Calcium-Dependent BK Channel by a Macromolecular
Complex: Implications for Cardiovascular Diseases”

191st meeting, New Haven (April 1, 2005)

Patty J. Lee, MD, Yale University School of Medicine: “The Heme
Oxygenase-1 System: A Cytoprotective Response to Acute Lung Injury”

192nd meeting, Boston (November 4, 2005)

Hanno Hock, MD, PhD, Massachusetts General Hospital: “The
Transcriptional Regulation of Hematopoietic Stem Cells and Leukemia”

193rd meeting, Baltimore (April 7, 2006)

Victor Velculescu, MD, PhD, Johns Hopkins University School of
Medicine: “Genetic Analysis of Signaling Pathways in Human Cancer”

194th meeting, Philadelphia (November 3, 2006)

Volker H. Haase, MD, University of Pennsylvania School of Medicine:
“The VHL/HIF Oxygen Sensing Pathway in Disease”

195th meeting, New York (March 30, 2007)

Licia Selleri, MD, PhD, Weill Cornell Medical College:

“Making Faces: Pbx Mutant Mice as Genetic Models of Cleft Lip and Palate”

196th meeting, New Haven (November 2, 2007)

Arya Mani, MD, Yale University School of Medicine: “Metabolic Phenotypes Linked by a Single Gene Mutation”

197th meeting, Boston (April 4, 2008)

Scott Armstrong, MD, PhD, Dana Farber Cancer Institute, Harvard University: “Genetic and Epigenetic Programs in Leukemia Stem Cells”

198th meeting, New York (November 14, 2008)

Jonathan W. Weinsaft, MD, Weill Cornell Medical College:

“Delayed Enhancement MRI for Left Atrial Appendage Thrombus Tissue Characterization”

199th meeting, Philadelphia (April 3, 2009)

Rebecca Wells, MD, University of Pennsylvania School of Medicine:

“Soluble and Mechanical Factors in Liver Fibrosis”

200th meeting, Baltimore (November 6, 2009)

Andrea Cox, MD, PhD, Johns Hopkins University School of Medicine:

“Reversing T Cell Inhibition in Chronic Viral Infection: From Bench to Bedside . . . and Back”

201st meeting, New Haven (March 26, 2010)

Clara Abraham, MD, Yale University School of Medicine: “Human

IL-23/Th17 Pathway Functions”

202nd meeting, Boston (November 5, 2010)

Dan Hung Barouch, MD, Harvard University School of Medicine:

“Novel Approaches to Vaccine Development”

203^d meeting, New York (April 1, 2011)

Ross Levine, MD, Memorial Sloan Kettering Cancer Center, Weill Cornell

Medical College: “Genetics and Therapy of Myeloid Malignancies”

204th meeting, Philadelphia (October 28, 2011)

Jordan Orange, MD, PhD, Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine: "The Human Immunobiology of Natural Killer Cells: Insights from and Opportunities for Rare Pediatric Disease"

205th meeting, Baltimore (March 30, 2012)

Andrew Mammen, MD, PhD, Johns Hopkins University School of Medicine: "Statin-Associated Autoimmune Myopathy"

206th meeting, New Haven (October 26, 2012)

Daniel Goldstein, MD, Yale University School of Medicine: "Novel Triggers of Inflammation after Cardiac Transplantation"

207th meeting, Boston (April 5, 2013)

Kimberly Stegmaier, MD, Harvard Medical School: "Integrating Genomic Approaches for Cancer Target and Drug Discovery"

208th meeting, New York (November 1, 2013)

Renier J. Brentjens, MD, PhD, Memorial Sloan Kettering Cancer Center: "Immunotherapy of Lymphoid Malignancies"

209th meeting, Philadelphia (April 4, 2014)

Gregory L. Beatty, MD, PhD, University of Pennsylvania School of Medicine: "Targeting Macrophages for Cancer Immunotherapy"

210th meeting, Baltimore (November 7, 2014)

Hans T. Bjornsson, MD, PhD, Johns Hopkins University School of Medicine: "Kabuki Syndrome: A Potentially Treatable Cause of Intellectual Disability"

211th meeting, New Haven (April 10, 2015)

Stephanie Halene, MD, Yale University School of Medicine: "Molecular Mechanisms of MDS and the Development of a Xenotransplantation Model"

212th meeting, Boston (November 13, 2015)

Duane Wesemann, MD, PhD, Harvard Medical School: "Microbes Shape the Primary Ig Repertoire"

Chapter 9

PROGRAMS OF RECENT INTERURBAN CLINICAL CLUB SCIENTIFIC MEETINGS



The overarching theme of the Interurban Clinical Club scientific meetings is “Advances in Medicine: An Ongoing Celebration of the Legacy of Sir William Osler”

212th Meeting — November 13, 2015

Brigham and Women’s Hospital, Harvard Medical School
Ballard Room, Francis A. Countway Library of Medicine, 10 Shattuck Street, Boston, MA 02115

- | | |
|---------|---|
| 7:30 am | Continental Breakfast |
| 8:00 am | Welcome Remarks and Opening
Bruce Levy, MD — Parker B. Francis Professor of
Medicine, Harvard Medical School/Chief, Division of
Pulmonary and Critical Care Medicine, Brigham and
Women’s Hospital |
| 8:15 am | “Kidney Disease in People of Recent African Ancestry”
Martin Pollak, MD — Professor of Medicine, Harvard
Medical School/Chief of Nephrology, Beth Israel
Deaconess Medical Center |
| 8:45 am | “Preeclampsia: Diagnosis to Therapy”
Anath Karumanchi, MD — Associate Professor of
Medicine, Harvard Medical School, Beth Israel
Deaconess Medical Center |
| 9:15 am | “Mutations and Mechanisms for Human Heart Failure”
Christine (Krocket) Seidman, MD — T.W. Smith
Professor of Medicine and Genetics, Harvard Medical
School/Director, Brigham and Women’s Cardiovascular
Genetics Center |
| 9:45 am | Break |

- 10:00 am “Resolvins & Novel Mediators in Resolution of Inflammation : Human Functional Metabolomics”
Charles N. Serhan, PhD, DSc (hc) — Simon Gelman Professor of Anaesthesia, Harvard Medical School/Director, Center for Experimental Therapeutics and Reperfusion Injury/Professor, Department of Oral Medicine, Infection and Immunity, Department of Biochemistry and Molecular Pharmacology, Harvard Medical School
- 10:30 am Sir William Osler Young Investigator Award: “Microbes Shape the Primary Ig Repertoire”
Duane Wesemann, MD, PhD — Assistant Professor of Medicine, Harvard Medical School, Division of Rheumatology, Immunology and Allergy, Brigham and Women’s Hospital
- 11:00 am “Inner Ear Function, Dysfunction and the Prospects for Gene Therapy”
Jeffrey Holt, PhD — Associate Professor of Otolaryngology, Harvard Medical School
- 11:30 am “The Blood Vessel and Its Disorders: An Early History of Vascular Biology and Medicine in Boston”
Joseph Loscalzo, MD, PhD — Hersey Professor of the Theory and Practice of Medicine, Harvard Medical School/Chairman, Department of Medicine/Physician-in-Chief, Brigham and Women’s Hospital
- 12:00 pm Lunch (members only)
Speaker: Jeffrey Flier, MD — Caroline Shields Walker Professor of Medicine, Harvard Medical School/Dean of the Faculty of Medicine, Harvard Medical School
- 12:45 pm Guided Tour (meet in Library Ware Room)
Topic: “From the Center for the History of Medicine Archives: A Lasting Legacy of ‘Medical Improvement,’”
by Scott Podolsky, MD — Associate Professor of Global Health and Social Medicine, Harvard Medical School/Director, Center for the History of Medicine

- 1:30 pm “On the Right Side of History — A Story from the Heart”
Calum Macrae, MD — Professor of Medicine, Harvard Medical School, Chief, Division of Cardiovascular Medicine, Brigham and Women’s Hospital
- 2:00 pm “From Genome Biology to Cancer Precision Medicine”
Levi Garraway, MD, PhD — Associate Professor of Medicine, Harvard Medical School/Co-Leader, Cancer Genetics, Dana-Farber Cancer Institute/Inaugural Director, Joint Center for Cancer Precision Medicine (CCPM) at the Dana-Farber Cancer Institute, Brigham and Women’s Hospital, and the Broad Institute
- 2:30 pm “An Epigenomic and Transcriptional Basis for Insulin Resistance” Evan Rosen, MD — Professor of Medicine, Harvard Medical School, Division of Endocrinology, Diabetes and Metabolism, Beth Israel Deaconess Medical Center/Institute Member, Broad Institute
- 3:00 pm Break
- 3:15 pm MD-PhD Student Talk: “Generation of Patient-Specific Lung Alveolar Epithelium from Pluripotent Stem Cells”
Anjali Jacob — Boston University School of Medicine
- 3:30 pm MD-PhD Student Talk: “Halofuginone: A Story Of How Target Identification of an Ancient Chinese Medicine and Multi-Step Evolution Informs Malaria Drug Discovery”
Jon Herman — Harvard Medical School
- 3:45 pm MD-PhD Student Talk: “Sterile Particles: Double-Edged Swords of Inflammatory Cell Death, in the Air and in Your Blood”Gregory Orłowski — University of Massachusetts Medical School
- 4:00 pm Business Meeting (members only)
- 6:00 pm Cocktail Reception and Black Tie Dinner
(Held at the Harvard Club, Massachusetts Room, 374 Commonwealth Avenue)

- 8:00 pm Keynote Address
César A. Hidalgo, PhD — Asahi Broadcast Corporation
Career Development Professor and Assistant Professor,
MIT Media Laboratory/Faculty Associate, Harvard
University Center for International Development
- 9:00 pm Conclusion

211th Meeting — April 10, 2015

Yale University School of Medicine

Medical Historical Library, 333 Cedar Street, New Haven, CT 06520

- 8:00 am Continental Breakfast
- 9:00 am Welcoming Remarks and Opening
Elizabeth Jonas, MD — *Associate Professor of Medicine
and of Neurobiology, Yale School of Medicine*
- 9:15 am “Integrin-Induced Effects on RNA Stability in Angiogenesis and Neuroinflammation” Jeffrey R. Bender, MD —
*Robert I. Levy Professor of Cardiology and of
Immunobiology/Director, Cardiovascular Research
Center/Associate Chief, Cardiovascular Medicine,
Yale School of Medicine*
- 9:45 am “Energy Sensor and Cell Survival in the Heart”
Lawrence Young, MD — *Professor of Medicine
(Cardiology) and of Cellular and Molecular Physiology/
Vice-Chairman, Department of Medicine, Yale School
of Medicine*
- 10:15 am Sir William Osler Young Investigator Award: “Molecular
Mechanisms of MDS and the Development of a
Xenotransplantation Model”
Stephanie Halene, MD — *Assistant Professor
(Hematology), Department of Internal Medicine
and Yale Cancer Center, Yale School of Medicine*
- 10:45 am Break
- 11:00 am “The Glycolytic Metabolon Meets Local Energy
Demands In Vivo at Neuronal Synapses”
Daniel Alfonso Colón-Ramos, PhD — *Associate
Professor of Cell Biology, Yale School of Medicine*

- 11:30 am “Getting Calcium into Milk: Unexpected Lessons for Breast Cancer”
John J. Wysolmerski, MD — *Professor of Medicine (Endocrinology), Yale School of Medicine*
- 12:00 pm “Innate Immune Recognition of Pathogens: From Mice to Men”
Barbara I. Kazmierczak PhD, MD — *Associate Professor of Medicine (Infectious Diseases) and of Microbial Pathogenesis/Director, MD-PhD Program, Yale School of Medicine*
- 12:30 pm “Child Abuse and Epigenetic Mechanisms of Disease Risk” Joan Kaufman, PhD — *Associate Professor of Psychiatry/Director, Child and Adolescent Research and Education (CARE) Program/Director, Child Welfare Unit, Zigler Center for Child Development and Social Policy*
- 1:00 pm Lunch (*members only*) (held in Giarman Room, Yale School of Medicine, 333 Cedar Street)
Speaker: “Academic Health Centers 2015,” by Robert J. Alpern, MD — *Ensign Professor of Medicine (Nephrology)/Dean, Yale School of Medicine*
- 2:00 pm Tour of the Yale Historical Library Collection
- 3:00 pm “Extended Release Guanfacine (Intuniv™) For the Treatment of Higher Cognitive Disorders: Successful Translation from Monkey to Man”
Amy F. T. Arnsten, PhD — *Professor of Neurobiology and of Psychology/Member, Kavli Institute of Neuroscience, Yale University*
- 3:30 pm MD-PhD Student Talk: “Genes and Mechanisms of Congenital Heart Disease: Converging Pathways in Developmental Disorders”
Samir Zaidi — *Yale School of Medicine*
- 3:45 pm MD-PhD Student Talk: “Characterizing the Genomic Architecture and Molecular Mechanisms Driving the Formation of Non-*NF2* Meningiomas”
Victoria E. Clark — *Yale School of Medicine*
- 4:00 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception and Black Tie Dinner
(Held at the Union League Café, 1032 Chapel Street)

8:00 pm “William Osler and Arthur Conan Doyle:
Partners in Detection”

Thomas Duffy, MD — *Professor Emeritus,
Yale School of Medicine*

9:00 pm Conclusion

210th Meeting — November 7, 2014

Johns Hopkins University School of Medicine

***Owens Auditorium, Koch Cancer Research Building, 1550 Orleans Street,
Baltimore, MD 21287***

8:00 am Continental Breakfast

9:00 am Welcoming Remarks and Opening

Landon S. King, MD — *Executive Vice Dean/
Professor Medicine and Biological Chemistry,
Johns Hopkins University School of Medicine*

9:15 am “Insights from Human Enteroids in Understanding
Intestinal Physiology and Host-Pathogen Interactions”

Mark Donowitz, MD — *LeBoff Professor of Medicine,
Johns Hopkins University School of Medicine*

9:45 am “Liquid Biopsy Approaches for Detecting and
Characterizing Human Cancer”

Victor Velculescu, MD, PhD — *Professor, Department of
Oncology, Johns Hopkins University School of Medicine*

10:15 am Break

10:30 am Sir William Osler Young Investigator Award: “Kabuki
Syndrome: A Potentially Treatable Cause of Intellectual
Disability”

Hans T. Bjornsson, MD, PhD — *Assistant Professor in
Pediatrics and Genetics, Johns Hopkins University
School of Medicine*

11:00 am “Found in Translation: New Insights into the
Pathogenesis and Treatment of Aortic Aneurysm”

Hal Dietz, PhD — *Victor A. McKusick Professor of
Genetics, Departments of Medicine, Pediatrics, and
Molecular Biology and Genetics, Johns Hopkins
University School of Medicine*

- 11:30 am “Applications of Engineering Principles in Cancer Research”
Denis Wirtz, PhD — *Vice Provost for Research/TH Smoot Professor, Chemical and Biomolecular Engineering, Pathology, Oncology, Johns Hopkins University and Johns Hopkins School of Medicine*
- 12:00 pm Lunch (*members only*)
- 12:45 pm Tour of Hopkins Hospital Dome
(meet at 601 North Broadway)
- 1:30 pm “Rebuilding Bodies: Regenerative Medicine From The Lab to The Clinic”
Jennifer Elisseff, PhD — *Professor, Wilmer Eye Institute and Department of Biomedical Engineering, Johns Hopkins University School of Medicine*
- 2:00 pm “Can Cancer Trigger Autoimmunity? Clues from systemic sclerosis”
Erika Darrah, PhD — *Assistant Professor, Department of Medicine, Johns Hopkins University School of Medicine*
- 2:30 pm Break
- 3:00 pm “A Serendipitous Finding Leading to a Potentially Novel Treatment for Obesity and Type II Diabetes”
Jonathan Powell, PhD — *Professor, Department of Oncology, Johns Hopkins University School of Medicine*
- 3:30 pm “Wireless Microrobots Perform Thousands of Biopsies In Vivo”
Florin Selaru, MD — *Assistant Professor of Medicine and Oncology, Johns Hopkins University School of Medicine*
- 4:00 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception and Black Tie Dinner
(Held at the Walters Art Museum, 600 N. Charles Street)
- 8:00 pm “From Smallpox to Ebola: Responding to Biological Threats” D.A. Henderson, MD, MPH — *Dean Emeritus, Bloomberg School of Public Health, Johns Hopkins University*
- 9:00 pm Conclusion

209th Meeting — April 4, 2014

University of Pennsylvania

Room 9-146, Smilow Center for Translational Research, 3400 Civic Center Blvd., Philadelphia, PA 19104

- 8:15 am Continental Breakfast
- 9:15 am Welcoming Remarks and Opening
Charles Abrams, MD — *Director, PENN-CHOP Blood Center for Patient Care & Discovery/Associate Chief, Division of Hematology-Oncology University of Pennsylvania*
Jonathan A. Epstein, MD — *William Wikoff Smith Professor of Medicine/Chair, Department of Cell and Developmental Biology/Scientific Director, Penn Cardiovascular Institute, University of Pennsylvania*
- 9:30 am “Stalking the Wards for Blood Disease as a Pediatric Physician Scientist” Mitchell J. Weiss, MD, PhD,
Jane Fishman Grinberg
Professor of Pediatrics The Children’s Hospital of Philadelphia
- 10:00 am “The BRCA Tumor Suppressor Network”
Roger A. Greenberg, MD, PhD — *Abramson Family Cancer Research Institute, University of Pennsylvania*
- 10:30 am Break
- 10:45 am “Using Genetics to Uncover Novel Antiviral Targets”
Sara Cherry, PhD — *Associate Professor, Department of Microbiology, University of Pennsylvania*
- 11:15 am Sir William Osler Young Investigator Award: “Targeting Macrophages for Cancer Immunotherapy”
Gregory L. Beatty, MD, PhD — *Assistant Professor, Division of Hematology-Oncology, University of Pennsylvania*
- 12:00 pm Lunch (*members only*) (held in Conference Room 9-100)
Speaker: “Opportunities for Treatment of Cancer Through Cancer Cell–Autonomous and –Non-Autonomous Mechanisms,”
by D. Gary Gilliland, MD, PhD — *Vice Dean & Vice President, Precision Medicine*

- 12:45 pm Guided Tour of the University of Pennsylvania Museum of Archaeology & Anthropology
(meet at 3260 South Street)
- 1:45 pm “Reactivation of Developmentally Silenced Globin Genes by Forced Chromatin Looping”
Gerd A. Blobel, MD, PhD — *Frank E. Weise III Endowed Chair of Pediatrics, The Children’s Hospital of Philadelphia*
- 2:15 pm “New Insights into Mammalian Physiology from Lymphatics”
Mark L. Kahn, MD — *Professor of Medicine, Penn Cardiovascular Institute, University of Pennsylvania*
- 2:45 pm “Hematopoietic Stem Cell Formation — Lessons from the Embryo”
Nancy Speck, PhD — *Professor of Cell and Developmental Biology, Cancer Biology, University of Pennsylvania*
- 3:15 pm Break
- 3:30 pm “The Development and Function of Brown and Beige Adipocytes”
Patrick Seale, PhD — *Assistant Professor of Cell and Developmental Biology, University of Pennsylvania*
- 4:00 pm “New Biology and Therapeutic Targets Inspired by Human Genetics”
Daniel J. Rader, MD — *Chief, Division of Translational Medicine and Human Genetics/Director, Preventive Cardiovascular Medicine and Lipid Clinic/Director, Clinical and Translational Research Center/Associate Director, Institute for Translational Medicine and Therapeutics/Director, Cardiovascular Metabolism Unit, Institute for Diabetes, Obesity, & Metabolism, University of Pennsylvania*
- 4:45 pm Business Meeting (*members only*)
- 6:00 pm Cocktail Reception and Black Tie Dinner
(Held at the Physick House, 321 S. 4th Street)
- 8:00 pm “Megatrends: Predictions for the Future of the American Health Care System”
Ezekiel J. Emanuel, MD, PhD — *Vice Provost for Global Initiatives, Chair, Medical Ethics and Health Policy, University of Pennsylvania*
- 9:00 pm Conclusion

208th Meeting — November 1, 2013
(Theme: The New York Cancer Landscape)

Memorial Sloan Kettering Cancer Center

**Lobby Auditorium, Zuckerman Research Center, 417 E 68th St,
New York, NY, 10065**

- 8:15 am Continental Breakfast (held in Room 136)
- 9:15 am Welcoming Remarks and Opening
Jose Baselga, MD, PhD — *Physician-in-Chief, Memorial Hospital Member, Human Oncology and Pathogenesis/Program Co-Chair, Center for Molecular Biology and Targeted Therapies, MSKCC*
Ross L. Levine, MD — *Associate Attending, Leukemia Service/Associate Member, Human Oncology and Pathogenesis Program MSKCC*
- 9:30 am Sir William Osler Young Investigator Award:
“Immunotherapy of Lymphoid Malignancies”
Renier J. Brentjens, MD, PhD — *Associate Attending, Leukemia Service MSKCC*
- 10:00 am “EZH2 Activation and Lymphomagenesis”
Ari M. Melnick, MD — *Professor of Medicine, Gebroe Professor of Hematology/Oncology, Weill Cornell Medical College*
- 10:30 am Break
- 10:45 am “Microbiome-Mediated Defense Against Bacterial Infection”
Eric G. Pamer, MD — *Chief, Infectious Disease Service, Head, Division of General Medicine/Director, The Lucille Castori Center for Microbes, Inflammation and Cancer MSKCC*
- 11:15 am “miRNA and Metastasis”
Sohail Tavazoie, MD, PhD — *Assistant Professor, Rockefeller University*
- 12:00 pm Lunch (*members only*) (held in Room 136)
Speaker: “MSKCC: History and Future,” by
Craig Thompson, MD — *President and CEO, MSKCC*
- 12:45 pm Historical Tour of Roosevelt House
- 1:45 pm “Molecular Therapy of Tuberculosis”
Michael S. Glickman, MD — *Department of Medicine, MSKCC*

- 2:15 pm “Repurposing Bisphosphonates for the Therapy of EGFR Family–Driven Cancers”
Mone Zaidi, MD, PhD — *Professor of Medicine and of Structural and Chemical Biology, Mount Sinai School of Medicine*
- 2:45 pm “Genome Sequencing to Uncover Therapeutic Vulnerabilities in Cancer”
David B. Solit, MD — *Associate Member, Human Oncology and Pathogenesis Program/Associate Attending, Genitourinary Oncology Service, MSKCC*
- 3:15 pm Break
- 3:30 pm “Targeting Leukemia Stem Cells”
Scott A. Armstrong, MD, PhD — *Member, Human Oncology and Pathogenesis Program/Vice Chair, Pediatrics/Director, Leukemia Center, MSKCC*
- 4:00 pm “Therapy Directed to Undruggable Targets in Cancer”
David S. Scheinberg, MD, PhD — *Interim Director, Sloan-Kettering Institute/Chairman, Molecular Pharmacology and Chemistry Program, Experimental Therapeutics Center, MSKCC*
- 4:45 pm Business Meeting (*members only*)
- 6:00 pm Cocktail Reception and Black Tie Dinner
(Held at New York Academy of Medicine, 1216 Fifth Avenue [corner of 102nd St. & 5th Ave])
- 8:00 pm “Lessons from the War on Cancer”
Siddhartha Mukherjee, MD, PhD —
Columbia University
- 9:00 pm Conclusion

207th Meeting — April 5, 2013

Harvard Medical School

***Ballard Room, Francis A. Countway Library of Medicine, 10 Shattuck St.
Boston, MA 02115***

- 8:30 am Continental Breakfast
- 8:50 am Welcoming Remarks and Opening
Mark Zeidel, MD — *President, ICC/Herrman Ludwig Blumgart Professor of Medicine, Harvard Medical School/Physician-in-Chief and Chairman,*

- Department of Medicine, Beth Israel Deaconess Medical Center*
Elizabeth Henske, MD — Boston Councilor, ICC/
Professor of Medicine, Harvard Medical School
Director, Center for LAM Research and Clinical Care
Brigham and Women's Hospital
- 9:00 am “The Promise of Genomics to Transform Infectious Disease Diagnostics”
Deborah Hung, MD, PhD — *Member, Broad Institute/*
Assistant Professor, Harvard Medical School
- 9:30 am “START Domain-Mediated Metabolic Regulation Reveals New Therapeutic Targets for Diabetes and Obesity”
David Cohen, MD, PhD — *Director of Hepatology, Division of Gastroenterology, Brigham and Women's Hospital/Director, Harvard-MIT Division of Health Sciences and Technology/Robert H. Ebert Professor of Medicine and Health Sciences and Technology, Harvard Medical School*
- 10:00 am “Targeting Cellular Metabolism and Autophagy in Lymphangiomyomatosis (LAM)”
Elizabeth Henske, MD — *Professor of Medicine, Harvard Medical School/Director, Center for LAM Research and Clinical Care, Brigham and Women's Hospital*
- 10:30 am Break
- 11:00 am “Changing Cell Fate as Therapy for Melanoma”
Leonard Zon, MD, PhD — *Grousbeck Professor of Pediatrics, Harvard Medical School/Director, Stem Cell Program, Boston Children's Hospital/Investigator, Howard Hughes Medical Institute*
- 11:30 am “Atherosclerosis: An Inflammatory Disease?”
Paul Ridker, MD — *Eugene Braunwald Professor of Medicine, Harvard Medical School/Professor of Epidemiology, Harvard School of Public Health/Director, Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital*
- 12:00 pm Lunch & Tour of Brigham and Women's Hospital Archives
- 1:30 pm Presentation
Jeffrey Flier, MD — *Dean of the Faculty of Medicine, Harvard University/Caroline Shields Walker Professor of Medicine, Harvard Medical School*

- 2:00 pm Break
- 2:15 pm “Pin1: A Pivotal Regulator and an Attractive Drug Target in Cancer and Alzheimer’s Disease”
Kun Ping Lu, MD, PhD — *Professor of Medicine, Harvard Medical School Beth Israel Deaconess Medical Center*
- 2:45 pm Sir William Osler Young Investigator Award:
“Integrating Genomic Approaches for Cancer Target and Drug Discovery”
Kimberly Stegmaier, MD — *Assistant Professor of Pediatrics, Harvard Medical School Dana-Farber Cancer Institute*
- 3:15 pm “Transcriptional Control of Brown and Beige Fat: Toward a New Generation of Therapeutics”
Bruce Spiegelman, PhD — *Stanley J. Korsmeyer Professor of Cell Biology and Medicine, Dana-Farber Cancer Institute, Harvard Medical School*
- 3:45 pm “Lipoxin A4 Regulates Innate Lymphoid Cells in Asthma”
Bruce Levy, MD — *Associate Professor of Medicine, Harvard Medical School/Medical Residency Director for Academics and Career Development, Brigham and Women’s Hospital*
- 4:15 pm Business Meeting (*members only*)
- 6:00 pm Cocktail Reception and Black Tie Dinner
(Held at the Harvard Club, 374 Commonwealth Avenue)
- 8:00 pm “The Play of Chance: The Evolution of Clinical Evidence”
Jeffrey M. Drazen, MD — *Editor-in-Chief, New England Journal of Medicine/Parker B. Francis Distinguished Professor of Medicine, Brigham and Women’s Hospital, Harvard Medical School*
- 9:00 pm Conclusion

206th Meeting — October 26, 2012

Yale University School of Medicine

Chapel and Library, Dwight Hall, Yale Old Campus, 67 High Street,
New Haven, CT 06520

- 8:30 am Continental Breakfast
- 8:50 am Welcoming Remarks and Opening
Michael Simons, MD — *New Haven Councilor, ICC/
R.W. Berliner Professor of Medicine and Cell Biology/
Chief, Section of Cardiovascular Medicine/Director, Yale
Cardiovascular Research Center, Yale School of Medicine*
- 9:00 am “Follicular Helper T Cells in Immunity and
Autoimmunity”
Joseph Edgar Craft, MD — *Paul B. Beeson Professor of
Internal Medicine, Rheumatology/Chief, Rheumatol-
ogy/Professor of Immunobiology/Director, Investigative
Medicine Program, Yale School of Medicine*
- 9:30 am “Fluid Shear Stress Mechanotransduction”
Martin A. Schwartz, PhD — *Professor, Internal Medicine
and Cell Biology, Yale School of Medicine*
- 10:00 am Break
- 10:30 am “Molecular Regulation of Glucose Uptake”
Jonathan Bogan, MD — *Associate Professor, Internal
Medicine, Endocrinology and Cell Biology,
Yale School of Medicine*
- 11:00 am “How Does Your Kidney Smell? New Signaling Pathways
in Polycystic Kidney Disease and Renal Olfaction”
Michael J. Caplan, MD, CNH — *Long Professor and
Chairman of Cellular and Molecular Physiology,
Yale School of Medicine*
- 11:30 am Sir William Osler Young Investigator Award: “Novel
Triggers of Inflammation After Cardiac Transplantation”
Daniel R. Goldstein, MD — *Associate Professor of
Internal Medicine and Immunobiology Yale School
of Medicine*
- 12:00 pm Lunch
Speaker: “Artificial Organs,” by Laura Niklason, MD —
*Professor of Anesthesiology and Biomedical Engineering
(SEAS)/Section Chief, Anesthesiology, Yale School
of Medicine*

- 12:45 pm “Vessel Branching Morphogenesis”
Anne C. Eichmann, PhD — *Professor, Internal Medicine (Cardiology), Yale School of Medicine*
- 1:15 pm “Novel Roles for TLR4 in Lung Injury and Repair”
Patty Lee, MD — *Associate Professor of Medicine/Director of Research, Section of Pulmonary, Critical Care, & Sleep Medicine, Yale School of Medicine*
- 1:45 pm Break
- 2:00 pm Tour of the Cushing Library, led by Lynn Sette
(Held at Cushing Whitney Medical Library, Sterling Hall of Medicine, 333 Cedar Street)
- 3:15 pm “An ATP Synthase Leak Conductance Controls Synaptic Plasticity and Neuronal Death”
Elizabeth Jonas, MD — *Associate Professor of Internal Medicine, Endocrinology and Neurobiology, Yale School of Medicine*
- 3:45 pm “Imaging the Complex Cellular Dynamics of Dementia Neuropathology”
Jamie Grutzendler, MD — *Associate Professor of Neurology and Neurobiology, Yale School of Medicine*
- 4:30 pm Business meeting (*members only*)
- 6:30 pm Cocktail Reception and Black Tie Dinner
(Held at the Union League Café, 1032 Chapel Street)
- 8:00 pm “The Future of the University” Professor John Martin —
Co-Director, Yale UCL Collaborative, Centre for Cardiovascular Biology & Medicine, University College London
- 9:00 pm Conclusion

205th Meeting — March 30, 2012

Johns Hopkins University School of Medicine

Albert H. Owens, Jr. Auditorium, David H. Koch Cancer Research Building, Sidney Kimmel Comprehensive Cancer Center, 1650 Orleans Street, Baltimore, Maryland 21231

- 8:30 am Continental Breakfast
- 8:50 am Opening of Meeting & Welcoming Remarks
Landon S. King, MD — *Baltimore Councilor, ICC/Vice Dean for Research, David Marine Professor of Medicine, and Director, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine*
- 9:00 am “Telomeres and Age-Related Lung Disease”
Mary Armanios, MD — *Associate Professor, Department of Oncology, McKusick-Nathans Institute of Genetic Medicine Johns Hopkins University School of Medicine*
- 9:30 am “The Epigenetic Basis of Common Human Disease”
Andrew P. Feinberg, MD, MPH — *King Fahd Professor of Medicine/Professor of Medicine/Chief, Division of Molecular Medicine/Professor of Molecular Biology and Genetics/Professor of Oncology, Johns Hopkins University School of Medicine/Director, Center for Epigenetics, Institute for Basic Biomedical Sciences*
- 10:00 am Break
- 10:30 am Sir William Osler Young Investigator Award:
“Statin-Associated Autoimmune Myopathy”
Andrew Mammen, MD, PhD — *Associate Professor of Neurology and Medicine/Co-Director, Johns Hopkins Myositis Center, Johns Hopkins University School of Medicine*
- 11:00 am “Making Molecular Imaging a Clinical Reality”
Martin Pomper, MD, PhD — *William Brody Professor of Radiology/Director, Small Animal Imaging Core/Director, Center for Translational Molecular Imaging, Johns Hopkins University School of Medicine*
- 11:30 am “Physiological and Pathological Responses to Hypoxia-Mediated by HIF-1”
Gregg L. Semenza, MD, PhD — *C. Michael Armstrong Professor of Pediatrics, Medicine, Oncology, Radiation Oncology, Biological Chemistry, and Genetic Medicine, Johns Hopkins University School of Medicine*

- 12:00 pm Lunch
Speaker: “Henrietta Lacks: A Story for All of Us,” by Landon S. King, MD — *Baltimore Councilor, ICC/Vice Dean for Research, David Marine Professor of Medicine, and Director, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine*
- 12:45 pm “TGF-Beta and Alveolar Airspace Homeostasis”
Enid R. Neptune, MD — *Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine, Johns Hopkins University School of Medicine*
- 1:15 pm “A Luminal View of Colorectal Cancer”
Cynthia L. Sears, MD — *Professor, Division of Infectious Diseases Johns Hopkins University School of Medicine*
- 1:45 pm Break
- 2:00 pm “Reverse Engineering of Cardiac Resynchronization: New Lessons for Heart Failure Therapy”
David A. Kass, MD — *Abraham and Virginia Weiss Professor of Cardiology/Professor of Medicine and Biomedical Engineering, Division of Cardiology, Johns Hopkins University School of Medicine*
- 2:30 pm “Natural Control of HIV-1 Infection: Highly Active Immune Responses?”
Joel N. Blankson, MD, PhD — *Associate Professor of Medicine, Division of Infectious Diseases, Johns Hopkins University School of Medicine*
- 3:15 pm Tour of the Charlotte R. Bloomberg Children’s Center (Johns Hopkins) and the Sheikh Zayed bin Sultan Al Nahyan Cardiovascular and Critical Care Tower (Johns Hopkins Hospital; opening April 2012)
- 4:15 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception & Black Tie Dinner
(Held at The Atrium, Robert H. and Clarice Smith Building/Johns Hopkins Wilmer Eye Institute, 400 North Broadway [corner of Broadway and Orleans Street])
- 8:00 pm Presentation
Introduction by Landon S. King
“Science as a Tool for Diplomacy,” by Peter C. Agre, MD — *Professor and Director, Johns Hopkins Malaria Research Institute, Bloomberg School of Public Health/2003 Nobel Laureate for Chemistry*
- 9:00 pm Conclusion

204th Meeting — October 28, 2011

Jefferson Medical College, Thomas Jefferson University
Jefferson Alumni Hall, 1020 Locust St., Philadelphia, PA 19107

- 8:30 am Continental Breakfast
- 8:50 am Opening of Meeting & Welcoming Remarks
Richard G. Pestell, MD, PhD — *Philadelphia Councilor, ICC/Director, Kimmel Cancer Center/Associate Dean, Cancer Programs, Jefferson Medical College/Vice President, Oncology Services, Thomas Jefferson University Hospital*
- 9:00 am “Therapeutic Strategies for Reactivating the p53 Tumor Suppressor in Cancer”
Steve McMahon, PhD — *Professor of Cancer Biology, Thomas Jefferson University*
- 9:30 am “Engineered T Cells: Establishing Good Memories for Bad Cancers”
Carl June, MD, PhD — *Professor of Pathology and Laboratory Medicine Director, Translational Research Program, Abramson Cancer Center, University of Pennsylvania School of Medicine*
- 10:00 am Break
- 10:30 am Myc and HIF Regulation of Metabolism and Therapeutic Targets”
Chi Dang, MD, PhD — *John H. Glick Professor, Professor of Medicine, and Director, Abramson Cancer Center Perelman School of Medicine, University of Pennsylvania*
- 11:30 am “Warburg in Reverse: The Autophagic Tumor Stroma Model of Cancer Metabolism”
Michael P. Lisanti, MD, PhD — *Professor and Chair, Department of Stem Cell Biology and Regenerative Medicine/Editor-in-Chief, American Journal of Pathology/Landenberger Endowed Professor in Breast Cancer Research and Professor of Cancer Biology, Medical Oncology, and Biochemistry, Kimmel Cancer Center, Thomas Jefferson University*

- 12:00 pm Lunch
Speaker: “Academic Medical Centers as Ecosystems,” by
J. Larry Jameson, MD, PhD — *Executive Vice President,
University of Pennsylvania for the Health System/Dean,
Raymond and Ruth Perelman School of Medicine,
University of Pennsylvania*
- 1:00 pm “Ups and Downs of Metabolism”
Mitchell A. Lazar, MD, PhD — *Sylvan H. Eisman
Professor of Medicine and Chief, Division of
Endocrinology, Diabetes, and Metabolism/Director,
Institute for Diabetes, Obesity, and Metabolism,
University of Pennsylvania*
- 1:30 pm “The Epigenetic Regulation of the Genome”
Shelley L. Berger, PhD — *Daniel S. Och University
Professor and Director, Epigenetics Program University
of Pennsylvania*
- 2:00 pm “The Arts of Jefferson”
F. Michael Angelo, MA — *University Archivist,
Thomas Jefferson University*
- 2:30 pm Sir William Osler Young Investigator Award:
“The Human Immunobiology of Natural Killer Cells:
Insights from and Opportunities for Rare Pediatric
Disease”
Jordan Orange, MD, PhD
- 3:00 pm Break
- 3:30 pm “Nature, Nurture, and Vitamin D: Rickets in the Tropics”
Michael Levine, MD — *Professor of Pediatrics and
Medicine, Perelman School of Medicine, University of
Pennsylvania/Chief, Division of Endocrinology and
Diabetes/Director, Center for Bone Health,
The Children’s Hospital of Philadelphia*
- 4:00 pm “Viral Entry Through Membrane Fusion: How HIV-1
gp41 Works”
Michael Root, MD, PhD — *Assistant Professor,
Department of Biochemistry & Molecular Biology,
Thomas Jefferson University*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception & Black Tie Dinner
Special Performance: The Arrhythmias
(Held at the Union League of Philadelphia,
Lincoln Memorial Room, 140 South Broad Street)

- 8:00 pm Presentation
Introduction by Mark L. Tykocinski, MD — *Anthony F. and Gertrude M. DePalma Dean, Jefferson Medical College/Senior Vice President, Thomas Jefferson University/President, Jefferson University Physicians*
“Mutation, Evolution, and Cancer,” by
Alfred G. Knudson Jr., MD, PhD — *Professor, Fox Chase Cancer Center*
- 9:00 pm Conclusion

203rd Meeting — April 1, 2011
*(Theme: Advances in Translational Medicine:
The New York Landscape)*

Mount Sinai School of Medicine

Atrium 4th Floor Conference Room, One Gustave L. Levy Place, New York, NY 10029

- 8:00 am Welcome & Continental Breakfast
Mone Zaidi, MD, PhD — *New York Councilor, ICC/Professor of Medicine and Director, Mount Sinai Bone Program, Mount Sinai School of Medicine*
- 8:30 am “Genetic Reprogramming in Regenerative Medicine”
Ihor Lemischka, PhD — *Henry M. Stratton Professor of Gene and Cell Medicine and Director, Black Family Stem Cell Institute, Mount Sinai School of Medicine*
- 9:00 am “The Role of Inflammation and Stem Cells in Cancer”
Timothy Wang, MD — *Dorothy L. and Daniel H. Silberberg Professor of Medicine and Chief, Division of Gastroenterology, College of Physicians and Surgeons, Columbia University*
- 9:30 am “Prenatal Diagnosis and Therapy of Congenital Adrenal Hyperplasia”
Maria New, MD — *Professor of Pediatrics and Director, Adrenal Steroid Disorders Program, Mount Sinai School of Medicine*
- 10:00 am Break
- 10:30 am Sir William Osler Young Investigator Award:
“Genetics and Therapy of Myeloid Malignancies”

- Ross Levine, MD — *Assistant Member and Geoffrey Beene Junior Chair, Memorial Sloan Kettering Cancer Center/Assistant Professor of Medicine, Weill Cornell Medical School*
- 11:00 am “Developing Vaccines that Elicit T-Cell Immunity”
Ralph Steinman, MD — *Henry G. Kunkel Professor and Senior Physician, Laboratory of Cellular Physiology and Immunology, Rockefeller University*
- 11:30 am “Central Regulation of Metabolism”
Christoph Buettner, MD — *Assistant Professor of Medicine, Division of Endocrinology, Diabetes, and Bone Diseases, Mount Sinai School of Medicine*
- 12:00 pm Display of Mount Sinai’s Own Treasures by Archivist Barbara Niss (Meet at 11th Floor, Annenberg Building, Mount Sinai School of Medicine)
- 1:00 pm Lunch (held in Board Room, 5th Floor, Annenberg Building)
Speaker: “Fulfilling the Promise of Biomedical Research: Nurturing Innovation at an Academic Medical Center,”
by Dennis S. Charney, MD — *Anne and Joel Ehrenkranz Dean, Mount Sinai School of Medicine/Executive, Vice President for Academic Affairs, Mount Sinai Medical Center*
- 2:00 pm “Targeted Molecular Therapies in Lung Cancer”
Goutham Narla, MD, PhD — *Assistant Professor of Medicine and of Genetics and Genomic Sciences, Mount Sinai School of Medicine*
- 2:30 pm “Insights into the Regulation of Skeletal Mass, Microstructure, and Remodeling by Parathyroid Hormone through Disorders of Parathyroid Function”
John Bilezikian, MD — *Dorothy L. and Daniel H. Silberberg Professor of Medicine, Professor of Pharmacology, and Chief, Division of Endocrinology, College of Physicians and Surgeons, Columbia University*
- 3:00 pm Break
- 3:30 pm “A Transition from Disease to Health — 2010–2020: Subclinical Cardiovascular and Mental Disease”
Valentin Fuster, MD, PhD — *Richard Gorlin, MD/Heart Research Foundation Professor and Director, Mount Sinai Heart, Mount Sinai School of Medicine*

- 4:00 pm “Mammals, Dinosaurs, and Fungi: Is There a Connection?” Arturo Casadevall, MD, PhD — *Leo and Julia Forchheimer Chair in Microbiology and Immunology, and Chairman, Department of Microbiology and Immunology, Albert Einstein College of Medicine*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception and Black Tie Dinner
(Held at the New York Academy of Medicine, 1216 Fifth Avenue at 103rd Street)
- 8:00 pm “Confronting the Limits of Biologic and Medical Determinism”
Barry Collier, MD — *David Rockefeller Professor of Medicine/Head, Allen and Frances Adler Laboratory of Blood and Vascular Diseases/Vice President for Medical Affairs, Rockefeller University*
- 9:00 pm Conclusion

202nd Meeting — November 5, 2010

Harvard Medical School

Benjamin Waterhouse Room, Gordon Hall, 25 Shattuck Street, Boston, MA 02115

- 8:00 am Continental Breakfast
- 8:15 am Opening of Meeting and Welcoming Remarks
Mark L Zeidel, MD — *Boston Councilor, ICC/Herrman Ludwig Blumgart Professor of Medicine, Harvard Medical School/Chair, Department of Medicine, Beth Israel Deaconess Medical Center*
- 8:30 am “Control of T cell Homeostasis by the Suppressor Gene PTEN”
Lawrence S. Turka, MD — *Lecturer of Medicine, Harvard Medical School/Co-Chief, Division of Transplant Immunology, Beth Israel Deaconess Medical Center*
- 9:00 am “The Noncoding Revolution”
Pier Paolo Pandolfi, MD, PhD — *George S. Reisman Professor of Medicine, Harvard Medical School/Chair, Department of Genetics, Beth Israel Deaconess Medical Center*

- 9:30 am “Disorders of Axon Guidance-Eye Movements
as a Paradigm”
Elizabeth Engle, MD — *Professor of Neurology, Harvard
Medical School/Department of Neurology, Children’s
Hospital Boston*
- 10:00 am Break
- 10:30 am Sir William Osler Young Investigator Award: “Novel
Approaches to Vaccine Development”
Dan Hung Barouch, MD — *Associate Professor of
Medicine, Harvard Medical School/Chief, Division of
Vaccine Research, Beth Israel Deaconess Medical Center*
- 11:00 am “Pathways Regulating Blood Stem Cell Self Renewal”
Leonard Ira Zon, MD — *Grousbeck Professor of
Pediatrics, Harvard Medical School/Director, Stem Cell
Research Program, Children’s Hospital Boston*
- 11:30 am “Functionalizing the Cancer Genome”
Lynda Chin, MD — *Professor of Dermatology, Harvard
Medical School/Scientific Director, Belfer Institute for
Applied Cancer Science, Dana-Farber Cancer Center*
- 12:00 pm Lunch
Speaker: “Harvard Medical School – Then and Now,” by
Jeffrey S. Flier, MD — *Dean of the Faculty of Medicine,
Harvard Medical School*
- 1:15 pm Tour of Countway Library Historical Archives
- 2:00 pm “Polycystic Kidney Disease – 3 Mini Stories”
Jing Zhou, MD, PhD — *Associate Professor of Medi-
cine, Harvard Medical School/Department of Medicine,
Brigham and Women’s Hospital*
- 2:30 pm “Targeting P13K for Cancer Treatment”
Lewis C. Chantley, PhD — *William Bosworth Castle
Professor of Medicine, Harvard Medical School/Chief,
Division of Signal Transduction, Beth Israel Deaconess
Medical Center*
- 3:00 pm Break
- 3:30 pm “Novel Mechanisms that Link Obesity and Diabetes Risk”
Barbara Kahn, MD — *George Richards Minot Professor
of Medicine, Harvard Medical School, Division of
Endocrinology, Diabetes and Metabolism, Beth Israel
Deaconess Medical Center*

- 4:00 pm “Quality Improvement: Raising the Bar”
Mark L. Zeidel, MD — *Herrman Ludwig Blumgart
Professor of Medicine, Harvard Medical School/Chair,
Department of Medicine, Beth Israel Deaconess Medical
Center of Medicine, Harvard Medical School*
- 4:30 pm Business Meeting (*members only*)
- 6:00 pm Cocktail Reception
(Held at the Harvard Club, 374 Commonwealth Ave.)
- 7:00 pm Black Tie Dinner
- 8:00 pm “Health Care Reform”
Stuart Altman, PhD — *Sol C. Chaikin Professor of
National Health Policy, Brandeis University/Chair,
Health Industry Forum/Chair, Council on the Economic
Impact of Health System Change*
- 9:00 pm Conclusion

201st Meeting — March 26, 2010

Yale School of Medicine

***Cohen Auditorium, Harris Building, Yale Child Study Center, 230 South
Frontage Road, New Haven, CT 06520***

- 8:00 am Continental Breakfast
(Held on the first floor of the Jane Ellen Hope Building,
Yale School of Medicine)
- 8:15 am Opening of Meeting and Welcoming Remarks
John Wysolmerski, MD — *New Haven Councilor, ICC/
Professor, Section of Endocrinology & Metabolism,
Yale University School of Medicine*
- 8:30am “New Treatments for Type 1 Diabetes”
Kevan Herold, MD — *Professor of Immunobiology,
Professor of Internal Medicine (Endocrinology),
Yale University School of Medicine*
- 9:00 am “Understanding Autoimmune Disease: from Genotype to
Phenotype”
David Hafler, MD — *Professor and Gilbert H. Glasser
Chair of Neurology, Yale University School of Medicine*
- 9:30 am “Stem Cells, Inflammation, and Tumor Immunity: From
Bedside to the Bench and Back”

- Madhav Dhodapkar, MD — *Arthur and Isabel Bunker Professor of Medicine and Chief, Section of Hematology, Department of Internal Medicine/Director of Hematologic Malignancies, Yale Cancer Center*
- 10:00 am Break
- 10:30 am Sir William Osler Young Investigator Award: “Human IL-23/Th17 Pathway Functions”
Clara Abraham, MD — *Assistant Professor of Internal Medicine, Section of Digestive Diseases, Yale University School of Medicine*
- 11:00 am “MicroRNAs and cancer”
Frank Slack, PhD — *Professor of Molecular, Cellular & Developmental Biology, Yale University*
- 11:30 am “Personalized Therapy of Lung Cancer 2010”
Thomas Lynch, MD — *Director of Yale Cancer Center and Physician-in-Chief, Smilow Cancer Hospital, Yale–New Haven Hospital*
- 12:00 pm Lunch
Speaker: “Undergraduate Science Curriculum Reform and Medical School Admissions,” by Robert Alpern, MD — *Professor of Internal Medicine and Dean, Yale School of Medicine*
- 1:15 pm Preview Tour of the Cushing Archive, led by Dennis Spencer, MD — *Professor of Neurosurgery*
- 2:00 pm “VEGF Signaling and Arterial Morphogenesis”
Michael Simons, MD — *Chief, Section of Cardiovascular Medicine/Professor of Medicine, Yale University School of Medicine*
- 2:30 pm “Insulin-Induced Hypoglycemia: The Brain-Diabetes Connection”
Robert Sherwin, MD, CNH — *Long Professor of Medicine, Section Chief, Section of Endocrinology & Metabolism, Yale University School of Medicine*
- 3:00 pm Break
- 3:30 pm “Immunology of Asthma”
Jack Elias, MD — *Chairman, Department of Internal Medicine Waldemar Von Zedtwitz Professor of Medicine and Chief, Beeson Medical Service, Yale–New Haven Hospital, Yale University School of Medicine*

- 4:00 pm “CFTR in the Immune Response”
Marie Egan, MD — *Associate Professor of Pediatrics
and Cellular and Molecular Physiology, Yale University
School of Medicine*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception
(Held at the Quinnipiack Club, 221 Church Street)
- 7:00 pm Black Tie Dinner
- 8:00 pm Performance by the Yale Opera Program
- 9:00 pm Conclusion

*200th Meeting — November 6–7, 2009
November 6, 2009*

Johns Hopkins University

*Conference Room 111, Cancer Research Building 2, 1550 Orleans
Street, Baltimore, MD 21231*

Organizing Committee

Honorary Chairperson: Eve Osler Hampson

Boston: Frank Austen, Ed Benz, Frank Bunn, Jeff Drazen,
Kurt Isselbacher, John Potts, Tom Stossel, Megan Sykes*, Mark Zeidel

New Haven: Jeffrey Bender, Arthur Broadus, Lloyd Cantley,
Thomas Duffy, Jack Elias, Bernie Forget, John Forrest, Steve Malawista,
John Wysolmerski*

New York: Craig Basson*, Leonard Chess, Edward Fisher, Rochelle
Hirschhorn, Richard Kitsis, Paul Marks, Aaron Marcus, David Shafritz,
Babette Weksler

Philadelphia: Barry Blumberg, Robert Coleman, Wafik El-Deiry*,
Stephen Emerson, Jon Epstein, William Kelley, Richard Shannon*,
Koneti Rao, Scott Waldman

Baltimore: Mark Donowitz, Diane Griffin, Tom Hendrix, Richard Johns,
Gerald Lazarus, Guy McKhann, Antony Rosen*, Richard Ross,
Cynthia Sears, Mike Weisfeldt

**Current ICC Officer or Councilor*

- 7:30 am Continental Breakfast
- 8:00 am Opening of Meeting and Welcoming Remarks
Richard P. Shannon, MD — *President, ICC/Frank Wister Thomas Professor of Medicine and Chair, Department of Medicine, University of Pennsylvania School of Medicine*
Antony Rosen, MD — *Baltimore Councilor, ICC/Professor and Director, Division of Rheumatology, Department of Medicine, Johns Hopkins University*
- 8:10 am “Welcoming Remarks from the Osler Family”
Eve Osler Hampson — *Great-Grand Niece of Sir William Osler, Ottawa, Canada/Honorary Chairperson, 200th ICC Meeting*
- 8:25 am “Welcome to Johns Hopkins and Baltimore”
Edward D. Miller, MD — *Frances Watt Baker and Lenox D. Baker Jr. Dean of the School of Medicine and Chief Executive Officer, Johns Hopkins Medicine*

Morning Scientific Session (I)

(Chair: Cynthia L. Sears, MD — *Professor of Medicine and Oncology, Johns Hopkins University*)

- 8:30am “The Cancer Genome and Its Implications for Patients”
Bert Vogelstein, MD — *Director, Ludwig Center at Johns Hopkins/Investigator, Howard Hughes Medical Institute*
- 9:00 am “The Human Microbiota in Health and Disease”
Claire Fraser-Liggett, PhD — *Professor of Medicine, Microbiology and Immunology and Director, Institute for Genome Sciences, University of Maryland School of Medicine*
- 9:30 am “Mechanistic Analysis of Wilson’s Disease Reveals New Metabolic Connections in the Liver”
Svetlana Lutsenko, PhD — *Visiting Professor of Physiology, Johns Hopkins University School of Medicine*
- 10:00 am Break

Scientific Session (II)

(Chair: Wafik S. El-Deiry, MD, PhD — *Secretary-Treasurer and Philadelphia Councilor, ICC/American Cancer Society Professor, Professor of Medicine [Hematology/Oncology], Genetics, and Pharmacology, University of Pennsylvania School of Medicine*)

- 10:30 am Sir William Osler Young Investigator Award: “Reversing T Cell Inhibition in Chronic Viral Infection: From Bench to Bedside...and Back”
Andrea Cox, MD, PhD — *Associate Professor of Medicine and Oncology, Johns Hopkins University*
- 11:00 am “Thromboregulation: Blood and Vascular Cell Control of Platelet Reactivity in Hemostasis and Thrombosis”
Aaron Marcus, MD — *Chief, Hematology/Oncology Section, Medical Service, VA NY Harbor Healthcare System*
- 11:30 am “Reflections on Academic Leadership”
William N. Kelley, MD — *Professor of Medicine, University of Pennsylvania School of Medicine*
- 12:00 pm Lunch
Introduction by Cynthia L. Sears, MD, Professor of Medicine and Oncology, Johns Hopkins University
Speaker: “Unlikely Allies: Sir William Osler, Mary Elizabeth Garrett and the Transformation of American Medicine,” by Kathleen Waters Sander, PhD — *Adjunct Professor of History, University of Maryland University College*
- 1:15 pm Option of Two Activities:
(i) Tour of Johns Hopkins’ Dome with Charles Wiener, MD — *Professor of Medicine and Physiology, Vice-Chair of Education, Director, Osler Medical Housestaff Program, Johns Hopkins University School of Medicine*
(ii) Video Presentation of “William Osler and the Teaching of Microscopy at McGill,” with an Introduction by Eve Osler Hampson

Afternoon Scientific Session

(Chair: Mark Donowitz, MD — *LeBoff Professor for Research in Digestive Diseases and Director, Johns Hopkins Center for Epithelial Disorders/President, American Gastroenterological Association [2006–2007]*)

- 2:00 pm “Cognitive and Neurological Outcomes after Cardiac Surgery” Guy McKhann, MD — *Professor of Neurology and Neuroscience, Department of Neurology, Center for Mind-Body Research, Johns Hopkins University*
- 2:30 pm “LTE4, the Overlooked Cysteinyl Leukotriene in Inflammation” Frank Austen, MD — *Astra Zeneca Professor of Respiratory and Inflammatory Diseases, Department of Medicine, Harvard Medical School and Brigham and Women’s Hospital*
- 3:00 pm Break
- 3:30 pm “Osler’s Legacy in the Interurban Clinical Club” Thomas Duffy, MD — *Professor of Medicine/Hematology and Director, Program for Humanities in Medicine, Yale University School of Medicine*
- 4:00 pm “Mechanisms of Hypoglycemia Associated Autonomic Failure” Stephen Davis, MD — *Incoming Professor, Physician-in-Chief, and Theodore Woodward Chairman of Medicine, University of Maryland School of Medicine*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception
(Held at the Engineers Club, 11 West Mount Vernon Place)
- 7:00 pm Black Tie Dinner
- 8:00 pm “Osler: Founding Father of American Clinical Medicine” Michael Bliss, PhD — *University Professor Emeritus, University of Toronto*
- 9:00 pm Conclusion

200th Meeting (cont.) — November 7, 2009

Johns Hopkins University
Hurd Hall, 600 North Wolfe Street, Baltimore, MD 21287

- 8:15 am Breakfast
- 8:40 am Opening of Grand Rounds and Welcoming Remarks
Cynthia Sears, MD — *Professor of Medicine and Oncology, Johns Hopkins University*

- 8:45am Presentations
“Grand Rounds Image of Osler,” by Amy E. Dezern, MD
— *Assistant Chief of Service, Janeway Firm, Department of Medicine, Johns Hopkins University*
“Maintaining Skeletal Muscle Mass: Lessons Learned from Muscular Dystrophy and Hibernation,” by Ronald Cohn, MD — *Assistant Professor, Pediatrics and Neurology, McKusick-Nathans Institute of Genetic Medicine, Director, Johns Hopkins Center for Hypotonia*
“Androgens, Androgen Action, and Prostate Cancer: New Insights into an Old Idea,” by William G. Nelson, MD, PhD — *Marion I Knott Professor and Director, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University*

9:45 am Break

Scientific session (held at Tilghman Auditorium, Turner Concourse)
(Chair: Richard J. Johns, MD — *Distinguished Service Professor of Biomedical Engineering, Johns Hopkins University*)

- 10:15 am “ Atovaquone for Malaria Prophylaxis: A Stitch in Time”
Theresa A. Shapiro, MD, PhD — *Professor of Medicine and Director, Division of Clinical Pharmacology, Johns Hopkins University School of Medicine*
- 10:45 am “How HIV informed Medicine”
John Bartlett, MD — *Stanhope Bayne-Jones Professor of Medicine (Infectious Diseases) and Professor of Epidemiology, Johns Hopkins University School of Medicine*
- 11:15 am Conclusion
John N. Forrest Jr., MD — *Professor of Medicine and Director, Office of Student Research, Yale University School of Medicine/Director, Mount Desert Island Biological Laboratory*

199th Meeting — April 3, 2009

College of Physicians of Philadelphia

Thomson Hall, 19 South 22nd Street, Philadelphia, PA 19103

- 8:00 am Continental Breakfast
- 8:20 am Opening of Meeting and Welcoming Remarks
Wafik S. El-Deiry, MD, PhD — *Philadelphia Councilor, ICC/American Cancer Society Research Professor, Professor of Medicine, Genetics, and Pharmacology and Co-Director, Radiation Biology and Imaging Program, Abramson Cancer Center, University of Pennsylvania School of Medicine*
- 8:30am “Wnt Signaling, Chromatin Structure, and Poised Transcription in Early Development”
Peter S. Klein, MD, PhD — *Associate Professor, Departments of Medicine and Cell and Developmental Biology, University of Pennsylvania School of Medicine*
- 9:00 am “Sleepless Flies: Probing the Genetics of Sleep”
Amita Seghal, PhD — *Professor of Neuroscience, University of Pennsylvania School of Medicine/ Investigator, Howard Hughes Medical Institute*
- 9:30 am “Stem Cells and Immunity in the 21st Century — The Quest for Vaccines against Stealthy Pathogens”
Steven L. Reiner, MD — *Professor, Department of Medicine, Division of Infectious Diseases and Abramson Family Cancer Research Institute/Chair, Immunology Graduate Group, University of Pennsylvania School of Medicine*
- 10:00 am “Challenges in Spanning the Biology-Medicine Chasm — Lessons from Ovarian Cancer”
Michael V. Seiden, MD, PhD — *President and CEO, Fox Chase Cancer Center*
- 10:30 am Break
- 11:00 am “Developmental Biology Rounds: Molecular Control of Pancreatic Development and Cancer”
Ben Stanger, MD, PhD — *Assistant Professor of Medicine, Division of Gastroenterology/Assistant Investigator, Abramson Family Cancer Research Institute, University of Pennsylvania School of Medicine*
- 11:30 am Sir William Osler Young Investigator Award: “Soluble

and Mechanical Factors in Liver Fibrosis”

Rebecca Wells, MD — *Assistant Professor, Departments of Medicine (Gastroenterology) and Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine*

12:15 pm

Lunch

Speaker: “Lessons Learned from the OTCD Trial,” by James M. Wilson, MD, PhD — *John Herr Musser Professor of Research Medicine and Professor, Department of Pathology and Laboratory Medicine/Head, Gene Therapy Program, University of Pennsylvania School of Medicine*

1:15 pm

Tour of the Mütter Museum

2:00 pm

“The Imaging Phenotype as a Tool for Disease Characterization”

Mitchell Schnall, MD, PhD — *Matthew J. Wilson Professor of Radiology and Vice Chair for Research, Department of Radiology, University of Pennsylvania School of Medicine*

2:30 pm

“An Aye for Gene Therapy: Preliminary Results from a Phase 1 Clinical Trial for Congenital Blindness”

Jean Bennett, MD, PhD — *F.M. Kirby Professor of Ophthalmology, Cell and Developmental Biology, Vice Chair for Research in Ophthalmology, and Senior Investigator, F.M. Kirby Center for Molecular Ophthalmology, University of Pennsylvania School of Medicine*

3:00 pm

“Caveolins in Breast Cancer Pathogenesis and Prevention: Role of the Tumor Micro-Environment”

Michael P. Lisanti, MD, PhD — *Director, Stem Cell Biology and Regenerative Medicine Center/Director, Basic and Translational Science, Department of Medical Oncology/Landenberger Endowed Professor in Breast Cancer Research and Professor of Cancer Biology, Medical Oncology, and Biochemistry, Kimmel Cancer Center, Thomas Jefferson University*

3:30 pm

“Pediatric Oncology at the Crossroads: Meeting the Challenge of Stagnating Cure Rates with Genomic Medicine”

John Maris, MD — *Chief, Division of Oncology/Associate Professor of Pediatrics/Director, Center for Childhood Cancer Research, Children’s Hospital of Philadelphia*

- 4:00 pm “Hair Follicle Stem Cells and Skin Regeneration”
George Cotsarelis, MD — *Albert M. Kligman Associate Professor of Dermatology/Director, Program on Epithelial Regeneration and Stem Cells, University of Pennsylvania Institute for Regenerative Medicine/ Director, University of Pennsylvania Hair and Scalp Clinic, University of Pennsylvania School of Medicine and Hospital of the University of Pennsylvania*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception
(Held at the Union League, 140 S. Broad Street)
- 7:00 pm Black Tie Dinner
- 8:00 pm “Progress & Promise in the Fight Against Cancer”
Margaret Foti, PhD, MD (hc) — *Chief Executive Officer, American Association for Cancer Research*
- 9:00 pm Conclusion

198th Meeting — November 14, 2008

Weill Medical College of Cornell University
Conference Room 460, Starr Pavilion, 510 E. 70th Street New York, NY 10021

- 8:30 am Continental Breakfast
- 8:50am Opening of Meeting and Welcoming Remarks
Craig T. Basson, MD, PhD — *Councilor, Gladys and Roland Professor of Medicine, Pediatrics, Cell & Developmental Biology, and Director, Center for Molecular Cardiology, Weill Cornell Medical College*
- 9:00 am “Genome-Wide Association Study for Cardiovascular Risk Factors on the Pacific Island of Kosrae”
Jan Breslow, MD — *Professor and Head, Laboratory of Biochemical Genetics and Metabolism, Rockefeller University/Senior Physician, Rockefeller Hospital*
- 9:30 am “Regulating Lymph Node Vascular Growth”
Theresa T. Lu, MD, PhD — *Assistant Professor of Microbiology and Immunology, Weill Cornell Medical College/Assistant Member, Autoimmunity and Inflammation Program and Pediatric Rheumatology, Hospital for Special Surgery*

- 10:00 am “Genetic Reprogramming of T cells and B cells to Generate Potent HIV-Specific Immunity”
Harris Goldstein, MD — *Professor of Pediatrics and Microbiology & Immunology, Director of Einstein/MMC Center for AIDS*
Research/Assistant Dean for Scientific Resources, Albert Einstein College of Medicine
- 10:30 am Break
- 11:15 am “Restoration of p53 Function for Induction of Apoptosis in Mutant p53 Cancer Cells by a p53 Custom Peptide: Design, Mechanisms, and In Vivo Efficacy”
Robert L. Fine, MD — *Irving Associate Professor of Medicine and Director of Experimental Therapeutics, College of Physicians and Surgeons, Columbia University*
- 11:45 am “Preparing the ‘Soil’ for the Metastatic Niche”
David Lyden, MD, PhD — *Stavros S. Niarchos Professor in Pediatric Cardiology, Department of Pediatrics, Weill Cornell Medical College*
- 12:15 pm Lunch
Speaker: “Training Physician-Scientists for the 21st Century: Challenges and Opportunities,” by Olaf S. Andersen, MD — *Professor of Physiology and Biophysics, Thomas H. Meikle, Jr. Professor of Medical Education, Weill Cornell Medical College/Director, Weill Cornell/Rockefeller/Sloan-Kettering MD-PhD Program*
- 1:25 pm Tour of the University Archives of the Weill Medical College, led by James L. Gehrlich — *Archivist*
- 1:55 pm “Evolutionary Dynamics of Cancer Stem Cells”
Franziska Michor, PhD — *Assistant Member, Computational Biology Program, Memorial Sloan Kettering Cancer Center*
- 2:25 pm “Targeting Calcium Cycling in Heart Failure”
Roger J. Hajjar, MD — *Arthur & Janet C. Ross Professor of Medicine and Director, Cardiovascular Research Center, Mount Sinai School of Medicine*
- 2:55 pm “Disorders of Sex Development: New Lingo, New Genes, New Mechanisms”
Harry Ostrer, MD — *Professor of Pediatrics, Pathology and Medicine and Director, Human Genetics Program, New York University Langone Medical Center*

- 3:25 pm Sir William Osler Young Investigator Award: “Delayed Enhancement MRI for Left Atrial Appendage Thrombus Tissue Characterization” Jonathan W. Weinsaft, MD — *Michael J. Wolk Clinical Scholar, Assistant Professor of Medicine, and Director, Cardiac MRI Program, Weill Cornell Medical College*
- 4:30 pm Business Meeting (*members only*)
- 6:30 pm Cocktail Reception
(Held at Ristorante Primavera, 82nd St. & 1st Ave.)
- 7:00 pm Black Tie Dinner
- 8:00 pm After-Dinner Speaker
Jeffrey D. Sachs, PhD — *Quetelet Professor of Sustainable Development, The Earth Institute, Columbia University/Special Advisor to UN Secretary General Ban Ki-moon*
- 9:00 pm Conclusion

BROADENING THE MISSION OF THE INTERURBAN CLINICAL CLUB



Jonathan Epstein

President, 2014–2016

In the fall of 2014, the councilors of the Interurban Clinical Club discussed and developed the idea of broadening the mission of the society to include mentorship and development of the next generation of physician-scientists. The membership includes outstanding role models and gifted teachers who have much to offer in terms of inspiring gifted trainees. In some cases, the ability of our most research-oriented members to interact with students during their clinical training or at early points in their post-graduate education is limited. In other cases, our emeritus members may have declining opportunities to transmit knowledge and to provide context and tradition for students. The ICC, we reasoned, might provide emerging physician-scientists with concentrated, valuable exposure to outstanding science presented by elite role models, as well as an opportunity for casual social interactions that catalyze mentor-mentee relationships. At the same time, the engagement of eager trainees at our meetings would inspire members, encourage attendance, and provide an additional worthy mission for our club. It was suggested that the dual-degree MD-PhD students at our various institutions would be an appropriate target audience for this initiative.

This concept was presented to the membership and unanimously approved, and we thus invited students enrolled in the MD-PhD program at Yale to join the 211th meeting on April 10, 2015, in New Haven. Barbara Kazmierczak, an active member from New Haven and the director of the MD-PhD program at Yale, worked tirelessly to engage the students and helped to select two outstanding candidates to present their research at the meeting. More than 20 students attended the scientific sessions and the black tie dinner at the Union League Café (students were excused from the requirement for black tie!), where Tom Duffy presented a fabulous and humorous after-dinner comparison between Sir William Osler and Sir Arthur Conan Doyle. The feedback from students and members was strongly positive, and many of the students wrote to me expressing their gratitude and praise

for the idea. The Yale MD-PhD program and medical school, the ICC, and individual ICC members contributed funds to cover the necessary costs so that the program and dinner were free to the students.

The success of the engagement with MD-PhD students at Yale encouraged the council to endorse continuation of this initiative, and Bruce Levy engaged Boston-area MD-PhD students for the 212th meeting in Boston, held at the Countway Library and the Harvard Club on November 13, 2015. Students from the University of Massachusetts, Boston University, Tufts University, and Harvard University were included, and three outstanding papers were presented. The discussions and interactions were inspiring, and the feedback from both members and students, many of whom sent personal letters or emails to me afterward, suggested that the format and mission are a success. Thus, a new chapter in the life of the ICC has dawned, in which Osler's conception of a society to promote the transfer of knowledge among the most accomplished physician-scientists in the Northeastern US will extend to the new generation.

*The First MD-PhD Student Speakers at
the Interurban Clinical Club*

211th meeting, New Haven (April 10, 2015)

Samir Zaidi, Yale School of Medicine: "Genes and Mechanisms of Congenital Heart Disease: Converging Pathways in Developmental Disorders"

Victoria E. Clark, Yale School of Medicine: "Characterizing the Genomic Architecture and Molecular Mechanisms Driving the Formation of Non-NF2 Meningiomas"

212th meeting, Boston (November 13, 2015)

Anjali Jacob, Boston University School of Medicine: "Generation of Patient-Specific Lung Alveolar Epithelium from Pluripotent Stem Cells"

Jon Herman, Harvard Medical School: "Halofuginone: A Story of How Target Identification of an Ancient Chinese Medicine and Multi-Step Evolution Informs Malaria Drug Discovery"

Gregory Orłowski, University of Massachusetts Medical School: "Sterile Particles: Double-Edged Swords of Inflammatory Cell Death, in the Air and in Your Blood"

At both meetings, many MD-PhD students attended the scientific sessions and the dinner.

INTERURBAN CLINICAL CLUB
CONSTITUTION
AND OFFICERS

Mone Zaidi,¹ John N. Forrest Jr.,² and Wafik S. El-Deiry³

¹*Secretary-treasurer, 2013–2016*

²*President, 1992–1993*

³*President, 2013–2014*

This chapter documents facts regarding the Interurban Clinical Club over nearly two decades. The ICC Constitution, initially drafted in 1905, is provided, along with amendments passed at the 212th meeting held in Boston on November 13, 2015. Two recent, notable changes to the Constitution, approved as amendments, are explained below. ICC presidents, secretary-treasurers, and councilors representing the five cities (Boston, New Haven, New York, Philadelphia, and Baltimore) from 2004 through 2016 are also listed.

Recent Amendments

At the 210th council meeting in Baltimore, Jonathan Epstein proposed using the ICC as a forum for nurturing the upcoming generation of physician-scientists. Toward this end, it was suggested that the meetings include talks by two MD-PhD students from institutions within the host city. Criteria for selecting such candidates would be developed and applied by the councilors in conjunction with the host institution's MD-PhD program director. The amendment, proposed by Epstein, was seconded by Mark Zeidel and approved unanimously at the business meeting. It was also discussed that a larger group of MD-PhD students be invited to attend the black-tie dinner (but not required to wear black-tie attire), which would give the students an opportunity to network with senior investigators. As a consequence, the Yale and Boston meetings included two and three student presentations, respectively. Epstein and Barbara Kazmierczak kindly provided funding for the initial MD-PhD student participation.

It was discussed both among the council and before the full membership during the 211th meeting at Yale whether to increase the age of active-to-emeritus transition to 60 years, and whether to increase the membership from each city. This was in response to the request from councilors to invite new members from each city, particularly those that had reached their membership limit. It was agreed that membership from each city would be increased from 12 to 15, to a maximum of 75 active members at any one time. It was also agreed that each city could have a maximum of 18 members, provided the total membership did not exceed 75 active members. The change was proposed by Zeidel, seconded by Jeffrey Bender, and approved unanimously by the membership.

The council gratefully acknowledges several chairs of departments of medicine for their generous contribution toward the publication of this volume. These include Gary Desir, Donald Landry, Joseph Loscalzo, Richard Shannon, Myron Weisfeldt, and Mark Zeidel.

Constitution and Amendments

1. The name is to be the "Interurban Clinical Club"
2. The objects of the Club are:
 - The stimulation of original work and investigation.
 - The development and improvement of methods of teaching.
 - Demonstration of work in the "border-line" subjects.
 - To give the members a better knowledge of physicians, methods, and work of other clinics. These objects are to be sought by meetings which are to be practical and at which few formal papers are to be allowed. The members will have the opportunity of showing work in medicine, either clinical or experimental. Special attention is to be given to the study of methods of teaching. The demonstration of work in other departments (e.g., pathology and physiology) is desired.
3. The members shall be active, emeritus, or honorary. The active members shall be under 55 years of age, and shall reside in Boston, New Haven, New York, Philadelphia, or Baltimore; the total number shall not exceed 60, and not more than 14 shall be from any one city. The emeritus members shall consist of those previously active members who have become 55 years of age or have changed their residence to some place other than the above-named cities. The honorary members shall be outstanding persons, either medical graduates or not, who have distinguished themselves in medical work and who have been elected unanimously by the Club. (See Amendment 3)

4. The officers of the Club shall be a president, secretary-treasurer, and a committee of five members, one to be chosen from each of the five cities (Boston, New Haven, New York, Philadelphia, and Baltimore). They shall be nominated at the annual meeting by a committee appointed by the president.

5. The president shall preside at the meetings and exercise the usual duties of the chair. The secretary-treasurer shall keep a record of the proceedings, conduct the correspondence, collect the fees, and submit an annual report to the Club.

6. The council (composed of all officers) shall determine the date and place of meeting; they shall have the supervision over the affairs of the Club, fix the yearly assessment, and appropriate money for the necessary expenditures.

7. Election of members. Nominations for membership shall be made in writing to the secretary-treasurer by any four members of the Club. Such nominations are to be acted on by the council, and a unanimous vote by its members shall be necessary for the submission of the name to the Club. Members may be elected at either the spring or the autumn meeting. The number of vacancies will be considered as that number that will exist at the time of the meeting following a physician's nomination to the Club by the council. The names of candidates approved by the council shall be transmitted to the members at least two months before the meeting. A four-fifths vote of the members of the Club present at the meeting shall be necessary for election. Not more than five new active members are to be elected in one year. Honorary members are to be elected at any meeting by a unanimous vote, which is to be taken by ballot. (See Amendment 3)

8. Meetings. Two meetings are to be held in each year, one in the fall and one in the spring. The latter is to be the annual meeting at which the officers shall be elected. As a rule, two days are to be given to each meeting, and if thought advisable by the council, two cities may be chosen. The local members in each city shall have charge of the meeting there and arrange the program, and the member of the committee in that city shall act as the local chairman in making arrangements for the meetings. The meetings are to be as practical as possible, and few formal papers are to be allowed. Demonstrations of methods of teaching, the giving of clinical demonstrations, showing experimental methods, etc., are the important aims of the Club. Free discussion and criticism are to be the features of the meetings.

Guests may be invited to the meetings and by invitation contribute to the program.

9. Absence from three consecutive meetings shall be considered an indication of a wish to discontinue active membership, and those who are absent from three consecutive meetings shall be reminded of this rule. (See Amendment 1)

10. Notice to amend the Constitution may be given at any meeting. This must be made in writing by at least three members and transmitted to the members of the Club before the next meeting, when action is to be taken on it. A two-thirds vote of the members of the Club present at the meeting shall be necessary for the adoption of the amendment.

Amendments

1. The Council shall have the privilege of determining the validity of excuses offered for absences; and in the event of three consecutive absences by a member, the Council may recommend to the Club either that the member remain active or be transferred to emeritus status. (Adopted at the 76th meeting, December 5, 1947)

2. All active members of the Club (regardless of attendance) and emeritus members who attend the dinner shall share alike the costs of the dinner and entertainment. (Adopted at the 76th meeting, December 5, 1947)

3. Not more than five new members may be elected at any one meeting. A total of 35 active members shall not be exceeded, nor more than nine active members from any one city. (Adopted at the 77th meeting, April 2, 1948)

4. Active members who move from one Club city to another Club city shall be transferred to the special category of "members at large" and shall continue to assume the same financial responsibilities as active members until the age of 55. (Adopted at the 104th meeting, December 1, 1961)

5. Change to Amendment 1: The council will have the privilege of determining the validity of excuses offered for absences, and in the event of three consecutive absences by a member, the council may recommend to the Club either that the member remain active or be dropped from membership. (Adopted at the 122nd meeting, December 4, 1970)

6. Active members are expected to present a paper at meetings held in the city from which they hold membership. (Adopted at the 127th meeting, April 6, 1973)
7. Change to Amendment 3: The active membership of the Interurban Clinical Club shall be increased from 35 to 40. This increase will be accomplished by increasing the maximum number of active members by one member each year for five years. No city shall have more than ten active members. (Adopted at the 150th meeting, December 7, 1984)
8. The limit of five new members that can be elected in a given year is removed; hence the maximum that can be elected will be determined by the number of active members at the time of each meeting and the ceiling on the number permitted by the Constitution at that time. (Adopted at the 153rd meeting, April 4, 1986)
9. Change to Amendment 7: The active membership of the Club shall be increased to 45. This increase will be accomplished by increasing the maximum number of active members by one member at each meeting for the next two and one-half years. At the third meeting after the passage of this amendment, the limit of ten active members per city will be increased to 11. (Adopted at the 161st meeting, April 6, 1990)
10. Formal acceptance of membership following election to the Club requires attendance at one of the two subsequent meetings, to be introduced to the Club. (Adopted at the 172nd meeting, November 3, 1995)
11. Change to Amendment 9: The active membership of the Club shall be increased to 60. This increase will be accomplished by increasing the maximum number of active members by five members at each meeting for the next three meetings. At the third meeting after the passage of this amendment, the limit of 11 active members per city will be increased to 14. (Adopted at the 173rd meeting, April 12, 1996)
12. Each meeting will have up to three speakers from the student body, either medical (MD) or joint-degree (MD-PhD) students, of the institutions within the city. (Adopted at the 210th meeting, November 7, 2014).
13. Change to Amendment 11: The membership from each city is increased to 15 active members, with no more than 18 active members from each city. The total number of active members shall not exceed 75 at any

time. (Adopted at the 211th meeting, April 10, 2015)

Interurban Clinical Club Council

Presidents

A. Koneti Rao (2004–2005)
Jeffrey Bender (2005–2006)
Stephen G. Emerson (2006–2007)
Cynthia L. Sears (2007–2008)
Richard N. Kitsis (2008–2009)
Richard P. Shannon (2009–2010)
John J. Wysolmerski (2010–2011)
Mark Zeidel (2011–2013)
Wafik S. El-Deiry (2013–2014)
Jonathan Epstein (2014–2016)

Secretary-Treasurers

Stephen G. Emerson (2004–2006)
Richard N. Kitsis (2006–2008)
Wafik S. El-Deiry (2008–2013)
Mone Zaidi (2013–2016)

Councilors

Charles Abrams (2013–2015)
C. William Balke (2002–2004)
Craig Basson (2006–2009)
Lloyd Cantley (2006–2008)
Wafik S. El-Deiry (2007–2009)
Barry Goldstein (2004–2006)
Elizabeth Henske (2011–2014)
Elizabeth Jonas (2014–current)
Landon S. King (2011–2015)
Richard N. Kitsis (2005–2006)
Ross L. Levine (2013–current)
Hyam I. Levitsky (2005–2008)
Bruce Levy (2015–current)
Susan McDonald (2003–2005)
Paul W. Noble (2004–2006)
Richard Pestell (2010–2012)

Antony Rosen (2008–2011)
David T. Scadden (2006–2006)
Michael Simons (2010–2014)
Edward Y. Skolnik (2003–2005)
Megan Sykes (2006–2009)
John J. Wysolmerski (2008–2010)
Mone Zaidi (2010–2013)
Mark Zeidel (2010–2011)

Those listed as “current” councilors were actively serving as of spring 2016.

BALTIMORE BIOGRAPHIES OF LIVING MEMBERS



Martin G. Pomper, MD, PhD

Martin Pomper was born on February 24, 1961, in Chicago, IL. He received his BS degree from the University of Illinois at Urbana-Champaign in 1982, followed by PhD and MD degrees in 1989 and 1990, respectively. His MD and PhD degrees were pursued in the Medical Scholars Program at the University of Illinois, a relatively new program at the time that was centered at the Urbana-Champaign campus and allowed study in areas not traditionally combined with medicine, such as organic chemistry, which was the area of Pomper's thesis research. He then moved to Baltimore for an internship in internal medicine on the Osler Medical Service of Johns Hopkins Hospital (1990–1991), followed by residencies in radiology and nuclear medicine (1991–1995), then a fellowship in neuroradiology (1996), all at Johns Hopkins. He was promoted to assistant professor at Johns Hopkins in 1996, to associate professor in 2002, and to full professor in 2007. He has several joint appointments, including pharmacology and molecular sciences (2003), oncology (2006), environmental health sciences (in the Bloomberg School of Public Health, 2006), psychiatry (2008), and pathology (2013). In 2011 he became the inaugural William R. Brody Professor of Radiology. He is board certified in diagnostic radiology and nuclear medicine.

From an early age Pomper decided to pursue a career in medicine, which stemmed from his interest in science and early reading, encouraged by his father, of classics such as *Microbe Hunters*. During college he became convinced to pursue chemical solutions to important biomedical problems, and he began to study with John A. Katzenellenbogen, a like-minded, biologically oriented organic chemist, in the Department of Chemistry at Illinois. In graduate school with Katzenellenbogen, Pomper developed site-directed imaging agents, focusing on the synthesis of positron-emitting steroids that home to steroid receptor-positive breast tumors, target areas of the brain, and can be used to image these tumors and target areas with positron emission tomography (PET). At the time — the middle to late 1980s — there were few PET centers in the US, so all of the radiochemical aspects of that work were undertaken in collaboration with Michael J.

Welch of Washington University, the leading center, which had a cyclotron, PET scanners, and other facilities for radiochemistry. When Pomper applied for internship and residency, Brody (then chair of the Department of Radiology at Johns Hopkins) felt that Pomper would be a good match for Johns Hopkins, as Brody was developing a PET program there throughout the 1980s and into the early 1990s.

Pomper began his independent research career at Johns Hopkins, focusing not only on radiopharmaceutical-based PET but also on molecular imaging — a more general area that involves studying biochemistry in vivo and non-invasively. He has maintained two themes, namely, molecular imaging of cancer and central nervous system disease, with a translational bent. Throughout his work he has benefitted from collaboration with many remarkable individuals at Johns Hopkins, with whom he developed new ways to image inflammation and infection, performed the first endogenous molecular-genetic imaging studies, and developed a series of imaging agents that target prostate cancer and that are emerging as standards in the field for a variety of imaging modalities, including and beyond radiopharmaceuticals. One such agent has been commercialized with the intent to offer intra-operative guidance to urologists performing prostatectomies by assuring a negative surgical margin at the end of the procedure. His research group consists of chemists, physicists, molecular biologists, and clinicians working together toward clinical molecular imaging.

Pomper is currently the director of the Johns Hopkins Small Animal Imaging Resource and associate director of the In Vivo Cellular and Molecular Imaging Center, both funded by the National Cancer Institute to support molecular imaging research. He is director of the Johns Hopkins Center for Translational Molecular Imaging. He is co-director of the Johns Hopkins Center of Cancer Nanotechnology Excellence and the Positron Emission Tomography Center. He is the immediate past editor-in-chief of Molecular Imaging and a past president of the Molecular Imaging Center of Excellence of the Society of Nuclear Medicine and Molecular Imaging. He has received several awards dating back to graduate school, including the R. C. Fuson Award for Excellence in Organic Chemistry, and has been co-author on abstracts for which he received, on three occasions (1988, 2007, and 2011), the Berson-Yalow Award from the Society of Nuclear Medicine. He has also received the Distinguished Service Award from the Society of Nuclear Medicine and is a distinguished investigator of the Academy of Radiology Research. He has served on the Clinical Molecular Imaging Probes Study Section at the NIH and on the Imaging and Informatics review panel

for the Cancer Prevention Research Institute of Texas. He serves as advisor to many academic and industrial programs involved in molecular imaging and lectures widely on the topic. He has numerous publications and patents related to medical imaging, many of which have been licensed, as well as several imaging agents undergoing clinical trials. He is a co-founder of Cancer Targeting Systems, Inc., and Theraly Pharmaceuticals.

Jonathan D. Powell, MD PhD

Jonathan Powell was born in New York City, NY, on January 20, 1964. He received his AB degree from Dartmouth College in 1986 and his MD and PhD degrees from Emory University in 1992. This was followed by a residency in internal medicine on the Osler Service at Johns Hopkins Medicine (1992–1995). He next pursued the clinical component of a fellowship in hematology-oncology at the Brigham and Women’s Hospital (1995–1996), followed by a postdoctoral fellowship in the laboratory of Ronald Schwartz at the National Institutes of Health (1996–2000). While in Schwartz’s lab his research involved dissecting the biochemical and molecular pathways involved in T cell anergy. It was at the NIH that he first began probing the role of mTOR in T cells, which has become a major focus of his own lab. In January of 2001 he joined the faculty of the Department of Oncology at Johns Hopkins as an assistant professor, and he has since risen through the ranks to his current position as full professor.

Powell headed to Dartmouth College intending to pursue a premed track and become a physician. During the summer after his freshman year, he worked in the lab of John Swaney at the Albert Einstein College of Medicine. This proved to be a transformative opportunity and enabled Powell to experience for the first time the excitement of discovery. Inspired by his time in Swaney’s lab, Powell began to work in the lab of Donald Schneider at Dartmouth during the academic year. In addition, during his semesters off from college, he worked with Peter Ward, then chairman of pathology at the University of Michigan. In both labs Powell studied neutrophils and the oxidative burst. At the end of college, now firmly committed to a research path, Powell decided to attend the MD-PhD program at Emory. Powell received his PhD under the tutelage of Aftab A. Ansari. His interests switched from the innate immune response to the adaptive immune response, and his thesis project involved the study of CD8⁺ T cells in a primate model of simian immunodeficiency virus infection. This work prompted him to take a more in-depth approach to studying T cell biology

and led him to Schwartz's lab at the NIH. There Powell worked on dissecting the molecular and biochemical pathways that promote T cell anergy. This included the elucidation of the role of the transcription factors CREM and Egr-2 and Egr-3. Furthermore, Powell was able to demonstrate that blocking mTOR activity promoted T cell anergy in Th1 cells, even in the presence of co-stimulation. Initially it was thought that the ability of mTOR inhibitors such as rapamycin to induce anergy was related to their ability to inhibit proliferation. However, through a series of genetic and pharmacologic experiments, it was shown that it was the inhibition of mTOR itself independent of proliferation that promoted this form of T cell tolerance.

Upon establishing his own lab at Johns Hopkins, Powell built upon his observations from studying T cell anergy in an attempt to understand how T cells integrate cues from the immune microenvironment to dictate the outcome of antigen recognition. By employing mice in which mTOR was selectively deleted in T cells, the Powell lab was able to demonstrate a critical role for this evolutionarily conserved kinase in promoting T helper cell differentiation. Furthermore, observations from these studies suggested a new paradigm whereby the default pathway for TCR engagement in the absence of mTOR is the generation of regulatory T cells. In a second series of experiments, the Powell lab demonstrated selective and critical roles for mTORC1 activity in regulating Th1 and Th17 differentiation, and for mTORC2 activity in regulating Th2 differentiation. More recently, the lab demonstrated a critical role for the mTORC2 target SGK1 in regulating Th2 differentiation. Furthermore, they demonstrated critical links between mTOR signaling and T cell differentiation and the regulation of metabolism. Findings from the lab have provided the preclinical rationale for the development of a novel regimen for non-myeloablative bone marrow transplantation in the treatment of sickle cell disease. In collaboration with John Tisdale of the NHLBI, a protocol was developed that promotes tolerance in patients and thus induces bone marrow chimerism. Furthermore, the basic findings revealed from these T cell studies have led to novel lines of inquiry in terms of new targets for enhancing immunotherapy for cancer, treating asthma, treating type II diabetes and obesity, and treating CNS malaria.

While at Hopkins Powell has trained eight PhD students and numerous clinical and research fellows and has served as the director for admissions for the graduate program in immunology. He is a member of the American Society for Clinical Investigation as well as the American Society for Hematology, the American Association of Immunology, and the Federation

of Clinical Immunology Societies.

Stuart Ray, MD

In 1963 Stuart Ray was born in Baltimore to a Presbyterian minister father and journalism-trained mother, moving to Nashville in 1967. He attended Caltech 1982-1984 and graduated with a BS in molecular biology from Vanderbilt University in 1986 and from Vanderbilt University School of Medicine in 1990. He trained at Johns Hopkins as an Osler intern and resident on the Barker Firm at Johns Hopkins Hospital (JHH) 1990-1993, followed by an infectious diseases fellowship at JHH 1993-1997, interrupted to serve as an assistant chief of service at JHH 1995-1996 under Edward Benz and David Hellmann. In 1997 he joined the faculty and, in 2011, was promoted to professor. He has a secondary appointment in oncology, and an adjunct appointment in health sciences informatics.

As a public school student in Nashville, Ray's scientific interest was piqued at Hillsboro High School by two years of chemistry with Jacqueline Turner, interests that were deepened during two years at Caltech where professors Richard Feynman (physics), Peter Dervan (chemistry), and Thomas Apostol (mathematics) provided charismatic and rigorous foundational teaching. He was recruited to transfer to Vanderbilt and major in Molecular Biology by his first laboratory mentor, Douglas Cavener, who schooled him in the basics of population genetics and phylogenetic analysis, culminating in a highly-cited two-author paper that broadened understanding of the Kozak consensus context around the start codon — an experience that taught Ray the importance of creating novel computational tools to solve biological problems. During medical school at Vanderbilt, he worked with Carl Hellerqvist, who trained him in bacterial glycobiology but also fostered his interest in computational tools with the development of an expert system for carbohydrate sequencing.

His fellowship research projects included a study of strain-specific anti-HIV cellular immune responses (coupling sequence variation with immunology), and sequencing of the first six full-length genomes from India. During the latter project, one of the genomes defied analysis using conventional tools — the phylogenetic pattern was a mosaic of known HIV clades. To resolve these, building from phylogenetic skills that Cavener had fostered, Ray created a program called Simplot and made it freely available. Since then, Simplot has been used in more than 1200 publications to study organisms ranging from the initial SARS coronavirus isolate to

eukaryotic chromosomes. In the nascent genomic era, Ray found that even informally-acquired phylogenetic skills could be valuable. Analysis of endosymbiont sequences under the direction of Steve Dumler led to a highly-cited reorganization of the order Rickettsiales. He continued to collaborate productively with Siliciano, whose lab meetings were always intellectually stimulating; but his real break came when David Thomas, a pioneer in the epidemiology and pathogenesis of HCV infection, asked him to engage full-time in the study of HCV evolution. Thomas had already assembled a unique cohort of injection drug users that had been followed prospectively with serial sampling before and after acute HCV infection, with some clearing the infection spontaneously (clearance) and some progressing to chronic HCV infection (persistence).

In the late 1990s, HCV evolution was attributed primarily to the high level of HCV replication and its error-prone polymerase. Ray and Thomas perceived more signal than noise in human HCV sequence variation within and outside hypervariable region 1 (HVR1), and demonstrated differences between persons with HCV clearance versus persistence in this sequence variation, findings that were subsequently confirmed by others. To show that variation in HVR1 is non-random, Ray and Thomas demonstrated that chimpanzees with poor antibody responses to E2 had little or no variation in HVR1, whether sampled during acute-phase passage or a decade of chronic infection. These publications laid the groundwork for increasingly mechanistic studies, joined by subsequent trainees including Chloe Thio (human and HBV genetics), Andrea Cox (cellular immunology), Ashwin Balagopal (inflammation and intrahepatic pathogenesis), Bill Osburn (diagnostics), Michael Chattergoon (innate/adaptive immunology), and Justin Bailey (humoral immunology). Sequence variation in HCV is directly relevant to treatment and prevention of HCV infection. With the advent of direct-acting antiviral agents (DAAs), specific targeting of viral proteins makes variation in these proteins more relevant, potentially limiting the effectiveness and durability of DAAs. HCV evolution will inform rational application of therapeutic and prophylactic measures against this supremely variable pathogen.

As a teacher, Ray is actively involved in classroom instruction of JHU undergraduates, graduate students, medical students (in all 4 years), residents, and fellows. He has been a member of the Firm Faculty of the Osler Medicine residency program since 2000, and has served as Janeway Firm Faculty Leader.

In 2009 Ray was elected to the American Society for Clinical Investigation (ASCI), and currently serves as JHU's institutional representative to ASCI. In 2012 Ray received the JHU School of Medicine Professors' Award for Excellence in Teaching in the Preclinical and Clinical Sciences. In 2015 Ray was named vice chair of medicine for Data Integrity and Analytics, and Research Director for the JHU Laboratory for Integrated NanoDiagnostics.

Antony Rosen, MBChB, MD

Antony Rosen was born in Cape Town, South Africa, on May 29, 1961. He received his medical degree with first class honors from the University of Cape Town in 1984 and completed a rotating internship at Groote Schuur Hospital in Cape Town in 1985. After a postgraduate year in medical biochemistry in Cape Town, he moved to New York City, where he pursued postdoctoral training in cell biology and immunology in the laboratory of Zan Cohn and Ralph Steinman at the Rockefeller University (1987–1990). This was followed by a residency in internal medicine (1990–1992) and fellowship in rheumatology (1993–1994) at Johns Hopkins Medicine. He joined the faculty in the Johns Hopkins rheumatology division in 1994, with a joint appointment in cell biology. In 2002 he became professor of medicine and division director. He was appointed vice dean for research at the Johns Hopkins School of Medicine in 2013.

Rosen's interest in research was inspired initially at medical school by Wieland Gevers and Mervyn Berman, outstanding physician-scientists and teachers who supervised active research groups and who modeled the reward and excitement that come from understanding basic biological processes that underlie human diseases. After moving to the Rockefeller University, Rosen worked with Alan Aderem on signaling in macrophages. This was an exceptionally rich environment, with numerous opportunities to interact and learn from Cohn and Steinman.

Rosen's research studies have focused on the mechanisms of the autoimmune rheumatic diseases, performed exclusively in the human model. In collaboration with his wife, Livia Casciola-Rosen, he has used the specificity of the immune response in distinct disease phenotypes to dissect pathways that initiate and drive rheumatic diseases. Specifically, they have used the distinct autoantibody responses in different rheumatic diseases as probes to understand events initiating and driving the autoimmune response in systemic lupus erythematosus, myositis, scleroderma, rheuma-

toid arthritis, and Sjogren's syndrome. In particular, their work has focused on changes in autoantigen structure and expression in both cancers and the target tissues in rheumatic diseases as important forces driving disease in the different syndromes. Their work has focused on two distinct stages in the autoimmune process: what initiates the immune response to highly specific molecules, and what drives this immune response in target tissues. In terms of the former stage, their recent work has demonstrated that mutation of specific autoantigens in cancer can initiate the disease-specific autoimmune response in scleroderma. This suggests that the rheumatic diseases like scleroderma and myositis might more generally reflect an immune response initiated by cancer. In terms of the latter stage, they have uncovered a previously unappreciated role for the target tissue in shaping and driving the immune response in the rheumatic diseases. The immune response in myositis is directed against a limited set of autoantigens, which are, interestingly, not expressed at significant levels in normal muscle. In contrast, these autoantigens are expressed at high levels in regenerating muscle cells in myositis muscle. These studies suggested that myositis reflects a feed-forward cycle of damage, in which immune-mediated injury induces high-level autoantigen expression, generating more damage and more antigen.

Rosen's leadership of the division of rheumatology at Johns Hopkins has been instrumental in creating and supporting several multidisciplinary specialty centers (for lupus, Sjogren's syndrome, scleroderma, myositis, arthritis, and vasculitis) that have been highly effective in providing multidisciplinary clinical care and an outstanding framework for discovery and scholarship. These centers have been powerful drivers of referral and discovery. During his tenure, he increased the division faculty from 14 individuals to 29.

Rosen has received multiple awards, including the Pew Scholar in the Biomedical Sciences award, a MERIT Award from the NIH, a Burroughs Wellcome Fund Translational Research Award, and the Henry Kunkel Young Investigator Award from the American College of Rheumatology. He was co-editor of *Arthritis & Rheumatism* (2010–2014). Rosen is a member of the American Society for Clinical Investigation and served as the Baltimore councilor of the Interurban Clinical Club.

Chloe L. Thio, MD

Chloe Thio was born in Dallas, TX, on June 9, 1965. She received a BA degree from University of Pennsylvania in 1987 and an MD from Yale University School of Medicine in 1992. This was followed by an internship and residency in internal medicine at the Hospital of the University of Pennsylvania (1992–1995), one year as a visiting physician at Sassoon Hospital in Pune, India (1995–1996), and a fellowship in infectious diseases at Johns Hopkins University (1996–2000). During her fellowship she was mentored by David Thomas and studied host genetic factors associated with hepatitis B virus (HBV) outcomes following acute HBV infection. During her fellowship she also became interested in HIV-HBV co-infection and began working with the Multicenter AIDS Cohort Study to pursue research in this area. In 2000 she was hired by John Bartlett for her first academic position, as an assistant professor of medicine in the Infectious Diseases Division of Johns Hopkins supported by an NIH NIDA Career Development Award. During this time she also had a clinical appointment at Johns Hopkins Hospital. In 2014 she became professor of medicine with a joint appointment in the Department of Molecular Microbiology and Immunology at the Johns Hopkins Bloomberg School of Public Health.

Thio first became interested in research during her undergraduate education, when she pursued a project on evolutionary genetics of the ribosomal RNA. It was at this time that she also became interested in pursuing a career in medicine. She pursued clinical research projects during medical school and residency, and then during her fellowship she applied her interest in human genetics to HBV infection. Her various research experiences inspired her to continue her investigative career after fellowship.

Thio's laboratory has developed several main focuses. Her primary area of interest is HIV-HBV co-infection. Her group was the first to discover that HIV increases HBV-related liver mortality. She has found HBV variants that are more common in HIV-infected patients that may be partially responsible for the more rapid progression of HIV. Her work has also led to an increased understanding of the development of drug-resistant HBV in the setting of HIV infection. She also has several ongoing molecular epidemiology projects in the United States and internationally that are designed to elucidate the anti-HIV and anti-HBV response to antiretroviral therapy in HIV-HBV co-infected patients. She and collaborators were also the first to discover that entecavir, a drug thought to be specific to HBV therapy, was also active against HIV and could lead to drug-resistant HIV.

Her second area of interest is in determining host genetic factors that are associated with recovery from HBV and HCV infections. To this end, Thio works with a large cohort of HBV-infected persons who have either recovered from the infection or remain chronically infected. She works with a second cohort of persons infected with HCV who have either recovered or remain chronically infected. Her group has discovered several candidate genes that influence HBV or HCV recovery or persistence.

Her third area of research is toward discovering a cure for chronic HBV infection. The current therapies do not cure HBV infection and thus usually require lifelong treatment. This fact, along with her findings that >95% compliance with therapies is required to maintain undetectable levels of HBV, has led to her interest in curing HBV. She is pursuing immunology studies in humans and mouse models to discover immunotherapies that can be given along with antiviral drugs.

Thio has also maintained an active clinical practice throughout her career. She has clinics in HIV-hepatitis co-infection and HIV mono-infection. She also attends on both the HIV service and the infectious diseases consult service at Johns Hopkins Hospital. In addition to mentoring students and fellows in research, she also mentors infectious diseases fellows in outpatient HIV medicine.

Thio is a fellow of the Infectious Diseases Society of America and a member of the American Association for the Study of Liver Disease and the American College of Physicians. She was also awarded membership in the American Society for Clinical Investigation. She has served as a reviewer for NIH and VA grants and is on the editorial advisory board for the *Journal of Infectious Diseases*.

Victor E. Velculescu, MD, PhD

Victor Velculescu was born in Bucharest, Romania on August 16, 1970 and moved to Westlake Village, CA at the age of 7. He credits his parents with instilling an interest in biomedical research from a young age. He began molecular biology research as an undergraduate at Stanford, receiving a BS degree with honors and distinction in biological sciences in 1992. Velculescu completed his MD degree, a PhD in human genetics and molecular biology, and postdoctoral studies at Johns Hopkins University. He remained on the faculty at Johns Hopkins and currently serves as professor

of oncology and pathology as well as co-director of cancer biology at the Sidney Kimmel Comprehensive Cancer Center.

Velculescu and members of his research group have pioneered approaches for discovering molecular alterations in human cancer and applying these discoveries to improve the diagnosis and treatment of cancer. In 1995 Velculescu developed SAGE (serial analysis of gene expression), a gene expression technology for the global and quantitative measurement of gene activity. The SAGE approach provided some of the first insights into gene expression patterns in eukaryotic cells and the identification of gene expression patterns in human cancer. These studies led Velculescu to coin the term “transcriptome” in a 1997 paper to describe the comprehensive gene expression patterns that could now be analyzed. SAGE contributed to the development of next-generation sequencing methods used for genome-wide expression analyses.

In the early 2000s, Velculescu and members of his laboratory devised new technologies for characterizing the cancer genome. These included digital karyotyping, which allows for quantitative characterization of amplifications and deletions at the DNA level. This approach provided the underlying methodology for next-generation sequencing analyses to detect chromosomal abnormalities in human cancer as well as in prenatal genetic testing.

Velculescu was an early developer of methods for high-throughput sequencing of human cancer. Through these approaches his group identified the gene *PIK3CA* as one of the most highly mutated cancer genes and demonstrated the importance of this gene for tumor growth and invasion. A variety of inhibitors targeting the *PIK3CA* gene product and its pathway have been developed and are currently in clinical trials.

In 2005, Velculescu extended these approaches, and together with Bert Vogelstein, Ken Kinzler and other colleagues at Johns Hopkins performed the first sequence analysis of the coding genome in human cancers, including breast, colorectal, brain, and pancreatic cancers. His group also led the effort to sequence the first pediatric tumor genome for medulloblastoma. These studies defined the genomic landscapes of human cancers and identified alterations in a variety of genes and pathways not previously known to be involved in tumorigenesis, including the genes *IDH1* and *IDH2* in gliomas, and chromatin modifying genes *MLL2/3* and *ARID1* in medulloblastomas, neuroblastomas and other tumor types. In 2010, Velculescu

and his group developed the PARE (personalized analysis of rearranged ends) technology that can help detect genomic tumor biomarkers circulating in the blood to enable the monitoring and personalized treatment of human cancer. Using this approach, his laboratory performed the first whole-genome analysis detecting chromosomal alterations in the blood of cancer patients.

Dr. Velculescu is a member of the Board of Directors of AACR, and has served as a member of scientific advisory boards of Bassett Research Center at University of Pennsylvania, the Starr Cancer Consortium, Quintiles, Helicos Biosciences, Inostics, and SoftGenetics. Velculescu co-founded the cancer genomics company Personal Genome Diagnostics (PGDx) in 2010 to bring individualized cancer genome analyses to patients, physicians, and researchers. PGDx was the first clinical laboratory to provide large-scale genomic analyses for cancer patients in 2011. He is the recipient of several awards for his work including the Grand Prize Winner of the Amersham/Pharmacia & Science Young Scientist Prize (1999), Sir William Osler Young Investigator Award from the Interurban Clinical Club (2006), Judson Daland Prize of the American Philosophical Society (2008), the European Association of Cancer Research and Carcinogenesis Young Investigator Award (2008), the AACR Award for Outstanding Achievement in Cancer Research (2009), the Paul Marks Prize for Cancer Research (2011), and the AACR Team Science Awards for Pancreatic (2013) and Brain Cancer Research (2014).

Baltimore active members without submitted biographies:

Landon King
Hyman Levitsky

BALTIMORE EMERITUS MEMBERS BIOGRAPHIES

Peter Agre, MD

The second of six children, Peter Agre was born in Northfield, MN, on January 30, 1949, to a second-generation Minnesota-Norwegian family. As chairman of chemistry at St. Olaf and Augsburg Colleges, Agre's father introduced his sons to science at early ages. Following a one-year sabbati-

cal at the University of California at Berkeley, the Agre family returned to Minnesota, but special reverence for science and great scientists, such as family friend Linus Pauling, always continued. After studying chemistry at Augsburg College (BA, 1970), Agre attended medical school at Johns Hopkins University (MD, 1974). As a medical student Agre developed interest in biomedical research while studying cholera in the laboratories of R. Bradley Sack and Pedro Cuatrecasas at Johns Hopkins. It was at this time that Agre met his future wife, Mary Macgill, a research assistant with Diane Griffin in the neurovirology laboratory at Johns Hopkins. The Agres were married in 1975.

When Charles C. J. Carpenter left Hopkins to become the chair of medicine at Case Western Reserve University Hospitals, Agre and several classmates followed to complete medical residency training in Cleveland. Agre then completed a hematology-oncology fellowship at the University of North Carolina at Chapel Hill, where his clinical mentor was John Parker, and he rejoined the Cuatrecasas research team, which had since moved to the Wellcome Laboratories in Research Triangle Park, NC. At that time he worked with his former medical school roommate, Vann Bennett, who had recently discovered ankyrin in red cells as well as non-erythroid ankyrins in brain and other tissues. Agre and Bennett characterized the first-known membrane skeleton defects that cause hereditary spherocytosis.

Agre joined the Johns Hopkins University School of Medicine faculty in 1981 and rose to the rank of professor of biological chemistry and medicine. Following one term as vice chancellor for science and technology at Duke University Medical Center, Agre returned to Johns Hopkins in 2008 to become director of the Johns Hopkins Malaria Research Institute at the Bloomberg School of Public Health. He currently oversees 20 faculty research groups as well as field activities in Zimbabwe and Zambia. In 2014, Agre was appointed Bloomberg Distinguished Professor at the Johns Hopkins Bloomberg School of Public Health and the Johns Hopkins School of Medicine.

Agre is best known for the discovery of aquaporins, a family of water channel proteins found throughout nature. Referred to as “the plumbing system of cells,” aquaporin water channels confer high water permeability to cell membranes. First discovered in human erythrocytes, AQP1 has been characterized biophysically, the atomic structure of AQP1 was solved, and AQP1-null humans were identified. Twelve homologous proteins exist in humans — transporting water (aquaporins) or transporting water plus

glycerol (aquaglyceroporins). These proteins are required for generation of physiological fluids (urine, cerebrospinal fluid, aqueous humor, sweat, saliva, and tears). Involvement of aquaporins is becoming recognized in multiple clinical states such as renal concentration, fluid retention, cataract, skin hydration, brain edema, neuromyelitis optica, thermal stress, glucose homeostasis, arsenic poisoning, and even malaria. Agre's work on aquaporins involved pivotal collaborations with multiple scientists, including Gregory Preston, Barbara Smith, William Guggino, Masato Yasui, and Landon King (Johns Hopkins University); Mark Knepper (NIH); Mark Zeidel (Harvard University); Søren Nielsen (Aarhus University); Andreas Engel and Tom Walz (University of Basel); Yoshinori Fujiyoshi (Kyoto University); and Ole Petter Ottersen and Mahmood Amiry-Moghaddam (University of Oslo).

In 2003 Agre shared the Nobel Prize in Chemistry with Roderick MacKinnon of Rockefeller University "for discoveries concerning channels in cell membranes." Agre is also a member of the National Academy of Sciences and the Institute of Medicine, for which he chaired the Committee on Human Rights. He holds 18 honorary doctorates from around the world. He has received the Distinguished Eagle Scout Award from the Boy Scouts of America and Commandership in the Royal Norwegian Order of Merit from King Harald V. From 2009 to 2011 Agre served as president and chair of the board of advisors of the American Association for the Advancement of Science. As part of the AAAS Center for Science Diplomacy, Agre led visits of US scientists to North Korea, Myanmar (Burma), Iran, and Cuba.

In 2015 the Agres celebrated their 40th wedding anniversary with their four grown children and two grandchildren.

John Bartlett, MD

John Bartlett was born on February 12, 1937 in Syracuse NY. He obtained his undergraduate degree from Dartmouth College in 1959 and an MD degree from Upstate Medical Center in Syracuse in 1963. He then completed a medical residency at the Brigham and Women's Hospital, Boston in 1965, served in the US Army in Vietnam, and did a senior medical residency at the University of Alabama in Birmingham, and an infectious disease fellowship at the Wadsworth VA Hospital and UCLA under Dr. Syd Finegold from 1969-72.

Dr. Bartlett was an assistant professor of medicine, UCLA/Sepulveda Veterans Admin Hospital from 1972-75, an associate professor and professor of medicine, Tufts University School of Medicine, Boston from 1975-80, a professor of medicine and chair Division of Infectious Diseases Division, Johns Hopkins University School of Medicine 1980–2006; and in 2013 became professor of medicine emeritus, Johns Hopkins University School of Medicine.

Dr. Bartlett was recruited in 1980 to Johns Hopkins to start a Division of Infectious Diseases. At time of stepping down as division director in 2006 the ID division was the largest in the Department of Medicine with 40 FTE faculty members and an annual research budget of \$40 million. Major divisional strengths included teaching, medical care and basic/applied research. The HIV/AIDS Service was always ranked #2 to San Francisco General Hospital. Other major divisional strengths included international health, hepatitis C, hepatitis B, infection control, tuberculosis, STDs, and diagnostic microbiology. Dr. Bartlett discovered *Clostridium difficile* as cause of antibiotic associated colitis in 1977.

His dominant research interests include anaerobic infections and pulmonary infections, community acquired pneumonia and diagnostic methods, bowel preparation for elective colon surgery, protected bronchoscopy and brush catheter, *C. difficile* infection, HIV/AIDS, bioterrorism, *C. difficile* infection, and antibiotic resistance.

Dr. Bartlett has published 471 original articles in peer-reviewed journals and written 333 book chapters and received many awards, including Best Medical Book, (Medical Writers Assoc-1993); HERO Award (HIV Care, 1983-93); Institute of Medicine (1999); Kass Award (IDSA, 2002); Master, American College Physicians (2004); Finland Award, (IDSA, 2005); Fleming Award (IDSA Lifetime Achievement, 2005); Oldendorf Award for Lifetime Achievement (UCLA, 2008); Insider Award (Lifetime achievement, Metro Foundation, Chicago, 2010); Cubist Award; ASM achievements in microbiology, 2011; Partnership Award, contributions to the fight against AIDS, CAEAR, 2013.

Bruce S. Bochner, MD

Bruce S. Bochner was raised in Evanston, Illinois, the youngest of three children of a dry cleaner and housewife/bookkeeper. He received a bach-

elor of arts degree with honors in natural sciences from Johns Hopkins University. He attended medical school at the University of Illinois College of Medicine in Chicago, where he again graduated with honors and was elected into the Alpha Omega Alpha Honor Medical Society. During medical school he was introduced to, and worked in the laboratory of, Max Samter, for whom Samter's Triad (asthma, nasal polyposis, and aspirin sensitivity, now termed aspirin-exacerbated respiratory diseases [AERD]) is named. After completing internal medicine residency training at the University of Illinois, he began his postdoctoral allergy and immunology training in the laboratory of Robert Schleimer at Johns Hopkins University School of Medicine in the Division of Allergy and Clinical Immunology of the Department of Medicine. His clinical interests extend from asthma to hypereosinophilic disorders such as eosinophilic esophagitis, from food allergy and anaphylaxis to mast cell disorders, as well as novel therapies to treat these conditions.

In 1988 he joined the faculty at Johns Hopkins, a career path that would not have been possible without financial support from his family and early-career awards such as an NIH R29 grant, a New Investigator Award from the American Lung Association, a Developing Investigator Award from the Asthma and Allergy Foundation of America, and a Developing Investigator Award from the Burroughs Wellcome Fund. In 1999 Bochner was promoted to the rank of professor of medicine and subsequently became a Cosner Scholar in Translational Research at Johns Hopkins. In January 2003 he succeeded Lawrence Lichtenstein as division director and remained in that position until 2013, when he was recruited by Schleimer to the Division of Allergy and Immunology at Northwestern University as the Samuel M. Feinberg Professor of Medicine. At Johns Hopkins he was honored and proud to lead a T32 training grant that funded MD postdoctoral education related to careers in allergy and immunology research. He has supervised over 35 MD, PhD, and MD-PhD visiting scientists, postdoctoral fellows, and graduate students and is gratified that most of his trainees have gone on to pursue successful careers in discovery.

As a physician-scientist devoting more than 80% of his efforts to NIH-funded research, his overarching research philosophy has been to delineate novel mechanisms of human allergic diseases, working whenever possible with primary human cells and tissues, and at the same time attempting to identify targets that might be amenable to the development of new therapies. He was among the first to explore the different roles of cytokines, chemokines, and adhesion molecules (especially VLA-4/VCAM-1) used

by eosinophils for their selective cell recruitment. In 2000 he co-discovered Siglec-8 from material isolated from a patient with hypereosinophilic syndrome as part of an effort to identify novel eosinophil molecules. Siglec-8 was also expressed on mast cells and to a weak extent on basophils, but on no other cells. Subsequent studies defined its inhibitory, pro-apoptotic biology and natural glycan ligands. Currently, most of his laboratory's ongoing efforts are focused on exploiting and optimizing antibody and glycan targeting of Siglec-8 on eosinophils and mast cells, while also exploring sialylated endogenous tissue ligands for this molecule; such work has already identified an important airway source of such ligands. These efforts introduced the lab to the world of glycobiology, resulting in collaborations with colleagues on a "glycobiology of inflammatory lung diseases" program project grant. Together with Schleimer and others, Bochner recently co-founded Allakos, Inc., a biotechnology company whose goal is to develop therapeutics for the treatment of eosinophil- and mast cell-related disorders.

Bochner has received several awards, including the David M. Levine Excellence in Mentoring Award from the Department of Medicine at Johns Hopkins. He is a fellow of the American Academy of Allergy, Asthma, and Immunology, the American College of Allergy, Asthma, and Immunology, and the American College of Physicians. He is a member of the American Association of Immunologists and was elected to membership in the American Society for Clinical Investigation and the Association of American Physicians. He has served on the executive committee of the International Eosinophil Society and was responsible for planning that society's July 2015 meeting in Chicago. He currently serves as secretary general of the Collegium Internationale Allergologicum, an organization limited to 250 international members of physicians and scientists who meet biannually to discuss scientific and clinical problems in allergy and related branches of medicine and immunology. He served as an associate editor of the *Journal of Allergy and Clinical Immunology* from 1993 to 2013 and is an associate editor of *Clinical and Translational Medicine*.

Bochner is also co-editor-in-chief of the Allergy and Immunology Section of the online journal *UpToDate* and a co-editor of the 6th, 7th, and 8th editions of the textbook *Middleton's Allergy: Principles and Practice*. He previously served on the boards of directors of the American Board of Allergy and Immunology and the American Academy of Allergy, Asthma, and Immunology. He is a former member of the Immunological Sciences Grant Review Study Section and a current member of the Hypersensitiv-

ity, Autoimmune, and Immune-Mediated Grant Review Study Section of the NIAID. He is the author of more than 235 peer-reviewed publications, reviews, and book chapters and has received research support since 1988 from the NIAID, NHLBI, and Dana Foundation.

Mark Donowitz, MD

Mark Donowitz was born in Neptune, NJ, on May 16, 1943. He received a BS degree from Brandeis University in 1964 and an MD from the Johns Hopkins University School of Medicine in 1968. This was followed by a residency in internal medicine at Hopkins (1968–1970), a senior residency at Albert Einstein College of Medicine (1970–1971), and a fellowship in gastroenterology at Yale, where he was mentored by Henry Binder and studied mechanisms of regulation of intestinal electrolyte transport. This was followed by research at the Walter Reed Army Institute of Research, where he studied the pathogenesis of bacterial diarrheal diseases with Sam Formal, to fulfill his Berry Plan deferred military obligation. During this time he also served as an assistant clinical professor of medicine at the George Washington School of Medicine. In 1977 he was hired by Sheldon Wolff for his first academic position, as assistant professor of medicine in the Gastroenterology Division of Tufts New England Medical Center, supported by an NIH NIDDK Research Career Development Award. In 1984 he became professor of medicine, with a joint appointment in physiology. In 1988 he moved to Johns Hopkins Medicine as professor of medicine and chief of the gastroenterology division, a position he held until 1996, when he assumed directorship of the Hopkins Center for Epithelial Disorders and the LeBoff Professorship for Research Disorders in Digestive Diseases.

In selecting medicine as a career, Donowitz, his brother, Jerry (now professor of medicine at the University of Virginia), and his sister, Arlene (practicing internal medicine in Chattanooga, TN), were inspired by their maternal uncle, Martin A. Entin, who was chairman of hand surgery at McGill University, and by their mother, who believed that education was the key to success. Although he had always been interested in science, Donowitz decided to pursue an investigative career after working in the Binder laboratory, where he developed an interest in the pathophysiology of diarrheal diseases. His decision was solidified during his first year on the faculty at Tufts, when he was a mentee of Geoffrey Sharp, one of the discoverers that cholera toxin activated the adenylyl cyclase system. Together they discovered that intestinal Na absorption and insulin secretion were regulated by

similar signaling pathways, and they formed a close collaboration that continued for more than 25 years.

The theme of regulation of intestinal Na absorption and how abnormalities in that absorption contribute to the pathophysiology of diarrhea have been the major foci of Donowitz's research. Upon moving to Hopkins he used molecular tools to clone the epithelial Na/H exchangers that are the major Na absorptive proteins in the intestine and proximal tubule. He was the first to recognize the existence of the mammalian Na/H antiporter gene family and cloned the two epithelial isoforms, NHE3 and NHE2. In addition, he recognized that multi-PDZ scaffolds were central to NHE3 regulation, identified and named the gene family involved, and cloned the second member of this family, now called NHERF2, which is a major regulator of Na absorption. He has pursued mechanisms of regulation of NHE3, showing that NHE3 is regulated by large complexes that form on its C terminus, which acts as a scaffold, with the complexes forming at the sites at which NHE3 is attached to the cytoskeleton but being changed in their components as part of NHE3 regulation. In addition, he helped to develop human 2D and 3D enteroid models for use in the study of human intestinal physiology, pathophysiology, and drug development.

As chief of gastroenterology at Hopkins, he expanded the clinical base, initiated therapeutic endoscopy and the liver transplant program, and greatly increased the number of women in the division. As director of the Hopkins Center for Epithelial Disorders, he brought together scientists interested in epithelial biology and the diseases resulting from abnormal transport in epithelial cells. The center served as the nidus that allowed Donowitz to successfully compete for NIH funding to create a GI core center, the Hopkins Digestive Diseases Basic Research Development Center. In 2011 Donowitz also became the founding director of the Hopkins Digestive Diseases Basic and Translational Research Core Center, which is a Silvio O. Conte Digestive Diseases Research Core Center funded by the NIH. Through the development of these centers, and with support from two program project grants at Hopkins in which he was named principal investigator, he created an environment in which collaborative basic science with a translational component could be carried out by MD and PhD investigators in the Department of Medicine working in collaboration with members of the Hopkins basic science faculty. At Hopkins he was strongly supported by Ann Hubbard, professor of cell biology; Joseph Handler, chair of nephrology; and Svetlana Lutsenko, professor of physiology, all of whom helped to develop and run the core centers and who were important in

forming interactions between Hopkins basic scientists and the investigators from the Department of Medicine.

Donowitz has received multiple awards, including the American Physiological Society Horace Davenport Career Achievement Award and its Distinguished Achievement Award in Gastroenterology. He is a fellow of the American Association for the Advancement of Science and a member of the American Society for Clinical Investigation and the Association of American Physicians. He belongs to the American Gastroenterological Association and the American Physiological Society. Donowitz has been president of the Gastroenterology Research Group, the Interurban Clinical Club (1992–1993), and the American Gastroenterological Association. He has taken two sabbaticals: one supported by the Grossman Sabbatical Prize from the American Gastroenterological Association and conducted with Heini Murer and Ernesto Carafoli in Zurich, and one supported by the Boursie Rothschild-Mayent Sabbatical Fellowship award from the Curie Institute and conducted with Daniel Louvard and Monique Arpin in Paris. He has served on the NIH GMA Study Section and the VA Merit Review Committee for Gastroenterology, the advisory councils of the NIDDK and the Dental and Craniopharyngeal Institutes, and on the editorial boards of the *Journal of Clinical Investigation*, the *American Journal of Physiology—Cell Physiology*, *American Journal of Physiology—Gastrointestinal and Liver Physiology*, *Physiology*, and the *Journal of Biological Chemistry*.

Andrew Feinberg, MD, MPH

Andrew Feinberg received his education at Yale (1969–1971) and Johns Hopkins University (BA in 1973, MD in 1976, and MPH in 1981). He performed his clinical training at the University of Pennsylvania and his postdoctoral research at the University of California, San Diego, and Johns Hopkins. He was a Howard Hughes investigator at University of Michigan, then returned to Johns Hopkins in 1994, where he is currently a Gilman Scholar and professor of medicine, oncology, and molecular biology and biostatistics and director of the Center for Epigenetics.

His early work included the discoveries of altered DNA methylation in human cancer, human imprinted genes and loss of imprinting (LOI) in cancer, the molecular basis of Beckwith-Wiedemann syndrome, and epigenetic risk of cancer. Most recently he pioneered genome-scale epigenetics (epigenomics), with the first whole genome bisulfite sequencing analysis of

human cancer, and the discovery of large hypomethylated blocks that correspond to nuclear lamina-associated heterochromatin, as well as a mechanism for disruption of these blocks in epithelial-mesenchymal transition. He has shown the close relationship between epigenomic changes in normal development, cancer, and stem cell reprogramming. He received the NIH Director's Pioneer Award to pursue a novel model of genetically driven stochastic epigenetic plasticity in evolution and development, which led to his discovery of the first evidence for methylation-mediated reversible behavior in a whole organism.

His honors include elected membership to the Association of American Physicians, the Institute of Medicine of the National Academy of Sciences, and the American Academy of Arts and Sciences. He was awarded the Fedor Lynen Medal, the Spinoza Chair of the University of Amsterdam, and honorary doctorates from the University of Uppsala and the Karolinska Institutet.

Diane Edmund Griffin, MD

Diane Edmund was born in Iowa City, Iowa, on May 12, 1940 and grew up in Oklahoma City where she attended Putnam City School. She earned a BA degree in Biology from Augustana College (Rock Island, IL) in 1962 and MD and PhD degrees from Stanford University in 1968 and 1970. From 1968-1970 she was intern and medical resident at the Stanford University Hospital; and from 1970-1973 a postdoctoral fellow in virology with Richard T. Johnson in the Department of Neurology at the Johns Hopkins University School of Medicine. She served as an assistant professor of medicine and neurology at Johns Hopkins from 1973-1979 and was an investigator of the Howard Hughes Medical Institute from 1975 to 1982. She was promoted to associate professor in 1979 and professor of medicine and neurology in 1986. In 1994, she became the Alfred and Jill Sommer Chair of the W. Harry Feinstone Department of Molecular Microbiology and Immunology (formerly Immunology and Infectious Diseases) in the Johns Hopkins Bloomberg School of Public Health. She held this position until January 2015 and is currently a Johns Hopkins University Distinguished Service Professor in the department.

As a PhD student at Stanford, Griffin was supported on an NIH predoctoral award. After one year of graduate study she entered the Stanford 5-year medical program that meant surrendering her NIH funding and reliance

on low interest loans and Stanford scholarships. Her thesis research in immunology under Sidney Raffel and Leon Rosenberg secured her interest in disease-oriented research. After graduation and two years of residency training she and her husband John W. Griffin (married June 1965 in Rock Island, IL) migrated to Baltimore and Johns Hopkins University School of Medicine. She joined Richard Johnson's multidisciplinary program to study the pathogenesis of viral infections, serving as the immunologist in the group. Her training was funded by the NIH. She learned virology and initiated the studies that evolved into her current research interests. Veterinary virologist Opendra (Bill) Narayan and neurologist Henry McFarland were fellows at the same time in the Johnson lab and had an important influence on her scientific development.

Much of her research time has been focused on the study of two types of virus diseases: acute alphavirus encephalitis and measles. The alphavirus work focuses on the determinants of virulence and the importance of the immune response to infection. The amino acid changes that determine virulence of the virus were defined and the mechanisms by which these alterations affect virulence were identified. She and her colleagues have demonstrated that there is local immunoglobulin synthesis in the CNS that is long lasting and that antibody can clear virus infection from neurons by a non-cytolytic mechanism. T cells producing interferon-gamma contribute to clearance of virus from spinal cord motor neurons, but T cells also contribute to immunopathology in the CNS. However, viral RNA is not totally eliminated by these mechanisms and continued presence of virus-specific immune cells is required to prevent reactivation of infection.

The measles work has shown that the immune suppression associated with infection is not due to destruction of lymphocytes, but is paradoxically associated with immune activation of T lymphocytes that secrete cytokines that suppress cellular responses. She has also shown that measles virus RNA persists in lymphoid cells and tissue for months after the rash has resolved and that this persistence is associated with multiphasic waves of T cell activation and continued maturation of the antibody response. Viral persistence may be necessary to establish the life-long protective immunity characteristic of recovery from measles.

Griffin is a member of numerous professional societies including the American Association of Immunologists, the American Society for Clinical Investigation, the Infectious Disease Society of America (fellow) and the American Association for Advancement of Science (fellow; Chair Med-

ical Sciences section). She has served as president of the American Society for Microbiology, the American Society for Virology, the Association of Medical School Microbiology and Immunology Chairs and US Chair for the US-Japan Cooperative Medical Sciences Program. She has served on numerous private and federal advisory committees including the Virology Study Section, NIH; National Multiple Sclerosis Society Advisory Committee on Research and Medical Advisory Board; Microbiology and Infectious Diseases Research Advisory Committee, NIAID (chair 1992-1994); Board of Scientific Councilors, NINDS; Board of Scientific Councilors, NIAID (co-chair); NIAID Advisory Council; WHO Steering Committee on Respiratory Viruses; US-Japan Panel on Viral Diseases (chair); FDA Vaccine and Related Biological Products Advisory Committee, Howard Hughes Medical Institute Scientific Review Board. She was co-director of the graduate program in Cellular and Molecular Medicine at Johns Hopkins (1993-1998). Griffin has served on the editorial boards of *Virology*, *Intervirology*, *Microbial Pathogenesis*, *Virus Research*, *Journal of Virology* (associate editor) and *Science* and is currently on the boards for *mBio*, *Current Opinion in Virology* and *Proceedings of the National Academy of Sciences*.

She has received the Alumni Achievement Award, Augustana College (1985); Javits Neuroscience Investigator Award (1990); International Society for NeuroVirology Pioneer Award (2009); University of Wurzburg Rudolf Virchow Medal (2010); Stanford University Wallace Sterling Lifetime Alumni Achievement Award (2011); Forbes Magazine Forty Women over 40 (2014), FASEB Excellence in Science Award (2015) and Maxwell Findland Award (2016). She has been elected to the American Neurological Association (2000), American Academy of Microbiology (2004; board of governors 2009-2014), Institute of Medicine/National Academy of Medicine (2004; Council 2012-2018), National Academy of Sciences (2004; council 2010-2013, vice-president 2013-present) and Maryland Women's Hall of Fame (2009).

William R. Hazzard, MD

William Russell (Bill) Hazzard is noted for having initiated three academic programs in Gerontology — at the University of Washington, Johns Hopkins University School of Medicine, and Wake Forest University School of Medicine — when there was no American precedent upon which to build

such programs.

Hazzard was born on September 5, 1936 in Ann Arbor, Michigan, where he was raised in a research-oriented family (both parents held Cornell PhDs) and received a strong academic education in the public schools of that quintessential college town. His father, Albert S. Hazzard, director of the Institute of Fisheries Research on the UM campus, was his first research mentor as champion of the catch-and-release approach to trout conservation. Like his parents, Hazzard attended Cornell University in Ithaca, NY, where he majored in zoology on a pre-medical course and was introduced to biomedical research by Samuel L. Leonard, a PhD reproductive endocrinologist.

His interest in research was further encouraged during medical school at Cornell by a strong clinical faculty, including Jerome Barondess, Marvin Schlesinger, Ed Hook and especially the study of human lipid metabolism and atherosclerosis by “Pete” Ahrens at Rockefeller Institute. Hazzard graduated with honors in 1962, and remained at New York Hospital for his medical internship (1962-63).

He was drafted into the Navy, where he served for two years at the Camp Lejeune Navy Hospital as a general medical officer, principally caring for the wives of marines, where he became fascinated with the metabolic side-effects of the newly-introduced oral contraceptives. This triggered a lifelong interest in the hormonal modulation of human lipid and carbohydrate metabolism and cardiovascular disease by sex hormones and ultimately an enduring interest in the biological basis of the gender differences in longevity.

He was recruited to Seattle by Robert H. Williams, famed endocrinologist and first chairman of medicine at the University of Washington. There he completed his medical residency (1966-67) and fellowships in Endocrinology and Metabolism, first under Williams at University Hospital and later and most transforming, at the Seattle VA Hospital in the laboratory led by Edwin L. Bierman and Dan Porte, in studies of patients with obesity, diabetes, and hyperlipidemia. There Hazzard pursued two problems, the metabolic effects of oral contraceptives in normal volunteers and the basis of a rare form of hyperlipidemia (“broad-beta disease”, Type III in the famous classification system of Frederickson, Levy, and Lees). These two avenues converged when Hazzard discovered that estrogen improved normalized lipoprotein patterns in women with Type III, proving that the blockade

in removal of triglyceride- and cholesterol-rich remnant intermediates in the catabolic cascade of chylomicrons and VLDLs was ameliorated by estrogens. The apex of Hazzard's research productivity, however, coincided with his contributions to the studies of a recently arrived fellow in Medical Genetics, Joseph L. Goldstein, who took by storm the laboratories of both Bierman at the VA, the Lipid Research Clinic at Harborview Medical Center (where Hazzard had recently moved as assistant professor), and the division of Medical Genetics led by Arno Motulsky in studies of 500 3-month survivors of myocardial infarction in King County reported by Goldstein *et al.* in a landmark trilogy published in the *Journal of Clinical Investigation* in 1973, entitled, "The Genetics of Hyperlipidemia in Cardiovascular Disease." Goldstein's precocious success was prescient of his sterling career in partnership with Michael Brown at Southwestern Medical School in Dallas that led to their receipt of the Nobel Prize in Physiology or Medicine 12 years later.

The arc of Hazzard's career was to change when he accepted the challenge proffered by department chairman Petersdorf to assume leadership of a nascent program in gerontology and metabolism started at the VA by Bierman and expand it into a full division of Gerontology and Geriatric Medicine, as recommended by his own mentor, Paul Beeson, who had recently returned from Oxford to Seattle as Distinguished Physician at the VA. Trusting in Petersdorf, Bierman, and Beeson for support and advice, and early successes resulted in his timely promotion to professor, election to prestigious societies such as the American Society of Clinical Investigation, Association of American Physicians, and, ultimately, the Institute of Medicine.

Hazzard's career thus pivoted to addressing this new challenge, enhanced by a sabbatical year in Oxford and London imbedded in the British approach to geriatric medicine. Informed by this experience, Hazzard returned to Seattle to develop his first of the three models of academic geriatric program development that were to consume his remaining years in academic medicine. In each case these were focused in attracting the best and the brightest talent, especially fellows, to this new program, providing dual training in clinical geriatric medicine and rigorous clinical research, and encouraging graduates to pursue academic careers in this new field wherever they could succeed and expand the ranks so limited in young leaders. Based at Harborview Medical Center, he initiated a clinical geriatric program while continuing a parallel (lipoprotein) research program as a nascent division; there he flourished for 7 years, attracting fellows, ad-

vancing clinical and laboratory lipoprotein research, and initiating clinical services in a geriatrics clinic and a new wing of Harborview with special geriatric programs and facilities.

At that juncture Hazzard accepted the second challenge, recruited by Victor McKusick as associate director (vice-chairman) of the department of medicine at Johns Hopkins, to launch a new program in gerontology and geriatric medicine from a small division of (General) Internal Medicine at the Johns Hopkins medical campus while linking it with the already promising programs in aging at the campus of the Baltimore City Hospital (BCH), loosely affiliated with Hopkins. There, while supporting the department at the main Hopkins hospital as vice-chairman and focusing on the students and residents on medical services and the Division of Internal Medicine at the Wolfe Street campus, Hazzard promoted development of the aging program principally at BCH, with exceptional clinical and educational leadership by John Burton, and research at the GRC by Reubin Andres and newly recruited clinical investigator Andrew Goldberg. This rapidly became one of the leading Geriatric Medicine programs in the US, attracting future leaders like Linda Fried, Jeremy Walston, and Walt Ettinger to the field. During that interval Hazzard was elected to membership in the Interurban Clinical Club and the Clinical and Climatological Society. That also coincided with publication of the first edition (With Andres and Bierman) of what has become Hazzard's *Geriatric Medicine and Gerontology*, the leading American textbook in this still evolving discipline (now in its 7th edition).

In 1986 as his academic career approached its zenith, Hazzard became chair of the Department of Internal Medicine at the Bowman Gray School of Medicine in Winston-Salem, NC with the explicit goal of building the academic reputation of the institution around the theme of aging — “gerontologizing” the medical school and university — in an “all-hands” effort to disseminate the science and clinical medicine of caring for an aging population of Americans born in the post WW2 era. This culminated a decade later with the opening of the J. Paul Sticht Center on Aging and Rehabilitation adjoining the North Carolina Baptist Hospital and Wake Forest School of Medicine in a continuing crucible of scientific, educational, and clinical activities focused on the aging process and care of the approaching wave of aging baby-boomers. A concurrent extramural extension of that approach coincided with Hazzard's leadership activities in the American Board of Internal Medicine, the American Geriatric Society, the Gerontological Society of America, the Association of the Professors (Chairs) of

Medicine, and the national dissemination of gerontological expertise and career development through such John A. Hartford Foundation and NIA programs as the Paul B. Beeson Scholars in Aging and a series of Geriatric Education Retreats (“GERs”) to stimulate research and education in aging and geriatrics throughout American academic health centers.

Upon retiring to emeritus status from Wake Forest in 1999, Hazzard’s career continued full circle with his return to Seattle, the University of Washington, the Division of Gerontology and Geriatric Medicine, and VA Puget Sound Health Care System as director of geriatrics and extended care for a decade before retiring to emeritus status — and once again coming full circle once to his current position as professor of internal medicine at Wake Forest with an office in the J. Paul Sticht Center on Aging.

Gerald S. Lazarus, MD

Gerald S. Lazarus was born in New York City on February 16, 1939. He is currently professor of dermatology and medicine and the founder of the John Hopkins Wound Healing Center. Before his move to Johns Hopkins, Lazarus held endowed professorships and chaired the dermatology departments at Duke University and the University of Pennsylvania, where his department was the top recipient of NIH support in cutaneous biology. As dean and CEO at the UC Davis Medical School and Health System, he organized multiple multidisciplinary research programs and, in cooperation with the School of Veterinary Medicine, led research on animal models of human disease and focused on molecular approaches. Between 1999 and 2002 he lived in Beijing with his wife, Audrey Jakubowski, where he served as an adviser to the Minister of Health of the People’s Republic of China and as senior professor at the Peking Union Medical College.

During his tenure at Johns Hopkins, he has been instrumental in developing collaborations with Walter Reed, the National Naval Medical Center, and the Center for Biofilm Research at Montana State University. He has published extensively on collagen metabolism, proteinase biochemistry, medical education, the bacterial ecology of chronic wounds using metagenomic methods, and the effectiveness of clinical interventions in chronic wound care.

After graduating from Colby College, he graduated from George Washington University School of Medicine with distinction. He did his internal

medicine training at the University of Michigan, followed by three years of connective tissue research at the NIH. He then took dermatology training at Massachusetts General Hospital, where he was the chief resident in dermatology at Harvard Medical School. He was awarded the Carl Herzog Fellowship and an ARA Junior Faculty Award, which allowed him to do further research training at the Strangeways Research Laboratory at the University of Cambridge, where he became a fellow at Clare Hall.

He is the author of over 300 scholarly papers and 7 books and has received multiple awards for research, distinguished teaching, and mentoring younger researchers — most notably the D. Martin Carter Award. As the founding president of the Milstein Medical Asian American Partnership Foundation, he developed medical and scientific partnerships between leading American and Chinese universities. He is a member of the American Society for Clinical Investigation and the Association of American Physicians and has served as president of the Society of Investigative Dermatology and as an associate editor of the *Journal of Investigative Dermatology*. He has been a member of the board of directors of the American Academy of Dermatology. Lazarus currently serves on the boards of the Milstein Medical Asian American Partnership Foundation, the American Skin Association, and the National Endowment for the Humanities Trust. He recently served a nine-year term as a trustee of George Washington University and vice chair of the medical center committee.

Stephen B. Liggett, MD

Stephen B. Liggett was born November 13, 1954, in Pensacola, FL. He obtained a BS in physics from the Georgia Institute of Technology and an MD from the University of Miami School of Medicine. He served his internship and residency in internal medicine, and his fellowship in pulmonary and critical care medicine, at Washington University School of Medicine and Barnes Hospital in St. Louis, MO.

This was followed by a laboratory-based postdoctoral fellowship at the Howard Hughes Medical Institute at Duke University, under the mentorship of Robert Lefkowitz (who won the Nobel Prize in Chemistry in 2012). He subsequently became an assistant professor of medicine and pharmacology at Duke University, then moved to the University of Cincinnati College of Medicine, where he served as the Taylor Endowed Professor of Medicine, Pharmacology and Molecular Genetics. He was also chief of the

pulmonary and critical care division. In 2005 he moved to the University of Maryland School of Medicine, where he was professor of medicine and physiology. In 2012 he moved to the University of South Florida College of Medicine in Tampa, FL, to serve as the vice dean for research and associate vice president for personalized medicine at USF Health. He is also professor of medicine and molecular pharmacology and physiology.

Liggett chose medicine as a career based on an early influence from his maternal grandfather, who was a physician in Pensacola, FL. During his undergraduate studies at Georgia Tech, he became interested in the physics of the cell and changed his degree program from theoretical to applied physics. At Washington University he was encouraged to pursue investigative medicine by David Kipnis (then chair of medicine), William Daughaday, and Philip Cryer. The critical influence came from the postdoctoral fellowship with, and mentoring by, Bob Lefkowitz at Duke. This occurred during the dawn of molecular biology, when the structure-function relationships of G protein-coupled receptors (GPCRs) were being to be defined. His excitement, enthusiasm, and intuition were contagious and gave rise to a large group of successful investigators worldwide.

This merger of classic pharmacology with molecular biology remains a cornerstone of Liggett's current research. His laboratory studies the fundamental biology and structure-function relationships of GPCRs as they relate to heart (chronic heart failure) and lung (asthma and COPD) disease. These endeavors include studies of the basic mechanisms of signal transduction and agonist and antagonist interactions in cells, human polymorphism discovery in candidate genes and their characterization *in vivo* and *in vitro*, the production of lung- and heart-specific transgenic mice, and omics-based drug discovery.

Charles Julian Lowenstein, MD

Charles J. Lowenstein was born in Boston, MA, in 1960. He graduated from Harvard College in 1982 and received his MD from the Harvard Medical School in 1986. His clinical training included a medical residency at Massachusetts General Hospital and a cardiology fellowship at the Johns Hopkins University School of Medicine. He then joined the faculty in the Division of Cardiology in the Department of Medicine at the Johns Hopkins University School of Medicine in 1993. He was promoted to professor at Hopkins in 2004 and awarded the Clarence Doodeman Professorship in

Cardiology in 2006. Lowenstein then became the chief of cardiology and the director of the Aab Cardiovascular Research Institute at the University of Rochester School of Medicine and Dentistry in 2009. He was awarded the Paul N. Yu Professorship in Cardiology in 2009.

Lowenstein began his research career as a postdoctoral fellow in the laboratory of Solomon Snyder in the Department of Neuroscience at the Johns Hopkins University School of Medicine. He assisted in cloning the neuronal nitric oxide synthase (NOS) cDNA, then cloned the inducible NOS (iNOS) cDNA. As an assistant professor, Lowenstein characterized the 5'-untranslated region of the iNOS gene. He then studied the role of iNOS and NO in innate immunity, identifying pathways through which NO inactivates viruses.

As an associate professor Lowenstein defined the role of endothelial NOS (eNOS) in ischemia and reperfusion injury in the heart. He also explored the role of iNOS in transplant vasculopathy. As a professor, Lowenstein discovered that NO inhibits vascular inflammation by blocking endothelial exocytosis of pro-inflammatory granules. He has continued to explore the molecular regulation of exocytosis and the role of granule secretion in vascular inflammation.

From 1989 to 1994 Lowenstein held a physician-scientist award from the NIH. He was awarded a National Established Investigator Grant from the American Heart Association in 2001. He received the Sir William Osler Young Investigator Award from the Interurban Clinical Club in 2003 and became a member of the Interurban Clinical Club in 2007. He has received grant support from the National Institutes of Health and the American Heart Association. He has served as a charter member of the NIH NHLBI Atherosclerosis and Inflammation of the Cardiovascular System Study Section.

Susan M. MacDonald, MD

Susan M. MacDonald was born on September 3, 1950, in Springfield, MA. She received her BS degree in chemistry cum laude from Regis College in 1972 and her MD degree from the University of Massachusetts Medical School in 1980. She did her residency training in internal medicine at the Johns Hopkins Hospital (1980–1983) and a fellowship in clinical rheumatology (1983–1984), was assistant chief of service on the Osler Medi-

cal Service at Johns Hopkins Hospital (1984–1985), and did a second postdoctoral research fellowship in the Division of Allergy and Clinical Immunology at Johns Hopkins (1985–1987). MacDonald joined the faculty of the Department of Medicine at Johns Hopkins University School of Medicine as an assistant professor in 1987, was named full professor in 2004, and currently remains at Johns Hopkins.

Both of her parents, although only high school educated, instilled in her the importance of higher education as the key to success. Her father gave her a black notebook embossed with the word “THINK” in gold when she was a child. Her mother insisted that reading was the key to higher education. MacDonald was the first person in her family to graduate from college. She chose to pursue medicine because she believed it allowed for a thoughtful approach to advancing the care of patients. Her interest in investigative medicine solidified between college and medical school, in the laboratory of K. Frank Austen at Harvard, where she learned how much she loved the idea of becoming a physician-scientist. During her second postdoctoral fellowship in allergy and clinical immunology at Johns Hopkins, the division director, Lawrence Lichtenstein, became her mentor.

MacDonald has enjoyed a distinguished career in academic internal medicine. Her laboratory was the first to clone a novel cytokine, termed histamine-releasing factor (HRF) (results published in *Science*, 1995). Her laboratory demonstrated that HRF in vitro activates cells important in allergy, namely basophils and eosinophils, and inhibits T cells. They also showed that HRF is found in vivo in biologic fluids in the late phase of an allergic reaction. Additionally, her laboratory uncovered a molecular basis for the hyperreleasability of basophils from allergic and asthmatic subjects, who have decreased levels of the intracellular signaling molecule SHIP, a phosphatase. Her work also focused on producing an HRF-inducible transgenic mouse that mimics signs of human allergic disease. Throughout all of her work, she maintained her status as an active, NIH-funded investigator.

MacDonald is a fellow of the American Academy of Asthma, Allergy and Immunology (AAAAI); a member of the American Association of Immunologists; was named to the executive council of the Collegium Internationale Allergologicum, a prestigious international allergy and immunology society with limited elected membership; and was elected to the membership in the Interurban Clinical Club. She has served as a guest editor for Springer’s *Seminars in Immunopathology* and for *Immunology and Allergy Clinics of North America* and has been a guest author of a chapter in

Current Opinion in Immunology. She has served as a scientific program chairperson for the AAAAI and as the first chair of the AAAAI Leadership Institute (2012–2014), which was established to groom future AAAAI members as leaders in the academy. Recognition of her accomplishments in allergic disease research includes being one of the first recipients of the AAAAI Women Physicians Leadership in Allergy Award (2001), the AAAAI Women's Involvement Special Recognition Award (2005), and the AAAAI Gail G. Shapiro Honorary Special Recognition Award (2008). She has served on the FDA Allergenic Products Advisory Committee and the academic advisory board for Pfizer's Visiting Professorships in Allergic Diseases and Asthma. Additionally, she served on NIH study sections and the VA Merit Review Committee for immunology for four years.

MacDonald's scientific accomplishments are particularly notable because of her ability to build scientific momentum while devoting substantial amounts of time, energy, and creativity to issues of faculty development. Her passion for mentoring junior faculty and fellows, both men and women, began when she became a key charter member of the Task Force for Women's Academic Careers in Medicine in the Johns Hopkins Department of Medicine, under department chair Jack Stobo. When she chaired this task force (1995–1997), she implemented a mentoring program for women fellows that exists today. In 2013 she and the current chair of the task force received an Association of American Medical Colleges organizational award for their work on the task force. Under the subsequent department chair, Edward Benz, she served as deputy director for faculty development (1997–2001). Since 2002 she has served as the first woman associate chair/vice chair of the Department of Medicine, the largest department in the School of Medicine, under Myron (Mike) Weisfeldt. For this administrative work, MacDonald was awarded the Women in Leadership Award from the Johns Hopkins University Women's Network (2002) and the Department of Medicine's David M. Levine Excellence in Mentoring Award (2003), and in March 2009 she was named the first recipient of the Vice Dean's Award for the Advancement of Women.

In April 2013 she was appointed as interim director of the Division of Allergy and Clinical Immunology, one of the largest freestanding allergy divisions in the country, known nationally and internationally for its focus on human allergic diseases.

Eduardo Marbán, MD, PhD

Eduardo Marbán is an international leader in cardiology and a pioneering heart researcher. His 25-plus years of experience in patient care and research into heart disease have led to key discoveries in gene and stem cell therapies and new drug treatments for heart attacks, heart failure and strokes. Those discoveries have formed the basis for multiple startup companies.

Marbán was born in Havana, Cuba on June 27, 1954, and was brought to the USA as a political refugee by his parents at age 6. He attended public schools through high school and later Wilkes College, where he earned a BS in Mathematics. Thereafter, Marbán matriculated at the Yale University School of Medicine in a combined MD/PhD program. Postgraduate training took him to the Osler Medical Service at the Johns Hopkins University, where he eventually spent 25 productive years. During his tenure there, he served in a variety of academic and research positions, including Chief of Cardiology.

His interest in research arose as an undergraduate. In medical school, an early influence was Dr. Barry Zaret, who first exposed Dr. Marbán to the rewards and challenges of clinical cardiology. The clinical richness in cardiology was seemingly unmatched by fundamental understanding. At the time, the physiology of the cardiovascular system was taught in terms of lead pipes and rheology, as if there were no underlying biology. Marbán thought there must be more to it, and sought out Richard W. Tsien as a PhD mentor. Marbán pursued fundamental studies of excitation-contraction coupling in heart muscle. The biology was indeed rich, and rewarding. In the course of Marbán's thesis research, Roger Tsien, then at Cambridge, visited the lab with some new microelectrodes that he had developed to measure intracellular calcium concentration. A collaborative project arose. The result was a *Nature* paper with Marbán as first author and two prominent mentors: Richard W. Tsien, who would go on to join the National Academy of Sciences, and Roger Tsien, who would later win a Nobel Prize. Thus, Marbán's standards for scholarly accomplishment were high from the outset.

After residency and cardiology fellowship training, Marbán began his independent scientific career as a cellular electrophysiologist with an interest in basic ion channel biology. Over the following years, nourished by continuous NIH funding, he has pursued an investigative trajectory increas-

ingly motivated by questions of relevance to heart disease (ischemia, heart failure and arrhythmias). Marbán approached all of these disease-motivated challenges from the unique perspective of a cellular physiologist/clinician, a feature which continues to define his thinking to the present day. The Marbán laboratory elucidated the fundamental pathogenesis of myocardial stunning, pioneered the concept of gene therapy to alter electrical excitability, and created the first *de novo* biological pacemaker as an alternative to electronic pacemakers. He first became interested in stem cells in 2002, building upon his work on biological pacemakers. Since 2004 the lab has been intensively studying cardiac progenitor cells, their origins and their therapeutic potential. The basic work has come full circle in that Marbán's cardiac-derived cell products form the basis for 3 NIH-funded clinical trials: one completed (CADUCEUS), and two ongoing (ALLSTAR, DYNAMIC). The CADUCEUS trial was the first to show that cell therapy can repair "irreversible" tissue damage caused by heart attacks, ushering in the concept of therapeutic regeneration in humans.

In 2007, Dr. Marbán became founding director of the Cedars-Sinai Heart Institute, a multidisciplinary entity which brings together adult and pediatric cardiologists, cardiac surgeons, imaging specialists and researchers to foster discovery and enhance patient care. The institute is built on a long tradition of excellence and innovation at Cedars-Sinai, including the invention of the Swan-Ganz catheter.

Among the many honors Dr. Marbán has received are the Basic Research Prize of the American Heart Association (AHA), the Research Achievement Award of the International Society for Heart Research, the Gill Heart Institute Award and the Distinguished Scientist Awards of the AHA and the American College of Cardiology.

Guy M. McKhann, MD

Guy Mead McKhann was born in Boston Massachusetts on March 20, 1932. He lived in Boston, Ann Arbor, Detroit, and Cleveland, while his father, Dr Charles Fremont McKhann, a Professor of Pediatrics, occupied various academic posts. After graduating from University School in Cleveland, McKhann attended Harvard College for 3 years and then moved on to Yale Medical School, graduating in 1955.

After a medical internship at New York Hospital, and a year of pediatric resi-

dency at Johns Hopkins, McKhann spent 3 years at the NINDS, NIH. There he first worked with Dr. Richard Masland in studies of cerebral palsy, and then switched to the Laboratory of Neurochemistry with Don Tower. While there he was greatly influenced by Milton Shy, an excellent clinical investigator. Following the NIH, McKahnn returned to Boston for a residency in Adult and Pediatric Neurology at the Massachusetts General Hospital.

His first academic job was at Stanford in Pediatrics and Medicine (Neurology). Stanford at that time was an incredibly dynamic place. Interactions between departments were wide open, and even a young upstart interacted with people like Dave Hamburg, Josh Lederburg, Eric Shooter, and Norman Kretchmer. When McKahnn came to Hopkins, he tried to create the interactive atmosphere that existed at Stanford. McKahnn led the neurology department at Hopkins for almost 20 years, as it went from being non-existent to being the number three or number one department in the country, depending on the year. Following giving up the Department, he started a research institute at Hopkins, The Zanvyl Krieger Mind/Brain Institute. He was the Acting Associate Director for Clinical Research and Acting Clinical Director at the NINDS, while Gerry Fischbach was Director.

McKhann's exposure to research began at an early age, as he was a substitute animal boy in his father's department during high school. In addition, he was exposed to an unusual group of inventors who operated near his house in Cleveland. Jim Rand was a free-lance inventor, who attracted an amazing group of inventors to his lab, by making his facilities available to them at night. Thus McKhann was exposed to a diverse group of projects such as the development of an alternating pressure mattress to prevent bed sores, an all-day diaper, and a machine that would deliver a single cup of coffee. From this group he learned that there were no boundaries to research, and that research could be great fun.

McKhann's formal training in research began at the NINDS, with Don Tower. There he worked on vitamin B6 deficiency, the role of gamma-aminobutyric acid in the brain, and studies of ammonia toxicity. At MGH, he started a long-term association with Hugo Moser, and his wife, Ann, on metachromat leukodystrophy and the metabolism of sulfolipids. This association continued when Hugo and Ann moved to the Kennedy Institute at Hopkins.

His major contributions came late in his career in three areas: The criteria for Alzheimer's disease; the delineating of a form of the Guillain-Barre

Syndrome (GBS) in China, and the cognitive and neurological outcomes related to heart surgery, particularly coronary bypass grafting (CABG). In 1984, he led a group that defined the clinical and cognitive criteria for Alzheimer's disease.

The studies of GBS in China started by accident. During a visit as a member of a delegation to the Beijing Children's Hospital, he was shown a ward full of paralyzed young children. His first reaction was to say "I didn't realize that they still had so much polio". His hosts' response was "that is not polio, it's the Guillain-Barre Syndrome, we have it every summer". Thus a research project was born that included Jack Griffin, Dave Cornblath and Tony Ho at Hopkins, Art Asbury and Irv Nachamkin at Penn, and C.Y. Lee at the 2nd Teaching Hospital in Shijizhuang, China. In summary, over 9-10 years, the group established that this was a yearly summer epidemic, involving children from rural communities, not cities, in northern China. The form of GBS, in contrast to the US and Europe forms, was an acute motor neuropathy. The mechanism was a form of molecular mimicry in which children are infected with *Campylobacter jejuni*, carried by chickens. They then develop antibodies to that organism that attack the person's motor axons, producing the axonal form of GBS.

The studies of neurological outcomes after cardiac surgery were carried out at Hopkins with Bill Baumgartner of cardiac surgery, Scott Zeger from statistics, Ola Selnes a neuropsychologist in the neurology department, and Maura Grega, an outstanding cardiac nurse. This group set out to answer whether there were long-term cognitive changes after surgery, and if so, were they associated with being on the bypass pump. They set up a four arm study: those undergoing conventional CABG, those undergoing surgery without the use of the bypass pump, those receiving medical care for heart disease, and a heart healthy control group. These 4 groups were followed annually over 6 years. The conclusion was that there were long-term cognitive changes but they were not confined to the CABG group, but occurred in all cardiac patients. Thus, the cognitive changes were related to underlying cardiac, and brain, vascular disease. These areas of research occurred after McKhann's 65th birthday and reinforced his views on mandatory retirement.

After being an assistant then associate professor at Stanford, McKhann became the founding director of the Department of Neurology at Hopkins. After that he became the founding director of the Zanyvl Krieger Mind/Brain Institute, at Hopkins. He has received a number of awards, includ-

ing John and Mary Markle Scholar in Academic Medicine (1964), Johns Hopkins Medical School Teaching Award (1964), Macy Faculty Award (1982, Institute of Medicine, National Academy of Sciences (1991), Honorary MD, Hebei Medical College, Shijiizhuang, PRC (1996), Fellow, Royal College of Surgeons (2002), American Academy of Neurology Presidential Award (2014), and Harvard-Mahoney Neuroscience Institute, David Mahoney Prize (2014)

Edward Miller, MD

Edward Miller was born on February 1, 1943, in Rochester, NY. He received his AB from Ohio Wesleyan University and his MD from the University of Rochester School of Medicine and Dentistry. He served as chief executive officer of Johns Hopkins Medicine and 13th dean of the Johns Hopkins University School of Medicine, from which he retired on June 30, 2012.

As part of Miller's vision to improve health care access through the development of a regional, integrated health care delivery system, Howard County General Hospital was acquired and integrated into Johns Hopkins Medicine. Miller also led efforts to integrate into Johns Hopkins Medicine the Suburban Hospital and Health System (Bethesda, MD), Sibley Memorial Hospital (Washington, DC), and All Children's Hospital (St. Petersburg, FL).

During his tenure as CEO, Johns Hopkins Medicine broadened its international presence to include relationships with hospitals and other health care-related institutions in the Americas, Europe, the Middle East, and Asia, including an agreement to help Malaysia develop its first fully integrated, private four-year graduate medical school and teaching hospital.

One of his most significant accomplishments as dean and CEO of Johns Hopkins was the massive rebuilding and renovation projects that transformed the East Baltimore medical campus into a medical center in which the most modern of buildings sit among the most historic. This transformation included one of the largest hospital construction projects in the nation — that of two new, state-of-the-art hospitals for adult and pediatric patients. In addition, clinical and research buildings for the Sidney Kimmel Comprehensive Cancer Center, the Broadway Research Building, the Anne and Mike Armstrong Medical Educational Building, and the new Robert H. and Clarice Smith Building (part of the Wilmer Eye Institute) were also built during his time at Johns Hopkins.

Under Miller's direction a new curriculum, termed "Genes to Society," was developed and introduced for the School of Medicine, representing the first wholesale academic overhaul at the school in two decades.

An anesthesiologist who has authored or co-authored more than 150 scientific papers, abstracts, and book chapters, Miller joined Johns Hopkins in 1994 as professor and director of the Department of Anesthesiology and Critical Care Medicine. He is a member of the Institute of Medicine of the National Academy of Sciences and is a fellow of the Royal College of Physicians and the Royal College of Anaesthetists. He and his wife, Lynne, are the parents of four adult children.

Neil R. Powe, MD, MPH

Neil R. Powe was born in Philadelphia, PA, on May 11, 1955. He attended Central High School in Philadelphia, received a BA degree cum laude from Princeton University in 1976, and jointly received an MD degree from Harvard Medical School and an MPH degree from Harvard School of Public Health in 1981. This was followed by residency in internal medicine and fellowship in the Robert Wood Johnson Clinical Scholars Program at the Hospital of the University of Pennsylvania under the mentorship of John Eisenberg. Hired as an instructor at the Johns Hopkins School of Medicine in 1986, he rose to full professor of medicine in 1998 and was appointed a Johns Hopkins University Distinguished Service Professor in 2008.

Powe's interest in medical science developed at Princeton, where his senior thesis advisor on red blood cell differentiation was Harold Weintraub, the noted late molecular biologist and pioneer of the linkage between gene expression and cell differentiation. At Hopkins in 1989, Powe led a national evaluation of the effectiveness of the then-new biotechnology recombinant human erythropoietin for treatment of anemia in patients with end-stage renal disease (ESRD). This work showed that effectiveness in routine clinical practice differs from efficacy in early-phase clinical trials. He went on to create, as principal investigator, a patient outcomes research team called the Choices for Health Outcomes in ESRD (CHOICE) Study, the first large national prospective study of dialysis care for incident ESRD patients. Since its inception in 1994, CHOICE has been funded continuously for 20 years and over 80 manuscripts have been published that involved collaborators from many institutions. These manuscripts address fundamental issues in etiology, prevention, risk factors, diagnosis, therapy,

prognosis, complications, access to care, quality of care, and resource use/treatment costs for kidney disease. Powe is also principal investigator of the Centers for Disease Control and Prevention's Chronic Kidney Disease Surveillance System, a national effort designed to prevent the progression of kidney disease, a disease that disproportionately affects minorities. Powe has worked to push the frontiers of knowledge about health care delivery and disparities in care — and to influence optimal allocation of health care resources by providers, payers, and the federal government — through the application of rigorous methods in clinical epidemiology, comparative effectiveness, and outcomes research. His work has also elucidated health disparities.

In 1998 Powe was asked to lead the Welch Center for Prevention, Epidemiology and Clinical Research at Johns Hopkins, following Paul Whelton's departure, and to serve as director of doctoral and masters degree programs in clinical epidemiology. Bridging the Johns Hopkins School of Medicine and the School of Public Health, he catapulted the Welch Center to become a major center of learning for medicine and public health students, residents, fellows, and junior faculty, thereby growing it in prestige, faculty, funding, trainee reach, and diversity. As principal investigator of two NIH Roadmap Programs in Clinical Research, he created rigorous training opportunities for students, fellows, and junior faculty. Powe has an unbridled enthusiasm for cultivating young physician-scientists who are addressing major problems in science, health, and health care delivery.

In 2009 Powe was called to serve as leader of the University of California, San Francisco, Medicine Service at San Francisco General Hospital (SFGH), a leading medicine department in a public hospital with strong basic and clinical research programs. As chief of the largest department at SFGH, he oversees 765 faculty and staff dedicated to improving the health of the public through practice, education, and research. He has nurtured this department to become a top NIH-funded department of medicine in a public hospital. The research programs are focused on major public health threats, including those affecting the most vulnerable (e.g., ethnic minorities, persons of low socioeconomic status, immigrants, and the homeless). The faculty members of his department are internationally known for their work in HIV, tuberculosis, liver disease, lung injury, kidney disease, health disparities, and health communication. Powe creates a supportive foundation for their thriving careers through his passion to improve discovery, education, and clinical practice in medicine; improve the ways in which academic organizations function; enhance scholarship and multidisci-

plinary collaboration; and develop future talent and leadership.

Powe has received the John M. Eisenberg National Award for Career Achievement in Research from the Society of General Internal Medicine, the Belding Scribner Award from the American Society of Nephrology, the Garabed Eknayan Award from the National Kidney Foundation, the Distinguished Educator Award from the Association for Clinical Research Training, and the Diversity Award from the Association of Professors of Medicine and was selected to the Central High School of Philadelphia Hall of Fame. He has been elected to the American Society for Clinical Investigation, the Association of American Professors, the American Epidemiologic Society, and the Institute of Medicine of the National Academy of Sciences. He is a master of the American College of Physicians. He has served on the Secretary's Advisory Committee on Human Subjects Protection of the US Department of Health and Human Services, the NIH Clinical Center Board of Scientific Counselors, the National Center for Health Statistics Board of Scientific Counselors, and Institute of Medicine committees on conflicts of interest in medical research, pay for performance, comparative effectiveness research, and ESRD. He has testified before the US Congress on the prevention of kidney disease and the role of value science for medical innovations. Powe was the first African American at Johns Hopkins to become a full professor of medicine, to be appointed a University Distinguished Service Professor, and to become a full professor at Hopkins Bloomberg School of Public Health.

Cynthia L. Sears, MD

Cynthia L. Sears was born in Reading, PA, on January 24, 1955. She received a BS degree from Pennsylvania State University in 1975 and an MD from Thomas Jefferson College of Medicine in 1977 as part of the Pennsylvania State University–Thomas Jefferson College of Medicine five-year combined undergraduate–medical school program. This was followed by a residency in internal medicine at the New York Hospital (Cornell Medical School; 1977–1980), a year of general internal medicine fellowship at the New York Hospital (1980–1981) under the leadership of Mary Charlson and Jeremiah Barondess, a clinical year of infectious diseases fellowship at Memorial Hospital–Sloan Kettering Institute (1981–1982) under the leadership of Donald Armstrong, and a subsequent three-year clinical and research infectious diseases fellowship at the University of Virginia (1982–1985) under the leadership of Gerald Mandell. After completing her infec-

tious diseases fellowship at the University of Virginia (UVA), she joined the UVA infectious diseases faculty as an assistant professor for three years (1985–1988). In 1988 she was recruited to Johns Hopkins University School of Medicine (JHU SOM) by Mark Donowitz, the new chief of the Division of Gastroenterology, and by John Bartlett, chief of the Division of Infectious Diseases. In 2001 Sears was promoted to professor of medicine at JHU SOM and, in 2006 and 2010, joined the Department of Oncology (JHU SOM) and Department of Molecular Microbiology and Immunology (Bloomberg School of Public Health).

The pivotal experience that guided Sears's career in research occurred during her senior internal medicine residency year and subsequent fellowship year at the New York Hospital, when she worked as part of the Cornell team at the Khao-I-Dang Holding Center located near Aranyaprathet, Thailand. Within this seven-square-mile enclosure, nearly 180,000 Cambodian, Vietnamese, and Burmese refugees were housed. She was deeply influenced and inspired by her experiences working with the refugees in Khao-I-Dang. Here she saw the profound impact of infectious diseases on the health of children and adults and took particular note of the adverse impact of diarrheal illnesses, including cholera. After her time at Khao-I-Dang, she was fortunate to meet Richard Guerrant, an individual passionate about improving the health of children in under-resourced areas of the world; she ultimately developed her initial research in his laboratory at UVA. With Guerrant as her mentor, Sears began her studies on the pathogenesis of bacterial diarrheal disease, initially focusing on bacterial toxin biology and pathophysiology. Her commitment to the field of infectious diseases was also profoundly influenced by her clinical experiences from 1979 to 1982, during the unfolding of what became the HIV epidemic in New York City. Her early experiences regarding the HIV epidemic led to a career-long commitment to this patient population, including conducting laboratory research on cryptosporidiosis and contributing to descriptions of opportunistic infections in HIV/AIDS.

The major focus of her research has been to understand how bacteria contribute to intestinal disease. Not long after her arrival at JHU SOM in 1988, R. Bradley Sack introduced Sears to enterotoxigenic *Bacteroides fragilis* (ETBF), a newly recognized bacterium that was identified as contributing to diarrheal disease in children in studies conducted by Sack in collaboration with Lyle Myles of Montana State University. Sack asked Sears to help identify an *in vitro* assay for ETBF, as the only assay available at the time to detect the biologic activity of ETBF was ligated intestinal loops in lambs.

Sears and her group successfully developed an in vitro colonic epithelial cell assay to identify ETBF and then pursued studies to purify the protein and to identify the gene encoding the detected in vitro cell-free biologic activity of ETBF. She discovered that the toxin secreted by *B. fragilis* (BFT) activates multiple colonic epithelial cell carcinogenic mechanisms, including E-cadherin cleavage, Wnt signaling, NF-kappaB signaling, oncogene expression, and DNA damage; these discoveries led to the novel hypothesis that ETBF colonization was an initiator or promoter of human colon cancer. Using the multiple intestinal neoplasia murine model, the Sears group demonstrated that ETBF strains are robust inducers of IL-17–dependent colon carcinogenesis; this was the first demonstration of the contribution of endogenous IL-17 to carcinogenesis, and the observation served as a springboard for studies of the contribution of IL-17 to oncogenesis. Human translational studies led by Sears then identified the *BFT* gene in the mucosa of nearly all human colon cancer, described the association of nearly all right colon cancer with colon mucosa biofilms, and provided the first link between a genetic subtype of human colon cancer (MSI) and expression in the tumor microenvironment of checkpoint molecules.

Her many professional honors include membership in Alpha Omega Alpha (1975), serving as an assistant chief resident during her residency at the New York Hospital (1980), membership in the American Society for Clinical Investigation (1996), election to the Interurban Clinical Club (2005) and serving as the club's president (2007–2008), selection as the Maxwell Finland Lecturer of the Infectious Diseases Society of America (2009), serving as president of the Anaerobe Society of the Americas (2010–2012), and presentation of numerous named university lectureships. Among the many professional societies to which she contributes, she is particularly proud of her service to the Infectious Diseases Societies of America (IDSA), for which she has served as chair of the annual meeting program committee (2002–2003), a member of the board of directors (2004–2007), vice chair of the IDSA Education and Research Foundation (2005–2007), treasurer of IDSA (2010–2015), and associate editor of the IDSA signature clinical journal, *Clinical Infectious Diseases* (2000–2016).

Theresa A. Shapiro, MD, PhD

Theresa Shapiro was born 25 November 1949 in Washington DC, the daughter of Army officers Ruth and Thomas Barry. By the age of 17 her family had moved 21 times, to postings that included Virginia, Kansas,

Pennsylvania, Washington State, North Dakota, and for four years, Germany. In 1972 she obtained a BS in Chemistry from Drexel University, in a work-study program that included nearly two years of research in industry and with a focus on synthetic organic chemistry. She attended Johns Hopkins for combined MD and PhD, the latter in Pharmacology (1976 and 1978, respectively). Graduate studies with pharmacologist Paul Talalay and molecular parasitologist Ernest Bueding on *Schistosoma mansoni* were the start of a career-long interest in new therapies for parasitic infections. After completing an internal medicine internship and residency at the University of Chicago, and concurrent Diplomate in Tropical Medicine from the University of London, in 1981 she returned to Johns Hopkins as an Assistant Professor. She has since remained at Hopkins, promoted through the ranks to Professor of Medicine, of Pharmacology and Molecular Sciences (School of Medicine), and of Molecular Microbiology and Immunology (School of Public Health).

Travels as a child in post-war Europe and the tropics led to Shapiro's first-hand appreciation of the health burden posed by infectious diseases, and her undergraduate research on the problem of devising chemical compounds that would be selectively toxic to tumors but not normal tissues, underpinned her choice of thesis research at Hopkins. The tremendous numbers of people with parasitic infections, intrinsically fascinating biology of parasites, and antiquity of many antiparasitic drugs, in conjunction with a general lack of pharmaceutical industry interest in this area, have made the discovery and development of antiparasitics particularly attractive for this academic clinical pharmacologist. Shapiro's work has ranged across the spectrum of pharmacology, with a focus on African trypanosomes (that cause sleeping sickness) and malaria.

Basic molecular studies utilizing chemical and genetic methods have validated the DNA topoisomerases and Hsp90 as vulnerable targets for antiparasitic drugs. She has discovered several new enzymes (including the trypanosome's structurally novel heterodimeric topoisomerase IB and a type IA mitochondrial topoisomerase with no ortholog in humans) and has studied the organization and replication of the massive and intricate network of thousands of interlocked DNA circles that constitute the mitochondrial genome of trypanosomes and related kinetoplastid pathogens. Her preclinical studies of promising drug leads have included chemical structure-activity analyses, scale-up synthesis, and animal toxicology evaluations. Her lab devised a novel in vitro system that exposes cells to dynamically changing drug concentrations, akin to those that occur in hu-

mans, in order to determine the pharmacokinetic governance of antimalarial and antitrypanosomal drugs. Clinical studies of experimental new drugs have included first-in-human Phase I trials, and Phase II efficacy trials in East Africa. Perhaps her most important contribution was the discovery, in an investigator-initiated study, of atovaquone's ability to prevent malaria in healthy volunteers challenged with *Plasmodium falciparum*-infected Anopheline mosquitoes. Deemed pivotal by the FDA for its approval of Malarone for malaria prophylaxis, this was the first (and to date, only) drug approved on the basis of its activity against liver-stage malaria parasites.

Since 2001 she has been the Wellcome Professor and director of the Division of Clinical Pharmacology at Johns Hopkins. This translational unit was established 60 years ago as a component of both the Department of Medicine and the Department of Pharmacology, and is dedicated to research, education and patient care, as they relate to the use of drugs in humans. Shapiro's contributions to the Division have included modernization of the analytical laboratories, bringing faculty and chromatography/mass spectrometry instrumentation that have made possible highly specific and sensitive measurement of drug and metabolite levels in human tissues and fluids obtained in clinical trials.

Shapiro was a Rockefeller Fellow and recipient of the Burroughs Wellcome Fund Scholar Award in Experimental Therapeutics. She is a fellow of the American Association for the Advancement of Science and member of the Association of American Physicians. She has twice been a member of the NIH MIDRC study section and ad hoc on many others; an Advisory Committee member and expert consultant to the FDA; a consultant to the US Pharmacopeia and Gates Foundation; and an Associate Editor of Pharmacological Reviews.

Carol O. Tacket, MD

Carol Tacket was born in Memphis, Tennessee on May 17, 1952. She received a BA degree from Wellesley College in 1974 and an MD from the Yale University School of Medicine in 1978. She completed a Residency in Internal Medicine at Yale-New Haven Hospital, under the Chairmanship of Samuel O. Thier. She served as an Epidemiology Intelligence Service officer in the Enteric Diseases Branch, Center for Disease Control, from 1981-83. The Branch was led by Paul Blake, MD and Mitchell Cohen, MD

While there, she investigated outbreaks of acute intestinal infections in the US and spent several months at the International Center for Diarrheal Disease Research, Dhaka, Bangladesh, where she studied the molecular epidemiology of shigellosis.

Because of her interest in enteric infections, Dr. Tacket came to the University of Maryland School of Medicine for a fellowship in infectious disease at the UM's Division of Infectious Diseases and the Center for Vaccine Development (CVD). There her clinical mentors included Frank Calia, Ellis Caplan, and John Warren. While working as an infectious diseases fellow with Myron Levine in the CVD, she identified and characterized a novel fimbrial colonization factor of enterotoxigenic *E. coli*. In 1986 she was hired as an Assistant Professor of Medicine in the Division of Geographic Medicine and Center for Vaccine Development at the University of Maryland.

With the support of a contract granted by NIAID to Dr. Levine, Dr. Tacket began conducting clinical research studies of novel oral vaccines against enteric infections, in collaboration with Mary Lou Clements at the CVD. Many of these studies involved delivery of an experimental vaccine by the oral route to healthy adult volunteers who resided on a research isolation ward in the University of Maryland Hospital. Typically such studies included an oral challenge with the infectious agent of interest to determine the protective efficacy of a vaccine or other biologic agent. These studies included challenges with *Vibrio cholera* O1 and O139, diarrheagenic *E. coli*, and *Shigella sonnei*.

Using the volunteer challenge model, Dr. Tacket conducted clinical studies of a number of novel live oral vaccines, e.g., vaccines against cholera, ETEC, and shigellosis. She led studies of the safety and prophylactic efficacy of numerous biologics, e.g., transgenic potatoes and transgenic corn expressing the nontoxic B subunit of *E. coli* enterotoxin, orally administered virus-like particle vaccines derived from norovirus capsid protein, and hyperimmune milk products against *E. coli*, *Shigella sonnei*, and *Cryptosporidium*. She also demonstrated the safety and immunogenicity of recombinant oral hybrid vaccines, such as tetanus toxoid administered in an attenuated *S. typhi* vector.

While at the CVD, Dr. Tacket led a trial of the first HIV vaccine rgp160, supported by NIAID, in collaboration with other Vaccine Testing and Evaluation Units in the U.S. She subsequently led a trial of immunotherapy us-

ing recombinant gp120 in individuals infected with HIV, in collaboration with Edmond Tramont at the UM Center for Biotechnology.

Immediately after 9/11, in response to bioterror threats, Dr. Tacket led the University of Maryland's role in a multi-center clinical trial of the venerable smallpox vaccine which had been stored for many decades.

From 2001 to 2010, Dr. Tacket was the founding Program Director of the University of Maryland's General Clinical Research Center and Co-Program Director of Maryland's Multidisciplinary Clinical Research Career Development Program. These two core programs provided much needed infrastructure for the expansion of clinical research in all disciplines at the University of Maryland.

Dr. Tacket was drawn to medicine by her interest in human biology and by several role models in her family, including her father Hall S. Tacket and grandfather Spencer T. Snedecor. Dr. Snedecor participated in surveys of overseas hospitals for the World Council of Churches and stirred her interest in infectious diseases and international health. In continuance of this tradition, her daughter Elizabeth T. Rogawski, PhD, is leading epidemiologic research in Limpopo, South Africa, and her son David S. Rogawski, M.D., Ph.D. (2018) has identified novel proteins of therapeutic use in cancer.

Myron L. Weisfeldt, MD

Myron Weisfeldt was born on April 25, 1940, in Milwaukee, WI. Following two years at Northwestern University, he entered the five-year medical school program at Johns Hopkins University School of Medicine, receiving his AB degree in 1962 and his MD in 1965. In 1963–1964 he was a postsophomore fellow in the cardiovascular laboratory of Stanley Sarnoff at the NIH. He was an intern and assistant resident in medicine at the Columbia-Presbyterian Medical Center in New York from 1965 to 1967. The following two years were spent at the NIH Gerontology Research Center. He completed his training as a clinical and research fellow in cardiology at Massachusetts General Hospital (1970–1972). In 1972 he returned to Johns Hopkins as an assistant professor of medicine and director of the Peter Belfer Laboratory for Myocardial Research. In 1975 he was promoted to associate professor and in 1978 became a full professor, being named the Robert L. Levy Professor of Cardiology in 1979. From 1975 to 1991 he was

director of the cardiology division in the Department of Medicine at Johns Hopkins. In October 1991 Weisfeldt became the Samuel Bard Professor of Medicine, chairman of the department of medicine, director of the medical service and head of the Cardiovascular Center at the Columbia-Presbyterian Medical Center in New York City. In 2001 he returned to Johns Hopkins to assume the positions of William Osler Professor of Medicine, director of the Department of Medicine, and physician-in-chief of Johns Hopkins Hospital. On relinquishing these positions in 2014, he was named University Distinguished Service Professor by the Johns Hopkins University.

During medical school he did several summers of research in cardiovascular surgery in Milwaukee and spent a pivotal year in research training in cardiovascular physiology under Sarnoff at the NIH, experiences that led him to a career in clinically based physiological research dealing with the heart and circulation. During his subsequent two years at the NIH, he studied cardiovascular aging, an experience that led to a long-term commitment to understanding age-associated changes in the heart and circulation and their responses to drugs and stress, including exercise. While at Johns Hopkins his research interests included the study of reperfusion injury following a period of ischemia or low blood flow, study of the relaxation phase of cardiac contraction and the relationship of relaxation properties to heart failure, and study of the mechanisms of blood movement during cardiopulmonary resuscitation. In recent years he has been a strong proponent of public use of automated defibrillators. He coined the term “public access defibrillation” to describe this program.

Weisfeldt has served on numerous editorial boards, including those of the *Journal of Molecular and Cellular Cardiology* (1975–1981 and 1987–1989), the *Journal of Clinical Investigation* (1983–1988), *Circulation* (1978–1981 and 1981–2004), the *American Journal of Cardiology* (1981–1983), the *Journal of Cardiovascular Ultrasonography* (1982–1984), *Circulation Research* (1985–1994), and the *Journal of the American College of Cardiology* (1987–1992).

From 1989 to 1990 Weisfeldt served as president of the American Heart Association, and from 1987 to 1990 was chairman of the cardiology advisory committee of the National Heart, Lung and Blood Institute of the NIH. Weisfeldt is a member of numerous professional organizations, including the American Federation for Clinical Research, the American Physiological Society, the American College of Cardiology, the American Society for Clinical Investigation, the Gerontological Society, the International So-

ciety for Heart Research, the InterAmerican Society of Cardiology (first vice president, 1989–1991), the Association of University Cardiologists, the Association of American Physicians, and the Institute of Medicine. Among his awards are the John Phillips Memorial Award from the American College of Physicians, the 2008 Diversity Award from the Association of Professors of Medicine (APM), and the 2015 Robert H. Williams, MD Distinguished Chair of Medicine Award, also from the APM.

Baltimore emeritus members without submitted biographies:

Douglas Fearon

Lawrence Lichtenstein

Richard Ross

Robert Ross

Jessie Roth

John Stobo

Jimmie Sylvaster

Gordon Tomaselli

Eric Walser

BOSTON BIOGRAPHIES OF LIVING MEMBERS



David E. Cohen, MD, PhD

David Cohen was born in Newburgh, NY, on February 27, 1960. He earned an AB degree from Harvard College in 1982, and in 1987 earned both an MD degree from the Harvard-MIT Division of Health Sciences and Technology at Harvard Medical School (HMS) and a PhD in physiology and biophysics from the Graduate School of Arts and Sciences at Harvard University. He completed his residency and served as a research fellow in internal medicine at HMS and Brigham and Women's Hospital (BWH) in Boston. Cohen subsequently completed clinical and research fellowships in gastroenterology at HMS and BWH, then served as a senior fellow in hepatology at BWH.

Cohen was appointed as instructor in medicine at HMS in 1995, and as assistant professor in 1996. In 1997 he moved to the Albert Einstein College of Medicine, where he held joint appointments in the Department of Medicine and Department of Biochemistry as a member of the Marion Bessin Liver Research Center. Cohen returned to HMS and BWH in 2004 as an associate professor of medicine and health sciences and technology. In 2004 Cohen was appointed director of hepatology at Brigham and Women's Hospital, and in 2007 he was appointed director of the Harvard-MIT Division of Health Sciences and Technology (HST), and master of the London Society at HMS. In 2011 Cohen became the Robert H. Ebert Professor of Medicine and Health Sciences and Technology at HMS and BWH.

Along with his two brothers, Mark and Steven, both of whom are physicians, Cohen was inspired to pursue a career in academic medicine by both his father, Murray Cohen (a board certified internist and former clinical assistant professor of medicine at New York University), and mother, Beverly Cohen (a professor in the Department of Environmental Medicine at New York University).

Throughout his career Cohen's research has contributed to our understanding of hepatic lipid, glucose, and lipoprotein metabolism as well as energy

homeostasis. He has described novel regulatory roles for phosphatidylcholine transfer protein (PC-TP). In the course of this research, he was the first to clone PC-TP, to characterize the gene and its transcription, and to solve its three-dimensional structure. He demonstrated that *Pctp*^{-/-} mice are protected against diet-induced diabetes and elucidated a novel mechanism whereby a complex of PC-TP and thioesterase superfamily member 2 (Them2) suppresses insulin signaling. He has further shown that PC-TP and Them2 suppress adaptive thermogenesis by reducing the sensitivity of brown adipocytes to stimulation by norepinephrine. In pivotal studies Cohen discovered small-molecule inhibitors of PC-TP and demonstrated their in vivo promise for treating type 2 diabetes. Recently Cohen has characterized Them1 as an acyl-CoA thioesterase and has elucidated its role in the pathogenesis of obesity and the metabolic syndrome.

As director of HST, Cohen oversees educational programs at Harvard, MIT, and affiliated teaching hospitals. This includes core and affiliated faculty as well as students enrolled in MD, PhD, and MD-PhD programs at HMS and MIT. As master of the London Society, he is charged with the academic oversight of the nearly 200 HST MD and MD-PhD students at HMS. He is a faculty member of the graduate Program in Biological and Biomedical Sciences and an affiliate of the Department of Biological Chemistry and Molecular Pharmacology, both at HMS. As director of hepatology at BWH, he supervises the clinical, research, and educational activities of the hepatology group, which comprises four investigators (two basic, two clinical). Cohen's own clinical practice specializes in the management of dyslipidemia in patients with liver disease.

Cohen has been the recipient of numerous awards, including the American Liver Foundation Research Prize, an American Liver Foundation Liver Scholar Award, an International HDL Research Award, a Hirschl Career Scientist Award, and an NIH MERIT Award. He was also an Established Investigator of the American Heart Association. He is a fellow of the American College of Physicians and the American Gastroenterological Association and a member of the American Society for Clinical Investigation. Cohen has received several grants from the National Institutes of Health for his research in liver diseases and has served as a member of the NIH Hepatobiliary Pathophysiology Study Section and as chair of the American Heart Association Lipoprotein and Lipid Metabolism Study Section, National Chapter. He has served on the editorial boards of the *American Journal of Physiology: Gastrointestinal and Liver Physiology* and the *Journal of Lipid Research* and currently serves on the editorial boards of *Hepa-*

tology, Trends in Endocrinology and Metabolism, and the Journal of Biological Chemistry and as an associate editor of *Seminars in Liver Disease*.

Glenn Dranoff, MD

Glenn Dranoff was born in Forest Hills, New York. He received his AB (summa cum laude and Phi Beta Kappa) in chemistry from Duke University and his MD (Alpha Omega Alpha) from Duke University Medical School, where he studied cancer chemotherapy with Nobel laureate Gertrude Elion and Darell Bigner. He served as an intern and resident in internal medicine at Massachusetts General Hospital and was an American Cancer Society clinical fellow in medical oncology at the Dana-Farber Cancer Institute. He worked as a postdoctoral fellow in genetics with Richard C. Mulligan at the Whitehead Institute for Biomedical Research, where he was the recipient of the Herbert and Margaret Sokol Prize for Cancer Research. Dranoff was recruited as an independent investigator to Dana-Farber Cancer Institute in 1994.

Dranoff has developed a basic and clinical research program to elucidate the cellular and molecular mechanisms underlying the generation of antitumor immunity. Work in his laboratory has given rise to 16 clinical protocols at Dana-Farber that have defined the biologic activity of several different cancer immunotherapies in patients with solid or hematologic malignancies. Dranoff has received numerous awards for these investigations, including the Eli Lilly Biochemistry Award in Gene Therapy and the Stohler Scholarship of the Leukemia & Lymphoma Society and membership in the Academy of Cancer Immunology, the American Society for Clinical Investigation, and (in 2008) the Interurban Clinical Club.

Dranoff is the leader of the Dana-Farber/Harvard Cancer Center Program in Cancer Immunology, a co-leader of the Dana-Farber Cancer Vaccine Center, the director of the Human Gene Transfer Laboratory at Dana-Farber, and the principal investigator of the Harvard Immunology Training Grant for Pre-Doctoral Students in Cancer Immunology.

He serves on the editorial boards of 11 major scientific journals and the scientific advisory boards of the Cancer Research Institute (for which he is associate director), the Pediatric Brain Tumor Foundation of the United States, the Brain Tumor Society, the Melanoma Research Alliance, and several university cancer centers.

Dranoff is a founding member of the steering committee for the Cancer Immunology Working Group of the American Association of Cancer Research and serves on the executive committee of the Cancer Research Institute/Sabin Cancer Vaccine Consortium and the Food and Drug Administration Cellular, Tissue, and Gene Therapies Advisory Committee.

Elizabeth C. Engle, MD

Elizabeth C. Engle was born in Columbus, OH. She received her BA *summa cum laude* in biology from Middlebury College (Middlebury, VT) in 1980 and her MD degree from Johns Hopkins University School of Medicine five years later. She then trained from 1985 to 1988 as an intern and resident in pediatrics at Johns Hopkins, from 1988 to 1989 as a fellow in neuropathology at Massachusetts General Hospital, and from 1989 to 1992 as a resident in adult and child neurology in the Longwood Neurology Training Program and Children's Hospital Boston. Toward the end of her neurology residency, Engle cared for a toddler who was born with a very odd fixed-eye position, droopy eyelids, and a backward head tilt. This young boy became the proband for Engle's research career, which has focused on the genetic and neurodevelopmental basis of cranial nerve maldevelopment. To understand the cause of the toddler's problem, she spent 1992–1996 as a research fellow in the genetics lab of Alan Beggs and Louis Kunkel and then established her own research lab at Children's Hospital Boston in 1997. In addition to her research, Engle continues to care for child neurology patients, primarily consulting for children and adults with rare eye movement disorders, now referred to as congenital cranial dysinnervation disorders.

Engle is professor of neurology and ophthalmology at Harvard Medical School and an investigator of the Howard Hughes Medical Institute. At Children's Hospital Boston she is a member of the departments of neurology, ophthalmology, and medicine (genetics), a member of the FM Kirby Neurobiology Center and the Program in Genomics, and a senior investigator for the Manton Center for Orphan Disease Research. She is also an associate member of the Broad Institute. She joined Interurban Clinical Club in November 2010.

Engle's honors include the E. Mead Johnson Award in Pediatric Research from the American Pediatric Society/Society for Pediatric Research, the Sidney Carter Award in Child Neurology from the American Academy of

Neurology, and a research grant from the Alcon Research Institute.

Elizabeth Petri Henske, MD

Elizabeth (Lisa) Petri Henske, a musician, runner, parent, and physician-scientist, was born on October 13, 1959, in Washington, DC. She attended Lafayette Elementary School and McLean High School, where she was valedictorian. She graduated summa cum laude from Yale University in 1981, where she majored in molecular biophysics and biochemistry and was one of 12 members of the junior class elected to Phi Beta Kappa. After graduating from Harvard Medical School, she was a resident in internal medicine and fellow in hematology-oncology at Massachusetts General Hospital.

Henske rose to the level of assistant professor at the Brigham and Women's Hospital (BWH) before moving to Fox Chase Cancer Center in Philadelphia. In 2008 she returned to BWH as the director of the Center for LAM Research and Clinical Care. She is professor of medicine at Harvard Medical School and has an appointment at the Dana-Farber Cancer Institute in the Lank Center for Genitourinary Oncology.

Henske's remarkable parents, William Arthur Petri, a chemical and missile engineer, and Ann Emmons Petri, an educator and author, have been continual sources of inspiration. Leading through example, they fostered excellence in science, research, writing, and service. Henske's older siblings, also academic physicians, have been role models: William Arthur Petri Jr. is professor of medicine at University of Virginia and Michelle Ann Petri is professor of medicine at Johns Hopkins University. Henske and Petri are believed to be the first sisters to attend Harvard Medical School. Their younger brother, Steven Richard Petri, is an assistant U.S. attorney in Florida.

Tuberous sclerosis complex (TSC) became the focus of Henske's career when she was a research fellow at Harvard, working under David Kwiatkowski. At Fox Chase Cancer Center, she became a colleague and friend of Alfred Knudson, who proposed the Knudson "two-hit" tumor suppressor gene model. One of Henske's first discoveries as an independent investigator was the physical interaction between the TSC1 and TSC2 proteins, which is now the centerpiece of the PTEN/Akt/TSC/mTOR signaling network. In addition to utilizing human tissues in her research, Henske has

used mice, *Drosophila*, and *Schizosaccharomyces pombe* models. Her laboratory discovered that the *TSC* genes regulate amino acid biosynthesis in *S. pombe*, Notch signaling in *Drosophila*, and estrogen-induced metastasis in mice. She developed the first mouse model of renal carcinoma in Birt-Hogg-Dubé syndrome and was one of the first to discover mutations in both alleles of the polycystic kidney disease 1 gene in renal cysts, leading to the two-hit model of cyst pathogenesis.

Henske is best known for her pioneering genetic research in lymphangi-leiomyomatosis (LAM). LAM is a devastating lung disease that affects almost exclusively women, often resulting in death in young adulthood. Henske's discovery that LAM is caused by somatic *TSC2* gene mutations catalyzed clinical and basic LAM research. Henske also discovered that LAM cells spread to the lungs via a metastatic mechanism. Because of this paradigm-shifting "benign metastasis" model of LAM pathogenesis, many investigators now view LAM as a neoplasm rather than an interstitial lung disease. Henske has been very active with foundations that support LAM research. One of her most valued possessions is a framed quilt given to her by women with LAM.

Henske has a long history of service to the medical research community. She chaired an NIH study section and has served on the scientific advisory boards of the Polycystic Kidney Disease Foundation, the LAM Foundation, and the Tuberous Sclerosis Alliance, where she is also an elected member of the board of directors and the chair of the international professional advisory board. At Harvard Medical School Henske is active in the teaching, advising, and mentoring of students and fellows. She is an elected member of the Harvard Medical School Alumni Council.

Henske's honors include the Manuel Gomez Award for "extraordinary scientific and humanitarian efforts to find a cure for tuberous sclerosis," the Scientific Advancement Award from the LAM Foundation, and the Medtronic Prize from the Society for Women's Health Research, granted to outstanding scientists "whose work has led or will lead directly to the improvement of women's health."

Henske's contributions to LAM and related diseases are only possible because of her enormously supportive husband, Robert Charles Henske, and their three children, Jessica, Brian, and Michael. Henske and her husband met as freshmen at Yale and graduated together from Yale and then again from Harvard, with Henske receiving her MD and her husband his MBA

on the same day in 1985.

Henske has run four marathons and qualified for the Boston Marathon. She was the principal flutist of the Yale Symphony Orchestra and studied flute at the Yale School of Music with Thomas Nyfenger. She continues to perform regularly, including at benefits for Fox Chase Cancer Center, the LAM Foundation, and Brigham and Women's Hospital.

Bruce D. Levy, MD

Bruce D. Levy was born in Saint Louis, MO, on December 13, 1961. He received a BA degree from the University of Pennsylvania in 1984 and an MD from the University of Pennsylvania School of Medicine in 1988. From the latter, he won the Department of Medicine's Lawrence Saunders Prize for clinical excellence. This was followed by an internship and residency at Brigham and Women's Hospital (1988–1991) and a fellowship in pulmonary and critical care medicine at the combined Brigham and Women's and Beth Israel Hospital program under the mentorship of Jeffrey M. Drazen. In 1993–1994, he was a chief medical resident at Brigham and Women's Hospital working closely with Marshall A. Wolf and Eugene Braunwald. After this, he completed a postdoctoral fellowship in biochemistry in the laboratory of Charles N. Serhan, where he began to investigate the formation and actions of a new family of arachidonic acid–derived mediators termed lipoxins. He was appointed to the faculty by Braunwald and Drazen as an instructor of medicine in the Pulmonary and Critical Care Medicine Division at Brigham and Women's Hospital. He received funding support for his postdoctoral research from the American Heart Association, Massachusetts affiliate (Paul Dudley White Award), followed by an NIH NHLBI K08 grant (Mentored Clinical Scientist Development Award), and then by NIH R01 funding in 2001. In 2006 he became an associate professor of medicine at Harvard Medical School. Beginning in 2000 under the chair of internal medicine, Victor Dzau, Levy became the director of academics and career development for the medical residency program at Brigham and Women's Hospital. In 2013 he was appointed chief of the Pulmonary and Critical Care Medicine Division at Brigham and Women's Hospital under the leadership of chairman Joseph Loscalzo.

Inspired by his parents, Morton, a specialist in hematology and oncology, and Marilyn, an experimental biologist, Levy developed an early affinity for studying the intersection of medicine and science. Early laboratory

experiences with Robert Senior and Robert Mecham at Washington University School of Medicine in Saint Louis led to his first discoveries and publications. Clinical training under Marshall Wolf opened his eyes to the art and science of evidence-based medicine and cemented his desire for a career as a physician-scientist. The lung and its delicate interface between the body and its external environment captured Levy's interest and led to a lifelong pursuit to better understand the inflammatory responses of the lung in health and disease. Mentorship from leading experts in the field of lipid mediators, namely Drazen and Serhan, inspired his fascination for autacoid regulators of cellular and organ function. The discovery by Serhan and Levy of novel counter-regulatory signaling pathways and lipid mediator class switching during the resolution of inflammation laid the foundation for both Levy's subsequent scientific contributions and a close, ongoing collaboration with Serhan for more than 20 years.

Levy led several important basic and translational research efforts into the molecular and cellular events that control the resolution of inflammation, in particular in the lung. These fundamental insights helped to uncover the pathophysiology of several lung diseases and provide potential novel therapeutic approaches. He has determined mechanisms of action for specialized pro-resolving autacoids, including lipoxins, resolvins, protectins, and maresins, in lung inflammation and elucidated intracellular signaling pathways that these mediators can use to regulate cell activation. Perhaps most notably, Levy identified defective formation of pro-resolving mediators in severe and uncontrolled asthma. The chronic inflammation and lung destruction in COPD that occurs despite smoking cessation stems from the inhibition of specific pro-resolving receptors, rather than defective generation of pro-resolving mediators. These findings of disrupted resolution of signaling circuits have led to a paradigm shift in our understanding of the pathophysiology of severe asthma, COPD, and more generally, diseases characterized by chronic inflammation.

Levy served for over a decade as the director for academics and career development of the medical residency program at Brigham and Women's Hospital. In this leadership position he worked to recruit and foster the academic careers of over 1,000 trainees, including hundreds of physician-scientists. Levy has served since 2013 as chief of the Division of Pulmonary and Critical Care Medicine at Brigham and Women's Hospital. The division is one of the nation's leaders in patient care, research, and education and has nearly 60 full-time academic faculty, one of the largest portfolios of research support in the country, as well as a fellowship dedicated to training

the next generation of academic physician-scientists. He initiated collaborative innovation projects for the division's physicians and scientists, including development of the Pulmonary Genetics Center, which integrates the latest advances in genetics and genomics with clinical medicine. He also catalyzed the formation of the Lung Research Center, through which research cores can facilitate the work of lung researchers throughout the hospital.

Levy has received multiple awards and honors, including the George Thorn Award in Internal Medicine and recognition for outstanding research achievement by *Nature Biotechnology* SciCafe. He is a fellow of the American College of Physicians and a member of the American Society for Clinical Investigation and Association of American Physicians. He belongs to the American Thoracic Society and serves in leadership capacities for its Assembly on Allergy, Immunology and Inflammation; is a member of the faculty of the F1000Prime Asthma & Allergic Rhinitis Section; and is a member, and serves on the leadership council of, the Society for Leukocyte Biology. He has served as a grant reviewer for the NIH and several foundations. Levy has served as an associate editor for the *American Journal of Respiratory and Critical Care Medicine* and as a section editor for the *Journal of Immunology*. He was a co-founder and serves as an associate editor for the *New England Journal of Medicine's* award-winning Interactive Medical Case Series.

Andrew D. Luster, MD, PhD

Andrew Luster was born in Brooklyn, NY, on August 28, 1959. He received his BS degree in 1981 summa cum laude from Duke University and was awarded the prize for the most distinguished graduating biology student. He then entered an NIH-funded medical scientist training program, and received his PhD from Rockefeller University in 1987 and his MD from Cornell University Medical College in 1988. He received the New York State Annual Medical School Research Award for his PhD studies under the mentorship of Jeffrey Ravetch and Zanvil Cohn. Luster pursued his residency in medicine and fellowship in infectious diseases at Massachusetts General Hospital, followed by a postdoctoral fellowship in Philip Leder's laboratory in the Department of Genetics at Harvard Medical School. In 1994 Luster established his laboratory at MGH, and in 2000 he was appointed chief of the new MGH Division of Rheumatology, Allergy and Immunology and director of the new Center for Immunology and Inflamma-

tory Diseases. He is the Persis, Cyrus and Marlow B. Harrison Professor of Medicine at Harvard Medical School.

Over the past two decades, Luster has been intimately associated with the birth, growth, and development of the chemokine field. He has been a pioneer in the chemokine field and has made multiple seminal contributions to this important field, demonstrating how chemokines function in immune cell trafficking and defining their roles in both host defense and inflammatory diseases. Luster identified one of the first chemokines, IP-10 (CXCL10), as an important mediator of effector T cell trafficking. He also described several other members of the chemokine family, including monocyte chemoattractant protein 4 (MCP-4, also known as CCL13) and MCP-5 (CCL12); eotaxin-1 (CCL11), a critical mediator of eosinophil trafficking; and most recently, CCL8, a mediator of T helper cell 2 trafficking.

Luster has been at the forefront of elucidating the role of chemokines in disease. He described roles for IP-10 and its receptor, CXCR3, in host defense against infectious pathogens, allograft rejection, and atherosclerosis; CCR2 in monocyte homing into the brain in multiple sclerosis and Alzheimer's disease; and STAT6-inducible chemokines in the control of Th2 cell trafficking in asthma and atopic dermatitis. Luster also discovered that cytotoxic T cells release chemokines that inhibit HIV-1 entry into cells and that the homing patterns of these cells influence anti-HIV immunity. More recently, Luster has expanded his interests to include lipid chemoattractants, such as leukotriene B₄ (LTB₄) and lysophosphatidic acid (LPA). He identified the long-sought-after receptor for LTB₄, BLT1, and has changed the thinking about the function of this chemoattractant by describing that it has potent activity for effector T cells. Similar to his work on chemokines, Luster has defined important roles for BLT1 in several disease processes, including arthritis, asthma, and atherosclerosis. He has established the concept that cascades of chemoattractants, including chemokines and lipid mediators, cooperate to guide the complex migratory patterns of leukocytes in vivo in health and disease. Finally, his lab recently identified LPA₁, the receptor for the lipid chemoattractant LPA, as the key mediator linking inflammation to fibroblast recruitment and activation in fibrotic diseases such as pulmonary fibrosis and scleroderma.

Luster has received numerous awards and honors, including a Damon Runyon–Walter Winchell Postdoctoral Fellowship Award, a Cancer Research Institute Investigator Award, a Charles E. Culpeper Scholarship in Medical Science Award, and an NIH MERIT Award. His work has been supported

by grants from the NIH, the Dana Foundation for human immunology, the Roche Organ Transplantation Research Foundation, the Massachusetts Life Sciences Center, and the Ragon Institute of MGH, MIT & Harvard. Luster has served on numerous NIH review panels, including chairing the Asthma and Allergic Diseases Cooperative Research Centers Review Group in 2006. Luster is a member of the American Association of Immunologists, the American Society of Leukocyte Biology, the American College of Rheumatology, and the American College of Allergy, Asthma and Immunology. He was elected to the American Society for Clinical Investigation in 1996, the Association of American Physicians in 2006, and the Interurban Clinical Club in 2008.

Calum MacRae, MD, PhD

Calum MacRae was born in Uig, Isle of Skye, United Kingdom, on October 25, 1961. He received a BSc with honors in mammalian physiology from the University of Edinburgh in 1984 and graduated with a degree in medicine in 1985 from the University of Edinburgh Medical School. Following a surgical internship with Sir Patrick Forrest, he completed a medical internship and residency at the Royal Infirmary of Edinburgh in 1987. He subsequently undertook additional training in internal medicine at the Hammersmith Hospital and Royal Postgraduate Medical School in London, then began his cardiology training under John Camm and William McKenna at St. George's Hospital. In 1992 he completed his initial cardiology training, which included periods in the national inherited heart disease clinic and in cardiac transplantation.

In 1992 MacRae began a postdoctoral fellowship in the laboratory of Jon and Cricket Seidman in the Department of Genetics at Harvard Medical School. There he worked on the genetics of cardiomyopathy and was fortunate to participate in the identification of several of the major disease genes in hypertrophic and dilated cardiomyopathy. In 1996 he was accepted into the internal medicine training program at Brigham and Women's Hospital under Marshall Wolf and went on to a cardiology fellowship at Massachusetts General Hospital. On completion of his clinical training, MacRae entered the laboratory of Mark Fishman, where he was trained in the developmental biology and genetics of zebrafish. He remained at MGH as a faculty member, and in 2002 he became the cardiology program fellowship director. He returned to Brigham and Women's Hospital in 2009, where he is currently clinical director of the genomic medicine program and associ-

ate professor of medicine at Harvard Medical School.

MacRae's work has focused on the human genetics of cardiovascular diseases and on the use of the zebrafish to understand the developmental basis of disease mechanisms. His work has helped to define the genetic underpinnings of atrial fibrillation, arrhythmogenic cardiomyopathies, and other disorders. He has also designed novel approaches to identify subclinical endophenotypes, to improve the mapping of the genetic loci with a view to gene identification. This human genetic work led to exploration of the cellular and developmental biology of arrhythmia diathesis. Using innovative approaches in the zebrafish, his group has identified the genetic and developmental basis of cellular heterogeneity within the heart, defining novel, highly specific cardiomyocyte cell circuits within the heart. These circuits are regulated by the pathways responsible for cardiac septation, and their findings suggest that these pathways are conserved in the simple two-chamber heart of the zebrafish. Ongoing work includes large-scale genetic and chemical screens to define the ontogenesis of lungs and the right heart. Recent efforts have defined a role for abnormalities of these same circuits in atrial fibrillation and have modeled several cardiac and vascular diseases in the zebrafish so that subsequent phenotype-driven chemical screens could be used to identify novel therapeutics. These chemical screens are already bearing fruit, as two compounds are undergoing additional evaluation prior to preclinical toxicology assessment.

MacRae has received several awards. He was elected into the American Society for Clinical Investigation in 2007 and was chosen as the keynote speaker at the NIH PRAT Symposium in 2011. He was awarded the George Thorn prize for clinical teaching in 2010 and a received a Burroughs Wellcome Fund Innovation in Regulatory Science Award for his work in toxicology using zebrafish. He is a fellow of the Royal College of Physicians of Edinburgh, the American College of Cardiology, and the American Heart Association. He is also a member of the American Society of Human Genetics, the Heart Rhythm Society, the North American Vascular Biology Organization, and the Heart Failure Society of America. He has served on several NIH study sections and is currently on the editorial boards of *Circulation* and *Circulation Cardiovascular Genetics*.

Martin Pollak, MD

Martin Pollak was born in Princeton, NJ, on October 12, 1960. He received

his early education at John Adams High School in South Bend, IN, from which he graduated in 1979, and at Princeton University, where he majored in mathematics and graduated in 1983. He received his MD degree from New York University School of Medicine in 1988 and did his internship and residency in internal medicine at the New York–Presbyterian/Columbia University Medical Center from 1988 to 1991. He followed this with a nephrology fellowship at Brigham and Women’s Hospital at Harvard, under Barry Brenner.

Pollak did not do much serious research until after his clinical training. He became generally interested in the genetic basis of disease and pursued this as a postdoctoral fellow starting in 1992. He found the genetic approach quite compelling because of the ability to find the most-upstream cause of disease. He began his postdoctoral research training in the laboratory of Jon and Cricket Seidman at Harvard Medical School, working on the genetic basis of familial hypocalciuric hypercalcemia and neonatal hyperparathyroidism. Both conditions turned out to result from mutations in the calcium-sensing receptor. This research involved collaboration with Ed Brown and Steve Hebert, who taught him molecular physiology. Toward the end of his time in the Seidman lab, Pollak decided to start work on the genetic basis of proteinuric kidney disease, which he has since pursued in his own lab, first at the Brigham and Women’s Hospital and now at Beth Israel Deaconess Medical Center.

Most of Pollak’s work has been on the genetic basis of human kidney disease and related issues in the molecular physiology of kidney disease. His lab first showed that mutations in the cytoskeletal actin-binding protein *a-actinin-4* cause an autosomal-dominant form of progressive kidney disease characterized by a focal segmental glomerulosclerosis injury pattern. He has continued to work on the mechanism of this disease, in which altered cytoskeletal biophysical behavior seems to cause abnormal glomerular function.

Pollak’s lab has shown that mutations in the *INF2* gene, another actin-regulating protein, cause a similar autosomal-dominant phenotype. Many independent mutations have now been found in this gene. Mutations all localize to the same domain and appear to both disrupt important intramolecular interactions and interfere with the ability of Rho to regulate actin dynamics. He has also characterized various aspects of the spectrum of mutations in other proteinuric kidney disease–associated genes, including *TRPC6*, *NPHS2*, and *PAX2*. Recently he showed that two common variants

in the apolipoprotein-L1 gene (*APOL1*) explain for the first time the high rate of kidney disease in Africans and African Americans. These variants, which alter the *APOL1* protein sequence, have come to a high frequency in Sub-Saharan Africa because of a protective effect provided by the variant forms of *APOL1* against types of African trypanosomiasis. Pollak's lab continues to study the molecular pathophysiology of *APOL1*-mediated disease as well as *ACTN4* and *INF2*, and to search for other genetic factors that mediate human kidney disease.

Pollak has served as instructor in medicine (1994–1998), as assistant professor of medicine (1998–2005), as associate professor of medicine (2005–2011), and as professor of medicine (2011–present) at Harvard Medical School. In 2009 he became an associate member of the Broad Institute of Harvard and MIT. Since 2010 Pollak has served as chief of nephrology at the Beth Israel Deaconess Medical Center and Harvard Medical School.

He has received numerous honors for his research, including election to the American Society for Clinical Investigation (2005) and the Association of American Physicians (2012). In 2012 he received the NephCure Foundation Marilyn Farquhar Award for Podocyte Research. In 2014 he was elected to the National Academy of Sciences.

Leonard I. Zon, MD

Leonard I. Zon, born September 8, 1957, in Hartford, CT, is the Grousbeck Professor of Pediatric Medicine at Harvard Medical School, an Investigator of the Howard Hughes Medical Institute, and director of the Stem Cell Program at Children's Hospital Boston. He is founder and former president of the International Society for Stem Cell Research and chair of the executive committee of the Harvard Stem Cell Institute (HSCI). In 2005 he completed a term as president of the American Society for Clinical Investigation. That same year, Zon was elected to the Institute of Medicine of the National Academy of Sciences. In 2008 Zon was elected to the American Academy of Arts and Sciences, and in 2010 he was awarded the E. Donnall Thomas Lecture and Prize from American Society of Hematology. In 2013 Zon received the Donald Metcalf Lecture Award from the International Society for Hematology and Stem Cells.

Zon received his BS in chemistry and natural sciences from Muhlenberg College and his MD from Jefferson Medical College. He subsequently did

an internal medicine residency at New England Deaconess Hospital and a fellowship in medical oncology at the Dana-Farber Cancer Institute. His postdoctoral research was in the laboratory of Stuart Orkin. Zon's initial interest in cancer research stemmed from the experience of watching a family member struggle with the disease.

Zon is internationally recognized for his pioneering work in the fields of stem cell biology and cancer genetics. He has been the preeminent figure in establishing the zebrafish as an invaluable genetic model for the study of the blood and hematopoietic development. His laboratory focuses on the developmental biology of hematopoiesis and cancer, and together, Zon and his team have identified over 30 genetic mutations that affect the hematopoietic system. Some of these mutations represent excellent animal models of human disease. The lab has also undertaken a chemical genetic approach to blood development and has found that prostaglandins upregulate blood stem cells. This has led to a clinical trial to improve engraftment for patients receiving cord blood transplants. The Zon lab recently developed the use of genetic suppressor screens and found that transcriptional elongation regulates blood cell fate.

His laboratory has also developed zebrafish models of cancer. They have used transgenics to generate a melanoma model in the zebrafish system. Transgenic fish develop nevi, and in combination with a p53 mutant, the fish develop melanomas. His group recently identified a histone methyltransferase that can accelerate melanoma and discovered a small molecule that blocks transcription elongation and suppresses melanoma growth.

Boston active members without submitted biographies:

Arlene Sharpe

Margaret Shipp

Jing Zhou

BOSTON EMERITUS MEMBERS BIOGRAPHIES

Seth L. Alper, MD, PhD

Seth Alper was born in Philadelphia, PA, on January 31, 1952. He received a BS degree in chemistry from Haverford College in 1973, where he was

inspired by research mentor and chemist Robert Gavin, cell biologist Ariel Loewy, and chemists Harmon Dunathan, John Chesick, Claude Wintner, and Colin MacKay. Alper's final undergraduate semester was at Leningrad State University's Department of Russian Language for Foreigners. Alper's doctoral studies at Yale University led to a PhD degree in pharmacology in 1979, under Paul Greengard, followed by an MD degree in 1980. Influential Yale mentors included James Jamieson, William Douglas, Murdoch Ritchie, Gary Rudnick, Joseph Hoffman, Gerhard Giebisch, Emile Boulpaep, George Palade, Robert Berliner, Sam Thier, Norman Siegel, Peter Aronson, John Forrest, and John Hayslett.

Alper's medical internship and residency under Eugene Braunwald and clinical fellowship in nephrology under Franklin Epstein (both of whom were, at that time, at Boston's Beth Israel Deaconess Medical Center [BIDMC]) were followed by postdoctoral training in molecular and cellular biology in the laboratory of Harvey Lodish at the Whitehead Institute and MIT. During this time Alper joined the faculty of the Harvard Medical School as instructor of medicine. He was promoted in 1989 to assistant professor of cellular and molecular physiology at Harvard Medical School, with his laboratory at the Molecular Medicine Unit of BIDMC and joint appointment to the Renal Division. He was also assistant professor of cell biology (in medicine) under Marc Kirschner, then promoted to associate professor of medicine in 1995 and to professor of medicine in 2001. He has remained at Harvard Medical School and BIDMC, serving as acting co-chief of the Molecular Medicine Unit, then as associate chief of the Molecular and Vascular Medicine Unit under William Aird. Alper also served as director of clinical and translational studies at the BI at Harvard Catalyst. In 2013 he was appointed associate member of the Broad Institute of Harvard and MIT.

Alper's investigative career has, until recently, been devoted to cell physiology, cell biology, and molecular genetics of ion transporters and channels. Alper's laboratory contributed to the molecular cloning and functional characterization of SLC4 anion exchanger kidney AE1 and non-erythroid exchangers AE2 and AE3, with a focus on their acute regulatory influences. The lab co-discovered and functionally characterized human AE1 mutations that cause hereditary spherocytosis and stomatocytic anemias and distal renal tubular acidosis. The collaboration of Dennis Brown, Carsten Wagner, Gary Shull, Ursula Seidler, and other colleagues was important in these studies. The Alper lab conducted investigations on SLC26 anion exchangers and the multiple human and murine diseases arising from their

mutations. Their recent studies have solved NMR structures of SLC26-related STAS domains and defined them as guanine nucleotide-binding proteins. An additional project has focused on the role of potassium transporters and channels as red cell volume regulators in sickle disease and hemoglobinopathies. These studies eventually led to a phase III trial of a KCNN4 inhibitor in sickle disease and were complemented by pharmacologic studies on intestinal epithelial cells. Alper's recent work has focused on erythroid Psickle function and its candidate mediators, including PIEZO1. His laboratory also contributed to mechanotransduction and purinergic signaling research in polycystic kidney disease and endothelial biology. In the last two years, the Alper lab has engaged in collaborative research with colleagues at the Broad Institute on pathogenic mechanisms of medullary cystic kidney disease caused by mutations in the epithelial mucin MUC1. The lab has also pursued studies on pathogenic mechanisms of APOL1-associated focal sclerosing glomerulonephritis with BIDMC nephrology colleagues Martin Pollak and David Friedman, and on peritoneal fibrosis with Dominik Alscher and Manoj Bhasin.

Alper was elected to the Red Cell Club in 1978 and to the Salt and Water Club in 1989, serving as secretary from 1997 to 1999. He was an established investigator of the American Heart Association and was elected a fellow of the American Association for the Advancement of Science. In 1998 he was recognized by the NIDDK with a MERIT award. In 1999 Alper co-organized an influential NIH meeting entitled, "Membrane Transport: Lessons from Model Organisms." Alper was elected a member of the Interurban Clinical Club in 2005. He has delivered keynote lectures to the Kidney Council of the American Heart Association and the Japanese Society of Nephrology, and at the University of Verona Hematology Conference and McGill University Undergraduate Research Day. He has also presented the Litchfield Lecture at the University of Oxford, the Schrier Lecture to the American Society of Nephrology, and the Hong Memorial Lecture at the University of Buffalo.

Alper's editorial responsibilities have included six years as associate editor of the *American Journal of Physiology—Cell Physiology*, four years as associate editor of *Physiological Genomics*, and service on the editorial review boards of many publications, including the *American Journal of Physiology—Renal Physiology*, *Journal of General Physiology*, *Journal of Membrane Biology*, *American Journal of Kidney Diseases*, *Histochemistry and Cell Biology*, *Clinical Medicine: Blood Disorders*, *Journal of Epithelial Biology*, and *World Journal of Biochemistry*. He served on a study sec-

tion for the American Heart Association and has reviewed for the NIH, National Science Foundation, Department of Defense, U.S. Department of Veterans Affairs, Cystic Fibrosis Foundation, and PKD Foundation, as well as for governmental agencies and charitable foundations from the UK, Ireland, Canada, Australia, France, Switzerland, Italy, Israel, Hungary, Singapore, and Hong Kong. His professional society memberships have included the American Society of Nephrology, National Kidney Foundation, American Society of Cell Biology, American Physiological Society, American Heart Association, Society of General Physiologists, and the Biophysical Society. He served a three-year term as a councilor for the Society of General Physiologists.

Alper's interests outside of nephrology are reflected in service on the Executive Board of the Harvard Digestive Diseases Center and as investigator of the BIDMC Program in Smooth Muscle, the Harvard-Dana-Farber Cancer Center, and the Boston Sickle Cell Center. He has served as training faculty for the BIDMC or Harvard Medical School training programs in nephrology, gastroenterology, pediatric gastroenterology and nutrition, cardiology, hematology, oncology/cancer biology, hematopathology, and endocrinology. Extramural activities have included service on the External Advisory Board of the Kansas State University Center for Biomedical Research Excellence in Epithelial Biology and ongoing service on the External Review Panel for the Swiss National Science Foundation's National Center of Excellence in Research on Membrane Solute Transporters and Channels.

Nancy Andrews, MD, PhD

Nancy Catherine Andrews was born in Syracuse, NY, on November 29, 1958. She simultaneously received her BS summa cum laude and MS degrees in molecular biophysics and biochemistry from Yale University in 1980, after conducting her thesis work in the laboratory of Joan Steitz. She moved to Boston to join the Harvard Medical School/Massachusetts Institute of Technology MD-PhD program (MSTP), where she worked with David Baltimore, to earn her PhD in biology from MIT in 1985. She earned her MD from Harvard Medical School in 1987, and also received the Richard C. Cabot and Pediatrics prizes. From 1987 to 1989 she served as intern and assistant resident in pediatrics at Children's Hospital Boston. From 1989 to 1991 she was a fellow in pediatric hematology and oncology at Children's Hospital and the Dana-Farber Cancer Institute, then joined

the Harvard faculty as an instructor in 1991. She was a research fellow with Stuart Orkin from 1990 to 1993. David G. Nathan was an important mentor, beginning in medical school and for decades after. Andrews served as assistant professor from 1993 to 1998, associate professor from 1998 to 2003, and full professor from 2003 to 2007 at Harvard Medical School. She held the titles of Leland Fikes Professor of Pediatrics from 2003 to 2006 and George Richards Minot Professor of Pediatrics from 2006 until she left Harvard in 2007.

Soon after starting her independent laboratory, Andrews became an investigator at Howard Hughes Medical Institute (1993–2006). Generous HHMI funding allowed her to enter a new area of study, iron biology. Iron had been a major area of research interest for hematologists during the 1950s and 1960s, but interest had waned because the technology was not yet available to understand fundamental molecular processes important in iron transport and its regulation. The Andrews group took a new approach, using genetic mapping to identify the genes defective in a series of mouse mutants described between the 1930s and 1990s. Her laboratory identified the first mammalian iron transporter, now known as divalent metal transporter 1 (DMT1), which imports iron into the cell, and assisted in the identification of ferroportin, an iron transporter that exports iron. They also identified several other novel proteins important in iron homeostasis, using classical mouse mutants. Once many of the important molecules had been identified, the Andrews lab turned its attention to understanding how iron homeostasis is disrupted in human iron disorders. They developed more than 20 new mouse models, using gene targeting and transgenic technology. They played a major role in working out the pathogenesis of hereditary hemochromatosis and the anemia of chronic disease, and also described a new genetic iron disorder, iron-refractory iron deficiency, which they showed results from mutations in the serine protease TMPRSS6. Andrews also contributed as a clinical hematologist with expertise in red blood cell and iron disorders.

In 1999 Andrews became director of the Harvard/MIT MD-PhD program, beginning her career in academic administration. Four years later the dean of the Harvard Medical School, Joseph B. Martin, asked her to serve as dean for Basic Sciences and Graduate Studies. Martin became a very important mentor for Andrews. When he decided to step down from his deanship in 2007, Andrews left Harvard to become the dean of the School of Medicine at Duke University. She was the first woman to become dean of a medical school ranked among the top ten in the nation. Soon after

arriving at Duke, she appointed three women as new department chairs, including Mary Klotman as chair of Duke's Department of Medicine. Prior to Klotman, very few women had chaired departments of medicine, and almost none at research-intensive schools.

Andrews has been elected to membership in many organizations, including the Society for Pediatric Research (1996), American Society for Clinical Investigation (1998; serving as its president in 2008–2009), American Pediatric Society (2004), Association of American Physicians (2004), Institute of Medicine of the National Academies (2006), and American Academy of Arts and Sciences (2007). She was also elected a fellow of the American Association for the Advancement of Science (2006) and has been a very active member of the American Society of Hematology.

Other honors include the Society for Pediatric Research's House Officer (1990), Young Investigator (1994), and E. Mead Johnson (2002) awards, the Samuel Rosenthal Prize for Excellence in Academic Pediatrics (1998), the American Federation for Medical Research Outstanding Investigator Award (2000), the Marcel Simon Award (2007), the Vanderbilt Prize in Biomedical Science (2010), and a variety of teaching and mentoring awards. She has delivered many named lectureships at institutions across the country. Andrews married Bernard Mathey-Prevot, PhD, in 1985. They have two children, Camille Mathey-Andrews (b. 1992) and Nicolas Mathey-Andrews (b. 1995).

K. Frank Austen, MD

K. Frank Austen was born in 1928 in Akron, OH. He attended Amherst College and received his medical degree from Harvard Medical School (HMS), then completed a medicine internship (1954), residency, and chief residency at Massachusetts General Hospital (MGH) (1961). Those years were interrupted by years at the Walter Reed Army Institute of Research and Walter Reed National Medical Center, where he was introduced to immunology and its likely role in disease, and by postdoctoral fellowships in immunology at the National Institute for Medical Research in England and the Johns Hopkins Medical School Department of Microbiology. He then joined the faculty of HMS at the MGH in 1962, initially in infectious diseases and then as chief of pulmonary medicine. In 1966 he moved to the Robert B. Brigham Hospital as physician-in-chief and chairman of the new Division of Rheumatology, Allergy and Immunology at HMS. He is

currently the AstraZeneca Professor of Respiratory and Inflammatory Diseases at HMS in the Division of Rheumatology, Immunology and Allergy of the Department of Medicine at the Brigham and Women's Hospital.

Austen's research has been focused on three innate effector pathways of the microenvironment of tissues that initiate inflammatory reactions while also priming for immune responses. His group identified factors D and H of the alternative complement pathway and established that these factors contribute to an amplification loop for all pathways that can activate complement, namely alternative (properdin), classical (IgG), and lectin. In the mast cell area, he used biochemical and then molecular approaches to characterize the secretory granules as complexes of cationic proteases and anionic glycosaminoglycan chains of proteoglycans with a serine/glycine-rich core. More recently, the focus has been to distinguishing the innate, T cell-independent sentinel mast cells from the adaptive, T cell-dependent induced mast cells that accompany an inflammation response. Austen was fascinated by the possibility that a moiety, termed slow-reacting substance of anaphylaxis (SRS-A), released from lung tissue and highly potent in constricting airway smooth muscle by an unknown mechanism might be involved in bronchial asthma. His group developed a purification technique and characterized the pharmacology of SRS-A in studies with Robert Murphy and Jeffrey Drazen. They then worked with the initial synthetic cysteinyl leukotrienes (cysLTs) provided by E. J. Corey, to show that SRS-A was composed of three moieties in which the glutathione adduct of the arachidonic acid-derived lipid portion (LTC_4) was cleaved to leave a dipeptide (LTD_4) and then merely a cysteinyl adduct (LTE_4). They cloned and named LTC_4 synthase, the human enzyme that forms the parent of the cysLTs with the glutathione adduct. After decades of addressing only the effector functions of the three cysLTs, provided by mast cells and eosinophils, they found that dendritic cells respond to house dust mites by also generating cysLTs via the carbohydrate receptor dectin-2. In early pharmacologic studies they had found evidence for three receptors, and the Austen group recently cloned the missing third receptor and showed that each cysLT had a preferred receptor.

Austen is the recipient of numerous medical awards, including the Gairdner Prize, the Waterford Prize, the Warren Alpert Foundation Prize, and the Kober Medal of the Association of American Physicians. He has been elected to the American Society for Clinical Investigation, the American Academy of Arts and Sciences, the National Academy of Sciences, and the Royal Society. Austen has served as president of the American Association

of Immunologists, the American Academy of Allergy, Asthma and Immunology, and the American Association of Physicians. He has received honorary doctorates from the University of Paris, Hofstra University, Akron University, and Amherst College. He has presented numerous named lectures, is currently on the editorial boards of the *Journal of Experimental Medicine* and *Advances in Immunology*, and has edited a series of textbooks in immunology. He has been the recipient of numerous research support awards since 1958. The Harvard Medical School established a K. Frank Austen Professorship, and a K. Frank Austen Visiting Professorship was added by the Brigham and Women's Hospital on his 80th birthday. He has served as the mentor for many pre- and postdoctoral research-trainees, who themselves have gone on to distinguished careers in medicine and medical research. He served three terms as a trustee of Amherst College and is currently a life trustee of the college.

Edward J. Benz Jr., MD

Edward Benz was born in Pittsburgh, PA, on May 22, 1946. He received his AB degree from Princeton University in 1968 and his MD degree from Harvard Medical School in 1973. From 1973 to 1975 he served as intern and assistant resident in medicine at the Peter Bent Brigham Hospital. During that period Benz was a clinical fellow in medicine (hematology). From 1975 to 1978 he was a research associate in the Molecular Hematology Branch at the NIH NHLBI. After a year as a hematology fellow at Yale, he served as assistant professor of medicine, then as associate professor of medicine and human genetics. In 1987 he became professor of internal medicine and human genetics and chief of hematology. From 1990 to 1993 he served as vice chairman of the department of medicine.

In 1993 he was appointed Jack C. Myers Professor and chairman of the department of medicine at the University of Pittsburgh School of Medicine, adjunct professor of biological sciences at Carnegie Mellon University, and a member of the Pittsburgh Cancer Institute. In 1995 he moved to Johns Hopkins as the Osler Professor of Medicine, director of the Department of Medicine, professor of molecular genetics and biology, and physician-in-chief at Johns Hopkins Hospital.

In 2000 Benz became president and CEO of the Dana-Farber Cancer Institute in Boston, CEO of Dana-Farber/Partners CancerCare, director and principal investigator of Dana-Farber/Harvard Cancer Center, and the

Richard and Susan Smith Professor of Medicine, professor of pediatrics, and professor of genetics at Harvard Medical School.

Benz's father, chief of pathology at St. Luke's Hospital in Bethlehem, PA, was the quiet inspiration for his academic career. Benz's interest in science and medicine started in elementary school and early high school. Raised in a family laced with medical relationships, he found clinical practice attractive but wanted to add other dimensions to his career. As an undergraduate at Princeton, he became fascinated by the embryonic field of molecular biology and was inspired by work in the laboratory of Arthur G. Pardee, his undergraduate thesis advisor. This experience sparked his interest in gene regulation and convinced him that he wanted a career that combined clinical care and basic research.

While a Harvard medical student, he met David G. Nathan, who was chief of the Division of Hematology Research at Children's Hospital. Nathan quickly tutored Benz in the nuances of hemoglobinopathies, and his career was underway. Most importantly, he made friends with Bernard G. Forget, one of Nathan's group who had been exposed to the molecular biologist Sherman Weissman. In friendly competition with Art Nienhuis and French Anderson from the NIH, Forget and Benz performed experiments demonstrating that defects in hemoglobin synthesis known to characterize common hemoglobinopathies, the thalassemia syndromes, were due to quantitative defects in the messenger RNA encoding each globin. Forget was influential in promoting Benz's stature as an equal partner in their research accomplishments. This allowed Benz to grow as an investigator during his years of clinical rotations. He entered his role as house officer with a growing national reputation as a member of a nascent community of molecular hematologists. He also had the good fortune to secure a research internship inaugurated at the Peter Bent Brigham Hospital by Eugene Braunwald, which permitted him to remain involved in research while obtaining first-rate clinical training.

At the NIH he joined the laboratory of Arthur Nienhuis. They worked out the basic molecular biology of hemoglobin switching in sheep and began to relate molecular events controlling globin gene expression with cellular events in early hematopoiesis. They joined the early ranks of the "gene splicers," cloning sheep globin genes and some human thalassemia mutations. Benz now had an established research career due to the advantages given him by his mentors, Pardee, Nathan, Forget, and Nienhuis.

Benz's major research accomplishments have been in the area of applying molecular genetics to the study of human diseases. In 1971 he published a paper with Forget that recorded the first successful attempt to dissect a human disease (thalassemia) at the level of the immediate gene products. These studies reoriented the focus of research in thalassemia to the study of the globin genes. Hemoglobinopathies have since become the model that is now widely applied in human pathology, and these studies made a significant early contribution to this change in perspective.

More recently Benz's group has demonstrated the importance of tissue-specific alternative mRNA splicing in the biogenesis of the red cell membrane. Their studies of protein 4.1 provided the basis for understanding how mutations in a gene expressed in multiple tissues can result in a phenotype expressed only in a limited subset of tissues, namely those dependent upon splicing events altered by the mutation. His laboratory remains active and focuses on the multiple roles of protein 4.1R that are modulated by tissue-specific alternative pre-mRNA splicing in a variety of tissues and physiologic states.

Benz attributes his contributions to the fact that he functioned in a very nurturing environment with outstanding mentors. Another important factor is that the system for funding biomedical research and the culture in academic medical centers during his period of development were very compatible with launching a successful career in clinical investigation. In the present climate only a few exceptional individuals can engage in intense bench research and still maintain competence as a clinician. These individuals are critical. Their continued presence should be maintained at all costs.

Benz has received many awards, including the Soma Weiss Award for Undergraduate Research (1972) and the Boylston Society Award (1973), as well as the Leon Resnick Memorial Award for Undergraduate Research. In 1979 he accepted the NIH Young Investigator Award and, the following year, the Basil O'Conner Award and Edward Paradisio Research Grant Award. He also received the Cooley's Anemia Foundation of New Jersey Award. In 1982 he received an NIH Research Career Development Award. He has served on many advisory committees, both federal and private, including the Hematology I Study Section at the NIH, which he chaired. He co-chaired the Director's Blue Ribbon Panel on Clinical Research at the NIH Clinical Center and served on the board of directors of the center, chairing it in 2007–2009.

Benz belongs to many prestigious societies, including the Institute of Medicine, the American Academy of Arts and Sciences, the American Society for Clinical Investigation, the Association of American Physicians, Phi Beta Kappa, Alpha Omega Alpha, Sigma Xi, the American Federation for Clinical Research, the Red Cell Club, the American Society for Human Genetics, and the American College of Physicians. He has been elected president of ASCI (1992), the American Society of Hematology (2000), Friends of the National Institute of Nursing (2006), the Association of American Cancer Institutes (2007–2009), and the American Clinical and Climatological Association (2012). In 1988 he held a Markey Fellowship at the Mount Desert Island Biological Laboratory. Benz has served as associate editor for the *New England Journal of Medicine* and *Blood* and served on numerous editorial boards, including those of the *American Journal of Hematology*, *Cellular and Molecular Biology*, and *American Journal of Medicine*. He is a founding co-editor with Ron Hoffman of the award-winning textbook *Hematology: Principles and Practice*, now in its sixth edition, and was an editor of the 4th edition of the *Oxford Textbook of Medicine*, which won the Royal Society of Authors First Prize for Textbooks in 2003.

Richard S. Blumberg, MD

Richard (Rick) Blumberg was born in Philadelphia, PA, on April 29, 1953. He received his BS degree from Carnegie-Mellon University in Pittsburgh (1974), where he studied chemistry and biological sciences. After a year in a PhD program in biochemistry at Pittsburgh, he matriculated to Jefferson Medical College and received his MD in 1979. This was followed by a residency in medicine at the New York Hospital of Cornell Medical College (1979–1982), where he served as assistant chief medical resident, followed by fellowship training in infectious diseases at Massachusetts General Hospital (MGH) (1982–1986) and in gastroenterology at Brigham and Women’s Hospital (1986–1990). His years at Pittsburgh and Jefferson were influenced by mentors Daisuke Nakada (biochemistry) and Dhodanand Kowlessar (gastroenterology). Daisuke instilled excitement and pleasure in undertaking scientific investigation, and Dhodanand served as a role model for academic medicine and helped Blumberg focus his innate abilities.

At New York Hospital (1979–1982) he was influenced by patients with the newly described acquired immunodeficiency syndrome (AIDS) and chose a fellowship in infectious diseases with Robert (Chip) Schooley, who

served as Blumberg's first mentor at MGH. There he studied the immune responses of AIDS patients to Epstein-Barr virus (EBV) infection and became enchanted with the host immune response and immunology in general. The laboratories of Schooley and Hirsch at MGH were among the earliest to initiate longitudinal studies of patients, providing ample clinical material that allowed Blumberg to hone his interests in immunology. After discovery of human T cell lymphotropic virus type III (HTLV-III) in 1983–1984, he studied the immune response to HTLV-III itself and demonstrated that anti-HTLV-III antibodies could function in cellular toxicity. Further, upon the discovery by others that B cells became permissive to HTLV-III infection upon immortalization with EBV, he recognized that he could superinfect the immortalized EBV lines from AIDS patients with HTLV-III and use their autologous peripheral blood T cells to detect HIV-specific cytotoxic T cells. This work was completed by his protégé, Bruce Walker. The recognition that HTLV-III was a mucosal infection piqued his interests in this field.

At Brigham and Women's Hospital (BWH) he received critical mentoring from Jerry Trier and Cox Terhorst, the first to clone CD3 genes. Under Jerry's direction, Blumberg spent three years in Terhorst's laboratory at the Dana-Farber Cancer Institute, studying T cell receptor (TCR)/CD3 structure and function. These were exciting times in T cell immunology and in Boston. The Terhorst laboratory was a fertile environment and trained numerous scientists who went on to distinguished careers, such as Hans Clevers, Katia Georgopolous, Steven Ley, Balbino Alarcon, Steven Balk, and Thomas Wileman. There, Blumberg made several important discoveries, including the recognition that the TCR/CD3 complex contained two CD3-epsilon chains; this was a critical clue to the stoichiometry of this receptor complex. From this, Blumberg acquired the molecular immunology expertise that allowed him to embark on his own independent program at BWH in 1990 and apply this expertise in mucosal immunology to the study of inflammatory bowel disease.

Blumberg was named chief of the Division of Gastroenterology, Hepatology and Endoscopy at BWH in 1998 and professor of medicine at Harvard Medical School in 2005. His research evolved into four areas of inquiry. Following his experience in the Terhorst lab, Blumberg spent the next 24 years studying CD1 proteins and the TCR repertoire in mucosal tissues, making crucial observations such as the recognition that microsomal triglyceride transfer protein is essential for CD1 lipidation in the endoplasmic reticulum akin to the acquisition of peptide antigens by classical MHC

class I molecules. His interests in MHC class I proteins led him to study the neonatal Fc receptor (FcRn) for IgG. He built this research program into one that had great translational impact and was the scientific founder of Syntonix Pharmaceuticals (acquired by Biogen in 2007), which was responsible for leveraging FcRn biology in the development of long-acting therapeutic proteins for the prophylaxis of hemophilia A and B. This culminated in the 2014 FDA approval of Eloctate (factor VIII-Fc) and Alprolix (factor IX-Fc), which use the monomeric Fc fusion protein technology developed by Blumberg and his colleagues. Blumberg was the first to recognize the role of carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1) as an activation-induced inhibitory molecule on mucosal and systemic T cells and, more recently, that CEACAM1 forms a heterodimeric complex with T cell immunoglobulin domain and mucin domain molecule 3 (TIM-3) to regulate the latter's ability to elicit tolerance in exhausted T cells. He showed that X box-binding protein 1 (XBP1), a molecule discovered by Laurie Glimcher, a collaborator of Blumberg's, determines Paneth cell function, and that intestinal inflammation can derive directly from this cell type in the small intestine.

Blumberg recognized the importance of collaboration and mentoring, and has helped build the careers of young scientists around the world. He has served the community in different capacities. He is the co-director of the Harvard Digestive Diseases Center, a P30 program supported by the NIH, is the incoming chair of the Brigham Research Institute, and serves as vice chair of the advisory committee of the Department of Medicine. He has served as member of the Immunology Sciences Study Section of the NIAID, member of the National Commission of Digestive Diseases of the NIDDK, scientific consultant to the Human Microbiome Project of the National Genome Research Institute, and member of the Vaccine Branch External Advisory Board of the National Cancer Institute, and has served on the Board of Scientific Councilors of the NIAID. He served as chair of the national scientific advisory committee of the Crohn's & Colitis Foundation of America and was president of the Society for Mucosal Immunology. Blumberg is an elected member of the American Society for Clinical Investigation and the Association of American Physicians and a recipient of an NIH MERIT Award (2005), the William Beaumont Prize from the American Gastroenterological Association (2012), and the Distinguished Scientific Achievement Award from the Crohn's and Colitis Foundation of America (2012).

Eugene Braunwald, MD

Eugene Braunwald was born on August 15, 1929, in Vienna, Austria. Following the Nazi occupation he emigrated to England in 1938, and then to the United States. He attended New York University, receiving the AB degree in 1949 and the MD in 1952. After internship and fellowship training in internal medicine and cardiology at Mount Sinai Hospital in New York, he became a fellow in the laboratory of Andre Cournand at Bellevue Hospital. In 1955 he joined the Intramural Program of the National Heart Institute. With the exception of one year of senior residency training in medicine at Johns Hopkins, he remained associated with the Heart Institute from 1959 to 1968, serving for a number of years as its clinical director. In 1968 Braunwald became professor and first chairman of the department of medicine at the new medical school at University of California, San Diego, and physician-in-chief of its university hospital. In 1972 he succeeded George Thorn as Harvard's tenth Hersey Professor of the Theory and Practice of Medicine and the fourth physician-in-chief of the Peter Bent Brigham Hospital. From 1980 to 1989 he was Herrman Blumgart Professor of Medicine at Harvard. With the changes in hospital affiliation at Harvard, he serves as physician-in-chief of Brigham and Women's Hospital.

Braunwald's earliest research work dealt with the hemodynamics of the normal and diseased heart. He and his colleagues made the first measurements of the pressure gradient across the stenotic mitral valve and described for the first time the time relationships of dynamic events in the cardiac chambers, pulmonary artery, and aorta in humans. While at the National Heart Institute, Braunwald and his collaborators developed a number of diagnostic techniques that have been applied widely, including the use of indicator dilution curves from the left heart and aorta for localization of left-to-right shunts and detection of valvular insufficiency, transbronchial left heart catheterization, transseptal left heart catheterization, indicator dilution techniques for the detection of pulmonic and tricuspid valvular regurgitation, the use of external precordial scanning in the detection of cardiac shunts, and the use of inhaled inert foreign gases in the detection of left-to-right shunts.

In studies with Sarnoff, Braunwald characterized the hemodynamic determinants of myocardial oxygen consumption and coronary blood flow, identifying the tension time index as a major determinant of myocardial oxygen consumption. He and his colleagues clarified the importance of Starling's law as a major determinant of myocardial performance in hu-

mans, and together with Andrew Morrow he contributed to the initial description of, and then named, idiopathic hypertrophic subaortic stenosis. With Tinsley Harrison he studied cardiac dimensions in intact unanesthetized patients in whom radiopaque markers had been sewn to the surface of the heart at the time of corrective cardiac operations. With Edmund Sonnenblick, he developed techniques for characterizing myocardial force-velocity relations in intact unanesthetized humans and identified velocity of cardiac contraction as a major determinant of myocardial oxygen consumption. Together with Stephen Epstein he carried out some of the earliest studies on β -adrenergic receptor-blocking drugs and identified reduction of cardiac tyrosine hydroxylase activity as the immediate cause of norepinephrine depletion in heart failure. Working with Epstein and his wife, Nina Braunwald, he demonstrated that implantation of a radio frequency-receiving unit connected to electrodes attached to the carotid sinus nerves could, when activated externally, relieve angina pectoris by electrical stimulation of the nerves. While in San Diego, Braunwald and his coworkers determined that the size of infarcted heart muscle is not irrevocably determined at the time of coronary occlusion but could be greatly augmented or reduced by a variety of interventions. After moving to Boston, Braunwald's major research efforts were devoted to extending to patients the concept of the reduction of infarct size following coronary occlusion.

Braunwald has written and edited a number of books and monographs on heart disease and cardiovascular physiology. In 1966 he replaced Harrison as cardiovascular editor of the textbook *Harrison's Principles of Internal Medicine*.

Braunwald is a member of a number of professional societies, including the National Academy of Sciences and the Institute of Medicine of the National Academy of Sciences, and is a fellow of the American Academy of Arts and Sciences. He has served as president of the American Society for Clinical Investigation, the American Federation for Clinical Research, and the Association of Professors of Medicine. He is a member of the Association of American Physicians. Awards received include the Abel Award for Research in Pharmacology, the Research Achievement and Herrick Awards of the American Heart Association, the Phillips Award of the American College of Physicians, the Williams Award of the Association of Professors of Medicine, and the Distinguished Scientist Award of the American College of Cardiology. He has served on many advisory committees, including the Panel of Biological and Medical Science of the President's Science

Advisory Committee, the President's Advisory Panel on Heart Disease, and the National Heart and Lung Advisory Council. He is also the recipient of a number of honorary degrees.

Barry M. Brenner, MD

Barry M. Brenner was born in Brooklyn, NY, on October 4, 1937. He received his BS in biology from Long Island University in 1958. He was awarded the MD degree by the University of Pittsburgh School of Medicine in 1962. He served as intern and assistant resident in medicine at the Bronx Municipal Hospital Center of the Albert Einstein College of Medicine from 1962 to 1965 and as chief resident the following year. He then spent three years in research training in renal physiology at the NIH in the laboratory of R. W. Berliner. During the subsequent seven years he served as chief of nephrology at the San Francisco VA Medical Center and rose to the rank of professor of physiology and medicine (1975) at the University of California, San Francisco, School of Medicine. From 1974 to 1976 he was a staff member at the Cardiovascular Research Institute of UCSF. In 1976 he moved to Boston as the Samuel A. Levine Professor of Medicine at Harvard Medical School and director of the Laboratory of Kidney and Electrolyte Physiology at Brigham and Women's Hospital (BWH). In 1979 he succeeded the late John P. Merrill as director of the Renal Division at BWH. In 1987 he became director of the Harvard Center for the Study of Kidney Disease.

Brenner is responsible in large measure for our current knowledge of hydrodynamic and permeability properties of the renal glomerular and peritubular capillary systems and the biophysical, physiologic, and hormonal factors that regulate them in health and disease. In the late 1960s Brenner developed microtechniques to directly measure capillary hydraulic and oncotic pressures. He applied these techniques to a mutant rat strain endowed with accessible glomeruli and feed/draining microvessels, thus permitting quantification of pertinent pressures, flows, and solute and fluid permeabilities. He and his associates derived highly predictive mathematical models to explain observed physiologic events, incorporating concepts of hydrodynamic and mass transfer theory. These models have since been shown to be applicable to other microcirculatory beds as well. Likewise, his discovery that a variety of vasoactive substances bind to specific membrane receptors in isolated glomeruli and modulate glomerular capillary function in vivo motivated the successful search for similar microvascular

hormonal control in peripheral capillary beds. He is also responsible for discovering that movement of macromolecules across glomerular capillary walls is strongly influenced by fixed negative charges, thus explaining the normally trivial filtration of albumin and other circulating polyanions. Disruption of this charge-selective barrier accounts for albuminuria and nephrotic syndrome, which are clinical hallmarks of glomerular injury in humans and animals. Similar fixed negative charges have since been found along the walls of non-renal capillary beds, accounting for the low albumin escape rates characteristic of the intact peripheral microvasculature.

Brenner discovered in 1981 that reduction in renal mass leads to adaptive glomerular hypertension and hyperfiltration, and he postulated that human renal disease follows its inexorably progressive downhill course due to this excess of glomerular pressures. This “final common pathway” hypothesis, a unifying explanation to account for all forms of progressive renal disease, allows for the possibility that clinical renal disease can be completely arrested in its early stages, thereby obviating the eventual need for the expensive “halfway” technologies of dialysis and transplantation. The concept of intra-organ hypertension, a key feature of Brenner’s hypothesis, has broad implications for progressive failure of other organs. In 1988 Brenner proposed that babies born too small or too soon are endowed with fewer nephrons than would be expected. This state of having low nephron number carries consequences in later life, such as hypertension and increased risk of chronic kidney disease.

Brenner received the George Heard Memorial Prize in 1962, at graduation from the University of Pittsburgh. He also received the George Brown Memorial Award from the American Heart Association in 1985; the Wilson Medal from the American Clinical and Climatological Association and the MERIT Award from the NIH in 1986; the Bright, Masugi, Volhard Medal from the Japanese Society of Nephrology, the Richard Bright Award from the American Society of Hypertension, and the President’s Medal from the American Society of Nephrology in 1987; and the 9th Centennial Silver Medallion from the University of Bologna in 1991. Brenner has received honorary degrees from Harvard University, Long Island University, the University of Paris IV (Pierre et Marie Curie University), Charles University in Prague, Complutense University of Madrid, and the Royal College of Physicians in London. More recent awards have included the Jean Hamburger Award, A.N. Richards Award, and ISN Amgen International Prize from the International Society of Nephrology; the David Hume and Donald W. Seldon Awards from the National Kidney Foundation; and the Homer W.

Smith Award, John P. Peters Award, and Robert G. Narins Award from the American Society of Nephrology.

Brenner is a member of numerous medical societies, including the American Society of Nephrology, the International Society of Nephrology, the American Federation for Clinical Research, the American Physiological Society, the American Society for Clinical Investigation, the Association of American Physicians, and the American Academy of Arts and Sciences. He has co-authored an authoritative textbook entitled *Brenner and Rector's The Kidney* with F.C. Rector Jr., first published in 1976, as well as volumes in the *Contemporary Issues in Nephrology* series (e.g., *Acute Renal Failure*, *Clinical Nephrology*), *Renal Physiology in Health and Disease*, *Renal Pathology with Clinical and Functional Correlations*, the *Perspectives in Hypertension* series, *Biologically Active Atrial Peptides*, *Advances in Atrial Peptide Research*, and *Hypertension: Pathophysiology, Diagnosis, and Management*. He has also served on numerous editorial boards, including those of the *American Journal of Physiology*, *Circulation Research*, *Journal of Clinical Investigation*, and *American Journal of Hypertension*.

He is a member of many professional committees both federal and private and has served as vice president of the American Society for Clinical Investigation and president of the American Society of Nephrology and the American Society of Hypertension.

Howard Franklin Bunn, MD

Franklin Bunn was born in Madison, NJ, on July 7, 1935. His high school chemistry and physics classes were complemented by a summer at The Jackson Laboratory in Bar Harbor, Maine, where he observed scientists design and execute experiments. He received an AB degree from Harvard in 1957 and an MD from the University of Pennsylvania School of Medicine in 1961. For the following three years he was intern and resident in medicine at New York Hospital. From 1964 to 1966 he was a research fellow at the Thorndike Laboratory under James Jandl; this experience began what would become a 20-year study of hemoglobin. He used chemical crosslinking reagents to show that hemoglobin is filtered by the glomerulus as the α/β dimer. After serving in the U.S. Army, Bunn spent a year working in the laboratory of Robin Briehl at Albert Einstein College of Medicine. His measurements of oxygen equilibria on human hemoglobins enabled him to conclude that the physiologically important modifier 2,3-BPG binds to

deoxyhemoglobin at the N-terminus of the beta chain as well as at beta-143 histidine. He sent his results to Nobel Laureate Max Perutz and was thrilled to receive a hand-written reply from Perutz explaining that he (Perutz) had fitted BPG into his model of deoxyhemoglobin and found agreement with Bunn's biochemical observations.

Further research on hemoglobin demonstrated the existence of asymmetrical hybrid hemoglobins *in vitro* and *in vivo*. Measurements of the rates of assembly of hemoglobin subunits into dimers and tetramers revealed that the charge on the subunit is an important determinant of the rate of assembly and therefore contributes significantly to the hematologic phenotype. His lab discovered and characterized several functionally interesting variants, including the first example of a frame-shift mutation. Identification of a partially N-acetylated variant that retains its initiator methionine prompted Bunn and Jean-Paul Boissel to prepare and express a complete set of site-directed mutants, leading to the establishment of sequence-dependent rules for the cleavage of the initiator methionine and N-acetylation.

In collaboration with Paul Gallop, Bunn showed that the minor hemoglobin component A1c contains glucose attached to the N terminus of the beta chain by a ketoamine linkage. The kinetics of this adduct formation both *in vivo* and *in vitro* provided the rationale for the clinical use of HbA1c as an index of long-term glucose control in diabetics. Subsequently his lab demonstrated similar ketoamine-linked glucose in albumin, red cell membrane proteins, lens crystalline, and glomerular basement membrane collagen. These studies suggested that this glucose-dependent modification is a likely contributor to the long-term complications of diabetes.

In 1984, following a sabbatical at the NIH, Bunn began to use recombinant DNA technology, and the focus of research has since been on erythropoietin (Epo). He and Mark Goldberg discovered two cell lines that, like the kidney and liver, produce Epo in response to hypoxia. Transfection experiments led to the identification of cis-acting elements in the Epo gene responsible for hypoxic induction, including steroid hormone response elements in a downstream enhancer. Bunn and Boissel subsequently examined structure-function relationships in Epo by the preparation and testing of over 50 site-directed mutants. Their results supported a 4 α -helical bundle model and revealed sites on the molecule that are involved in the binding of Epo to its receptor.

Other investigators showed that the oxygen-dependent regulation of Epo (and a large number of other physiologically relevant genes) is regulated by a heterodimeric hypoxia-induced transcription factor (HIF). Bunn and Eric Huang found that in oxygenated cells HIF α is rapidly degraded in the proteasome, owing to a highly conserved oxygen-dependent degradation (ODD) domain that is necessary and sufficient for rapid destruction of HIF α in oxygenated cells.

The 20-year devotion of Bunn's lab to hemoglobin led to a search for novel heme proteins and the cloning and characterization of the novel 58-kDa protein Ncb5or, which has a cytochrome b₅-like domain at the N terminus and a flavin-binding cytochrome reductase like domain at the C terminus. A global knockout of this gene produced mice with insulin-deficient diabetes, lipoatrophy, and a defect in $\Delta 9$ desaturation of fatty acids, even when their diabetes was corrected by treatment with insulin. Thus Ncb5or may function as a substitute or a supplement to the classic cytochrome b₅ and cytochrome b reductase complex in mediating fatty acid desaturation.

From 1976 to 1982 Bunn served as director of the hematology division at Brigham and Women's Hospital. From 1977 to 1989 he was an investigator at the Howard Hughes Medical Institute. In 1990 Bunn assumed responsibility for the Harvard-Markey program in Biomedical Sciences, which provides graduate students with an additional year of training in human biology and the pathophysiology of disease. In 2013 he won a Harvard Medical School Faculty Prize for sustained excellence in teaching, and in 2015 he won an award for his teaching of first- and second-year students.

Bunn is a member of the American Society of Hematology (president 1992–1993). He was recipient of their Stratton Medal in 1996 and their Coulter Award in 2009 for lifetime achievement in hematology. He has also been a member of the American Society for Clinical Investigation, the American Society for Biological Chemists, the Interurban Clinical Club (president 1991–1992), and the Association of American Physicians and is a fellow of the American Academy of Arts and Sciences. He has served on the editorial boards of the *Journal of Clinical Investigation*, *Blood*, *Hemoglobin*, *American Journal of Hematology*, *Blood Cells, Molecules and Diseases*, and *Diabetes*.

Stephen B. Calderwood, MD

Stephen Calderwood was born in Brooklyn, NY on April 9, 1946. He received his BA degree from Harvard University in 1971 and MD degree from Harvard Medical School in 1975. This was followed by residency in internal medicine at Massachusetts General Hospital (MGH) in 1975–1978 and fellowship in infectious diseases at MGH in 1978–1980, where he was mentored by Morton Swartz and Robert Moellering and studied antimicrobial resistance in enterococci. He did a chief residency at MGH in 1981. Following a period on the faculty in the Division of Infectious Diseases at MGH as the fellowship training program director and clinical director, he did three years of additional postdoctoral research fellowship training under the mentorship of John Mekalanos at Harvard Medical School, studying the pathogenesis of enteric infection in both *Vibrio cholerae* and *Escherichia coli* O157. He returned to the faculty in the Division of Infectious Diseases at MGH in 1988, to set up his own laboratory, which has continued to the present. He became the chief of the Division of Infectious Diseases at MGH in 1990, a position he still holds. Since 1988 his research interests have focused on immune responses to enteric infections, microbial pathogenesis, microbial-host interactions, regulation of gene expression in the human host, human genetic polymorphisms related to susceptibility to enteric infections, and enteric vaccine development. His clinical interests are in antimicrobial agents and antimicrobial resistance, gastrointestinal infections, endocarditis, and central nervous system infections. He is currently the Morton N. Swartz MD Academy Professor of Medicine (Microbiology and Immunobiology) at Harvard Medical School.

Calderwood was heavily influenced in his career choice of internal medicine and infectious diseases by his mentors at MGH, Swartz and Moellering. Following his clinical training and chief residency, he was initially drawn to clinical practice infectious diseases. After his postdoctoral research fellowship with Mekalanos, however, he decided to shift his focus to translational research in the area of enteric infections.

Calderwood originally focused in his laboratory at MGH on in vitro and animal studies of *V. cholerae* gene regulation and pathogenesis. Following several years of NIH-funded research in these areas, he shifted the focus of his research in 2000 to studying cholera infection directly in humans, as principal investigator on an NIH International Collaborations in Infectious Disease Research (ICIDR) grant, conducted in collaboration with the International Centre for Diarrhoeal Disease Research in Dhaka, Bangladesh

(ICDDR,B). His collaborative studies since 2000 have focused on studying the immune responses that follow cholera infection; characterizing the immune responses that mediate protective immunity upon exposure to the organism from an infected individual in the household; studying the differences in immune response to infection versus immune response to cholera vaccination, with the goal of discerning why vaccination produces shorter-lived, less-protective efficacy than does natural infection; and characterizing the host genes involved in modulating the severity of cholera and the subsequent immune responses to natural infection or vaccination. In addition to receiving NIH funding for his research, Calderwood has also been the principal investigator of Fogarty International Center training grants that have facilitated both research training in Bangladesh for U.S. medical students and postdoctoral fellows as well as training in the U.S. for Bangladeshi physicians and scientists.

During Calderwood's time as chief of the Division of Infectious Diseases at MGH, the faculty in the division has grown to include 46 individuals, more than half of whom are NIH-funded investigators. The division currently conducts research on a broad range of topics, including HIV and other viral infections, microbial pathogenesis, vaccine development, immunology, global health, and clinical and translational research on antimicrobials and vaccines.

In addition to his research, clinical, and administrative activities, Calderwood is also the director of undergraduate medical education at MGH and directs the principal clinical experience for 50–58 third-year students at Harvard Medical School during their twelve months of core clinical rotations. Calderwood is the vice chair of the Department of Medicine and oversees the education of students, residents, and fellows in the department.

Calderwood has received multiple honors, including fellowship in the American College of Physicians, the Infectious Diseases Society of America, the American Society of Tropical Medicine and Hygiene, the American Academy of Microbiology, and the American Association for the Advancement of Science. He is an elected member of the Association of American Physicians and the president-elect of the Infectious Diseases Society of America. He has served on the NIH Bacteriology and Mycology 1 Study Section (including two years as chair), served as chair of division B (microbial pathogenesis) of the American Society for Microbiology, served for three years as chair of the Merck Irving Sigal Memorial Award selection

committee for the American Academy of Microbiology, served on the editorial board of *Infection and Immunity*, and currently serves as co-editor-in-chief for the infectious diseases sections of *UpToDate*. He has published over 200 journal articles, reviews, and book chapters on a variety of topics related to infectious disease and microbiology. In 2012 he received the Williams Silen Lifetime Achievement in Mentoring Award from Harvard Medical School.

Martin C. Carey, MD, DSc

Martin C. Carey was born on June 18, 1939, in Clonmel, County Tipperary, Ireland. He received MB, BCh, and BAO degrees summa cum laude and an MD, all from University College Dublin (UCD). In 1984 he was awarded the DSc degree from the National University of Ireland. He was a medical intern at St. Vincent's Hospital in Dublin, a resident in pediatrics and medical obstetrics at the Maternity Hospital in Dublin, a medical resident at St. Luke's Hospital, and a research fellow in gastroenterology at St. Vincent's Hospital. He came to the US in 1967 on a Fogarty fellowship and a Fulbright grant and received research training in gastroenterology, followed by training in lipid biophysics at Boston University School of Medicine, where he remained until 1975.

In 1975 he joined the Peter Bent Brigham Hospital. He rose through the ranks and became a tenured full professor at Harvard in 1988. From 1983 to 2014 he was a faculty member in the Graduate School of Arts and Sciences and associate member in the Department of Cell and Molecular Physiology at Harvard. Since 1982 he has been in the Gastroenterology Division at Brigham and Woman's Hospital. He retired in 2014, becoming professor of medicine, emeritus.

Carey's research interests were in the physical chemistry of bile and the pathophysiology of gallstones. Carey described low fasting and postprandial serum folate levels in homocystinuric children and suggested that folate was employed in the remethylation of homocysteine to methionine. He and his coworkers documented that the steroid antibiotic fusidic acid and its congeners were soluble, detergent-like molecules that formed micelles similar in size and properties to those of the common bile salts. When the carboxylic side chain of fusidate was amide-linked with glycine or taurine, the steroid lost its antibiotic properties but important detergent properties — especially resistance to acidic pH and calcium ions — were enhanced.

It was discovered years later that micellar solutions of fusidate conjugates could deliver peptides such as calcitonin, growth hormone, and insulin across epithelial surfaces, to enter the bloodstream in metabolically active form. Based on this work he and colleagues Jeffrey Flier and Alan Moses were awarded three U.S. patents for nasal drug delivery.

In 1978 he published a study with Donald M. Small, his first U.S. mentor, defining the equilibrium cholesterol solubility in model bile solutions composed of bile salt, egg yolk lecithin, cholesterol, and water. A paper published in 1979 by Carey and John Patton in *Science* reported the first visualization of the physicochemical processes that occur during fat (triglyceride) digestion with pancreatic lipase-colipase in the duodenum.

A 1981 paper published with S. P. Lee and J. T. LaMont was significant because it demonstrated that (a) *ex vivo* organ culture of gallbladder explants was feasible; (b) through the use of a radiolabelled glucosamine precursor, mucin hypersecretion occurred in response to delivery of lithogenic hepatic bile into the gallbladder; and (c) gallbladder mucus gel was a powerful nucleation matrix for biliary cholesterol crystallization. This work opened up new approaches to gallstone prevention by suppressing mucin production. In 1992 Carey and F. Konikoff showed that in bile salt-rich model bile, cholesterol precipitated as filamentous crystals that subsequently underwent changes in habit, often through metastable helical and tubular intermediates to achieve plate-like forms. This work opened up a new field of research into cholesterol crystallization from biologic fluids and challenged previously held beliefs concerning crystallization pathways in bile.

Research in the 1990s with colleagues (for which Beverly Paigen was principal investigator) at the Jackson Laboratory in Maine discovered the first cholesterol gallstone genetic locus (*Lith1*) in the C57L inbred mouse. Together with MIT colleagues Kirk J. Maurer and James G. Fox (the latter of whom was the study's principal investigator), it was demonstrated that a family of enterohepatic helicobacter species such as *H. hepaticus* is essential for the high prevalence of cholesterol gallstones in some strains of mice. Carey and colleagues were also the first to systematically define the physical chemistry of a natural conjugated bile pigment, bilirubin ditaurate, and together with his colleagues at MIT he described a new model of impaired CCK-induced gallbladder contraction involved in spontaneous formation of "black" pigment gallstones in germ-free Swiss Webster mice.

Carey received a Guggenheim grant in 1975, an academic career devel-

opment award from the NIH in 1976, MERIT awards in 1986 and 2004, the Adolf Windaus Prize from the Falk Foundation (Freiburg) in 1984, and the Fitzgerald Medal from UCD in 1993. He was awarded the Ismar Boas Medal from the German Society for Gastroenterology at their Annual Meeting in Bonn in 2002 and became an honorary fellow of the faculties of medicine at the UCD School of Medicine & Medical Science and at National University of Ireland in 2003. He is a fellow of Royal College Physicians of Ireland and the American Association for the Advancement of Science and was a member of the Gastroenterology Research Group (vice chairman of its steering committee) and the American Society for Clinical Investigation. He was a member of the American Gastroenterological Association, received its distinguished achievement award in 1990 and the Beaumont Prize in 2000, and was named as fellow in 2006. He is also a member of the American Oil Chemists Society, the Biophysical Society, the Interurban Clinical Club, the American Association for the Study of Liver Disease, the American Association of Physicians, and the Royal Irish Academy.

Carey has served on many advisory committees and on several editorial boards, including those of the *American Journal of Physiology*, *Journal of Lipid Research*, *Hepatology*, *Gastroenterology*, and *Archives of Gastroenterology*. Carey holds honorary degrees from Harvard (AM, awarded in 1989) and the National University of Ireland (LLD awarded in 1992 and DSc awarded in 2010).

William W. Chin, MD

William W. Chin was born in New York, NY, on November 20, 1947, of parents who were first-generation immigrants from southeast China. His early education was obtained in the New York City public school system, and he graduated from Jamaica High School in Jamaica, NY, in 1964.

He received his AB in chemistry summa cum laude from Columbia College in 1968 and his MD from Harvard Medical School in 1972. He then completed a residency in internal medicine at the Beth Israel Hospital from 1972 to 1974, a research fellowship in molecular virology at the National Institute for Child Health and Development (NICHD) at the NIH (1974–1976), and a fellowship in endocrinology and metabolism at Massachusetts General Hospital (MGH) (1976–1978).

Chin joined the Harvard Medical School (HMS) faculty at MGH in 1978 and subsequently moved to the Brigham and Women's Hospital (BWH), where he became professor of medicine at HMS in 1993 and professor of obstetrics, gynecology, and reproductive medicine in 1996. He served as senior physician and founded the Division of Genetics in the Department of Medicine at BWH (1987–1999) and also served as an investigator at the Howard Hughes Medical Institute (1979–1995).

He is a molecular endocrinologist who pioneered an understanding of the mechanisms of hormonal regulation of pituitary hormone gene expression as well as aspects of nuclear receptor action, with a focus on thyroid, estrogen, and other hormones. Together with many wonderful students and postdoctoral fellows, he engaged in pioneering work in this field, cloning cDNAs for the α and β subunits of thyrotropin, lutropin, and follitropin as well as the thyroid hormone receptors. In turn, these important molecular reagents were then used to explore the regulation of gene expression by hormones and hormone action and biosynthesis, including the definition of key coactivators and other transcriptional factors involved in nuclear hormone receptor action.

The inspiration for a life in science and medicine came early for Chin, from Herman Gillary, chairman of biology at Jamaica High School, who inculcated the importance of query. In college Chin had Charles R. Cantor as a research mentor, a collaboration that led to his first publication, which was focused on the physical chemistry of oligo RNA:DNA complexes. In medical school, his experience in a first-year lecture on the thyroid by Sidney H. Ingbar set in motion a life-long desire to understand the regulation of the hypothalamic-pituitary-thyroid axis and, in particular, the mechanism of negative regulation of thyrotropin synthesis by thyroid hormones. Other influential mentors included Louis Sherwood, who focused his interest in other pituitary hormones; Jacob V. Maizel, Philip Leder, Phil Sharp and Alex Rich in molecular biology and genetics; Farahe Maloof and Chip Ridgeway in clinical thyroidology; and Joel F. Habener in molecular endocrinology.

As head of the Division of Genetics at BWH, Chin was responsible for the early deployment of clinical genetics, genomics, and bioinformatics in the practice of adult medicine. He has been author or co-author of more than 300 original papers, invited chapters, or books and has served on numerous editorial boards and private and governmental review panels. In addition, he has practiced endocrinology with a focus on thyroid and pituitary

disease and taught Harvard medical and graduate students in these fields for much of his academic career.

He joined Eli Lilly and Company in 1999 to turn his focus toward translational science and medicine. He served in a number of executive roles in drug discovery and development, including vice president and senior vice president of discovery research and clinical investigation and member of the senior management council (2005–2010).

In 2010 Chin returned to HMS as the executive dean of research, Bertarelli Professor of Translational Medical Science, and professor of medicine. While there he catalyzed new programs in therapeutic sciences and industry — academic collaborative partnerships — to speed innovation to patients through translational research.

Since 2013 he has been executive vice president of science and regulatory affairs and chief medical officer of PhRMA in Washington, DC. He advocates for policies that foster biopharmaceutical science and innovation and regulatory decision-making, including interactions with pharmaceutical industry members, the Food and Drug Administration, and the NIH.

Chin has served on the NIH endocrinology and biochemical endocrinology study sections (and has chaired the former) and as member of the boards of scientific counselors for the NIDDK and NICHD. He is currently a member of the global advisory board at Takeda Pharmaceutical Company and of the science advisory board at the Agency for Science, Technology and Research (A*STAR). He has also been active in his local community, including service as an overseer of the New England Conservatory of Music and a member of the boards of directors at the Indianapolis Museum of Art and the Indianapolis Prize Jury (the largest monetary prize for wildlife conservation in the world).

Finally, he has provided leadership on the councils of several professional societies, including service as president of the American Thyroid Association and the Interurban Clinical Club (1998–1999). He has received many accolades, among which are the Robert H. Williams Distinguished Leadership Award from the Endocrine Society, the Sidney H. Ingbar and Van Meter Awards from the American Thyroid Association, the Bowditch Award from the American Physiological Society, the AFCR Young Investigator Award, and election to the American Society for Clinical Investigation and the American Association of Physicians.

William Crowley, MD

William Crowley was born on December 28, 1943, in Meriden, CT. He is a graduate of Holy Cross College (AB with honors, 1965), Tufts Medical School (MD, 1969), and the Internal Medicine Residency Program and Endocrinology Fellowship Program at Massachusetts General Hospital (MGH). He has remained on the faculty at Harvard Medical School since completing his training. He is currently the Daniel K. Podolsky Professor of Medicine at Harvard Medical School, chief of the Reproductive Endocrine Unit of the Department of Medicine at MGH, and served as the founding director of clinical research at MGH (1996–2014). He has also been director of the NICHD-funded Harvard Reproductive Endocrine Sciences Center at HMS for the past 28 years.

Crowley's research program has provided new insights into the mechanisms of reproductive disorders of men, women, and children and also pioneered newer and more effective diagnoses for these disorders as well as elucidated their genetic control. These new treatments have included the first use of GnRH agonist-induced pituitary desensitization of the gonadotropes as a therapy for children with precocious puberty. This work provided the proof of principle for GnRH α therapy in men with prostate cancer and women undergoing IVF and with endometriosis. He also developed pulsatile GnRH administration to induce ovulation in infertile women and a normal puberty and fertility in men and women who fail to undergo normal puberty as a result of diagnoses such as Kallmann syndrome and idiopathic hypogonadotropic hypogonadism. To accomplish these tasks, he has used a wide spectrum of research approaches, including the study of normal men and women in tandem with several human disease models, by which he discovered underlying defects in the hypothalamic control of reproduction in the human. Most recently he has combined this detailed phenotyping information with various new tools derived from the Human Genome Project, using various biochemical, cellular, genetic and animal approaches wherever appropriate. Using these approaches he and his colleagues discovered the kisspeptin and prokinetic 2 signaling systems that control sexual maturation in humans. These master regulators of GnRH secretion are now known to control reproduction in all mammals and are the focus of both basic and clinical research groups throughout the world.

During the course of his discoveries, Crowley established a remarkable track record of training 85 pre- and postdoctoral physician-scientists for careers in academic biomedical research. Of these trainees, over 80% re-

main in academic medicine and are funded by peer-reviewed mechanisms, over 50% of those who trained with him 10 or more years ago are now full professors, and 68% are women. In recognition of these training accomplishments, Crowley received the Mentor Award from Women in Endocrinology in 2000, the first time this award was given to a male. In 2001 he received the Fred Conrad Koch Award, the Endocrine Society's highest scientific award. He also received the Fuller Albright Award from the Peripatetic Society, clinical investigator awards from both the NIH and the Endocrine Society, and the IPSEN Foundation's International Endocrine Award, the highest juried international prize in endocrinology.

Daniel Deykin, MD

Daniel Deykin was born in New York City on October 29, 1932. He attended Harvard College, and Harvard Medical School. Following internship and residency at the Beth Israel Hospital he then had a Research Associate appointment at the National Heart Institute in Bethesda. In 1962 he joined the Harvard Medical School faculty with a clinical appointment at the Beth Israel Hospital. His primary mentors were Hermann Blumgart, Stanford Wessler, and De Witt Goodman, all of whom were avatars of excellence of clinical and research excellence.

His research interests were sparked when he was fourth year medical student. He had just heard a lecture by Dr. Benjamin Alexander on the new understanding of the blood clotting cascade. This was followed by his presenting a patient with deep vein thrombosis on rounds at the MGH. He was struck by apparent lack of understanding of the pathogenesis of thrombosis by the most senior attending physicians. He decided then to embark on a research career to try to link hemostasis and thrombosis, leading to his first publication in 1960, followed by some 200 additional reports over the next thirty five years, reflecting both clinical and basic research studies. One key finding was the discovery and characterization of a novel and hitherto unknown transacylase that plays a key role in the metabolism of platelet and endothelial eicosanoid metabolism.

In 1972, while on a Guggenheim Fellowship to study platelet membrane structure at the National Institute for Medical Research in London, he received and accepted an invitation to become chief of the medical service at the Boston VA Hospital and professor of medicine at both Boston University and Tufts Medical Schools, becoming the newly established Maurice

Strauss Professor of Medicine. In 1985 he took on a new role as chief of the VA's national Cooperative studies program, and in 1988, adding the position of director of the VA's Health Services Research and Development program, moving both to Boston, where he kept his laboratory in full swing. He retired from the VA in 1996, receiving the VA's Secretary Award for Distinguished Service. He retained his appointments as professor of medicine, biochemistry and public health at Boston University. He retired fully in 2004, becoming emeritus professor of medicine and public health. He serves a consultant to the Clinical Trials and Epidemiology Research program at the Boston VA Medical Center.

Deykin is a Fellow of the American College of Physicians, and a member of the American Association of Physicians, the American Society for Clinical Investigation, the American Society for Hematology, Physicians for Social Responsibility, The American Clinical and Climatological Association, the Interurban Club, and the Roxbury Medical Improvement Society.

At Harvard College Deykin was awarded the Bowen Prize for his thesis on Walter Lippmann. He has taken three sabbaticals: the first in 1972, sponsored by the Guggenheim Foundation; the second in 1981 at Boston University where he joined a team studying practice variations in the management of diabetic ketoacidosis, which served as an introduction to health services research; and in 1995, sponsored by the Robert Wood Johnson Foundation to help evaluate the British National Health Services' nascent Health Services Research Program.

Although he maintains an active medical license, Deykin's current interest is studying Jewish biblical texts. He has joined the Harvard Institute for Learning in Retirement, where he will lead a seminar on the works of Primo Levi.

Jeffrey Mark Drazen, MD

Jeffrey Drazen was born on May 19, 1946, in Saint Louis, MO, and raised in Clayton, MO. He received an SB degree from Tufts University in 1965 and an MD degree four years later from Harvard Medical School. Between 1972 and 1977 Drazen served as intern, assistant resident physician, and senior resident physician at the Peter Bent Brigham Hospital, while simultaneously holding positions as clinical fellow in medicine (1972–1974; 1976–1977) and research fellow in medicine (1974–1976). In 1977 he became

assistant professor of medicine at Harvard and associate physician at Peter Bent Brigham. Drazen was promoted to associate professor in 1981 and to full professor in 1989. In 1990 he was appointed the Parker B. Francis Professor of Medicine at Harvard. At the Harvard School of Public Health, he became assistant professor of physiology in 1980, associate professor of physiology in 1981, and professor of physiology in 1991. In 1985 Drazen was appointed physician at Beth Israel Hospital and chief of its pulmonary division. In 1987 he became director of the Ina Sue Perlmutter Laboratory and associate chief for research in the Pulmonary Division of Boston Children's Hospital. In 1989 he assumed the directorship of the combined pulmonary divisions of Beth Israel Deaconess Medical Center and Brigham and Women's Hospital. He remained in that role at Beth Israel until 1994 and at Brigham and Women's until 2000, when he left to assume the job of editor-in-chief of the *New England Journal of Medicine*.

Drazen's interest in research was first kindled by his high school chemistry teacher, Frank Quiring. As an undergraduate at Tufts, he worked in the solid-state physics laboratory and developed techniques for measuring the Hall effect in semi-conductor thin films. During medical school Drazen worked in the physiology laboratory of Clifford Barger and J. Allen Herd. A course taught by Jeremiah Mead and John Pappenheimer at Harvard convinced him that his research interest lay in the respiratory field. As a third-year medical student, he worked with K. Frank Austen "to discover the cause and ultimately the cure for asthma." Drazen began to examine the airway effects of slow-reacting substance of anaphylaxis (SRS-A), research that he was able to continue during his residency years through a program created by Eugene Braunwald. He demonstrated that SRS-A had a unique peripheral airway effect in the guinea pig and was able to show that the peripheral airway activity of SRS was related to the unique distribution of receptors for this material. With the structural elucidation of SRS-A as a collection of the cysteinyl leukotrienes, leukotrienes C_4 , D_4 , and E_4 , Drazen showed that inhalation of these compounds in animals caused severe bronchoconstriction. He later demonstrated that cysteinyl leukotrienes were all potent bronchoactive agonists in normal human subjects when administered by inhalation. On the molar basis, LTC_4 and LTD_4 were approximately 3,000- to 10,000-fold more potent than histamine as bronchoactive agonists, making them the most potent bronchoconstrictor agonists known in normal humans. Drazen realized that the importance of leukotrienes in the asthmatic response could best be understood by studying the effects of leukotriene synthesis inhibitors or receptor antagonists on the asthmatic response. He worked with other investigators involved in phar-

maceutical development to design and execute a trial of the effects of the first-generation leukotriene receptor antagonist LY1 71883 on asthma induced by cold air inhalation. There was a significant protective effect of the antagonist on this induced asthmatic response. These investigations were extended to a series of leukotriene receptor antagonists or synthesis inhibitors. In each case it was shown that the cysteinyl leukotrienes contribute in an important way to asthmatic airway narrowing, thus introducing a new therapeutic approach to asthma. Eventually this work, along with that of many others, led to the licensing of four novel drugs to treat asthma; by 2010, over 10 million people used at least one of these drugs on a daily basis. Based on the variance of the response to leukotriene antagonists among patients, Drazen reasoned that there may be a genetic reason for these differences. He identified a promoter polymorphism in the *ALOX5* gene that was associated with less of a response to this class of drugs, a finding that has been widely replicated.

During Drazen's tenure as editor-in-chief, the *New England Journal of Medicine* has published major papers advancing the science of medicine, including the first descriptions of SARS, timely coverage of the Ebola epidemic, and modifications in the treatment of cancer, heart disease, and lung disease, and it has been at the forefront of the worldwide effort to register all clinical trials. Under his leadership the ISI Impact Factor of the journal has increased from the mid-20s to over 50; from 2008 through the present, it has had the highest impact factor of any medical journal that publishes original research.

Drazen is a member of the American Thoracic Society, the American Physiological Society, the American Federation for Clinical Research, the American Society for Clinical Investigation, the American Society for Pharmacology and Experimental Therapeutics, the Association of American Physicians, and the Institute of Medicine and is a fellow of the American Academy for the Advancement of Science. He holds honorary degrees from the University of Ferrara, the University of Modena and Reggio Emilia, and the National and Kapodistrian University of Athens.

Victor J. Dzau, MD

Victor J. Dzau was born on October 23, 1946, in Shanghai, China. When he was still young, his family fled China to Hong Kong. His childhood experiences with poverty and disease in postwar China greatly influenced

his life's passion for medicine. At age 18 he left his family to attend McGill University, where he received his bachelors and medical degrees. He completed his residency in medicine at Peter Bent Brigham Hospital and his clinical and research fellowships at Massachusetts General Hospital and Harvard Medical School.

Dzau is currently the eighth president of the Institute of Medicine of the National Academy of Sciences. He is the James B. Duke Professor of Medicine at Duke University, where he is chancellor emeritus, and is past president and CEO of Duke University Health System. He is also the executive director of the Mandel Center for Hypertension and Atherosclerosis Research at Duke University. Dzau was the Hersey Professor of Theory and Practice of Medicine and chairman of medicine at Harvard Medical School's Brigham and Women's Hospital. He worked previously at Stanford University, where he was chair of medicine, director of the Falk Cardiovascular Research Center, and director of the American Heart Association (AHA) and the Bugher Foundation's Center for Molecular Biology. He has served much of his career as a physician-scientist, leader, and mentor of young and future leaders.

Dzau's career as a physician-scientist was very much influenced during his residency and fellowship by his mentors, Eugene Braunwald and the late Edgar Haber and Clifford Barger, whose works truly exemplified the "bench-to-bedside" philosophy of pursuing discoveries that have direct human significance. Following in their footsteps, Dzau dedicated his career to translational research and has made a significant impact on modern medicine through his seminal works in cardiovascular medicine and genetics, his pioneering the discipline of vascular medicine, and recently his leadership in health care innovation. His work on the renin-angiotensin system (RAS) paved the way for the contemporary understanding of the RAS in cardiovascular disease and the development of RAS inhibitors as therapeutics. Dzau also pioneered gene therapy for vascular disease, and his recent work on the stem cell "paracrine mechanism" and the use of microRNA in direct reprogramming have provided novel insight into stem cell biology and regenerative medicine.

Dzau has authored over 600 publications, including over 300 original contributions to the scientific and medical literature. He has co-authored 11 books, including *Cardiovascular Pharmacology and Therapeutics* and *Vascular Medicine*. Dzau is editor-in-chief and founding editor of the *Journal of Vascular Biology and Medicine* as well as of the American Physiological

Society's Physiological Genomics.

In his role as a leader in health care, Dzau has led efforts in health care innovation. His vision is for academic health sciences centers to lead the transformation of medicine through innovation, translation, and globalization. Leading this vision at Duke, he and colleagues developed the Duke Translational Medicine Institute, the Duke Global Health Institute, the Duke–National University of Singapore Graduate Medical School, and the Duke Institute for Health Innovation. These initiatives create a seamless continuum from discovery and translational sciences to clinical care, and promote transformative innovation in health.

In 2011 he led a partnership between Duke University, the World Economic Forum, and McKinsey & Co. to found the nonprofit organization International Partnership for Innovative Healthcare Delivery (now called Innovations in Healthcare). This organization aims to increase access to quality health care globally by reducing the barriers to the scale-up of innovative health care delivery models. He currently chairs its board of directors.

As one of the world's preeminent academic health leaders, Dzau advises governments, corporations, and universities worldwide. He has served on the council of the Institute of Medicine and as chair of the AHA's Council on Artherosclerosis, Thrombosis, and Vascular Biology. He also has been advisor to numerous divisions and committees of the NIH and served on the NIH Advisory Committee to the Director. He currently serves as chair of the steering committee and scientific advisory board of the NIH NHLBI Progenitor Cell Biology Consortium. Dzau chaired the board of directors of the Association of Academic Health Centers and is on the board of directors of the Gairdner Foundation.

Dzau's advisory work extends far beyond North America and is driven by his desire to improve health globally. Dzau is currently a member of the board of directors of the Singapore Health System, the governing board of Duke–National University Singapore Medical School, and the expert advisory board of Imperial College Health Partners, and is senior health policy advisor to Her Highness Sheikha Moza (the chair of the Qatar Foundation). He is also on the board of health governors of the World Economic Forum and chaired its Global Agenda Council on Personalized and Precision Medicine.

Among his honors and recognitions are the Gustav Nylin Medal from the

Swedish Royal College of Medicine; the Max Delbruck Medal from Humboldt University, Charité, and Max Planck Institute; the Commemorative Gold Medal from Ludwig Maximilian University of Munich; the Inaugural Hatter Award from the Medical Research Council of South Africa; the Polzer Prize from the European Academy of Sciences and Arts; the Novartis Award for Hypertension Research; the Distinguished Scientist Award from the AHA; the Outstanding Service Award from the National University of Singapore; the Order of the Long Leaf Pines Award conferred by North Carolina Governor Pat McCrory; the Henry G. Friesen International Prize in Health Research from the Canadian Institutes of Health Research; and the 2010 AHA Research Achievement Award for his contributions to cardiovascular biology and medicine. He has received six honorary doctorates from universities around the world.

Dzau is member of several professional societies, including the American Academy of Arts and Sciences, the European Academy of Sciences and Art, the Republic of China National Academy of Science, the Institute of Medicine, the Interurban Clinical Club, the Association of American Physicians, and the American Society for Clinical Investigation.

Jeffrey S. Flier, MD

Jeffrey S. Flier was named the 21st dean of the faculty of medicine at Harvard University on July 11, 2007. Flier, an endocrinologist and an authority on the molecular causes of obesity and diabetes, is also the Caroline Shields Walker Professor of Medicine at Harvard Medical School. Previously he had served as faculty dean for academic programs at Harvard Medical School and chief academic officer for Beth Israel Deaconess Medical Center (BIDMC).

Flier was born in New York City in 1948. He received a BS from the City College of New York in 1968 and an MD from Mount Sinai School of Medicine in 1972, graduating with the Elster Award for highest academic standing. Following residency training in internal medicine at Mount Sinai Hospital from 1972 to 1974, Flier moved to the National Institutes of Health as a clinical associate. In 1978 he joined the faculty of medicine at Harvard Medical School, serving as chief of the Diabetes Unit at Beth Israel Hospital until 1990, when he was named chief of the hospital's Division of Endocrinology.

In 2002 Flier was named chief academic officer of Beth Israel Deaconess Medical Center, a newly created senior position responsible for research and academic programs. He worked with BIDMC academic department chairs to ensure the quality and breadth of the academic programs, through which most Harvard Medical School students pass. He also served as the formal liaison to Harvard Medical School, sitting on the council of academic deans.

Flier is one of the country's leading investigators in the areas of obesity and diabetes. His research has produced major insights into the molecular mechanism of insulin action, the molecular mechanisms of insulin resistance in human disease, and the molecular pathophysiology of obesity. He was one of the first to demonstrate that diet-induced obesity in rodents is associated with increased leptin expression and that short-term starvation is associated with decreased leptin expression and blood levels. His proposal that leptin serves as a switch from the fed to the starved state has fundamentally shaped the discourse of the field.

Flier has authored over 200 scholarly papers and reviews, has held many editorial positions, including associate editor of the *Journal of Clinical Investigation*, and has served on the editorial boards of *Molecular Endocrinology*, the *Journal of Clinical Endocrinology and Metabolism*, and the *American Journal of Medicine*. He is currently on the board of consulting editors of *Science*.

An elected member of the Institute of Medicine and a fellow of the American Academy of Arts and Sciences, Flier's honors also include the Eli Lilly Award of the American Diabetes Association, the Berson Lecture of the American Physiological Society, and an honorary doctorate from the University of Athens. He has been the recipient of a five-year, \$500,000 Unrestricted Research Grant from Bristol-Myers Squibb and the 2003 Edwin B. Astwood Lecture Award from the Endocrine Society. In 2005 he received the Banting Medal from the American Diabetes Association, its highest scientific honor. In 2010 Flier was awarded an honorary doctor of science degree from the University of Edinburgh, and in 2011 he received the Rolf Luft Award from the Karolinska Institute.

Flier is married to Eleftheria Maratos-Flier, who is also on the faculty of Harvard Medical School and with whom he has collaborated on research in the area of neuroendocrine control of body weight. They have two daughters, Lydia and Sarah, and live in Newton, Massachusetts.

Laurie H. Glimcher, MD

Laurie H. Glimcher is the Stephen and Suzanne Weiss Dean of Weill Cornell Medical College in New York, New York, where she is also professor of medicine. In addition, Glimcher is provost for medical affairs of Cornell University. Previously, she was the Irene Heinz Given Professor of Immunology at Harvard School of Public Health, director of its Division of Biological Sciences, and professor of medicine at Harvard Medical School, where she headed one of the top immunology programs in the world. She also served as senior physician and rheumatologist at the Brigham and Woman's Hospital.

Glimcher received her postdoctoral training at Harvard and in the Laboratory of Immunology at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, and is board certified in internal medicine and rheumatology. She received her BA degree from Radcliffe College and her MD from Harvard Medical School.

Glimcher's research focus is on immune and endoplasmic reticulum (ER) stress responses in disease processes, skeletal biology, and the study of cancer. As an immunologist she has elucidated the molecular pathways that regulate CD4 T helper cell development and activation. The complex regulatory pathways governing T helper cell responses are critical for both the development of protective immunity and for the pathophysiologic immune responses underlying autoimmune, infectious, and malignant diseases. Her research laboratory has studied the transcriptional pathways that control this important immune checkpoint, leading to many discoveries, including the c-Maf, T-bet and XBP1 transcription factors, which regulate a variety of adaptive and innate immune functions. Her laboratory also discovered XBP1, the first transcription factor required for plasma cell differentiation and the endoplasmic reticulum stress response. They demonstrated a link between ER stress and proinflammatory/autoimmune diseases in intestinal epithelial cells and in macrophages. Most recently they discovered a key role for XBP1 in both tumor cells and in host immune responses. In addition, her laboratory has identified new proteins that control osteoblast and osteoclast commitment and activation in skeletal biology, which has significant implications for diseases of bone, including osteoporosis, rheumatoid arthritis, osteoarthritis, and cancer metastasis to bone.

Glimcher is the recipient of numerous awards and honors, including the Soma Weiss Award for Undergraduate Research, the Distinguished Young

Investigator Award from the American College of Rheumatology, the Arthritis Foundation Lee S. Howley Award, the FASEB Excellence in Science Award, the American Society for Clinical Investigation Young Investigator Award, the American Association of University Women Educational Foundation Founders Distinguished Senior Scholar Award, the American Association of Immunologists–Huang Foundation Meritorious Career Award, the AAI Excellence in Mentoring Award, Harvard’s Dean’s Award for Leadership in the Advancement of Women, the American College of Rheumatology Distinguished Investigator Award, the Ernst W. Bertner Memorial Award, the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology, and a L’Oreal Foundation award, among others. She is a fellow of the American Academy of Arts and Sciences, a member of the Institute of Medicine of the National Academy of Sciences, and a member of the National Academy of Sciences. She is a former president of the American Association of Immunologists. She is a member of the American Asthma Foundation, Cancer Research Institute, and Health Care Ventures scientific advisory boards and served on the boards of the Burroughs Wellcome Fund and Howard Hughes Medical Institute. She sits on the boards of trustees of Cornell University, Weill Cornell Medical College, Memorial Sloan Kettering Cancer Center, and the New York Blood Foundation and is on the corporate boards of directors of the Bristol-Myers Squibb Pharmaceutical Corporation and the Waters Corporation.

As president of the American Association of Immunologists, she started a pilot program to provide supplementary funds for postdoctoral fellows who are primary caregivers of dependents.

Glimcher has contributed to more than 350 scholarly articles in the medical literature.

Howard Hiatt, MD

Howard Hiatt was born on July 22, 1925, in Patchogue, NY. He attended Harvard College and received his MD from Harvard Medical School in 1948. He is trained in clinical medicine, biochemistry, and molecular biology and has been on the Harvard University faculty since 1955. His early research focused on the application of molecular biology to medical problems, particularly cancer. He was a member of the team at the Pasteur Institute in Paris that first identified and described messenger RNA, and he was among the first to demonstrate messenger RNA in mammalian cells.

From 1963 to 1972 Hiatt served as the first Herrman L. Blumgart Professor of Medicine at Harvard Medical School and as physician-in-chief at Beth Israel Deaconess Medical Center (BIDMC). During his tenure BIDMC was among the first of the nation's teaching hospitals to seek methods to apply molecular and cell biology to clinical medicine and among the first to develop teaching and research programs in primary care. From 1972 to 1984, while he was dean of the Harvard School of Public Health, the school strengthened and broadened greatly its work in the quantitative analytic sciences, introduced molecular and cell biology into its research and teaching, began its program in health policy and management — the first in a public health school — and promoted integration of its teaching and research programs with those of other Harvard faculties.

Since 1985 Hiatt has served as professor of medicine at Harvard Medical School and as senior physician at Brigham and Women's Hospital. He helped develop the Research Training in Clinical Effectiveness Program, which trains physicians to carry out research on issues of quality and costs of medical care. His present research concerns social aspects of health. He is a co-founder, and for the past ten years has been associate chief of, the Division of Global Health Equity.

Hiatt is a widely published author. His research articles have appeared in such publications as the *Journal of Molecular Biology*, the *Journal of Biological Chemistry*, the *New England Journal of Medicine*, and the *Journal of the American Medical Association*. He has written for the lay press in areas of disease prevention, health services, and health implications of the nuclear arms race. His book, *Medical Lifeboat: Will There Be Room for You in the Health Care System?* (Harper & Row, 1989), described ways to deal with some major problems of the nation's health care system.

He is a member of the Association of American Physicians, the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, the American Society for Clinical Investigation, the American Society for Biochemistry and Molecular Biology, and the American Public Health Association as well as other organizations. He has served for several years on the boards of Physicians for Human Rights, the Institute for Health Care Improvement, Partners in Health, and the Gateway Institute for Pre-College Education.

Kurt Julius Isselbacher, MD

Kurt Isselbacher was born in Wirges, Germany, on September 12, 1925. He attended Harvard College and received his MD degree from Harvard Medical School in 1950. From 1950 to 1953 he served on the medical house staff at Massachusetts General Hospital. He spent the next three years at the National Institutes of Health where, working with Herman Kalckar, he received excellent basic training in biochemistry. He made two outstanding contributions there: first, he helped to describe the biochemical reactions whereby important corticosteroids such as cortisone are metabolized in the liver. Second, along with Kalckar, he recognized and described the specific enzyme defect in the hereditary disorder galactosemia. As a result, an enzyme assay was developed to detect the disease in newborns.

Although he had had little formal training in gastroenterology, Isselbacher was appointed chief of the gastrointestinal unit at MGH in 1957. With on-the-job training he developed an outstanding clinical and research gastroenterological unit. From 1958 to 1962 Isselbacher carried out studies on the glucuronideconjugating system and partially purified the important enzyme glucuronyl transferase. He discovered and isolated another bilirubin derivative, bilirubin sulfate, and observed that this metabolite is normally excreted in bile.

Together with Alan Cohen in 1960, he published results from electron-microscopic studies carried out on intestinal mucosal biopsy specimens obtained from a patient with Whipple disease. These studies revealed macrophages in the intestinal mucosa that contained numerous “bacillary bodies” that had a structure similar to bacteria. This added confirmatory evidence to the current understanding of the infectious nature of this disease.

In the 1960s Isselbacher and John Senior elucidated the biochemical steps involved in the intestinal absorption of fat. They demonstrated that lipid esterification is a required step in the transport of fatty acids across the intestinal mucosa. The important role of monoglycerides in fat absorption and the major enzymatic steps involved in the formation of mono- and diglycerides were identified and characterized. In the middle and late 1960s, Isselbacher collaborated with Seymour Sabesin, Norton Greenberger, and Robert Ockner to perform a number of additional fundamental studies on the mechanisms involved in intestinal transport of lipids and lipoproteins. These studies had important clinical implications and served as a model for studying the hereditary disorder abetalipoproteinemia. A series of studies

that compared the transport of short- and medium-chain triglycerides and of long-chain fatty acids across the intestinal mucosa provided a sound physiological basis for the use of medium-chain triglycerides in the treatment of disorders of malabsorption. Additional studies were performed on the structure and function of the intestinal brush border and the microvillous membrane, including the demonstration of the biosynthesis of sucrose-isomaltase, the enzyme lacking in sucrase deficiency.

Isselbacher and his colleagues clarified the pathogenesis of abetalipoproteinemia and isovaleric acidemia. Isselbacher formulated the key concept that a basic lesion in abetalipoproteinemia is defective lipid transport, which results from impaired synthesis of b-lipoproteins in the liver and the gut. Exciting detective work was involved in the identification and description of the defect in the inborn error of leucine metabolism associated with lack of the enzyme isovaleryl CoA dehydrogenase, which catalyzes the decarboxylation of isovaleric acid. Isselbacher showed that this compound is responsible for the clinical syndrome in which children have recurrent episodes of acidosis, coma, and a peculiar odor (the sweaty-foot smell).

In 1970 Isselbacher worked in the laboratories of M.G. Stoker at the Imperial Cancer Research Fund Laboratories in London. He conducted an important study in which animal cells were virally transformed in tissue culture into malignant cells. It was demonstrated that these malignant cells transport sugar and amino acids at a greater rate than comparable non-transformed cells. This implied that there may be an oncogenic mechanism that changes the characteristics of the cell membrane, to permit an inordinate influx of nutrients. Thus, malignant cells have evolved a mechanism to take up nutrients more efficiently than normal cells, a process that in turn leads to the “starvation” and death of adjacent normal cells.

In 1984 and 1985 Isselbacher was a named Fogarty Scholar at the NIH, and he spent four months of each year learning molecular biology in the Laboratory of Molecular Virology with the late George Khoury. He studied the role of the immune system in tumorigenesis, specifically the role of the major histocompatibility complex (MHC) class I antigens. He found that tumor cells frequently lack the expression of MHC class I antigens on their surface; as a result they are not recognized by cytotoxic T cells and thus can escape destruction. Additional research extended Isselbacher’s earlier finding of enhanced nutrient transport (especially glucose) by tumor cells. This phenomenon is related to the original observation of Otto Warburg that tumor cells have an increased rate of glycolysis. Isselbacher and his

colleagues have turned their attention to the genetic factors that regulate and influence glucose transport by normal versus malignant cells.

In 1986 Isselbacher stepped down as chief of the gastrointestinal unit and accepted the challenge of becoming director of the Cancer Center of MGH. This involved recruiting new senior and junior faculty to occupy the laboratories he designed at a new MGH campus at Charlestown Navy Yard. At this new facility, known as MGH East, he developed a group of over 100 scientists and research associates to study the major problems of cancer causation and treatment at both the basic and the applied levels. He became director emeritus in 2003 but has continued his research on environmental agents in the causation of cancer.

Isselbacher's publications include nearly 400 journal articles and book chapters. He has served on the editorial boards of the *Journal of Clinical Investigation* and *Gastroenterology* and was a consulting editor of *Medicine*. His leadership in medicine is also recognized nationally and internationally by virtue of his role as an editor of *Harrison's Principles of Internal Medicine*, a book viewed by many as the leading text in internal medicine.

Isselbacher has been a member and officer in many professional associations, including the National Academy of Sciences (NAS), the National Research Council, the American Academy of Arts and Sciences, and the Institute of Medicine. He has served as president of the American Gastroenterological Association and the Association of American Physicians. He has also served as a member of the science advisory board of the Food and Drug Administration. Isselbacher had received many awards and honors, including the Distinguished Achievement Award and the Friedenwald Medal of the American Gastroenterological Association, the John Phillips Memorial Award for Distinguished Achievement in Clinical Medicine from the American College of Physicians, and the Bristol-Myers Squibb/Mead Johnson Award for Distinguished Achievement in Nutrition Research. In 2001 he received the Kober Medal of the Association of American Physicians, which is the highest recognition that this association can bestow upon its members, and an honorary doctor of science degree from Northwestern University.

Elliott Kieff, MD

Elliott Kieff was born in Philadelphia on February 2nd, 1943 to Florence, a

Philadelphia grammar school teacher, and Irving Kieff, a Senior Deputy Attorney General for the Commonwealth of Pennsylvania. His primary education was at the Blaine School. He commuted to a magnet Junior high school and attended Central High school, a magnet school for Urban Philadelphia teenagers, where he played tennis and participated in a club that was attempting to resurrect a dysfunctional cyclotron.

He received a High School Science Prize from Swarthmore College and enrolled in the General Honors Program at the University of Pennsylvania. There he met Jacqueline, my future bride of 50+ years. Dr. Kieff used the flexibility of the University's General Honors Program to teach physics to discharged war veterans, who were seeking employment in the electronics industry in New Jersey, and worked at night in research laboratories of the Hospital of the University of Pennsylvania, learning polysaccharide biochemistry. In his last year at the University of Pennsylvania, he switched to studying mitochondrial biochemistry and P/O ratios. Despite the absence of a college biology course, the chairs of the basic science departments at Johns Hopkins spent 2 hours with Elliot and immediately admitted him to Medical School.

After three years of mostly clinical studies at Hopkins, Kieff became enamored with human herpes virus research and was allowed to graduate early from Hopkins. During his internship at the University of Chicago, he pursued human herpes virus research, at night, in Bernard Roizman's Laboratory, at Chicago. There, Kieff isolated and characterized the size and structure of the first intact herpes virus genome, using T4 phage genomes as markers. As a result of this and other laboratory accomplishments, and the quality of his clinical teaching, Kieff was asked to start an infectious disease program at the University of Chicago. He recruited first class clinical teachers and investigators from Harvard and the CDC. Luckily, a review team from the NIAID included a well known senior virologist who awarded him a training grant based on his basic research. This enabled Kieff to recruit outstanding basic research trainees.

After overseeing the clinical and research Infectious Disease Division and his own independent herpes virus research, Kieff began to obtain R01 grant support and undertake major problems in herpes virus research. The discovery of Epstein Barr virus by Anthony Epstein in 1964 opened up a new area of potential virus oncology research. Kieff has devoted much of his laboratory and teaching career to improved molecular understanding of the mechanisms through which oncogenic viruses cause cancers.

Dr. Kieff is grateful to the American Cancer Society for early support of his research and to the National Institutes of Health for continuous support of his research since 1972. In 1985-86, Bernard Fields and Daniel Tosteson recruited Kieff and his research group to Harvard to continue a basic cancer virology research program in the department of microbiology and to reinvigorate the BWH infectious disease program. After 1994, Kieff recruited outstanding clinical HIV infection related teaching colleagues, who were well able to take advantage of new pharmacophores to deal with the complex dilemmas of the HIV pandemic.

Dr. Kieff received many honors including election to the American Society for Clinical Investigation, the Interurban Club, the Association of American Physicians, and the American Academy of Arts and Sciences. In 2008-2009 Kieff was elected president of Association of American Physicians (AAP). Kieff was the Karl Meyer Visiting Professor UCSF in 1991; Outstanding Investigator Award NCI, NIH in 1994-2001; Outstanding Investigator Award; 2011-Distinguished Alumni Award, University of Chicago; 2011-Howard Taylor Ricketts Award, University of Chicago; 2014- Howard Taylor Ricketts Award, University of Chicago; 1996 Brockman Memorial Lectureship, University of Michigan; 2006 Lamb Visiting Professor, Vanderbilt University; 2007 Vice President; 2009 President AAP; 1994 Alumni AOA award Johns Hopkins School of Medicine.

Lewis Landsberg, MD

Lewis Landsberg was born in New York City on November 23, 1938. Landsberg graduated summa cum laude from Williams College in 1960 and from the Yale University School of Medicine in 1964. Following residency training in internal medicine at Yale–New Haven Hospital, he pursued a research fellowship at the NIH in the laboratory of Nobel Laureate Julius Axelrod. After two years on the faculty of Yale, Landsberg was recruited to Harvard Medical School, where he was promoted to professor of medicine in 1986. In 1990 he joined the faculty of Northwestern University as the Irving S. Cutter Professor and chairman of the Department of Medicine at the medical school and as physician-in-chief at Northwestern Memorial Hospital. In August of 1999 Landsberg was appointed vice president of medical affairs at Northwestern University and dean of Northwestern University Feinberg School of Medicine.

During his tenure as dean at Northwestern, he appointed eight new center and institute directors along with 17 new department chairs. Extramural

research support doubled, and space devoted to research increased by more than 70 percent. On the occasion of his retirement as dean of Northwestern Memorial Hospital, the hospital's medical staff and the Northwestern Medical Faculty Foundation made an extraordinary gift of endowment to create and name the Lewis Landsberg Deanship. Landsberg now serves as the Irving S. Cutter Professor of Medicine, dean emeritus, and director of the Northwestern Comprehensive Center on Obesity.

The author of over 230 publications, he has an international reputation in the fields of the sympathetic nervous system, the regulation of metabolism, hypertension, and obesity. Landsberg's life-long interest in catecholamines and the sympathetic nervous system developed during his time working with Axelrod, but his initial interest in research was stimulated by his honors thesis at Williams College, which involved the administration of insulin to frogs and the subsequent determination of blood glucose responses. For his thesis requirement at Yale, he studied the effect of fat malabsorption induced by cholestyramine on intestinal calcium absorption. After completing his chief residency at Yale, he received a clinical investigatorship at the West Haven Veterans Hospital, where he undertook a series of experiments to study the metabolism and pharmacology of L-dopa in the rat. He demonstrated that glucuronide conjugation in the liver was a major metabolic pathway and that significant aspects of the pharmacology of L-dopa were due to the *in vivo* generation of dopamine which, as an indirectly acting sympathomimetic amine, released norepinephrine from sympathetic nerve terminals. In 1972 Landsberg and James B. Young systematically explored the role played by catecholamines in the regulation of metabolism. Applying norepinephrine turnover techniques to the assessment of sympathetic activity in the rat, they were able to demonstrate that fasting suppressed, while overfeeding stimulated, the sympathetic nervous system. This was the first evidence that diet influences autonomic nervous system activity. The fact that fasting suppressed sympathetic activity initially appeared counterintuitive, as starvation had been thought to be associated with increased sympathetic activity. Subsequent studies demonstrated that diet-induced changes in sympathetic activity were important in regulating energy expenditure in accord with nutritional status. The decrease in metabolic rate that accompanies starvation or low-energy diets is due, in large part, to the suppression of sympathetically mediated thermogenesis. Conversely, the increase in metabolic rate associated with overfeeding, known as dietary thermogenesis, is related to an increase in sympathetic activity. They demonstrated that insulin played an important role in the relationship between diet and sympathetic activity, and that

insulin-mediated glucose metabolism that occurred in neurons related to the ventromedial hypothalamus was a critical component of this relationship. Landsberg and his associates have extended these observations to the pathogenesis of obesity-related hypertension. In population studies conducted with Scott Weiss of the Channing laboratory at Harvard, utilizing data from the Normative Aging Study in Boston, they were able to provide evidence that the hyperinsulinemia of obesity, a consequence of insulin resistance, drives sympathetic activity and participates in obesity-related hypertension, the pathogenesis of which had previously been obscure.

In 1960 Landsberg received the Conant-Harrington Prize in Biology (from Williams College) and in 1964 the Parker Prize from Yale Medical School. In 1984 he received the S. Robert Stone Award for Teaching from Harvard and in 1993 the Outstanding Clinical Teaching Award from Northwestern. He has been a member of many advisory committees, both federal and private. He has held editorial positions at a variety of journals, including the *American Journal of Physiology, Endocrinology and Metabolism* and the *Proceedings of the Society for Experimental Biology and Medicine*. Landsberg is a member of many professional societies, including the American Federation for Clinical Research, the Endocrine Society, the American Heart Association, the American Society for Pharmacology and Experimental Therapeutics, the American Physiological Society, the American Society for Clinical Investigation, the Association of American Physicians, the Society for Experimental Biology and Medicine, and the American Clinical and Climatological Association. His recent honors include being granted the Franz Volhard Award from the International Society of Hypertension, election to fellowship of the American Association for the Advancement of Science, and appointment as master of the American College of Physicians.

Judy Lieberman, MD, PhD

Judy Lieberman was born in Boston, MA, on September 5, 1947. She received her AB summa cum laude from Harvard University in 1969, a PhD in theoretical physics from Rockefeller University in 1974, and an MD from the Harvard-MIT Program in Health Sciences and Technology in 1981. Before entering medical school she was a member of the Institute for Advanced Study in Princeton, NJ, and a research associate in theoretical physics at Fermi National Accelerator Laboratory in Batavia, IL, where she studied the theory of subatomic particles. She received her clinical training in internal medicine from 1981 to 1984 and in hematology-oncology from

1986 to 1987 at Tufts New England Medical Center. She was a Damon-Runyon postdoctoral fellow (1984–1986) and visiting scientist (1987–1988) in the laboratory of Herman Eisen in the Center for Cancer Research at MIT, where she studied the biology of cytotoxic T lymphocytes. She joined the hematology-oncology division of Tufts New England Medical Center as an assistant professor in 1987, where she ran a laboratory that studied the mechanism by which killer lymphocytes induce cell death and the T cell response to HIV and developed T cell immunotherapy for AIDS. She also served as a clinical hematologist. In 1995 she joined the Center for Blood Research (currently the Immune Disease Institute) and the Department of Pediatrics at Harvard Medical School, where she was promoted to associate professor in 1998 and to professor in 2004. She also served as director of the Division of AIDS at Harvard Medical School from 2005 to 2009.

The Lieberman laboratory studies the molecular pathways used by cytotoxic T cells and natural killer cells to induce death of virus-infected cells or tumors. They have defined a novel form of programmed cell death induced by the most abundant cytotoxic granule serine protease, granzyme A. This caspase-independent cell death pathway has all the morphological features of apoptosis but involves single-stranded DNA damage, not double-stranded DNA breaks. It does not involve caspase activation, and cells that are resistant to the caspase pathway are sensitive to granzyme A. Granzyme A activates a novel form of mitochondrial damage without releasing cytochrome c by entering the mitochondrial matrix to cleave and inactivate a key component of electron transport and disrupt mitochondrial function. A special target of this cell death pathway is an oxidative stress response complex called the SET complex, which contains DNA repair enzymes and proteins that modify chromatin and activate transcription in response to oxidative stress. Two nucleases in the SET complex are activated by granzyme A to cause DNA damage during killer cell-mediated death. They also found that one of the SET complex nucleases Trex1 plays an important role in the innate immune response, autoimmunity, and HIV infection. Recent work has elucidated an unexpected mechanism by which perforin delivers the death-inducing granzyme proteases to cells targeted for destruction. The Lieberman laboratory also studies how CTL function is dysregulated in the setting of chronic infection, with a particular emphasis on HIV infection. They were the first to show that most CD8 T cells in HIV infection are profoundly dysfunctional.

The Lieberman laboratory was the first to demonstrate in an animal model

that RNA interference (RNAi) could be used to protect animals from disease. Her laboratory has been actively working to harness RNAi for therapeutic use to treat or prevent HIV infection and for cancer treatment. They have developed novel strategies for cell-specific targeting of small interfering RNAs that are effective in vivo. They have also shown that small RNAs can be used topically to prevent sexual transmission of herpes virus type 2 and HIV in small animal models. The lab has also investigated the role of the endogenous microRNA pathway in hematopoietic cell differentiation, cellular transformation, stem cells, cancer and metastasis, and viral infection. They have identified microRNAs that regulate stem cell properties of breast tumor-initiating cells, breast cancer metastasis, cell cycle progression, the proliferative response to growth factors, and DNA repair.

Lieberman received a Clinical Investigator Award from the NCI (1990–1995) and a Pew Scholar Award (1991–1997). She was elected to the Association of American Physicians in 2004, the Interurban Clinical Club in 2005, and the American Academy of Arts and Sciences in 2008. She received the Hope is a Vaccine Award from the GAIA Foundation for her work on AIDS vaccines in 2007 and the Heath Memorial Award for outstanding contributions to cancer research from the MD Anderson Cancer Center in 2009. She was elected chair of the Medical Sciences Section of the American Association for the Advancement of Science (2010–2011). She currently serves on the AIDS Research Advisory Council at the NIH, the scientific advisory board of Alnylam Pharmaceuticals, the board of trustees of the Association of Members of the Institute for Advanced Study, and the executive committees of the Harvard University Program on Global Health, the PhD Program in Immunology at Harvard Medical School, and the Immune Disease Institute.

Joseph Loscalzo, MD, PhD

Joseph Loscalzo was born in Camden, NJ, on October 26, 1951. He is the Hersey Professor of the Theory and Practice of Medicine at Harvard Medical School, chairman of the Department of Medicine, and physician-in-chief at Brigham and Women's Hospital. He received his AB degree summa cum laude, his PhD in biochemistry, and his MD from the University of Pennsylvania. His clinical training was completed at Brigham and Women's Hospital, where he served as resident and chief resident in medicine and fellow in cardiovascular medicine.

Loscalzo joined the Harvard faculty and staff at Brigham and Women's Hospital in 1984. He rose to associate professor of medicine, chief of cardiology at the West Roxbury VA Medical Center, and director of the Center for Research in Thrombolysis at Brigham and Women's Hospital. He joined the faculty of Boston University in 1994, first as chief of cardiology and then as Wade Professor and chair of medicine, professor of biochemistry, and director of the Whitaker Cardiovascular Institute. He returned to Harvard and Brigham and Women's Hospital in 2005.

Loscalzo has received many awards for teaching and research, including the Clinician-Scientist Award, the Distinguished Scientist Award, the Research Achievement Award, and the Paul Dudley White Award from the American Heart Association; a Research Career Development Award, a Specialized Center of Research in Ischemic Heart Disease Award, and a MERIT Award from the National Institutes of Health; the George W. Thorn Award for Excellence in Teaching from Brigham and Women's Hospital; the Educator of the Year Award in Clinical Medicine from Boston University; the William Silen Lifetime Achievement in Mentorship Award from Harvard Medical School; and the Glaxo Cardiovascular Research Award and Outstanding Investigator Prize from the International Society for Heart Research. He was elected to the American Society for Clinical Investigation, the Association of American Physicians, the American Academy of Arts and Sciences, and the Institute of Medicine of the National Academy of Sciences. He has served on several NIH study sections and editorial boards and chaired the Gordon Conference on Thrombolysis. He was an associate editor of the *New England Journal of Medicine* for nine years, chair of the Cardiovascular Board of the American Board of Internal Medicine, chair of the research committee of the American Heart Association, chair of the scientific board of the Stanley J. Sarnoff Society of Fellows for Research in the Cardiovascular Sciences, and chair of the Board of Scientific Counselors of the National Heart, Lung, and Blood Institute of the National Institutes of Health. He is currently editor-in-chief of *Circulation*, senior editor of *Harrison's Principles of Internal Medicine*, a former member of the Advisory Council of the National Heart, Lung, and Blood Institute, and a former member of the Council of Councils of the National Institutes of Health.

The simple molecule nitric oxide (NO) has played a key role in Loscalzo's scientific career, and it was not until he remembered an experience as a graduate student at the University of Pennsylvania that he realized how much it had crossed his path. At the time, the biochemistry depart-

ment's library was down the hall from the laboratory in which he worked, and he spent a considerable number of hours working at a desk in that quiet place throughout his student days. Scattered about the walls of the library was a collection of photomicrographs of hemoglobin crystals taken by David Drabkin, a professor at Penn who developed a biochemical reagent for measuring hemoglobin. One form of hemoglobin that Drabkin crystallized was nitrosylhemoglobin, whose crystals were striking for their brilliant hue. That particular photomicrograph hung just above the desk at which Loscalzo sat. Little did he know at that time how much the simple molecule responsible for the striking color of the hemoglobin crystals would consume his interests and energies ten years later.

Loscalzo's studies of the vascular effects of NO began when he was a cardiology fellow in a hematology laboratory. He developed an interest in thrombosis at a time when most cardiologists had little interest in the area. The seminal article by DeWood and colleagues on the role of thrombosis in acute myocardial infarction was not published until 1980, and it took several years for the cardiology community to accept the importance of this pathobiology in coronary heart disease. Loscalzo realized that this new-found focus on the role of thrombosis in atherosclerotic disease represented an opportunity as he struggled with how best to justify his presence as someone interested in thrombosis within a cardiovascular division. For this reason he began to examine the role of nitrates on platelet function and, finding no real effect at pharmacologically relevant concentrations, reviewed earlier work by Needleman, who showed that the vasorelaxing effects of nitrates could be potentiated by thiols. Taking a cue from this earlier work, Loscalzo showed that thiols potentiated the antiplatelet effects of nitrates. He went on to demonstrate that this effect was, in part, a consequence of the metabolism of organic nitrates to *S*-nitrosothiols. Furthermore, he showed that *S*-nitrosothiols are a unique class of molecules that regulate NO bioavailability and function, and that they represent a unique form of posttranslational modification of proteins with many functional consequences.

Loscalzo has been a visiting professor at many institutions, holds two honorary degrees, has authored more than 700 scientific publications, has authored or edited 33 books, and holds 31 patents for his work in the field of NO and redox biology. He has received many grants from the NIH and industry for his work in the areas of vascular biology, thrombosis, atherosclerosis, redox biology, and more recently, systems biology. His most recent work has established the field of network medicine, a paradigm-changing

discipline that seeks to re-define disease and therapeutics from an integrated perspective, using systems biology and molecular network science.

Joseph B. Martin, MD, PhD

Joseph B. Martin's life journey has taken him from humble beginnings as a Mennonite farm boy to the highest levels of academic and medical leadership. Along the way he has led and witnessed many of the discoveries and events central to the turbulent transformation of medicine that began in the second half of the twentieth century.

Martin was born in 1938 in Bassano, Alberta, Canada, and grew up near the village of Duchess. The first in his family to obtain an education beyond high school, he received his BS degree from Eastern Mennonite College (now Eastern Mennonite University). He went on to receive his MD degree from the University of Alberta in 1962 and his PhD from the University of Rochester in 1971.

Martin's first appointment as professor was at McGill University, and he became chair of the Department of Neurology and Neurosurgery in 1977. He subsequently joined the faculty of Harvard Medical School and chaired the Department of Neurology at Massachusetts General Hospital. His lab at MGH identified a biomarker that led to the location of the gene for Huntington's disease, which was the first proven link between genetics and disease. In 1984 he was key to the establishment of the Massachusetts Alzheimer's Disease Research Center.

In 1989 Martin joined the University of California, San Francisco, as dean of the School of Medicine, for which he later became chancellor. During his tenure at UCSF, he inaugurated the W. M. Keck Foundation Center for Integrative Neurosciences, which is dedicated to combining studies of the brain and behavior, and the Gladstone Institute of Virology and Immunology, dedicated to the research of AIDS. As chancellor, Martin also led efforts to identify a second campus that resulted in the establishment of the UCSF campus at Mission Bay.

Appointed dean of the faculty of medicine at Harvard Medical School in 1997, Martin helped create the Dana-Farber/Harvard Cancer Center, which brought together seven Harvard-affiliated institutions to collaborate on research into the diagnosis, prevention, and treatment of cancer.

In 2001 he formed the Harvard Center for Neurodegeneration and Repair, a decentralized community of over 500 neurology and neuroscientist faculty and researchers working together to translate neuroscience research into the treatment and prevention of a wide array of neurodegenerative diseases.

As dean at Harvard, Martin also led efforts to redesign the entire medical school curriculum. Under his leadership, in 2003 the Harvard Medical School formed the Department of Systems Biology, one of the first department-level systems biology programs in the US and the first new basic science department at the school in over 20 years. He stepped down as dean in 2007 and continues to serve Harvard Medical School as the Edward R. and Anne G. Lefler Distinguished Professor of Neurobiology.

Martin is the author or co-author of more than 300 scientific articles and reviews. He is a former editor of the widely used textbook *Harrison's Principles of Internal Medicine* and has served on the editorial boards of the *New England Journal of Medicine*, *Annals of Neurology*, and *Science*. He is a member of multiple medical and scientific societies, including the Institute of Medicine of the National Academy of Sciences. Martin chaired the committee at the Institute of Medicine that examined the feasibility of mapping of the human brain. He is a fellow of the American Academy of Arts and Sciences, a member of the Association of American Physicians, and a member and past president of the American Neurological Association. Martin has received numerous honorary degrees and awards, including the Association of American Medical Colleges Abraham Flexner Award, which he received in 1999.

Martin and his wife, Rachel (née Wenger), have four children and nine grandchildren. Martin recently published his autobiography, *Alfalfa to Ivy: Memoir of a Harvard Medical School Dean* (University of Alberta Press, 2011).

John Potts, MD

John T. Potts Jr. was born on January 19, 1932, in Philadelphia. He earned his BS from LaSalle University in 1953 and his MD from the University of Pennsylvania in 1957. After completing his medical training at Penn, Potts did his internship and residency at Massachusetts General Hospital from 1957 to 1959 and at the National Heart Institute. He was employed at the

National Heart Institute from 1959 to 1968, where he became the head of the section on polypeptide hormones. He returned to Massachusetts General Hospital as chief of the endocrine unit in 1968. Potts then served as the chairman of the Department of Medicine and the physician-in-chief from 1981 to 1996.

In his role as director of research at Massachusetts General Hospital (1995–2004), Potts was responsible for developing policies and strategies to preserve and strengthen the extensive scientific research effort at the hospital, an endeavor which he continues to the present. He was the Jackson Distinguished Professor of Clinical Medicine at Harvard Medical School and Massachusetts General Hospital from 1981 to 1996.

An internationally recognized authority on calcium metabolism and the hormonal mechanisms that govern it, Potts has been a pioneer in the chemistry and biology of parathyroid hormone (PTH) and its role in clinical disorders of bone and mineral ion metabolism. He conducted research on protein chemistry at the National Institutes of Health with Nobel Laureate Christian Anfinsen. His career spans more than 50 years of distinguished service in science and medicine. An author or co-author of over 500 scientific publications, Potts's accomplishments have been recognized with a series of honors, including election to the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. He holds active and honorary memberships in numerous scientific and professional organizations. His honors and awards include the William Silen Lifetime Achievement in Mentoring Award from Harvard Medical School (2003); the Robert H. Williams, MD Distinguished Chair of Medicine Award from the Association of Professors of Medicine (2002); the Biomedical Science Career Program Hope Award (2001); the Fred Konrad Koch Award from the Endocrine Society (1991); and the William F. Neuman Award from the American Society for Bone and Mineral Research (1987). He is a board member of BioSante, a founder and board observer of Radius, a board observer of ZELTIQ, a member of the medical and scientific advisory board of MPM Capital, and a consultant for Pfizer and Quest Diagnostics.

Michael Rosenblatt, MD

Michael Rosenblatt was born in Lund, Sweden, on November 27, 1947. His parents were Polish Jewish refugees who survived Auschwitz and the

Holocaust before immigrating to the United States. Rosenblatt was raised in New Jersey.

Rosenblatt currently serves as executive vice president and chief medical officer of Merck & Co., Inc. He is the first person to hold this appointment. In his role he serves as an independent voice of the patient at the highest levels of the company and represents Merck and industry externally in areas of medicine and health. Previously he was dean of Tufts University School of Medicine (2001–2006). Prior to that he held the appointments of George R. Minot and Robert H. Ebert Professor at Harvard Medical School (HMS) and president of the Beth Israel Deaconess Medical Center (BIDMC). Rosenblatt was dean of Harvard Faculty, senior vice president for academic programs at CareGroup and BIDMC, and a founder of the Carl J. Shapiro Institute for Education and Research at HMS and BIDMC, a joint venture that promotes academic innovation.

As director of the Harvard-MIT Division of Health Sciences and Technology, he led a medical education organization that trained MD, PhD, and MD-PhD students. Prior to that role, he served as senior vice president for research at Merck Sharp & Dohme research laboratories, where he co-led the worldwide development of alendronate (Fosamax), Merck's bisphosphonate product for the treatment of osteoporosis. In addition, he directed drug discovery efforts in molecular biology, bone biology, virology, cancer, lipid metabolism, and cardiovascular disease in the United States, Japan, and Italy. During this period he established new research institutes in Japan and Italy.

Rosenblatt received the Fuller Albright Award for his work on parathyroid hormone (PTH), the Vincent du Vigneaud Award in peptide chemistry and biology, and the Chairman's Award from Merck. His research is in the field of hormone-receptor interactions, osteoporosis, and cancer metastasis to bone. His major research projects address the design of peptide hormone antagonists for PTH and PTH-related protein, mapping of hormone-receptor interactions, osteoporosis and bone biology, and elucidation of the mechanisms by which breast cancer metastasizes to bone.

He has been active in the biotechnology industry and was a founder of ProScript, the company that discovered bortezomib (Velcade; now Takeda Millennium's drug for multiple myeloma and other malignancies) and Radius Health, a women's health company. He has served on the board of directors and scientific advisory boards of several biotech companies

and one publicly traded company (Shire). He was a member of the Board of Scientific Counselors of the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH. He was elected to membership in the American Society for Clinical Investigation and the Association of American Physicians, to fellowship in the American Association for the Advancement of Science and the American College of Physicians, and to the presidency of the American Society for Bone and Mineral Research. In 1997 he testified before a US Senate hearing on biomedical research priorities, and in 2011 he testified before the US President's Council of Advisors on Science and Technology.

From 1981 to 1984 he served as chief of the Endocrine Unit at Massachusetts General Hospital (MGH). He received an AB degree summa cum laude from Columbia University and an MD degree magna cum laude from Harvard. Internship, residency, and endocrinology training were all completed at MGH.

Rosenblatt's interest in research began when, as an undergraduate at Columbia, he worked in the organic chemistry laboratory of Gilbert Stork. At HMS he turned to endocrinology. George Cahill advised him to join the laboratory of John Potts at the MGH. Working with Geoffrey Tregear, his first project was directed at designing and synthesizing an analog of PTH for use in developing a radioreceptor membrane-binding assay. He received the HMS Soma Weiss Award for this research. After internal medicine residency training, he joined the MGH Endocrine Unit, working on the design of PTH antagonists. He and colleagues mapped the functional domains within PTH by chemically synthesizing over 100 fragments and analogs of the hormone molecule. They identified the principal binding domain of PTH and delineated a small region of the molecule critical for activating PTH receptors once binding occurred. This led eventually to the generation of hormone antagonists effective *in vivo*.

The Rosenblatt lab was the first to chemically synthesize PTH-related protein, a newly discovered hormone that is secreted by solid tumors and responsible for many cases of hypercalcemia of malignancy. The group later mapped the bimolecular interface between PTH or PTHrP and their shared receptor at the level of amino acid to amino acid point contacts.

During his first period at Merck (1983–1992), Rosenblatt built a new bone biology group together with Gideon Rodan and brought the novel bisphosphonate alendronate from the laboratory to clinical trials. Rosenblatt then

co-led with Reynold Spector the development of alendronate. The drug subsequently became the leading osteoporosis therapy in the world. At Merck he also directed research on AIDS, glaucoma, and gastrointestinal and cardiovascular disease.

In 2001–2002 Rosenblatt took a sabbatical with Robert A. Weinberg at the Whitehead Institute of MIT, where he investigated mechanisms by which breast cancer metastasizes to bone. Afterward, this topic became a focus of his research.

Rosenblatt has served since 2009 as Merck's chief medical officer, generating global policy around medicines, vaccines, healthcare, and translational research. He interfaces with patient groups to bring perspectives of benefit and risk into drug discovery and development.

David Scadden, MD

David Scadden was born in Passaic, NJ. He is the Gerald and Darlene Jordan Professor of Medicine at Harvard University. He graduated from Bucknell University cum laude with honors in English. After a year of post-graduate premed studies at Columbia University, he went to Case Western Reserve Medical School, where he received his MD (Alpha Omega Alpha) and won the Edward C. Garvin Senior Prize. He trained in internal medicine at Brigham and Women's Hospital (BWH) and then in hematology and medical oncology at BWH and the Dana-Farber Cancer Institute, respectively.

He worked on murine retroviral interactions with host cells in the Howard Hughes Medical Institute laboratory of James Cunningham at BWH as a fellow, and then became involved in the care of patients with AIDS-related hematologic and oncologic complications. He helped found, and for a time led, the NCI-sponsored AIDS Malignancy Consortium, an effort to combine clinical testing of new therapeutics with laboratory evaluation on patient samples. He led a program in AIDS oncology first at Beth Israel Deaconess Medical Center and then at Massachusetts General Hospital and Dana-Farber/Harvard Cancer Center. He led or participated in studies that resulted in new therapies for Kaposi sarcoma and tested T cell and stem cell transplantation therapies for HIV and AIDS-related lymphoma, respectively. His laboratory provided evidence for hematopoietic stem cell resistance to HIV infection and was active in developing methods for iso-

lating and characterizing human hematopoietic stem cells to improve stem cell-based therapies.

Scadden joined with Doug Melton to establish the Harvard Stem Cell Institute (HSCI) at a time when evidence was accumulating to indicate that stem cells were not restricted to the hematopoietic system and when the use of human embryonic stem cells was being established (also a time when HIV therapies markedly reduced the incidence of AIDS-related malignancies). HSCI was a multi-institutional effort that emphasized accelerating stem cell discovery and facilitating development of stem cell therapies, and it brought together over 150 faculty members, to create the largest such program in the world. Due to the strong interest of students in the HSCI, Harvard permitted the founding of the Department of Stem Cell and Regenerative Biology, which was co-chaired by Melton and Scadden. This was a first-of-its-kind, cross-school department at Harvard. It has established an undergraduate curriculum that heavily emphasizes human biology.

Scadden's laboratory work has focused largely on defining how hematopoietic stem cells are regulated. He defined the role for a number of cell intrinsic mediators of cell cycle and metabolism and showed their impact on the physiology of hematopoiesis in animal models. He also provided evidence for the role of specific components of bone in regulating hematopoiesis, thus indicating the existence of a hematopoietic stem cell niche. He documented that this niche could be targeted pharmacologically to alter the outcome of stem cell harvests and transplants in animals, and these findings subsequently formed the basis for multi-institutional clinical trials. He demonstrated that genetic alteration of niche elements can result in disordered hematopoiesis, including the development of dysplasia and leukemia. He also defined regulation of hematopoietic stem cell localization in the bone marrow niche. His laboratory was the first to show that modulating CXCR4 could result in stem cell mobilization into the blood. Further, he discovered that Gas signaling and the calcium-sensing receptor are essential for bone marrow homing and engraftment of hematopoietic stem cells.

Scadden is an elected member of the Institute of Medicine of the National Academy of Sciences, the Association of American Physicians, and the American Society for Clinical Investigation. He has received honorary doctorates from Lund University in Sweden and Bucknell University, the William Dameshek Prize from the American Society of Hematology, and distinguished alumnus awards from both Bucknell and Case Western Re-

serve. He has served on the Board of Scientific Counselors for the NIH National Cancer Institute and the Board of External Experts for the NIH National Heart, Lung and Blood Institute and has served leadership roles for the International Society of Stem Cell Research, the International Society of Experimental Hematology and Stem Cells, and the American Society of Hematology. He has received awards from the Doris Duke Foundation, the Burroughs Wellcome Foundation, and the Ellison Medical Foundation; served as associate editor of *Blood* and on the editorial boards of *Cell Stem Cell*, *Stem Cells*, and *Experimental Hematology*; and served as a trustee of Bucknell University.

Allen Caruthers Steere Jr., MD

Allen Steere was born in Fort Wayne, IN, on April 11, 1943. He received the BA degree from Columbia College in New York in 1965 and the MD degree in 1969 from the Columbia College of Physicians and Surgeons. From 1969 to 1973 he was intern, assistant and senior resident, chief resident, and instructor of medicine at Saint Luke's Hospital, Columbia University College of Physicians and Surgeons. The following two years he served as an epidemiologist for the Hospital Infections Branch of the US Public Health Service at the Centers for Disease Control and Prevention in Atlanta.

His time at the CDC proved critical in his discovery and description of Lyme disease, which occurred four months after beginning a rheumatology fellowship at Yale in 1975. He had the opportunity to evaluate a cluster of children in Lyme, CT, who were thought to have juvenile rheumatoid arthritis. He showed instead that they had a previously undescribed arthropod-borne illness, which was named Lyme arthritis or Lyme disease. Since that time he has continued to work on the elucidation of Lyme disease, first as a junior faculty member at Yale (assistant professor of medicine, 1981–1987), then at the New England Medical Center and Tufts University School of Medicine (professor of medicine and chief of rheumatology and immunology, 1987–2002), and most recently at Harvard Medical School (professor of medicine, 2002–present) and the Translational Research in Rheumatology at Massachusetts General Hospital (director, 2002–present).

Steere's major research focus for 39 years has been the elucidation of Lyme disease, including its clinical characteristics, etiology, pathogenesis, diagnosis, treatment, and prevention. He and his associates are currently study-

ing the pathogenesis of Lyme arthritis, particularly antibiotic-refractory Lyme arthritis, as a model for other forms of chronic inflammatory arthritis, including rheumatoid arthritis. He and his fellow investigators have shown that excessive inflammation, immune dysregulation, and infection-induced autoimmunity are key factors in this disadvantageous outcome.

He has received many awards for his research. In 1984 he received the Citation of the Infectious Diseases Society of America (awarded for the elucidation of Lyme disease), and in 1985 he was awarded the Ciba-Geigy Rheumatology Prize by the International League against Rheumatism (presented for his studies of Lyme disease: its initial description, clinical characteristics, epidemiology, etiology, pathogenesis and treatment). He has received numerous other awards, including an award from the National Institute of Arthritis and Musculoskeletal and Skin Diseases for the discovery of Lyme disease (1988); the Richard and Hinda Rosenthal Memorial Award from the American College of Physicians (presented to the physician-scientist, clinician, or scientific group whose recent innovative work is making a notable contribution to improve clinical care in the field of internal medicine); the Joseph Mather Smith Prize from the College of Physicians and Surgeons (presented to the alumnus whose research is decided to be most meritorious); the Zucker Faculty Prize from Tufts (for excellence in the study of Lyme disease); and the National Medical Research Award from the National Health Council (for singular contributions to identifying the clinical characteristics, pathogenesis, etiology, epidemiology and treatment of Lyme disease). He has received honorary doctor of science degrees from Indiana University (1992), the State University of New York (1997), and Ohio Wesleyan University (2008) and an honorary masters degree from Harvard Medical School (2002, the year he began his tenure there as professor of medicine). He has also received the Lee C. Howley, Sr. Prize from the Arthritis Foundation (1993; for outstanding research in the field of arthritis), the Howard & Martha Holley Research Prize in Rheumatology from the American College of Rheumatology (1995), the Albert Sabin Vaccine Institute Gold Medal (1998; for vaccine studies of Lyme disease), the Astute Clinician Award from the National Institutes of Health (1999; for observation of an unusual clinical occurrence, and by investigating it, opening an important new avenue of research), the Alumni Award from Columbia College of Physicians and Surgeons (2001; for distinguished academic accomplishment), the Research Hero Award from the Arthritis Foundation on the 50th anniversary of its fellowship program (2001), the Marian Ropes Physician Achievement Award from the Massachusetts Chapter of the Arthritis Foundation (2006; for outstanding

contributions to rheumatology), and the Clinical Investigator Award from the American College of Rheumatology (2009; for the elucidation of Lyme disease). Additionally, in 2000 he received an award from the American Lyme Disease Foundation in recognition of pioneering research and distinguished contributions to the understanding of Lyme disease. Steere is a member of the American Federation for Clinical Research, the American Society for Clinical Investigation, and the American College of Rheumatology. From 1977 to 1980 he was a research fellow of the Arthritis Foundation and, from 1981 to 1986, a senior fellow.

Thomas P. Stossel, MD

Thomas P. Stossel was born on September 10, 1941, in Chicago, IL. He graduated from Princeton University (summa cum laude) and Harvard Medical School (cum laude) and trained in internal medicine, hematology, and research at Massachusetts General Hospital, Boston Children's Hospital, and the National Institutes of Health. He served as head of hematology-oncology at Massachusetts General Hospital (1976–1991) and as head of experimental medicine (1991–1998), hematology (1998–2007), and translational medicine (2007–2014) at Brigham and Women's Hospital. He also served as president of the American Society for Clinical Investigation (1987) and the American Society of Hematology (1997), as editor-in-chief of the *Journal of Clinical Investigation* (1982–1987) and *Current Opinion in Hematology* (1995–present), and on the jury for the Lasker Award (1997–2009).

For his research into the mechanisms by which cells move about the body, he was elected to the American Society for Clinical Investigation (1975), the Association of American Physicians (1981), the Interurban Clinical Club (1985), the American Clinical and Climatological Association (1998), the National Academy of Sciences (1997), the American Academy of Arts and Sciences (1996), and the Institute of Medicine of the National Academy of Sciences (1998) and received honorary degrees from Linköping University and Geneva University, an NIH MERIT Award, and the Dameshek and Thomas awards of the American Society of Hematology.

He authored 293 publications and two textbooks and is an inventor on 11 issued patents. He was a scientific advisor to Biogen (1987–2002) and Dyax (1991–2001) and currently is director of Velico Medical and founding scientist of BioAegis Therapeutics, companies that are undertaking

clinical development of his discoveries concerning, respectively, blood transfusion and inflammation control and innate immunity. For his policy work regarding the medicine-industry interface, he received the Academy of Pharmaceutical Physicians' Sherwood award and the American Medical Writers Association's McGovern award. With his wife, Kerry Maguire, and others, Stossel co-founded in 2006 the 501(c)(3) charity Options for Children in Zambia, which provides voluntary dental and medical care in that Sub-Saharan African country. For this effort he received the 2012 Humanitarian Award of the Brigham & Women's Hospital Hippocrates Society. His book *Pharmaphobia: How the Conflict of Interest Myth Undermines American Medical Innovation* was published by Rowman-Littlefield in 2015. He is currently senior physician in the Hematology Division of Brigham and Women's Hospital and a visiting scholar of the American Enterprise Institute.

Terry Strom, MD

Terry Strom, born November 30, 1941, in Chicago, was educated in Chicago's public schools and at the University of Illinois as an undergraduate and medical student. Upon graduation from medical school (1966), he trained in internal medicine at the University of Illinois Research Hospital. Following two years of military service, he completed clinical training in internal medicine at Beth Israel Hospital (1970–1971) and in nephrology at Peter Bent Brigham Hospital (PBBH) (1971–1973). His interests in renal disease and immunology began as a medical student at a time when pioneering systematic studies of percutaneous renal biopsies were ongoing at the University of Illinois and during a period in which systemic lupus erythematosus (SLE) nephritis was intensely studied. During this period and under the direction of Victor Pollak, he studied the effects of polyclonal anti-lymphocyte antibody treatment in mice that develop SLE-like nephritis.

As a fellow in John Merrill's renal division at PBBH, his interests turned to clinical renal transplantation. In parallel, he studied the cellular basis of rejection and tolerance under the guidance of C. Bernard Carpenter. His first-ever studies on the role of donor-reactive, allograft-infiltrating T lymphocytes in transplant rejection, and his studies on the cell biology of cytotoxic T cells, in turn led to the discovery that lymphocytes possess functionally important receptors for certain hormones and neurotransmitters, and that activated lymphocytes express numerous "activation" proteins,

including the insulin receptor, that are not expressed on resting T cells.

In parallel, Strom also studied signal transduction pathways, especially the cyclic AMP pathway, that govern T cell function. Because CD25, the IL-2 receptor α -chain, is a T cell activation protein, this work led to his development of anti-CD25 antibodies as a therapy. Anti-CD25 monoclonal antibodies are still used to treat transplant recipients and individuals with autoimmune disease. In collaboration with John Murphy, he conceived of the first gene fusion protein, an IL-2 diphtheria toxin-related protein, which was approved for the treatment of patients with malignant T cell disorders. He was among the first to study the essential role of regulatory T cells in transplant tolerance and, together with Laurence Turka, demonstrated that activation-induced apoptotic reduction of the enormous mass of donor-reactive T cells is crucial to establish regulatory T cell-dependent transplant tolerance (their publication of these findings has over 1,000 citations). In these studies they discovered the inhibitory effect of calcineurin inhibitors and the enhancing effect that rapamycin creates in tolerance induction. These results have guided clinical studies aimed at tolerance induction to this day. He also demonstrated that IL-2 promotes activation-induced apoptotic death of newly activated T cells, a cell population that transiently expresses the high-affinity IL-2R, without harming regulatory T cells. These studies led to his development of long-lived IL-2/Ig fusion proteins for treatment in mouse and monkey models of transplantation and in mouse models of type 1 diabetes. IL-2 is now being used successfully in humans with graft-versus-host disease and autoimmune disease.

Simon Robson and Strom demonstrated that co-expression of the ATP-splitting and adenosine-producing CD39 and CD73 ectoenzymes is a major effector of regulatory T cell immunoregulation (over 1,000 citations). In other work centering on the influence of innate immunity upon adaptive immunity, his collaboration with Vijay Kuchroo led to the discovery that, while TGF-beta promotes the differentiation of newly activated T cells to the regulatory T cell phenotype, the addition of IL-6 (over 4,500 citations) or IL-21 (over 1,500 citations) diverts differentiation to the pro-inflammatory Th17 phenotype, a phenotype most important for pathogenesis of autoimmune disease. More recently his studies highlighting the importance of innate immunity in influencing adaptive immunity demonstrate that treatment with α_1 -antitrypsin, an anti-inflammatory protein, while grossly and directly modifying innate but not isolated T cell function, actually exerts immunosuppressive and tolerance-promoting effects *in vivo*. This work demonstrates the governing role, albeit indirect, of in-

nate immunity on T cell function in transplantation and autoimmunity. As a direct consequence, Strom and others are testing α_1 -antitrypsin in clinical trials for transplantation and the treatment of type 1 diabetes. In the course of studies by Strom concerning the biology of TIM family proteins, the quintessential importance was discovered of the TIM-3 death pathway present in terminally differentiated T cells for tolerance induction. As a result, blockade of the TIM-3 pathway is being developed by industry as an immunotherapy for malignant disease.

Since his postgraduate training, Strom has remained at Harvard Medical School as a faculty member in the immunology program and as the medical director of the transplant program at PBBH/Brigham and Women's Hospitals and later at Beth Israel Hospital/Beth Israel Deaconess Medical Center. Currently he is scientific director of the Transplant Institute at BIDMC and a professor of medicine and surgery at Harvard. He is also an adjunct professor at King's College London.

Strom's awards and honors include an Illinois State Scholarship; an NIH Career Development Award; the Lilly Lectureship of the Royal College of Physicians; the mentorship, mid-career, and lifetime achievement awards of the American Society of Transplantation; lifetime achievement awards from both the American Society of Nephrology and the International Society of Nephrology; and the Thomas E. Starzl Prize in Surgery and Immunology. Strom is a founding member and past president of both the American Society of Transplantation and the Clinical Immunology Society. He is a member of several honorific professional societies and has served as an officer of several professional societies, a member of biomedical journal editorial boards, and as a scientific or medical board member of pharmaceutical and biotech companies.

Ralph Weissleder, MD, PhD

Ralph Weissleder is a physician-scientist at Massachusetts General Hospital (MGH) and the Thrall Professor of Radiology and professor of systems biology at Harvard Medical School (HMS). He was born in Germany and attended the University of Freiburg (1977–1979) and the University of Heidelberg (1979–1985), from which he received his doctoral degrees. He did a medical internship at the Universidad Autónoma de Nuevo León in Monterrey, Mexico, followed by a postdoctoral research fellowship at MGH in magnetic resonance imaging (1986–1989). From 1989 to 1993

Weissleder was a radiology resident at MGH. He became assistant professor of radiology at HMS in 1994, associate professor in 1996, professor of radiology in 2001, and professor of systems biology in 2007.

Weissleder is currently director of the Center for Systems Biology (CSB), one of five thematic research centers at MGH. CSB is currently home to over 200 scientists. The large, multidisciplinary group of researchers works collaboratively to analyze the body's complex networks in healthy and diseased states and, using powerful and innovative technologies, translates that knowledge into practical applications. In 1994 Weissleder also established the Center for Molecular Imaging Research at MGH, then one of the first of its kind in the United States. Weissleder is also an attending interventional radiologist and practices one day per week.

Weissleder's research is focused on creating new technologies for the development of medicines and diagnostics, including approaches at the interface of chemistry, biology, and engineering. His world-renowned expertise, combined with his passion for innovative solutions, have led to the development of novel molecular imaging techniques, tools for the early detection of cancer, and new miniaturized sensing technologies. His goal is to use these tools to obtain quantitative and system-wide global measurements, to perform dynamic serial measurements, to integrate multiple and various data sets into models, and to enable earlier, faster, and simpler diagnostics. His recent work has been focused on translational aspects such as cancer phenotyping in single cells, large-scale analysis of new sensing approaches (e.g., mNMR, hall sensors, SPR, holography), and creating databases of molecular profiles of human cancers in different populations. Weissleder has spearheaded the development of over 50 different imaging drugs. Several of his research developments have been evaluated in clinical trials and/or are being commercialized. He is a co-founder of VisEn Medical (acquired by PerkinElmer in 2012), T2 Biosystems (public in 2014), and Lumicell, Inc. (private).

Weissleder is a founding member of the Society for Molecular Imaging Research, for which he served as president in 2002. He has served on innumerable local, national, and international scientific committees. He currently serves, or has served, on the editorial or advisory boards for *Science Translational Medicine* (2009–present), *Angewandte Chemie International Edition* (2014–present), *ACS Nano* (2014), *Bioconjugate Chemistry* (1999–date), *Cancer Biology and Therapy* (2001–present), *Molecular Imaging* (2001–2007), *The Oncologist* (2002–2009), *Radiology* (1996–2007); *PLoS*

Medicine (2004–date), *ChemMedChem* (2005–2013), *Nanotechnology* (2006–2009), and *Diagnostics and Therapeutics* (2006–2009). Weissleder is the principal investigator of several large federally funded research studies and is the author of more than 750 peer-reviewed, published papers. He has over 30 patents and has written several major textbooks. He has trained over 200 postdoctoral fellows, many of whom are now professors.

In 2009 he was elected to membership in the Institute of Medicine of the National Academy of Sciences. In recognition of his outstanding contribution to research, Weissleder's work has been honored with numerous awards, including the J. Allyn Taylor International Prize in Medicine, the Millennium Pharmaceuticals Innovator Award, the Association of University Radiologists Memorial Award, the American Roentgen Ray Society President's Award, the Society for Molecular Imaging Lifetime Achievement Award, the Academy of Molecular Imaging 2006 Distinguished Basic Scientist Award, the Radiological Society of North America 2008 Outstanding Researcher Award, and the 2011 Gold Medal of the European Society of Radiology. Weissleder has received honorary degrees from the Universidad Autónoma de Nuevo León (2007) and Harvard University (2001).

Mark L. Zeidel, MD

Mark L. Zeidel was born in 1954 at Beth Israel Hospital in Boston, where he now chairs the Department of Medicine. He was educated in the Natick, Massachusetts, public schools and at Phillips Exeter Academy. He received a combined BS and MS degree in molecular biophysics and biochemistry, graduating summa cum laude from Yale in 1972, and completed his MD Alpha Omega Alpha from Columbia University College of Physicians and Surgeons in 1976. He completed his medicine internship and residency and renal fellowship at the Brigham and Women's Hospital.

Zeidel's interest in biomedical research was kindled initially by his biology teacher at Exeter, Andrew Polychronis, and by a preceptor for summer research work at the Worcester Foundation (Yutaka Kobayashi, the developer of the coincidence counting scintillation counter). This interest was honed by numerous mentors at Yale and Columbia, including Joseph Fruton, Qais Al-Awqati, and Richard Rifkind, as well as Michael Dunn, who precepted Zeidel during research stints at the University of Vermont and at Case Western Reserve University. When Zeidel began his internship, he

was considering ID or renal as potential directions. Despite an early and very positive exposure to Bernard Fields, Zeidel was drawn to homeostasis as a general topic and decided to pursue fellowship training in nephrology with Barry Brenner. The Brenner group included Julian Seifter and Steve Hebert, who helped Zeidel develop expertise in tubular transport mechanisms.

Zeidel's work began with the first measurements of intracellular pH in renal epithelia. When atrial natriuretic peptide was discovered, he examined its effects in renal tubular epithelium, demonstrating that it blocks collecting duct salt reabsorption and defining the receptors and signaling pathways that mediate this response. He then began a series of studies focused on mechanisms of water flow across biological membranes. Working with Peter Agre, he reconstituted what became known as aquaporin-1 from red cells into proteoliposomes and defined the biophysical properties of the pore. These studies formed the foundation for the atomic-level description of how water crosses water channels; the seminal paper describing this work was one of two cited by the Nobel committee in awarding the Nobel Prize in Chemistry to Agre. Zeidel characterized a number of other aquaporins and has helped define how biological membranes can block the permeation of water and other normally permeant substances. Because mammalian bladder is such an effective barrier, he performed much of his early work on the cell biology of urothelium. He now focuses much of his research efforts on understanding the causes and potential treatments of disorders of bladder filling and voiding.

From an early stage Zeidel has had a strong interest in the delivery of medical care, medical teaching, and medical administration. From 1986 to 1994 he created and ran the renal section of the West Roxbury VA Medical Center. In 1995 he was recruited by Ed Benz to serve as chief of the Renal-Electrolyte Division of the University of Pittsburgh Department of Medicine. Soon after Benz left for Hopkins, Zeidel was made interim chair of medicine and then permanent chair, a position he held until 2005, when he was recruited back to Boston to his current position, as Herrman L. Blumgart Professor of Medicine at Harvard Medical School, chair of the Department of Medicine, and physician-in-chief at the Beth Israel Deaconess Medical Center.

During his time in Pittsburgh, Zeidel trained in systematic quality improvement with Brent James at Intermountain Healthcare and developed, within the departments at Pitt and BIDMC, robust quality improvement

efforts that led to markedly improved care. He also oversaw the training of numerous faculty members whose academic contributions focus on improving the care of patients.

An active teacher Zeidel co-wrote a textbook of renal physiology that uses computer-driven animations, rather than static images, to convey concepts of renal physiology. He has also developed novel courses for the Mount Desert Island Biological Laboratory on comparative physiology (for students and residents) and renal physiology (for renal fellows and students interested in pursuing a career in nephrology).

Zeidel has received a Young Investigator Award from the American Physiological Society and the Williams Award from the Association of Professors of Medicine. He was elected to membership in the American Society for Clinical Investigation and the Association of American Physicians. He married Susan Freedman in 1979, and they have three children and two grandchildren.

Boston emeritus members without submitted biographies:

Dennis Ausiello

Joseph Avruch

George Cahill

Alan Cohen

Alessio Fasano

Barbara Kahn

Dennis Kasper

Henry Kronenberg

Seymour Reichlin

LI Rubin

NEW HAVEN BIOGRAPHIES OF
LIVING MEMBERS



Linda Bockenstedt, MD

Linda Bockenstedt was born in Dayton, OH, on August 3, 1957. A recipient of a Westinghouse Science Talent scholarship, she entered Harvard College at the age of 17 and graduated three years later, in 1977, with an AB degree in chemistry and physics. She received her MD degree from Ohio State University School of Medicine in 1981 and completed a residency and chief residency in internal medicine at Yale–New Haven Hospital (1981–1985) during a period when Sam Thier served as chair. She pursued fellowship training in rheumatology at the University of California, San Francisco, where she was mentored in the laboratory by Arthur Weiss, and studied mechanisms of signal transduction in human lymphocytes. She joined the Yale rheumatology faculty first as an associate research scientist from 1990 to 1991, to establish her laboratory, and subsequently rose to the rank of professor of medicine in 2006. She currently also serves as associate dean for faculty development and diversity and divides her time among research, clinical/teaching, and administrative activities.

Bockenstedt's interest in science was nurtured by her engineer father, who believed that girls could understand math and science as well as boys, and by her sister Paula (now a hematologist at the University of Michigan), who served as a role model by showing a pathway for success. Although initially Bockenstedt was interested in how the brain worked (her Westinghouse project was on stuttering), it was the field of immunology that captured her attention in medical school and prompted her to spend a year at Harvard Medical School in the laboratory of Edward Goetzl, studying chemotaxis of human neutrophils. Her experiences in residency and fellowship solidified her decision to pursue an investigative career in academic rheumatology, and she came to Yale with the intent of applying her training in basic immunology toward understanding disease mechanisms. Her interests complemented those of the group at Yale studying Lyme disease, a tick-borne infection with the spirochete *Borrelia burgdorferi*, and she has focused her research program on the immunopathogenesis of Lyme disease.

Bockenstedt's investigations have explored the roles of innate and adap-

tive immunity in host defense, mechanisms of spirochete immune evasion, and, through application of novel, state-of-the-art imaging techniques, interactions of the pathogen with ticks and mammalian host tissues. Her early work explained that the lack of an early antibody response to Osp A, the most dominantly expressed spirochete lipoprotein in the tick midgut, was due to the rapid loss of expression of this protein after infection; she showed this via the first ex vivo demonstration of antigenic variation of the organism. Her subsequent studies of T cell responses to the pathogen overturned dogma on the role of T cells in disease susceptibility and resistance. She showed that the most important host defenses against this pathogen were at the level of innate immunity, with both B cells and TLR/MyD88-associated immune mechanisms necessary for controlling pathogen burden and pathology. She demonstrated a dual role for antibodies, with T cell-independent antibodies beneficial to the host and FcR engagement by IgG affecting disease severity. More recently, she pioneered the use of two-photon intravital microscopy to study *B. burgdorferi* infection in the living anesthetized mouse. The use of two-photon microscopy allowed her to demonstrate where spirochetes preferentially reside within the joint (in the entheses) and that inflammatory antigenic and DNA remnants of the spirochete can be detected for many months at these sites after antibiotic therapy has eliminated viable organisms, a finding with significant implications for Lyme arthritis pathogenesis and persistence.

For her contributions to the field of Lyme disease, Bockenstedt was the recipient of the Interurban Clinical Club Sir William Osler Young Investigator Award in 2000 and is an elected member of the Interurban Clinical Club, the Henry Kunkel Society, and the CT Academy of Science and Engineering. She has been a frequent invited speaker and chair of sessions at major international Lyme disease conferences, including the Gordon Research Conference on the "Biology of Spirochetes" and the "International Conference on Lyme Borreliosis and Other Tick-Borne Diseases", the latter of which she co-chaired in 2013. In addition to serving as a standing member on the NIH Immunity and Host Defense Study Section, she has been an invited speaker at a several NIH workshops on Lyme disease, the 2010 Institute of Medicine Workshop on "Critical Needs and Gaps in Understanding Lyme Disease", and a 2014 HHS/NIH/CDC Special Webinar on Lyme disease and *Borrelia* persistence. She is presently co-chair of the trisociety (Infectious Diseases Society of America [IDSA], American Academy of Neurology, and American College of Rheumatology [ACR]) panel that is updating the 2006 IDSA Lyme Disease Clinical Practice Guidelines.

In addition to her scientific accomplishments, Bockenstedt has been a key contributor to the academic community at Yale and beyond. She served as director of the Yale Training Program in Investigative Rheumatology for nearly a decade and chaired the ACR Committee on Training and Workforce Issues subcommittee on curriculum development. She served on the ACR Research and Education Foundation board of directors and its scientific advisory council. Since 2006 she has served as director for Professional Development and Equity at Yale School of Medicine, and in 2014 she was named associate dean for Faculty Development and Diversity to facilitate the career advancement of all faculty, especially women and minorities. She remains an active clinician and teacher and has been listed among best doctors in rheumatology for many years.

Jonathan S. Bogan, MD

Jonathan S. Bogan was born March 7, 1964, in New Haven, CT. He graduated from Hopkins School in New Haven in 1982 and received his BS degree from Yale College, where he majored in electrical engineering. During 1985–1987 he worked in the laboratory of Robert G. Shulman at Yale, where he designed and constructed electronic instruments to facilitate in vivo nuclear magnetic resonance studies of metabolism. This experience gave him an appreciation for how technological advances can lead to new knowledge, and also piqued his interest in metabolism. In 1987 he matriculated at Harvard Medical School in the Harvard/MIT Division of Health Sciences and Technology. To learn more about novel developments in molecular genetics, Bogan joined the laboratory of David C. Page at the Whitehead Institute and MIT. There, during 1988–1991, he constructed a genetic deletion map of the human Y chromosome and characterized the fine structure of the sex determining region. He completed coursework in the MIT biology graduate program, received his MD summa cum laude in 1992, and was awarded Harvard's Leon Resnick Memorial Prize for excellence in research for his MD thesis and its defense. Bogan went on to an internal medicine residency (1992–1994) and endocrinology fellowship (1994–1998) at Massachusetts General Hospital. For the research component of his fellowship, he joined the cell biology laboratory of Harvey F. Lodish at the Whitehead Institute and MIT. Both his engineering and genetics training influenced his work in Lodish's laboratory. To study insulin action in cultured adipocytes, Bogan adapted deconvolution microscopy techniques, developed retrovirus vectors, and conceptualized a dual-tagged reporter protein to facilitate the quantitative measurement

of GLUT4 glucose transporters at the plasma membrane. He used these tools to study the cell type specificity of insulin-responsive GLUT4 trafficking and to construct a mathematical model to account for the kinetics of GLUT4 movement. He became an assistant professor of medicine at Massachusetts General Hospital and Harvard in 2001 and moved to Yale University School of Medicine in 2002.

Bogan's major scientific contribution has been the discovery of a proteolytic mechanism by which insulin stimulates glucose uptake. His recent and ongoing work shows that this mechanism coordinates glucose uptake with other aspects of physiology, metabolism, and energy expenditure. In fat and muscle cells, insulin stimulates glucose uptake by causing the exocytic translocation of GLUT4 glucose transporters from intracellular membranes to the cell surface. Bogan saw that the tools he had developed made possible a genetic screen to identify regulators of GLUT4 targeting. This screen identified the TUG protein as a functional tether that sequesters GLUT4 proteins away from the plasma membrane in cells not stimulated with insulin. Insulin releases the tether to translocate GLUT4 to the cell surface, thereby promoting glucose disposal in adipose and muscle. Bogan's research team showed that TUG traps GLUT4-containing vesicles on specific Golgi proteins, that insulin triggers site-specific TUG cleavage to liberate these vesicles, and that during ongoing insulin exposure, endocytosed GLUT4 bypasses this proteolytic mechanism. This arrangement obviates the need for ongoing TUG destruction, which would be energetically expensive, during sustained insulin action. Together with other results, the data support the idea that this proteolytic pathway senses and responds to glycemic load. Insulin-regulated TUG proteolysis controls GLUT4 targeting and glucose uptake in muscle as well as adipose and is modulated in response to nutritional cues by cytosolic NAD^+ . Recently it has also become clear that the exocytic translocation of vesicles is a mechanism to coordinately regulate distinct physiologic effects, controlled by different cargo proteins present uniquely in the TUG-regulated vesicles. One of these, IRAP, limits vasopressin action, which may promote vasodilation during increased metabolic activity in muscle. Other vesicle cargos likely control lipoprotein metabolism. The actions of these vesicle proteins are coupled with potential effects of a TUG cleavage product, which is hypothesized to regulate genes controlling energy expenditure and to contribute to the thermic effect of food. Bogan's ongoing work in this area may thus have broad significance for understanding pathogenesis of metabolic syndrome.

Bogan is presently a tenured associate professor of medicine (endocrinology) and of cell biology at Yale University School of Medicine. He received the Richard and Susan Smith Family Foundation Award for Excellence in Biomedical Research in 2000 and was named as a W. M. Keck Foundation Distinguished Young Scholar in Medical Research in 2006. He was elected to membership in the American Society for Clinical Investigation in 2014 and to the Interurban Clinical Club in 2015.

Erol Fikrig, MD

Erol Fikrig was born in Istanbul, Turkey, on December 15, 1959. His mother was Scottish and his father Turkish. He moved to New York City the next year, when his father took a position as professor of pediatrics at SUNY Downstate Medical Center. He attended the United Nations High School in Manhattan, then majored in chemistry at Cornell University, graduating Phi Beta Kappa with honors and distinction in all subjects in 1981. He then attended Cornell University Medical College, spending part of his second and fourth years in Brazil, where he studied mucocutaneous leishmaniasis with Warren Johnson and Steve Reed. After completing his medical residency at Vanderbilt University Hospital in 1988, Fikrig went to Yale University for a fellowship in infectious diseases. There he studied immunobiology with Richard Flavell and, in collaboration with Stephen Barthold and Fred Kantor, developed a recombinant vaccine against Lyme disease that was approved for human use by the US Food and Drug Administration in 1998. Fikrig joined the Yale faculty in 1992 as an assistant professor of medicine, was promoted to associate professor in 1996, and became professor of medicine in microbial pathogenesis, epidemiology, and public health in 2002.

His laboratory focuses on understanding the pathogenesis of arthropod-borne diseases, including Lyme disease, anaplasmosis, West Nile encephalitis, dengue fever, and malaria. His group has advanced the paradigm that microbes alter the expression of tick and mosquito salivary gland genes and then use these differentially expressed proteins to facilitate infection of the mammalian host. This understanding of such interactions is being used to develop new vaccines and therapeutics for infectious diseases.

Fikrig was a Pew Biomedical Scholar, an established investigator of the Arthritis Foundation and the American Heart Association, and the recipient of a Burroughs Wellcome Clinical Scientist Award. He has served as a

member of the NIH Bacteriology and Mycology Study Section. He was the Hermann Boerhaave Visiting Professor at Leiden during a sabbatical in 2005, and is a member of the American Society for Clinical Investigation and the Association of American Physicians. In 2007 Fikrig was appointed the von Zedtwitz Professor of Medicine and chief of the Section of Infectious Diseases at Yale, and in 2008 he became an investigator of the Howard Hughes Medical Institute.

Kevan C. Herold, MD

Kevan Herold was born in Philadelphia, PA on December 28, 1956. He did his undergraduate and medical school training in the accelerated program with Pennsylvania State University and Jefferson Medical College. He remained in Philadelphia, at Temple University, for housestaff training in Internal Medicine and then completed a fellowship in Endocrinology at The University of Chicago. While a fellow, he studied glucagon metabolism including counterregulation mechanisms to hypoglycemia in patients with diabetes. His interest in immunology began then, and he completed a post-doc in the laboratory of Dr. Frank Fitch where he studied the molecular control of cytokine gene expression and began to work with murine models of autoimmune diabetes and biologics. He then was a Staff Scientist at the Hagedorn Research Laboratory in Gentofte Denmark before returning to the faculty at the University of Chicago. His studies as a junior faculty member involved tolerance and manipulation of tolerance in autoimmune disease models. He showed that intrathymic transplantation of islets of Langerhans would prevent induction of autoimmune diabetes induced with low doses of streptozotocin. He also at that time showed that this disease could be prevented with non-FcR binding anti-CD3 monoclonal antibody in collaboration with Dr. Jeffrey Bluestone. His studies identified the control of autoimmunity with anti-B7 antibodies. It was also at that time that he identified a family with hypoglycemia and a mutation of the glucokinase gene. This observation and the evaluation of the control of glucose in this family was one of the key findings that led to the concept of glucokinase as the regulatory of insulin secretion in the beta cells.

He left Chicago in 1997 and served as the Chief Scientific Officer at the Juvenile Diabetes Research Foundation in N.Y. briefly before returning to academics at the Naomi Berrie Center at Columbia University. At that time, Dr. Bluestone had produced a humanized non-FcR binding anti-CD3 antibody that had been tested in transplant recipients. Dr. Herold wrote an

IND for studies of this agent in new onset Type 1 diabetes and showed that a single course of treatment could significantly preserve insulin secretion for at least 2 years. This study led to several additional investigations with non-FcR binding anti-CD3 antibodies and other biologics. Studies that have continued in Dr. Herold's lab have identified the mechanisms for clinical responses and the characteristics of the responders that might be used to determine those who would benefit most from drug treatment. A part of these investigations, he collaborated with Dr. Richard Flavell to identify a mechanism whereby anti-CD3 mAb causes migration of T cells to the lamina propria where tolerance is induced. He showed this mechanism with human cells in humanized mice and more recently has identified an important role for the microflora in regulating this response. In addition, he has carried out studies in preclinical models that have led to new treatment protocols for patients.

The studies in the field were hampered by the reliance on metabolic studies that were affected by environmental factors and did not directly evaluate beta cell killing that was the cause of the disease. He developed a novel assay to measure beta cell killing in vivo by detecting beta cell derived DNA with epigenetic modifications that indicate its source. This assay was used to determine the kinetics of beta cell killing in those at risk for the disease and the response of individuals to the biologics.

Dr. Herold has served as a mentor for more than 20 post-docs, medical students, and fellows. He has been the director of the training program in Human and Translational Immunology at Yale and teaches the Immunobiology course for Medical Students. He is currently the program director for the Federation of Clinical Immunology Societies (FOCIS).

Dr. Herold's studies involve translational immunology and use both animal models of human disease together with clinical studies that entail metabolic investigations and immunologic studies. He serves as a deputy director of the Yale Center for Clinical Investigation and the director of the Yale Diabetes Center. He has received the Mary Tyler Moore and S. Robert Levine Award for Excellence in Clinical Research from the Juvenile Diabetes Foundation and is a member of the Association of American Physicians.

Thomas Gill, MD

Thomas Gill was born in Chicago, Illinois, on June 20, 1961. He received his BS degree (1983) and BA degree (1985) from Loyola University, Chicago, and his MD degree from the University of Chicago Pritzker School of Medicine (1987). During the following three years, he was an intern, resident, and chief resident in the primary care internal medicine program at the University of Washington in Seattle. After a year (1990–1991) as an acting instructor at the University of Washington Medical Center, where he worked in the HIV Vaccine Trials Unit under Larry Corey, Gill moved to Yale for his research training in clinical epidemiology as a Robert Wood Johnson Clinical Scholar (1991–1993) under Alvan Feinstein and Ralph Horwitz.

After completing an additional year as a geriatrics fellow (1993–1994) under Leo Cooney and Mary Tinetti, he joined the Yale faculty as an assistant professor of medicine (geriatrics) in 1994. Gill was promoted to associate professor in 1999 and to professor of medicine, epidemiology, and public health in 2006. In 2005 he was appointed to the graduate school faculty in the investigative medicine program, and in 2009 he was named the Humana Foundation Professor of Geriatric Medicine. Gill has directed Yale's training program in geriatric clinical epidemiology and aging-related research since 1999, served as co-director of the Yale Program on Aging/Claude D. Pepper Older Americans Independence Center from 2006 to 2010, and assumed leadership as the director of the Program on Aging/Pepper Center in 2010. In 2008 he established the Yale Center for Disability and Disabling Disorders.

Gill's research has focused on the epidemiology and prevention of disability, a challenging and complex problem of immense importance in geriatrics. He has devoted particular attention to rigorously evaluating the natural history of disability, investigating the mechanisms by which older persons become disabled, and developing innovative strategies to prevent the onset and progression of disability. In an initial set of studies, Gill demonstrated that simple tests of physical capabilities, including a 20-foot walk and single chair stand, can be used to effectively identify older persons who are at increased risk for becoming disabled. Based on his work these tests (often referred to as "geriatric vital signs") are increasingly being used, both in clinical practice and in clinical trials, to identify frail older persons for preventive interventions. Subsequently, Gill was the first to show that impairments in physical capabilities and cognitive status contribute inde-

pendently to the risk of disability.

Gill's most remarkable achievement may be his ongoing longitudinal study, which includes monthly assessments of functional status and potential precipitants of disability over a 13-year period, along with home-based assessments performed at 18-month intervals, in a large cohort of older persons. Gill has provided compelling evidence to support an emerging paradigm of disability as a reversible, and often recurrent, event, more similar to falls and delirium than to progressive disorders such as Alzheimer's disease. He has shown that disability often occurs insidiously, particularly among older persons who are physically frail, and that illnesses and injuries leading to either hospitalization or restricted activity, particularly falls and fall-related injuries, represent important sources of disability regardless of the presence of physical frailty. Most recently Gill demonstrated that the course of disability at the end of life does not follow a predictable pattern for most decedents, raising questions about how resources should be properly allocated to care for older persons at the end of life.

Informed by his epidemiologic studies, Gill was the first to show that a home-based program targeting underlying impairments in physical capabilities can reduce the progression of functional decline among physically frail, elderly persons who live at home. During the course of this trial, Gill demonstrated that current guidelines regarding exercise stress testing are not applicable for the vast majority of older persons who are interested in restoring or enhancing their physical function through a program of physical activity and exercise.

Through the support of an NIH midcareer investigator award in patient-oriented research, Gill has mentored a large number of junior faculty and fellows, generating new knowledge on an array of important topics in geriatrics and gerontology, including disabling back pain, depression, frailty, sleep complaints, and the deleterious effects of low levels of serum micronutrients. In recent years he and colleague Carlos Vaz Fragoso have developed new strategies to more accurately assess pulmonary function and diagnose chronic obstructive lung disease across the lifespan.

Gill is the recipient of numerous awards, including the Paul Beeson Physician Faculty Scholars in Aging Research Award, the Robert Wood Johnson Generalist Physician Faculty Scholar Award, the Outstanding Scientific Achievement for Clinical Investigation Award from the American Geriatrics Society, and the Ewald W. Busse Research Award in the Biomed-

cal Sciences. His research accomplishments have been recognized through receipt of a MERIT Award from the NIH and election to the American Society for Clinical Investigation and Association of American Physicians. He joined the Interurban Clinical Club in 2008.

Daniel R. Goldstein, MD

Daniel R. Goldstein was born in Wimbledon, England, on April 22, 1968. He was raised in England and attended medical school at St. George's Hospital Medical School at the University of London from 1986 to 1992. After completing a houseman's year that consisted of six months of internal medicine and six months of general surgery in London, he moved to the United States due to family reasons, where he started an internal medicine residency at Johns Hopkins Bayview Medical Center (formerly the Francis Scott Key Medical Center) in Baltimore, Maryland, in 1993. After completing his residency in 1996, he undertook training in cardiovascular diseases at the University of Alabama at Birmingham (1996–2000). During this time he received postdoctoral fellowship research training in transplantation immunology and also undertook a fellowship in advanced heart failure and cardiac transplantation at UAB from 2000–2001. He started on the faculty at Yale in 2001 as an assistant professor and was supported by a K08 career development grant from the NIAID. He has since remained at Yale, where he became a full professor in 2013.

Goldstein's interest in medicine was inspired by his father, who suffered from polio as a child and was rendered physically handicapped. He was intrigued by the story that led to the development of the polio vaccine and attended the medical school at which Edward Jenner developed the first vaccine (for cowpox). Since medical school he has been interested in immunology and inflammation. The focus of his laboratory has been in examining how aging affects inflammation and how inflammation is initiated after organ transplantation.

For more than a decade, Goldstein has defined how activation of specific inflammatory pathways results in organ rejection after transplantation. His laboratory was the first to define the role of the Toll-like receptors (TLRs) in organ transplantation, by showing that TLRs were required for murine skin graft rejection (findings published in the *Journal of Clinical Investigation [JCI]* in 2003). The lab then defined the functions of TLRs and downstream mediators (e.g., MyD88) in acute cardiac allograft rejection

(*American Journal of Transplantation* [*AJT*], 2004) and in transplantation tolerance (*Journal of Immunology* [*Jl*], 2006; *Journal of the American Society of Nephrology*, 2009). The group identified an extracellular matrix component, hyaluronan, which activates TLRs to enhance alloimmunity, and demonstrated that elevated hyaluronan levels correlate with human chronic lung rejection (*AJT*, 2006). Recently, via a proteomic screen, they identified haptoglobin as a unique activator of MyD88 that enhances skin graft rejection (*JCI*, 2012). This work has been clinically translated and has led to the development of TLR inhibition strategies in solid organ transplantation.

Goldstein's laboratory has also examined the interplay between aging and inflammation and was the first to show that dysregulated inflammation during viral infection with aging has lethal consequences (due to reduced levels of type I interferon coupled to elevated IL-17 levels) (*Jl*, 2008; *Cell Host and Microbe*, 2009). This work indicates that anti-inflammatory therapies may be beneficial. In addition, the group has discovered pathways by which aging induces increased inflammation in vascular smooth muscle cells (*Arteriosclerosis, Thrombosis, and Vascular Biology*, 2012) and increased macrophage apoptosis (*Aging Cell*, 2013), findings that may explain how aging enhances atherosclerosis. In sum, the work done in Goldstein's laboratory addresses the core principles and potential clinical translation of elevated inflammation in age-associated phenotypes.

As a fellow Goldstein received the Walter B. Frommeyer Award in investigative medicine and the Bernard Amos Award in transplantation immunology. As a faculty member he received an American Society of Transplantation investigator award in 2007, the Paul Beeson Career Development Award in aging research in 2005, an Established Investigator Award from the American Heart Association in 2008, a mid-career development award from the NIA in 2008, and the Osler Young Investigator Award from the Interurban Clinical Club in 2012. He was inducted into the American Society for Clinical Investigation in 2010, served as a section editor for *Jl*, served as a regular member of the NIH Transplantation, Tolerance and Tumor Immunology Study Section from 2008–2012, and joined the NIH Cellular Mechanisms in Aging and Development Study Section in 2014. Beginning in 2013 he served on the board of directors for the International Society for Heart and Lung transplantation and on the publication committee of the American Association of Immunologists.

Elizabeth Ann Jonas, MD

Elizabeth Ann Jonas was born on April 14, 1960. She was educated from the age of four at the Ethical Culture School in New York City and the high school of the Ethical Culture Society known as the Fieldston School. She attended Yale University and resided in Branford College. She majored in history with a concentration in British naval history of the eighteenth century. Having completed her premedical requirements during college, upon graduation from Yale she immediately enrolled at New York University School of Medicine, where she was elected to the Alpha Omega Alpha society.

After medical school Jonas interned at Yale–New Haven Hospital in internal medicine and carried out neurology residency training at Yale. She was elected chief resident in neurology and received the first Hugh L. Dwyer Award for excellence in clinical medicine and teaching. Following her neurology training she obtained board certification in neurology. She began a postdoctoral fellowship in the Department of Pharmacology at Yale, in the laboratory of Leonard Kaczmarek, where she focused on the role of intracellular calcium in synaptic vesicle release and neuropeptide granule fusion. In Kaczmarek's laboratory she described the activity of insulin receptor in neurons and found that insulin induces intracellular calcium release from neuropeptide granules, to foster the fusion of the granules with the plasma membrane during the process of neuropeptide release. Based on these findings, Jonas suggested that calcium-release channels on intracellular membranes could be recorded intracellularly, and she created a technique to perform this feat. Notable outcomes of this technical achievement included finding a calcium–re-release channel in mitochondrial membranes, the activity of which was required for short-term plasticity in neuronal synapses. Shortly after publishing these reports, she began her appointment as assistant professor in internal medicine (endocrinology) at Yale. She completed her training in internal medicine and became board certified in internal medicine in 2002.

Jonas then continued to study mitochondrial ion channels, using adaptations of mitochondrial recording techniques. She demonstrated that the anti-apoptotic protein Bcl-xL induces channel activity in part to regulate short-term synaptic plasticity. In the course of her studies in invertebrate systems, Jonas described a possible metabolic role for Bcl-xL in the synapse. She examined this more closely in mammalian hippocampal neurons. Long-term changes in activity of hippocampal neurons produce

learning and memory formation in the brain; in contrast, dysfunction of these cells leads to neurodegenerative disease. Jonas described that hippocampal neurons are dependent on Bcl-xL for increases in the number and size of synapses, changes that are correlated with healthy memory formation. She found that Bcl-xL, by interacting directly with the ATP synthase, enhances the efficiency of energy production by mitochondria in neurons. Jonas and her collaborators then found that a non-selective channel that leaks protons resides within the membrane portion of the ATP synthase. Closing of this channel increases metabolic efficiency, and opening of the channel decreases efficiency but provides a conduit for calcium re-release during normal synaptic transmission and synaptic plasticity.

Calcium accumulation in mitochondrial matrix predisposes to pathologic changes to mitochondria, including opening of a widely known cell death channel, the mitochondrial permeability transition pore. This channel is implicated in producing ischemic, traumatic, and degenerative cell death. When channel opening occurs in injured cardiac cells, neurons, and other cell types, it contributes to cell death in stroke, heart disease, neurodegenerative disease, and cancer. Based on the evidence provided by Jonas's group, the Bcl-xL-sensitive leak channel within the ATP synthase forms the mitochondrial permeability transition pore. Understanding the regulation of this pore in health and disease now forms the focus of Jonas's lab work. She is studying models of Parkinson's disease, brain ischemia, Fragile X mental retardation syndrome, and hippocampal neurodegeneration.

Jonas currently holds a position as associate professor of medicine (endocrinology) and neuroscience at Yale. She teaches in internal medicine and is active clinically as an attending physician on the Fitkin Medicine service at Yale–New Haven Hospital and at the Primary Care Clinic of Yale–New Haven Hospital. She participates in the Emergency Medicine Lecture series at Yale and the VA medical center. She also teaches as part of the Affiliated Hospitals Program lecture series. She teaches neuroanatomy of clinical cases in the preclinical program at Yale Medical School as part of her duties in the neurobiology department. Jonas is an active member of the Yale intern selection committee.

In addition to training her own postdoctoral fellows and several graduate students, Jonas teaches and trains undergraduates in her laboratory at Yale, as part of two lecture classes at Brown University and as part of the NSF Research Experience for Undergraduates program at the Marine Biological Laboratory in Woods Hole, MA. At the Marine Biological Laboratory,

she also frequently serves as an advisor to the prestigious Grass Fellowship Program. She has completed service as a permanent member of the NIH Neural Oxidative Metabolism, Mitochondria and Cell Death Study Section. She maintains board certifications in neurology and internal medicine. She has been awarded the prestigious Jacob Javits Award for Achievement in Neuroscience.

Barbara Kazmierczak, MD, PhD

Barbara Kazmierczak was born in Chicago, IL, on October 10, 1964. She received her BA in biological sciences and her MS in biochemistry and molecular biology from the University of Chicago in 1986, then entered the medical scientist training program at The Rockefeller University. She joined Norton Zinder's laboratory of genetics and worked with Marjorie Russel and Peter Model on mechanisms of filamentous phage assembly. She obtained her PhD from Rockefeller in 1993 and her MD from Cornell University Medical College in 1994. This was followed by a short-track residency in internal medicine (1994–1996) and fellowship training in infectious diseases (1996–1999) at the University of California, San Francisco. At UCSF Kazmierczak began studying interactions of the opportunistic pathogen *Pseudomonas aeruginosa* with polarized epithelia under the joint mentorship of Joanne Engel and Keith Mostov and supported by a Postdoctoral Research Fellowship for Physicians from the Howard Hughes Medical Institute. She was appointed an assistant adjunct professor in medicine (1999–2001) and continued her studies supported by an NIH NIAID K08 Career Development Award. She was recruited to Yale in 2001, where she joined the Department of Medicine (infectious diseases) as an assistant professor, with a joint appointment in the Section of Microbial Pathogenesis. She served as director of graduate admissions for the microbiology track (2004–2007), was promoted to associate professor in 2007, and was granted tenure in 2011. Since 2010 she has also served as an associate director of the MD-PhD program at Yale.

Scholarship was highly valued in Kazmierczak's family. Her parents, Stanislaw Kazmierczak and Irena Wozniak, were displaced from their homes in Poland during World War II, and each came to America in the early 1950s with little in the way of possessions save what they carried in their heads. An engineer and a teacher, respectively, they transmitted their love of learning to their daughters, Barbara and Krystyna (who is a microbiologist and director of molecular services at IHMA in Chicago). An early interest

in mathematics and science was reinforced by Kazmierczak's experiences at the University of Chicago, where teachers and mentors such as Howard Tager, Wolf Epstein, Malka Moscona, and Lucia Rothman-Denes demonstrated how complementary approaches of biochemistry and molecular genetics could elucidate the rules governing complex signaling and regulatory pathways. During her PhD work with Russel and Model, the tools of biochemistry and genetics allowed Kazmierczak to describe the role of a phage-encoded outer membrane pore, or secretin, in filamentous phage assembly and secretion by *E. coli*. The recognition that similar secretins were obligate components of bacterially encoded secretion and conjugation systems (type II, type III, and type IV) led to her subsequent interest in the assembly and regulation of type III secretion systems (T3SS) of Gram-negative pathogens and in the activities of type III secreted effectors after their injection into eukaryotic cells by these pathogens.

Since moving to Yale, Kazmierczak has continued her studies of *P. aeruginosa* pathogenesis, focusing on the bacterial factors important for establishment of disease, as well as host responses to infection. She described the first sensor kinase/response regulator system (RtsM/RetS) required for expression of the *P. aeruginosa* T3SS, then showed that bacteria expressing the T3SS elicited more rapid and robust neutrophilic responses in acute pneumonia than did their T3SS-negative counterparts. Working with Suterwala and Flavell, she demonstrated that the NLRC4 inflammasome recognized T3SS-expressing bacteria, and that flagellin was not required for inflammasome activation. More recently, she has collaborated with Romberg and Lifton to characterize the molecular defects associated with the first de novo NLRC4 mutation described in human patients, which is responsible for a syndrome of enterocolitis and autoinflammation. Kazmierczak's research group has also continued to make seminal contributions to understanding the basic cell biology of *P. aeruginosa* and how it contributes to bacterial fitness during both acute and chronic infections, e.g., pneumonia versus persistent colonization of the cystic fibrosis airway. She and her trainees have described novel regulators that control localization and assembly of surface organelles (flagella and type IV pili) and have elucidated the signaling pathways and second messengers (cAMP, cyclic-di-GMP) that allow bacteria to respond to surface attachment and to initiate biofilm formation. Her most recent work, done in collaboration with Marie Egan, director of the Cystic Fibrosis Center at Yale, examines the acquisition of bacterial commensals and pathogens by infants with cystic fibrosis over time, with the goal of identifying bacterial and inflammatory biomarkers in the airway and gut that predict progression of clinical air-

way disease. In all of these studies, Kazmierczak's goal is to identify new therapeutic targets for improving clinical outcomes associated with *P. aeruginosa* infection.

Kazmierczak has been recognized with numerous awards. She was a Presidential Scholar (1982) and a Phi Beta Kappa and Sigma Xi inductee (1985), and she was named a 2002 Hellman Family Fellow, a Donaghue Investigator of the Donaghue Medical Research Foundation (2002–2007), and an Investigator in Pathogenesis of Infectious Diseases of the Burroughs Wellcome Fund (2007–2012). She has been a fellow of the Infectious Diseases Society of America since 2008 and served on its annual meeting program committee (2009–2012). She was elected to membership in the Polish Institute of Arts and Sciences in America (2009) and the American Society for Clinical Investigation (2014). Kazmierczak spent a sabbatical in the laboratory of Arturo Zychlinsky at the Max Planck Institute for Infection Biology (Berlin) as a recipient of a Deutscher Akademischer Austausch Dienst Research Visit Grant. She is currently a section editor for *PLoS Pathogens* and has sat on the NIH Bacterial Pathogenesis Study Section and the Host Interactions with Bacterial Pathogens Study Section. Kazmierczak is also an accomplished pianist: she appeared as soloist with the Chicago Symphony Orchestra at age 16, won the Louis Sudler Prize in the Performing Arts at the University of Chicago (1986), and continued to present recitals as a soloist and chamber musician during her medical and scientific training in New York and San Francisco. Currently she performs as guest pianist with the Manesse Quartett, with recent concerts in Swaebisch-Gmuend, Berlin, Rostock, and New Haven.

Michael Simons, MD

Michael Simons was born in St. Petersburg, Russia, on July 19, 1957. After moving to the United States, he received a BS from Massachusetts Institute of Technology, then an MD cum laude from Yale University School of Medicine in 1984. This was followed by an internship and residency at the New England Medical Center in Boston, a medical staff fellowship at the National Heart, Lung and Blood Institute, a cardiology fellowship at Beth Israel Hospital, and a postdoctoral fellowship in molecular cell biology at MIT under supervision of Robert D. Rosenberg.

In 1993 Simons was recruited by William Grossman to his first academic position as an assistant professor of medicine at Beth Israel/Harvard Medi-

cal School. In 1996 he became an associate professor at Beth Israel, and in 2001 he moved to Dartmouth School of Medicine to serve as chief of cardiology. In 2008 he moved back to Yale, where he is currently the Robert W. Berliner Professor of Medicine and Cell Biology.

Throughout his career Simons pursued an integrated program of clinical, translational, and basic research. While at Beth Israel he developed applications of newly discovered angiogenic growth factors to treat advanced coronary disease. His studies in animal models established the feasibility of this approach and elucidated many of the issues associated with dosing and delivery. This work led to clinical trials of therapeutic angiogenesis in patients with coronary and peripheral artery diseases. Simons led a number of early trials in this field and developed many of the current approaches to patient selection and evaluation of outcomes. The lack of clear-cut benefit of these therapies in a variety of clinical settings led him to examine the underlying molecular reasons and to elucidate in detail the signaling pathway(s) responsible for arteriogenesis. During the course of these studies, his laboratory established the central role of vascular endothelial growth factor (VEGF)-activated ERK signaling in the endothelium in this process and worked out various regulatory checkpoints involved. These discoveries allowed for developments of new therapeutic strategies aimed at stimulating arteriogenesis by bypassing the critical blocks that typically prevent the effective use of angiogenic growth factors and lead to endothelial pathology in patients with atherosclerosis, diabetes, and other diseases.

Since VEGF signaling is central to a number of key vascular processes including angiogenesis and arteriogenesis, Simons's laboratory focused on elucidating molecular details of VEGF receptor signaling pathways. In the course of these studies, he demonstrated that VEGFR2 endocytosis and the subsequent intracellular trafficking are critical to VEGF activation of ERK signaling. Elucidation of this pathway opened the possibility of new therapeutic approaches toward the activation of VEGF signaling that may be of considerable clinical importance.

Other studies of fundamental importance from his laboratory demonstrated that ongoing fibroblast growth factor (FGF) signaling input is critical to the maintenance of vascular normalcy. When FGF signaling input is disrupted, blood vessels begin to lose their structural integrity, leading to increased permeability, occasional frank hemorrhage, and most critically, development of endothelial-to-mesenchymal (EndMT) transition. The lat-

ter appears to be the key process underlying neointima growth and atherosclerosis progression.

Finally, Simons is one of the pioneers in the field of syndecan biology. Syndecans are an incompletely understood family of transmembrane proteoglycans that are involved in a number of biological processes. His laboratory made major contributions to the understanding of syndecan-4 signaling, establishing a number of key points in its biology. In particular, he demonstrated its involvement in control of PKC- α activity, regulation of FGF signaling, and control of endothelial polarity.

Simons has received a number of awards, including the Alfred A. Richman Research Award from the American College of Chest Physicians, the Clinician-Scientist Award and Established Investigator Award from the American Heart Association, and honorary citations from the Japanese Circulation Society and India Cardiovascular Society. He has received an honorary fellowship from University College London and a visiting professorship from the British Heart Association. Simons has been elected to fellowships in the American Physiological Society, the American College of Cardiology, and the American Heart Association. He is a past president of the North American Vascular Biology Organization and a former councilor of the New Haven chapter of the Interurban Clinical Club. He is also an elected member of the American Society for Clinical Investigations, the Association of American Physicians, and the Association of University Cardiologists.

John J. Wysolmerski, MD

John J. Wysolmerski was born in Rutland, VT, on December 15, 1960. He received his BS degree from Yale College in 1982 and his MD degree from Yale Medical School in 1986. His childhood interest in science was nurtured by professors at Yale such as Frank Ruddle, Harry Wasserman, and John Trinkaus. During medical school he was awarded an NIH medical student research fellowship and worked in the laboratory of Ronald Germain at the NIAID. His interest in endocrine research was sparked by his medical school thesis work in the laboratory of Andrew Stewart. Wysolmerski went on to serve as an intern and resident in internal medicine at Tufts–New England Medical Center in Boston from 1986 to 1989. His decision to become an endocrinologist was heavily influenced by his interactions with Seymour Reichlin at Tufts. He practiced general internal

medicine at the Faulkner Hospital in Boston for one year before returning to Yale to train in endocrinology in 1990. He joined the laboratory of Arthur Broadus, who served as his research mentor. He joined the faculty at Yale as an assistant professor in 1995 and rose through the ranks to become professor in 2008. He currently serves as associate chief of endocrinology for research at Yale.

Wysolmerski's research has been at the interface between mineral and bone metabolism and mammary gland biology and breast cancer. As a medical student he participated in studies that led to the purification and characterization of parathyroid hormone-related protein (PTHrP) from the breast tumor of a hypercalcemic patient. After returning to Yale as an endocrine fellow, he turned his attention to elucidating the physiologic function of PTHrP in the breast. Using a series of genetic models in mice, he discovered that PTHrP was required for breast development and characterized a series of mesenchymal responses to PTHrP that were necessary for the survival and three-dimensional morphogenesis of embryonic mammary epithelial cells. His laboratory also showed that during lactation, PTHrP was produced by the mammary gland and was secreted into the systemic circulation to enhance bone resorption and liberate skeletal calcium stores for milk production. Furthermore, the Wysolmerski laboratory demonstrated that the calcium-sensing receptor (CaSR) was expressed by mammary epithelial cells during lactation and controlled the production of PTHrP as well as calcium and water transport into milk. These studies highlighted the fact that the breast contributes to the regulation of systemic mineral and bone metabolism during lactation and described a previously unrecognized endocrine feedback loop between breast and bone that regulates the flow of calcium from maternal skeletal stores into milk. More recent studies have demonstrated how this normal feedback loop is altered during malignant transformation in order to support the development of systemic hypercalcemia and osteolytic bone metastases.

Wysolmerski has studied the mechanisms by which CaSR stimulates calcium transport into milk and has identified calcium pumps that are necessary for transepithelial calcium transport across the mammary epithelium. Recent studies have focused on a particular calcium-ATPase, PMCA2, which is required for calcium transport into milk but also appears to play a critical role in the regulation of epithelial cell apoptosis during mammary gland involution and in resistance to apoptosis in breast cancer. His lab has also helped to elucidate the hormonal regulation of bone loss during lactation and the recovery of bone loss after weaning, studies which suggest that

changes in the skeleton during lactation may represent an evolutionary rationale for postmenopausal bone loss in older women.

Wysolmerski is a member of Alpha Omega Alpha, the Endocrine Society, the American Society for Bone and Mineral Research (ASBMR), and the American Society for Clinical Investigation. He has been the recipient of young investigator awards from the Endocrine Society, the Advances in Mineral Metabolism Meeting, and the ASBMR. He has served on the editorial boards of *Endocrinology*, *Bone*, the *Journal of Bone and Mineral Research*, and the *FASEB Journal*. He is an associate editor of the *Journal of Mammary Gland Biology and Neoplasia*. He is a past recipient of the Sir William Osler Award from the Interurban Clinical Club, served as New Haven councilor from 2007 through 2010, and was president from 2010 to 2011.

Lawrence Young, MD

Lawrence Young was born in Boston, MA, on November 24, 1954. He graduated from Milton Academy, then earned his BA degree from Brown University in 1976 and his MD degree from Yale University School of Medicine in 1980. He did his Yale Medical School thesis under the guidance of Ralph DeFronzo, studying skeletal muscle glucose transport, which sparked his career interest in metabolism. He completed his residency in internal medicine at Yale (1980–1983) under Samuel Thier and his fellowship in cardiology at Yale (1983–1986) under Barry Zaret. During his research cardiology fellowship, he was mentored by Eugene Barrett and studied mechanisms that regulate cardiac amino acid transport. He joined the Yale faculty as assistant professor of medicine in the Cardiology Division in 1986, with the support of an NIH NHLBI Research Career Development Award. In 1990 he became associate professor of medicine, and he was promoted to professor in 2000 with a secondary appointment in cellular and molecular physiology.

In selecting medicine, and ultimately cardiology, as a career, Young was inspired by his father Eliot, who was a cardiologist at Peter Bent Brigham Hospital, Beth Israel Deaconess Hospital, and Harvard Medical School. His father trained a generation of fellows and students in electrocardiography and instilled in him a deep appreciation for the importance of investigation and education in medicine. While always fascinated by clinical cardiology and cardiac physiology, Young decided to study fundamental

cellular and molecular responses to pathological stress, in particular myocardial ischemia. His initial work focused on cellular mechanisms that regulate glucose transport, and he revealed the fundamental importance of translocation of the glucose transporter 4 from intracellular vesicles to the sarcolemma during ischemia. Recognizing that a molecular sensor of energy deprivation that regulated the metabolic response to ischemia might be important, his laboratory discovered that a protein kinase activated by changes in adenine nucleotide concentration plays a critical role during ischemia. In 1997 Raymond Russell in his laboratory first presented work that indicated that AMP-activated protein kinase (AMPK) indeed was a potent regulator of glucose transporter translocation in the heart. Together with independent discoveries in skeletal muscle, these findings set off a great deal of interest in the role of AMPK as a metabolic regulator and as a potential target for the treatment of type 2 diabetes.

Experimental work in the Young laboratory defined AMPK as a critical pathway in the ischemic heart and provided the first evidence that pharmacologic therapy to activate AMPK might prevent injury during myocardial infarction. His interests then extended to the role of autocrine-paracrine factors in the ischemic heart. Together with his colleague Richard Bucala, a rheumatologist at Yale, he discovered that cardiomyocytes within the heart expressed a cytokine called macrophage migration inhibitory factor (MIF). They found that MIF secreted from cardiomyocytes during ischemia had an unanticipated physiologic effect to promote glucose metabolism, AMPK activation, and cell survival during ischemia. They also noted that patients who express a common polymorphism in the MIF gene promoter, which leads to low-level MIF expression, also have impaired cellular AMPK activation. They observed that action of MIF is mediated by the cell surface receptor CD74, and Young then discovered that the heart also expresses a second ligand for CD74. This curious ligand was D-dopachrome tautomerase, which also possesses a vestigial tautomerase activity but has no known physiological substrate in mammalian species.

Based on his interest in metabolism, Young also promoted multi-disciplinary clinical research at the interface of diabetes and cardiovascular disease at Yale. He served as the principal cardiologist for the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study, which showed that routine stress testing in asymptomatic patients with type 2 diabetes has no effect on outcomes; as a result, the then-common practice of routine screening for asymptomatic coronary artery disease was ended. He also serves as the principal cardiologist for the Insulin Resistance Intervention in Stroke

(IRIS) trial, which is assessing the role of metabolic therapy in pre-diabetic patients as a novel strategy for secondary cardiovascular prevention.

Young has held several leadership roles at Yale, including as director of the Myocardial Biology Program, director of the Yale cardiovascular fellowship program, and vice chairman for faculty affairs in internal medicine. He has mentored numerous trainees within his own laboratory, and more broadly in the cardiovascular medicine section, department, and school. He serves on the faculty of the Yale Investigative Medicine Program, which provides PhD training for clinically trained MDs during their subspecialty fellowships. He has been a spokesman for the importance of investigation and scholarship in medicine and has inspired many trainees and young faculty to pursue careers as physician-scientists.

Young has also had an important clinical presence at Yale. He trained fellows in cardiovascular physiology in the Yale cardiac catheterization laboratory for many years. He maintains an active cardiology practice and teaches incoming housestaff and fellows as an attending physician in the Coronary Care Unit every summer. Outside of Yale, Young has held several leadership roles with the American Heart Association and serves a member of the NIH/NHLBI Myocardial Ischemia and Metabolism Study Section. He is an elected member of the Association of American Physicians.

NEW HAVEN EMERITUS MEMBERS BIOGRAPHIES

Philip W. Askenase, MD

Philip W. Askenase was born on June 7, 1939, in Brooklyn, NY. He was awarded an AB degree by Brown University in 1961 (*magna cum laude* and Junior Phi Beta Kappa) and an MD by Yale University School of Medicine in 1965 (*cum laude* and Alpha Omega Alpha). When Askenase was a medical student, he was profoundly influenced by Paul Beeson, who recommended he join the Harvard Medical Unit/Thorndike Laboratory at Boston City Hospital for further training. There, the clinical director, Charles Davidson Jr., asked about future plans. Askenase said he wanted to join the Peace Corps. Davidson put an arm around his shoulders and said: "Phil, that kind of thinking was all right when you were at Yale, but you are

a ‘Harvard man’ now, and I want you to look at NIH.”

Askenase went to the NIH determined to have a clinical experience, but he found it deficient, as the facilities available for patient care during clinical studies were more minimal than those of the Boston City Hospital. He was trained in rheumatology by John Decker and Norman Talal. Recognizing that there were no therapies beyond toxic steroids and aspirin, he began research with Edward J. Leonard, a second lab descendent of Albert Szent-Györgyi (who won the Nobel Prize in 1937 for his discovery of vitamin C). Leonard was embarking on research in immunochemistry to help solve problems, so Askenase and Leonard learned laboratory immunology together. This led to their discovery of the ability of antigen and antibodies to adhere to test tubes for immune assay, which led to the development of ELISAs and Western blots. Askenase’s research problem was to search for circulating immune complexes in humans with acute glomerulonephritis. He and Leonard developed the first solid-phase radioimmunoassay based on antibody bonding spontaneously to a surface. They were able to take a dilute solution of antibody and demonstrate that putting it in a test tube resulted in small amounts sticking to the surface yet having available antibody-combining sites, enabling them to do a competition between radioactive antigen and test antigen in the tube. They found that not only were complexes present in patient sera, but that an equal amount of complexes were present in the age- and sex-matched controls. They had difficulty publishing their results, which contradicted the current dogma that immune complexes were pathogenic. An important paper published in 1970 presented solid-phase immunoassay of C3, the first tube or platebinding assay.

Askenase was smitten with research and so completed a fellowship in England with Geoffrey Asherson, then returned to Yale in the Inflammatory Disease Section, which encompassed research in infectious diseases (Elisha Atkins and Vince Andriole), rheumatology (Bill Hollingsworth and Steve Maliwista), and allergy and clinical immunology (Fred Kantor).

Askenase’s early career skyrocketed after the discovery that B cell antibodies could mediate a new kind of delayed sensitivity featuring basophil infiltrates. This led to the concept that allergic diseases featured this type of delayed inflammation in the newly recognized late phase, as in asthma. He did a sabbatical in London at Mill Hill in immunoparasitology with Bridgette Ogilvie, aiming to understand the usefulness of allergy. Upon returning to Yale, Askenase showed that these basophil reactions reject-

ed ectoparasite ticks, leading later to his participation in the discovery of Lyme disease. He then turned to analogous studies in mice, with Richard Gershon, and discovered the required roles of antibodies, mast cells, complement, and NKT cells.

In 2015 at 75 years of age, Askenase has turned his focus to the newly recognized extracellular nanovesicles called “exosomes,” which are made by all cells, present in all fluids, and made in some form by all species (including bacteria and fungi) and thus are fundamental particles of life. Remarkably, exosomes transfer miRNAs, then function genetically in the acceptor cells. His laboratory’s system has been suppressor T cells that make antigen-specific exosomes due to a coating of immunoglobulin light chains that are induced, by antigen high-dose tolerance, to suppress effector T cells. The initial system was a mouse model of allergic cutaneous contact dermatitis (e.g., poison ivy, nickel sensitivity), but this has since been extended to delayed-type hypersensitivity to the protein antigens, in order to study allergies and autoimmunity.

A remarkable aspect of this system is that these tiny vesicles, which contain only 0.2 attoliters (10^{-21} liters), can antigen-specifically transfer specific miRNA at femtomolar amounts (10^{-15} moles), to function in vivo in an endocrine manner to genetically suppress the function of distant effector T cells at sites of active immune responses. Now that the role of exosomes in immune cell interactions has been uncovered, Askenase’s laboratory is now researching the use of exosomes made by mesenchymal stem cells as a therapy for spinal cord injury, multiple sclerosis, and autism. It is interesting that basic allergy research on poison ivy has led to the consideration of entirely new therapies for neurologic and psychiatric diseases.

Askenase recalls that at his first day at Yale Medical School, someone said the word “pathology” and he asked, “What is pathology?” This confirmed what seemed to be a quick decision by Tom Forbes, the director of admissions at Yale, when, during Askenase’s admissions interview in 1960, Forbes said, “Do you want to go to Yale Medical School? Congratulations.” This led to 300 peer-reviewed publications and 30 years as chief of Allergy and Clinical Immunology at Yale.

Askenase has served on the NIH NIAID Allergy, Immunology and Transplantation Committee, NIH Pathology A Study Section, NIH Immunological Sciences Study Section, Wellcome Trust, and Medical Research Council. He received a Career Development Award from the NIAID and

an NIH MERIT Award. He belongs to numerous professional societies, including the American Society for Clinical Investigation, American Association of Immunologists, and American Academy of Allergy and Clinical Immunology.

Michele Barry, MD

Michele Barry was born in New York City on June 13, 1952. She studied for three years at Bryn Mawr College, and then for three years at Albert Einstein College of Medicine, where she received her MD degree. She spent one year in the laboratory of Louis Weinstein at Peter Bent Brigham Hospital, then completed her internal medicine residency and chief residency at Yale–New Haven Hospital (YNHH). She followed this with a fellowship in rheumatology at YNHH and obtained a tropical medicine diploma from Walter Reed Army Medical Center.

Barry became interested in studying refugee health and working with the underserved populations in New Haven. She started the first mobile van project for the homeless, for which she was awarded the Elm-Ivy Award by the mayor of New Haven. She also started the first refugee health clinic at YNHH for “boat people” from Southeast Asia, for which she was granted humanitarian awards from both Catholic Charities and the Global Health Educational Consortium.

Barry’s academic and scholarly writing has tackled the ethical issues around the practice of Western research overseas, travel and tropical diseases, the role of the tobacco industry overseas, and pharmaceutical access in low-resource countries. She has worked extensively overseas, in Ecuador, South Africa, and Zimbabwe, with her spouse, Mark Cullen, and their two children.

Barry was elected as president of the American Society of Tropical Medicine and Hygiene (ASTMH) after she spearheaded the development of tropical medicine diploma courses and certifications for the United States. She was elected to the Institute of Medicine of the National Academy of Sciences, for which she chaired the first global health interest group committee. The ASTMH awarded Barry the Ben Kean Medal (which is awarded only once every three years) for her dedication to clinical tropical medicine.

Barry is currently the inaugural senior associate dean for global health and

director of the Center for Innovation in Global Health at Stanford University. She sits on the advisory boards of the NIH Fogarty Center, the Foundation for Advancement of International Medical Education and Research, and the Consortium of Universities for Global Health.

Jeffrey R. Bender, MD

Jeff Bender was born in Hartford, CT, in 1953. He received his BS degree from Brandeis University in 1975 and an MD from the University of California, San Francisco, in 1979. He completed an internal medicine residency and chief residency at Yale in 1983, after which he moved to Stanford for his clinical cardiology fellowship and postdoctoral immunology research training in Ed Engleman's T cell regulation laboratory. This is where he began studying interactions between human lymphoid and endothelial cells (ECs), initially in the context of allograft rejection. It was then that he began working with Ruggero Pardi, a postdoc from Milan, Italy, who would become a lifelong collaborator. In 1988, his bicoastal journey brought him back to Yale, where he joined the Department of Internal Medicine (cardiology) faculty.

At that time, the field of cardiovascular inflammation and immunity was in its infancy. Bender's laboratory evolved a focus on leukocyte $\beta 2$ integrins, initially in their affinity modulation (inside-out signaling), followed by downstream consequences of engagement (outside-in signaling). His laboratory discovered that, upon engagement of $\beta 2$ integrin and leukocyte (T cell and monocyte) adhesion to inflamed, activated endothelium or to antigen-presenting cells, gene expression profiles are dynamically altered via a kinase cascade that modulates the RNA-binding and -stabilizing protein HuR. That is, a wide spectrum of typically labile mRNAs are stabilized by this adhesion-dependent pathway. Upon tissue-specific targeting of the *HuR* gene, his laboratory described the importance of this posttranscriptional switch in myeloid cells (monocyte/macrophages) in neovascular, arteriogenic responses to tissue ischemia.

A second major area of Bender's research has been the effects of ovarian steroid hormone on the endothelium, initially studied in the context of vascular inflammation. Amid swirling controversies regarding the clinical benefit (or detriment) of hormone replacement therapy in postmenopausal women, his laboratory has addressed the biologic effects of estrogen on ECs. They discovered how a splice isoform of the classical estrogen

receptor is targeted to the plasma membrane and can even conform to an integral transmembrane protein. Upon engagement by ligand, this receptor is capable of rapidly activating a sequential kinase cascade, resulting in strongly enhanced production of the atheroprotective molecule nitric oxide. This work was part of a very early wave of international scientific investigation into rapid responses to steroid hormones, which is now a well-established scientific community.

During these years of biomedical research, Bender maintained a strong clinical presence in the Cardiology Section, including as an attending physician at the Yale Cardiac Catheterization Laboratory for 15 years. His dedication to education and training includes the directorship of Yale's first NIH postdoctoral training grant in vascular research. This program is directed to physician-scientists training in broad basic and translational aspects of vascular biology and medicine.

Bender has been a leader in cardiovascular medicine and at Yale, and has been the associate chief for 10 years. He holds the Yale endowed chair of Robert I. Levy Professor of Preventive Cardiology. He is a member of the American Society for Clinical Investigation and the Association of American Physicians and is currently president of the Association of University Cardiologists. He has been a member of the Interurban Clinical Club since 1998 (and was its president in 2005).

Nancy Berliner, MD

Nancy Berliner was born in Washington, DC, on March 17, 1954. She graduated from Yale University with a BA in combined literature in 1975 and received her MD from Yale Medical School in 1979. She was a resident in internal medicine and a fellow in hematology at Brigham and Women's Hospital from 1979 to 1985. She did her postdoctoral research with Philip Leder, during which she studied genes that cooperated with the c-Myc oncogene in the pathogenesis of malignancy and also performed studies using immunoglobulin and T cell receptor gene rearrangements as markers of clonality of lymphoproliferative disease. In 1985 to 1986 Berliner served as the first female medical chief resident at Brigham.

In 1986, following her chief residency, Berliner was hired by Bernard Forget as assistant professor of medicine in the Hematology Division of Yale Medical School. She was supported by a K08 award from the NIDDK, for

which her mentor was Edward Benz, who has continued as a valued mentor throughout her career. She rose through the ranks at Yale, and became professor of medicine and genetics in 2000. In 2007 she was recruited to Brigham as chief of the Division of Hematology.

Berliner's research has focused on the regulation of neutrophil-specific gene expression and its disruption in leukemia and myelodysplasia. She cloned the genes encoding for the neutrophil secondary granule proteins and demonstrated that they are coordinately regulated at the transcriptional level in a stage-specific manner, and that this is uniformly disrupted in leukemic cells. She went on to characterize the transcriptional regulators of these genes, demonstrating that the transcriptional regulators of late neutrophil-specific gene regulation are closely related to those that regulate lineage commitment and early maturation of the myeloid lineage.

In other studies Berliner has investigated the pathophysiology of anemia in the elderly. She has characterized the role of inflammatory mediators in the development of anemia in a healthy aging population and has linked these pathways to the anemia of HIV as a model of premature aging. She is currently involved in large cohort studies correlating hematologic outcomes with studies of the impact of anti-inflammatory agents on cardiovascular outcomes.

Berliner also has broad-based interests in clinical hematology and a major commitment to teaching and mentoring. As chief of the Hematology Division at Brigham, she has expanded the research faculty, recruiting a cadre of talented young scientists at the forefront of research in the biology of platelets, red cells, neutrophils, myelodysplastic syndromes, and leukemia. In addition, she has revamped the hematology portion of the Dana-Farber Cancer Institute/Partners CancerCare hematology-oncology fellowship and tripled the number of trainees opting for extra clinical training in clinical hematology. She is co-director of the hematology course for the Harvard-MIT Program in Health Sciences and Technology. She continues to have an active clinical practice in hematology and attends the hematology service at Brigham. Berliner has expanded the clinical program at Brigham through the recruitment of new clinical faculty. Under her leadership, the division has also taken over the responsibility for outpatient anticoagulation management at Brigham and DFCI and has created a hemostasis and thrombosis stewardship program for the appropriate inpatient management of novel intravenous anticoagulants and factor concentrates.

Berliner was the recipient of a scholar award from the Leukemia Society of America in 1992 and received the LSA Stohlman Prize in 1997. She is a fellow of the American Association for the Advancement of Science and the American College of Physicians. She was elected to the American Society for Clinical Investigation in 1994 and the Association of American Physicians in 2004. She has had a longstanding involvement with the American Society of Hematology and was president of that society in 2009. She was elected to the Institute of Medicine in 2010.

Joseph R. Bertino, MD

Joseph R. Bertino was born in Port Chester, NY, on August 16, 1930. In 1950 he graduated from Cornell University, and in 1954 he received his MD from Downstate Medical Center, State University of New York. He completed his residency in internal medicine at the University of Pennsylvania Graduate Hospital and the Philadelphia VA hospital in 1956. After spending two years doing research at the Army Chemical Center at Edgewood, he became a postdoctoral fellow at the NIH with Clement Finch, an expert in hematopoiesis, and Frank Huennekens, who was at the forefront in elucidating the biochemistry of folate enzymes. In 1961 Bertino was recruited by Arnold Welch to the pharmacology department with a joint appointment in medicine at Yale University School of Medicine. The Yale pharmacology department was recognized as the top pharmacology program in the country. In 1966 Bertino succeeded Paul Calabresi as head of medical oncology at Yale. From 1973 to 1975 he served as the first head of the Yale Cancer Center, under Lewis Thomas, dean of the School of Medicine. In 1975 he stepped down as a condition for being named an American Cancer Society Research Professor. During his time at Yale, his research was supported by ACS and NCI/NIH grants, and he was the primary investigator on several program project grants. In 1987 he was recruited by Memorial Sloan Kettering Cancer Center to become head of the Molecular Therapeutics and Clinical Investigation Program. At MSKCC Bertino built a strong program in cancer pharmacology and clinical investigation and served as attending physician in medicine on the lymphoma service and co-chair of the joint Cornell-MSKCC graduate program in pharmacology. In 2002 he was recruited to join the Cancer Institute of New Jersey(CINJ) at the Robert Wood Johnson Medical School/University of Medicine and Dentistry (now called Rutgers Cancer Institute of New Jersey) as university professor of medicine and pharmacology, associate director, and chief scientific officer. He was the interim director of the Stem Cell Institute of New Jersey and served as interim director of CINJ from 2007 to 2008.

Although always interested in science, in medical school Bertino developed a keen interest in hematology (an elective) that was influenced by the late Janet Watson. That led him to join the outstanding hematology training program established by Clem Finch at the University of Washington. This training included spending time in a basic science department, where he learned folate biochemistry from Huennekens.

In 1976, while on a sabbatical at Stanford University, Bertino and colleagues Robert Schimke, Rodney E. Kellems, and Frederick W. Alt made a groundbreaking discovery. They discovered that amplification of the dihydrofolate reductase gene was a mechanism of methotrexate resistance. Bertino's continued research into methotrexate yielded the discovery that defective uptake of methotrexate and low-level amplification of *DHFR* caused resistance to the drug in patients with leukemia and soft-tissue sarcomas. These and other discoveries eventually led to new analogs and treatments for these patients.

Some other highlights of Bertino's research accomplishments include the use of leucovorin rescue following high-dose methotrexate, as well as development of the methodology and elucidation of the pharmacology of this reduced folate in humans. He isolated and characterized carboxypeptidase G1, an enzyme that metabolizes methotrexate, recently approved by the FDA for clinical rescue use following high-dose administration of methotrexate. At Yale he developed one of the first curative regimens for some patients with advanced diffuse large cell lymphoma. While at CINJ he published a paper that showed a novel mechanism of methotrexate resistance: mutations in the 3' UTR of the methotrexate target enzyme dihydrofolate reductase abrogated binding of microRNA-34a, leading to increased expression of DHFR mRNA and protein. His work with fluorouracil included a seminal paper that showed that this drug produced cytotoxicity by different mechanisms that were dependent on the drug administration schedule, findings translated into current clinical regimens that use both pulse and infusional fluorouracil administration.

During his long history of research, Bertino trained over 16 graduate students and 50 postdoctoral fellows, many of whom have gone on to leadership positions in academia.

Bertino has received several awards, including the Experimental Therapeutics Award from the American Society of Pharmacology and Experimental Therapeutics (1969), the Richard Hilda Rosenthal Award from the

American Association of Cancer Research (1978), the Karnofsky Award from the American Society for Clinical Oncology (1992), the American Cancer Society Medal of Honor for Research (1992), the Bob Pinedo Cancer Care Prize from the Medical Knowledge Institute (2007), the Distinguished Service Award for Scientific Achievement from the American Society for Clinical Oncology (2008), and the Joseph H. Burchenal Award for Outstanding Achievements in Clinical Research from the American Association for Cancer Research (2008). He was also named as a fellow of AACR (2012). Bertino served as founding editor of the *Journal of Clinical Oncology* and is on the editorial boards of several other journals.

James Lorenzen Boyer, MD

James L. Boyer was born in New York City on August 28, 1936. He received his AB in 1958 from Haverford College and his MD in 1962 from the Johns Hopkins University School of Medicine. After spending two years (1962–1964) on the medical house staff at the New York Hospital–Cornell Medical Center, he joined the US Public Health Service and was assigned to the Johns Hopkins International Center for Medical Research and Training in Calcutta (1964–1966). While there he developed an interest in hepatology and performed definitive studies on the pathophysiology of idiopathic portal hypertension. In 1966 he was a senior assistant resident in medicine at Yale and then studied hepatology under the late Gerald Klatskin, supported by an NIH postdoctoral training fellowship. He published with Klatskin a classic description of the role of sub-acute hepatic necrosis in determining the prognosis in viral hepatitis.

Boyer's laboratory pioneered research in the basic physiological mechanisms of bile secretion and cholestasis. He was stimulated initially by observing an isolated perfused rat liver secreting bile and discovering that almost nothing was known about the mechanisms involved. Boyer's work would later transform the field, when his studies determined that the hepatocyte, a highly polarized cell, resembled a classic epithelial cell with respect to transport functions and that absorptive and secretory mechanisms might resemble those of other epithelial cells. The development of techniques to purify isolated canalicular membranes enabled transport studies to be performed in membrane vesicles from the apical secretory domain. His most important technical advance, however, was the development of the hepatocyte couplet model. Hepatocyte couplets represent the primary bile secretory unit and can be maintained in short-term primary culture.

This allowed electrophysiological approaches to define driving forces for canalicular secretion for the first time and facilitated morphological studies of secretion in the liver cell. His lab subsequently developed the isolated bile duct unit, which allowed insights into mechanisms of water and electrolyte transport in bile duct epithelia. Based on this body of work, Boyer was awarded the Adolf-Windaus Prize in 1988 for outstanding scientific achievements in the field of bile acid research and the Distinguished Achievement Award from the American Gastroenterology Association in 1989. In the 1990s his lab was one of the first to examine the adaptive response of bile transporters at the molecular level in cholestatic liver injury. At the Mount Desert Island Biological Laboratory, Boyer studied marine skates with a colleague, the late Ned Ballatori. Together they discovered the organic solute transporter ab, which turned out to be the basolateral ileal bile acid transporter, the missing link in the enterohepatic circulation of bile acids. His research has been continuously supported by NIH grants for nearly 40 years. He is the recipient of a second MERIT Award from the NIH.

In 1972, after three years on the Yale faculty, Boyer went to the University of Chicago, where he developed the university's first liver study unit. In 1978 he returned to Yale as professor of medicine and director of the liver study unit. In 1983 the gastrointestinal and liver groups were combined, and Boyer became the first chief of the Division of Digestive Diseases. For 25 years, beginning in 1984, he directed the NIH-supported Liver Center, a multidepartmental and multidisciplinary center devoted to studies of liver structure and function.

Boyer was president of the American Association for the Study of Liver Disease in 1979–1980, the year in which the society's journal *Hepatology* was founded. In 1998 he received the society's Distinguished Achievement Award. In 1988–1990 he served as president of the International Association for the Study of Liver. He was also a founding board member of the American Liver Foundation and chaired its board of trustees from 2004 to 2008. He was a member of the NIDDK National Advisory Council (1985–1989) and is a member of the American Society for Clinical Investigation, the Association of American Physicians, the American Gastroenterology Association, and the American Clinical and Climatological Association.

Since 1971 he has been an investigator at the MDI Biological Laboratory, where he pursued a special interest in the use of marine organisms as alternative models for studies of bile-secretory physiology. There he also served

as director of the National Institute for Environmental Health Sciences Center for Membrane Toxicity Studies from 1992 to 2010 and was chair of the laboratory's board of trustees in 1995–2003 and 2001–2013. He has been a member of the board of managers of Haverford College since 2009.

Arthur E. Broadus, MD, PhD

Arthur E. Broadus was born in Knoxville, TN, on March 28, 1941. He received an AB degree from Washington and Lee University in 1964, where his interest in science was awakened by a legendary professor of organic chemistry, James K. Shillington. Broadus entered Vanderbilt Medical School in 1964, where he worked with three of the class acts in American science, Joel Hardman (later chairman of pharmacology), Grant W. Liddle (the most notable clinical investigator in endocrinology of his generation and member of the National Academy of Sciences), and Earl W. Sutherland (solo winner of the Nobel Prize in Physiology or Medicine in 1971). Broadus graduated as valedictorian from Vanderbilt in 1971 with combined MD-PhD degrees, but more importantly, armed with the ideals and instincts learned at the feet of these remarkable men.

Broadus did an internship and residency in internal medicine at Massachusetts General Hospital, followed by a fellowship in endocrinology at the NIH. He joined the Endocrine Section at Yale in 1976, recruited by Howard Rasmussen with the mandate to develop a program in clinical mineral metabolism. Broadus was much influenced in approach by the legendary work of Fuller Albright, and he studied a variety of mineral metabolism disorders using a similar approach to that of Albright, supported by a laboratory capable of measuring parathyroid hormone (PTH), the vitamin D metabolites, and nephrogenous cyclic AMP (NcAMP). Broadus had developed NcAMP as an *in vivo* bioassay of the effects of circulating PTH as a graduate student and fellow. There followed in the late 1970s and early 1980s a series of studies targeted at pathophysiologic mechanisms in a variety of hypercalcemic and hypercalciuric syndromes.

One of these studies involved patients with malignancy-associated hypercalcemia (MAHC), the underlying mechanism of which was the subject of considerable controversy at the time. The key finding was that three-quarters of an unselected population of patients with MAHC displayed increased NcAMP excretion together with suppressed PTH and $1,25\text{-(OH)}_2\text{D}$. These findings led to the proposal that such patients had a humoral

form of MAHC that was in certain ways “PTH-like” but in others ways “PTH-unlike”. This syndrome was referred to as humoral hypercalcemia of malignancy (HHM). It was hypothesized that a circulating factor that displayed such actions *in vivo* should display the same features *in vitro*, and Broadus used a PTH-sensitive renal membrane adenylate cyclase assay to show that this was the case. In this assay, extracts from HHM-associated tumors contained potent activity that was inhibited by competition with synthetic PTH receptor binding analogs but was not inhibited with anti-PTH antisera. This assay (and a great deal of elbow grease) led to the isolation of an aminoterminal fragment that had homology to human PTH proximally but diverged distally in sequence. This sequence was used to fashion probes that allowed the isolation of a cDNA and subsequently the gene. Several other groups using similar strategies simultaneously isolated peptide or cDNA sequences, and all such sequences were identical. By consensus this product was referred to as PTH-related protein (PTHrP).

While the identification of PTHrP answered a longstanding question as to the nature of the factor responsible for most instances of HHM, from a biological perspective this work corresponded to the discovery of a novel gene and gene product in a bad neighborhood. The next question of interest was the nature of the normal biological function(s) of PTHrP. This question was pursued principally via modern gene-manipulation techniques in mice, which allow one to overproduce, delete, or modulate a gene almost at will and in almost any location. Overall, these studies have been very fruitful, for PTHrP turns out to have many regulatory functions. For example, during development it regulates processes as diverse as the formation and growth of long bones, the eruption of teeth, and the formation of the mammary epithelium. In the adult, PTHrP regulates the tone of smooth muscle structures such as the stomach and uterus, the provision of calcium to milk during lactation, the preservation of intact articular chondrocytes in the joints, and the sculpting of long bone surfaces associated with modeling bone size and shape as well as tendon and ligament attachment.

Broadus rose through the ranks at Yale to become section chief of the Endocrine Division for 20 years and vice chair for research in the department for ten years. He was appointed Ensign Professor of Medicine at Yale in 1987. He was a member of a number of societies including the AFCR, the American Society for Clinical Investigation, the Association of American Physicians, and the Endocrine Society and served on the boards of the principal bone journals as well as the American Journal of Physiology and the Journal of Clinical Investigation. Broadus was a Guggenheim Fellow in

1982 and received the Frederic C. Bartter Award of the American Society for Bone and Mineral Research in 1989, an NIH MERIT Award in 1990, and the Distinguished Alumni Award from Washington and Lee University in 2014.

Broadus spent his entire career at Yale and considered being on the Yale faculty a privilege. An even greater privilege was to have mentored the development of outstanding young physician scientists such as Andy Stewart, Karl Insogna, and John Wysolmerski.

Richard Bucala, MD, PhD

Richard Bucala was born in 1957, grew up in greater Hartford, CT, and matriculated at Yale College, where he received a combined BS/MS degree summa cum laude. He entered the Cornell/Rockefeller MD-PhD program in 1979 and performed dissertation work in biochemistry under Anthony Cerami in the area of posttranslational modification. After a visiting fellowship in molecular genetics at the Institut Pasteur laboratory of Maxime Schwartz in Paris, he completed internship and residency training in internal medicine at Brigham and Women's Hospital and Harvard Medical School. In 1988 he was awarded a Brookdale National Fellowship and returned to Rockefeller for a postdoctoral fellowship together with subspecialty training in rheumatology under Charles Christian at the Hospital for Special Surgery. During his postdoctoral research he observed that vascular glycation products quenched the recently discovered vasodilator nitric oxide, and he developed the first immunoassay for measuring glycation damage in vivo. He was appointed assistant professor at Rockefeller in 1990 and subsequently was recruited to the newly established Picower Institute, where he became scientific director in 1999. His investigations during this period encompassed the cloning of the cytokine macrophage migration inhibitory factor (MIF), the discovery of the circulating fibrocyte, and the cloning of a novel phosphofructokinase gene responsible for the Warburg effect. Bucala joined Yale as professor of medicine in 2002 and was appointed to its School of Public Health in 2006.

In selecting medical research for a career, Bucala drew inspiration from his early reading of the biography of Louis Pasteur, and specifically from the fact that Pasteur's practical investigations in such areas as rabies vaccination, germ theory, and energy metabolism led directly to clinical or societal benefit.

Bucala studies the regulation of the immune system, with a focus on the mechanisms by which protective responses can lead to immunopathology and disease. His research has led to novel therapies in clinical evaluation to correct imbalances in immunologic, metabolic, and repair responses. The laboratory's main emphasis has been in the area of MIF family cytokines, their genetics, and their therapeutic targeting. The Bucala group discovered that MIF regulates glucocorticoid immunosuppression, which made possible the development of novel approaches to immunotherapy. The group also identified the two-component MIF receptor and discovered functional polymorphisms in the gene for MIF, which show global population stratification. Depending on the nature of the immune, infectious, or invasive provocation, variant *MIF* alleles either protect from disease or contribute to pathology in conditions such as autoimmunity, sepsis, malaria, autism, and tumor progression. The laboratory has developed facile biochips to determine *MIF* polymorphisms in resource-limited settings, and these have application for predicting susceptibility to malaria and tuberculosis. The Bucala group has enjoyed longstanding collaborations with the Macha Malaria Research Institute and Mission Hospital, the University of Zambia, and the KwaZulu-Natal Research Institute for Tuberculosis and HIV in South Africa.

The Bucala group has led efforts to develop MIF-based therapies tailored to an individual's genetic makeup. An anti-MIF antibody from the laboratory has been humanized for clinical application in autoimmunity and cancer, and an anti-CD74 antibody targeting the MIF receptor is in phase II studies for leukemias/lymphomas. Close collaborative work in structure-based drug design has further led to orally active, small-molecule MIF antagonists that are in advanced preclinical testing. Small-molecule MIF agonists also have been developed for application as immune adjuvants and in ischemic tissue protection. The function of the MIF-like genes expressed by the parasites responsible for malaria, leishmaniasis, and hookworm infection additionally have been investigated and found to suppress host immunity by reducing T cell memory.

Bucala is also credited with the discovery of the fibrocyte, which is a circulating connective tissue cell that contributes to the pathogenesis of different systemic and organ-specific fibrosing disorders. Fibrocytes are prognostic biomarkers for interstitial lung disease, and a fibrocyte-directed therapy is currently in phase 2 clinical trials.

Bucala attends at Yale–New Haven Hospital on the rheumatology consult

service and in internal medicine on Yale's physician-scientist service. He teaches in the School of Medicine and School of Public Health and in Yale College on the topics of inflammation, autoimmunity, immunotherapy, and malaria. His sabbaticals have included public health and human genetic projects in Africa. Under the auspices of the International League Against Rheumatism, he spearheaded the development of the first rheumatology training program in Zambia and the founding of the Rheumatologic Association of Zambia, and he serves as a medical advisor to the University Teaching Hospital in Lusaka.

Bucala is an inventor on over 35 issued patents, with licensed technologies that include a diagnostic ELISA for protein aging, the Warburg enzyme, anti-MIF and anti-MIF receptor antibodies, genetic tests for MIF, and small-molecule cytokine modulators. His discoveries have contributed to the founding of biotechnology companies, and he has served on several scientific advisory boards for industry, academia, and private foundations.

Bucala was elected to the American Society for Clinical Investigation and the Association of American Physicians. He has been a permanent member of two NIH study sections and served on several editorial boards, including co-editorship of *Arthritis & Rheumatology*.

Lloyd Cantley, MD

Lloyd Cantley was born in Charleston, WV, in 1956 and attended West Virginia Wesleyan College, where he graduated summa cum laude with degrees in biology and chemistry in 1977. He then attended West Virginia University Medical School, where he was inducted into the Alpha Omega Alpha honor society. Cantley performed his internal medicine internship and residency at the University of North Carolina, Chapel Hill, followed by a clinical nephrology fellowship at Beth Israel Deaconess Medical Center and Brigham and Women's Hospital in Boston. During the research component of his fellowship with Franklin Epstein at the Beth Israel, Lloyd received a physician-scientist award from the NIH. He spent the next two years at Harvard College, studying chloride transporters in the laboratory of Guido Guidotti, followed by two years at Tufts University Medical School in the laboratory of his brother, Lewis Cantley, studying the mechanisms of ouabain resistance by the murine Na,K-ATPase.

This excellent trio of mentors inspired in Cantley an understanding of the

importance of both patient care in helping to focus research questions and in properly designing the necessary experiments to understand disease pathogenesis. During his time at Lewis Cantley's laboratory, Lloyd became focused on the rapidly expanding field of signal transduction. In 1990 he began his own laboratory at Beth Israel, where he began his studies of hepatocyte growth factor signaling and how the signaling induced epithelial tubulogenesis. These studies led to the identification by his laboratory that lipid products of PI3K are direct inducers of cell migration via activation of atypical PKC; his laboratory also identified the role of phospholipase C as a regulator of PI3K activity. Lloyd remained on the faculty at Harvard until 2000, when he moved his laboratory to Yale University.

At Yale Cantley was promoted to professor with tenure in both internal medicine and cellular and molecular physiology in 2007 and was named the C. N. H. Long Professor of Medicine in 2008. For his work in defining pathways of kidney injury and repair, Cantley has been inducted into the American Society for Clinical Investigation, the Interurban Clinical Club, and the Association of American Physicians. His laboratory was the first to identify an in situ switch from pro-inflammatory macrophage activation to alternative macrophage activation as regulators of kidney injury and then repair, respectively, and has identified tubule-secreted GM-CSF as a novel inducer of that switch. Cantley has served as an associate editor of the *Journal of the American Society of Nephrology* and is the chair of the ASN 2015 program committee.

Lawrence S. Cohen, MD

Lawrence Cohen was born in New York City on March 27, 1933. He received the AB degree from Harvard College in 1954 and the MD from the New York University School of Medicine four years later. An MA degree (with honors) was awarded to Cohen by Yale University in 1970. From 1958 to 1960 he was an intern and then assistant resident in medicine at the Yale–New Haven Medical Center. He spent the next two years (1960–1962) in the Epidemiology Intelligence Service of the US Public Health Service as a research fellow in infectious diseases stationed at the Johns Hopkins Hospital in Baltimore. It was there that his interest in cardiovascular physiology and coronary circulation was born. After this he returned to New Haven (1964–1965) as senior assistant resident in medicine at Yale under Paul Beeson. He then moved to the National Heart Institute, where he spent three years (1965–1968) as a senior investigator and head of the

clinical service, cardiology branch, under Eugene Braunwald. In 1968 he joined the faculty of the University of Texas Southwestern Medical School as chief of clinical cardiology. Cohen returned to Yale in 1970 as a professor of medicine and chief of the Division of Cardiology in the Department of Medicine. In 1981 he became the Ebenezer K. Hunt Professor of Medicine. From 1991 to 1992 he was acting deputy dean at Yale. In 1992, while continuing to teach, see patients, and remain active in cardiologic clinical trials, Cohen was appointed deputy dean at Yale University School of Medicine; from 1995 to 2007 he served as special advisor to the dean. In both of these roles, one of his responsibilities was that of research integrity officer for the school.

In the early 1960s the study of hemodynamic and natural history of patients with valvular heart disease and primary myocardial disease was at its peak. His interest in this approach led Cohen to a series of investigations in the cardiac catheterization laboratory, where he studied coronary blood flow utilizing Krypton 85. During his time working under Braunwald at the NIH, Cohen's research focused on measurements of coronary blood flow in normal and in cardiac patients under a variety of pharmacologic stimuli. There, his clinical interest burgeoned and he focused his studies on cardiovascular physiology. While working with Jere Mitchell at Southwestern, Cohen became interested in assisted circulation and performed studies on patients using external cardiac assist devices.

Cohen served as program chairman for the annual scientific sessions of the American Heart Association from 1977 to 1980. From 1984 to 1986 he was president of the Connecticut Heart Association. He was also college governor for Connecticut and a member of the board of trustees of the American College of Cardiology. From 1971 to 1981 he was a member of the subspecialty board of cardiovascular diseases. He has been counselor, secretary-treasurer (1987–1989), and president (1991) of the Association of University Cardiologists. From 1984 to 1996 and 1987 to 1989, he chaired the clinical trials review committee of the National Heart, Lung and Blood Institute. He is on the editorial board of *Circulation*, the *American Journal of Cardiology*, the *American Heart Journal*, the *Journal of the American College of Cardiology*, and the *American Journal of Geriatric Cardiology*. Cohen is also a member of the American Federation for Clinical Research, the American College of Physicians, and the Southern Society for Clinical Investigation. In 1974 he received the Francis Gilman Blake Award for Outstanding Teaching of the Medical Sciences and in 1989 was Recipient of The Lawrence S. Cohen Teaching and Meeting Facility from the Con-

necticut Heart Association in Wallingford, CT. He was an honorary consultant at Brompton Hospital in London from January to September of 1985.

Cohen has chaired a number of endpoint committees for the NIH and for industry clinical trials on thrombolytic and lipid-lowering agents. He has lectured internationally since 1992 in Argentina, Kenya, the UK, Russia, China, Pakistan, and Korea. In 2007 he became professor emeritus at Yale and continues to teach, advise, and remain active in the clinical trial arena.

Thomas P. Duffy, MD

Thomas Duffy was born in New York City on March 17, 1937. He received the AB degree from St. Peter's College (Jersey City, NJ) in 1958 and the MD degree from Johns Hopkins University School of Medicine four years later. From 1962 to 1965 he served as medical intern and assistant resident in medicine at the Johns Hopkins Hospital. The following year (1965–1966) he was a postdoctoral fellow at Johns Hopkins University School of Hygiene and Public Health. Duffy then served for two years (1966–1968) in the Medical Corps of the US Army with the rank of captain, stationed at the Walter Reed Hospital in Washington, DC. Duffy then served as chief resident in medicine under A. McGehee Harvey at the Johns Hopkins Hospital (1970–1971). From 1971 to 1976 he was assistant professor of medicine at Johns Hopkins, working in the hematology division under C. Lockard Conley, and in 1975–1976 he also served as associate director of the Office of Continuing Education.

In 1976 he moved to the Yale University School of Medicine, where he served as associate professor of medicine (1976–1981), promoted to full professor of medicine in 1981. Since 1976 he has also been an attending physician at the Yale–New Haven Hospital. In 1988 he became chief of the Klatskin Firm in the Yale University Department of Medicine. From 1982 to 1990 he was chairman of the Clinical Education Curriculum Committee in the Yale Department of Medicine. During his tenure at Yale, he established a national reputation as a diagnostician in internal medicine and hematology. Duffy is now professor emeritus of internal medicine at the Yale School of Medicine.

Duffy's contributions originated in his role as a clinician and medical educator. While working under C. Lockard Conley in the hematology division at John Hopkins, he performed studies on heparin-induced throm-

bocytopenia, adriamycin-induced cardiotoxicity, hepatic toxemia, and aluminum-induced anemia, all of which had their origins in the interface between the patient population and the physician team caring for them. This same resource constituted the subject material for the Clinical Reasoning series in the *New England Journal of Medicine*. This forum allowed Duffy to present to a large audience the principles and practices that he was exposed to during his years on the medical service at Johns Hopkins under the leadership of A. McGehee Harvey.

Duffy's allied involvement has been in the field of medical ethics, and he was one of the earliest physicians in the field of bioethics. He was a founding member of the Yale–New Haven Hospital Ethics Committee over 20 years ago. This committee framed the initial guidelines for the care of the terminally ill, and these guidelines are now in use in hospitals throughout the country. He has been an ethicist scholar of the Yale Bioethics Consortium and continues to serve on the board of the Yale Bioethics Center. During this same period he has been heavily engaged in teaching clinical ethics to house staff and students. He is a board member of the Fellowship at Auschwitz for the Study of Professional Ethics (FASPE), AmeriCares Health in Harmony, and the board of the Cuniff-Dixon Foundation, which recognizes national leaders in oncology care.

Duffy was the commencement speaker at Johns Hopkins in 1977 and at Yale in 1979 and 1990. He was awarded Yale's Francis Gilman Blake Award for outstanding teacher of medical sciences in 1980 and its Bohmfalk Teaching Award in 1992. He has published over 150 articles and essays. Duffy has shared editing and authorship of the books *Medical Complications of Pregnancy* and *Making Sense: Beauty, Creativity, and Healing*.

Over the last decade Duffy has served as director of the Program for Humanities in Medicine at Yale School of Medicine. His tenure has seen the establishment of the Yale Medical Symphony Orchestra and numerous other options for students to keep alive their passion for the humanities.

Philip Felig, MD

Philip Felig was born in New York City on December 18, 1936. He received the AB degree from Princeton University in 1957 and the MD from Yale University School of Medicine four years later. From 1961 to 1963 he was intern and assistant resident in medicine at the Yale–New Haven Hospi-

tal. For the next two years he was a research investigator with the rank of captain in the US Air Force, stationed at the Aerospace Medical Research Laboratories at Wright-Patterson Air Force Base. He returned to Yale from 1965 to 1967 as assistant resident and chief resident in medicine. For the following two years, he was a research fellow at the Elliot P. Joslin Research Laboratory in Boston under George F. Cahill Jr.

In 1969 he returned to Yale as an assistant professor of medicine; he was promoted to associate professor in 1972 and to full professor in 1975. Felig was program director of the General Clinical Research Center at Yale from 1971 to 1980, during which time he also held the C. N. H. Long Professorship of Medicine. From 1975 to 1980 he was chief of the Section of Endocrinology at Yale as well as vice chairman of the Department of Medicine. From 1984 to 1988 he was clinical professor of medicine at Yale and, in 1988, became clinical professor of medicine at New York Medical College. For two months in 1980 he was Samuel Bard Professor, chairman of the Department of Medicine at Columbia University College of Physicians and Surgeons, and director of medical service at Presbyterian Hospital in New York City. In 1984 Felig became president of the Sandoz Research Institute in East Hanover, New Jersey. In 1987 he entered private practice in endocrinology in New York City. Since 1987 he has been an attending physician at the Lenox Hill Hospital and principal consultant of the Rachmiel Levine Diabetes Center of the New York Medical College.

Under Cahill's tutelage Felig undertook studies on prolonged starvation, which identified alanine as the key gluconeogenic precursor utilized by the liver and the limitation of substrate outflow as the mechanism for regulating gluconeogenesis in starvation. At Yale he pursued further studies of amino acid metabolism. Work with John Wahren on amino acid metabolism in exercise led to the identification of the glucose-alanine cycle, a key regulatory cycle in gluconeogenesis. He identified a defect in the uptake of branched-chain amino acids by muscle tissue in insulin-dependent diabetics and demonstrated hyperaminoacidemia in obesity. His studies in pregnancy established that the response to starvation is accelerated and that ketones are transferred to amniotic fluid. In other studies he found that the liver was identified as a key site of insulin action and glucose disposal, and he showed that in healthy humans the liver is more sensitive than muscle tissue to small increments in circulating insulin. He also identified hepatic resistance to insulin action as a key aspect of altered carbohydrate metabolism in human obesity. His subsequent studies in diabetics identified the liver as a key site of diminished utilization of orally administered glucose

and showed the important role of the route of glucose uptake. In a series of studies, he investigated the role of glucagon in glucose homeostasis and demonstrated that glucagon has an evanescent rather than persistent effect on hepatic glucose production, that hyperglucagonemia fails to induce diabetes in the absence of insulin deficiency, and that the glucose-lowering effect of somatostatin is not due to inhibition of glucagon secretion but is rather a consequence of decreased glucose absorption. In another series of studies undertaken between 1970 and 1986 on the metabolic response to exercise, Felig demonstrated that (a) glucose is the key fuel utilized during short-term exercise and that fatty acids are the key fuel utilized during prolonged exercise, (b) glucose uptake and insulin sensitivity are augmented during recovery from exercise, (c) during exercise recovery, glycogen is redistributed from previously resting muscle to previously exercising muscle, (d) exercising diabetics have increased hepatic ketogenesis and utilization of muscle ketone, and (e) insulin secretion and liver glucokinase activity are decreased after physical training. At the Sandoz Research Institute he reorganized the Diabetes and Lipid Research Programs, which resulted in the development of a new HMGCoA reductase inhibitor (Sinvastatin) and the discovery of several oral antidiabetic drugs that are now in various stages of development.

Felig has received a number of special honors, including the Commendation Medal from the US Air Force for “distinguished and meritorious service” as a research investigator, the Alverenga Prize from the Swedish Medical Society (1975), the Lilly Award (1976) and Established Investigator Award (1977–1982) from the American Diabetes Association, a Research Career Development Award from NIH (1972–1977), the Mary Jane Kuel Award from the Juvenile Diabetes Foundation (1977), an honorary doctor of medicine degree from the Karolinska Institutet (1978), and the Jonathan May Award from the Connecticut Diabetes Association (1979), among others.

Felig belongs to numerous professional societies, including the American Society for Clinical Investigation, the American Physiological Society, the American Society for Clinical Nutrition, the Endocrine Society, the American Federation for Medical Research, the American Diabetes Association, the American College of Physicians, and the Association of American Physicians. He has served as a consultant and member of advisory committees at the NIH and the Institute of Medicine, among other organizations. He has held editorial positions with many journals, including *Clinical Research*, the *Archives of Internal Medicine*, the *Annals of Internal Medicine*,

Diabetes, the American Journal of Medicine, and the American Journal of Physiology.

Bernard G. Forget, MD

Bernard G. Forget was born in 1939 in Fall River, MA. He attended the University of Montreal and received his BA degree in 1959. In 1963 he received his MDCM from McGill University and was awarded the Holmes Gold Medal. During the following two years he served as intern and resident in internal medicine at Massachusetts General Hospital. From 1965 to 1967 he was a clinical associate in the metabolism branch of the National Cancer Institute, where he worked in the laboratory of Sherman M. Weissman. The following year he served as a resident in pathology at MGH, after which he did a year of postdoctoral research in molecular biology as a special NIH fellow, working in the laboratory of Roger Monier in Marseilles, France. Between 1969 and 1971 he completed a combined pediatric and adult hematology fellowship at Boston Children's Hospital and Peter Bent Brigham Hospital. He was appointed instructor in pediatrics at Harvard Medical School in 1971, then promoted to assistant professor the following year and to associate professor in 1975. During that time he developed his research program in the hematology division of Boston Children's Hospital. In 1976 he was recruited to Yale to be chief of the hematology section and associate professor of medicine and human genetics; he was promoted to full professor in 1978. At Yale he served as associate dean for research affairs from 1987 to 1989 and as director of the Cooperating Graduate Programs from 1989 to 1992, then reassumed the position of chief of the hematology section from 1993 to 2005. He retired and became professor emeritus in 2011.

In 1965 Frederick Sanger published his paper on RNA fingerprinting technology. Forget and Weissman used this technique to study the structure of various low-molecular RNAs, in particular the 5S ribosomal RNA from human (KB tissue culture) cells. They attempted to determine the entire nucleotide sequence of KB cell 5S RNA, which was known to be approximately 120 nucleotides long. Sanger and his colleagues had decided to sequence *E. coli* 5S RNA, and so the race was on. Forget and Weissman published their sequence in *Science* in 1967, a few months after the Sanger group published theirs in *Nature*.

While at the NIH Forget had his first contact with patients suffering from

beta-thalassemia. At Boston Children's Hospital in 1969 he decided to apply the RNA isolation and analytical techniques to the purification and characterization of human globin mRNA, with the long-term goal of studying the molecular basis of beta-thalassemia. Forget succeeded in purifying an RNA species from normal and beta-thalassemic reticulocytes that was of the expected size, but a functional assay was needed. Working with Edward Benz, they quickly demonstrated the functional properties of their mRNA preparations. Similar work was being done at the NIH by Nienhuis and Anderson using blood samples from the same beta-thalassemia patients that Forget had cared for in 1965–1967. Techniques were developed by Forget and David Housman, of MIT, to establish a cDNA-mRNA hybridization assay to accurately measure the relative abundance of alpha and beta mRNAs in RNA preparations. The group was successful in demonstrating quantitative deficiency of beta-globin mRNA in beta-thalassemia and quantitative deficiency of alpha-globin mRNA in alpha-thalassemia. They also used similar assays to demonstrate absence or deletion of beta-globin gene sequences in the syndrome of hereditary persistence of fetal hemoglobin.

In collaboration with Weissman, who had left the NIH to join the Yale faculty in 1967, Forget decided to study the nucleotide sequence of human globin mRNA. This collaboration (which required frequent exchanges of samples between Boston and New Haven) resulted in the elucidation of the complete nucleotide sequence of human beta-globin mRNA.

After Forget moved to Yale in 1976, Weissman and Forget continued to pursue studies of the molecular genetics of the human globin gene system and analysis of the molecular basis of human hemoglobinopathies, in particular beta-thalassemia. One of their major accomplishments was the demonstration that one of the common forms of beta-thalassemia results from a substitution in an intron of the beta-globin gene that causes alternative splicing of the precursor globin mRNA —this was one of the first descriptions of this mechanism as the molecular basis of a human genetic disorder.

Forget's laboratory also carried out detailed mapping, cloning, and characterization of the beta-gene cluster in deletion forms of hereditary persistence of fetal hemoglobin and delta-beta-thalassemia. Subsequently, the emphasis in Forget's laboratory shifted to the molecular analysis of genes encoding erythrocyte membrane skeleton proteins such as spectrin and ankyrin, with a long-term goal to elucidate the molecular basis of heredi-

tary hemolytic anemias due to abnormalities of the red cell membrane, such as hereditary elliptocytosis (HE) and hereditary spherocytosis (HS). The cDNAs and/or genes for alpha spectrin, beta spectrin and ankyrin were cloned and their structures determined. In addition, specific point mutations of these genes were identified in association with different cases of HE and HS. More recently, his laboratory studied the gene expression profile of hematopoietic stem/progenitor cells, with the goal to elucidate transcriptional regulatory circuits during hematopoiesis.

Forget held a Research Career Development Award from the NIH NIA-MD (1972–1976), and his research was continuously supported by various grants from the NIH, including a MERIT Award, until his retirement in 2011. Memberships include the American Federation for Clinical Research, the American Society of Hematology (councilor, 1989–1993), and the American Society of Biological Chemists, and as well as elected memberships in the American Society for Clinical Investigation and the Association of American Physicians. He is a diplomat of the American Board of Internal Medicine and the subspecialty board of hematology. He has served on a number of scientific peer review committees for the NIH, including the NHLBI Research Review Committee B and the NHLBI Board of Scientific Counselors. He has had editorial assignments on several journals, including *Blood*, *Hemoglobin*, and the *New England Journal of Medicine*. He has been a member of numerous other advisory boards, both private and federal. He is the author or co-author of over 280 publications in various scientific and medical journals and textbooks. In 1996 he was awarded the Henry M. Stratton Medal of the American Society of Hematology for distinguished research in hematology. In 2007 he was elected to membership in the American Academy of Arts and Sciences. In 2013 he received the Yale Cancer Center Lifetime Achievement Award.

John Nevins Forrest Jr., MD

John N. Forrest Jr. was born in Palmerton, PA, on July 20, 1938. He received his BS degree from Ursinus College in 1960 and his MD degree from the University of Pennsylvania School of Medicine in 1964. He became interested in the renal concentrating mechanism while a medical student, after attending a lecture by Robert Winters on the discovery of the renal countercurrent multiplication system. He began work in the laboratory of J. Russell Elkinton, and in 1963 Elkinton arranged for Forrest to do research in the laboratory of R. A McCance, in the Department of Experi-

mental Medicine at Cambridge University. Papers titled “Renal Concentrating Ability in the Adrenalectomized Rat” and “Kidney Composition and Renal Concentrating Ability in Young Rabbits” resulted from his studies as a medical student.

Forrest was an intern and assistant resident at the Grace–New Haven Hospital under Paul Beeson (1964–1966). He was attracted to Yale by Frank Epstein’s studies on renal concentrating defects in hypercalcemia and hypokalemia. Members of Beeson’s department, including Epstein, Tom Amatruda, Thomas Ferris, David Seligson, Elisha Atkins, and Gerald Klatskin, had a strong influence on Forrest’s academic development.

From 1967–1969 Forrest was an officer of the Epidemiology Intelligence Service (EIS) of the CDC and surgeon in the U.S. Public Health Service, assigned to Boston teaching hospitals. As an instructor in medicine at Harvard, he organized the first study on the incidence of hepatitis among patients and staff in dialysis units in the United States. Forrest transported equipment to Dacca, East Pakistan, to measure the arterial blood pH in patients with cholera and subsequently published two papers on the use of an oral glucose electrolyte solution for initial fluid replacement in this disease.

In 1969–1970 Forrest was chief resident in medicine (with Lewis Landsberg) at Yale, under Philip Bondy. In 1970 he was a research fellow with Franklin Epstein, and the following year he was appointed assistant professor of medicine by Louis Welt. Forrest carried out landmark studies (published in the *Journal of Clinical Investigation*) on the mechanism of lithium-induced diabetes insipidus, which defined the incidence of this disorder and the cellular basis for the renal effects of lithium. Together with Irwin Singer he described the first use of declomycin in the treatment of the syndrome of inappropriate secretion of ADH (published in the *New England Journal of Medicine*).

In 1970 at the Mount Desert Island Biological Laboratory (MDIBL) in Maine, Forrest developed an interest in the study of ion transport in marine species. In collaboration with Epstein and others, he defined the mechanism of active chloride secretion by the shark rectal gland, a model that he used extensively in the study of chloride transport. Forrest has been an investigator at MDIBL since 1973 and was a trustee and member of its executive committee for many years. His career was influenced by other senior investigators at MDIBL, including John Boylan, Thomas Maren, Roy Forster, and Michael Field. From 1998 until 2009 he was the director of

MDIBL and raised funds from the NIH and the State of Maine to initiate a year-round program that attracted 10 investigative groups, build four new buildings, and renovate the summer labs.

Forrest directed the Renal Consultation Service at Yale and since 1986 has been director of the Office of Student Research and chairman of the thesis committee at the Yale University School of Medicine. He is the former co-chief of the Beeson Firm in the Department of Medicine at Yale.

In his research, Forrest capitalized on the unique elements of the shark rectal gland as a homogeneous, single-cell tubular epithelial model for ion transport. Together with Beyenbach and Gregor, he carried out the first studies on the isolated perfused tubule of the rectal gland and established the sequence of events involved in the signal transduction of cyclic AMP-mediated hormones and natriuretic peptides that activate chloride transport. Forrest used the rectal gland to define the role of stimulatory and inhibitory adenosine receptors in the dual regulation of chloride secretion, providing the first evidence that adenosine receptors modulate ion transport in epithelia. Together with Valentich he developed the first system for primary culture of rectal gland cells that retain full expression of hormone receptors and chloride channels. He worked with Raymond Frizzell to characterize CFTR-type chloride channels, and with medical students and Hugo DeJonge to clone and express multiple receptors in the gland.

Forrest took sabbaticals at the NIH (working with Joe Handler at the Laboratory of Kidney and Electrolyte Metabolism in 1982 and 1989) and at the Medical Research Council in Cambridge, UK (working with Sidney Brenner in the Molecular Genetics Unit in 1996), and was a visiting fellow at Kings College London. Together with Paul Scofield and Stephen Jones he cloned the first gene in the dogfish shark and, later, identified C-type natriuretic peptide as a unique cardiac hormone that increases chloride secretion through CFTR in the rectal gland. In 1992 he and Michael Zasloff discovered squalamine, a unique sterol antibiotic isolated from shark tissues that is effective against bacterial and fungal infections.

Forrest was an established investigator of the American Heart Association and president of the American Heart Association, Connecticut affiliate. He has been elected to the American Society for Clinical Investigation, the Association of American Physicians, the American Clinical and Climatological Association, and the Eastern Salt and Water Club. He is a member of the American Physiological Society, the American Society of Nephrology,

the American Heart Association, and the International Society of Nephrology. He served on two NIH study sections and on the research committee, board of directors, and executive committee of the American Heart Association, Connecticut affiliate, and was co-chairman of the cardio-renal study section of the national American Heart Association. He received an honorary doctor of science degree from Ursinus College in 2001.

Fred Sanford Gorelick, MD

Fred Gorelick was born in Springfield, MO, on February 2, 1948. He studied premed at Drury College from 1966 to 1969 and received his MD from the University of Missouri at Columbia in 1973. This was followed by an internal medicine residency at the University of Missouri (1973–1976) and a gastroenterology fellowship at Yale University (1976–1979). There he joined the laboratory of James D. Jamieson in the Department of Cell Biology, where he studied the mechanisms regulating pancreatic acinar cell function. Working with Jamieson he described the fourth protein kinase, calcium/calmodulin-dependent protein kinase II (CaMKII). In 1979 he joined the faculty of Yale University School of Medicine as an assistant professor and received an NIH Clinical Investigator Award, with Jamieson as the sponsor.

Although Gorelick came to Yale to pursue clinical gastroenterology, his interests in academic medicine were motivated by his father, a pathologist and member of the faculty at the University of Missouri School of Medicine, and by his experiences while a gastroenterology fellow at Yale. Soon after arriving at Yale, he began to interact with Henry Binder, who has continued to serve as a mentor to Gorelick throughout his academic career. His interest in pancreatic physiology was kindled by presentations given by George Palade and Jamieson at Yale during the first and second year of Gorelick's fellowship. Palade and Jamieson had characterized the protein secretory pathway using the pancreatic acinar cell as the model system, and these studies led to Palade being awarded the 1974 Nobel Prize in Physiology or Medicine.

One of the outstanding issues when Gorelick joined Jamieson's laboratory was understanding how hormones transduced their signals to elicit biologic responses, such as secretion, in the pancreatic acinar cell. At that time preliminary data suggested that an increase in intracellular calcium had a role, but the targets of calcium remained unknown. A few years before Gorelick began working in Jamieson's laboratory, both the calcium-acti-

vated protein, calmodulin, and protein kinases were described. Reasoning that a calcium/calmodulin kinase might mediate responses in the acinar cell, Gorelick worked with Jamieson and another fellow, Jon Cohn (now professor of medicine at Duke University) to purify and characterize CaMKII, one of the first protein kinases. Since few laboratories had expertise in performing functional studies involving these enzymes, Gorelick soon joined Paul Greengard's laboratory at The Rockefeller University. Greengard, the 2000 recipient of the Nobel Prize in Physiology or Medicine, is known for his pioneering work on protein phosphorylation. Gorelick's work with Greengard helped to establish CaMKII as a molecule involved in molecular memory. The training Gorelick received in Greengard's laboratory involved the nervous system but was later applied to his studies of the gastrointestinal tract.

During the 1980s most of Gorelick's work focused on kinase enzymology and was limited in its applicability to normal physiology or disease. In 1989 he was approached by Steven Leach (then a Yale resident and now director of the Center for Pancreatic Cancer Research at Memorial Sloan Kettering) to do research related to acute pancreatitis. Together with Leach, Gorelick investigated whether zymogens of digestive enzymes, particularly proteases, could be activated within the acinar cell and initiate acute pancreatitis. Their studies were the first to demonstrate regulated activation of these enzymes and to implicate a low-pH compartment in this response. Gorelick's subsequent work has been dedicated to characterizing the compartments and signaling pathways that mediate this important disease response. His more recent studies may be clinically applicable and include the observation that an extracellular acid load accentuates pancreatitis responses by driving pathologic intracellular calcium signaling, and that lactate, acting through a specific G protein-linked receptor (GPR81) is a potent inhibitor of pancreatitis responses. Focused primarily on issues related to pancreatic cell biology and disease, Gorelick's research has been continuously funded since 1979 and supported by the NIH and the US Department of Veterans Affairs.

While at Yale, Gorelick served as the associate chief of the Digestive Diseases Section during the time when James M. Anderson led the section, and was the fellowship program director from 1995 to 2000. In 2005 he took over leadership of the training program in investigative gastroenterology after 30 years of leadership by Henry Binder. In 1996 he became a professor of internal medicine and cell biology. He has also served as a permanent member and chair of NIH NIDDK study sections. Gorelick has

had a long-standing interest in education and directs courses for first-year Yale medical students and a graduate course for MD-PhD students. His involvement with the MD-PhD students led to his appointment as an associate director of the MD-PhD program in 1998. In 2011 he was appointed its deputy director, and he continues to work closely with Jamieson, its director. Finally, Gorelick continues to collaborate with Greengard and holds an appointment as a visiting scientist at The Rockefeller University.

Gorelick's achievements have been recognized both locally and nationally. A Morton Grossmann Research Award in 1986 (from the American Gastroenterological Association) supported his sabbatical work in Greengard's laboratory. He was elected to the American Society for Clinical Investigation in 1989, the Interurban Clinical Club in 1991, and the Association of American Physicians in 2011. From 1993 to 1997 he served on the American Gastroenterological Association research council, and from 1999 to 2000 he served as president of the American Pancreatic Association. His efforts as an educator at Yale University have been recognized by his receipt of the Alvan R. Feinstein Award, the Howard M. Spiro Faculty Teaching Award, and the Bohmfalk Prize in basic science.

Margaret Kendrick Hostetter, MD

Margaret Kendrick Hostetter was born in Toledo, OH, on May 29, 1948. She graduated from Denison University with a BA in English, then studied English in graduate school at Rice University prior to her acceptance at Baylor College of Medicine, where she graduated first in her class in 1975.

She completed her pediatric residency and fellowship in pediatric infectious diseases at Children's Hospital Boston before moving with her family in 1982 to the University of Minnesota to serve as an instructor in pediatric infectious diseases. Over the next 16 years she became director of the Division of Infectious Diseases, the vice chair for research, and the American Legion Heart Research Professor in Pediatrics. In 1998 she moved to Yale to become director of the Division of Immunology, and in 2002 she became chair of the Department of Pediatrics and Jean McLean Wallace Professor of Pediatrics. She moved to Cincinnati Children's Hospital in 2010, where she was named the Albert B. Sabin Professor of Pediatrics and director of the Division of Infectious Diseases. On July 1, 2014, she became the B. K. Rachford Professor of Pediatrics, chair of the Department of Pediatrics, and director of the Cincinnati Children's Research Foundation.

Hostetter's interest in infectious diseases was piqued when, recovering from pneumococcal pneumonia at four years of age, she was given a picture book entitled *Handbook of the Common Acute Infectious Diseases* (published in 1949) that her mother had used as a general practitioner in Kankakee, Illinois. Prominent physician-scientist role models such as Martha Yow (at Baylor) and Mary Ellen Avery and Fred Rosen (once at Children's Hospital Boston) encouraged her interest in research.

From the laboratory of the protein biochemist Brian F. Tack, she published the first description of the transesterification reaction that mediated covalent binding of C3b via its internal thioester bond (published in *Nature* in 1982). She subsequently defined the mechanisms of C3b-mediated opsonization of *Streptococcus pneumoniae* and *Candida albicans* and was one of the first to identify candidal genes involved in adhesion, filamentous growth, and virulence (*Science*, 1998). Since 1996 she has directed the NIH-funded Pediatric Scientist Development Program, which has trained more than 180 pediatric scientists in the US and Canada. Other current extramural funding comes from the Bill & Melinda Gates Foundation and the Global Alliance to Prevent Prematurity and Stillbirth.

Together with colleagues at the University of Minnesota, her clinical research has focused on the medical evaluation of internationally adopted children, with publications in the *New England Journal of Medicine* and *JAMA*, among others.

Hostetter's honors include the American Academy of Pediatrics Award for Excellence in Research, the Samuel Rosenthal Award for contributions to academic pediatrics, the E. Mead Johnson Award for Research in Pediatrics from the American Pediatric Society/Society for Pediatric Research, and the Maxwell Finland Lecture from the Infectious Diseases Society of America. She has received the Mentor's Award from the Eastern Society for Pediatric Research and the Founders' Award from the Midwest Society of Pediatric Research. She is a past president of the Society for Pediatric Research and is the president-elect of the American Pediatric Society. She is a member of the Society for Pediatric Research, the American Pediatric Society, the American Society for Clinical Investigation, the Association of American Physicians, and the Institute of Medicine of the National Academy of Sciences.

Keith A. Joiner, MD, MPH

Keith Joiner was born in Denver, CO, on March 4, 1948. He received his undergraduate degree from the University of Chicago in 1970 and an MD degree from the University of Colorado in 1974. His internal medicine residency training was at the Royal Victoria hospital of McGill University, Quebec (1974–1976) and at Dartmouth (1976–1977). Infectious diseases fellowship training was done at Tufts–New England Medical Center (1977–1980). Following his fellowship, he spent nine years (1980–1989) working at the National Institutes of Health, where he was senior investigator and chief of the Unit of Microbial Pathogenesis.

In 1989 he moved to Yale University School of Medicine as chief of the Section of Infectious Disease. During nearly 15 years at Yale University School of Medicine, he was the associate chairman of the Department of Medicine; the Waldemar von Zedtwitz Professor of Medicine, Cell Biology and Epidemiology; and professor of cell biology and epidemiology. One of his major accomplishments was to develop and direct the Investigative Medicine Program, an accelerated PhD program for physicians with at least 2 years of residency training.

In 2004 he moved to the University of Arizona to serve as dean of the College of Medicine and vice provost for medical affairs, a position he held for 5 years. In 2009 he was a senior scholar at the Association of Academic Health Centers (Washington, DC), and in 2010 he moved to the Eller College of Management at the University of Arizona. In that position he created the Center for Management Innovations in Health Care, which he currently directs. He is a professor of medicine, economics, and health promotion sciences at the University of Arizona.

His interest in biomedical research was spawned in high school, when he worked in the physiology laboratory of Basil Reeves at the University of Colorado School of Medicine. He continued this work during summers throughout his undergraduate education. His research training was cemented during his infectious diseases fellowship at Tufts, where he worked with John Bartlett, Jeffrey Gelfand, and Keith McAdam. He was encouraged by Sheldon Wolff to move to the NIH; there he joined the Laboratory of Clinical Investigation, directed by Michael Frank, where he expanded his research training. Additional training occurred during two sabbaticals at Yale, one with Ira Mellman, the second with Peter Novick, both in the Department of Cell Biology.

The initial theme of Joiner's research was the interaction of the complement system with bacteria. Beginning with back-to-back papers in the *Journal of Experimental Medicine* in 1982, and continuing throughout the 1980s, he was acknowledged as the premier authority on complement-microbial interactions. In the late 1980s he transitioned his research to the cell biology of intracellular parasitism, focusing initially on *Toxoplasma gondii* and later on *Plasmodium falciparum*. Work resulted in highly cited papers in *Science*, *Cell*, *Nature*, *PNAS*, the *Journal of Cell Biology*, and *Nature Cell Biology*, among others. This work, in aggregate, identified novel membrane transport pathways by which intracellular parasites acquire essential nutrients from the host cells in which they reside.

As Joiner took on more administration roles at Yale, he developed an interest in management, which culminated in the decision to earn an MPH degree (2002–2003), with coursework conducted almost exclusively in the Yale School of Management. The consequence was a shift in research focus, to models on optimizing resource allocation in academic health centers. This in turn led to his decision to seek a deanship and, later, to move to the Eller College of Management, where he created the Center for Management Innovations in Health Care. Joiner now works closely with economists at the University of Arizona and elsewhere, conducting health economics research. Over the last 12 years, he has published extensively on financial management strategies in academic health centers, and his work has gathered substantial national attention. His current work focuses on payment reform in health care.

Honors include election to membership in the American Society for Clinical Investigation, the American Association of Physicians, and the Society of Medical Administrators and fellowship in the American Association for the Advancement of Science and the Infectious Disease Society of America. He served for five years as chairman of the training program directors committee of the Infectious Disease Society of America, and while doing so organized the first series of regional and national meetings of infectious disease program directors to develop uniform criteria for fellowship training.

Joiner was extremely successful in obtaining extramural grant support while at Yale University. In only 15 years in the extramural program (1989–2004), he was above the 95th percentile in distribution of NIH grant funds over the 25-year period of 1980–2004. Among other funding and recognition, he received the Burroughs Wellcome Fund Scholar Award in Molecular Parasitology and the Burroughs Wellcome Fund New Initiatives in

Malaria Research Award.

Fred S. Kantor, MD

Fred S. Kantor was born in Brooklyn, NY, on July 2, 1931. He had a strong interest in electronics and so attended Brooklyn Technical High School, but his attention had shifted to biology by the time he entered Union College. After spending his junior year at St. Andrew's University in Scotland, he graduated with honors from Union College (BS, 1952) and then from the New York University School of Medicine (1956). His experience as a student in the laboratory of Gene Stollerman directed him toward a career in academic medicine. He interned at the Barnes Hospital in St. Louis (1956–1957) and then worked as a research associate in infectious diseases for two years at the NIH (1957–1959). In 1959 he joined the resident staff in medicine at Yale, following which he served as fellow with Paul Beeson. Beeson wished to establish a unit of clinical immunology separate from that in infectious disease and so urged Kantor to spend a year or two getting specialized training for such a venture. In 1961 Kantor worked with Baruj Benacerraf at New York University, and in mid-1962 he returned to Yale as instructor in medicine and the first director of a new section of allergy and clinical immunology. In 1968, as associate professor, he spent nine months of his sabbatical leave at the Walter and Eliza Hall Institute in Melbourne, Australia, and then completed the year in the laboratory of Michael Sela at the Weizmann Institute in Israel. In 1973 he was promoted to professor of medicine and two years later spent a second sabbatical year in the laboratory of zoology (tumor immunology) with N.A. Mitchison at University College London. He then traveled as a visiting professor of medicine to Pahlavi University in Shiraz, Iran, and to the Hebrew University Hadassah Medical School in Jerusalem. Kantor became the Paul B. Beeson Professor of Medicine when the post was established in the early 1980s. Outside of medicine, an important interest of Kantor's has been in piloting small aircraft, which he has done continuously since 1957.

Kantor's research began with study of the immunobiology of streptococcus. This work, carried on at the NIH, culminated in the finding that streptococcal M protein binds to fibrinogen, leading to a macromolecular complex that is deposited in the kidney. He first conducted studies on cell-mediated immunity in Benacerraf's laboratory that formed the basis for a major part of his research interest. Of importance was the early finding that certain guinea pigs were responders, and others nonresponders,

to two unrelated synthetic polyaminoacid antigens, DNP-polylysine and glutamyllysine. This finding heralded the appearance of much work on the immune response gene by others and the discovery of more than 30 different such systems, and it established clearly the genetic basis of the immune response.

In the late 1960s and early 1970s, Kantor's research interest turned to the regulation of delayed hypersensitivity, with particular reference to the shut-off mechanisms involved normally and in disease states. In 1970 he proposed that anergy was an extension of a normal shut-off mechanism and was an active process rather than a deficiency of cell-mediated immunity. Since that time, a variety of models using viral agents and protein antigens have been used to elucidate the mechanism of immunologic unresponsiveness.

During the later 1980s he became interested in autoimmunity and together with collaborators investigated experimental autoimmune myasthenia gravis. It was discovered that there were regulatory cells, particularly suppressor cells, involved in this disease, and they attempted to implicate the immune network first described by Jerne as a means of regulation of this disease both in mice and humans. In the 1990s he called together the diverse groups at Yale that were studying Lyme disease, in an effort to produce a body of information concerning protection against the Lyme spirochete, with a view to developing a vaccine. This proved highly successful.

Kantor was a fellow of the Helen Hay Whitney Foundation (1960–1962) and recipient of a Research Career Development Award (1962–1972). He has served on the editorial boards of the *Annals of Internal Medicine*, the *Journal of Allergy*, and the *Journal of Immunology* as well as on the NIH immunology study section and the NIH Allergy and Clinical Immunology Research Committee. He has served on numerous other advisory committees, both federal and private. He has been chief of the J. P. Peters firm at the Yale–New Haven Hospital since 1988 and holds the Paul B. Beeson Chair at Yale. He is a member of the Association of Immunologists, the American Academy of Allergies, the American Society for Clinical Investigation, and the Association of American Physicians. In 2014 Kantor was honored at a dinner with students, colleagues, and friends, where he presented the Leadership in Biomedicine Lecture at Yale Medical School.

Michael Harris Nathanson, MD, PhD

Michael Harris Nathanson was born in Detroit, MI, on August 9, 1955. He was raised in Oak Park, MI, and graduated from Oak Park High School in 1973. He received a BS degree in mathematical statistics from the University of California, Berkeley, in 1976 and an MS degree in biomedical engineering from the Massachusetts Institute of Technology in 1977. He went on to receive a PhD in biomedical engineering from Case Western Reserve University in 1983, followed by an MD in medicine in 1985. For his doctoral research, he investigated the mechanism of dietary iron absorption under the joint mentorship of Gordon McLaren and Gerald Saidel. In 1990 he received his postdoctoral degree in digestive diseases from Yale University School of Medicine, and then was jointly hired as an instructor in the digestive diseases section and the cell biology department. He has remained at Yale, where he currently is the Gladys Phillips Crofoot Professor of Medicine, professor of cell biology, and chief of the digestive diseases section.

As a medical student at Cleveland's MetroHealth Medical Center, he was mentored by three of the country's most distinguished hepatologists — Bruce Bacon, Art McCullough, and Anthony Tavill — all of whom have served in leadership positions with the American Association for the Study of Liver Disease. Nathanson's decision to specialize in hepatology led him ultimately to Yale University, and to the labs of two physician-researchers, James Boyer and the late Anil Gautam. Gautam was interested in newer forms of light microscopy, while Boyer was developing new cell models for liver function, including isolated hepatocyte couplets and isolated bile duct units. Nathanson combined these two developments to investigate signaling and secretion at the single-cell and subcellular level.

Nathanson traces his interest in science to an antique microscope given to him by his grandfather when he was a child. Even now, his research interests have involved questions that typically use techniques such as confocal, multi-photon, and super-resolution microscopy. He is also the founder and director of Yale's Center for Cell and Molecular Imaging.

Nathanson currently serves as principal investigator on six awards: a program project grant to investigate signaling mechanisms in the nucleus of hepatocytes, an R01 grant to investigate regulation of secretion in hepatocytes, an R03 grant to support a scientific collaboration with an investigator at Universidade Federal de Minas Gerais in Brazil, a digestive diseases

research core center grant to provide support for the Yale Liver Center, a postdoctoral training grant in investigative hepatology, and a grant to investigate mechanisms of carcinogenesis in the liver. He also is co-investigator on a three-year grant to support a separate, ongoing collaboration in Brazil and is also working informally to develop new techniques and applications in endomicroscopy.

Nathanson has served on multiple NIH and VA study sections, three of which he has chaired. He received the FAPESP Fulbright Scholar Award, the Howard M. Spiro Teaching Award, the American Liver Foundation Liver Scholar Award, and an Established Investigator Award from the American Heart Association. He has served on numerous editorial boards and is currently the editor-in-chief of *Hepatology*. Nathanson is a member of the Association of American Physicians, the American Society for Clinical Investigation, and the Interurban Clinical Club. He was secretary-treasurer of the American Federation for Medical Research, for the Eastern Section in 1994–1995 and nationally in 1995–1999. As a member of the American Association for the Study of Liver Diseases, he has served on the basic research committee (1999–2001), the abstract review committee (2001–2004 and 2007–2010), and the nominating committee (2008–2009).

Paul Wesley Noble, MD

Paul W. Noble was born on September 20, 1958 in Orlando Florida. He spent the formative years of early education outside of Detroit, Michigan and then attended public high school in Spring Valley, New York. He attended Haverford College in Haverford, Pennsylvania and majored in biology (1976–1980). During his senior year he was elected to the Honor Council and was captain of the golf team. He attended medical school at New York University (1980–1984). It was during the time at NYU where he was exposed to some tremendous individuals such as Dr. Gerald Weissmann that introduced him to laboratory research in inflammation. He was very fortunate to obtain internal medicine residency training and then served as chief resident at UCSF (1984–1988). He then obtained a pulmonary and critical care medicine fellowship at the University of Colorado and The National Jewish Medical Center in Denver (1988–1992). During this period his research interests were greatly influenced by Dr. Peter Henson. At this time his career-long interests in the mechanisms of lung inflammation and fibrosis was formed. His clinical focus in interstitial lung diseases also emerged under the tutelage of Drs. Marvin Schwarz and Talmadge King, Jr.

His academic career further developed as an assistant professor at Johns Hopkins from 1992–97 and then Yale University from 1997–2006 where he became professor with tenure. During this period he uncovered the role of the extracellular matrix glycosaminoglycan hyaluronan as a fundamental mediator of non-infectious lung inflammation and fibrosis in both in vitro and in vivo studies. He was among the first to develop the concept that endogenous matrix fragments generated during inflammation can serve as ligands for innate immune receptors. These studies have spanned over two decades of investigation and have been supported by the National Institutes of Health. During this period he was elected to the American Society of Clinical Investigation, Interurban Clinical Club and Association of American Physicians. He subsequently moved to Duke University as professor and chief of the Division of Pulmonary and Critical Care Medicine (2006–2013) and then became the chair of the Department of Medicine at Cedars-Sinai Medical Center and director of the Women’s Guild Lung Institute in Los Angeles in 2013.

In addition to studying the basic mechanisms of lung fibrosis, he also is a clinical leader in interstitial lung diseases and established clinics at Johns Hopkins and Yale that continued after his departure. He contributed to the clinical trials that led to the first FDA-approved treatments for idiopathic pulmonary fibrosis in 2014.

Herbert Y. Reynolds, MD

Herbert Y. Reynolds was born in Richmond, VA, on August 20, 1939. He was awarded the BA degree by the University of Virginia in 1961 and the MD degree (Alpha Omega Alpha) from its medical school four years later. He was an intern in medicine and assistant physician from 1965 to 1967 at the New York Hospital–Cornell Medical Center. For the next three years he worked at the NIH as a clinical associate in the Laboratory of Clinical Investigation (LCI) of the Institute of Allergy and Infectious Diseases, and from 1968 to 1969 he was chief clinical associate under the direction of Sheldon M. Wolff. After a year as chief medical resident at the University of Washington Hospital (1970–1971) under Robert G. Petersdorf, he returned to the LCI as a senior investigator from 1971 to 1976. In 1976 he moved to Yale University School of Medicine to serve as an associate professor of internal medicine and director of the Pulmonary Division in the Department of Medicine, which was directed by Samuel Their, and in 1979 he was promoted to full professor. He spent a sabbatical year (1982–1983)

as a senior scientist at the *Institute Nationale de la Sante et de la Recherche Medicale* at *Hôpital Laennec* (Paris Descartes University, under Jacques Chretien). In September 1988 he moved to the Milton S. Hershey Medical Center at Penn State College of Medicine as the J. Lloyd Huck Professor of Medicine and chair of the Department of Medicine. He remained there until November 2002, when he returned to the NIH as a medical officer in the Lung Biology and Disease Branch of the Division of Lung Diseases at the NHLBI, a position that he held until March 2011. He was involved in the program management of grants and research for interstitial lung diseases and related immunologic problems. He was an adjunct professor of medicine at the F. Edward Hebert School of Medicine of the Uniformed Services University of Health Sciences in Bethesda, Maryland (2003). He has been an emeritus professor at Penn State since 2002.

After completing his work in the Division of Lung Diseases at the NHLBI, Reynolds returned to Hershey, where he resumed a part-time faculty position at the Hershey Medical Center in October 2011. His major activities have been in teaching medical students, precepting in the pulmonary fellows outpatient clinic, helping to mentor faculty, and participating in educational and clinical research programs. He served as interim division chief of the Pulmonary, Allergy, and Critical Care Medicine Section from July 2012 to June 2014, during the recruitment of a new division chief.

His first opportunity to participate in research came after his third year in medical school, when he worked during the summer with Calvin M. Kunin, professor of medicine and preventive medicine, who helped him design and manipulate a sepsis-initiated model of cerebral infection in order to examine host resistance. In a nearby laboratory Quentin Myrvik and colleagues were studying respiratory immunity in rabbits and lavaging lungs to retrieve macrophages. Reynolds utilized this method in his studies of lung defenses in rabbits, dogs, and monkeys, and he and colleagues later applied it to human studies when the first fiberoptic bronchoscopes became available around 1972. Particularly stimulating was the atmosphere at the NIH, where Wolff fostered the research careers of many outstanding investigators, including Anthony Fauci, John Gallin, Richard Root, John Johnson, and John Atkinson. While he focused on examining lung responses to infection and describing components of respiratory immunity, a second opportunity developed to study humans with various forms of interstitial pulmonary disease and fibrosis. Using bronchoalveolar lavage and in collaboration with Ronald G. Crystal at the NHLBI, studies were made to define immunologic changes in a variety of patients with interstitial lung

disease. This approach provided a major avenue for lung investigation and helped to move the field of lung research from the physiology of lung mechanics and gas exchange into the arena of lung cellular immunity. Reynolds's medical research continued to concentrate on pulmonary host immunity and the lung's response to infection, on inflammatory mechanisms involving cytokines such as interleukin 8, and on mechanisms involved with interstitial lung diseases such as idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, and sarcoidosis. Over the years he and research and clinical colleagues have published 335 research, clinical, and review articles and textbook chapters.

Reynolds is a member of the American Association of Immunologists, the American Federation of Clinical Research, the Infectious Diseases Society of America, the American College of Physicians (from which he received a Laureate Award in 2013 from the Pennsylvania chapter), the American Society for Clinical Investigation, the American Thoracic Society (president, 1991), the American College of Chest Physicians, the American Clinical and Climatological Association (president, 2002), the Association of American Physicians, and the Academy of Medicine of Washington, DC. From 1978 to 1982 he was a member of the Pulmonary Disease Advisory Committee of the NHLBI, and from 1984 to 1988 he served on the NHLBI Board of Scientific Counselors. From 1980 to 1986 he was a member of the pulmonary infections committee of the Cystic Fibrosis Foundation and served on the executive committee of the Association of Pulmonary Program Directors. From 1991 to 1992 he chaired the committee on research and development of the American Board of Internal Medicine. He has served as an associate editor or editorial board member of the following journals: *Journal of Clinical Investigation*, *Journal of Applied Physiology*, *American Review of Respiratory Disease*, *American Journal of Medicine*, and *Lung*. He served in the US Public Health Service from 1967 to 1970 and from February 1975 to July 1976 as surgeon. During his employment in the Division of Lung Diseases at the NHLBI, he received NIH MERIT Awards (2004, 2006, and 2009), a DLD Director's Award (2005), and an NIH Director's Award (2007 and 2011). He has been included in Best Doctors in America (1992–2012) and was a medical health care provider at the Mercy Health Clinic in Montgomery County, Maryland (2003–2012).

Gerald I. Shulman, MD, PhD

Dr. Gerald I. Shulman was born in Detroit, Michigan on February 8,

1953. He is an Investigator of the Howard Hughes Medical Institute and the George R. Cowgill Professor of Medicine and Cellular & Molecular Physiology at Yale University. He is also co-director of the Yale Diabetes Research Center. Dr. Shulman completed his undergraduate studies in biophysics at the University of Michigan, and he received his MD and PhD degrees from Wayne State University. Following internship and residency at Duke University Medical Center, he did an endocrinology fellowship at the Massachusetts General Hospital/Harvard Medical School and additional postdoctoral work in molecular biophysics and biochemistry at Yale before joining the faculty at Harvard Medical School. He was subsequently recruited back to Yale and has remained there ever since.

Dr. Shulman has pioneered the use of magnetic resonance spectroscopy to non-invasively examine intracellular glucose and fat metabolism in humans and using this approach he has conducted ground breaking basic and clinical investigative studies on the cellular mechanisms of insulin resistance in humans that have led to several paradigm shifts in our understanding of type 2 diabetes (T2D). Insulin resistance plays a primary role in the pathogenesis of T2D and Dr. Shulman's group has pioneered the development of novel magnetic resonance spectroscopy (MRS) methods to assess intracellular lipid and glucose metabolism in normal, prediabetic and T2D humans, noninvasively and in an organ specific manner for the first time.

These studies in turn have provided unique insights into the cellular mechanisms of insulin resistance that could not have been obtained at the bench. Using this approach his group made the first "real time" measurements of glycogen synthesis in human skeletal muscle and showed that a defect in insulin-stimulated muscle glycogen synthesis was the major factor responsible for insulin resistance in patients with T2D. Using ^{31}P MRS his group went on to show in the *JCI* and *NEJM* that this could be attributed to decreased insulin-stimulated glucose transport activity. His group then extended these observations to both obese and nonobese prediabetic individuals and found that they have a similar defect in insulin-stimulated muscle glucose transport/ phosphorylation activity demonstrating that this is an early abnormality in the pathogenesis of T2D. His group went on to show in *PNAS* that the insulin resistance in these offspring of T2D patients could be reversed by exercise training and that this improvement in insulin action was mainly due to an improvement in insulin-stimulated muscle glycogen synthesis, which could be attributed to increased glucose transport/phosphorylation activity. In cross-sectional studies his group ex-

plored possible contributing factors to the occurrence of insulin resistance in these otherwise young-healthy-lean individuals and found a strong inverse relationship between plasma fatty acid concentrations and insulin sensitivity.

Dr. Shulman's group was the first to use ^1H NMR, to assess intramyocellular triglyceride content, to demonstrate that an increase in intramyocellular triglyceride content was the best predictor of insulin resistance in both adults and obese children. Dr. Shulman's group went on to explore the mechanism by which fatty acids cause insulin resistance in humans and in a combined $^{13}\text{C}/^{31}\text{P}$ NMR approach they found that an increase in plasma fatty acid concentrations induced insulin resistance through a reduction in insulin-stimulated muscle glycogen synthesis, which could be attributed to reduced glucose transport/phosphorylation. These findings led to a paradigm shift in our understanding of the molecular mechanism of lipid-induced insulin resistance, which differed from Randle's original postulated mechanism for the inhibitory effect of fatty acids on glucose uptake in muscle. Dr. Shulman then went on to show that this defect could be attributed to decreased insulin-stimulated glucose transport activity due to a defect in proximal insulin signaling. This led to the novel hypothesis that intracellular diacylglycerol (DAG) blocks insulin-stimulated glucose transport activity in human skeletal muscle by interfering with insulin signaling at the level of insulin receptor substrate-1 (IRS-1) through activation of a serine kinase cascade involving activation of PKC. In strong support of this hypothesis he demonstrated that PKC-gamma knockout mice were protected from lipid-induced insulin resistance in skeletal muscle. His group has gone on to show in publications in the *JCI* and *JBC* that a similar mechanism explains hepatic insulin resistance associated with non-alcoholic fatty liver disease (NAFLD) where intracellular diacylglycerol activates PKC-gamma leading to inhibition of the insulin receptor kinase activity.

His group has translated these observations from rodent models of NAFLD to humans by demonstrating that DAG-induced PKC-gamma activation is the best predictor of insulin resistance in obese humans with NAFLD undergoing bariatric surgery. Furthermore, he found that NAFLD and hepatic insulin resistance can be reversed with modest weight reduction in T2D patients and leptin treatment in patients with severe lipodystrophy. Parallel studies in lipodystrophic mice led him to hypothesize that any imbalance between fatty acid delivery and fatty acid oxidation in liver and muscle cells leads to net increases in intracellular DAG content that in turn

activate nPKCs leading to decreased insulin signaling and insulin action in liver and muscle. This unifying hypothesis of ectopic lipid (DAG)-induced insulin resistance explains liver and muscle insulin resistance in both obese and lipodystrophic individuals as well as the mechanism of action of the thiazolidinediones

In order to further test the potential role of mitochondrial dysfunction predisposing individuals to ectopic lipid accumulation his group developed and validated a novel MRS approach to noninvasively assess mitochondrial oxidative-phosphorylation activity in human skeletal muscle for the first time. He then applied this technique to healthy lean elderly subjects and demonstrated that an age-associated decline in mitochondrial function contributes to intramyocellular lipid accumulation and muscle insulin resistance in the elderly which he subsequently demonstrated could be attributed to cumulative reactive oxygen species damage of the mitochondria and prevented by targeted catalase overexpression to the mitochondria

His group has gone on to apply this NMR method to demonstrate reduced mitochondrial function in patients with a novel mitochondrial tRNA mutation that results in hypomagnesemia and hypertension and in young insulin resistant offspring of parents with T2D, which he found could be attributed to reduced mitochondrial content. His group went on to apply these novel MRS methods to examine the pathogenesis of the metabolic syndrome and found that primary defects in insulin-stimulated muscle glycogen synthesis can lead to increased plasma triglyceride concentrations and reductions in plasma HDL concentrations and to non-alcoholic fatty liver disease (NAFLD) by altering the distribution of carbohydrate from liver and muscle glycogen synthesis to increased hepatic de novo lipogenesis. Furthermore, his group found that a single-bout of exercise reversed muscle insulin resistance and decreased hepatic de novo lipogenesis and hepatic triglyceride synthesis, thus proving a key role of muscle insulin resistance in the pathogenesis of NAFLD and the metabolic syndrome

Dr. Shulman's group also discovered two common gene variants in the insulin response element of apolipoprotein C3 that predispose lean individuals to nonalcoholic fatty liver disease (NAFLD) and insulin resistance. This is the first common gene variant described that predisposes healthy lean individuals to NAFLD and insulin resistance and this finding has now been replicated by other groups. The role of ApoC3 as a predisposing factor in the pathogenesis of NAFLD was further verified genetically in apoC3 transgenic mice, which were shown to develop hepatic steatosis associated

with hepatic insulin resistance, increased hepatic DAG content and PKC-gamma activation. Prof. Shulman has developed a novel ^{13}C MRS method to directly assess rates in hepatic mitochondrial oxidative metabolism in humans for the first time (*Nat Med* (20):98-102) and most recently his group has developed novel liver-targeted uncoupling agents which safely reverses hypertriglyceridemia, NAFLD/NASH, hepatic insulin resistance and diabetes in rodent models of NAFLD/NASH and T2D, which are now in clinical development. Most recently his group has solved the long-standing riddles for the glucose lowering effects of metformin (*Nature* 2014; 510:542-46) and leptin (*Nat Med*, 2014; 20(7):759-63) in diabetes and discovered a key role for hepatic acetyl CoA in linking adipose tissue inflammation to hepatic insulin resistance and type 2 diabetes (*Cell*, 160; 745-58).

Dr. Shulman has authored and co-authored over 400 peer-reviewed publications, and he has also trained more than 60 postdoctoral fellows and graduate students, many of whom now direct their own independent laboratories around the world. Dr. Shulman has been elected to the American Society for Clinical Investigation, the Association of American Physicians, the National Academy of Medicine and the National Academy of Sciences and has won many awards, including Distinguished Alumni Award, Wayne State University, Outstanding Investigator Award for Clinical Research, American Federation for Medical Research, Diabetes Care Research Award, JDRF International/Boehringer Mannheim, Outstanding Scientific Achievement Award (Lilly Lecture), American Diabetes Association, the Novartis Prize in Diabetes, the E.H. Ahrens Jr. Award, Association for Patient-Oriented Research, Distinguished Clinical Scientist Award, American Diabetes Association, Naomi Berrie Award for Outstanding Achievement in Diabetes Research, Columbia University, and the Stanley J. Korsmeyer Award, American Society for Clinical Investigation.

Frederick J. Suchy, MD

Frederick J. Suchy was born in Bridgeport, CT on April 9, 1947. He is professor of pediatrics and chief research officer, director, The Children's Hospital Colorado Research Institute, and associate dean for Child Health Research, University of Colorado School of Medicine, Denver. There he is responsible for overseeing a large and well-funded pediatric research enterprise.

He is a graduate of the University of Cincinnati College of Medicine and completed pediatric residency and fellowship training at Cincinnati Children's Hospital Medical Center. Between 1988-1996 he was professor of pediatrics and cellular and molecular physiology at Yale University School of Medicine and chief of the Pediatric Gastroenterology/Hepatology Section. Dr. Suchy was the Herbert H. Lehman Professor of Pediatrics and chairman, Department of Pediatrics, Mount Sinai School of Medicine (1996-2009). He has served as president of the American Association for the Study of Liver Diseases and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.

He is the recipient of the Shwachman Award for major, life long scientific contributions to the field of pediatric gastroenterology, hepatology, and nutrition from North American Society for Pediatric Gastroenterology, Hepatology and Nutrition and Distinguished Service Award from American Association for the Study of Liver Diseases. His clinical and research interests focus on pediatric liver disease including the role of nuclear receptors in regulating bile acid homeostasis in health and disease. The NIH has funded him continuously for over 30 years. Dr. Suchy is a member of the American Society for Clinical Investigation and the Association of American Physicians.

Samuel O. Thier, MD

Samuel O. Thier was born in Brooklyn, NY, in June 1937. He attended Cornell University and received his MD degree from the State University of New York at Syracuse in 1960. After an internship and first-year residency in internal medicine at Massachusetts General Hospital, Thier spent two years in the clinical endocrinology branch of the NIH, working under the supervision of Stanton Segal. He returned to MGH in 1966 to serve as a clinical teaching fellow in nephrology and chief resident in medicine, before joining the hospital staff in January 1967. He was appointed associate in medicine at the Harvard Medical School in July 1967. Thier became director of the MGH renal unit and in 1969 was promoted to assistant professor at Harvard Medical School. In July of that year, he joined Arnold Relman's department at the University of Pennsylvania, serving initially as associate professor of medicine and associate director of the medical service at the Hospital of the University of Pennsylvania. In 1972 he became professor of medicine and vice chairman of the Department of Medicine at the University of Pennsylvania School of Medicine. In January 1979 Thier

accepted the position of David Paige Smith Professor, chairman of the Department of Internal Medicine at Yale University School of Medicine, and chief of medicine at the Yale–New Haven Hospital. He was made Sterling Professor in 1981. In 1985 he accepted the position as president of the Institute of Medicine of the National Academy of Sciences, where he remained until his appointment as president of Brandeis University in 1991. From 1994 to 1997 he served as president of Massachusetts General Hospital. Thier was president and chief executive officer of Partners HealthCare, Inc. (founded by MGH and Brigham and Women’s Hospital), from July 1996 to December 2002. He is professor emeritus of medicine and health care policy at Harvard Medical School.

Thier spent the major part of his investigative career in studies of renal tubular function, work that began under the supervision Segal at the NIH. Initially Thier and his colleagues demonstrated that sugars and amino acids interact in utilizing renal tubular transport systems. They later showed the dependence of renal amino acid transport on the presence of extracellular sodium and defined the kinetics of this transport interaction. A series of studies into the mechanisms of cystinuria were also initiated at the NIH. Thier and colleagues demonstrated transport abnormalities *in vitro* in the kidney and the intestine, which led to subsequent investigations *in vivo* that demonstrated a genetically controlled defect in the board of the kidney and the intestine that was expressed in cystinuria. These studies not only increased the understanding of the disorder of cystinuria, but also enlarged knowledge of the physiology of amino transport. They demonstrated that amino acid transport was bidirectional in the kidney and that secretion of amino acids occurred. They also demonstrated that amino acid transport and incorporation into protein in the intestine was a far more polar process, with the majority of transport and metabolism occurring as a result of luminal surface transport. They also showed the coupling of a genetic defect of the kidney and intestine *in vitro* in Hartnup’s disease and Lowe’s syndrome, which suggested that the genetic expression of transport dysfunction in both tissues was a broadly applicable concept. Thier and his coworkers studied the familial occurrence of Hashimoto’s thyroiditis, the usefulness of long-acting glucagon in the treatment of hypoglycemia, and the incidence and mechanism of renal tubular dysfunction in transplantation patients. The latter findings extended to more specific investigations of renal tubular acidosis in the post-transplant patient and were pursued in further studies of the effects of acidosis on potassium excretion.

Thier had a special interest in medical education. He directed the medical

residency and student training programs at the Hospital of the University of Pennsylvania and served as chairman of the medical school curriculum committee from 1970 to 1973. While at Pennsylvania he was awarded the Christian R. and Mary F. Lindback Foundation Distinguished Teaching Award. At Yale he participated in extensive use of Yale facilities for continuing education in the State of Connecticut. He was a member of the American Board of Internal Medicine (chairman, 1984–1985). Thier served as director on the boards of Charles River Laboratories and Merck & Co., Inc.

Thier was a member of the editorial board of the *New England Journal of Medicine* (1978–1981) and of the NIH Advisory Committee to the Director (1980–1985). He is a member of numerous distinguished professional societies, including the American Federation for Clinical Research (past president), the American Society of Nephrology, the American Physiological Society, the Institute of Medicine of the National Academy of Sciences, the National Academy of Sciences, and the Association of American Physicians (Kober Medal). He was named a master of the American College of Physicians and a fellow of the American Academy of Arts and Sciences. Thier holds sixteen honorary degrees and is the recipient of the UC Medal of the University of California, San Francisco.

Barry Lewis Zaret, MD

Barry L. Zaret was born in Brooklyn, New York, on October 3, 1940. He was awarded the BS degree from Queens College, New York, in 1962 and the MD degree from the New York University School of Medicine four years later. From 1966 to 1969 he was an intern and assistant resident in medicine at the Bellevue Hospital under Saul J. Farber. Zaret spent the following two years as a fellow in the cardiology division at Johns Hopkins Hospital under the direction of Richard Ross. There he had his initial exposure to research and, supported by the NIH, began to study the use of nuclear medicine approaches in the assessment of patients with cardiovascular disease. From 1971 to 1973 Zaret was a major in the US Air Force Medical Corps stationed at Travis Air Force Base in California. He accepted an appointment at Yale Medical School in 1973 as an assistant professor of medicine and diagnostic radiology and was promoted to associate professor in 1976 and to full professor of medicine in 1982. In 1984 he was named the Robert W. Berliner Professor of Medicine. From 1978 until 2004 he was chief of the section of cardiovascular medicine at Yale School

of Medicine. A major force in his career was the influence of Samuel Thier.

Zaret has pioneered the development of non-invasive cardiology, particularly nuclear cardiology, as a means of diagnosing and understanding cardiovascular disease. He has done seminal work in equilibrium and first-pass radionuclide angiocardiology, stress perfusion imaging, assessment of ventricular function in the ambulatory patient, and myocardial metabolism. Zaret is a member of the American Federation for Clinical Research, the American Society for Clinical Investigation, the Association of American Physicians, the Association of University Cardiologists, the American College of Cardiology, the American Physiological Society, and the American Heart Association. In 1993 he became editor-in-chief of the *Journal of Nuclear Cardiology*. He also serves or has served on the editorial boards of *Circulation*, the *American Journal of Cardiology*, the *Journal of the American College of Cardiology*, the *Journal of Cardiovascular Medicine*, the *American Journal of Cardiac Imaging*, *Clinical Cardiology*, and the *Journal of Congestive Heart Failure*. He was an established investigator of the American Heart Association. He received the Casimir Funk Award from the Society of Military Surgeons in 1973 and the Herrmann Blumgart Award from the New England chapter of the Society of Nuclear Medicine in 1978. He was president of the Association of Professors of Cardiology (1992) and was a Louis Sudler Lecturer and Medalist at Rush-Presbyterian Medical College in 1993. He has served on numerous committees, both private and federal, including the cardiology advisory committee of the NHLBI, the NIH Nuclear Medicine and Diagnostic Radiology Study Section, the American College of Cardiology committee on cardiac imaging, and the Institute of Medicine committee to evaluate the Nuclear Regulatory Commission. In 2004 Zaret received an Ellis Island Medal of Honor for his outstanding contributions to American medicine.

New Haven emeritus members without submitted biographies:

Joseph Craft

Richard Edelson

Jack Elias

Stuart Finch

Karl Insogna

Ralph Horwitz

Patrick Mulrow

Leon Rosenberg

Andrew Stewart

NEW YORK CITY BIOGRAPHIES OF LIVING MEMBERS



Renier Brentjens, MD, PhD

Renier Brentjens was born in Amsterdam, the Netherlands, on November 6, 1966. He moved to the United States with his family at the age of 10 and was raised in Buffalo, NY. He received his BA in history from Davidson College, NC, in 1989. Immediately following college graduation Renier entered medical school at the State University of New York in Buffalo. During his second year of medical school, he applied to and was accepted into the school's MSTP program. Over the next three years he completed a PhD in microbiology/immunology and ultimately graduated with a dual MD-PhD in 1996. Renier completed a short-track residency in internal medicine at Yale–New Haven Hospital and subsequently completed a fellowship in medical oncology at Memorial Sloan Kettering Cancer Center in 2002. He remained at MSKCC, initially as an instructor on the Leukemia Service, with subsequent promotions to assistant member and associate member at Memorial Hospital. He is currently also an associate professor of medicine at the Weill Cornell Medical College of Cornell University. Most recently he was made chief of the MSKCC Cellular Therapeutics Center (CTC), directing the clinical arm of the institution's adoptive T cell program.

Brentjens was inspired to pursue a career in medicine at a very early age. Specifically, he had both his father, Jan, and mother, Vero, as role models. The former was a nephrologist who also had a combined MD-PhD degree and whose research career focused heavily on immune-related kidney disease, and the latter was a practicing dermatologist. Of note, medicine was a clear family tradition, as Brentjens's grandfather had been a family physician in the Netherlands and he had four aunts and uncles who were physicians. Although his father was influential in his choice to pursue a medical career in the context of laboratory research, Brentjens was also inspired by Julio Ramirez, a young professor at Davidson College who took Brentjens under his wing at his neurology laboratory and introduced Brentjens to the world of scientific research.

Brentjens spent the summer after his first year of medical school as an intern in the laboratory of Stanley Spinola, learning about microbiology and

becoming versed in molecular therapy. Inspired by this experience, one year later he joined the Spinola laboratory as a graduate student, studying the pathogenesis *Haemophilus ducreyi*, the causative agent of chancroid. As a fellow in medical oncology, he joined the laboratory of Michel Sad-elain, where he initiated studies into the development of T cells retrovirally modified to express chimeric antigen receptors (CARs), which are artificial T cell receptors targeted to the CD19 antigen expressed on both normal B cells and most B cell malignancies.

The concept of CAR T cells for the treatment of cancer, certainly in the early years of his work, failed to receive much attention in the field. Nonetheless, during his fellowship years he was able to demonstrate significant and promising preclinical efficacy of these gene-modified T cells to warrant not only his own laboratory space at the institution as a primary investigator, but more significantly to warrant translation of this work to the clinical setting. To this end, Brentjens spearheaded a program to allow for initial first-in-human testing of CD19-targeted CAR T cells in patients with relapsed B cell malignancies. Although an initial trial to treat patients with relapsed chronic lymphocytic leukemia (CLL) met with modest clinical outcomes, a second trial in patients with relapsed B cell acute lymphoblastic leukemia (B-ALL; a patient population with very poor prognosis) demonstrated remarkable clinical outcomes. In 2013 Brentjens and his colleagues were the first to publish these remarkable therapeutic outcomes in the setting of B-ALL. Since that time, this trial, as well as trials in lymphoma and CLL, have continued to enroll patients and have shown validating and promising outcomes.

Currently Brentjens continues to develop this CAR T cell platform for therapy of both hematologic and solid tumors through the generation of CARs targeted to additional cancer-associated antigens. More significantly, he has pioneered work on the development of potent modified CAR T cells, termed “armored CAR” T cells, designed to overcome the immune-suppressive tumor microenvironment and engage the patient’s own endogenous antitumor immune response via CAR T cell secretion of pro-inflammatory cytokines and co-stimulatory ligands. These approaches have been validated in the preclinical setting and await timely translation to the clinical setting.

Throughout his training and professional career, Brentjens has received numerous honors and awards. In college Brentjens was a Kendrick Kelly History Scholar, voted as a member of the Davidson College chapter of Phi

Beta Kappa, and graduated with a *cum laude* degree with honors in history. In medical school Brentjens won first prize in the annual student research forum after his first year. As a fellow, he was awarded the Errol and Gladys Cook Fellowship from the Cure for Lymphoma Foundation and received physician-scientist development awards, a Career Development Award from the Conquer Cancer Association, and — most significantly — a Damon Runyon Clinical Investigator Award. As a faculty member Brentjens was awarded the Outstanding New Investigator Award from the American Society of Gene and Cell Therapy, the Sir William Osler Young Investigator Award, the NY Intellectual Property Law Association Investigator of the Year Award, and the Society of Hematologic Oncology 2014 Distinguished Lecturer Award. Most recently Brentjens was awarded membership in the American Society for Clinical Investigation. He has served as a reviewer for numerous journals and is member of the editorial boards for several journals, including *Clinical Cancer Research*, *Cancer Immunology Research*, *Molecular Therapy—Oncolytics*, and *Reviews on Recent Clinical Trials*.

Arturo Casadevall, MD, PhD

Arturo Casadevall was born in 1957 in the old province of Las Villas in the city of Sancti Spiritus, Cuba. He completed 6th grade in Cuba and became a political exile in the United States at age 11. After settling with his family in Queens, New York, he attended public and catholic schools and graduated from Mater Christi High School in 1975. Afterward, he majored in chemistry at Queens College of the City University of New York. In 1979 he was accepted to the MD-PhD program at New York University; he received his PhD in physical biochemistry in 1984 and his MD in 1985. He completed internship and residency in internal medicine at Bellevue Hospital in New York City, followed by subspecialty training in infectious diseases at the Montefiore Medical Center at the Albert Einstein College of Medicine.

Since joining the faculty at Albert Einstein College of Medicine in 1992, Casadevall has risen through the ranks. From 2002 to 2006 he served as director of the Division of Infectious Diseases at the Montefiore Medical Center, where he oversaw the expansion of its research program. He is currently the Leo and Julia Forchheimer Professor of Microbiology & Immunology and chairman of the Department of Microbiology and Immunology. He has mentored dozens of graduate students, postdoctoral fellows, and junior faculty, and many of his trainees have gone on to have successful careers in science and medicine. He was elected to the Leo M. Davidoff So-

ciety and has received the Samuel M. Rosen Award, both in recognition for excellence in teaching. In 2008 he was recognized by the American Society of Microbiology with the William Hinton Award for mentoring scientists from underrepresented groups.

Casadevall's major research interests are in fungal pathogenesis and the mechanism of antibody action. He has authored over 600 scientific papers. Casadevall showed that antibodies mediated protection against intracellular pathogens for which humoral immunity was thought to have no role. That work catalyzed a renaissance in studies of antibody function and vaccine development. The Casadevall laboratory established *C. neoformans* as an intracellular pathogen and defined the contribution of melanin to microbial pathogenesis. Together with Ekaterina Dadachova he developed radioimmunotherapy for infectious disease and brought to clinical trials the therapeutic uses of mAbs to *C. neoformans* and melanin. Casadevall has also made several highly influential conceptual contributions. Together with Liise-anne Pirofski he proposed the "damage-response framework of microbial pathogenesis" theory, which was the first theory to reconcile the contributions of the host and microbe in virulence. He devised the first formula to compute the weapon potential of a microbe. He hypothesized that virulence of soil fungi emerged from their interactions with other microbes, thus relating fungal virulence to ecology. He has also put forth recommendations to reform science, based on rigorous research showing that misconduct has been responsible for most retractions of scientific papers.

Casadevall has been elected to membership in the American Society for Clinical Investigation, the American Academy of Physicians, and the American Academy of Microbiology. He was elected a fellow of the American Academy for the Advancement of Science and has received numerous honors, including the Solomon A. Berson Medical Alumni Achievement Award in Basic Science from the NYU School of Medicine, the Maxwell L. Littman Award (mycology award), and the Rhoda Benham Award from the Medical Mycology Society of America. He presented the Kass Lecture of the Infectious Disease Society of America in 2008 and was the ICAAC Lecturer in 2012. In 2013 he delivered the Kinyoun Lecture of the NIAID. Casadevall has organized numerous symposia and conferences, was the chair of the program committee of the Infectious Disease Society of America in 2006, and was the program chair for the American Society for Microbiology general meeting in 2013–2015. Casadevall is the editor-in-chief of *mBio*, the first open-access general journal of the American Society for Microbiology. He has served on the editorial boards of the *Journal of In-*

fectious Diseases, the *Journal of Clinical Investigation*, and the *Journal of Experimental Medicine*. He has served on numerous NIH committees, including those drafting the NIAID Strategic Plan and the Blue Ribbon Panel on Biodefense Research. He served on the National Science Advisory Board for Biosecurity from 2005 to 2014 and was a member of the National Academy panel that reviewed the scientific evidence in the FBI anthrax investigation.

Benjamin Chen, MD

Benjamin Chen is a first generation Taiwanese-American born in New York City on April 25th, 1968. His father immigrated to the United States to New York City for residency training in pediatrics and his family settled in suburban Long Island in Huntington Station, New York where Ben attended public school. He matriculated to Stanford University for undergraduate studies in biology and philosophy. As an undergraduate he became enthralled with virology after pursuing summer research project in herpesvirus biology. He learned virology and basic molecular cloning approaches in the laboratory of Edward Mocarski, an influential herpes virologist in the department of microbiology and immunology. This experience inspired him to expand his goals to study both medicine and research and ultimately gave rise to a lifelong commitment to study virus host interactions.

In the fall of 1990, Ben entered the joint MD, PhD training program at Cornell University Medical College. For his PhD studies, he was accepted into the laboratory of Nobel laureate, David Baltimore, the discoverer of reverse transcriptase, to study HIV-1 latency at the Rockefeller University. At the time, the HIV/AIDS epidemic represented one the greatest modern challenges in virology and medicine, and the Baltimore lab had an active group studying HIV-1 along with other investigators in the lab studying fundamental molecular immunology, transcription and signaling in immune cells. As a graduate student, Ben studied diverse mechanisms HIV gene regulation that contribute to pathogenesis. To interrogate the transcriptional activity of HIV in latent cell lines, he developed infectious luciferase-expressing viral clones, which provided a convenient and sensitive tool to measure the efficiency of infection and viral transcription in different cell environments. These constructs allowed him to discern whether HIV was latent because of factors that influence one specific integrated provirus, or whether the transcriptional milieu was more generally limiting. In other fundamental studies of HIV biology he quantified the effects of the viral

genes that cooperate to downmodulate the HIV receptor, CD4, in infected cells. Lastly, he discovered the context dependent requirements of the NF-kappa B transcription factor in maintaining optimal HIV transcription in different T cell environments. In all these projects, a key component was the development of new recombinant reporterviruses that facilitated the measurement of viral and host gene expression in HIV infected cells. In addition to being enabling for his own studies these tools have also been broadly exploited by the HIV-1 research community.

After finishing his medical degree, Ben continued his pursuit of HIV virology as a postdoc in the laboratory of Dr. Peter S. Kim at the Whitehead Institute at MIT. The Kim laboratory had a vigorous HIV program studying mechanisms of viral entry. There he participated in HIV vaccine studies and pursued fundamental mechanisms of viral assembly. Ben studied murine cells that were unable to support HIV assembly to determine what host factors may be participating in the assembly process. He identified small portions of the MLV genome from the matrix domain of Gag that could greatly enhance viral assembly in murine cells. The studies indicated that species-specific MA cofactors factors that were absent from murine cells were required to support HIV assembly.

In 2003, Ben started his own laboratory at Mount Sinai School of Medicine, to continue studying HIV assembly. The development of a molecular clone of HIV that carried green fluorescent protein (GFP) inserted into a functional Gag protein helped to advance this work. Video rate confocal fluorescence imaging of fluorescent viruses allowed his group to directly visualize the formation of infectious cell-cell contacts called virological synapses (VS). His group observed the direct translocation of HIV from T cell to T cell through VS. Surprising observations from a key publication revealed that recruitment of the viral structural protein Gag occurred after an Env-dependent cell-cell adhesion process and that the transfer process occurred in heterogeneous packets that appeared to be endocytic in nature. The Chen group has continued to study how the VS influences HIV pathogenesis. After measuring the high efficiency of viral transfer across the virological synapse the group examined how the VS transmission enhances the multiplicity of infection. This study in turn led to others in the field to study how the high multiplicity of infection can contribute to drug resistance to certain classes of antiretrovirals drugs. They learned that the regulation of fusion within endosomes is critical during cell-cell transmission. Additionally, studies from the Chen lab were among the first to describe the high degree to which cell-cell transmission can resist neutralizing an-

tibodies. These studies are relevant for the ongoing efforts to develop an effective preventive vaccine against HIV. With collaborators, his group has also investigated how HIV-infected T cells may cause pathology by interacting with non-immune cells in other organs such as the liver or kidney.

Currently, Ben is an associate professor in the Division of Infectious Disease, in the Department of Medicine at the Icahn School of Medicine at Mount Sinai. The work from the Chen lab on T cell virological synapses has been recognized with a Hirschl Career Scientist Award, a Burroughs Wellcome Infectious Diseases Investigator Award, an NIH/National Institutes of Drug Abuse Avant Garde Award for Innovative HIV research. He is a member of the American Association for Clinical Investigation. His group continues to study the cellular mechanisms of VS formation and viral transfer, and also has been studying how the VS contributes to viral dissemination *in vivo* using live imaging approaches in humanized mouse models. In ongoing studies, his group has been working to apply genetic approaches in humanized mice to identify and characterize viral reservoirs to learn how to eradicate HIV from these hidden sites.

Paul S. Frenette, MD

Paul Frenette was born in Rivière-du-Loup, Québec, Canada, in 1965. He was raised near Quebec City and received his college degree from the Séminaire St-Augustin and MD at Université Laval in 1988 in Quebec. As he was interested to pursue a career in academic medicine, programs in the United States offered then the best opportunities to combine clinical and basic research training. To palliate a limited knowledge of the English language, he moved to Montréal for a residency in internal medicine at the Montreal General Hospital of McGill University prior to enrolling in a hematology-oncology fellowship at the New England Medical Center in Boston under the tutelage of Jane Desforges, Bob Schwartz, and Bruce Furie. He joined the laboratory of Denisa Wagner for his research training, developed novel intravital microscopy model systems to assess platelet-endothelial interactions *in vivo*, and generated knockout mice of the selectin family of adhesion molecules in close collaboration with Richard Hynes at the Massachusetts Institute of Technology to carry out genetic analyses of their functions.

Frenette was recruited in 1998 by Barry Collier (then chair of the department of medicine) at Mount Sinai School of Medicine, with the support of

a Scholar Award from an NHLBI-funded Comprehensive Sickle Cell Center (headed by George Atweh) to use intravital microscopy for dissecting the adhesion mechanisms mediating vaso-occlusive events in sickle cell disease. His laboratory made the paradigm-shifting discovery that neutrophils played a direct role in sickle cell vaso-occlusion by interacting with circulating sickle red blood cells. They have identified selectins as a key signal leading to the activation of adherent neutrophils, the regulating activity of gamma immunoglobulins and Fc receptors, and later described that the microbiota promoted neutrophil aging, a newly identified pro-inflammatory subset that drives vaso-occlusive events. He has conducted pre-clinical studies using newly developed selectin antagonists in sickle cell vaso-occlusion, which have led to multi-center placebo-controlled randomized clinical trials. If the promising results are confirmed in a large ongoing phase III trial, selectin antagonists may represent the first targeted therapy to treat acute vaso-occlusive events.

During his postdoctoral years, Frenette showed that the selectins contributed to hematopoiesis and to hematopoietic stem and progenitor (HSPC) homing to bone marrow after transplantation. As junior faculty, he conducted studies to assess the molecular mechanisms mediating HSPC mobilization from bone marrow. In the course of these studies, his group made the ground-breaking discovery that signals from the sympathetic nervous system (SNS) regulated the enforced HSPC mobilization and the circadian release of HSCs from the bone marrow under homeostasis. The notion that adrenergic signaling from SNS nerves regulated the microenvironment suggested that the cellular target might play a role in the stem cell niche. His laboratory then identified Nestin⁺ mesenchymal stem cell as a putative niche for HSCs in the bone marrow and developed whole-mount 3D imaging system to characterize Nestin⁺ niche subsets in distinct vascular structures (arterioles and sinusoids). His laboratory also identified CD169⁺ macrophage as key regulatory niche cells promoting HSC retention in the niche and demonstrated the existence of the long hypothesized erythroblastic island, and the feedback contribution of an HSC-derived progeny (megakaryocyte) in the maintenance of HSC quiescence. Frenette's laboratory has also uncovered critical functions of neural signals in the regulation of inflammatory responses via circadian expression of chemokines and endothelial adhesion and the contributions of innervation in cancer progression in models of acute myelogenous leukemia and prostate cancer.

In 2010, Frenette was recruited to become the founding Director and Chair of the Ruth L. and David S. Gottesman Institute for Stem Cell and Regen-

erative Medicine Research at Albert Einstein College of Medicine, Bronx, New York. He is an elected member of the American Society for Clinical Investigation and the Association of American Physicians and the author more than 120 research articles and reviews, most of which in high-impact journals (h-index 62). He has served on the editorial boards of *Blood*, the *Journal of Clinical Investigation*, *Stem Cell Report*, the Medical Advisory Board of the New York Stem Cell Foundation, as chair of a scientific committee of the American Society of Hematology, and on the Sickle Cell Advisory Council of National Heart, Lung, and Blood Institute and multiple other panels at the NIH. He was elected and served as president of the International Society of Experimental Hematology for its annual meeting in Kyoto, Japan in 2015. Other selected honors include Médaille Gloire de l'Escolle, Prix Grands diplômés from Université Laval, Nobel Lecturer at Karolinska Institutet, Stockholm, Sweden, and several other national and international keynote and named lectures.

Ross L. Levine, MD

Ross Levine was born January 26, 1972, in New York. He received his AB from Harvard College and his MD from Johns Hopkins School of Medicine. Levine is a member of the Human Oncology and Pathogenics Program and an attending physician on the Leukemia Service in the Department of Medicine at Memorial Sloan Kettering Cancer Center, where he also holds the Laurence Joseph Dineen Chair in Leukemia Research. Levine served as a resident in internal medicine at Massachusetts General Hospital and subsequently as a hematology-oncology fellow at the Dana-Farber Cancer Institute. He then joined Gary Gilliland's laboratory at the Broad Institute as a postdoctoral fellow, where he performed kinome sequencing to identify JAK2V617F and MPL mutations in patients with myeloproliferative neoplasms (MPN). His subsequent work during fellowship training included genomic and functional studies of mutant JAK2/MPL disease alleles.

In September 2007 he was recruited to the Human Oncology and Pathogenesis Program at MSKCC; in addition to his work in that program, he also sees patients on the Leukemia Service. His laboratory has identified alleles that predispose patients to MPN and has characterized somatic genetic alterations in MPN patients. This work has improved our understanding of the genetic basis of MPNs. In addition, his lab performed pre-clinical studies of JAK kinase inhibitors and HSP90 inhibitors that have led to clinical trials. His laboratory also identified a mechanism by which

MPN cells develop resistance to JAK inhibitors; this knowledge has led to the development of novel mechanism-based clinical trials.

His lab also investigates the role of somatic mutations in epigenetic modifiers in acute myeloid leukemia (AML). This includes functional studies that have elucidated the role of mutations in TET2, IDH1/2, WT1, and ASXL1 in hematopoietic transformation. He and his colleagues also performed detailed genomic profiling of patients with AML, with the aim to develop a robust prognostic algorithm for AML that can be used in the clinical setting. These genomic tests are now being used as part of clinical care for AML patients at MSKCC and nationwide. In addition, the Levine lab developed murine models of AML based on mutations in epigenetic modifiers, and studies of these mice have led to novel insights into AML pathogenesis and the development of novel AML therapies.

Levine serves on the editorial boards of *Blood*, the *Journal of Clinical Investigation*, *Haematologica* (associate editor), and *Clinical Cancer Research*. He serves on the medical and scientific advisory board of the Leukemia and Lymphoma Society. He has earned a Scholar Award from the Leukemia and Lymphoma Society, a Young Investigator Award from the American Society of Clinical Oncology, a Scholar Award from the American Society of Hematology, and a Clinical Scientist Development Award from the Doris Duke Charitable Foundation. In 2011 he was elected to the American Society for Clinical Investigation and received the Boyer Award for Clinical Investigation from MSKCC.

Barbara Murphy, MD, MB, BAO, BCh

Barbara Murphy was born in Dublin, Ireland. She received her MD from the Royal College of Surgeons in Dublin in 1989. She completed a residency and a clinical nephrology fellowship at Beaumont Hospital in Dublin, followed by a nephrology fellowship in the Renal Division of Brigham and Women's Hospital and Harvard Medical School, where she worked with Charles Carpenter and Mohamed Sayegh, specializing in transplant immunology.

She was first recruited to Mount Sinai Hospital as director of transplant nephrology in 1997 and was named chief of the Division of Nephrology in 2003. In 2011 she was appointed dean for clinical and population-based research, director of Conduits — Institutes for Translational Science, and

principal investigator of the institute's Clinical and Translational Science Award. She was named Murray M. Rosenberg Professor of Medicine and chair of the Samuel Bronfman Department of Medicine at the Icahn School of Medicine at Mount Sinai in 2012. Murphy is the first female chair of medicine at an academic medical center in New York City.

In addition to maintaining a busy clinical transplant practice, Murphy has been continually funded by the NIH since 1994. Through her research Murphy has made significant contributions to the field of transplant in several areas. Major contributions include an early paper demonstrating that the indirect pathway of allorecognition plays a significant role in acute and chronic rejection, shifting the paradigm from the previously held believe that allo-MHCs were recognized solely through the direct pathway of allorecognition. She subsequently published multiple important papers demonstrating that soluble MHC peptides not only contribute to the promotion of the alloimmune response but, under certain circumstances, can indeed inhibit the immune response. She elegantly demonstrated that this occurs via the generation of allospecific regulatory T cells, which suggests an alternative role for soluble MHC peptides in the serum. Murphy was one of the first investigators to examine the impact of genetic variability on graft outcomes, in particular the effect on the susceptibility of an allograft to ischemia reperfusion, acute rejection, and graft survival. These studies led to a larger, multicenter study that applied genetics and genomics to risk stratifications in renal transplantation. This work is ongoing — several papers are under journal review or in development — and forms the basis for two patents and one provisional patent filed in the past year.

Murphy has not limited her research to the lab. She is one of a small group of investigators to develop the protocol for, and participate in, an NIH-sponsored study to determine the outcomes of solid organ transplantation in HIV-positive individuals. At a time when antiretrovirals had only recently been introduced, this study was a radical departure from mainstream clinical practice. This work led to a paper in the *New England Journal of Medicine* that demonstrated that outcomes for HIV-positive patients who received a renal transplant met clinically acceptable survival rates and were not significantly different from those of HIV-negative individuals. This work changed clinical practice, and renal transplantation for HIV-positive patients is now regarded as standard of care.

She is a past president of the American Society of Transplantation and a member of the American Society of Nephrology and has held numerous

leadership roles at a national level, including membership of the board of the American Society of Transplantation, chair of the education committee of the American Society of Transplantation, and co-chair of the American Society of Transplantation public policy committee. She has served on the editorial boards of the *Clinical Journal of the American Society of Nephrology* and the *American Journal of Transplantation*, among others. She was the program chair for the World Transplant Congress 2014. Among her numerous honors, Murphy was named Nephrologist of the Year by the American Kidney Fund in 2011, received the Wyeth Basic Science Investigator Award (the single most prestigious award for young physician-scientists in the transplant field) from the American Society of Transplantation in 2003, and is the recipient of the Jacobi Medallion for distinguished service to Mount Sinai.

Yaron Tomer, MD

Yaron Tomer was born in Petach-Tikva, Israel, in 1959. He received his MD degree from the Sackler School of Medicine at Tel Aviv University in 1985. He trained in internal medicine at Sheba Medical Center, Israel, and continued his training in internal medicine and in endocrinology at the Mount Sinai Medical Center.

During his fellowship in endocrinology, he began studying the immunogenetics of autoimmune thyroid disease under the mentorship of Terry Davies. After completing his training in 1997, he joined the Mount Sinai Division of Endocrinology as an assistant professor. In 2003 he was promoted to associate professor. In 2005 he was recruited by James Fagin to join the University of Cincinnati Division of Endocrinology, where he was appointed professor of medicine. In Cincinnati Tomer expanded his research focus to study the immunogenetic association between type 1 diabetes and autoimmune thyroiditis. In 2009 Tomer was recruited by Paul Klotman to return to Mount Sinai School of Medicine, where he became the vice chair for research in the Department of Medicine. In 2011 Tomer assumed the position of chief of the Division of Endocrinology at Mount Sinai School of Medicine.

Tomer's research focuses on the immunogenetic, epigenetic, and environmental mechanisms that cause thyroid autoimmunity and type 1 diabetes. His group was the first to show that CD40 is a major gene involved in thyroid autoimmunity; this finding led to the discovery that CD40 is asso-

ciated with several autoimmune diseases, including rheumatoid arthritis. Tomer's group also discovered an HLA amino acid signature that is associated with both autoimmune diabetes and thyroiditis. His team is currently studying genetic-epigenetic interactions that play a role in the development of autoimmune thyroid disease and type 1 diabetes. Tomer is a member of the American Society for Clinical Investigation and a fellow of the American College of Physicians. He has received several awards, including the American Thyroid Association Van Meter Award.

Timothy Cragin Wang, MD

Timothy Wang was born in Allentown, PA, on March 27, 1957. He was raised primarily in St. Louis, MO, graduated from John Burroughs Preparatory School in 1975, and matriculated at Williams College, where he graduated in 1979 *summa cum laude* with a BA in chemistry. He then went to Columbia University College of Physicians & Surgeons (the alma mater of his grandfather and great-grandfather), where he received his MD degree (Alpha Omega Alpha) in 1983. There he was inspired by John Lindenbaum to do research in hematology, and by Robert Glickman to pursue gastroenterology. This was followed by a residency in internal medicine at Barnes Hospital and Washington University (1983–1986) and fellowship in gastroenterology at Massachusetts General Hospital. Following his initial year of clinical training in gastroenterology, he was mentored in basic research by Steven Brand, studying the regulation of gastrin gene expression, and then by Emmett Schmidt in the MGH Cancer Center, a new cancer unit developed by Kurt J. Isselbacher, where Wang learned the methodology involved in the creation of transgenic mice and set up the first Transgenic Mouse Core at MGH. In his first high-impact study with Schmidt, Wang demonstrated that cyclin D1 was a true oncogene by overexpression in mammary epithelium, which led to a breast cancer phenotype.

During this second postdoctoral fellowship at MGH Cancer Center, Wang focused on developing transgenic models of gastrin overexpression. He obtained a K08 grant for his research and was hired in 1990 to serve as an instructor in medicine in the gastroenterology unit at MGH by Daniel Podolsky, who had taken over as chief of the division and who went on to become the primary mentor for Wang. Wang was promoted to assistant professor of medicine at MGH and Harvard in 1993 and a year later received his first R01 grant on “the regulation of histidine decarboxylase.” This was followed, over the next four years, by two more R01 grants, on

“the role of gastrin in colon cancer” and “mouse models of gastric cancer.” He was promoted to associate professor of medicine and made associate chief of the division in 1998. In 2000 Wang was recruited to the serve as division chief of gastroenterology at the University of Massachusetts Medical School, and in 2004 he moved to a similar position as chief of digestive and liver diseases at his alma mater, Columbia University Medical Center.

As a junior faculty at MGH in the early 1990s, Wang began exploring ways to combine his training in molecular biology and transgenic mice with his clinical interest in gastroenterology. During medical school and residency, he had co-authored several papers on gastric cancer with Peter H. R. Green and Ray Clouse. In addition, during his gastroenterology fellowship he organized a clinical project at MGH to determine the prevalence of *Helicobacter pylori* infection in patients with dyspepsia undergoing endoscopy. In 1991, the first convincing reports appeared linking *H. pylori* infection to gastric cancer, and Wang quickly developed a collaboration with James G. Fox at MIT to develop a *Helicobacter*-dependent model of gastric cancer. This work progressed quickly, and the INS-GAS transgenic mouse was found to be highly susceptible to gastric cancer following infection with either *H. pylori* or *H. felis*. Wang began to focus increasingly on the role of infection and inflammation in the both initiation and progression of cancer, and the role of specific immune cells and cytokines in this process.

After moving in 2000 to the University of Massachusetts in Worcester to serve as division chief, Wang continued to explore the role of inflammatory cells, and their interaction with stem cells, during *H. felis* infection. He began to examine the role of bone marrow cells during chronic *H. felis* infection and showed an important contribution of these cells to epithelial dysplasia. In addition, he overexpressed the cytokine IL-1beta and showed for the first time that upregulated expression of IL-1beta is able to induce gastric cancer in the absence of *Helicobacter* infection or carcinogen exposure. This led to his early hypothesis that inflammation, by altering the gastric stem cell niche, may be an initiator of cancer.

In 2004 Wang was recruited to the Columbia College of Physicians & Surgeons as the Dorothy L. and Daniel H. Silberberg Professor of Medicine and chief of the Division of Digestive & Liver Diseases. He was also appointed the director of the gastroenterology cancer program at the Herbert Irving Comprehensive Cancer Center. His research continued to focus on the role of inflammation and cancer, and Wang went on to explore the role of myeloid-derived suppressor cells (MDSCs), cancer-associated fi-

broblasts (CAFs), and nerves in the development of solid malignancies. He started a lab in the NCI-sponsored Tumor Microenvironment Network (TMEN) at Columbia, and also generated a mouse model of Barrett's esophagus via overexpression of IL-1beta, which formed the basis for a developing a research center in the NCI-sponsored Barrett's Esophagus Translational Research Network (BETRNet). His focus on the early origins of gastrointestinal tumors led to further studies, specifically to investigate markers for gut progenitors using Cre lineage-tracing techniques, and in 2014 Wang became a member of the NIH Intestinal Stem Cell Consortium (ISCC). In particular, Wang has focused on studying quiescent and reserve stem cells in the gastrointestinal tract.

Wang is a member of the American Society for Clinical Investigation and the Association of American Physicians and the author of more than 250 original research and review articles. He was an associate editor of the journal *Gastroenterology* for 10 years and is the senior deputy editor of *Cancer Prevention Research* and the founding editor and editor-in-chief of *Therapeutic Advances in Gastroenterology*. He is an associate editor of *Yamada's Textbook of Gastroenterology* and is currently vice president of the American Gastroenterological Association.

Jedd Wolchok, MD, PhD

Jedd Wolchok was born in Staten Island, NY, on January 31, 1965. He received an AB from Princeton University in 1987, an MS from New York University (NYU) in 1991, a PhD from NYU in 1993, and an MD from NYU School of Medicine in 1994. His PhD research was performed in the laboratory of Jan Vilček and focused on the role of TNF and IFN-beta in regulating expression of MHC class I antigen. This was followed by a residency in internal medicine at NYU-Bellevue Hospital (1994–1996) and a fellowship in medical oncology at Memorial Sloan Kettering Cancer Center (MSKCC), where he was mentored by Alan Houghton (1996–2000) and studied the use of xenogeneic plasmid DNA vaccines as means to engender antigen-specific immunity to self proteins on cancer cells. He also served as chief fellow in medical oncology and hematology from 1997 to 1998. In 2000 he was appointed to MSKCC, Memorial Hospital, and Weill-Cornell Medical College as assistant member, assistant attending, and assistant professor of medicine, respectively.

Wolchok's interest in translational immunology research dates back to

1984, when he worked with Lloyd Old and Alan Houghton as a summer student after his freshman year in college. The project focused on developing a pharmacokinetic assay for R24, a mouse monoclonal antibody to the disialoganglioside GD3. The experience of working with specimens from patients currently being treated with a novel immunotherapy was unique, as was the exposure to the team of dedicated and successful physician-scientists working in this area at MSKCC (including Old, Houghton, David Scheinberg, Paul Chapman, Richard Cote, and Neil Bander). The bidirectional equilibrium between the laboratory and the clinic was fully evident and portended a career path in academic medicine with both laboratory and clinical experiences.

Wolchok used his experiences in translational immunotherapy and molecular mechanisms of MHC class I regulation to begin a series of studies of xenogeneic DNA vaccines as means to overcome immunologic ignorance and tolerance, which constrain response to self molecules on cancer. He performed preclinical studies to determine the mechanisms utilized by distinct antigens to induce protective tumor immunity and launched both a clinical program in patients with cancer (melanoma, prostate, breast, and renal cell carcinoma) as well as a unique collaboration with veterinary oncologists in which the human tyrosinase DNA vaccine was successfully developed and approved for use in dogs with melanoma. This product (ONCEPT) is recognized as the first licensed therapeutic cancer vaccine in the US. Recognizing that therapeutic immunity to cancer requires additional immune potentiation, Wolchok began a collaboration with Jim Allison, focused on the clinical development of the CTLA4-blocking antibody ipilimumab. He led numerous clinical trials of ipilimumab, including a randomized, dose-ranging trial and a phase 3 trial of ipilimumab plus dacarbazine for patients with metastatic melanoma. Correlative research endeavors during this time (2004–present) have resulted in several important publications. One publication described the novel response kinetics associated with ipilimumab with a proposed set of novel response criteria, known as the immune-related response criteria (irRC). Another publication presented an in-depth case study of a patient who demonstrated a clear example of the abscopal effect, including supportive immune correlates, following administration of a combination of ipilimumab and radiation therapy. More recent publications have been focused on the clinical activity of concurrent CTLA4 and PD-1 blockade and the mechanisms underlying the effects of agonist antibodies to OX40 and GITR. Other areas of current research interest are the immunologic effects of targeted pathway inhibition and the role of both “passenger” mutations in generating potentially immunogenic

neo-epitopes.

Wolchok is currently full member and attending physician at MSKCC and Memorial Hospital, respectively. He is also an associate professor of medicine and graduate biomedical sciences at Weill-Cornell and has a joint appointment to the Sloan Kettering Institute. In 2012 he was named the Lloyd J. Old Chair for Clinical Investigation/Virginia and Daniel K. Ludwig Chair in Clinical Investigation, and in 2013 he was named chief of the Melanoma and Immunotherapeutics Service in the Department of Medicine. He founded the Immunotherapeutics Core, a phase 1 clinical trials unit specifically focused on novel immunotherapies and combinations. He is also an associate member of the Ludwig Institute for Cancer Research and serves as associate director of the Ludwig Center for Cancer Immunotherapy at MSKCC and director of the CVC Trials Network, a joint effort of the Ludwig Institute and the Cancer Research Institute. In 2014 Wolchok was inducted into the American Society for Clinical Investigation. He has received multiple awards, including the American Association for Cancer Research Richard and Hinda Rosenthal Memorial Award, a Doctor of the Year award from the Melanoma International Foundation, humanitarian awards from the Melanoma Research Foundation and the Live-Love-Laugh Foundation, and the Julia Zelmanovich Young Alumni Award from NYU School of Medicine. He is section editor of the *Journal of Immunology*, senior editor for *Cancer Immunology Research*, and has served as a full and ad hoc member of the NCI Clinical Oncology Study Section.

Mone Zaidi, MD, PhD

Mone Zaidi was born April 30, 1960, in Lucknow, India, as the only child of Sibte H. Zaidi, a physician-scientist, and Qamar Zaidi, a child psychologist. His interest in science and medicine was sparked at an early age, in visits to the laboratory of his father, who had then discovered the actions of asbestos and coal dust on lung. In 1983 Zaidi obtained his medical degree (MBBS) from King George's Medical University, receiving honors in medicine and the Stott Medal in pathology. After completing residency and house jobs in internal medicine, he and his wife, Meenakshi Zaidi, also a physician, immigrated to the United Kingdom. Their two children, Neeha Zaidi (currently a postdoctoral fellow at the NIH Vaccination Research Center) and Samir Zaidi (currently an MD-PhD student at Yale University) were born in London.

In 1984 Zaidi joined his long-term mentor, Iain MacIntyre (famed for his discovery of calcitonin), as a Lady Tata Memorial Fellow at the Wellcome Endocrine Unit of the Hammersmith Hospital (Royal Postgraduate Medical School, now Imperial College of Science, Technology and Medicine). He obtained his PhD (1987) in biochemistry and molecular biology and thereafter completed his clinical training as registrar and senior registrar (the equivalents of US senior and chief residents). Zaidi was also appointed as university lecturer with tenure at age 27. A year later he received three independent research grants, including one from the Medical Research Council (MRC). At age 29 Zaidi was appointed to a senior lecturer and consultant position (the youngest ever to be appointed to this position) at St. George's Hospital Medical School of the University of London, where his research thrived and remained well funded over the next 5 years.

In 1996 Zaidi was recruited by Tom Andreoli to join the University of Arkansas as professor of medicine. After a brief stint there, he moved to the University of Pennsylvania as associate professor and then to the Medical College of Pennsylvania as professor of medicine. He also served administrative functions as associate dean for academic affairs for the VA and associate chief of staff for geriatrics and extended care at the Philadelphia VA. In these latter roles he singlehandedly established from inception a Geriatrics and Extended Care Program at the Philadelphia VA by implementing an innovative strategic plan to redesign the traditional departmental structure into a capitated model for elder care. This effort resulted in the first of what is now a widely used care model in the entire VA system.

In 1999 Zaidi was recruited by Barry Collier (then chair of medicine) and Arthur Rubenstein (then dean) to Mount Sinai School of Medicine, where he is currently professor of medicine, geriatrics, and structural and chemical biology and founding director of the Mount Sinai Bone Program. He also served as chief of the Division of Endocrinology and associate director for research, as well as director of the newly established Geriatric Research Education and Clinical Center (GRECC) at the James J. Peters VA Medical Center in Bronx, NY. In these leadership roles Zaidi recruited 32 faculty and led the research, educational, and clinical missions of the GRECC, including the creation of an interdisciplinary geriatrics curriculum, programs in musculoskeletal biology and health services research, and a clinical program in palliative care medicine. In 2012 Zaidi received an MBA from the University of Massachusetts.

Zaidi's research in bone biology and endocrinology began at a very early

point in his career. In the mid-1980s the MacIntyre lab was deeply involved in studies on the molecular regulation and functions of the calcitonin gene peptides and other calcium-regulating hormones. Zaidi's graduate studies involved characterizing the origin and function of the newly discovered alternative splice product of the calcitonin gene, calcitonin gene-related peptide (CGRP). In a series of papers, one in collaboration with Piers Emson at the MRC, Zaidi demonstrated a neural, rather than thyroid, origin for circulating CGRP. In collaborative studies with Tim Chambers, then professor and chair of pathology at St. George's Hospital Medical School, Zaidi developed the first assays to examine the bone-resorbing activity of osteoclasts *in vitro* and demonstrated direct effects of calcitonin, CGRP, and amylin in inhibiting the function of osteoclasts.

In 1989 Zaidi's group, then at St. George's Hospital Medical School in London, discovered a pathway that controls the function of the osteoclast. He found that rising local ionized calcium (Ca^{2+}) levels during hydroxyapatite dissolution shut off the activity of resorbing osteoclasts as part of a negative feedback mechanism. This discovery coincided with the description by Ed Brown and Ed Nemeth of Ca^{2+} sensing in parathyroid cells, which laid the premise for the existence of a new class of Ca^{2+} -sensing receptors. These studies also showed how changes in extracellular Ca^{2+} in the micro- and millimolar range evoked nanomolar changes in cytosolic Ca^{2+} , which were measured for the first time in bone cells by the Zaidi group. A set of pharmacologic and electrophysiologic studies done over the next decade characterized the putative osteoclast Ca^{2+} sensor as being part of a ryanodine receptor activation complex, which was activated by cyclic ADP-ribose formed through the cyclization of NAD^+ by an extracellular ADP-ribosyl cyclase CD38. Physiologic relevance was proven by findings of enhanced osteoclastic activity and bone loss in CD38-deficient mice. In separate studies, Zaidi and his coworkers showed that cytosolic Ca^{2+} transients in osteoclasts and osteoblasts activated the Ca^{2+} /calmodulin phosphatase calcineurin to perturb cell function; the absence of calcineurin in knockout mice thus resulted in profound bone loss reminiscent of the osteoporosis seen with calcineurin inhibitors in organ transplant patients. Overall, these studies established a primary mechanism through which pathways evoked by extracellular Ca^{2+} regulate bone remodeling.

Parallel studies in bone cells confirmed Ole Peterson's initial report that ryanodine receptor-gated Ca^{2+} channels had a more ubiquitous distribution than was previously envisaged. Zaidi demonstrated that ryanodine and IP_3 receptors were located within the inner nuclear membrane, and gated cal-

cium fluxes across it. In an extension of this work, published in *Nature Cell Biology*, the group identified functionally active CD38 protein selectively in the inner nuclear membrane, thus offering a full explanation for the genesis of Ca^{2+} signals within the nuclear subcompartment. These studies together provide a compelling argument for the independence of nuclear Ca^{2+} homeostasis from cytosolic calcium regulation in eukaryotic cells.

Another early breakthrough in Zaidi's career occurred in a collaborative study with Nobel Laureate Sir John Vane and MacIntyre, in which they first demonstrated an inhibitory effect of nitric oxide on the osteoclast (results published in *PNAS*, 1991). It was subsequently shown that endothelial nitric oxide synthase-deficient mice were osteoporotic, thus establishing the physiologic context of Zaidi's pharmacologic observations. As a result of this work, novel nitric oxide donors are now being tested for use in osteoporosis. Around the same time as the above study, Zaidi and his group showed that endothelin and reactive oxygen species also directly affect bone resorption, thus setting the stage for extended studies on the vascular regulation of bone remodeling.

Over the past decade, Zaidi and coworkers have focused on the mechanisms underlying the bone loss associated with various medical conditions. In doing so, they defined a new pituitary-bone axis in which anterior pituitary hormones directly affect the skeleton, bypassing their primary endocrine targets. As a result, both thyroid-stimulating hormone (TSH) and follicle-stimulating hormone (FSH) have since been implicated in the pathophysiology of thyrotoxic and postmenopausal osteoporosis, respectively. These studies, published in *Cell*, have revolutionized the way in which we view endocrine physiology by shifting the paradigm from the traditional, one disease-one hormone model to that of a multifaceted disease pathophysiology for osteoporosis and ultimately revealing novel potential therapeutic targets. The idea that thyrotoxic osteoporosis arises solely from thyroid hormone excess is no longer viable, for low TSH also causes bone loss, as demonstrated by the group and validated clinically in multiple cohorts across the globe. The contribution of a rising FSH to postmenopausal bone loss beyond that resulting from estrogen decline was proven through the demonstration of osteoprotection by a novel anti-FSHb antibody. This opened a new direction for future human studies aimed at treating early postmenopausal disease. Zaidi's group more recently demonstrated opposing functions of posterior pituitary hormones, namely oxytocin and arginine vasopressin (AVP), in regulating bone mass. Notably, they found that oxytocin is a potent skeletal anabolic and that changes in circulating levels

may contribute to the osteoporosis that is associated with pregnancy and lactation. Likewise, AVP is a potent inhibitor of bone formation, and elevated levels in conditions such as chronic hyponatremia could potentially account for the profound bone loss that has been noted in conditions such as SIADH (syndrome of inappropriate antidiuretic hormone secretion). These studies, published over the past ten years, prompt a change in the way we understand and treat various types of osteoporosis.

A more recent set of observations related to the understanding and treatment of rare genetic diseases have challenged the conventional wisdom that Gaucher's disease is solely a macrophage disorder. Zaidi and coworkers have documented a vast array of immune, hematopoiesis, and skeletal defects in mice that lack the glucocerebrosidase-1 gene. Work on another rare disease, congenital adrenal hyperplasia, in collaboration with Maria New, has provided a compendium of structural alterations in the mutated enzyme 21-hydroxylase that correlate with and can predict disease severity. Finally, Zaidi and his group have used genomic connectivity mapping, computational modeling, and traditional pharmacology to show that bisphosphonates, the most commonly used class of drugs for osteoporosis and skeletal metastases, can bind to and inhibit the EGFR family of receptors. This finding could potentially repurpose bisphosphonates for treatment and prevention of EGFR family-driven cancers, such as lung, breast, colon, head and neck, and gastric cancers. This work has also served to bridge the bone field with other disciplines in the quest for interdisciplinary research.

In addition to over 350 publications (h index of 58), Zaidi has provided leadership in the fields of bone and mineral biology, endocrinology, and geriatrics. In addition to serving on a large number of national review and advisory committees, he chaired the Musculoskeletal and Orthopedics Study Section (now the Skeletal Biology Structure and Regeneration Study Section) of the NIH and, for three separate terms, chaired a VA merit review subcommittee. He founded the journal *MARROW*, which is a new interdisciplinary journal to be published in collaboration with the New York Academy of Sciences. He also developed the New York Skeletal Biology and Medicine Conferences, which brought in distinguished speakers from around the globe to share research in diverse areas and provided junior investigators with a platform to network and present their best work. He also serves on the program planning committee of the Association of Professors of Medicine and is associate editor of *Insight*, a publication of the Alliance of Academic Internal Medicine. Finally, Zaidi has mentored a

large number of graduate students, postdoctoral and clinical fellows, and faculty, who have gone on to hold senior faculty, government, and pharmaceutical industry positions.

Zaidi is member of the Association of Professors of Medicine (2014), the Association of American Physicians (2004), the Interurban Clinical Club (2004; has served as councilor and secretary-treasurer), the Association of Osteobiology (2005), the American Society for Clinical Investigation (2000), and the Institute of Biologists of England (1996). He is also a fellow of the Royal College of Physicians of Ireland (1994) and London (1998), as well as of the Royal College of Pathologists (1997). He was elected as an honorary member of the International Chinese Musculoskeletal Research Society (2014) and is honorary professor at Wuhan University (2011). He has delivered, among others, the ESICON Oration of the Endocrine Society of India (2013), the 40th James Platt White Memorial Lecture (University of Buffalo, 2012), the Larry Raisz Keynote Lecture (New England Bone Club, 2013), *Lectio Magistralis* (University of Bari, 2010), the Leo Sreebny Distinguished Lecture (Stony Brook University, 2010), the Steven Goodman Lecture (Yale, 2009), the Rudin-Kase Dean's Lecture (Mount Sinai, 2007 and 2009), the Marookian Lecture (University of Pennsylvania, 2009), the 8th Annual Professor S. H. Zaidi Memorial Oration (Lucknow, 2008), and a Dorothy Dillon Eweson Lecture (American Federation for Aging Research, 2002). He was a Kramer Distinguished Visiting Professor of Biochemistry at Rush University (2014), a visiting professor at Dartmouth Medical School (2007), a highlight speaker at the National Institute on Aging (NIA) Council (2006), and a guest lecturer at the Japanese Bone and Mineral Society (Tokyo, 2006). Zaidi was awarded an honorary doctor of medicine degree from the University of Bari (2010) and an honorary doctor of science degree from the Sanjay Gandhi Post Graduate Institute of Medical Sciences (2013) for his contributions to science.

New York City active members without submitted biographies:

Andrew Dannenberg

Jill Tardiff

NEW YORK CITY EMERITUS MEMBERS BIOGRAPHIES

Qais Al-Awqati, MD, ChB

Qais Al-Awqati was born in Baghdad, Iraq, on August 18, 1935. He attended a high school there founded by Boston Jesuits and graduated from the medical school of the University of Baghdad in 1962. After his military service he returned to the medical school hospital for his residency training in medicine (1965–1967). During the Baghdad cholera epidemic of 1966, he participated in a team organized to render treatment to these patients. Based on his knowledge of glucose-coupled sodium adsorption in the intestine, he started a successful oral treatment program independent of similar programs in Calcutta and Dacca.

In 1967 Al-Awqati came to the United States as a fellow in medicine on the Johns Hopkins service at the Baltimore City Hospitals (now the Francis Scott Key Hospital), where he served as a senior resident under Julius Krevens in 1968. In 1969 he moved to the Johns Hopkins Hospital as a fellow under W.B. Greenough III, participating in the research program concerning the role of cyclic AMP in the generation of diarrhea in cholera. In 1970 he transferred to the Massachusetts General Hospital and, after a year of clinical training, conducted research in the group headed by Alexander Leaf, working with Mortimer Civan. In 1973 he moved to the University of Iowa College of Medicine as an assistant professor of medicine. After three years at Iowa, Al-Awqati joined the Columbia University College of Physicians and Surgeons as an associate professor of medicine and physiology, and in 1983 was promoted to full professor, the same year in which he became the Robert F. Loeb Professor of Medicine and Physiology (a position which he still holds). Since 1977 he has been director of the renal division at New York–Presbyterian Hospital.

Al-Awqati's major field of interest has been ion transport in epithelial cells, although most of his investigations currently deal with the cell biology of ion transport proteins. He is studying the targeting of these proteins into the different membrane domains of the epithelial cell as well as investigating the development of epithelial polarity during the embryogenesis of the kidney. He is also interested in the pathophysiology of such diseases as cystic fibrosis, a disease in which a defect in a chloride channel leads to abnormalities in glycosylation of proteins and lipids. His group has attempted to

provide molecular description of the mechanism by which ion transport in the Golgi apparatus could lead to abnormal sialylation of proteins and gangliosides.

Al-Awqati belongs to numerous scientific societies, including the American Society of Nephrology, International Society of Nephrology, American Federation for Clinical Research, Society of General Physiologists, American Physiological Society, Central Society for Clinical Research, American Society for Cell Biology, American Society for Clinical Investigation, and Association of American Physicians. He also serves on various advisory committees, federal and private. He has been a member of various editorial boards, including those of the *Journal of Clinical Investigation*, *Science*, the *American Journal of Physiology—Cell Physiology*, the *Journal of Membrane Biology*, the *Journal of General Physiology*, and the *Journal of Cell Biology*.

Michael Artman, MD

Michael Artman was born in Hays, KS, on December 10, 1952. He grew up in Hays and attended Fort Hays State University, graduating in 1974 summa cum laude with an AB in chemistry. It was during his college summer research in organic chemistry under the mentorship of Robert Dressler that Artman became interested in a career that would include research and teaching. He received an MD from Tulane University in 1978, followed by pediatric residency and pediatric cardiology fellowship training at Vanderbilt University Medical Center. Artman completed his training in pediatric cardiology under the direction of Thomas P. Graham Jr. and received additional research mentoring from Robert C. Boerth and Robert Boucek. His research during fellowship training included studies of the pathophysiology of acute iron toxicity and cardiovascular pharmacology in the immature heart.

It was his interest in cardiovascular pharmacology that led Artman to take his first independent faculty appointment in the Department of Pediatrics and Department of Pharmacology at the University of South Alabama College of Medicine in Mobile, AL, in 1984. Boerth had recently moved to the University of South Alabama and recruited Artman to join him in the Department of Pediatric Cardiology. Artman was given a joint appointment and laboratory space in the Department of Pharmacology. His mentors in pharmacology, Sam Strada and Joe Thompson, were instrumental

in helping to focus his research program on the mechanisms of drug effects and regulation of contractile function in the developing heart, with an emphasis on elucidating the role of phosphodiesterase enzymes in immature myocardium. During this time Artman was heavily involved in teaching cardiovascular pharmacology to medical students, and he developed a popular fourth-year student elective course in clinical pharmacology.

Artman's research program became increasingly focused on the role of the cardiac sodium-calcium exchanger as a key modulator of cardiac function and responses to interventions in the immature heart. Artman's group was the first to show that exchanger expression and activity peaked at birth in rabbit and rat myocardium. In order to pursue functional and mechanistic studies of the sodium-calcium exchanger, Artman worked with William Coetzee in the Rayne Institute at St. Thomas' Hospital in London during the spring of 1993. This began a collaborative relationship and friendship with Coetzee that persisted for decades. Coetzee taught Artman the fundamentals of single-cell patch clamping techniques to measure the sodium-calcium exchange current. These studies confirmed the higher activity of the exchanger in immature animals and set the stage for future studies to better characterize the role of the exchanger in the regulation of contractile function.

In 1994 Artman was recruited by Wade Parks to direct the Division of Pediatric Cardiology at New York University School of Medicine in New York City. In addition to developing the clinical programs in pediatric cardiology, Artman established an entirely new research program and laboratory in molecular and cellular cardiology at NYU. He recruited Coetzee and Peter Haddock from the Rayne Institute to join the efforts to develop the research program in excitation-contraction coupling and regulation of contractile function in the immature heart at NYU. Working together, the group demonstrated that sodium-calcium exchange alone was sufficient for contraction and relaxation in the heart of newborn rabbits. These studies set the foundation for additional work to understand mechanisms of calcium transport and responses to inotropic agents during maturation of the heart.

While at NYU, Artman began exploring opportunities to lead a department of pediatrics. He was recruited to become chair of the Department of Pediatrics at the University of Iowa College of Medicine in 2004. During his tenure at Iowa, Artman focused on enhancing the clinical, educational, and research programs within the department. The success of these efforts

culminated in plans to build a new Children's Hospital at the University of Iowa. However, the project was completed after Artman left Iowa, as he was recruited to become chair of Pediatrics and pediatrician-in-chief at Children's Mercy Hospital and the University of Missouri–Kansas City School of Medicine in Kansas City, MO, in 2010. In 2013 talks were initiated with Kansas University Medical Center in an effort to combine the pediatric departments at Children's Mercy/University of Missouri–Kansas City and Kansas University School of Medicine into a single department. This culminated with Artman being named chair of the departments of pediatrics at both institutions in January 2014.

Artman has been involved in a variety of national and international committees, peer review, and related activities. He was given the Outstanding Young Alumni Award from Fort Hays State University in 1984 and was honored with the Alumni Achievement Award in 2006. He was elected into membership of Alpha Omega Alpha upon graduation from medical school. Artman has been active in the American Heart Association at the local, regional, and national levels throughout his career and is an inaugural fellow of the AHA. He has served on numerous NIH, AHA, and other national peer review committees, including membership in the NIH Electrical Signaling, Ion Transport and Arrhythmias Study Section from 2004 to 2007 and chairing the section from 2007 to 2009. He was a member of the FDA Cardiovascular and Renal Drugs Advisory Committee from 2000 to 2003. Artman has been chair of the Protocol Review Committee for the NHLBI Pediatric Heart Network since its inception in 2002. He is an active member of the Association of Medical School Pediatric Department Chairs, served on its board of directors (2010–2013), and became chair of its membership committee in 2015. He mentors faculty nationally through the Pediatric Leadership Development Program. He is a member of the Steering Committee for the NICHD Pediatric Scientist Development Program and is actively involved in mentoring fellows accepted into this program.

Craig T. Basson, MD, PhD

Craig T. Basson was born in New York, NY, in 1963. He graduated from Washington University in 1982 (BA in biology and French, MA in biology) and then was awarded a Marshall Scholarship at the University of Oxford (1984; MSc in physiological sciences). Basson completed his MD and PhD at Yale Medical School (1990) and received the John F. Fulton Prize in History of Medicine and the Milton C. Winternitz Prize in Pathology. Basson

trained in internal medicine at Johns Hopkins Hospital (1990–1992) and completed his clinical cardiology fellowship at Harvard Medical School and Brigham and Women’s Hospital, along with a research fellowship in cardiovascular genetics. He began his independent laboratory there in 1996 before moving to Weill Cornell Medical College in 1997.

Basson has devoted his career to deciphering the molecular genetic basis of inherited congenital and adult onset cardiovascular disease. Basson’s commitment to clinical care and investigation in cardiovascular disease was sparked by his graduate work, on mitochondrial creatine kinase with Robert Roberts at Washington University and on vascular integrin signaling with Joseph Madri at Yale. At Brigham and Women’s Hospital, Basson further trained with Christine and Jonathan Seidman, who inspired his care of patients with inherited cardiovascular disease and investigation of molecular genetic etiologies of these disorders.

Beginning with his collaboration with Dr. Seidman, Basson identified the *TBX5* transcription factor gene and the mutations in that gene that cause human septal defects and conduction disease in the setting of limb deformity (Holt-Oram syndrome). These represented the first identified molecular basis for a human monogenic congenital heart malformation, and he performed the first preimplantation genetic diagnosis of such an inherited congenital heart disease. Basson’s team subsequently demonstrated roles for *TBX5* in cell growth and differentiation as well as vasculogenesis. Basson also demonstrated that mutations in *PRKAR1A* and in *MYH8* cause familial cardiac myxoma syndromes and further showed a role for these genes in male infertility. He has also defined molecular genetic causes for several other disorders, including familial atrial septal defects (*NKX2.5*), cardiac lipomatosis (chromosome 19 rearrangements), hypertrophic cardiomyopathy (*RyR2*), arrhythmogenic right ventricular cardiomyopathy (*PKP-2*), right ventricular outflow tract tachycardia (G-protein signaling pathway mutations), and nonsyndromic familial aortic aneurysms (locus on chromosomes 11q and novel TGF-beta receptor mutations).

Basson has received the American Heart Association Samuel A. Levine Young Clinical Investigator Award and been named a Tolly Vinik Foundation Scholar, an Irma T. Hirschl Scholar, and an AHA Established Investigator. He was elected to the American Society for Clinical Investigation, the Harvey Society, and the Association of University Cardiologists and is a fellow of the AHA and the New York Academy of Medicine. Basson was elected to the Interurban Clinical Club in 2005 and served as its New York

councilor from 2005 to 2008. In 2009 Basson was awarded the Michael Potter & Veronique Dhieux Cardiovascular Genetics Prize at the University of Ottawa. At Cornell he was promoted to professor of medicine with tenure in 2004 and was named the Gladys and Roland Harriman Professor of Medicine in 2008. He was director of the Center for Molecular Cardiology and director of cardiovascular research at Cornell. At Cornell, Basson played a pivotal role in educating and training physician scientists, was associate director of the Weill Cornell/Rockefeller/Sloan-Kettering Tri-Institutional MD-PhD Program, and was associate director of the Clinical and Translational Science Center Mentored Clinical Research Program. Basson was also appointed senior lecturer at Harvard School of Medicine in 2014.

Basson has played a key role in developing cardiovascular investigation at other institutions. For a decade he served on the scientific advisory panel of the Donald W. Reynolds Foundation Cardiovascular Translational Medicine Centers from their inception to their conclusion. He served on and chaired the scientific advisory board of the National Marfan Foundation and served on the scientific advisory committee of the Coriell Institute for Medical Research and on the research committee of the AHA Heritage Affiliate. Basson has served on and/or chaired a number of NIH and AHA study sections, including the NIH Clinical Cardiovascular Science Study Section, the NIH Cardiovascular Differentiation and Development Study Section, and the AHA National CV Development Study Section. He has served on the editorial boards of *Circulation*, *Circulation Research*, and the *Journal of the American College of Cardiology* and has served as senior guest editor for *Circulation—Cardiovascular Genetics*.

Basson moved to a new position at Novartis in 2010. As vice president and head of Global Translational Medicine (Cardiovascular and Metabolism) at Novartis Institutes for Biomedical Research, Basson has spearheaded new global programs to translate basic findings into novel therapeutics. Basson's team has established new therapies in atherosclerosis, heart failure, diabetes, and metabolism.

Martin J. Blaser, MD

Martin J. Blaser was born in New York on December 18, 1948 and raised in Queens, NY. He graduated from the General Honors Program (now Benjamin Franklin Scholars) at the University of Pennsylvania, majoring in economics. He received his medical degree from the New York University

School of Medicine. His internship and residency in internal medicine and fellowship in infectious diseases were completed at the University of Colorado School of Medicine. Following two years at the Centers for Disease Control, he joined the University of Colorado faculty in 1981. In 1989 he moved to Vanderbilt University to become the Addison B. Scoville Professor of Medicine, director of the Division of Infectious Diseases, and professor of microbiology and immunology.

From 2000 to 2012 Blaser served as the Frederick H. King Professor of Medicine and chair of the Department of Medicine of the New York University School of Medicine and as director of medical services at Tisch and Bellevue Hospitals. At NYU he has emphasized the traditional academic missions and worked to build the clinical, research, and humanistic aspects of the department. In addition to his own research, Blaser has engaged in furthering medical and scientific education through teaching and mentoring. Since 2013 he has been the Muriel and George Singer Professor of Medicine, professor of microbiology, and director of the Human Microbiome Program at the NYU School of Medicine.

Blaser is interested in understanding the relationships between persistently colonizing bacteria and their multicellular hosts and the epidemic spread of pathogens in the community. His research career began when he was a fellow in infectious diseases and studying three pathogenic bacteria. His work over the past 30 years has largely focused on *Helicobacter pylori* and *Campylobacter* species, which are important as pathogens and as model systems, as well as on anthrax, SARS, influenza, and other acute respiratory diseases. Recent approaches have dealt with genetic and mathematical analyses of population diversity and structure. *H. pylori* interactions with humans have become a model for understanding interactions with other commensals in the human body, and influenza a model of epidemics. He is actively studying the relationship of the human microbiome to health and disease, with major emphasis on obesity and diabetes. Over the past 30 years, Blaser has served as advisor to a large number of graduate students and postdoctoral fellows. He holds 24 US patents relating to his research into bacterial diseases and the microbiome. Blaser has authored over 500 original articles.

Blaser served as president of the Infectious Diseases Society of America (IDSA). He is a member of the American Society for Clinical Investigation, the Association of American Physicians, the American Epidemiologic Society, and the American Clinical and Climatological Association. He

is a fellow of the American Academy of Microbiology and a master of the American College of Physicians. Blaser has received the Oswald Avery and Kass Awards from the IDSA, the Wade Hampton Frost Lecture Award from the American Public Health Association, and the American Association for Cancer Research/American Cancer Society Research Award in cancer epidemiology. He has served as chair of the Board of Scientific Counselors of the National Cancer Institute, as chair of the Advisory Board for Clinical Research of the National Institutes of Health, and on the scientific advisory board of the Doris Duke Charitable Foundation. In 2011 he was elected to the Institute of Medicine, and in 2013 to the American Academy of Arts and Sciences. In 2014 he received the Alexander Fleming Award from the IDSA, which is the association's highest award, for lifetime achievement.

Leonard Chess, MD

Leonard Chess was born in New York City on April 9, 1943. He received the BS degree from the Massachusetts Institute of Technology in 1964 and, four years later, the MD from The State University of New York Downstate, in Brooklyn. From 1968 to 1970 he was a medical intern and resident at the Columbia-Presbyterian Medical Center in New York City. The following two years were spent as a clinical associate at the National Cancer Institute Center at Francis Scott Key Medical Center in Baltimore. From 1972 to 1973 he was a senior medical resident at Massachusetts General Hospital and a clinical fellow at Harvard Medical School. Chess was a research associate at the Sidney Farber Cancer Institute in Boston, an assistant physician at the Beth Israel Hospital, and an assistant professor of medicine at Harvard Medical School from 1974 to 1977. From 1977 to 1982 he was an associate professor of medicine at Columbia and associate attending physician at the New York–Presbyterian/Columbia University Medical Center. In 1977 he was made director of the Division of Rheumatology in the Department of Medicine, and in 1982 he served as attending physician at NYP/Columbia University Medical Center and professor of medicine at Columbia.

At the NIH Chess was introduced to the new field of cellular immunology and became intrigued with the biological functions of lymphocytes, establishing some of the early methods for assaying human lymphocyte functions *in vitro*. In 1973, while working as a research fellow with Stuart Schlossman at Beth Israel Hospitals, he developed new methods for isolating human T cells and B cells and studying their detailed functions *in vitro*.

During his period at the Sidney Farber Institute he developed antibodies that permitted the isolation of functionally unique subsets of human T cells, now referred to as CD4 and CD8 T cells.

Since returning to New York, Chess's studies have continued to focus on the biology and differentiation of T cells, particularly on the surface molecules that dictate T cell function. In the early 1980s he used monoclonal antibodies to probe the functions of CD4 and CD8 molecules. These studies were extended, in collaboration with Richard Axel at Columbia, to the isolation of the genes encoding CD4 and CD8 molecules, ultimately leading to the discovery that CD4 functioned as the HIV receptor as well as to clinical trials of recombinant soluble CD4 in the treatment of AIDS. In 1986 Chess isolated the first human T cell lines expressing the $\alpha\beta$ T cell receptor and demonstrated that these T cells could function to secrete lymphokines and kill tumor cells in vitro. More recently Chess and colleagues isolated and defined the cDNA sequence and function of a novel structure on the surface of activated CD4⁺ T cells, termed T cell-B cell activating molecule (T-BAM, also known as CD40 ligand). This molecule has been shown to mediate the helper activity of T cells, because patients with mutation in the gene encoding T-BAM have markedly reduced and defective antibody responses and succumb to pyogenic infections.

Chess is a member of the American Association of Immunologists, the American Society for Clinical Investigation, the American College of Physicians, and the Association of American Physicians. He is a recipient of the Irma T. Herschl Foundation Scholar Award and an NIH Merit Award. He has served on the NIH immunobiology study section, the Transplantation and Clinical Immunology Study Sections, the merit review board for immunology of the Veterans Administration, the advisory board in immunobiology of the American Cancer Society, the immunology and microbiology study section of the American Heart Association, and the Irvington Institute for Biomedical Research scientific board. He is a section editor of the *Journal of Immunology*.

Lynda Chin, MD

Lynda Chin was born in Guangzhou, China, on January 2, 1966, and immigrated to the United States in her teens. She graduated as valedictorian from public high school in New York City and graduated magna cum laude from Brown University. Her interest in science began during her under-

graduate years at Brown, where she was fascinated by bat echolocation and was able to combine her interests in engineering, computer science, and biology in her research. She received her medical degree from Albert Einstein College of Medicine in 1993 and completed an internship at New York–Presbyterian/Columbia University Medical Center in 1994, then returned to Albert Einstein College of Medicine for her dermatology residency training. She conducted her dermatology residency training in the hospital in parallel to carrying out her molecular biology postdoctoral fellowship in the laboratory of Ronald A. dePinho at Albert Einstein College of Medicine. She excelled in both, as was demonstrated by her selection as the program's chief resident and an exceptional publication record of eight peer-reviewed manuscripts (including three first or co-first authorships in *Cell*, *PNAS*, and *Genes & Development*). Her work as a postdoctoral fellow led to advances in understanding how telomere dysfunction can fuel the development of cancer. She also developed the first bona-fide mouse model of spontaneous cutaneous melanoma.

In 1998 Chin joined the Dana-Farber Cancer Institute and Harvard Medical School as an assistant professor of dermatology and ultimately was promoted to professor in 2009. That same year she became the scientific director of the Belfer Institute of Applied Cancer Science. In 2011 Chin was recruited to the University of Texas MD Anderson Cancer Center to become the founding chair of the Department of Genomic Medicine. Her mission in that role was to integrate genomics into the practice of medicine, using a model of integration, collaboration, and cooperation between research and clinical care enterprises to bring to bear the power of big data on the cancer problem. She also serves as scientific director of the Institute of Applied Cancer Science, an organization designed to bring together the best attributes of academia and industry in a new construct to rapidly translate cancer genomics knowledge into actionable clinical endpoints.

During 15 plus years of her research career, Chin ran a program spanning the fields of transcription, telomere biology, mouse models of human cancer, cancer genomics, and personalized cancer medicine. Chin has held leadership roles in The Cancer Genome Atlas (TCGA) since its pilot phase, including serving on its executive subcommittee. She conceived and led the establishment of the Disease Working Group, a structure through which disease experts outside of TCGA can interact with genomic and computational scientists at TCGA. Together with Matthew Meyerson she led the first publication from TCGA (on glioblastoma). She has also chaired the disease working groups for both glioblastoma and melanoma. Internation-

ally Chin has played a role in the formation of the International Cancer Genome Consortium, serving as leader of the working group that drafted the policy on clinical and pathological issues, and is a member of its scientific steering committee. Chin's productivity and impact as an academic researcher are reflected by her election to membership of the Institute of Medicine of the National Academies in 2012 and to the Association of American Physicians in 2015.

In recent years Chin has returned to her undergraduate interests in computer science and technology, now combined with her medical expertise and research experience to leverage, develop, and deploy innovative technology-enabled solutions to improve access to, and affordability of, quality health care. Starting with cancer, in partnership with IBM, PricewaterhouseCooper (PwC), and AT&T, Chin has led the MD Anderson team in developing the Oncology Expert Advisor™ system and associated suite of technology-enabled solutions, designed to power democratization of cancer care knowledge and expertise beyond Houston, so that future patients all over the world will have access to the most appropriate, evidence-based cancer care regardless of geographic or socioeconomic status.

Charles L. Christian, MD

Charles L. Christian, a Kansan by birth and childhood, was educated in the public school system of Wichita, served in the US Navy from 1944 to 1946, received his BS degree from Wichita State University, and received his MD from Western Reserve Medical School (in 1953), then came to New York City for postdoctoral training. He served on the medical house staff at the New York–Presbyterian/Columbia University Medical Center (under Robert F. Loeb, chair of medicine). After completing a rheumatology fellowship under the mentorship of Charles A. Ragan, he joined the faculty of the Columbia University College of Physicians and Surgeons, acquired tenure status, and succeeded Ragan in 1959 as director of the Edward Daniel Faulkner Arthritis Program at Columbia. In 1969 Christian moved across town in New York City to accept positions at Cornell, including physician-in-chief at the Hospital for Special Surgery (HSS), professor of medicine at Cornell, and adjunct professor at Rockefeller University. At Rockefeller, he recruited four new full-time faculty members who had experience in both the clinical and research aspects of rheumatic disease. The proximity of premier rheumatology and orthopedics departments at HSS, along with the scientific expertise of the Cornell/Rockefeller community,

was a an important factor in the development of exemplary patient care, research, and training programs; these programs have been ranked in the highest tiers in all national surveys. Christian holds great pride in the success of the rheumatology training program at HSS. During his tenure as director, 80 postdoctoral candidates have spent two or more years in the program; a great majority of these individuals remain in academic roles in the US and abroad, many hold leadership roles, and three have served as president of the American College of Rheumatology.

Christian's research interests have been in the sphere of immunology, particularly autoimmunity and the role of infection in the initiation of inflammatory rheumatic syndromes. During his fellowship he demonstrated that the in vitro precipitation from mixing rheumatoid sera with IgG was dependent on presence of aggregates in the latter; this led to a series of studies showing that IgG aggregates and antigen-antibody complexes share biological properties and the hypothesis that rheumatoid factors develop in response to hyper-immunization. Christian and colleagues were the first to recognize and study the association of hepatitis B infection with a pattern of vasculitis characteristic of polyarteritis nodosa. In laboratory models of immune complex disease, the variations in host reactivity with epitopes on complex antigens were shown to influence the character of vascular lesions.

Christian's extramural activities have included serving as editor of *Arthritis & Rheumatism* (1970–1975), president of the American College of Rheumatology (1976), chairman of the National Arthritis Advisory Board (1977–1978), consultant to the US Public Service (including participation in study sections, a training grant committee, and the council of NIAMS; 1965–1988), president of the New York chapter of the Arthritis Foundation (1987–1990), a John & Mary Markle Foundation Scholar (1962–1967), and recipient of the Charles B. Harding Medal from the Arthritis Foundation (1983) and the Presidential Gold Medal from the American College of Rheumatology (1996).

For 10 years following his retirement (which began in 1995), Christian worked on a part-time basis as chief of rheumatology at the University of Florida/Shands Jacksonville Medical Center. Since 2010 his only clinical activity has been as a voluntary physician at a Nassau County clinic in Fernandina Beach, Florida. He retains titles of adjunct professor at the University of Florida and Weill Cornell Medical College and emeritus physician-in-chief at the Hospital for Special Surgery.

Christian and his constant companion, Molly Rinehart, travel widely on visits to Egypt, Jordan, the Balkans, Italy, Ireland, and the Danube River from Nuremberg to Budapest. For a 2-month period (March and April of 2010) Christian was involved in bedside teaching in Taiwan and China, and a planned visit (spring of 2011) to Australia and New Zealand. He spends most of the summer months in Chautauqua, NY, with frequent trips to New York City and Chapel Hill, NC, to visit his three children and four grandchildren.

Rody Powell Cox, MD, MACP

Rody P. Cox was born June 24, 1926, in Beaver Falls, PA. He attended Geneva College for one year before entering the US Army in 1944. He served as a laboratory technician in Africa until 1946. After the war he graduated from Franklin and Marshall College and entered the medical school of the University of Pennsylvania, receiving his MD degree in 1952. Cox then served as intern and junior medical resident at the University of Michigan Hospital. In 1954 he returned to the Hospital of the University of Pennsylvania, where he was senior resident and then chief medical resident. He established a tissue culture laboratory in research medicine under Colin MacLeod. He studied the production of oncofetal alkaline phosphatase in cancer cells and the increase in enzyme catalytic efficiency induced by glucocorticoids. He spent a year in the Department of Genetics at Glasgow University, working with Guido Pontecorvo. In 1961 Cox joined the faculty of the New York University Medical Center and rose through the ranks to become professor of medicine and pharmacology in 1971. He was the first director of one of the first medical scientist (MD-PhD) training programs, at New York University. In 1972 he established and directed the interdepartmental Division of Human Genetics. In 1978 Cox went to Case-Western Reserve University as chief of the medical services at the Cleveland Veterans Administration Medical Center and as vice chairman of the Department of Medicine. In 1988 he was recruited to the University of Texas Southwestern Medical School in Dallas as dean of the medical school and professor of internal medicine. After 16 months of full-time administration, he relinquished the deanship to return to teaching and research.

Cox's research contributions have centered on the regulation of gene expression by chromatin modification and on Mendelian inherited deficiencies of mitochondrial multienzyme complexes. His laboratory selected

maple syrup urine disease (MSUD), a disorder of the branched-chain amino acid metabolism, as a model system. This severe metabolic disease is produced by a deficiency of the mitochondrial E_1 subunit of branched-chain keto acid dehydrogenase (BCKAD) complex. Six genetic loci encode subunits of the BCKAD complex. Cox's laboratory has completed the cloning of cDNAs for three specific subunits— E_1 a, E_1 b, and E_2 —of both bovine and human BCKAD complexes. They have localized E_1 b and E_2 genes to human chromosomes 6p21–6p22 and 1p31, respectively. They have elucidated the structural organization of human E_1 a (45-kb) and E_2 (68-kb) genes and have identified over 50 mutations in E_1 a and E_2 loci. They have also developed efficient prokaryotic and eukaryotic expression systems for characterizing these mutations. The availability of these molecular tools has enabled them to characterize the promoter region of three of the BCKAD complex genes and elucidate the transcriptional elements needed to coordinate basal gene expressions. Recently the laboratory has crystallized E_1 and E_2 and carried out x-ray diffraction studies at 1.8 Å and 2.0 Å resolution.

Cox has been a member of the Interurban Clinical Club since 1973, and is a member of the American Society of Human Genetics, the American Society for Clinical Investigation, the Association of American Physicians, the American Clinical and Climatological Association, and the Central Society for Clinical Research. He is a master of the American College of Physicians and was a career scientist of the Health Research Council of New York City. Cox was a member of the NIH Metabolism Study Section from 1970 to 1974 and chairman of the NIH Mammalian Genetics Study Section from 1978 to 1982. He was a member of the panel on clinical sciences for the National Research Council from 1976 to 1985.

Cox has received many teaching awards, including the Aesculapius Award for Excellence from St. Paul University Hospital in 2005, the Laureate Award from the American College of Physicians, Texas Chapter in 2005, the Socrates Award in 2006, and the Clinical Educator Award in 2008.

Bruce N. Cronstein, MD

Bruce Cronstein was born in Cincinnati, OH, on May 24, 1951. He received his BA from Lake Forest College in 1972, then returned to Cincinnati to attend medical school at the University of Cincinnati College of Medicine, and received his MD in 1976. Cronstein completed an internship in in-

ternal medicine at the University of Cincinnati Medical Center in 1977, followed by a year of residency in anatomic pathology at New York University Medical Center. He then completed his training in internal medicine at Lenox Hill Hospital in New York City. In 1980 Cronstein began his fellowship in rheumatology under the leadership of Gerald Weissmann.

Although he had not been involved in research of any sort prior to his fellowship, he joined the laboratory of Rochelle Hirschhorn to study the role of purine metabolism in the regulation of inflammation and immunologic reactions. He subsequently carried out research under the supervision of both Hirschhorn and Weissmann, examining the role of adenosine and its receptors in the regulation of neutrophil function and inflammation. Cronstein subsequently established an independent research program at NYU School of Medicine, initially within the Division of Rheumatology and then within the Division of Translational Medicine, of which he is the founding director. Cronstein subsequently founded the NYU Clinical and Translational Science Institute within the Division of Translational Medicine, funded by a Clinical and Translational Science Award from the NIH, in 2008. Cronstein is the Paul R. Esserman Professor of Medicine at NYU School of Medicine.

Cronstein chose to pursue a career in medicine with the intention of becoming an internist with an interest in rheumatology. Although Cronstein had an interest in science, he had not participated directly in any type of research until his fellowship in rheumatology. Although his initial projects in the laboratory did not achieve great success, his discovery with Hirschhorn and Weissmann that adenosine regulates superoxide production by stimulated neutrophils awoke a deep interest in science and stimulated his engagement in research as a full-time occupation. This interest was further stimulated by Cronstein's subsequent demonstration that the anti-inflammatory effects of low-dose methotrexate, the anchor drug for the treatment of rheumatoid arthritis, is mediated by increased release of adenosine. Because his training was based in clinical medicine, Cronstein's subsequent research into the physiology and pharmacology of adenosine receptors has generally been informed by patients and their illnesses.

Cronstein has been a leader in the field of adenosine receptor physiology and pharmacology. Following his initial exploration of the role of adenosine in the regulation of inflammation and neutrophil function, Cronstein demonstrated a role for adenosine and its receptors in the process of wound healing and, subsequently, fibrosis. Moreover, his demonstration

that adenosine mediates the anti-inflammatory actions of methotrexate resulted in the exploration of the hypothesis that some of the toxicities of low-dose methotrexate were also due to adenosine and its receptors. Thus, the Cronstein laboratory has demonstrated that adenosine production, which is stimulated by ingestion of methotrexate, ethanol, fructose, and other agents, in turn stimulates the development of fatty liver and hepatic fibrosis via A1, A2A, and A2B receptors — a problem in patients who take methotrexate. Similarly, fibrosis in the lungs and elsewhere may result from adenosine receptor stimulation. Many of these observations have been carried to the clinic.

Cronstein has received a number of awards, including the Lee C. Howley Sr. Prize for Arthritis Research and the Senior Arthritis Investigator Award from the Arthritis Foundation. Cronstein is a fellow member of the American College of Rheumatology, the American Association of Immunology, the American Society for Bone and Mineral Research, the American Society for Pharmacology and Experimental Therapeutics, the American Society for Investigative Pathology, and the American Society for Clinical Investigation. Cronstein has been a member of various committees for the American College of Rheumatology and has chaired the committee on research for the American College of Rheumatology. Cronstein has also been a member and chair of both the Arthritis, Connective Tissue, and Skin Study Section for the NIH and the Immunology Merit Award Review Committee for the VA. He edits the journals *Inflammation* and *Current Rheumatology Reports*. In addition, Cronstein is the chair of the medical and scientific committee for the S. L. E. Lupus Foundation and is a member of the national advisory board of the Arthritis Foundation. He has also served on the boards of directors of the Vilcek Foundation and the Rheumatology Research Foundation.

Mary K. Crow, MD

Mary K. Crow, known as Peggy, was born in New Rochelle, NY, on August 22, 1947. After attending Westchester public schools through most of her early education, Crow completed high school at a private school, along with a class of 23 other young women. Having been immersed in English, French, and history courses throughout high school, it was only after experiencing biology and physics classes in college, with particular inspiration provided by a physics teacher at Manhattanville College, that she recognized her interest in science.

Following college graduation Crow worked as a research assistant in an immunology laboratory at Cornell University Medical College and, with great good fortune, was expertly mentored by her supervisor, Marc Weksler. Crow was allowed a remarkable level of independence in pursuing the laboratory's interest in lymphocyte interactions. She implemented experiments designed to identify the cell populations that respond *in vitro* to allogeneic stimulator cells and observed that self-reactive T cells could recognize and proliferate in response to autologous non-T cells in a reaction that was termed an "autologous mixed lymphocyte reaction". In further experiments she observed that the T cells activated by self-reactive non-T cells could generate suppressor activity as precursors of what are now termed "T regulatory cells". The implications of self-reactivity for the development of autoimmune disease were recognized, and Crow initiated a career-long interest in understanding the origins and mechanisms of systemic lupus erythematosus, the prototype autoimmune disease.

Encouraged to pursue medicine by Weksler, Crow attended Cornell Medical College, then completed an internal medicine residency at New York Hospital. During medical school clerkships and house-staff training, Crow was particularly compelled by the striking presenting features and high morbidity experienced by patients with lupus. During her senior resident year she was selected to participate in a research training program at Rockefeller University and joined the laboratory of Henry Kunkel, a remarkable mentor and creative scientist who had made seminal contributions to the characterization of autoantibodies in lupus and rheumatoid arthritis. During her five years at Rockefeller, while also completing rheumatology fellowship training at the Hospital for Special Surgery, Crow characterized the features of the mononuclear cells most effective in activating autologous T cells, in the process identifying and characterizing human dendritic cells as the most potent of such stimulators.

Crow joined the medical staff and faculty of the Hospital for Special Surgery and Weill Cornell Medical College in 1983 and established a laboratory focused on defining the mechanisms of systemic autoimmune disease. She studied the capacity of CD4⁺ T cells to provide cognate help to B cells, work that led to the recognition of the important role of CD40 ligand in driving B cell differentiation. Studies of blood from patients with lupus showed that expression of CD40L was elevated on their T cells and was sustained after T cell activation, contributing to the identification of CD40L as a rational therapeutic target. In collaboration with colleague Keith Elkon, Crow used a recombinant ribosomal P protein to identify autoantigen-re-

active T cells in patients with lupus; this was likely the first demonstration of autoantigen-specific human T cells. In the early 2000s Crow utilized the relatively new microarray technology to characterize the prominent features of gene expression in blood of lupus patients. In 2003, along with two other groups, Crow identified the type I interferon signature in lupus blood and then described the striking association of that signature with the presence of autoantibodies targeting RNA-associated proteins, thus indicating that RNA and Toll-like receptors are mediators of interferon production. A study of lupus families performed with a talented rheumatology fellow, Tim Niewold, suggested an important role for genetic factors in the elevated type I interferon produced by lupus patients, and disease-associated polymorphisms in interferon regulatory factor 5 were identified as associated with increased production of interferon, thus supporting the role of Toll-like receptors in interferon production. Taken together, this line of work has identified the interferon pathway as central to lupus pathogenesis and as a therapeutic target in lupus, a direction that is being pursued by numerous pharmaceutical companies. Crow's current work uses longitudinal biologic samples from carefully characterized patients to identify the molecular pathways mediating disease and predictors of lupus flare.

Crow is currently physician-in-chief and chair of the Department of Medicine at the Hospital for Special Surgery, professor of medicine and chief of the Rheumatology Division at Weill Cornell Medical College, and professor of immunology at the Weill Cornell Graduate School of Medical Sciences. She is the Joseph P. Routh Professor of Rheumatic Diseases in Medicine at the medical college. Crow is also senior scientist and co-director of the Mary Kirkland Center for Lupus Research and director of the Autoimmunity and Inflammation Program at the Hospital for Special Surgery, where she holds the Benjamin M. Rosen Chair in Immunology and Inflammation Research. Crow was president of the American College of Rheumatology from 2005 to 2006. She is also a past president of the Henry Kunkel Society, is chair of the scientific advisory board of the Alliance for Lupus Research, and is a member of the board of trustees of the Arthritis Foundation, New York chapter. She is currently chair of the NIH Arthritis, Connective Tissue, and Skin Study Section. Crow was named an "Arthritis Hero" by the Arthritis Foundation in 2001 and received the Margaret D. Smith Lifetime Achievement Award from the Arthritis Foundation, New York chapter, in 2010.

Terry Francis Davies, MD

Terry Davies was born in Manchester, United Kingdom, on August 24, 1947. He received the MBBS degree in 1971 from Newcastle University and the MD degree in 1978. In 1971–1972 he was an intern at the Royal Victoria Infirmary (in Newcastle-Upon-Tyne) and the following three years (1972–1975) a medical resident at the Royal Victoria Infirmary and General Hospital. From 1975 to 1977 he was honorary senior medical registrar for the Newcastle Health Authority and senior research associate in the Department of Medicine at Newcastle University. The following two years he served as visiting investigator in the Endocrinology and Reproduction Research Branch of the NIH. In 1979 he became assistant professor of medicine at Mount Sinai Hospital and in 1982 was promoted to associate professor and chief of the thyroid section of the Division of Endocrinology. In 1986 he was made professor of medicine and in 1988 became professor of obstetrics and gynecology at Mount Sinai. He is currently the Florence and Theodore Baumritter Professor of Medicine at the Icahn School of Medicine at Mount Sinai and director of the Division of Endocrinology, Diabetes & Metabolism at the James J. Peters VA Medical Center in New York.

Davies was introduced to laboratory medicine while working under Reginald Hall and Bernard Rees Smith (1975–1977) in Newcastle-Upon-Tyne, as the recipient of a Medical Research Council training fellowship. His studies focused principally on the human thyroid stimulating hormone receptor (TSHR) and autoantibodies to the TSHR. This work formed the basis of his MD thesis. Davies then came to the US as a recipient of a US Public Health Service Award, to pursue studies of peptide receptors with Kevin Catt and Maria Dufau in the Reproductive Sciences Branch of NICHD. These were the first studies of the human LH receptor and its regulation, and they demonstrated specificity crossover by hCG for the TSH receptor in patients with hydatidiform mole and choriocarcinoma, as well as described heterologous receptor regulation.

Davies has had a continuing interest in the receptor for TSH, which is the principal antigen for Graves' disease. In 1981 he demonstrated the utility of porcine, rather than human, thyroid for TSH receptor autoantibody assessment, which opened the way to the commercial development and widespread clinical application of this assay. While pioneering human thyroid cell culture, in 1987 his laboratory described an intrathyroidal human thyroid-specific cytotoxic T cell; in 1991 they showed the oligoclonality of

the T cell infiltrate in Graves' disease thyroid. In 2002 the Davies laboratory was the first to isolate and report a monoclonal antibody to the TSHR that acted as a stimulating antibody similar to those found in Graves' disease. Since that time, the availability of such antibody probes have allowed for a series of studies that examine the post-translational features of the TSHR, including the recognition of TSHR multimerization and the discovery of small molecules capable of specifically activating the TSHR. Since 2006 the Davies laboratory has also focused on the role of stem cells in thyroid pathology, and in 2014 they successfully induced human embryonic stem cells to develop into functional thyroid follicles.

In the clinical area, Davies pioneered the use of TSHR antibody measurements in the diagnosis and prediction of Graves' disease outcomes from 1977 through the present. His group described in 1984 the use of highly sensitive assays for autoantibodies to thyroglobulin and thyroid peroxidase; this led to the rejection of hemagglutination testing. Davies and his colleagues also described the now-well-known association between thyroid antibodies and increased loss of pregnancy. Since 1992 the Davies laboratory has pursued studies in the genetics of the autoimmune thyroid diseases (AITD), with an emphasis on defining non-MHC contributions. In a series of publications with his colleague Yaron Tomer, Davies's group described the major susceptibility loci linked to AITD, including site GD-1 (1997), which proved to be the TSHR itself.

In 1980–1985 Davies held the Irma T. Hirschl Career Scientist Award, and in 1987 he received the Distinguished Research Award from the Mount Sinai School of Medicine. In 1986 he was elected fellow of the Royal College of Physicians, in 1988 he was elected to the American Society for Clinical Investigation, and in 2000 he was elected to the American Association of Physicians. He is a member of the Society for Endocrinology, the Endocrine Society, and the European Thyroid Association, and he is a past president of the American Thyroid Association. Davies has published over 400 papers and reviews in the area of AITD. He has received continuous support from the NIH since 1980, from the VA Merit Award program since 2006, and from generous private sources. He has served on many editorial boards, including those of *Endocrinology*, *Autoimmunity*, and the *Journal of Clinical Endocrinology and Metabolism*. He was the editor of *Thyroid* from 2000 to 2008 and is currently the thyroid editor for *Frontiers in Endocrinology*. In 2012 he was awarded a fellowship *honoris causa* by Newcastle University.

Betty Diamond, MD

Betty Diamond was born in Hartford, CT, in 1948. She grew up primarily in New York City and attended Radcliffe College, then Harvard Medical School. An interest in research predated medical school education, and so in medical school she spent a year at Northwick Park in London, in a newly established clinical research facility led by Peter Medawar and dedicated to studies of human immunology.

Her focus on immunology was the product of fabulous medical school lectures by Kurt Bloch and by Pogo's famous dictum "We have met the enemy and he is us." During her year at Northwick Park, she studied lymphocyte migration with Eugene Lance and Stella Knight. Her lifelong interest in lupus reflects a staunch feminism and the fact that throughout medical school she was devoted to reading works by Southern women writers who suffered from rheumatologic disease.

After completing a residency in internal medicine at New York–Presbyterian/Columbia University Medical Center, she joined the laboratory of Mathew Scharff at the Albert Einstein College of Medicine for postdoctoral training. It was the early era of hybridoma technology, and she exploited the availability of monoclonal antibodies to demonstrate the specificity of Fc receptors for IgG isotypes.

She assumed a faculty position at Einstein and began her studies of systemic lupus. Her salient contributions include the demonstration that autoantibodies can acquire autospecificity by somatic mutation in the course of a germinal center response. This observation led to a paradigm shift in understanding the origins of pathogenic autoantibodies. She subsequently demonstrated that a subset of anti-DNA antibodies in lupus cross-react with the *N*-methyl-D-aspartate receptor and went on to show, in murine models, that these antibodies can alter brain function in ways that depend on the region of brain they penetrate and can alter fetal brain development. These studies opened the field of research into brain-reactive antibodies in autoimmune disease and provided a potential explanation for the neuropsychiatric manifestations of lupus.

In 2004 she moved from Einstein to Columbia University Medical Center and two years later to the Feinstein Institute, where she currently directs the Center for Autoimmune and Musculoskeletal Disease.

She is a member of the American Society for Clinical Investigation, a counselor of the Association of American Physicians. She has served on the board of scientific counselors and the scientific advisory board of NIAMS. She has served on the board of directors of the American College of Rheumatology and is a past president of the American Association of Immunologists. She is a member of the Institute of Medicine and a fellow of the American Association for the Advancement of Science.

Edward A. Fisher, MPH, MD, PhD

Edward A. Fisher was born in New York City and graduated from the Bronx High School of Science. He was a mathematics major at Harpur College at the State University of New York at Binghamton. He received his medical degree from New York University in 1975, then began a residency in pediatrics at Duke University. While there, he was influenced by James Sidbury, a biochemical geneticist, who encouraged him to apply to an MIT-Harvard program for physicians with an interest in metabolism and nutrition. He first earned his MPH degree in epidemiology (1978) from the University of North Carolina at Chapel Hill (working with Allan Smith, who is now at the University of California, Berkeley), where he studied algorithms to monitor risk exposure in the chemical industry. At MIT he began studies with Nevin Scrimshaw, then began a laboratory project in human lipoprotein metabolism at Boston Children's Hospital with Jan Breslow (currently at Rockefeller University). His PhD thesis was in the area of apolipoprotein E (apoE) metabolism and its relationship to plasma lipid and lipoprotein levels, with a focus on the functional consequences of the human isoforms that had recently been defined by the Breslow laboratory. His studies at MIT introduced him to the power of the rapidly evolving field of molecular biology, and he undertook postdoctoral training at the NIH (1981–1984) in the laboratory of Gary Felsenfeld on the regulation of gene expression by chromatin organization. At the NIH he used ultracentrifugation techniques to demonstrate directly that the chromatin containing an actively expressed gene was less condensed than that containing an inactive gene.

Using his combined training in lipoprotein metabolism and molecular biology, Fisher embarked on an independent career, first at the University of Pennsylvania (in the Genetics Division of the Department of Pediatrics at Children's Hospital of Philadelphia, 1984–1987), then at the Medical College of Pennsylvania (MCP) (Department of Biochemistry, 1987–1995). He was particularly influenced by Julian B. Marsh, a former chair at MCP,

who led him to study the metabolism of apoB, the major structural protein of atherosclerosis-causing VLDL and LDL. This work led him back to areas of cell biology with which he was unfamiliar, so in 1994 he joined the highly stimulating laboratory of Gunter Blobel as a sabbatical visitor. Unfortunately, MCP went bankrupt after an ill-fated merger, so in 1995 Fisher joined the Mount Sinai School of Medicine as director of lipoprotein research in the Cardiovascular Research Institute, which had been recently formed by Valentin Fuster. As luck would have it, from 1995 to 1997 his laboratory was located at Rockefeller, in close proximity to his former PhD mentor, Breslow, and his sabbatical host, Blobel. This allowed rapid progress in defining the three major pathways of protein degradation by which apoB and VLDL secretion are regulated, including the proteasome and autophagy, which ultimately made him and his collaborators — particularly Jeffrey Brodsky (University of Pittsburgh), Henry Ginsberg (Columbia University), and Kevin Williams (Temple University) widely recognized in this area.

During the time that his lab was at Rockefeller, he also began to develop a mouse model of atherosclerosis regression. This work continued at Mount Sinai and has followed him to his current position at NYU School of Medicine, where, since 2003, he has been the Leon H. Charney Professor of Cardiovascular Medicine, director of the Marc and Ruti Bell Program in Vascular Biology, and director of the Center for the Prevention of Cardiovascular Disease. To study cells in atherosclerotic plaques on a molecular level, he introduced into the field of vascular biology the use of laser capture microdissection. By applying this and another techniques to novel models of regression, his laboratory has shown that under certain conditions the macrophage population in plaques can be reduced in number (in some cases by emigrating) and be made to become anti-inflammatory. To follow these changes non-invasively, he has also pioneered the use of naturally occurring HDL lipoprotein particles to carry into plaques imaging agents detectable by MRI, in partnership with imaging expert Zahi Fayad (at Mount Sinai).

He has received a number of honors. These include election to the Interurban Clinical Club (initially nominated by Herb Samuels in 2004), the NYU Solomon Berson Award for research achievement, election to the American Association of Physicians, the Special Recognition Award from the American Heart Association for contributions to arteriosclerosis, election to the Alpha Omega Alpha Medical Honor Society, and selection as the George Eastman Visiting Professor at Oxford University. The esteem of his col-

leagues is also reflected by his being chosen as chair of the Atherosclerosis Gordon Conference (2011) and the Keystone Symposium on atherosclerosis (2012) and by his appointment as editor-in-chief of the American Heart Association journal *Arteriosclerosis, Thrombosis, and Vascular Biology*. He has also served on numerous editorial boards, including those of the *Journal of Biological Chemistry* and the *Journal of Clinical Investigation*.

In addition to his own accomplishments, he is proud of the many trainees who have gone on to important independent academic careers, including Joseph Bass (current chief of the Division of Medicine–Endocrinology at Northwestern University), Robin Choudhury (director of the Oxford Acute Vascular Imaging Centre), Ling Li (VFW Endowed Chair at the University of Minnesota), and Raanan Shamir (director of the Institute of Gastroenterology, Nutrition and Liver Diseases at Schneider Children’s Medical Center of Israel).

Linda P. Fried, MD, MPH

Linda Fried was born in New York, NY, on May 14, 1949. She received a BA degree in history from the University of Wisconsin in 1970. She worked for several years in Chicago, leading the paralegal department of a Chicago law firm, serving as a caseworker for the Chicago Department of Public Aid, and advocating for patients in a free health clinic. She also studied and taught aikido. She finished a pre-med curriculum at Loyola University and received her MD in 1979 from Rush Medical College. An internship and residency in medicine at Rush Presbyterian–St. Luke’s Medical Center followed. In 1980 she received the Intern of the Year Award from Rush. She went on to complete a Kaiser Family Foundation fellowship in internal medicine at Johns Hopkins University (JHU) under the clinical mentorship of Philip Tumulty and the research mentorship of Thomas Pearson. She obtained her MPH degree from the Johns Hopkins School of Hygiene and Public Health in chronic disease prevention and completed a post-doctoral fellowship in cardiovascular epidemiology. During 1982–1985 she conducted research to understand the role of smoking and alcohol consumption in coronary artery diameter at the Johns Hopkins Preventive Cardiology Center.

In 1985 Fried joined the Johns Hopkins Medical Institution’s new Welch Center for Prevention, Epidemiology and Clinical Research as a founding core faculty member. She initiated research on the role of physical

activity in cardiovascular disease in women and served as director of the Atherosclerosis Risk in Communities study. She was recruited by William Hazzard into geriatric medicine at Hopkins. Fried created and directed the Johns Hopkins Geriatric Assessment Center, where she led a multi-disciplinary team in the evaluation of frail geriatric patients with complex needs. She conducted research describing models of illness presentation in older adults that went beyond the diagnoses identified per Occam's razor. She received a Henry A. Kaiser Faculty Scholar Award in 1988 for her proposal to characterize preclinical disability in older adults as a precursor stage for disability and an opportunity for prevention. She developed novel theories that proposed a phenotype of frailty based on energy dysregulation, operationalized this phenotype, hypothesized that it represented a medical syndrome, and offered evidence for a physiologic explanation for this phenotype. In 2014 an international consensus group in geriatric medicine published a report recommending — based heavily on Fried's work — that frailty be considered a new medical syndrome.

Fried has led multiple population-based studies to characterize the causes of ill health associated with aging and the outcomes of cardiovascular disease in older adults. Fried was the founding principal investigator of the Cardiovascular Health Study and of the Women's Health and Aging Study and received a MERIT Award for study of the pathophysiology of disability in older women. Fried was a principal investigator of the Johns Hopkins Older Americans Independence Center. All of this work supported the development of her ground-breaking science on the presentations, causes, natural history, and opportunities for prevention and treatment of both frailty and disability in older adults. She is also the co-designer and co-founder of Experience Corps, an evidence-based program that harnesses the social capital of older adults to improve the success of children in public elementary schools. Fried has published over 400 peer-reviewed publications and in 2014 was included by Thomson Reuters in their list of the top 1% of scientists and the "world's most influential scientific minds" of the last decade.

Fried was promoted to professor of medicine in 1997, and in 1999 she founded the Johns Hopkins Center on Aging and Health, which spanned the schools of medicine, public health, and nursing. She served as the deputy director for clinical epidemiology and health services research in the Johns Hopkins Department of Medicine. In 2003 she was also named director of the Division of Geriatric Medicine and Gerontology at Hopkins and Mason F. Lord Professor of Geriatric Medicine. In the division, she

supported and extended the geriatric models of care delivery, built a broad range of research on frailty as well as strong clinical, basic, and population-based research, and brought the division to a *US News and World Reports* ranking of the #1 division in the United States.

Fried was asked by John Stobo in 1989 to found and lead the Johns Hopkins Task Force on Women's Academic Careers in Medicine. This task force transformed the culture and longevity of women in medicine in this department. An initial publication in *JAMA* by Fried, Stobo, and colleagues in 1996 reported the success of the interventions they put in place to support the success of women academic physicians. Fried was appointed, in 2000–2004, by Johns Hopkins President William Brody to chair the JHU Task Force on the Status of Women, which recommended the next generation of university-wide interventions.

In 2008 Fried was recruited to be dean at Columbia University Mailman School of Public Health, where she is the DeLamar Professor of Public Health, professor of medicine in the College of Physicians and Surgeons, and senior vice president of Columbia University Medical Center.

Fried was elected to Institute of Medicine, the Interurban Clinical Club, and the Association of American Physicians, for which she serves on the governing council and as treasurer. She is also a member of the World Economic Forum Global Agenda Council on Aging. Fried has received numerous honors and awards, most recently the Alliance for Aging Research Silver Scholar and Silver Innovator Awards and the Fondation Ipsen Longevity Prize. In 2004 she was named a Living Legend in Medicine by the US Congress and National Library of Medicine.

Marvin Carl Gershengorn, MD

Marvin Gershengorn was born on May 26, 1946, in the Bronx, NY. He received the BS degree from the City College of New York in 1967 and four years later the MD degree from the New York University School of Medicine. From 1971 to 1973 he was intern and assistant resident in medicine at the Strong Memorial Hospital in Rochester, NY. The next three years he served as a clinical associate in the Clinical Endocrinology Branch of the National Institute of Arthritis, Metabolism and Digestive Diseases. He returned to New York in 1976 to join the faculty at New York University Medical Center as an assistant professor of medicine, and from 1979 to

1980 he held the same rank in the Graduate School of Arts and Sciences. From 1980 to 1983 he was director of the honors program at the medical school, during which time he was associate professor. He moved to Cornell in 1983 as professor of medicine, professor of physiology and biophysics (medicine), and chief of the Division of Endocrinology and Metabolism. In 1984 he became the Abby Rockefeller Mauze Distinguished Professor of Endocrinology in Medicine. In 1985 he was made professor of cell biology and genetics (medicine), and in 1993 he became professor of medicine and director of the Division of Molecular Medicine. In 2001 he moved to Bethesda, MD, to become the director of the Division of Intramural Research at the National Institute of Diabetes and Digestive and Kidney Diseases, and in 2008 became chief of the Laboratory of Endocrinology and Receptor Biology.

During the majority of his career in research, Gershengorn has studied the biology of two G protein-coupled receptors — those for thyrotropin-releasing hormone (TRH) and thyrotropin (thyroid-stimulating hormone [TSH]). He has been interested in the intracellular pathways that mediate signaling by these receptors; in the regulation of expression of these receptors, especially in cells other than those in the anterior pituitary gland (for TRH) and the thyroid gland (for TSH); and in the development of small-molecule, “drug-like” ligands that can be used as probes of receptor function and as lead compounds for treatment of human disease. On the clinical side he has had a long-term interest in Graves’ disease, thyroid cancer, and disorders of the hypothalamic-pituitary-thyroid axis.

He is a member of numerous professional societies, including the American Federation for Clinical Research, the Endocrine Society, the American Thyroid Association, the American College of Physicians, the American Society for Clinical Investigation (councilor, 1988), the American Society of Biological Chemists, the American Physiological Society, and the Association of American Physicians. He has held editorial board appointments for *Endocrinology*, the *Journal of Neuroendocrinology*, the *Journal of Biological Chemistry*, and the *Journal of Basic and Clinical Physiology and Pharmacology*. In 1979 he was awarded an NIH Research Career Development Award and in 1981 an Irma T. Hirschl–Monique Weill–Caulier Career Scientist Award. In 1985 he received the Van Meter Award from the American Thyroid Association, in 1994 the Boots Pharmaceuticals Mentor Award for Outstanding Thyroid Research from the Endocrine Society, in 1998 the Sidney H. Ingbar Distinguished Lectureship Award from the American Thyroid Association, in 1999 the Solomon A. Berson Medical

Alumni Achievement Award in Clinical Science from New York University School of Medicine, in 2000 the Gerald D. Aurbach Lecture Award from the Endocrine Society, in 2004 the Boris Catz Lectureship from the Cedars-Sinai Medical Center/UCLA, in 2007 an honorary degree in medicine (laurea ad honorem in medicine and surgery) from the University of Chieti-Pescara, Italy, and in 2013 the NIDDK Director's Award for Translational Research.

Robert M. Glickman, MD

Robert M. Glickman was born on June 23, 1939, in Brooklyn, NY. He received the AB degree from Amherst College in 1960 and the MD degree from Harvard Medical School in 1964. After serving as an intern and assistant resident of the Second and Fourth Medical Services of Boston City Hospital, he was a research and clinical fellow in gastroenterology under the guidance of Kurt Isselbacher at Massachusetts General Hospital. Following a two-year period of service in the US Army, he returned to Massachusetts General Hospital as assistant professor of medicine. He then went to the Beth Israel Hospital in Boston, where he served as chief of the gastroenterology division from 1975 to 1977. In 1977 he moved to Columbia University College of Physicians and Surgeons in New York, where he was associate professor of medicine and chief of the gastroenterology division. In 1982 he was promoted to a professorship in medicine, became chairman of the Department of Medicine, and was awarded the Samuel Bard Professorship in Medicine. In 1990 Glickman return to Boston as physician-in-chief at Beth Israel and as Herrmann L. Blumgart Professor of Medicine at Harvard Medical School. After the merger of the New England Deaconess Hospital with the Beth Israel Hospital, he served as chairman of medicine for the combined hospital. He left Harvard in 1998 to serve as dean of the New York University School of Medicine and as CEO of the Tisch Hospital. In 2007 he stepped down from this position to accept an endowed chair in medicine and gastroenterology at NYU, where he remains. He has concentrated on the clinical teaching of medical students, housestaff, and gastroenterology fellows and continues to carry out these duties.

As a trainee in the laboratory of Kurt Isselbacher, Glickman became interested in the process of fat absorption and chylomicron formation. Specifically, he investigated impaired protein synthesis in an animal model and studied the lymphatic secretion of chylomicron during experimental conditions of impaired protein synthesis. His work initially showed that

when important proteins limiting for the chylomicron surface, particle size increased, and fat transport was largely unaltered through this compensatory increase in particle size. He pursued these studies in the ensuing years, and perhaps his principal scientific achievement was the discovery that the intestine represented a significant source of apoproteins, which are synthesized in the intestinal mucosa. Specifically, apoprotein A-I, an apoprotein shared by chylomicrons and high-density lipoproteins, was produced in the intestine, which accounted, both in animals and in humans, for perhaps as much as 50% of the total daily synthesis of this apoprotein. His studies quantitated this apoprotein in the intestinal mucosa and studied its output in lymph, and he extended these studies to humans, in which he documented the effect of fat feeding on the levels of this apoprotein in plasma. The culmination of many studies supported the concept that the intestine actively synthesized this apoprotein at a high rate and that this protein made a significant contribution to plasma high-density lipoproteins subsequent to the metabolism of chylomicrons.

Glickman's laboratory also co-discovered that another apoprotein, apoprotein A-IV, was dominantly produced by the intestine. His studies in patients with chyluria stood as important human confirmation that the intestine was a major synthetic site for apoprotein A-IV. In addition, his laboratory was the first to demonstrate that high-density lipoproteins could be recovered from mesenteric lymph in the rat, and he accumulated evidence to indicate that many of the components of these lymph high-density lipoproteins were locally synthesized in the intestine. This raised the interesting concept that the intestine could produce high-density lipoproteins in addition to triglyceride-rich chylomicrons. He conducted subsequent studies of lipoproteins isolated from the intestinal mucosa, from which he confirmed that high-density lipoproteins could be isolated from Golgi vesicles within the mucosa.

Glickman's recent studies relate to the quantitation of lipoprotein synthesis and mRNA levels in human intestinal mucosa. His latest work indicates a significant reproducible variability among human volunteers in synthetic rates and mRNA levels of apoproteins. These are thought most likely to be genetically influenced, since dietary manipulations do not appear to regulate the apoprotein synthesis in the short term. Studies are currently in progress to explore regulatory elements within these genes that might explain individual variations in basal and synthetic rates of these apoproteins. Thus, this body of work has concentrated on the role of the intestine in the synthesis of chylomicrons and high-density lipoprotein components

that affect the circulating levels of these important constituents.

Glickman is a member of numerous scientific societies, including the American Society for Clinical Investigation (president, 1983–1984), the Association of American Physicians (councilor), and the American Gastroenterological Association (president, 1989). He was on the council and was president of the Association of Professors of Medicine. He has served on many scientific advisory boards, both federal and non-federal, has been a reviewer for major scientific journals, and was elected to the Institute of Medicine.

Lee Goldman, MD, MPH

Lee Goldman was born in Philadelphia on January 6, 1948. Lee Goldman, MD, MPH, is currently the Harold and Margaret Hatch Professor, executive vice president and dean of the faculties of health sciences and medicine, and CEO of Columbia University Medical Center. He received his BA and MPH degrees from Yale University. He did his internal medicine training at the University of California, San Francisco, and Massachusetts General Hospital and his cardiology training at Yale. From 1978 to 1995 positions at Harvard included professor of medicine and professor of epidemiology, while positions at Brigham and Women's Hospital included vice chair of medicine and chief medical officer. From 1995 to 2006 he was the Julius R. Krevans Professor, chair of medicine, and associate dean for clinical affairs at UCSF.

Goldman's work has focused on evaluating cardiac risk in non-cardiac surgery, determining which patients with chest pain require hospital admission, establishing priorities for the prevention and treatment of coronary disease, and changing the way medical care is delivered by establishing the scientific basis for the now-ubiquitous chest pain evaluation units and the first academic hospitalist program. Under his mentorship more than 45 trainees have published their research as first authors in peer-reviewed publications.

Goldman is a member of the American Society for Clinical Investigation; a past president of the Association of American Physicians, the Society of General Internal Medicine, and the Association of Professors of Medicine; and a member of the Institute of Medicine of the National Academy of Sciences. He has received the highest awards granted by the Society of General Internal Medicine (the Glaser Award), the American College of Physicians

(the John Phillips Award), and the Association of Professors of Medicine (the Williams Award). Goldman is the lead editor of the *Goldman-Cecil Medicine*, the medical textbook with the longest continuous publication in the United States.

He holds an honorary MA degree from Harvard University and an honorary doctor of science degree from the University of Glasgow. The University of California, San Francisco, created the Lee Goldman MD Endowed Chair in Medicine in his name.

Katherine Amberson Hajjar, MD

Dr. Katherine Hajjar is professor of pediatrics, professor of pediatrics in medicine, the Brine Family Professor of Cell and Developmental Biology, and associate dean for research at the Weill Cornell Medical College. She has been a member of the faculty at Weill Cornell Medical College (Cornell University) for over thirty years.

Dr. Hajjar was born on October 29, 1952 in Rochester, New York. She graduated from public high school in Westwood, Massachusetts (1970), serving her senior year as an exchange student at the Tweede Vrijzinnig Christelijk Lyceum in The Hague, the Netherlands under the auspices of the American Field Service (1969–1970). She received her undergraduate degree *cum laude* with highest honors in biochemistry from Smith College in 1974, and her MD degree from the Johns Hopkins University School of Medicine in 1978. She completed her residency in Pediatrics at Children's Hospital of Pittsburgh (1978–1981), where she also served as Chief Pediatric Resident from 1981–1982. She returned to Johns Hopkins for fellowship training in pediatric hematology-oncology (1982–1984), before coming to Weill Cornell in 1984. There, Dr. Hajjar has served in the Departments of Pediatrics and Medicine, as chief of Pediatric Hematology-Oncology (1992–1994), and as chair of the Department of Cell and Developmental Biology (2002–2014). Under her leadership, the department achieved a unique gender balance, more than doubled in size, and tripled in federal funding. In 2014, Dr. Hajjar assumed the position of associate dean for research at Weill Cornell. Dr. Hajjar held the Stavros S. Niarchos Chair in Pediatric Cardiology (1997–2002), and currently holds the Brine Family Chair in Cell and Developmental Biology.

Dr. Hajjar's interest in science and research was sparked in early child-

hood by visits to the American Museum of Natural History in New York with her grandfather, Dr. J. Burns Amberson, Jr., and also by the cheerful acquiescence of her mother, Shirley Huber Kuntz, to setting up a home “chemistry lab.” Later, at Smith College, Professor Jeanne Powell inspired Dr. Hajjar’s honors thesis work on the *in vitro* differentiation of murine myocytes in the presence of cultured neurons. At Weill Cornell, Dr. Hajjar began her independent investigations on endothelial cells under the transformational mentorship of Dr. Ralph L. Nachman, Professor of Medicine. She was also profoundly influenced by many other eminent physician-scientists, including Drs. William H. Zinkham, Vann Bennett, Peter Agre, Barry S. Collier, and Aaron J. Marcus. Dr. Hajjar is largely responsible for the concept that generation of the protease plasmin occurs on cell surfaces as well as within a fibrin milieu. She discovered the major endothelial cell fibrinolytic receptor, the annexin A2 complex, and defined its binding interactions with plasminogen and its activator. She demonstrated its *in vivo* relevance to fibrin clearance in genetically engineered mice, and defined its role in human hemostasis (acute promyelocytic leukemia) and thrombosis (antiphospholipid syndrome and cerebral thrombosis). She also defined the unexpected role of annexin A2-mediated fibrin clearance in promoting pathologic angiogenesis in a model of retinopathy of prematurity and diabetic retinopathy. Her current research explores the role of the annexin A2 complex in secretion of macromolecular proteins, hemostasis, vascular permeability, and inflammation.

As an educator, Dr. Hajjar has mentored more than 10 graduate and medical students, more than 20 postdoctoral and clinical fellows, and several junior faculty members in her lab. She lectures regularly in both the medical school and graduate school curriculum, and frequently teaches small focus groups on selected topics in biomedicine. In various outreach programs, her lab has hosted many college and high school students for summer rotations. She has contributed chapters on fibrinolysis and vascular biology in many definitive textbooks of hematology.

Dr. Hajjar is a member of the American Society for Clinical Investigation, the Association of American Physicians, and the American Clinical and Climatological Association. She is the recipient of numerous prizes and awards including an Established Investigator Award from the American Heart Association (1989-1994), the Syntex Scholar Award (1989-1992), the Irvine Page Award from the American Heart Association (1991), and the Key to Life Award from the Children’s Blood Foundation (1993). She was elected a Fellow of the American Society for the Advancement of Science

in 2014. She received the Gwendolyn Stewart Memorial Award to Honor Women in Biomedical Sciences (1997), was elected an honorary fellow of the Weill Cornell Medical Alumni (2014), and received the George Papanicolaou Grand Award from the Hellenic Medical Society (2015). She has organized numerous international meetings and workshops, and served on multiple review panels and editorial boards. She is a frequently invited speaker at national and international conferences. She was president of the New York Society for the Study of Blood (2003–2004), and of the Harvey Society (2009–2010). She served as president of the Interurban Clinical Club from 2002 to 2003.

Barbara Hempstead, MD, PhD

Barbara Hempstead was born in Ithaca, NY, on February 22, 1954. She received her BS degree from Tufts University in 1976 and her MD and PhD (cell biology) degrees from Washington University School of Medicine in 1982. During her PhD studies she focused on identifying the IgE receptor complex and was mentored by Charles Parker and Anthony Kulczycki. This was followed by an internship and residency in internal medicine at the New York Hospital (1982–1985) and a fellowship in hematology and medical oncology at Cornell Medical College, where she was mentored by Moses Chao and studied the mechanisms of receptor signaling by nerve growth factor.

In selecting biomedical research as a career, Hempstead was inspired by her father, Charles Hempstead, a physicist at Bell Laboratories who believed that asking questions and embracing unexpected results was the key to success. Her initial forays into laboratory investigation were supported by Edward Greenberg at Tufts, and her research interests in receptor protein structure and signaling, with a focus on defining the subunits of the IgE receptor and mechanisms of activation in mast cells, were solidified under the mentorship of Parker and Kulczycki.

The theme of receptor signaling in the nervous system was the focus of studies during her postdoctoral fellowship, under the guidance of Chao. She used molecular tools to identify signaling cascades downstream of nerve growth factor (NGF) and was a member of the team that first identified the Trk receptor tyrosine kinase as an NGF receptor. Hempstead was the first to recognize the importance of neurotrophic factors in regulating vascular development and the vascular response to injury; she did this

by developing animal models of altered neurotrophin or neurotrophin receptor expression that exhibited abnormal vascular development. Importantly, she recognized that the precursor form of neurotrophins (pro-neurotrophins) were independent ligands that selectively engaged p75 and sortilin receptors, rather than Trk receptors, to mediate apoptosis or acute negative remodeling of the neuronal cytoskeleton. She identified the pro-neurotrophins as antagonists of mature neurotrophin function and documented their activities in brain development, synaptic plasticity, brain injury, and vascular injury. Most recently, she has identified the isolated prodomain of BDNF as a third neurotrophin ligand that can also antagonize the effects of mature neurotrophins to acutely regulate neuronal morphology via direct actions on the neuronal cytoskeleton.

As co-chief of the Division of Hematology and Medical Oncology at Cornell (2004–2012), she jointly supervised the growth of the division, overseeing the recruitment of numerous basic and translational scientists to newly renovated laboratories. In these efforts she coordinated the research activities of vascular biology, thoracic oncology, hematology/oncology, and tissue banking and the Epigenomics Core Facility to develop an integrated interdisciplinary program. Hempstead was also very active in fostering intercampus activities with Cornell University in Ithaca and, together with Harold Craighead, was the recipient of a Physical Sciences–Oncology Center grant from the NCI, which focused on defining the physical characteristics of the tumor microenvironment. In 2012 Hempstead was asked to develop and head a new Office of Faculty Development as associate dean. In this role she has developed a college-wide annual review process for all faculty and overseen a re-evaluation of promotion procedures and tracks and is developing a college-wide mentorship program. At Weill Cornell she has been strongly supported by Ralph Nachman and Andrew Schafer, former chairs of the Department of Medicine, in her activities to promote interdisciplinary research and by Laurie Glimcher, dean of the medical college, and Gary Koretzky, dean of the graduate school, for enabling college-wide activities in faculty development and diversity.

Hempstead has received multiple awards, including the Rose Klosk Fellowship Award, the Andrew T. Mellon Award, NCI Clinical Investigator Award, the American Cancer Society Junior Faculty Award, and the Irma T. Hirschl/Monique Weill-Caulier Trust Research Award. Hempstead has been named an established investigator of the American Heart Association and elected to membership in the American Society for Clinical Investigation, and has served as a national counselor for the American Society for

Clinical Investigation. In 1999 she received the Burroughs Wellcome Clinical Scientist Award in Translational Research. In 2002 Hempstead was named to the O. Wayne Isom Professorship in Cardiovascular Medicine at Weill Cornell Medical College. Hempstead is a member of the Association of American Physicians, has served as vice chair and chair in 2003 and 2005 of the Gordon Conference on Neurotrophic Factors. She is a member of the Board of Scientific Councilors at the NICHD division of the NIH. Hempstead is a member of the Practitioner's Society as well as the Inter-urban Clinical Club. In 2013 she was selected as a fellow in the Executive Leadership in Academic Medicine program.

Rochelle Hirschhorn, MD

Rochelle Hirschhorn was born on March 19, 1932, in Brooklyn, NY. She received the AB degree from Barnard College of Columbia University in 1953 and the MD degree from the New York University School of Medicine four years later. The following year she was a research associate at the Institute of Human Genetics in Uppsala, Sweden. From 1958 to 1959 she was an intern at the NYU-Bellevue Fourth Medical Division. The next three years she was a part-time physician at the Bellevue Well Baby Clinic (1960–1963). From 1963 to 1965 she worked as a research fellow and teaching assistant, part time, at NYU. She followed this with work in the NYU Department of Medicine as an associate research scientist, then spent three years serving as a fellow in rheumatology and instructor in medicine. She became an assistant professor of medicine in 1969, a position that she held until 1974. She worked with Harry Harris for a year at the Galton Laboratory of Human Genetics and Biometry, University College, London. In 1974 she was promoted to the position of associate professor of medicine at NYU and to full professor in 1979. From 1984 until 2008 she served as head of the Division of Medical Genetics in the Department of Medicine. From 1985 to 1986 Hirschhorn was a visiting professor in the laboratory of Stuart Orkin at Harvard Medical School. She is now a research professor of medicine at the NYU School of Medicine and professor emerita of medicine, cell biology, and pediatrics at NYU.

The year she spent in Sweden, and the physician-scientists she interacted with, as well as prior interactions with the late Charles Wilkinson and other members of the NYU faculty actively engaged in research, provided the basis for Hirschhorn's initial attraction to research. However, she did not fully commit to a research career until she did her fellowship under Gerald

Weissmann. The individuals who most influenced her early research career were Weissmann, her husband Kurt Hirschhorn, and the late Edward Franklin and Lewis Thomas. Harris and Fred S. Rosen also provided important influence and support.

In her research career Hirschhorn has elucidated the pathophysiologic mechanisms and delineated the molecular and biochemical defects of ADA deficiency and acid α -glucosidase deficiency, clarifying genotype-phenotype relationships. Hirschhorn initially elucidated the biochemistry of the enzyme involved in adenosine deaminase deficiency and participated in the first demonstration that the severe combined immunodeficiency associated with this enzyme deficiency can be cured by histocompatible bone marrow transplantation. She provided the first prenatal diagnosis and carrier testing for this disease, showed that enzyme therapy, in the form of red cell transfusions, could ameliorate the immunodeficiency, and demonstrated that deoxy-ATP is the major toxic metabolite responsible for the pathophysiology. During the past several years, in ongoing studies, she has described numerous mutations in the *ADA* gene and showed that different mutations resulted in varying severity of the disease. She was also one of the first to demonstrate that CpG dinucleotides represented mutational hot spots. In related studies she characterized the role of adenosine receptors in modulating responses of PMNs.

Hirschhorn's work on acid α -glucosidase deficiency (glycogen storage disease type II) includes initially defining carrier testing, discovering a major normal polymorphism by using a new technique of affinity gel electrophoresis, and purifying and biochemically characterizing the enzyme. Recently she has isolated both the cDNA and the structural gene and, as mentioned above, has defined a number of mutations associated with varying severity of the disease. She has also been instrumental in characterizing several neutral α -glucosidases, one of which is important in the processing of N-linked glycoproteins.

From 1966 to 1969 Hirschhorn was a fellow of the Arthritis Foundation. She followed this with three years as a senior investigator of the New York Heart Association. She held a Research Career Development Award from 1972 to 1977. Her research has been continuously supported by the NIH since 1970. She has received the Solomon A. Berson Medical Alumni Achievement Award in Clinical Science (1989), an NIH MERIT Award (1990), and the Jeffrey Modell Foundation Lifetime Achievement Award. In 1993 she was made a member of the Institute of Medicine of the National

Academy of Sciences. She has been a member of numerous advisory committees in health-related organizations, including the NIH Study Section in Allergy and Immunology; the NIH Allergy, Immunology and Transplantation Advisory Committee; the Board of Scientific Counselors of the NIH NIAID; the clinical research committee of the March of Dimes; the fellowship review committee of the Arthritis Foundation; and the boards of trustees of the NIH NIAID and the AIDS Medical Foundation. She has served on the editorial board of the *Journal of Clinical Immunology*, *Clinical Immunology and Immunopathology*, the *Journal of Clinical Investigation*, the *Journal of Immunology*, and the *American Journal of Human Genetics*. She is a member of numerous professional societies, including the American Society for Clinical Investigation, the Association of American Physicians, the American Association of Immunologists, the American Society of Human Genetics, the American Federation for Clinical Research, the American College of Rheumatology, the Society for Inherited Metabolic Diseases, and the Harvey Society.

In 1985 Hirschhorn was the first woman to be elected to membership of the Interurban Clinical Club, and she served as president of the club in 1987.

In 2003 Hirschhorn was named a distinguished alumna of Barnard College, in 2010 she was named a master scientist of NYU Langone Medical Center, in 2013 she and Kurt Hirschhorn jointly won the Victor McKusick Leadership Award of the American Society of Human Genetics, and in 2014 she received the Thomas Waldman Human Immunology Award.

Gerard Karsenty, MD, PhD

Gerard Karsenty was born in Oran, Algeria, on February 12, 1954. He received his high school education in Beauvais France and medical education at the University of Paris V Medical School, and was a student of Interne Des Hopitaux de Paris from 1978 to 1985. During his internship Karsenty developed an interest in nephrology and endocrinology. He obtained a PhD in the laboratory of T. Drueke, where he pursued his graduate studies on the nongenomic action of vitamin D3.

Upon completion of his internship, Karsenty moved to the NIH in 1986 to become a postdoctoral fellow in the laboratory of B. de Crombrughe at the NCI and then at the M.D. Anderson Cancer Center in Houston, TX,

where the laboratory of de Crombrughe moved in 1987. Karsenty learned techniques and concepts of molecular biology as it applies to the study of gene expression in mammalian cells. After his postdoctoral fellowship Karsenty was offered a tenure-track assistant professor faculty position in the Department of Molecular Genetics at M.D. Anderson Cancer Center.

Karsenty's scientific activity has focused on the study of bone biology. This choice was justified by several reasons. First, given his expertise in the study of gene regulation, he felt there was an opportunity to identify a master transcription factor that determines the differentiation of mesenchymal cells into osteoblasts. Second, he believed that the understanding of molecular and genetic controls of the functions of the skeleton, bone modeling, bone remodeling, and bone mineralization was still only rudimentary. Third, in the early 1990's, Houston was one of the few cities where it was possible to learn how to generate mice lacking any gene of interest. This constellation explains why his laboratory developed along two distinct axes — one developmental, aimed at understanding the molecular bases of cell differentiation along the osteoblast lineage; the second centered around a genetic approach to bone physiology, with an interest in the control of bone extracellular matrix (ECM) mineralization and bone mass accrual.

Karsenty used as a tool the promoter of the mouse osteocalcin gene he had cloned. An analysis of the promoter allowed his laboratory to identify the only two known osteoblast-specific cis-acting elements (OSE1 and OSE2). He then used OSE2 as bait to identify what remains to this day the earliest determinant of osteoblast differentiation, the transcription factor Runx2. He showed that haploinsufficiency at the *RUNX2* locus causes a relatively frequent skeletal dysplasia called cleidocranial dysplasia. In subsequent studies he identified a role for Runx2 during chondrogenesis as well as negative regulators of Runx2 function during development in mice and in humans. The study of OSE1 allowed him to identify AFT4 as a second osteoblast differentiation factor that acts downstream of Runx2 and is needed for amino acid uptake in osteoblasts. In perspective, there are three osteoblast-enriched transcription factors involved in osteoblast differentiation, and Karsenty's laboratory identified and characterized two of these, Runx2 and ATF4.

Karsenty pursued from a genetic perspective an understanding of why extracellular matrix mineralization occurs only in bone and teeth. He used the then-nascent mouse genetic technology to study the functions of two

related proteins, osteocalcin and matrix Gla protein (MGP), that undergo the same posttranslational modification. This modification confers to protein high affinity for minerals. MGP is a chondrocyte and vascular smooth muscle cell-specific protein, whereas osteocalcin is an osteoblast-specific protein. The analysis of Mgp-deficient mice was a breakthrough in the study of the control of ECM mineralization. In *Mgp*^{-/-} mice all arteries of the body and all cartilaginous structures are mineralized; this indicates that ECM mineralization is negatively regulated outside the skeleton. In subsequent work Karsenty provided a comprehensive genetic analysis and explanation for why ECM mineralization occurs only in bone.

The study of osteocalcin functions did not shed light on the molecular bases of bone ECM mineralization, but instead opened two new areas of study in bone biology. The two main characteristics of the osteocalcin-deficient mice were that they were fat and extremely poor breeders. This led Karsenty to propose that there must be a common control of bone mass accrual, energy metabolism, and reproduction. This has been the overarching hypothesis of the physiological aspect of his work in the last 15 years. He discovered that leptin is likely the most powerful regulator of bone mass and identified a roadmap in the brain whereby leptin regulates bone mass, demonstrating the existence of a central control of bone mass. Karsenty also demonstrated that osteocalcin is a hormone that regulates energy metabolism and male fertility. This body of work verified genetically in mice and in humans that there is a coordinated regulation, endocrine in nature, of bone mass accrual, energy metabolism, and reproduction. Karsenty identified the receptor of osteocalcin and showed that it has the same function in mice and humans. He showed that osteocalcin crosses the blood-brain barrier, is needed for spatial learning and memory, and prevents anxiety and depression in the mouse. Furthermore, he demonstrated that maternal osteocalcin crosses the placenta and is necessary for hippocampal development in the embryo and for the establishment of memory, thus providing the first molecular basis for the long-noticed maternal influence on the neurological and psychological development of the offspring.

After Karsenty served as an assistant and associate professor of molecular genetics at M. D. Anderson Cancer Center, he moved to the Department of Human and Molecular Genetics at Baylor, where he worked as an associate and then full professor. Since 2006 he has been the Paul Marks Professor and chairman of the Department of Genetics & Development at Columbia University Medical Center. Karsenty has received several awards, such as the Edith and Peter O'Donnell Award from the Academy of Medi-

cine, Engineering and Science of Texas; the Drieu-Cholet Award from the French National Academy of Medicine; the Lee C. Howley Prize for Arthritis Research from the Arthritis Foundation; the Richard Lounsberry Award given jointly by the National Academy of Sciences (USA) and the French Academy of Sciences; the Jacobaeus Prize given by the NovoNordisk Foundation in Denmark; the Herbert A. Fleisch ESCEO-IOF Medal from the International Osteoporosis Foundation; and the William F. Neuman Award from the American Society for Bone and Mineral Research. He is also a member of the Association of American Physicians and of the Institute of Medicine.

John A. Kessler, MD

John (Jack) Kessler was born in Philadelphia, PA, on December 5, 1946. He received his AB degree from Princeton University in 1967 and his MD from Cornell University Medical College in 1971. He then completed his residency in internal medicine at Mount Sinai Hospital in New York City, spent two years as a research fellow at the National Cancer Institute, and completed a neurology residency at New York Hospital/Cornell Medical Center. He became an assistant professor of neurology at Cornell in 1978 and was promoted to associate professor at Cornell in 1982. In 1983 he moved to Albert Einstein College of Medicine, where he remained until 2000. He became professor of neurology at Einstein in 1987 and served as associate director of the Rose Kennedy Research Center from 1984 to 1993, then as the center's director from 1993 to 1998. He also served as vice chairman of neurology at Einstein and as chief of service of neurology at Jacobi-North Bronx Medical Center. In 2000 he moved to Northwestern University Feinberg School of Medicine, where he served as chairman of the Ken and Ruth Davee Department of Neurology from 2000 to 2012. He was the Benjamin and Virginia T. Boshes Professor of Neurology from 2000 to 2006 and was named the Ken and Ruth Davee Professor of Stem Cell Biology in 2006. He was appointed director of the Feinberg Clinical Neuroscience Institute in 2000 and director of the Northwestern University Stem Cell Institute in 2006. He became a member of the board of directors of Northwestern Memorial Foundation in 2001 and a member of the board of directors of the Rehabilitation Institute of Chicago in 2002.

Kessler was always fascinated by science and mathematics, and he majored in chemistry at Princeton. His interest in research was kindled by his senior thesis work in the chemistry laboratory of Charles Gilvarg. Although

he enjoyed working in the physical sciences, he decided that he wanted a career that would allow him to more directly interact with, and help, other people. His interest in medicine was further stimulated by his older brother Jeffrey, who had chosen a medical career. Although he did not take a single course in biology during his three years at Princeton, he decided on a career that combined medical research with the delivery of health care. He was interested in neurosurgery when he went to medical school, and he published 13 papers as a medical student working in a neurosurgery laboratory. However, he was inspired by the chairman of neurology, Fred Plum, who sparked his interest in becoming a research neurologist. During his time in the neurosurgery laboratory, Kessler was astonished to discover that virtually nothing could be done to actually repair a damaged nervous system. He decided as a medical student that he would devote himself to finding ways to regenerate the nervous system, the theme underlying his work over the following decades.

He decided that the key for developing tools for neural regeneration would be to define factors that regulate nervous system development, and he focused his initial work on the biology of growth factors. This remained one of the foci of his studies over the ensuing years. Since he believed that the peripheral nervous system would be the best initial target for neural regeneration, he established animal models of different neuropathies and demonstrated that growth factor administration could promote regenerative responses. This work led to several clinical trials of recombinant proteins in diabetic and other forms of neuropathy, which failed. However, his commitment to the endeavor persisted, and eventually he directed successful non-viral gene therapy trials of hepatic growth factor in diabetic neuropathy. In the early 1990s he recognized the potential power of neural stem cells to promote regeneration, and he became one of the early investigators in this area. He defined the role of bone morphogenetic proteins in promoting astrocyte lineage commitment and demonstrated their role in regulating adult neurogenesis. He decided that stem cells and growth factors alone would be insufficient to promote neural regeneration without the provision of an appropriate extracellular matrix. As part of a bioengineering research partnership, he pioneered the use of nanoengineered materials for promoting neural repair. A major portion of this work has focused on spinal cord injury.

Although the Department of Neurology at Northwestern was small and relatively unknown when Kessler became chairman, within a few years it was ranked among the top ten departments nationally by virtually ev-

ery research and clinical metric. Its clinical programs grew 22% annually, compounded over twelve years, and its subspecialty programs in sleep, cognition, neuromuscular disease, and movement disorders, among others became national leaders. The department's research funding also grew exponentially during this time, and Northwestern joined the top tier in neurology research. Kessler was awarded one of three NIH Centers of Excellence in human embryonic stem cell research and subsequently received a large program award for induced pluripotent stem cell research. The intent of these awards — and the goal of the entire neurology department — was to integrate the basic and clinical sciences and to develop new tools for treating the damaged or diseased nervous systems. Kessler's own work was continuously funded by the NIH for more than 35 years.

Kessler has received multiple awards and has served in numerous roles in addition to his primary academic missions. He is the founding editor-in-chief of the *Annals of Clinical and Translational Neurology*, served as associate editor of several other scientific journals, and served on the editorial board of *Nature Reviews Neurology*. A documentary film about his life and research was awarded a Peabody Award. He became a member of the Interurban Clinical Club in 1997 and a member of the Association of American Physicians in 2005. He has served on many scientific advisory panels, including the March of Dimes, the Peripheral Nerve Foundation, and the Brain Research Foundation. He served as a councilor of the American Neurological Association and was a member of many NIH and other scientific review panels.

Gary A. Koretzky, MD, PhD

Gary Koretzky was born in Orange, NJ. He received his AB from Cornell University and obtained his MD and PhD (immunology) degrees at the University of Pennsylvania. Koretzky then pursued clinical training in internal medicine and rheumatology at the University of California, San Francisco. He re-entered the laboratory as a postdoctoral fellow, examining the molecular events associated with T cell activation. Koretzky moved to the University of Iowa in 1991, where he continued his research examining the biochemistry and molecular biology of signal transduction in hematopoietic cells. He joined the faculty at the University of Pennsylvania in 1999 in the Department of Pathology and Laboratory Medicine and as director of the Signal Transduction Program of the Abramson Family Cancer Research Institute. Koretzky served as the chief of the Division of

Rheumatology from 2006 to 2008 and is currently the Francis C. Wood Professor of Medicine and vice chair for research and chief scientific officer in the Department of Medicine of the University of Pennsylvania School of Medicine. In addition to these responsibilities, Koretzky is an associate director of the combined-degree MD-PhD program and is on the executive committees of the Graduate Program in Immunology and the Graduate Program in Cellular and Molecular Biology. Koretzky is also the co-leader of the immunobiology program of the University of Pennsylvania Abramson Cancer Center.

Koretzky's research aims to better understand the signal transduction events that occur following engagement of the T cell antigen receptor. He has been continuously funded by the National Institutes of Health for 20 years, as the laboratory has expanded its interests to study more globally the molecular events important for immune cell development, differentiation, and function. Initial studies focused on the CD45 tyrosine phosphatase as a positive regulator of immunoreceptor signaling. This work led naturally to an examination of the key biochemical events that occur following receptor engagement. The Koretzky lab approach was to identify novel regulators of signal transduction following T cell receptor ligation, and their studies led to the isolation, characterization, and molecular cloning of several adapter molecules that are critical for the integration of signaling pathways. The laboratory has identified three such molecules, including SH2 domain-containing leukocyte protein of 76 kDa (SLP-76), adhesion and degranulation-promoting adapter protein (ADAP), and promyelocytic leukemia RAR α -regulated adapter molecule-1 (PRAM-1). There are ongoing projects studying the role of each of these molecules not only in T cells but also in other hematopoietic cells. In addition to studies of these positive regulators of immune signaling, the Koretzky laboratory has also had a long-standing interest in signals that interfere with activation events in T cells. This interest led to studies of FAS and FAS ligand and, more recently, the role of diacylglycerol kinases as terminators of lymphocyte activation.

Koretzky has published more than 200 research articles. He has been a member of the Interurban Clinical Club since 2007. He is a past president of the American Society for Clinical Investigation, a fellow of the American Association for the Advancement of Science, a councilor of the Association of American Physicians, and a member of the Institute of Medicine of the National Academy of Sciences, and he serves as the editor-in-chief of *Immunological Reviews* and as deputy editor of the *Journal of Clinical*

Investigation.

Donald W. Landry, MD, PhD

Donald W. Landry was born in Jersey City, NJ, on May 19, 1954, to Donald O. and Gloria A. Landry. An early interest in academics was fostered by his mother, who revered learning; a specific interest in science was fostered by his father, who rose through the ranks from loading dock laborer to senior plant superintendent at an industrial chemical company in New Jersey. Landry became the first in his family to attend college, graduating in three years *summa cum laude* and Phi Beta Kappa from Lafayette College with a BS degree in chemistry in 1975. He won a National Science Foundation Graduate Fellowship and a spot at Harvard, where he was accepted into the research group of Nobel laureate R.B. Woodward — the father of modern organic chemistry. In 1979 he received his PhD in organic chemistry and, anticipating the increasingly biological future of organic chemistry, promptly went off to medical school at Columbia University's College of Physicians and Surgeons. He graduated Alpha Omega Alpha and went to Massachusetts General Hospital for internship and residency in internal medicine. He short-tracked through the 3-year program in 2 years and returned to Columbia as a National Institutes of Health physician-scientist in 1985 at the rank of instructor in medicine. He has since remained at Columbia, rising through the ranks to become the Samuel Bard Professor and chair of the Department of Medicine and physician-in-chief of New York Presbyterian Hospital/Columbia University Medical Center.

In 1991 Landry established a laboratory at Columbia that focuses on organic chemical solutions to intractable medical problems. He developed the first transition-state analogs for cocaine hydrolysis, and his report in *Science* on the first artificial enzymes to degrade cocaine was voted by the American Chemical Society as one of the 25 most important chemistry papers in the world in 1993. One of the enzymes he developed has advanced to clinical development.

Landry's clinical training in nephrology evolved into an interest in critical illness complicated by renal failure due to shock. In the context of this interest, he made a clinical observation that led to the discovery of a new hormone-deficiency state, vasopressin deficiency in vasodilatory shock. He pioneered the use of vasopressin to treat vasodilatory shock, and vasopressin replacement therapy is estimated to have saved thousands of lives worldwide. In 2003 he became director of the Division of Nephrology.

In 1998 he founded the Division of Experimental Therapeutics in the Department of Medicine to bring individuals with PhDs in synthetic organic chemistry into Columbia's Health Sciences Campus. Landry also founded and directed Columbia's Doris Duke Clinical Research Fellowship Program, which became the largest and most prolific of the ten Doris Duke programs.

Landry also pioneered an alternative method for the production of human embryonic stem cells that relies on harvesting live, normal cells from embryos that, by objective, peer-reviewed criteria, have died of natural causes. Cells harvested from dead embryos are covered under the established ethics undergirding transplantation of essential organs from deceased donors.

Landry is a member of the Empire State Stem Cell Board ethics committee, the American Chemical Society, the New York Academy of Sciences, the American Society for Clinical Investigation, and the Association of American Physicians. He was a member of the President's Council on Bioethics from 2008 to 2009 and is co-chairman, along with Robert P. George, of the Witherspoon Council on Ethics & the Integrity of Science. Landry received the Presidential Citizen's Medal, the nation's second-highest civilian honor, from President George W. Bush at the Oval Office in 2008 for "diverse and pioneering research and his efforts to improve the well-being of his fellow man."

John Nichols Loeb, MD

John N. Loeb was born in New York City on December 17, 1935. He graduated summa cum laude from both Harvard College and Harvard Medical School, and after an internship at Massachusetts General Hospital he moved to New York City for a year as an assistant resident on the medical service of the Presbyterian Hospital. After two years as a research associate with Gordon M. Tomkins in the Laboratory of Molecular Biology at the Institute of Arthritis and Metabolic Diseases at the National Institutes of Health, he returned to New York to serve as chief resident in medicine at the Presbyterian Hospital and instructor in medicine at the College of Physicians and Surgeons of Columbia University. He has remained affiliated with both institutions and since 2005 has been professor emeritus of medicine and special lecturer in medicine at Columbia University. He continues to serve as an attending physician at New York–Presbyterian Hospital.

Loeb's research was principally focused on the mechanisms of hormone action, the physical chemistry of receptor-ligand interactions and their quantitative relationship to biological response, and the regulation of glucose and monovalent cation transport. During his investigative career he chose to maintain a relatively small laboratory so that he could devote considerable time to bench-work; his work was continuously supported by the National Institutes of Health from 1967 to 1999, with support during the final ten years coming from an NIH MERIT Award.

From 1997 until 2003 Loeb served as associate chairman for research in the Department of Medicine and, from 2003 until his retirement, as vice chairman for academic affairs. Throughout his career he has had an abiding interest in teaching, particularly in bedside teaching, and for a number of years was director of the third-year clinical clerkship in the Department of Medicine. He has received numerous teaching awards at Columbia and has devoted substantial time to teaching abroad. He is a member of the American Society for Clinical Investigation, the Association of American Physicians, and the Practitioners Society of New York and is a fellow of the American Association for the Advancement of Science. He was elected to membership in the American Philosophical Society in 1998 and received a Distinguished Service Award from the Columbia University College of Physicians and Surgeons in 2007.

Aaron J. Marcus, MD

Aaron J. Marcus was born in Brooklyn, NY, on November 6, 1925. He received his early education in Boys' High School in New York, followed by a BA degree from the University of Virginia in 1948. He served as a medic in the Fleet Marine Force of the US Navy from 1944 to 1946, then received his medical education from New York Medical College in New York City in 1953. He followed this with a residency in internal medicine at Montefiore Hospital in New York (1955–1956) and a research fellowship in hematology (1956–1958).

The genesis of his interest in research originated during his tenure in the US Fleet Marine Force, where he took care of severe casualties and had the opportunity to treat patients with a new pharmaceutical agent known as penicillin. When Marcus began studying the mechanisms of hemorrhage, coagulation, and thrombosis, he found that calcium shortened the time for the blood coagulum to form; substances that were capable of accelerating

the clotting time were said to be “thromboplastic.” Marcus then decided to develop thromboplastic moieties, which would shorten the clotting time in the absence of platelets. New technological methods made possible the separation of lipid components of cells, such as platelets, in order to identify one or more platelet lipids from extracts of whole platelets. His studies of lipids in coagulation gave rise to the partial thromboplastin time (PTT) test, which is used to detect abnormalities in coagulation, such as prolonged coagulation in hemophilia, and is used worldwide. Subsequently, he performed experiments involving radiolabeled aspirin and platelets, to ascertain the aspirin-binding site on platelets. In these studies he used one preparation of aspirin with a radioactive acetyl group and a separate preparation with a radioactive hydroxyl group. He found that only the acetyl group was taken up by the platelets, and he believed this was the definitive experiment to demonstrate that only the acetyl group was involved in platelet inhibition.

During his studies involving metabolic interactions between heterologous cells, it became obvious that no further inroads could be made into the comprehension of thrombosis unless techniques were developed to allow simultaneous study of several cells, so that the metabolic interactions of intermediate and end products between multiple cells could be observed. Marcus developed the locution “transcellular metabolism” and originated a classification system for the entire group of cells under study. He then initiated studies of cell-cell interactions, and observed that combined cells showed altered biological behavior. Through these studies he demonstrated that there is a close metabolic relationship between inflammation and thrombosis. When he initiated studies between activated blood platelets and endothelial cells, he made an unanticipated observation that set the stage for future research.

The critical aspect of his research is based on his discovery that platelets in motion, and in proximity to endothelial cells, could not respond to any platelet agonist. Marcus obtained similar results when he admixed platelets and endothelial cells in a suspension or admixed platelets over an endothelial cell monolayer in a flask. This inhibition, he found, was due to an ectonucleoside triphosphate diphosphohydrolase known as NTPDase-1. He demonstrated that this enzyme metabolizes prothrombotic ADP from an activated platelet releasate to AMP. The enzyme was cloned and identified as CD39. This enzyme is an integral membrane protein; it has two transmembrane domains at the N and C termini and short cytoplasmic tails. Subsequently, Marcus generated a recombinant, soluble form of hu-

man CD39 (solCD39), which retained nucleotidase activities and inhibited agonist-induced platelet reactivity. A CD39-knockout mouse was created that could not withstand a stroke, but Marcus showed that this could be corrected by administration of solCD39 prior to, during, and after stroke. In addition, in a porcine model of acute coronary balloon injury, solCD39 resulted in a trend toward decreased platelet and fibrin deposition. Moreover, Marcus showed that systemic administration of solCD39 profoundly affects injury-induced cellular responses, minimizing platelet deposition and leukocyte recruitment and suppressing neointimal hyperplasia.

His 19 years of research on CD39 and 57 years of research on hemostasis led Marcus to propose that CD39 represents the main control system for blood fluidity and a new treatment for stroke in patients. Many molecular biological aspects of CD39 are now under exploration, such as its endocytic recycling and participation in the inflammatory response. Studies are currently underway to increase production of CD39 for larger animal studies, and eventually for administration to thrombosis patients, whose platelets have low thresholds for reactivity and thereby are prothrombotic. At present, three groups of stroke patients (those with cryptogenic stroke, stroke-prone sleep apnea, and atherothrombotic stroke) are under study for their threshold of platelet reactivity to multiple agonists.

Marcus is currently professor of medicine and of pathology and laboratory medicine at Weill Cornell Medical College in New York. He has received multiple awards, including the Interurban Clinical Club, the International Senior Aspirin Award from Bayer (2001), the Distinguished Career Award from the International Society on Thrombosis and Haemostasis, and the Wallace H. Coulter Award for Lifetime Achievement in Hematology from the American Society of Hematology. He was also the originator of the educational program of the American Society of Hematology and received the citation for distinguished service from the American Society for Clinical Investigation (for which he also served as a member of the editorial committee of the *Journal of Clinical Investigation*). He was also the William B. Castle Lecturer at Harvard Medical School and a Henry M. Stratton Lecturer of the American Society of Hematology. Moreover, he was the recipient of an NIH NHLBI MERIT Award (2004–2014).

Paul A. Marks, MD

Paul Marks was born on August 16, 1926, in New York City. He received his AB from Columbia College in 1945 and his MD from the Columbia University College of Physicians and Surgeons in 1949. After serving as intern and resident in medicine at the Presbyterian Hospital in New York, he spent two years as an associate in the laboratory of enzymology at the National Institute of Arthritis and Metabolic Diseases. He then returned to Columbia to begin research on the mechanisms of cell differentiation and hereditary diseases that affect red blood cells. Marks rose through the ranks from instructor in medicine (1955–1956) to the Frode Jensen Professor of Medicine (1967–1980) and professor of human genetics and development (1969–1980). Prior to assuming the positions of dean and vice president of medical affairs in 1970, he was chairman of the department of human genetics and development. He was the first director of the Comprehensive Cancer Center and vice president for health sciences at Columbia University (1973–1980). In 1961–1962, he served as a visiting scientist in the laboratory of cellular chemistry at the Pasteur Institute in Paris. He was president and chief executive officer of the Memorial Sloan Kettering Cancer Center from 1980 until 2000 and is now president emeritus.

Marks is a specialist in hematology-oncology and human genetics, and his research in recent years has centered on the mechanisms of differentiation and neoplastic transformation of blood cells. His research activities, related to cellular and molecular aspects of erythroid cell differentiation and globin synthesis, have provided contributions to our understanding of (a) the genetic basis of glucose-6-phosphate dehydrogenase deficiency, (b) the synthesis and function of globin mRNA, (c) the structure and function of polyribosomes, (d) the nature of the genetically determined defect in thalassemia syndromes, (e) the mechanisms of action of erythropoietin in erythroid cell differentiation, and (f) the mechanism of erythroid cell differentiation in virus infected cells. He has also contributed to the isolation of the precursor cell of erythroid cells, which is induced to differentiate by erythropoietin in cell culture, and to the development of polar/planar molecules, induce differentiation in transformed cells and which have been approved by the FDA to treat leukemia and lymphoma.

Marks was the first to show that a selective decrease in glucose-6-phosphate (G6P) dehydrogenase activity was an important aspect of the determinants of red blood cell life span. Studies on G6P dehydrogenase defined the genetically determined deficiency of this enzyme, which predisposes

to a wide variety of clinically important hemolytic anemias. Marks provided the initial evidence for genetic heterogeneity of G6P dehydrogenase deficiency. In collaboration with Frangois Gros, Marks was one of the first to establish that mRNA for globin is stable and continues to be translated for a considerable time after RNA synthesis has ceased. Studies of globin mRNA translation provided some of the initial evidence for the structure and function of polyribosomes. Marks and his associates demonstrated the reversible polyribosome association and dissociation in reticulocytes, and the conservation of globin mRNA under conditions in which it was not translated.

Marks also showed that the genetic abnormality in thalassemia syndromes causes a decrease in one or another globin mRNA associated with polyribosomes, and that this accounts for the selective deficiency in synthesis of β globin in beta-thalassemia. The hemolytic anemia in thalassemia is fatal in the homozygous state. This anemia results from the instability of the excess α over β chains formed which precipitate intracellularly and lead to the early destruction of erythroid cells. In subsequent studies on erythroid cell differentiation, he established a cellular basis for the changing pattern of hemoglobin synthesis that occurs during fetal and postfetal development. He also showed that in Friend virus infected cells, the induction of erythroid differentiation by dimethylsulfoxide requires DNA synthesis to initiate transcription of the globin structural gene.

He and his colleagues identified and synthesized a group of polar/planar compounds exemplified by hexamethylene bisacetamide that are potent inducers of differentiation of various transformed cells. Marks collaborated with Richard Rifkind and Ronald Breslow for 35 years on these studies, and they demonstrated that induced differentiation is a multistep process that involves modulation and expression of a number of genes, including those that control the production of various proteins involved in the regulation of cell-cycle progression (particularly the progression from G1 phase to S phase). In collaboration with colleagues at Sloan Kettering and the MD Anderson Cancer Center, Marks reported the first clinical trials demonstrating that the cyto-differentiation inducers HMBA and SAHA (Zolinza) can cause both partial and complete remission, albeit transient, in myelodysplastic syndrome and leukemias and lymphomas.

Marks is a past president of the American Society for Clinical Investigation, the Harvey Society, and the American Society of Hematology and is a past editor-in-chief of the *Journal of Clinical Investigation* and *Blood*. He

has served as an advisor to the National Institutes of Health, the National Science Foundation, and other government bodies. He served as a member of the President's Cancer Panel, the President's Biomedical Research Panel, and the President's Commission on the Accident at Three Mile Island. He was a member of the council of the National Academy of Sciences and the council of the Institute of Medicine and was chair of the National Research Council Division of Medical Sciences of the National Academy of Sciences.

Marks has received a number of honors, including the Distinguished Achievement Medal from the Columbia University College of Physicians and Surgeons. Columbia University had previously awarded him the Jane-way Prize, the Joseph Mather Smith Prize, the Stevens Triennial Prize, and the Bicentennial Medal. In 1994 he was awarded the Gold Medal of the Alumni of the Columbia University College of Physicians and Surgeons for academic achievement. He received a medal from the Japan Foundation for Cancer Research, the Centenary Medal of the Pasteur Institute, and honorary degrees from six universities. In 1991 he received the presidential National Medal of Science.

Andrew R. Marks, MD

Andrew R. Marks was born February 22, 1955, in New York City. He received his undergraduate degree from Amherst College in 1976, where he was the first student in the history of the college to graduate with honors in two subjects (biology and English), and his MD degree from Harvard Medical School in 1980. Following an internship and residency in internal medicine at Massachusetts General Hospital (MGH), he was a postdoctoral fellow in molecular genetics at Harvard Medical School and then a clinical cardiology fellow at MGH. He is board certified in internal medicine and in cardiology. In 1987 Marks joined the faculty of the cardiology division at Brigham and Women's Hospital. In 1990 he moved back to his hometown of New York City to serve as an assistant professor of molecular biology and medicine at Mount Sinai School of Medicine, where he also served as an attending physician in cardiology. In 1995 he was named the Fishberg Professor of Medicine at Mount Sinai. He was recruited to Columbia University College of Physicians & Surgeons in 1997 to serve as the founding director of the Clyde and Helen Wu Molecular Cardiology Center and as the Clyde and Helen Wu Professor of Medicine and Pharmacology. In 2003 Marks was appointed chair and professor of the Department of Physiology and Cellular Biophysics at Columbia University.

He was elected to the council of the American Society for Clinical Investigation (ASCI; 1997–2000) and from 2002 to 2007 served as editor-in-chief of the *Journal of Clinical Investigation*.

His honors include the Established Investigatorship Award (1993) and the Basic Research Prize (2005) from the American Heart Association, the Distinguished Clinical Scientist Award from the Doris Duke Charitable Foundation (2000), the Dean's Distinguished Lecturer in Basic Science from Columbia, and memberships in ASCI (1995) and the Association of American Physicians (1999). He was elected in 2004 to the Institute of Medicine of the National Academy of Sciences and, in 2005, to the American Academy of Arts and Sciences and the National Academy of Sciences. He has received an honorary doctor of science degree from Amherst College (2009), the ASCI Stanley J. Korsmeyer Award (2010), the Pasarow Foundation Award for Cardiovascular Research (2011), and the Ellison Medical Foundation Senior Scholar in Aging Award (2011). In 2015 Marks was chosen to present the Ulf von Euler lecture at Karolinska Institutet. Marks has served on the NHLBI Advisory Council (2007–2011) and scientific advisory boards for Centocor and Novartis, and is on the advisory committee of the Gladstone Institute of Cardiovascular Disease and the Harrington Discovery Institute. Marks chairs the scientific advisory board of ARMGO Pharma, Inc., a company he founded in 2006 to develop novel therapeutics for heart, muscle, and CNS diseases, and is the inventor on nine US patents for these new treatments. In 2001 he founded the Summer Program for Under-Represented Students (SPURS) at Columbia, which provides mentored research training at Columbia for minority students from the New York City public colleges and universities. In 2002 Marks founded the International Academic Friends of Israel, a nonprofit organization devoted to promoting and supporting the free and open exchange of ideas and information in the international academic community that seeks to ensure that Israeli academics and scientists are included and accepted in global academic and scientific circles.

Marks's interest in fundamental biological processes and translating new understandings into therapies for patients first led to his identification of the mechanism of action of rapamycin in the inhibition of vascular smooth muscle proliferation and migration. This discovery was the basis for the development of the first drug-eluting stent (coated with rapamycin) for treatment of coronary artery disease, which substantially reduced the incidence of in-stent restenosis. He also showed that rapamycin reduced accelerated arteriopathy following cardiac transplantation. Over the past 25

years the major focus of his work has to elucidate the role of intracellular calcium in regulating fundamental cellular processes such as cardiac and skeletal muscle contraction, lymphocyte activation, cognitive function, and glucose metabolism. Marks defined the structure, function, and regulation of the intracellular calcium release channels known as ryanodine receptors and inositol-1,4,5-trisphosphate receptors. In 2014 he reported the high-resolution structure of the mammalian type 1 ryanodine receptor/calcium release channel (required for excitation-contraction coupling in skeletal muscle), which he had cloned and worked on since 1989. He discovered that “leaky” intracellular calcium release channels contribute to heart failure, fatal cardiac arrhythmias, impaired exercise capacity (e.g., in muscular dystrophy), post-traumatic stress disorder (PTSD), Alzheimer’s disease, and diabetes. Marks developed in his laboratory a new class of small molecules, called Rycals, that target leaky ryanodine receptor channels and have been shown in preclinical studies to effectively treat cardiac arrhythmias, heart failure, and muscular dystrophy and prevent stress-induced cognitive dysfunction. Phase II clinical trials are currently underway to study the efficacy and safety of Rycals in the treatment of heart failure and cardiac arrhythmias, and additional clinical trials are beginning to test their use in the treatment of Duchenne muscular dystrophy.

Carl Nathan, MD

Carl Nathan is the R. A. Rees Pritchett Professor and chairman of the Department of Microbiology and Immunology at Weill Cornell Medical College and co-chair of the Program in Immunology and Microbial Pathogenesis at Weill Graduate School of Medical Sciences of Cornell University.

After graduation from Harvard College and Harvard Medical School, he trained in internal medicine and oncology at Massachusetts General Hospital, the National Cancer Institute, and Yale before joining the faculty of Rockefeller University from 1977 to 1986. At Cornell since 1986, he has served as Stanton Griffis Distinguished Professor of Medicine, founding director of the Tri-Institutional MD-PhD Program, senior associate dean for research, and acting dean. Nathan is a member of the National Academy of Sciences and the Institute of Medicine, a fellow of the American Academy of Microbiology, associate scientific director of the Cancer Research Institute, and a governor of the Tres Cantos Open Lab Foundation. He serves on the scientific advisory boards of the American Asthma Foundation and the Rita Allen Foundation and on the juries of the Lurie Prize

and the Paul Marks Prize.

He served for ten years on the scientific advisory board of the Cambridge Institute for Medical Research and on the board of trustees of the Hospital for Special Surgery. He has been an editor of the *Journal of Experimental Medicine* since 1981 and joined the editorial board of *PNAS* in 2014. He was awarded the Robert Koch Prize in 2009 for his work on tuberculosis and the Anthony Cerami Award in Translational Medicine in 2013.

Nathan's research deals with the immunological and biochemical basis of host defense. He established that lymphocyte products activate macrophages, that interferon- γ is a major macrophage-activating factor, and that mechanisms of macrophage antimicrobial activity include induction of the respiratory burst and inducible nitric oxide synthase (iNOS). He and his colleagues purified, cloned, knocked out, and characterized iNOS biochemically and functionally; discovered the cofactor role of tetrahydrobiopterin in NOSs; and introduced iNOS as a therapeutic target. Although iNOS helps the host to control *Mycobacterium tuberculosis*, the leading cause of death from bacterial infection, *M. tuberculosis* resists sterilization by host immunity. Nathan's lab now focuses on the biochemical basis of this resistance. They have used genetic and chemical screens to identify enzymes that *M. tuberculosis* requires to survive during non-replicative persistence, including the mycobacterial proteasome and components of pyruvate dehydrogenase that serve in peroxynitrite reductase.

His group is identifying compounds that kill non-replicating bacteria and, in doing so, is testing new collaborative models between academia and industry to help invigorate antibiotic research and development.

Benjamin G. Neel, MD, PhD

Ben Neel was born just outside of Philadelphia on April 13, 1956. He received his AB from Cornell University in 1977, his PhD in viral oncology (under William S. Hayward in the laboratory of Hidesaburo Hanafusa) from Rockefeller University in 1982, and his MD from Cornell University Medical College in 1983. He then completed residency training in internal medicine at the former Beth Israel Hospital (now Beth Israel-Deaconess Medical Center) from 1983 to 1987, with an overlapping postdoctoral fellowship in the laboratory of Raymond Erikson in the Department of Cellular and Developmental Biology at Harvard University. He was appointed

assistant professor of medicine at Harvard Medical School and a member of the Molecular Medicine Unit at Beth Israel in 1988. He rose through the ranks at HMS, becoming professor of medicine in 1999. He served as the director of the Cancer Biology Program beginning in 1994, and as deputy director for basic research in the Hematology/Oncology Division at Beth Israel–Deaconess Medical Center beginning in 2003. In 2006 he was appointed to the William B. Castle Chair of Medicine at HMS. In 2007 he relocated to Toronto, where he was appointed director of research at the Princess Margaret Cancer Center/Ontario Cancer Center and senior scientist and Tier 1 Canada Research Chair in the departments of medical biophysics and biochemistry at the University of Toronto. In 2015 he became director of the Isaac and Laurie Perlmutter Cancer Center and professor of medicine at NYU Langone Medical Center.

When he was young, Neel's grandmother Ida encouraged him to become a physician, and he spent much of his time watching medical shows like *Dr. Kildare*, *Ben Casey*, and *Medical Center*. He spent the summer of 1972 at the NSF-sponsored program in biochemistry at the Windsor School, which sparked his passion for biomedical research. Ida's death the following year from non-smoking-associated lung cancer triggered his interest in cancer biology and medicine, which was accentuated by a particularly influential genetics course at Cornell taught by Peter Bruns and by organic and physical chemistry courses taught by Jerry Meinwald, Harold Scheraga, and Ben Widom.

Oncogenic mechanisms and cell signaling have been major foci of Neel's research. His graduate work established that slowly transforming retroviruses cause cancer by activating cellular oncogenes. This set the stage for further research into the cognate mechanism by which many cancer-associated chromosomal translocations are oncogenic. As an independent investigator he has made multiple contributions to the signal transduction field, particularly regarding protein-tyrosine phosphatases (PTPs) and their binding proteins. His group identified many PTPs, including PTP1B, SHP1 (identified with Bob Rosenberg), and SHP2. He provided evidence for the "zip code" model for PTP regulation by showing that PTP1B localizes to the ER via a specific targeting sequence, and together with Philippe Bastiaens, he found that receptor tyrosine kinases (RTKs) traffic past the ER to be dephosphorylated. In a 15-year collaboration with Barbara Kahn, he established PTP1B as a key regulator of insulin and leptin signaling and an attractive target for diabetes/obesity and cancer. He identified SHP2 as the first PTP required for vertebrate development, established its reg-

ulatory and signaling mechanisms, and uncovered the molecular pathogenesis of SHP2 mutations in Noonan syndrome, LEOPARD syndrome, metachondromatosis, and various cancers. He purified/cloned the SHP2 binding protein GAB2 and established its key role in allergy, chronic myeloid leukemia, and breast cancer. He identified SHP1 and, in collaboration with Cliff Lowell and Pam Ohashi, has elucidated its cellular roles in inflammation and autoimmunity. His lab has generated multiple widely used mouse models of RASopathies and cancer. Most recently, he has expanded his interest to include breast cancer functional genomics and ovarian cancer biology.

As director of the Cancer Biology Program and deputy director for basic research at Beth Israel, Neel recruited several new investigators and helped substantially increase the funding and impact of the division. As director of research at Princess Margaret Cancer Center, he recruited over 20 investigators, more than half from out of the country. During his tenure extramural funding and philanthropy increased by approximately 50% each, and there were substantial increases in high-impact publications by researchers from the center. The center also launched new programs in clinical genomics (including the only NGS-based tumor sequencing program in Canada), tumor immunology/immunotherapy (including the only tumor-infiltrating lymphocyte program in Canada), epigenetics, and computational biology (including a High-Performance Computing Initiative for Health, in collaboration with the Hospital for Sick Children). He also co-founded Northern Biologics, the largest biotech startup in Canadian history.

Neel is the author of more than 200 original papers, several in leading scientific journals such as *Cell*, *Molecular Cell*, *Developmental Cell*, *Science*, *Nature*, *Nature Medicine*, and *Nature Genetics*. He is a member of the board of directors of the American Association for Cancer Research (AACR) and served as program chair for the association's 2012 annual meeting. He received a Junior Faculty Research Award from the American Cancer Society, was the inaugural recipient of the Gertrude Elion Award of the AACR, received the Premier of Ontario's Summit Award (Ontario's highest scientific honor) in 2009, and received an NIH MERIT Award. He has served on study sections and ad hoc review panels for the NIH, the American Cancer Society (Massachusetts division), the Starr Foundation, and the California tobacco and breast cancer research programs. He also was an editor of *Molecular and Cellular Biology* (2000–2010) and currently serves on the editorial boards of *Cancer Cell*, *Molecular Cell*, the

Journal of Experimental Medicine, the *Journal of Clinical Investigation*, and *Cancer Discovery*. He is a member of the scientific advisory board of Kolltan Pharmaceutical, Inc., an antibody drug discovery company, on the scientific advisory board and board of directors of Northern Biologics, and was a long time member of the scientific advisory board for CEPTYR, Inc., a biotechnology company whose goal was to discover PTP inhibitors for the treatment of diabetes, obesity, and cancer.

Maria I. New, MD

Honorary member

Maria New was born in New York, NY, on December 11, 1928. New earned her undergraduate degree from Cornell University and a distinguished MD degree from the Perelman School of Medicine at the University of Pennsylvania. She completed an internship in medicine at Bellevue Hospital in New York, followed by a residency in pediatrics at the New York Hospital. From 1957 to 1958 she studied renal function under a fellowship from the NIH. She was a research pediatrician to the Diabetic Study Group of the Comprehensive Care Teaching Program at the New York Hospital–Cornell Medical Center from 1958 to 1961 and completed a second NIH fellowship under Ralph E. Peterson from 1961 to 1964, to study specific steroid hormone production during infancy, childhood, and adolescence.

In 1964 New was appointed chief of pediatric endocrinology at Cornell University Medical College, a position she held for 40 years. In 1978 she was named Harold and Percy Uris Professor of Pediatric Endocrinology and Metabolism. In 1980 New was appointed chairman of the Department of Pediatrics at Cornell University Medical College and pediatrician-in-chief of the Department of Pediatrics at New York–Presbyterian Hospital. She was one of the few women in the country to serve as chair of a major department of a medical college, and her distinguished tenure lasted for 22 years. While chairman, New founded and directed the eight-bed Children’s Clinical Research Center, one of the nation’s most productive clinical research centers in pediatrics, which conducted groundbreaking research in pediatric endocrinology, hematology, and immunology during the emergence of AIDS. In 2004 New was recruited to the Mount Sinai School of Medicine as professor of pediatrics and human genetics and director of the Adrenal Steroid Disorders Program. She is currently adjunct professor of genetics at Columbia College of Physicians and Surgeons and associate dean for research at the Herbert Wertheim College of Medicine

at Florida International University.

New is recognized as one of the world's leading pediatric endocrinologists. Though always concerned with the well-being of her patients, New had been interested in the mechanisms of disease and decided to enhance her clinical work by pursuing investigative science. Her career exemplifies the link between clinical and basic science. She has remained in the vanguard of science, pioneering the use of molecular genetic diagnosis and prenatal diagnosis and treatment. Although steroid physiology was well understood when New began her scientific career, little of the knowledge had been applied to the understanding of steroid disorders in children. New's seminal research on the mechanism and genetics of steroid disorders has established standards for pre- and postnatal care for patients with congenital adrenal hyperplasia and apparent mineralocorticoid excess (AME). During a 43-year period, New held the NIH grant with the longest continuous funding, "Androgen Metabolism in Childhood," which supported research to characterize the diverse clinical spectra of patients with rare steroidogenic enzyme defects, such as congenital adrenal hyperplasia, and the metabolic consequences of those defects.

In 1977 New first described AME in a Zuni girl. Her team was the first to publish mutations on the 11 β -hydroxysteroid dehydrogenase type 2 (11 β -HSD2) enzyme (encoded by the *HSD11B2* gene), which causes this potentially fatal form of low-renin hypertension. New opened a new field of research into receptor biology by demonstrating the action of the 11 β -HSD2 enzyme at the mineralocorticoid receptor of the distal renal tubule to metabolize cortisol to cortisone and thus protect the receptor. This was the first demonstration of the metabolism of a ligand to down-regulate its action on receptor activation.

In 1979 New described a form of mild steroid 21-hydroxylase deficiency, called nonclassical 21-hydroxylase deficiency, which is characterized by diverse hyperandrogenic symptoms that appear postnatally in males and females. New documented in 1985 the remarkable prevalence of a mild form of CAH in 1 of 27 Ashkenazi Jews, and the genetic frequency of the mutation is 1 in 3 in the Ashkenazi Jewish population. These studies established non-classical 21-hydroxylase deficiency as the most frequent disorder of all autosomal recessive diseases in humans. Although a spectrum of severity of CAH had always been observed, New was first to identify the mild form with specific molecular mutations.

Her current primary research emphasis is on genetic steroid disorders. New continues to study three monogenic disorders: 21-hydroxylase deficiency, 11 β -hydroxylase deficiency, and apparent mineralocorticoid excess, with an emphasis on genotype/phenotype correlation and prenatal diagnosis and treatment. She has published more than 640 academic articles in a wide range of journals and, in 2014, a book entitled *Genetic Steroid Disorders*. She has received numerous awards and recognition for her work treating mothers and children affected with the disorder.

New is an active member of the New York State Public Health Council, the Public Health Policy Advisory Board, the National Advisory Research and Resources Council of the National Institute of Child Health and Human Development, the national advisory committee for the Harold Amos Medical Faculty Development Program of the Robert Wood Johnson Foundation, the Task Force on Childhood Violence, and the Leading Edge Endowment Fund of British Columbia. She also serves as a consultant for the New York State Newborn Screening Program and for the US Food and Drug Administration's Endocrinologic and Metabolic Drugs Advisory Committee, was president of the Endocrine Society in 1992, and was editor-in-chief of the *Journal of Clinical Endocrinology and Metabolism* for over six years. In 2006 she was awarded the Allan Munck Prize conferred by Dartmouth Medical School. New was elected to the Hall of Honor of the NIH, has received an NIH MERIT Award, and served as editor for over 15 leading medicals journals and textbooks. New has received two grants from the Genesis Foundation of New York to study Jewish genetic disorders. In 1996 she was elected to the National Academy of Sciences, and she is one of two pediatricians to be members of the Academy. New was honored with the Fondation IPSEN 2014 Endocrine Regulations Prize for "outstanding work" in pediatric endocrinology and her "fundamental advances".

Mark Philips, MD

Mark Philips was born at Mount Sinai Hospital in New York City on April 21, 1956, the oldest child of a teacher and a medical illustrator. In 1961 his father, Gerald Philips, founded Kallir, Philips, Ross, Inc., which grew to become the largest pharmaceutical advertising company in the world. Raised in Scarsdale, NY, Philips attended Harvard College (BA, 1978) and Columbia University College of Physicians and Surgeons (MD, 1982). At Harvard he completed an honors thesis in genetics in the laboratory of Richard Kes-

sin, who later became dean of science at Columbia, and studied immunology with Baruj Benacerraf and John David at Harvard Medical School. At Columbia his work with Leonard Chess led to a heightened interest in immunology. Philips trained in internal medicine at Bellevue Hospital during the cataclysmic early phase of the AIDS epidemic. He remained at New York University and Bellevue for a fellowship in rheumatology. As a rheumatology fellow Philips joined the laboratory of Gerald Weissman, where he studied neutrophil activation and adhesion. He continued his training at NYU in cell biology in the laboratory of David Sabatini, where Philips studied the role of small GTPases in neutrophil degranulation.

His postdoctoral work led him to study the post-translational modification of Ras and other small GTPases, an area in which he has focused his independent research career. Philips has made seminal contributions to the cell biology of small GTPases. In 1998 he cloned isoprenylcysteine carboxyl methyltransferase (Icmt), the third of three enzymes that modify CAAX proteins including Ras. This work led to discoveries that elucidated the subcellular trafficking and endomembrane signaling of Ras. As a consequence of his contributions to Ras biology, Philips's focus shifted from inflammation to cancer biology and his funding source shifted from the NIAID to the NCI. In 2002 he joined Steven Burakoff at the revitalized NYU Cancer Institute as associate director for basic research. A champion of training for physician-scientists, in 2011 Philips became the seventh director of the NYU Medical Scientist Training Program, which is among the three oldest federally funded MD-PhD programs in the nation (initially funded in 1964).

Philips was a recipient of the Young Scholars Award from the Arthritis Foundation as well as the Burroughs Wellcome Fund Clinical Scientist Award in Translational Research, the Orloff Award for Biomedical Research, and the NYC BioAccelerate Prize. Since 1991 he has been continuously funded by the NIH. He is a member of the American Society for Clinical Investigation, the Association of American Physicians, and the Interurban Clinical Club.

Philips is married to Sylvia Stein, a marketing and innovations consultant. They have three children: Sarah Rose, who is a medical student; Elliot Abraham, who is enrolled in an MD-PhD program; and Eva Pearl, who is beginning engineering at Tufts.

Herbert H. Samuels, MD

Herb Samuels was born in New York City on November 12, 1939. Samuels attended Tufts College and graduated from the NYU School of Medicine in 1965. During his time at the NYU Samuels became interested in research. From 1965 to 1967 he was an intern and resident in the Department of Medicine at Albert Einstein College of Medicine under Irving London. He then went to the NIH for the next two years as a Research Associate under Gordon Tomkins, head of the Laboratory of Molecular Biology. In July 1969, he accepted the invitation of Saul Farber to join the Department of Medicine at the NYU School of Medicine as an Instructor. From 1970-1974 he was an Assistant Professor and from 1975-1977 was an Associate Professor. In 1977, he was promoted to professor of medicine and became Director of the Division of Molecular Endocrinology. He was also co-director of the Honors Program at NYU and an Attending Physician at the NYU-Tisch and Bellevue Hospitals. In 1998 Samuels became Head of the Division of Diabetes, Endocrinology and Metabolic Diseases, a position he held until 2003 when he became the Kimmelman Professor and Chair of the Department of Pharmacology at NYU.

As a medical student, he worked with Robert Warner, a professor of biochemistry, and Charles Weissmann, then an assistant professor of biochemistry at NYU. Their research focused on analyzing the mechanism of action of RNA polymerase of *Azotobacter vinelandii*, one of the first RNA polymerases to be purified. Samuels devised a method to quantitatively analyze DNA-RNA hybrid intermediates in the polymerase reaction. While in Tomkins' laboratory at the NIH his research focused on the mechanism of stimulation of tyrosine aminotransferase by glucocorticoid hormones in cell culture systems.

When he returned to NYU, he initiated research on the mechanism of thyroid hormone action at the molecular level. Having experienced the utility of cell culture systems, he examined various established cell lines for biologic responses to T3 and T4. In 1973 he and his colleagues examined a rat pituitary tumor cell line (GH1), that produced both growth hormone and prolactin. He showed that these cells were responsive to physiological concentrations of T4 and T3 and these hormones stimulated the production of growth hormone and inhibited the production of prolactin, thus mimicking the effects of thyroid hormone *in vivo*. With the availability of L-[¹²⁵I]T3 they identified that these cells contained a nuclear L-[¹²⁵I]T3-binding factor that functioned as a receptor that mediated the activity of

the thyroid hormones. This receptor was ubiquitously expressed in a wide variety of cells and tissues.

Samuels and his co-workers made a number of seminal contributions to the area of thyroid hormone action including: (1) identification of auto-regulation of thyroid hormone receptor (TR) synthesis and degradation by ligand; (2) analysis of the role of TR in stimulating the transcription rate of the growth hormone gene; (3) identification of multiple isoforms of TR prior to cloning of the TRs. They developed the first photoaffinity label probe for TR and showed by covalent modification that the GH1 cells contained three different forms of TR. These forms did not represent degradation products and exhibited different half-lives and synthetic rates. Based on these studies they proposed that these multiple receptor forms were products of alternative splicing of different genes. This was confirmed four years later when the TR mRNAs were cloned; (4) identification of DNA and protein-protein interactions of TR in chromatin. By analyzing the chromatin organization of TR they showed that the receptor is organized in chromatin in association with another protein bound to a DNA fragment of about 35 base pairs. That factor was subsequently shown to be retinoid X receptor (RXR) which functions as a heterodimerization partner of the TRs and the retinoid acid receptors (RARs); (5) identification of the thyroid hormone responsive sequences of the rat growth hormone gene; (6) identification of the dimerization domain of the TRs and RARs; (7) purification of TR- α and human RAR- α to homogeneity and clarification of the mode of interaction of homodimers and heterodimers with DNA response elements exhibiting marked diversity in sequence and organization; and (8) role of ligand in mediating conformational changes in TR and RAR and identification of the domains of these receptors critical for mediating transcriptional activation of these receptors.

Recently the Samuels laboratory cloned and characterized three novel coregulators: NRC (nuclear receptor coregulator); NIF-1 (NRC interacting factor-1) and NRIF3 (nuclear receptor interacting factor-3). NRC has been shown to be essential for development and to play an important role in wound healing. NIF-1 is not only important for transcriptional activation by nuclear receptors but is essential for neural stem cell renewal and brain development. NRIF3 is important for TR and RAR action. However, it also plays a receptor-independent role in breast cancer cells where its expression rapidly leads to apoptosis through the rapid expression of the FASTKD2 pro-apoptotic gene.

Samuels was the recipient of a Research Career Development Award (NIH) and the Van Meter Prize of the American Thyroid Association for major contributions in thyroid hormone research, the Parke-Davis Distinguished Lectureship Award from the American Thyroid Association, and the Solomon A. Berson Alumni Achievement Award of NYU School of Medicine. He also received the Borden Research Award and was the recipient of a MERIT Award from the NIH-NIDDK. Samuels has been a member of the American Society for Biochemistry and Molecular Biology, the American Society for Clinical Investigation, the Association of American Physicians, the American Federation for Clinical Research, the American Society for Cell Biology, the American Society for Microbiology, the American Thyroid Association, the American Chemical Society, the Endocrine Society, the Tissue Culture Association and the Interurban Clinical Club. He has served on the editorial board of the *American Journal of Physiology*, *Endocrine and Metabolic Physiology*, *Endocrinology*, *Molecular and Cellular Endocrinology*, *The Journal of Clinical Investigation*, *Endocrine Reviews*, and *Molecular Endocrinology*. He has been a member of numerous advisory committees both federal and private.

Charles L. Sawyers, MD

Charles L. Sawyers was born in Nashville, TN, on January 26, 1959. He received a BA from Princeton University in 1981 and an MD from Johns Hopkins University School of Medicine in 1985. This was followed by an internship and residency at the University of California, San Francisco, from 1985 to 1988, a fellowship at the University of California, Los Angeles, from 1988 to 1991, and postdoctoral training at UCLA/Howard Hughes Medical Institute under the mentorship of Owen Witte from 1989 to 1993. Sawyers quickly rose through the ranks in a number of teaching and research positions at UCLA; these included clinical instructor (1991–1993), assistant professor (1993–1997), member (1993–2006), full member (1993–2006), associate chief (1996–2006), associate professor (1997–2000), and professor (2000–2006) with joint appointments in the Department of Urology and Department of Molecular & Medical Pharmacology. In addition, he provided clinical care at inpatient rounds at UCLA from 1993 to 2006. After more than 20 years at UCSF and UCLA, Sawyers joined Memorial Sloan Kettering Cancer Center in 2006, where he currently serves as chair of the Human Oncology and Pathogenesis Program and conducts cancer research as an investigator of the Howard Hughes Medical Institute. He is also a professor in the Cell and Developmental Biology Program at Weill Cornell Graduate School of Medical Sciences.

Sawyers studies mechanisms of cancer drug resistance with an eye toward developing novel therapies. He co-discovered the anti-androgen drug enzalutamide, which was approved by the FDA in 2012 for treatment of advanced prostate cancer. He was a co-recipient of the 2009 Lasker-DeBakey Clinical Medical Research Award for the development of the ABL kinase inhibitor imatinib for patients with chronic myeloid leukemia and the second-generation ABL inhibitor dasatinib to overcome imatinib resistance. Sawyers was one of the recipients of the 2013 Breakthrough Prize in Life Sciences, the 2013 Giants of Cancer Care Award, and the 2013 Taubman Prize for Excellence in Translational Medical Science.

Sawyers was inducted in 2014 as a member of the American Academy of Arts and Sciences, is a 2014 Hope Funds for Cancer Research Honoree, and is a member of the National Academy of Sciences and the Institute of Medicine. He is past president of the American Association for Cancer Research, was appointed to the NIH NCI National Cancer Advisory Board by President Obama, and serves on the board of directors of Novartis.

David A. Scheinberg, MD, PhD

David A. Scheinberg was born in New York City. He obtained his BA degree at Cornell University, and his MD and PhD degrees at the Johns Hopkins University School of Medicine. He is currently Vincent Astor Chair and chairman of the Molecular Pharmacology and Chemistry Program at the Sloan Kettering Institute. He also founded and chairs the Center for Experimental Therapeutics and founded and was chair (2010–2014) of the Center for Molecular Imaging & Nanotechnology. He is additionally professor of medicine and pharmacology and co-chair of the pharmacology graduate program at the Weill Medical College of Cornell University and professor in the Gerstner-Sloan Kettering Graduate School of Biomedical Sciences at Memorial Sloan Kettering Cancer Center. He is a founder and director of the Therapeutics Discovery Institute, a nonprofit drug discovery corporation formed with Weill Cornell Medical College, Rockefeller University, and Sloan Kettering Institute.

From 1992 until 2003 Scheinberg was chief of the MSKCC Leukemia Service. He has been elected into the American Society for Clinical Investigation, the Association of American Physicians, and the Interurban Club. His other awards include the Doris Duke Distinguished Clinical Science Professorship, the Lucille P. Markey Scholarship, the Emil J. Freireich Award,

Leukemia and Lymphoma Society Translational Investigator Awards, and CapCure Awards. He is an advisor to charitable foundations and cancer centers and sits on the boards of directors of public biotech companies.

Scheinberg is a physician-scientist who specializes in the care of patients with leukemia and investigates new therapeutic approaches to cancer, both in the hospital and in the laboratory. The focus of his research is on the discovery and development of novel, specific immunotherapeutic agents. These include monoclonal antibodies that target the cell surface or intracellular proteins of cancers, targeted radiopharmaceuticals that deliver radioactive particles (e.g., alpha particles or alpha particle nanogenerators), targeted nano-devices for selective cell kill, therapeutic vaccines that target the oncogene products that cause cancers, and antibodies to intracellular proteins. Eight different therapeutic agents developed by Scheinberg in his laboratory have reached human clinical trials, among them the first humanized antibodies to treat acute leukemia, the first targeted alpha particle therapies and alpha generators, and the first tumor-specific fusion oncogene product vaccines. Scheinberg has published more than 250 papers, chapters, or books in these fields.

James Scheuer, MD

James Scheuer was born in New York City on February 21, 1931. He received the AB degree from the University of Rochester (1952) and the MD degree from Yale University School of Medicine four years later. He served his internship in the Cornell division at Bellevue Hospital. He was an assistant resident in medicine at Mount Sinai Hospital in New York (1959–1960). In 1957 and 1959 he was an NIH postdoctoral fellow in cardiology and internal medicine at Mount Sinai. From 1959 to 1960 he was chief resident in medicine at Mount Sinai. From 1960 to 1962 he served in the US Army Medical Corps (one year in Korea and one year at the Dewitt Army Hospital in Fort Belvoir, Virginia). In 1962–1963 he served as a research associate at the Institute for Muscle Disease in New York City, then spent two years as a trainee in metabolism and nutrition with the Department of Biochemistry and Nutrition in the University of Pittsburgh Graduate School of Public Health. From 1964 to 1968 he was director of the Central Heart Station at Presbyterian-University Hospital in Pittsburgh and an assistant professor of medicine at the University of Pittsburgh School of Medicine. From 1968 to 1972 he held a Research Career Development Award from the NIH. In June 1970 he was appointed associate professor

of biochemistry, then in 1971 was appointed co-director of the Division of Cardiology and director of cardiovascular research at Pittsburgh. He then became professor of medicine and associate professor of physiology at Albert Einstein College of Medicine and chief of cardiology at the Montefiore Medical Center. From 1980 to 1987 he was vice chairman of the Department of Medicine at Einstein, and in 1987 became interim chairman and physician-in-chief at Einstein and Montefiore, respectively. In 1990 he was made Baumritter Professor and Louis Leiter Physician-in-Chief, a position he held until 1999. He stepped down to return to cardiology and run the fellowship training program. Scheuer was named University Chairman of Medicine Emeritus and Distinguished Professor Emeritus in 2011. In 2014 the Division of Cardiology was renamed in Scheuer's honor.

Scheuer's research was in myocardial metabolism and biochemistry. His laboratory was among the first to elucidate physiologic and biochemical responses of the heart to exercise training. His group demonstrated that the cardiac hypertrophy of exercise training and of systolic overload produced opposite effects on contraction and relaxation parameters and on myosin ATPase and isoenzyme patterns, thus revealing the disparate biochemical and physiologic patterns of different kinds of hypertrophy. The group also described effects of diabetes, aging, myocardial infarction, and estrogen and androgen on heart muscle function and biochemistry.

Scheuer served on numerous study sections and review panels for the NIH, the American Heart Association, and the New York Heart Association. He also served on editorial boards for *Circulation*, *Circulation Research*, the *Journal of Applied Physiology*, the *Journal of Molecular and Cellular Cardiology*, and the *American Journal of Cardiology*, among others. He has held several executive board positions, including that of president of the New York Cardiological Society. He has served on the boards of several councils of the American Heart Association and its New York City chapter. He is a member of the American Federation for Clinical Research, the American College of Physicians, the American Heart Association, the American College of Cardiology, the American Physiological Society, the Cardiac Muscle Society, the Central Society for Clinical Research, the Association of University Cardiologists, the American Society for Clinical Investigation, and the Association of American Physicians. His research support has come from the NIH and the American Heart Association.

David Andrew Shafritz, MD

David Shafritz was born in Philadelphia, PA, October 5, 1940. He graduated from the College of Arts and Sciences of the University of Pennsylvania in 1962 (AB degree). He received the MD degree from the University of Pennsylvania School of Medicine in 1966, having been simultaneously enrolled in the Graduate School of Arts and Sciences (molecular biology; 1962–1964). From 1966 to 1968 he was intern and assistant resident in medicine under Theodore Woodward at the University of Maryland Hospital in Baltimore. The following year he was a research associate at the National Heart Institute Laboratory of Clinical Biochemistry under Herbert Weissbach, and then from 1969 to 1971 worked at Section on Molecular Hematology in the Molecular Diseases Branch of the National Heart and Lung Institute, under W. French Anderson. In 1971 he moved to Massachusetts General Hospital (MGH) for research and clinical training in gastroenterology under Kurt J. Isselbacher and was appointed instructor in medicine at Harvard. In 1973 he was promoted to assistant professor and assistant in biochemistry (medicine) at MGH. Later, in 1973, he moved to Albert Einstein College of Medicine, where he held the following positions: assistant professor of medicine and cell biology (1973–1976), associate professor (1976–1981), and professor of medicine, cell biology and pathology (1981–present). In 1992 he was given the Herman Lopata Endowed Chair in Liver Diseases Research at Einstein, and from 1985 to the present he has served as director of the Marion Bessin Liver Research Center.

As an undergraduate at Pennsylvania, Shafritz began research in the laboratory of Philip George, an expert in thermodynamics. As a medical student he worked with John R. Senior, who had trained with Isselbacher. During this period (1965–1966) he devised methods to study pyrimidine biosynthesis in the intestine, using small amounts of tissue as might be obtained by peroral biopsy. These methods were subsequently utilized to study adult celiac disease.

At the NIH, Shafritz was introduced to molecular biology by Weissbach, and his subsequent studies with Anderson resulted in the first isolation and characterization of initiation factors for protein biosynthesis in eukaryotic cells. In Boston he worked on cell-free systems for protein synthesis and messenger RNA isolation from the liver. He has continued his research on liver gene regulation since moving to Einstein.

Shafritz and his colleagues were among the first to utilize molecular hy-

bridization methods as a diagnostic tool in clinical medicine. This work involved specific use of HBV DNA probes to study the pathogenesis of chronic liver disease when HBV sero-immunologic tests produced confusing or negative results. They showed that in some patients HBV persisted in the liver and continued to replicate and cause inflammatory liver disease many years after the patient had developed antibodies to some or all known viral proteins. They also demonstrated that the virus had become integrated into the host liver cell genome in some long-term HBV carriers, and that in nearly all carriers who developed hepatocellular carcinoma, HBV DNA was integrated into the tumor cell genome. This was the first study to use molecular methods to demonstrate *in vivo* the monoclonal origin and expansion of tumors and their metastasis, and their findings were published in 1981 as one of four lead articles in the bicentennial issue of the *New England Journal of Medicine*. In 1982, along with Jack Wands and Isselbacher, he proposed the presence of mutant or variant forms of HBV in the serum of patients with no clear evidence of active HBV infection and suggested a possible role of these mutant forms in idiopathic liver disease.

During the last two decades, Shafritz's attention has turned to molecular studies of liver cell growth control; liver cell differentiation; genes controlling liver regeneration; and the identification, activation, and differentiation of progenitor cells in the adult liver. His current work is devoted to repopulating the liver by transplanted cells, and he has developed a rat model system in which he routinely achieves 25% replacement of the normal adult liver with fetal liver stem/progenitor cells. The transplanted fetal liver cells become fully incorporated into the liver parenchyma, differentiate into both hepatocytes and bile duct epithelial cells, exhibit normal hepatic function, and remain in the host liver for the remainder of the rat lifetime. The mechanism for liver repopulation by fetal liver cells is cell competition, during which more rapidly proliferating transplanted fetal liver cells replace more slowly growing host hepatocytes by inducing their apoptosis, a mechanism originally described as occurring in *Drosophila* during wing development. During aging in the rat liver, the proliferation of potential hepatocytes is reduced (senescence), cell competition between transplanted fetal liver cells and host hepatocytes is increased, and liver repopulation can be increased to 50% of total liver mass. Studies now are underway to determine how these various processes and mechanisms, discovered in rodent systems, can be employed to achieve effective repopulation of human liver by transplanted cells.

Shafritz is a member of numerous professional societies, including the

American Association for the Study of Liver Diseases, the American Gastroenterological Association, the American Society of Biologists and Molecular Biologists, the American Society of Investigative Pathology, the American Society for Clinical Investigation (emeritus), the Association of American Physicians (emeritus), and the International Association for the Study of Liver. He has served on numerous advisory committees, including the American Association for the Study of Liver Disease research committee, the metabolic pathology study section (NIH), and as chairman of the NIH NIDDK Division of Digestive Disease and Nutrition Study Section for training grants and career awards. He held an NIH Research Career Development Award from 1975 to 1980 and a Career Scientist Award from the Irma T. Hirshl Charitable Trust of New York (1974–1979). He has served on the editorial boards of several journals, including those of *Hepatology* (associate editor, 1981–1986), the *Journal of Medical Virology*, and the *Journal of Virology*. He is co-editor of a major textbook dealing with basic clinical aspects of the liver and its diseases (*The Liver: Biology and Pathobiology*; Raven Press). In 2000 Shafritz was given the Distinguished Research Achievement Award from the American Liver Foundation, and in 2007 he received the American Gastroenterological Association Foundation Mentors Honoree Research Scholar Award.

Martin I. Surks, MD

Martin Surks was born in New York City on May 21, 1934. He attended public schools in New York City, received the AB degree from Columbia College in 1956 and received the MD degree from New York University Bellevue College of Medicine in 1960. He then spent two years as a house officer at the Montefiore Medical Center in Bronx, NY, followed by a year of medical residency at the Veterans Administration Hospital (Bronx, NY) and a year as a postdoctoral research fellow in the laboratory of Jack H. Oppenheimer (National Institute of Arthritis and Metabolic Diseases). He then served as a captain in the US Army, assigned to the Radioisotope Section of the Physiology Division of the US Army Medical Research and Nutrition Laboratory at Fitzsimmons General Hospital (Denver, CO) from 1964 to 1966. After his army service, he returned to Bronx, NY, where he entered the private practice of internal medicine and endocrinology and started a research laboratory at the Montefiore Medical Center. In 1967 he became a full-time member of the division of endocrinology and metabolism at Montefiore and an assistant professor of medicine at Albert Einstein College of Medicine. In 1976 he became head of the division at

Montefiore and, in 1978, professor of medicine at Einstein. In 1980 he did a sabbatical as a visiting scientist in the department of developmental biology and cancer at Einstein (in the laboratory of Jerard Hurwitz). In 1985 he received the additional appointment of professor of laboratory medicine at Einstein. Since 1981 he has been an attending physician at Montefiore Medical Center.

Surks began his research career under Oppenheimer and developed an interest in the physiology and actions of thyroid hormones. While in the Army he conducted studies on the impact of exposure to high altitude on the thyroid hormone system, fluid compartments, and protein metabolism. In his own laboratory he continued studies of hypoxia and thyroid hormone regulation, thyroid hormone metabolism, regulation of the thyroid system, and thyroid hormone action. He developed methods to measure triiodothyronine in human serum and, with Oppenheimer, showed that triiodothyronine affects most of the activity of the thyroid system. Subsequently, he published numerous studies concerning the impact of nonthyroidal illness on thyroid hormone metabolism and action. His subsequent work concerned the definition of the molecular basis by which thyroid hormone regulates cell growth, and he conducted many clinical studies.

Since 1990 he has worked in the center of research that showed that TSH distribution shifts to higher concentrations with age. Based on this knowledge, he determined that about 50% of geriatric patients previously considered to have subclinical hypothyroidism, based on TSH concentration, actually have levels within their age-specific reference range. Thus, in collaboration with colleagues, Surks estimated that about 5 million older people in the US are unnecessarily treated with levothyroxine.

Surks has received a Research Career Development Award from the NIH (1973–1977), and in 1973 he received the Van Meter Prize from the American Thyroid Association. He has served on several editorial boards, including those of *Endocrinology* (associate editor, 1986–1987), *the American Journal of Physiology, Endocrinology and Metabolism*, and the *Journal of Clinical Endocrinology and Metabolism* (1991). From 1976 to 1979 he served on the merit review board of the Veterans Administration (endocrinology) and, from 1981–1985, on the endocrinology study section of the NIH. Since 1986 he has been a member of the subspecialty board of endocrinology, diabetes, and metabolism of the American Board of Internal Medicine, and has served as its chairman. He is also a director of the American Board of Internal Medicine. He is a member of numerous

professional societies, including the American Society for Clinical Investigation, the American Thyroid Association (secretary, president, and past president), the Association of American Physicians, the American Federation for Clinical Research, the American College of Physicians, and the Endocrine Society.

He helped to develop the Endocrine Self-Assessment Program of the Endocrine Society and served as editor-in-chief of the program for 5 years. He was also a founder of the Association of Program Directors in Endocrinology and Metabolism and subsequently served as its president. Surks has published two books and more than 200 peer-reviewed papers.

In the last decade Surks was granted the Distinguished Service Award by the American Thyroid Association (2002), a Mastership by the American College of Physicians (2003), and the Sidney H. Ingbar Distinguished Service Award by the Endocrine Society (2009). He continues to serve as the program director for endocrinology at Albert Einstein College of Medicine.

Megan Sykes, MD

Megan Sykes was born in Toronto, Ontario, Canada, on May 29, 1958. She entered medical school after two years as an undergraduate at the University of Western Ontario and received her MD in 1982 from the University of Toronto. She entered medical residency at Montreal General Hospital at McGill University and returned to Toronto to complete her residency at the University of Toronto in 1985. She became fascinated with immunology during her clinical training and joined the laboratory of David H. Sachs at the NIH NCI in 1985 as a Fogarty Visiting Fellow, to conduct research in transplantation immunology. She began her own laboratory program and was promoted to senior staff fellow and laboratory leader in 1989, before moving to Massachusetts General Hospital and Harvard Medical School in December 1990, to serve as an assistant professor, with support from two NIH R01 awards and an American Cancer Society Junior Faculty Award. She moved up the academic ladder and received an honorary master of arts degree from Harvard University upon her promotion to tenured professor of surgery and medicine (immunology) at Harvard Medical School in 1999. She served as associate director of the Transplantation Biology Research Center (TBRC) at Massachusetts General Hospital and headed the Bone Marrow Transplantation Section of the TBRC from 1994 to 2010.

She held the Harold and Ellen Danser Chair in Surgery at Harvard from 2004 until 2010. In 2010 she moved to New York to establish and direct the Columbia Center for Translational Immunology (CCTI) at Columbia University, where she is the Michael J. Friedlander Professor of Medicine, professor of surgical sciences, and professor of immunology. By 2014 the CCTI had grown to include 13 full-time faculty in various fields of applied and basic immunology and more than 100 staff members.

Sykes has published 400 papers and book chapters based around her early interest in the immune system's ability, or failure, to distinguish self from non-self. Her work spans the fields of hematopoietic cell stem transplantation (HSCT), antitumor immunity, organ allograft tolerance induction, xenotransplantation tolerance, and type 1 diabetes.

Sykes has investigated HSCT directed toward three clinical applications: the treatment of hematologic malignancies, the induction of specific transplantation tolerance, and curing type 1 diabetes. She developed novel approaches to separating the effects of graft-vs-host disease (GVHD) from those of graft-vs-leukemia/lymphoma (GVL), one of which involves the non-myeloablative establishment of mixed chimerism, followed by delayed donor lymphocyte infusions (DLIs). Her lab demonstrated that DLIs administered under such conditions mediate GVL without GVHD because of a lack of inflammation in the epithelial GVHD target tissues. Her group demonstrated that such inflammation serves as a checkpoint for the transmigration of GVH-reactive T cells from the lymphohematopoietic system to the epithelial GVHD target tissues. Sykes and her colleagues have translated this approach into novel clinical trials of non-myeloablative, mixed-chimerism induction across HLA barriers, followed by delayed DLI, in an effort to achieve GVL without GVHD.

Sykes has focused on the development of non-toxic, non-myeloablative conditioning regimens using monoclonal antibodies to eliminate host resistance to engraftment of allogeneic and xenogeneic hematopoietic cells and allow the induction of mixed chimerism without the usual risks of hematopoietic cell transplantation, to achieve transplantation tolerance. She and her colleagues, including long-time collaborator Sachs, developed novel animal models and translated them to trials that for the first time achieved kidney allograft tolerance in patients. She has obtained a mechanistic understanding of T, B, and NK cell tolerance in the animal models and humans receiving these protocols.

Sykes showed in NOD mice that the mixed-chimerism approach can be used to simultaneously reverse the autoimmunity of type 1 diabetes while inducing donor islet allograft tolerance. This approach cured diabetes without risk of rejection or autoimmune recurrence. Sykes has initiated a preclinical large-animal program at Columbia in order to bring these strategies toward clinical application.

Sykes and her collaborator Yong-Guang Yang developed and studied humanized mice with robust human immune systems derived from human fetal thymus tissue and hematopoietic stem cells. She has used this model to obtain fundamental information on human lymphocyte development and homeostasis. She applied this knowledge to a method of xenograft tolerance induction that she first pioneered in mice, namely xenogeneic thymic transplantation, to demonstrate the capacity of porcine thymic transplantation to support development of a centrally tolerized, normal human T cell repertoire. Her group adapted the humanized mouse model to generate immune systems from adult human bone marrow stem cells. This “personalized immune” mouse model is being used to understand the fundamental immunoregulatory abnormalities that underlie autoimmune diseases.

Sykes has served numerous society leadership, committee, reviewing, editorial, and teaching roles in the above fields. She has been president of the International Xenotransplantation Association, vice president of The Transplantation Society (TTS), on the board of directors of the Federation of Clinical Immunology Societies, a councilor of the Interurban Clinical Club, and a recurrent member of the TTS council. She has received numerous honors and awards, including the American Society of Transplantation Basic Science Established Investigator Award, the TTS Roche Award for Outstanding Achievement in Transplantation Science, and the TTS Recognition Award for Outstanding Achievement in Transpalntation, and she was a distinguished lecturer at an annual meeting of the American Association of Immunologists. She is a fellow of the AAAS and a member of the Association of American Physicians and was elected to the Institute of Medicine of the National Academy of Sciences in 2009.

Harvey J. Weiss, MD

Harvey Weiss was born in New York City on June 30, 1929. He received the AB degree from Harvard College in 1951 and the MD degree from the

Harvard Medical School in 1955. William B. Castle's lectures at the medical school stimulated his early interest in hematology. Weiss was an intern on Dickinson W. Richard's Columbia Medical Service at Bellevue Hospital (NYC) in 1955–1956, and he spent the following two years as a resident in medicine at the Manhattan VA Hospital in New York City. He then spent a year as Dazian fellow in hematology with Louis R. Wasserman at the Mount Sinai Hospital in New York City. From 1959 to 1962 Weiss was fortunate to be assigned during his military service to William H. Crosby's division of hematology at the Walter Reed Army Institute of Research in Washington, DC, where he was chief of the coagulation section. He then returned to New York City and, after several years (1962–1969) at the New York University School of Medicine and Mount Sinai School of Medicine, he moved to the Roosevelt Hospital (in 1969), where he established the division of hematology-oncology in Nicholas P. Christy's Department of Medicine. He held this position until his retirement from the hospital in 1996. Throughout his career at Roosevelt, and later at Mount Sinai St. Luke's/Mount Sinai Roosevelt, Weiss was a member of the faculty of the Columbia University College of Physicians and Surgeons, achieving the rank of professor of medicine in 1975 and retiring as professor emeritus of medicine in 1996. In 1980–1981 and 1987–1988 he was a visiting scientist at the Institute for Cellular Biology in Paris, France.

Weiss' original contributions were in the field of hemostasis and thrombosis. His were the first reports of the inhibitory effect of aspirin on platelet aggregation (1967) and the demonstration that aspirin could inhibit the formation of platelet thrombi in several experimental models of thrombosis. These experimental studies provided the basis for the use of aspirin as an antithrombotic agent in cardiovascular disease. Weiss has made important contributions to the field of platelet function disorders. He was the first to report that defects in platelet aggregation, distinct from thrombasthenia, could account for the impaired hemostasis observed in some patients with bleeding disorders. In collaboration with Holm Holmsen, he showed that in some patients, impaired hemostasis is caused by decreased content of a specialized, non-metabolic pool of adenosine diphosphate (ADP) that is stored in platelet-dense granules (termed storage pool deficiency [SPD]). Further studies by Weiss and colleagues identified subgroups of SPD that were characterized by a deficiency of substances stored in dense granules, alpha granules, or both. These disorders are currently referred to as d-SPD, a-SPD, and ad-SPD, respectively. Weiss has also described patients whose bleeding disorder is the result of impaired platelet procoagulant activity, including a unique disorder (Scott syndrome) in which collaborative stud-

Correction made at the request of Dr. Harvey Weiss

Near the end of the first paragraph on page 438, the text erroneously reads: “Throughout his career at Roosevelt, and later at Mount Sinai St. Luke’s/Mount Sinai Roosevelt, Weiss was a member of the faculty of the Columbia University College of Physicians and Surgeons,…….”

The correct text should instead read:

“Throughout his career at Roosevelt, and later at St. Luke’s-Roosevelt, Weiss was a member of the faculty of the Columbia University College of Physicians and Surgeons,…….”

ies with Dutch and American investigators have identified the defect as an inability of activated platelets to translocate phosphatidylserine from inner to outer plasma membrane.

Weiss has been a major contributor to the study of von Willebrand factor (vWF) and Factor VIII. Together with Leon W. Hoyer, he showed that vWF could be separated from Factor VIII and provided evidence that these were two separate molecules. His laboratory was the first to establish the two major physiological functions of vWF. He demonstrated with Hans R. Baumgartner and others both its shear rate–dependent role in mediating platelet adhesion to subendothelium (as well as the complementary role of the GPIb receptor for vWF) and, with other colleagues, its role as the carrier molecule for Factor VIII, which serves to stabilize its activity in plasma. Weiss also developed an assay that, with modification, is currently used to measure vWF in plasma (ristocetin cofactor assay). He also described several subtypes of von Willebrand disease (vWD), including heterogeneous defects among patients with the type IIA variant; the type I, New York variant; and the platelet disorder known as pseudo-vWD.

Weiss is a member of, among others, the American Society for Clinical Investigation, the Association of American Physicians, the American Physiological Society, the American Society of Hematology, and the International Society for Thrombosis and Haemostasis. He has served on many editorial boards, including those of *Blood*, the *American Journal of Medicine*, the *Journal of Thrombosis and Haemostasis*, and *Arteriosclerosis and Thrombosis*. He has also been a member of the council on thrombosis of the American Heart Association, the senior advisory council of the International Society on Thrombosis and Haemostasis, and the committee on certification in hematology of the American Board of internal Medicine, as well as other national and international committees. In 1995 he received a Distinguished Career Award from the International Society on Thrombosis and Haemostasis.

Gerald Weissmann, MD

Gerald Weissmann was born in Vienna, Austria, on August 7, 1930. He received the AB degree from Columbia College in 1950 and the MD degree from the New York University College of Medicine in 1954. He spent 1954 to 1955 as an intern at Mount Sinai Hospital in New York City. The following two years were served as a captain in the US Army Medical Corps,

after which he returned to Mount Sinai as an assistant resident physician (1957–1958). Weissmann was a research fellow of the Arthritis and Rheumatism Foundation from 1958 to 1959, working in the departments of biochemistry and medicine under Severo Ochoa and Maxwell Schubert at New York University. The following year he was a research assistant under Lewis Thomas in the Department of Medicine as well as chief medical resident. Weissmann spent one year studying biophysics at the Strangeways Research Laboratory in Cambridge, England, under H. B. Fell and Sylvia Filton-Jackson. He then returned to New York where, from 1961 to 1965, he was a senior investigator of the Arthritis and Rheumatism Foundation. He then served as a career research scientist at the Health Research Council of New York City (1966–1971). In 1964 and 1969 he was a visiting investigator at the A. R. C. Institute of Animal Physiology in Babraham, Cambridge, UK. From 1973 to 1974 Weissmann was at the Centre de Physiologie et d'Immunologie Cellulaires, Hôpital St-Antoine, Paris, as a visiting investigator; he held the same role at the William Harvey Research Institute of London in 1987. He progressed through the academic ranks at NYU School of Medicine, beginning with his first appointment in 1959, to become professor of medicine in 1970. He was director of the division of cell biology (medicine) at NYU School of Medicine from 1969 to 1973 and then director of the division of rheumatology from 1973 to 1999. He is now emeritus professor of medicine (rheumatology), research professor of medicine, and director of the Biotechnology Study Center at NYU School of Medicine. He is also editor-in-chief of the *FASEB Journal*.

Lewis Thomas had the greatest influence in stimulating Weissmann to pursue a career in biomedical research. Since 1969 he has made numerous seminal contributions in this long-term study of inflammation, including the determining that lysosomes are subcellular organelles that contain not only tissue-degrading enzymes, but also inflammatory substances (findings published in 1962 with Thomas). He also determined that human neutrophil lysosomal constituents can break down cartilage proteoglycans, thereby producing joint destruction and inflammation, and that the release of lysosomal constituents occurs from intact, rather than dead or dying, neutrophils. Furthermore, he observed that the secretion of lysosomal enzymes and O_2 generation are not only responses to phagocytosis of particles but can also be elicited by soluble stimuli, and that neutrophil Fe receptors are more efficiently engaged by immune complexes on surfaces than in bulk phase. Similarly, he found that release of lysosomal enzymes, generation of O_2 , and formation of eicosanoids (LTB₄) are regulated in a yin/yang manner by cyclic AMP/cyclic GMP and by the assembly of

cytoplasmic microtubules; that intracellular but not extracellular Ca determines these messenger effects; and that neutrophil lysosomal enzyme release and O₂ generation are usually accompanied by homotypic cell/cell aggregation. Additionally, Weissmann determined that prostaglandins are feedback inhibitors rather than promoters of inflammation *in vitro* and *in vivo*, and they act via their receptors to raise cyclic AMP. He found that NSAIDs inhibit homotypic cell/cell adhesion not only of neutrophils but also of Microciona cells (which cannot synthesize prostaglandins). NSAIDs also exert anti-inflammatory effects not only by inhibiting cyclooxygenase, but also via their indirect effects on receptors, which provoke increments of cyclic AMP. Similarly, he observed that adenosine, another agonist that provokes changes in cAMP, inhibits O₂ generation via A₂ receptors. Later, he described how the vascular crises of systemic lupus erythematosus are due to the release of C3a and C5a set into the circulation, thus causing leukoaggregation and adult cerebral distress syndrome via CD11b/CD18-mediated hemotypic cell adhesion. In collaboration with A. D. Bangham, Weissmann helped to discover and name liposomes, and he was the first to complex them with an effective drug (amphotericin), encapsulate an enzyme (lysozyme), and develop a specific targeting ligand for intracellular delivery. He was co-founder (with E. C. Whitehead) and a director (1982–2000) of The Liposome Company, Inc. Two drugs based on his liposome work are now approved for clinical use (Abelcet® and Myocet®). Weissmann also provided evidence that phosphatidic acid and arachidonate are direct intracellular messengers in neutrophil activation. He has shown that NSAIDs such as salicylate and indomethacin inhibit cell/cell aggregation by interfering with affinity but not frequency modulation of CD11b/CD18. NSAIDs inhibit not only homotypic adhesion, but also heterotypic adhesion to the endothelium. During the past few years, he has continued to pursue these important studies.

Weissmann has received the Lila and Murray Gruber Cancer Research Award, two residencies at the Rockefeller Foundation Bellagio Center, the Allesandro Robecchi and Paul Klemperer awards for inflammation research, and the Distinguished Investigator Award from the American College of Rheumatology. He is a foreign member of the Accademia Nazionale dei Lincei of Rome and the Royal Society of Medicine of London. He is a master and past president of the American College of Rheumatology, a past president of the Harvey Society, and a fellow of the AAAS and the New York Academy of Medicine. He is on the board of the New York Academy of Sciences, and a trustee emeritus of the Marine Biological Laboratory in Woods Hole, Massachusetts. He was a founding member of

the advisory board of the Ellison Medical Foundation and founding chairman of the jury for the Prix Galien USA. A member of PEN, his essays and reviews of cultural history have been published in the *New Republic*, the *London Review of Books*, and the *New York Times Book Review* and have been collected in ten volumes, from *The Woods Hole Cantata: Essays on Science and Society* (1985) to *Epigenetics in the Age of Twitter: Pop Culture and Modern Science* (2012).

Babette Barbash Weksler, MD

Babette Weksler was born in New York City on January 18, 1937. She received the AB degree at Swarthmore College in 1958 with highest honors and the MD degree at Columbia University's College of Physicians and Surgeons in 1963, where she was elected to Alpha Omega Alpha. She is a third-generation woman physician, following her mother and maternal grandmother. She interned at the Bronx Municipal Hospital Center (1963–1964) and took her medical residency at Georgetown University Hospital in Washington, DC (1965–1967). She completed a research fellowship year in microbiology at the WrightFleming Institute (1967–1968) under R. E. O. Williams. During that time, she studied the effect on leukocytes of staphylococcal virulence factors. She then returned to New York, where she undertook hematology training at the New York Hospital–Weill Cornell Medical Center under Ralph Nachman (1968–1970); she held an American Cancer Society fellowship the first year and an NIH traineeship the second. She then joined the hematology division, under a US Public Health Service special postdoctoral fellowship (1970–1972), and was appointed as assistant professor of medicine (1970–1975), associate professor (1975–1981), and full professor of medicine. In 1983 she was also appointed professor of cell biology.

At Cornell her first research focused on the inflammatory functions of blood platelets, including the identification of bactericidal, permeability-enhancing, and complement-activating proteins contained in platelet granules; this was a modern updating of observations first made by Octave Gengou at the Pasteur Institute almost a century earlier. This led naturally to studies that demonstrated enhanced platelet function in different types of arteriosclerosis.

When prostacyclin (PG₁₂) was identified as a platelet-inhibitory eicosanoid produced by blood vessels, she was the first to show that endothe-

lial cells were a major source of PG12. These studies represented a productive collaboration with Eric Jaffe, who had developed the technique of culturing human vascular endothelial cells. Subsequently, she showed that after vascular injury, the denuded, de-endothelialized vessel wall rapidly regained the capacity to produce prostaglandins. Today, this is clearly attributed to rapid induction of the cyclooxygenase-2 (COX-2) enzyme that regulates cholesterol ester metabolism, changes in blood flow, and inflammatory stimuli (such as smoking) that induce COX-2. Complementary clinical investigations were undertaken into the effects of low-dose aspirin on platelet and endothelial functions in patients with atherosclerosis, with stroke, or who are undergoing coronary artery bypass surgery. More recently she engineered immortalized lines of bone marrow, cardiac, and human brain endothelial cells as research tools; these have been utilized by over 400 research laboratories throughout the world. The human brain endothelial cell line became the first good human model of the blood-brain barrier. A number of these projects were done at the Institut Cochin in Paris, France, where she spent two sabbatical years and was a visiting scientist for 20 years. She held grants from NIH and/or the American Heart Association over a 25-year span.

These activities stimulated her participation in research societies, starting with the American Federation for Clinical Research, for which she was the first woman chairperson of a regional section, and the American Society of Hematology, for which she chaired the annual education program (1987), then chaired the Education Committee, and later became a member of the society's advisory board. She served on the executive committee (and chaired the nominating and membership committees) of the council of thrombosis of the American Heart Association. Weksler is a member of numerous other professional societies, including the New York Society for the Study of Blood (president, 1986), the American Society for Clinical Investigation, and the Association of American Physicians. She was a member of the National Research Council Panel on Clinical Sciences (1978–1986) and the NIH Hematology Study Section (1979–1983). She has served on the editorial boards of *Stroke*, *Blood*, the *Journal of Lipid Research*, *Circulation*, the *American Journal of Medicine*, *Translational Research*, *Atherosclerosis*, and *FASEB Journal*. She was the third woman to be elected to the Interurban Clinical Club.

Her teaching and clinical work were concentrated in the areas of benign hematology, hemostasis/thrombosis, platelet disorders, and sickle cell anemia until her retirement from Weill Cornell Medical College in June 2014

as professor emerita.

Marc E. Weksler, MD

Marc Edward Weksler was born in New York City on April 16, 1937. He received an AB degree with honors from Swarthmore College in 1958 and an MD degree from Columbia University's College of Physicians and Surgeons with Alpha Omega Alpha academic honors in 1962. After two years of training in internal medicine at Bronx Municipal Hospital Center, he joined the US Public Health Service as a research associate in the laboratories of Robert Schimke and Harry Gelboin at the National Institutes of Health (1964–1966).

He chose to return to clinical medicine and was drawn to work with patients with chronic renal disease, for which novel immunotherapies were then being introduced. He spent one year studying chronic hemodialysis in the renal unit led by George Schreiner at Georgetown University Hospital in Washington, DC. However, it rapidly became clear that hemodialysis was not a satisfactory method to treat most patients with chronic renal failure when compared with renal transplantation. For this reason, and with a USPHS fellowship in transplant immunology, Weksler joined the clinical renal transplant unit directed by W. S. Peart at St. Mary's Hospital in London. This unit collaborated with the experimental transplantation unit at Mill Hill, which was then directed by the Nobel Laureate Peter Medawar.

In 1968 Weksler returned to the US as a special fellow with the USPHS, to care for patients with chronic renal disease, and study the cellular pathology of human lymphocyte biology, on the renal transplantation service at Cornell University Medical College. Initially the goal was focused on the limited success of renal dialysis or renal transplantation for patients with chronic renal failure (studies published in the *Journal of Clinical Investigation* [JCI], 1970). Subsequently he showed that immune responses occurred to autologous as well as allogenic lymphocytes (JCI, 1972).

At that time Alexander Bearn had just been recruited from Rockefeller University to chair the Cornell Department of Medicine and strengthen its research activities. He promoted Weksler to assistant professor of medicine and encouraged him to extend his studies in immunotherapy of chronic renal disease, after learning that Weksler had been awarded an American Cancer Society clinical investigatorship in 1970 and soon thereafter an

NIH Research Career Development Award. Bearn advised Weksler to “get into the laboratory and let your research merit election to the American Society for Clinical Investigation.” The Weksler lab was adjacent to that of Greg Siskind, who had recently been recruited from the lab of Baruj Benacerraf (who later won a Nobel Prize for his immunologic research). Under Siskind’s tutelage, Weksler extended his studies of autologous immune responses and the effect of human aging on lymphocyte proliferation. He discovered that human immune responses declined with age (JCI, 1974; *Journal of Experimental Medicine* [JEM], 1976, 1977). Weksler was elected to the American Society for Clinical Investigation in 1977.

In 1978 Weksler was selected as the first Irving S. Wright Professor of Medicine at Cornell University Medical College, the first endowed professorship dedicated to geriatrics and gerontology at a US medical school, and he held this chair for 34 years. His studies became increasingly focused on the effects of aging on immune function in elderly humans (JCI, 1981, 1986; *Annals of Internal Medicine*, 1983; JEM, 1986).

Weksler served as director of the Division of Geriatrics and Gerontology at Weill Cornell Medical College from 1977 to 2012 and trained numerous clinical and research geriatricians. As would be expected, his research evolved to include many inter-institutional studies of aging. He led a program project on the biology of aging in experimental animals and humans in collaboration with Robert Good at the Sloan Kettering Institute. During the last decade, Weksler organized phase 1, 2, and 3 studies of IVIg as a potential therapy for Alzheimer’s disease.

Throughout this time Weksler received numerous honors and professional awards, including participation in the NIH Aging Review Committee (1975), and membership in the American Society for Clinical Investigation (1977), the Association of American Physicians (1985), and the Interurban Clinical Club (1992). He was associate editor of the *Journal of Immunology* (1976) and the *Journal of Clinical Immunology* (1994) and served on the editorial boards of the *Journal of Immunology* (1980) and *Immunity & Ageing* (2004). He has chaired the FASEB Conference on Aging and Immune Responses (1984) and the WHO Aging Immunology Program (1990) and served as president of the American Federation for Aging Research (1990), as a consultant for the biotech directorate of the Organisation for Economic Co-operation and Development (1999), and as a counselor for the Henry Kunkel Society (2009).

Weksler was named professor emeritus of medicine at Weill Cornell Medical College upon his retirement in 2014. During his entire tenure at the medical college, his research, conducted in both humans and experimental animals, focused on the relationship between aging with immunosenescence that leads to neoplasia and the diseases of aging.

Allan Wolkoff, MD

Allan Wolkoff was born in Brooklyn, NY, on March 7, 1948. He received an AB degree from Dartmouth College in 1968 with high distinction in mathematics. He then entered Dartmouth Medical School, a two-year school at the time, and received a BMS degree in 1970, after which he entered the Albert Einstein College of Medicine, receiving an MD degree in 1972. At Einstein, he did research with Irwin Arias on inheritance of Dubin-Johnson and rotor syndromes. This sparked his now long-standing interest in pathobiology of the liver. He completed his internship and residency in internal medicine at Einstein (Bronx Municipal Hospital Center), then went to the National Institutes of Health as a clinical associate in gastroenterology-hepatology. At the NIH Wolkoff worked with Paul Berk in the Liver Unit, where he developed his interest in hepatocyte transport mechanisms and hepatology. He also collaborated with William Jakoby regarding the role of GSH-transferases as important cellular determinants of organic anion disposition. Wolkoff returned to Einstein in 1976 as an assistant professor of medicine in the Division of Gastroenterology, working his way up to tenured professor of medicine and anatomy and structural biology. He currently holds the Herman Lopata Chair in Liver Disease Research. He has remained at Einstein throughout his career, with the exception of a one-year sabbatical at the National Institutes of Health in 1982–1983, where he worked with Richard Klausner and Gilbert Ashwell on cell biology of receptor-mediated endocytosis in the liver.

Wolkoff established a program on liver cell membrane proteins and vesicular trafficking that was funded by the NIH (NIDDK) for 22 years. He served as associate director of the Marion Bessin Liver Research Center from 1993 to 2012 and now serves as director. A major aspect of his research is focused on elucidating mechanisms by which the hepatocyte takes up organic anions from the circulation. Based upon his studies of overnight-cultured hepatocytes and his synthesis of ³⁵S-sulfobromophthalein (BSP) of very high specific activity, he was able to develop an assay that, in collaboration with Peter Meier and colleagues in Zurich, permitted the

expression cloning of a transport protein that was initially termed organic anion transport protein (OATP) and is now known as OATP1A1, the first member of a previously undescribed family of organic anion transporters that are expressed in many cell types throughout the body. Wolkoff's more recent studies have examined the subcellular trafficking of OATPs and their requirement for interaction with PDZ proteins, microtubules, and molecular motors. A second major focus of Wolkoff's research has been receptor-mediated endocytosis and vesicular trafficking. Over the last 15 years, his laboratory has been able to reconstitute microtubule-based endocytic vesicle and trafficking in vitro using video microscopy. This has enabled discovery of novel vesicle-associated motor proteins and accessory proteins such as Rabs, enabling new paradigms of vesicle processing to be developed and tested in intact cells and animal models.

In addition to his research efforts, Wolkoff served as program director of the NIH training grant in hepatology from 1985–2008 and as director of the Belfer Institute for Advanced Biomedical Studies at Einstein from 2003–2008. The Belfer Institute provides a focus for integrating all post-doctoral training programs at Einstein and serves as an advocate for over 300 postdoctoral fellows. In 2007 he was made founding chief of the newly established Division of Liver Diseases at Einstein and Montefiore Medical Center. He and his colleagues established a liver transplant program and integrated many of its activities into the Liver Research Center, which had previously not had a major clinical focus. In 2010 he integrated hepatology back into the Division of Gastroenterology, and he now serves as chief of the Division of Gastroenterology and Liver Diseases at Einstein and Montefiore Medical Center. Under his leadership this division has seen a great deal of growth and academic integration between its clinical components and basic investigators at Einstein.

Wolkoff has been the recipient of a number of awards, including the Distinguished Service Award of the American Association for the Study of Liver Diseases (2006), the George Jamieson Humanitarian Award of the American Liver Foundation (2011), the Distinguished Scientific Achievement Award of the American Liver Foundation (2012), and designation as Physician of the Year of the Greater New York Division by the American Liver Foundation (2015). He is a member of the American Society for Clinical Investigation and the Association of American Physicians and a fellow of the American Gastroenterological Association and the American Association for the Study of Liver Diseases. He has served as councilor (1997–2000) and president (2000–2001) of the Interurban Clinical Club.

He has been a councilor for the American Association for the Study of Liver Diseases and the American Physiological Society, gastroenterology section, and has served on the steering committee of the Gastroenterology Research Group. He has been an active participant in the American Liver Foundation and served as chair of its board of directors (2007–2011). He has been a frequent member of NIH study sections and is the former chair of the Hepatobiliary Pathophysiology (HBPP) Study Section (2004–2007). He has also had multiple editorial positions, which include serving as associate editor of *Hepatology* (1990–1996) and associate editor of the *American Journal of Physiology—Gastrointestinal and Liver Physiology* (2003–2009). He is currently topic editor of the Hepatobiliary Physiology section of *Comprehensive Physiology* (Wiley-Blackwell).

New York City emeritus members without submitted biographies:

Paul Cannon
NP Christy
QB Deming
Jules Hirsch
Attallah Kappas
Richard Kitsis
IM London
Ronald Nagel
Wade Parks
Edward Skolnik
WJ William
David Zakim

PHILADELPHIA BIOGRAPHIES OF LIVING MEMBERS



Charles Abrams, MD

Charles Abrams received his BES degree from Johns Hopkins University in 1980 and his MD from Yale University School of Medicine in 1984. He was an intern at Temple University Hospital, then a resident in medicine and a hematology/oncology fellow at the Hospital of the University of Pennsylvania. In 1992 he joined the faculty at the University of Pennsylvania and is currently Francis C. Wood Professor of Medicine and a professor of pathology and laboratory medicine. He serves as vice chair for research and chief scientific officer of the Department of Medicine. He is also director of the PENN-CHOP Blood Center for Patient Care & Discovery.

Throughout his career Abrams has focused on the area of phospholipid signaling in hematopoietic cells. He found that phosphoinositides are synthesized in discrete microdomains within cells, and these lipid in turn regulate actin-binding proteins and proteins required for exocytosis. His research program has received longstanding federal support, and he has served as principal investigator of multiple R01, P01, and K12 awards. His publications have appeared in journals such as *Science*, *Journal of Clinical Investigation*, and *Blood*. In addition, Abrams has chaired many scientific review committees for the National Institutes of Health and the American Heart Association. He is the recipient of a National Research Service Award and a Physician Scientist Award and was elected to the American Society for Clinical Investigation in 2000 and the Association of American Physicians in 2007.

In addition to his interest in basic research, Abrams has specialized clinically in disorders of thrombosis and hemostasis. He participated in several clinical trials evaluating thrombocytopenia in ICU patients, heparin-induced thrombocytopenia, and the use of thrombopoietin receptor agonists. As a testimony to his dedication of mentoring of young investigators and clinicians, he is the recipient of the John Glick Prize for Teaching Excellence in Hematology-Oncology, the Donald B Martin Teaching Service Award, and the DuPont Guerry Mentoring Award. Abrams has held many roles with the American Board of Internal Medicine including serving on

its board of directors, and currently serves on its hematology board. In 2013 he was elected as vice president of the American Society of Hematology and will serve as their 58th president in 2016.

Zoltan Arany, MD, PhD

Zoltan Arany was born in Brussels, Belgium, on May 31, 1967. He emigrated to the US in 1979. He received a BA in biochemistry summa cum laude from Harvard College in 1989 and an MD-PhD in 1998 from the Harvard Medical School/MIT combined program and Harvard Graduate School of Arts and Sciences. During his PhD, he studied cancer biology under the mentorship of David Livingston at the Dana-Farber Cancer Institute. He then completed a residency in internal medicine at Massachusetts General Hospital (1998–2001), a fellowship in cardiology at Brigham and Women's Hospital (2001–2004), and a postdoctoral fellowship and instructorship with Bruce Spiegelman at Dana-Farber Cancer Institute (2004–2008), studying mechanisms of metabolism regulation in the heart and skeletal muscle and supported by an NIH NHLBI K08 Research Career Development Award. In 2008 Arany was recruited by Anthony Rosenzweig to initiate his own laboratory as assistant professor at Beth Israel Deaconess Medical Center Cardiovascular Institute and Harvard Medical School. In 2013 Arany became associate professor of medicine. In 2014 he moved to the Cardiovascular Institute at the University of Pennsylvania, where he is currently associate professor of medicine with a joint appointment in the Cell Developmental Biology Program.

Arany began his career studying mathematics but quickly became inspired by the burgeoning revolution in molecular biology that occurred in the late 1980s. The emerging and exciting possibilities in the arena of medical sciences led him to pursue a career in medicine. He developed an interest in gene regulation and cancer biology while working at the Livingston laboratory, where he discovered the transcriptional co-activator activity of the adenovirus oncoprotein E1A-associated p300 protein and its key role as a co-activator of hypoxia-inducible factor 1a (HIF-1a) and its hypoxic induction of VEGF and other angiogenic factors. Clinical interests then led him to the field of cardiology where, as a cardiology fellow, he rediscovered metabolism as a live, promising, and growing area of research (in contrast to his first impressions during college biochemistry courses) that was highly relevant to clinical care. This interest led him to work with Spiegelman, where he showed that the transcriptional coactivator PGC-1a

is a key regulator of ATP-producing metabolic programs in the heart in both physiologic and pathologic settings and used novel, high-throughput methods to identify small molecules to modulate this pathway.

The themes of metabolism and cardiovascular health and disease have been the major focus of Arany's research. As instructor at Harvard Medical School, he first became interested in the relationship between cellular metabolism and the vasculature. He showed that PGC-1 co-activators co-regulate mitochondrial biogenesis (fuel consumption) with powerful angiogenesis (fuel delivery), achieved via the coordinated induction and secretion of numerous angiogenic factors, including VEGF. This work paved the way for the notion that metabolic regulation reaches beyond the plasma membrane and modulates the cellular environment to suit the metabolic needs of the cell. Arany has continued to study the PGC-1 α metabo-/angiogenic pathway in numerous contexts in which both angiogenesis and metabolism play prominent roles. One of these, the heart, led to important insights into the orphan disease peripartum cardiomyopathy (PPCM), a disease that can be devastating to mother and newborn child and whose cause remained unknown. His work showed that the disease is caused by an angiogenic imbalance, triggered in part by the secretion from the placenta of anti-angiogenic factors such as soluble VEGFR1. PPCM is thus a vasculo-metabolic disease with an important endocrine component. The findings have significantly altered how the disease is understood. Arany continues to actively study this disease as well as vascular metabolism and the role of the vasculature in systemic metabolism, using tools spanning from molecular studies to mouse models and clinical investigations.

Arany has received numerous awards, including the American Heart Association Established Investigator Award, the Irvine H. Page Young Investigator Award, the Hal Dvorak Young Investigator Award in Translational Research, and the inaugural Yale Calabresi Prize in Vascular Biology. He is a member of the American Society for Clinical Investigation, has served on NIH study sections and other funding review mechanisms, and is a regular reviewer for numerous journals, including *Nature*, *New England Journal of Medicine*, *Circulation*, and *Journal of Clinical Investigation*. Arany is also committed to teaching and mentoring. He designed and co-directed with Thomas Michel for 5 years (2007–2011) the widely acclaimed course "Human Metabolism and Disease" at Harvard Medical School. In 2011 he designed and codirected for 3 years a new course, "Scholarship in Medicine," which is now required for all incoming Harvard medical students. He has lectured on communication skills in leadership development

courses at Harvard Medical School and has received a number of teaching and mentoring awards, including the John and Christine Seidman Prize for Research Mentoring.

Anne Rentoumis Cappola, ScM, MD

Anne Rentoumis was born in Houston, TX, on July 12, 1969, and moved to Fort Lauderdale, FL, in 1977. She received a BA in biochemistry from Harvard University in 1990 and an MD from the University of Pennsylvania School of Medicine in 1994. This was followed by a residency in internal medicine at Brigham and Women's Hospital (1994–1997), where she met her husband, Thomas Cappola, a co-resident. She began her fellowship in endocrinology at Massachusetts General Hospital (1997–1998) and completed it at Johns Hopkins Hospital (1998–2000). Concurrently, she completed a fellowship in the epidemiology of aging (1999–2001) and earned an ScM degree in clinical epidemiology at the Johns Hopkins Bloomberg School of Public Health (2001), where she was mentored by Linda P. Fried (1999–2001) and studied hormonal changes in older individuals. She was appointed an assistant professor of medicine in the Division of Endocrinology, Diabetes, and Nutrition at the University of Maryland in 2001 and recruited to the Division of Endocrinology, Diabetes and Metabolism at the University of Pennsylvania in 2003. In 2011 she was promoted to associate professor of medicine with tenure.

As a biochemistry major at Harvard College, she performed basic laboratory research with J. Larry Jameson at Massachusetts General Hospital, where she studied the molecular regulation of thyroid hormone action and earned a Hoopes Prize for her thesis work. It was the hunch of her biochemistry advisor, who thought Jameson's lab would be a good fit for her, that led her to the career-defining experience of working in the Jameson lab. She loved working in the lab, but, influenced by the endocrine fellows she met there, she decided to attend medical school, following in the footsteps of her maternal grandmother, a 1922 medical graduate. Throughout her medical training she remained interested in both endocrinology and biomedical research, and her clinical experiences sparked a desire to study human subjects. She met Fried during her endocrinology fellowship at Johns Hopkins Hospital and became her mentee, thus embarking on the interdisciplinary training in gerontology and epidemiology that subsequently defined her research program.

Cappola is recognized as a leader in translational research at the intersection of endocrinology and geriatrics, combining population-based and mechanistic research studies to identify the hormonal underpinnings of human aging. Her scientific contributions have led to changes in treatment recommendations for older individuals with subclinical thyroid dysfunction. In addition, she is developing the first therapeutic agent to treat age-associated frailty.

Early in her career she identified a critical gap in the field, that is, that there were no hormonal data in older people with illness and disability, who are arguably the patients who have the most to gain from hormonal interventions. She has since developed a new paradigm in hormones and aging that has illuminated the complex interplay among multiple hormonal axes and their evolution over time in older individuals. In particular, her research on multi-hormonal dysregulation and frailty has taken her field in a completely new direction that embraces the complexity of the aging process and has strong translational potential. The opening of this direction is very challenging but critical, because single-hormone replacement trials aimed at counteracting the phenotypic effects of aging have universally yielded disappointing results.

Her innovative research has made important contributions toward improving the care of three common, debilitating clinical problems in older adults: thyroid disorders, sarcopenia, and frailty. Her most significant research contribution has been to define the parameters for treating thyroid disorders in older individuals. She has also characterized the role of endogenous androgens in the health of older women, paving the way for therapies to treat muscle wasting in this population. In a third area of investigation, Cappola has pioneered studies in human subjects that seek to determine the role of endocrine abnormalities in age-associated frailty. Her body of work demonstrates that in the frailty syndrome, simultaneous physiologic alterations occur in multiple hormones, and more broadly, across organ systems. She completed the first randomized trials that studied the effects of ghrelin administration in frail older people. Administration of ghrelin resulted in a dramatic improvement in food intake, supporting a role for this hormone as the first therapeutic agent to combat unintentional weight loss in frailty.

She has a broad commitment to advancing translational research, and serves as director of the Commercialization and Entrepreneurship in Translation Program at the Perelman School of Medicine, director of re-

search education for the Division of Endocrinology, and core faculty mentor in the University of Pennsylvania's Masters in Translational Research Program.

Cappola has received multiple awards, including the Endocrine Society's Thyroid Clinical Research Mentor Award and the American Thyroid Association's Van Meter Award, and she has been elected to the American Society for Clinical Investigation. She has served on the editorial board of the *Journal of Clinical Endocrinology and Metabolism* and is an associate editor of *JAMA*. She recently completed a sabbatical at the University of Cambridge as a senior honorary visiting fellow.

Thomas P. Cappola, ScM, MD

Thomas Cappola was born in New Brunswick, NJ, on June 27, 1969. He received an AB in chemistry from Princeton University in 1991 and an MD from Harvard Medical School in 1995. He trained in internal medicine at Brigham and Women's Hospital (1995–1998), where he met and married co-resident Anne Rentoumis (now Anne Cappola). He then completed training in cardiovascular medicine and heart failure/transplant medicine at Johns Hopkins Hospital (1998–2002). While at Hopkins, he earned an ScM from the Graduate Program in Clinical Investigation, with a focus on translational science. He also trained in applied genomics in the Hopkins/NHLBI Program in Genomic Applications. He was appointed assistant professor of medicine in 2002 and moved to the University of Pennsylvania School of Medicine in 2003. In 2012 he was promoted to associate professor of medicine with tenure, and he became director of the Clinical and Translational Research Center at Penn in 2013.

Cappola became inspired to become a scientist while in high school, when he discovered and began to read textbooks from his father's PhD coursework. He was captivated by the idea of understanding complexity through fundamental principles of science. At Princeton he worked with Clarence Schutt, studying the structure of actin, but he sought a more translational path and chose medicine. During medical school and his residency, he focused on clinical excellence and developed a strong interest in cardiovascular disorders. During his fellowship training he was inspired by his primary mentor, Joshua Hare, as well as by Eduardo Marban and David Kass, to return to science with a specific focus on human heart failure. This required that he gain skill sets in translational medicine and genome

science, the latter of which was emerging as a powerful tool to understand common complex diseases.

Since moving to Penn he has established a broad research program that uses clinical investigation and applied genomics to understand human heart failure. His laboratory provided the first proof that the peripheral blood transcriptome provides a biomarker to track cardiac transplant rejection, an approach that is now used in clinical practice. He used genome-wide transcriptomic approaches applied to human myocardium to uncover a link between FOXP repressors and human heart failure. He developed and is principal investigator of the Penn Heart Failure Study, an ongoing NHLBI-sponsored multicenter, longitudinal cohort study of advanced heart failure. He has used this resource to uncover 1p36 as the first genetic risk locus for non-familial heart failure. In subsequent work he determined that the underlying mechanism is a loss-of-function variant in the CLCNKA transporter. He has also elucidated roles for circulating sFlt-1 and neuregulin in heart failure progression, both of which have potential as novel diagnostics.

More recently Cappola spearheaded the formation of the Myocardial Applied Genomics Network, a multicenter consortium for human myocardial transcriptomics and eQTL mapping. This consortium brings together laboratories from multiple institutions to form the world's largest human myocardial biobank for "omic" research. The consortium has uncovered genetic regulatory mechanisms in humans that lead to myocardial disease and conduction disorders. He also co-leads the Mid-Atlantic Heart Failure Network, which includes four hospitals in Pennsylvania and Maryland. This network is one of nine regional nodes in the NHLBI Heart Failure Clinical Research Network, the goal of which is to design and implement phase 2 trials of new heart failure therapies. He is currently national co-principal investigator on the Functional Impact of GLP-1 for Heart Failure Treatment (FIGHT) clinical trial, which will test whether or GLP-1 agonists improve clinical stability in patients with heart failure and reduced ejection fraction.

Cappola's leadership extends beyond his laboratory to the translational science community. He is currently director of the Clinical and Translational Science Award-funded Clinical and Translational Research Center at Penn. Beyond Penn, he serves on the steering and genetics committees of the NHLBI Heart Failure Clinical Research Network and is program chair for the American Heart Association Council on Functional Genomics and

Translational Biology. He has received numerous awards for his research accomplishments, most notably the Presidential Early Career Award for Scientists and Engineers (PECASE) and election to the American Society for Clinical Investigation. Most recently he served as an honorary senior visiting fellow at the University of Cambridge in 2013–2014, before returning to Penn in the summer of 2014.

Lewis A. Chodosh, MD, PhD

Lewis Chodosh was born in Framingham, MA, on November 26 (Thanksgiving Day), 1959. He began his academic career as an undergraduate at Yale University, from which he graduated summa cum laude and Phi Beta Kappa in 1981 with distinction in molecular biophysics and biochemistry. In 1989 Chodosh received his MD from Harvard Medical School magna cum laude and his PhD in biochemistry from the Massachusetts Institute of Technology under the mentorship of Nobel Laureate Phillip Sharp.

Following his graduation from the Harvard MD-PhD program, Chodosh performed clinical training at Massachusetts General Hospital, where he completed his internship and residency in internal medicine as well as a clinical fellowship in endocrinology. In 1992 Chodosh joined the laboratory of Philip Leder in the Department of Genetics at Harvard Medical School as a postdoctoral fellow. There, his interests in endocrinology and cancer biology coalesced in studying the pathogenesis of breast cancer and the impact of developmental regulatory programs on cancer susceptibility. These themes have remained a focus of his subsequent research.

Chodosh joined the faculty of the University of Pennsylvania School of Medicine as assistant professor in 1994, where he has remained for the past 20 years. He currently serves as chairman of the Department of Cancer Biology at the Perelman School of Medicine, associate director for basic science at the Abramson Cancer Center, director of cancer genetics for the Abramson Family Cancer Research Institute, and co-director of the 2-PREVENT Breast Cancer Translational Center of Excellence. Chodosh previously served as director of the Breast Cancer Program of the Abramson Cancer Center, vice chairman of the Department of Cancer Biology, and founding co-director of the Penn Medicine Small Animal Imaging Facility. Chodosh is a tenured professor in the Department of Cancer Biology and in the Department of Medicine in the Division of Endocrinology, Diabetes & Metabolism.

In selecting medicine and biomedical research as a career, Chodosh was inspired by his father, Sanford Chodosh, who was a physician-scientist at Boston City Hospital. As a high school student, he spent several summers in his father's clinical research laboratory studying the biochemistry and cytology of sputum specimens from patients with chronic bronchitis, asthma, and emphysema. This experience, together with witnessing the impact of the physician-patient relationship in the setting of clinical investigation, set Chodosh on his current path. His interest in laboratory-based biomedical research solidified during his graduate studies with Sharp at the Massachusetts Institute of Technology, during which time Chodosh made important contributions to our understanding of the mechanisms by which genes are regulated in mammalian cells.

As a physician-scientist Chodosh has pioneered new approaches to the study of breast cancer through a laboratory research program focused on understanding breast cancer etiology and progression. Through detailed analysis of a series of genetically engineered mouse models developed in his laboratory, Chodosh has made important inroads into understanding oncogene addiction, on which many targeted therapies for cancer are predicated, and the mechanisms by which cancers progress to more aggressive states. These studies have led to the novel identification and characterization of molecular pathways that contribute to breast cancer progression, particularly as they relate to tumor cell dormancy, metastasis, and tumor recurrence, which together represent the principal causes of death from this disease. Through the development of animal models that faithfully recapitulate human disease, Chodosh has had an important impact on the study of breast cancer pathogenesis and is a highly regarded leader in the cancer biology community.

As chairman of the Department of Cancer Biology, Chodosh leads the newest department at the Perelman School of Medicine at the University of Pennsylvania, a department that has grown substantially under his direction over the past six years. Chodosh was elected to the American Society for Clinical Investigation in 2002 and to the Association of American Physicians in 2008. He has received numerous honors, including the Emerson Tuttle Cup for Distinguished Academic Achievement from Yale University, the Leon Reznick Memorial Prize for excellence in research from Harvard Medical School, the Charles E. Culpeper Foundation Scholarship in Medical Science, and the AACR-Sidney Kimmel Cancer Research Scholar Award. Chodosh currently serves as an advisor to the Harvard Nurses' Health Study I and II and to the Dana-Farber/Harvard Cancer Center. He

also has served as principal investigator for a site of the National Cancer Institute's Mouse Models of Human Cancers Consortium, director of a congressionally directed Breast Cancer Center of Excellence at the University of Pennsylvania, and editor-in-chief of *Breast Cancer Research*.

George Cotsarelis, MD

George Cotsarelis was born in Harrisburg, PA, on November 24, 1961. Cotsarelis serves as the Milton B. Hartzell Professor and chairman of the Department of Dermatology at the University of Pennsylvania School of Medicine. He is also the director of the Program on Epithelial Regeneration and Stem Cells at the University of Pennsylvania Institute for Regenerative Medicine. His research focuses on epithelial stem cells, hair follicle biology, epithelial carcinogenesis, wound healing, and skin regeneration. As a medical student at Penn, Cotsarelis first localized epithelial stem cells of the cornea to the limbal epithelium. This finding eventually changed the practice of ophthalmology and led to new treatments for certain types of blindness.

His research interests then shifted to epithelial stem cells in the skin. In 1990 he was the first to localize presumptive hair follicle stem cells to the bulge area. He hypothesized that these quiescent cells were multipotent and responsible for the continual turnover of the cutaneous epithelium. After his dermatology residency at Penn, his laboratory discovered a molecular marker (cytokeratin 15) for bulge cells in both mouse and human skin. This finding allowed him to develop transgenic mouse models to test his hypotheses. Using flow cytometry and genetic lineage tracing, he isolated hair follicle stem cells and demonstrated their multipotency in a skin reconstitution assay that he developed. When injected into an immunodeficient mouse, the isolated hair follicle stem cells formed new hair follicles and all ten of the epithelial cell types within the skin. These findings have clinical implications for developing cell-based treatments for hair loss and chronic wounds.

Using genetic lineage analysis he studied the fate of hair follicle stem cells during wound healing. This small population of cells was responsible for providing 30% of the cells within a re-epithelialized wound. Remarkably, his lab discovered neogenic hair follicles regenerating in the newly formed epidermis during wound healing. This process was controlled by factors, such as Wnts, that are necessary for hair follicle development but are nor-

mally turned off in adult somatic stem cells. More recently, using global gene expression analysis, he discovered other growth factors produced by immune cells that control hair follicle regeneration in adult animals. These findings led to the formation of a startup company that is attempting to develop new treatments for hair and skin loss.

Cotsarelis developed means for isolating different populations of stem and progenitor cells from human skin. Using these techniques his laboratory showed that hair follicle stem cells remain intact in human balding scalp, while a population of progenitor cells decreased. This suggests that a defect in stem cell activation is responsible for male pattern baldness. His laboratory then discovered that prostaglandin D2 (PGD2) was elevated in balding scalp and inhibited hair growth through the PGD2R2 receptor. One company is planning to conduct a clinical trial using a compound that inhibits PGD2R2 for the treatment of male pattern baldness.

Cotsarelis's laboratory continues to work on the role of epithelial stem cells in normal skin biology, skin regeneration, wound healing, aging, and tissue engineering. The current hypothesis in the laboratory is that the expression of a modest number of genes in the skin determines whether skin regenerates or simply repairs with scarring after wounding. He is working on identifying these genes and epigenetic changes to better understand skin regeneration and to develop new treatments for skin disorders.

Cotsarelis heads the University of Pennsylvania Hair and Scalp Clinic. He is an expert in alopecia, including alopecia areata, androgenetic alopecia, and cicatricial alopecia. He served a term as president of the North American Hair Research Society. He was a permanent member of the NIH Arthritis and Musculoskeletal and Skin Diseases Study Section and is a member of the American Society for Clinical Investigation, the Association of American Physicians, and the American Dermatological Association.

Massimo Cristofanilli, MD, FACP

Massimo Cristofanilli, a knight of the Order of the Star of Italian Solidarity, was born on March 11, 1960. Cristofanilli is an Italian oncologist known for his contributions to the detection of micro-metastatic disease in breast cancer and research into inflammatory breast cancer (IBC), the most aggressive form of breast cancer. He currently serves as deputy director of translational research and director of the Jefferson Breast Cancer Center at

the Sidney Kimmel Cancer Center at Thomas Jefferson University.

A native of Nettuno, Italy, Cristofanilli graduated high school from the Scientific Liceum “Innocenzo XII” in Anzio, and received a degree in medicine and surgery from the University of Rome “La Sapienza” in 1986. He completed training in medical oncology under the direction of Alberto Pellegrini, who convinced him to dedicate his professional activity to the study and treatment of breast cancer. As a clinical research fellow in oncology, he focused his research on clinical trial design and assumed increasing responsibilities for patient care, research, and education of trainees and medical students.

Cristofanilli pursued additional training in clinical pathology, as he recognized the importance of molecular diagnostics in the management of cancer patients. His clinical and research activities brought him close to Italian oncology leaders such as Gianni Bonadonna. Cristofanilli realized that his research in breast cancer could be enhanced by extended training experience in the US, and so in 1993 he moved to New York for medical residency training at the Cabrini Medical Center of New York Medical College, where he served as chief medical resident. In 1996 he accepted a medical oncology fellowship at the University of Texas MD Anderson Cancer Center (MDACC) under director Richard Pazdur.

Cristofanilli completed two years of medical oncology fellowship and did his clinical rotations with Gabriel Hortobagyi at the Nellie B. Connally Breast Center. He treated a large number of patients with locally advanced breast cancers and IBCs and became responsible for the clinical trials for these patients. This initial experience convinced him of the need for a more comprehensive and focused approach toward IBC as a unique and rare clinical and biological entity. He spent last year of his fellowship training in the laboratory of Mien-Chi Hung, developing an approach to cancer cell sorting and single-cell molecular analysis, with the intention to understand the role of micro-metastatic disease in breast cancer patients.

In 1998 Cristofanilli joined the Department of Breast Medical Oncology, led by Hortobagyi. As an assistant professor, his first objective was to pursue an innovative concept to the detection of micro-metastatic disease in advanced breast cancer. He had just published a paper demonstrating that dielectrophoresis can distinguish cancer cells from normal breast epithelium and other mononuclear cells. Moreover, individual breast cancer cells could be further discriminated for the level of HER-2 protein expression.

He developed and initiated a prospective study for the longitudinal study of circulating tumor cells (CTCs) in metastatic breast cancer. The analysis of the study was published in 2004 in the *New England Journal of Medicine*. This was followed by a series of subsequent analyses confirming the prognostic value of CTCs irrespective of disease subtype, site of recurrence, or type of therapy.

The resulting technology, CellSearch[®], has been approved by the US Food Drug Administration for use in testing the prognosis of patients with certain metastatic cancers, and the technology was recognized with the Prix Galien, awarded by the Galien Foundation, in 2009. The detection of CTCs was incorporated in the 7th edition of the American Joint Committee on Cancer. The biological concept is that CTCs constitute seeds for growth of additional tumors (metastasis) in vital distant organs, triggering a mechanism that is responsible for the vast majority of cancer-related deaths. The revolutionary concept of a “liquid phase” of solid tumors has stimulated research and investments in this field that are currently focused on the molecular analysis of those cells for therapeutic targeting. Cristofanilli’s more recent work is in expanding the use of blood-based diagnostics to include circulating tumor DNA (ctDNA) and circulating immune cells.

In 2006 Cristofanilli started the first multidisciplinary clinic and research program that is focused mainly on IBC. Cristofanilli and Robertson received a Promise Grant from American Airlines and Susan G. Komen for the Cure (\$7.5M), which resulted in a number of discoveries and the development of IBC-focused trials. Understanding the need for collaboration and education, Cristofanilli established the International IBC Conference, the first of which was held in Houston, TX, in 2008 and was attended by more than 200 physicians, scientists, and advocates. The conference continues to be held, alternating between the US and Europe, and has led to the creation of an International IBC Consortium. Cristofanilli is also the co-founder of the IBC Foundation, an advocacy organization dedicated to raising awareness of the disease through increased education.

Wafik El-Deiry, MD, PhD

Wafik El-Deiry was born in Alexandria, Egypt on January 23, 1961. His parents moved to the U.S. in 1971-1972 to medical residency programs in New York City. He attended Martin Van Buren High School in Queens, NY and Coral Gables High School in Florida. He was interested in both

medicine and research at a young age due to the influence of his parents and physicians in his extended family. During high school and college he worked in the laboratory of William Awad, MD, PhD on purification and post-translational modifications of proteolytic enzymes trypsin and chymotrypsin at the University of Miami School of Medicine. He attended the University of Miami where he majored in chemistry and math, graduating in 1981. He attended the University of Miami School of Medicine and earned MD and PhD degrees by 1987. For his thesis, he worked with Antero So, MD, PhD, on manganese mutagenesis and error discrimination properties of *E. coli* DNA polymerase I.

Dr. El-Deiry moved to Baltimore in 1987 for internal medicine residency on the Osler Medical Service, and joined the medical oncology fellowship program at the Johns Hopkins Oncology Center in 1990. He joined the laboratory of Stephen Baylin, MD as a senior medical resident and cloned the first human DNA methyltransferase (DNMT1) and used its cDNA to analyze its expression in stages of human colon cancer. As a senior clinical fellow in medical oncology, he worked in the laboratory of Bert Vogelstein, MD doing research on the p53 tumor suppressor gene and protein. In the Vogelstein lab he discovered the DNA-binding response element for human p53, published in the first issue of a new journal, *Nature Genetics*, in 1992. This consensus sequence continues to be used to determine whether p53 protein directly regulates genes that it binds to and that may mediate its various effects in tumor suppression. Dr. El-Deiry discovered the gene encoding p21(WAF1) as a p53 target gene, universal cell cycle inhibitor and tumor suppressor that for the first time explained the mammalian cell stress response. The discovery of p21 as a p53 target gene and potential mediator of tumor suppression by p53 was the most highly cited work published in *Cell* over the next 20 years.

Dr. El-Deiry joined the faculty at the University of Pennsylvania School of Medicine as assistant professor of medicine and genetics in 1994, associate professor with tenure in 1999 and full professor of medicine, pharmacology and genetics by 2005. He was an Investigator of the Howard Hughes Medical Institute from 1995-2004. He served as co-program leader of the Radiobiology & Imaging Program at the Abramson Comprehensive Cancer Center and as associate director for Physician-Scientist Training in Hematology-Oncology at the University of Pennsylvania.

He made several discoveries in cell death and tumor suppressor genes, including discovery of TRAIL death receptor DR5 as a target of the p53

tumor suppressor. His laboratory characterized the TRAIL signaling pathway and explored its use as an anti-cancer agent in combination with chemotherapy, radiation, or targeted agents. His lab discovered that c-Myc is a major determinant of TRAIL sensitivity and found a potent synergy between TRAIL and the multi-kinase inhibitor sorafenib. His lab created a knockout mouse for the pro-apoptotic TRAIL receptor and described a role for the extrinsic cell death pathway in the *in vivo* response to radiation. For over a decade Dr. El-Deiry's laboratory performed functional small molecule discovery screening and *in vivo* validation/efficacy testing to accelerate the identification and development of molecularly-targeted anticancer therapeutics targeting mutant p53, hypoxic sensitization and the TRAIL cell death pathway. Dr. El-Deiry founded Oncoceutics, Inc. that licensed the first-in-class TRAIL pathway-inducing small molecule TIC10 for clinical development as ONC201. ONC201 completed first-in-human clinical testing in 2015 and entered multiple phase II trials for cancer patients. He founded p53-Therapeutics, Inc. in 2013.

Dr. El-Deiry moved to Penn State University as the Rose Dunlap Professor of Medicine and chief of the Hematology/Oncology Division, Milton S. Hershey Medical Center and the Penn State College of Medicine, associate director for translational research and program leader of experimental therapeutics at the Hershey Cancer Institute. He became one of 40 active American Cancer Society Research Professors in 2009 recognizing both scientific accomplishments and mentoring. He became interested in personalized cancer therapy for colorectal cancer, including demonstrating that pharmacokinetically guided dose adjustment of 5-fluorouracil can reduce toxicity and improve quality of life. He was interested in the genomic profiling of metastatic lesions in colorectal cancer and derived insights for potential therapies in various subtypes of this disease. Dr. El-Deiry's lab discovered an off-target effect for the EGFR/Her2 inhibitor lapatinib and published this in *Science Translational Medicine*. His group also published the discovery of TIC10/ONC201 and worked on its mechanism of action.

Dr. El-Deiry has over 300 peer-reviewed publications, h-index 99 and >50,000 citations by 2015. He has served on editorial boards including as associate editor for the *Journal of Clinical Investigation* and as the founding editor-in-chief of *Cancer Biology and Therapy*. El-Deiry is active in the NIH review system, and was also named a highly cited researcher by Thompson ISI in molecular biology and genetics and as one of America's Top Oncologists by the Consumer Research Council of America. He is a member of the Faculty of 1000 in cell growth and division.

Dr. El-Deiry is a member of several national honor societies including the Interurban Clinical Club (president 2013-2014), the American Society of Clinical Investigation and the American Association of Physicians, and is a fellow of the American College of Physicians. He received the Michael S. Brown Junior Faculty Research Achievement Award from the University of Pennsylvania, the Elizabeth and John Cox Award for Molecular Advances in GI Diseases and Cancer from Georgetown University, the international Kuwait Prize in Applied Sciences for "Cancer Diseases," the Distinguished Speaker Award from the Thomas Jefferson University School of Graduate Studies, the Dean's Award for Excellence in Teaching at the Penn State College of Medicine and the Department of Medicine's Excellence in Mentoring Award. He was inducted as a member of the Johns Hopkins University Society of Scholars in 2014.

In 2014, he was named deputy director for translational research and co-leader of the Molecular Therapeutics Program at Fox Chase Cancer Center in Philadelphia. He serves as professor of medical oncology and treats patients with colorectal cancer. His laboratory at Fox Chase is funded by multiple grants from the NIH and the American Cancer Society. As of January 2016, Dr. El-Deiry holds the William Wikoff Smith Endowed Chair in Cancer Research at Fox Chase Cancer Center.

Jonathan Alan Epstein, MD

Jonathan A. Epstein was born at the Yale–New Haven Hospital on May 19, 1961, and occasionally returned to the hospital as a child to join his father, Franklin H. Epstein (a past member of the Interurban Clinical Club) on his rounds. Jon Epstein moved to Brookline, MA, at age 12, where he attended the John D. Runkle School and then Brookline High School. He excelled at academics, auto mechanics, and woodworking. Summers included apprenticeships at the Mount Desert Island Biological Laboratory in Bar Harbor, ME, where he learned the joy of scientific discovery from his father and his mentor and friend Patricio Silva. There he met his future wife, the girl next door, Margaret (Maggie) Myers. At Harvard College he majored in biochemistry, studied with Lewis Cantley, captained the ultimate frisbee team, and graduated *magna cum laude* in 1983. After a brief stint as a technician with David Housman at MIT, he entered Harvard Medical School, studied with Claude Lechene, and continued his work with Cantley. He graduated *magna cum laude et thesis propria* and won the Leon Reznick Memorial Prize for excellence in research in 1988. He performed his internship and residency at Brigham and Women's Hospital as part of the

research-residency program under Eugene Braunwald and completed a cardiology fellowship at Brigham with Thomas W. Smith. He met Richard Maas while on rounds at Brigham and joined his developmental biology laboratory, with help from a Howard Hughes postdoctoral fellowship for physicians. This represented a significant change in research focus, from biochemistry to developmental biology, which set the stage for a subsequent career in developmental cardiology.

In 1996 Epstein accepted a position as assistant professor of medicine in the Division of Cardiology at the University of Pennsylvania. He was promoted to associate professor in 2001 and became the William Wikoff Smith Professor in 2004. In 2004 he was appointed scientific director of the Penn Cardiovascular Institute and, in 2006, chairman of the Department of Cell and Developmental Biology. In 2007 he collaborated with the renowned stem cell biologist Ralph Brinster, to create the Institute for Regenerative Medicine at Penn.

Epstein directed the physician-scientist program in the Department of Medicine at the University of Pennsylvania and has been a proponent of maintaining a vital role for the physician-scientist in academic medicine. He has trained numerous MD, PhD, and MD-PhD students and fellows in his laboratory.

Epstein was elected to the Interurban Clinical Club in 2004 and served as president in 2014–2015. He has been the recipient of numerous awards, including the Sir William Osler Young Investigator Award from the Interurban Clinical Club (2001) and the Outstanding Investigator Award from the American Federation for Medical Research (2006). He was elected to the American Society for Clinical Investigation in 2001 and served as councilor (2004–2010) and president (2010). He was elected to the American Association of Physicians in 2006 and to the Institute of Medicine of the National Academy of Sciences in 2008. He has served on numerous editorial boards and was associate and deputy editor of the *Journal of Clinical Investigation*. He has contributed to numerous NIH and American Heart Association study sections as both a member and chair. Epstein also has devoted time and energy to several scientific and medical foundations, including the Stanley J. Sarnoff Endowment Scientific Committee, the Children's Tumor Foundation, the Ara Parseghian Medical Research Foundation Scientific Advisory Board, the Verto Institute Board of Scientific Advisors, the Sanford-Burnham Institute Scientific Advisory Board, and the National Neurofibromatosis Foundation.

Epstein's research has focused on the molecular mechanisms of cardiovascular development and implications for understanding and treating human disease. His group has been at the forefront of utilizing animal models (mouse and zebrafish) of congenital heart disease to determine the genetic and molecular pathways required for cardiac morphogenesis, with implications for pediatric and adult cardiovascular disease. Stem cell, angiogenesis, and epigenetic studies have had direct implications for the development of new therapeutic agents for heart failure and myocardial infarction. Epstein is considered among the world experts in the roles of neural crest in cardiovascular development, and his group contributed to the identification of *TBX1* as a causative gene in DiGeorge syndrome. His studies have elucidated the genetic and developmental causes of aortic arch malformations, cardiac valve defects, and cardiac conduction abnormalities, including Wolff-Parkinson-White syndrome. He has been a proponent of utilizing information gleaned from the study of embryogenesis to inform regenerative approaches for cardiac disease.

In addition to his research commitments, Epstein practices medicine in the cardiac intensive care unit at the Hospital of the University of Pennsylvania and the Philadelphia VA Medical Center.

Michael S. Parmacek, MD

Michael Scott Parmacek was born on January 19, 1955, on Coronado Island, CA, where his father was a naval officer. Parmacek attended public schools in Highland Park, IL, where his interest in biology was catalyzed by a remarkable high school AP biology teacher. Parmacek received the John Holder award as the outstanding student-athlete in his graduating high school class. He matriculated at Tufts University and, as a freshman, started at linebacker on the football team, but his football career was cut short by injury. Parmacek spent summers performing neurochemical research at Rush Medical College, where he published his first papers. At Tufts, he majored in biology and psychology and graduated *magna cum laude* in the spring of 1977.

Parmacek attended Northwestern School of Medicine, from which he received his MD in 1981. He then completed his internship and residency in medicine at the University of Michigan and was elected by his peers as the "most outstanding house officer in medicine." He was influenced strongly by William Kelley, chair of medicine at Michigan, who encouraged Par-

macek to obtain the basic research experience required for a career as a physician-scientist. Following residency Parmacek joined the laboratory of Michael Lesch, chief of cardiology at Northwestern. He examined the molecular pathways that regulate protein synthesis and degradation in the heart. Parmacek completed a two-year clinical cardiology fellowship and served as chief fellow during his final year of fellowship training.

Kelley recruited Parmacek back to Michigan for a postdoctoral research fellowship in the laboratory of Jeffrey Leiden. Leiden, who later served as president of the American Society for Clinical Investigation (ASCI), was at the time an assistant investigator of the Howard Hughes Medical Institute (HHMI). Kelley suggested that Parmacek and Leiden apply molecular methods to examine mechanisms that regulate cardiac development and the pathogenesis of cardiovascular disease. As a postdoctoral fellow Parmacek cloned and characterized the cardiac and skeletal troponin C genes. Parmacek and Leiden also performed translational studies to demonstrate the feasibility of gene transfer to the heart and vasculature. During this period, Parmacek met his wife, Lisa R. Gottschalk, an immunologist who was also a postdoctoral fellow in the HHMI/Leiden laboratory.

In 1990 Parmacek was appointed assistant professor of medicine at Michigan and established an independent laboratory focused on molecular cardiology. In 1992 he joined the faculty of the Department of Medicine at the University of Chicago, which was led by Arthur Rubenstein. Rubenstein, who would later become dean at the University of Pennsylvania, provided valuable counsel and advice to Parmacek throughout his career. From 1992 to 1996 Parmacek served as co-director of the University of Chicago Cardiology Fellowship Training Program. At Chicago he made his first important discovery, in which he demonstrated that the cell lineage-restricted transcription factor GATA4 plays a key role in the molecular program governing cardiomyocyte differentiation and cardiac morphogenesis. These studies highlighted the central role that cardiac-restricted transcription factors play in the morphogenetic program that underlies heart development and adaptation of the heart to stress. It is now recognized that mutations in GATA4 are associated with common forms of congenital heart disease. Edward Morrissey, a postdoctoral fellow with Parmacek, cloned and characterized two related GATA family members, GATA5 and GATA6. They discovered that GATA6 controls the differentiation of visceral endoderm, which is required for embryonic development.

John Lepore, another postdoctoral fellow with Parmacek, reported that

GATA6 plays a critical role in neural crest patterning of the cardiac outflow tract and underlies commonly observed forms of congenital heart disease.

In 1998 Parmacek joined the faculty of the University of Pennsylvania as the Herbert C. Rorer Associate Professor of Medical Sciences and chief of the Division of Cardiology. In 2002 he was promoted to professor and, in 2005, was named founding director of the University of Pennsylvania Cardiovascular Institute. Parmacek's second important contribution to the field of cardiology was to characterize critical functions mediated by myocardin-related transcriptional coactivators in the cardiovascular system. Parmacek discovered that the muscle-restricted transcriptional coactivator myocardin binds to the MADS box transcription factor SRF, to activate the contractile smooth muscle cell gene program. He demonstrated that forced expression of myocardin in embryonic stem (ES) cells activates multiple endogenous smooth muscle cell genes. Consistent with this observation, ablation of the mouse myocardin (*Myocd*) gene in smooth muscle abolishes the smooth muscle cell contractile gene expression associated with aortic aneurysm and dissection. Several myocardin-activated target genes, including *Acta2* and *Myh11*, cause heritable forms of thoracic aneurysm and dissection (TAAD). Parmacek also discovered that a closely related transcriptional coactivator, myocardin-like protein 2 (MKL2), regulates TGF- β signaling required for vascular stabilization required for cardiovascular homeostasis. Mutations in the *MKL2* gene are associated with common forms of congenital heart disease. The Parmacek laboratory discovered that myocardin is required for cardiomyocyte proliferation required for heart development and sarcomeric structure required for maintenance of the adult heart.

Under Parmacek's direction, the Division of Cardiovascular Medicine and the Penn Cardiovascular Institute have undergone a renaissance. The Penn CVI is home to over 180 investigators in 19 departments. In 2014 the heart and heart surgery program at Penn was ranked among the top 10 programs in the United States by *U.S. News & World Report*.

In 2014 Parmacek was appointed as the Francis C. Wood Chair of the Department of Medicine at the University of Pennsylvania Perelman School of Medicine. He leads the largest department in the Perelman School of Medicine and the University of Pennsylvania Health System. The Department of Medicine at Penn is the oldest in the country, dating back to 1765 when John Morgan assumed leadership of the first medical school in the 13 Colonies. Today the department includes 600 full-time faculty and is

ranked #3 in terms of NIH funding among all departments of medicine in all US medical schools.

As a nationally recognized leader in academic medicine, Parmacek has been named to multiple local, regional, and national leadership positions. He has served on the Advisory Council of the National Institutes of Health/ National Heart, Lung, and Blood Institute and on the Commonwealth of Pennsylvania Health Research Advisory Council, as president of the Association of Professors of Cardiology, and as an established investigator of the American Heart Association, and maintains membership in the ASCI and Association of American Physicians.

Richard P. Shannon, MD

Richard Shannon was born on April 30, 1954, in Bridgeport, CT, and attended Hopkins Grammar School in New Haven. The intimacy between Hopkins and Yale led to his first research experience in the laboratory of Marvin Sears in the Department of Ophthalmology at the Yale School of Medicine, and he published his first paper in 1976. Shannon matriculated at Princeton, where he majored in biology and played rugby football. At Princeton Shannon had a fabulous laboratory experience, studying adrenergic control of the estrous cycle in hamsters, which led to a career in medicine. He attended the University of Connecticut School of Medicine, where he served as the commencement speaker. He then trained in internal medicine at the Beth Israel Hospital at Harvard, where his early career was shaped by Franklin Epstein, Lewis Landsberg, and Eugene Braunwald, for whom he was chief resident. After two years of research, studying the sodium sensitivity of baroreceptors, Shannon studied cardiology at the Massachusetts General Hospital under Roman DeSantis and George Thibault. In 1987, when Shannon was a first-year fellow, Edgar Haber directed him to the laboratory of Steve Vatner to study cardiovascular integrative physiology, and there began a ten-year partnership that launched his academic career. At the same time, he served as program director in internal medicine under Braunwald and Bob Glickman and saw patients in the cardiology division of the Beth Israel Hospital under Bill Grossman. In 1993 Shannon took on the roles of director of the cardiovascular division at West Roxbury VA Hospital and associate director of the cardiovascular division at Brigham and Women's Hospital under Tom Smith.

When Braunwald stepped down from his position at Beth Israel and Tom

Smith died after a valiant battle with mesothelioma, Shannon made a bold move to become the chair of medicine at Allegheny General Hospital in Pittsburgh. While those years were productive in the lab, where his group discovered the cardiovascular actions of incretins, they were also nearly professionally fatal, as he was embroiled in the bankruptcy at the Allegheny Health, Education, and Research Foundation (AHERF). The 15 recruits that he brought to Pittsburgh from Harvard had to be relocated. It was a time in which Shannon learned painful lessons, and was also a time of a great personal sadness. But amidst professional and personal turmoil, Shannon met Paul O'Neill, CEO of Alcoa, who challenged him to remake American medicine through the elimination of waste, a cause that he continues to work on to this day. Redemption came in the form of the opportunity to move to Penn, where Shannon was named the Frank Wister Thomas Professor of Medicine and chair of the oldest department of medicine in the US. He owes this opportunity to dean Arthur Rubenstein. Penn enjoyed a period of unprecedented growth in the seven years in which Shannon served, and he has never been more professionally challenged or happy.

Shannon now presides over the re-creation of the UVA Health System in a time of unprecedented change in American medicine as the Louise Nerancy Professor of Health Science Policy and as executive vice president for health affairs at the University of Virginia. Shannon is rebuilding there the academic enterprise and reforming care delivery systems to achieve high performance and value. Through many stops, Shannon has been privileged to share in the academic medical enterprise, which he will always cherish and for which he will always be grateful.

Laurence A. Turka, MD

Laurence A. Turka was born in New York, NY, on April 15, 1957. He received his BA degree in biochemistry summa cum laude from Colgate University in 1978 and his MD from Yale University in 1982. He did his internship and residency in internal medicine at Yale–New Haven Hospital from 1982 to 1985, followed by a fellowship in nephrology at Brigham and Women's Hospital and Harvard Medical School. Upon completion of his fellowship in 1988, Turka accepted his first faculty position, as assistant professor of internal medicine at the University of Michigan, where he became a tenured associate professor in 1993. In 1994 Turka moved to the University of Pennsylvania, where in 1998 he was promoted to professor

of medicine and became the chief of the Renal-Electrolyte and Hypertension Division. From 1999 to 2009 he was the C. Mahlon Kline Professor of Medicine and held secondary appointments as professor in the Department of Surgery, Department of Pediatrics, and Department of Pathology and Laboratory Medicine. In 2009 he was recruited to the Beth Israel Deaconess Medical Center (Harvard Medical School), to serve as co-director of the Transplant Institute and co-chief of the Division of Transplantation Immunology. In 2010 he became co-director of the newly created Harvard Institute of Translational Immunology.

Turka's research interests were kindled while a medical student at Yale, when, in 1983, he was a summer intern in Dennis Ausiello's lab at Massachusetts General Hospital. While at Yale, Sam Thier and John Forrest were important mentors to Turka, helping to guide him toward a career in academic medicine and steering him toward clinical and research work in nephrology. Based upon patient experiences while a renal fellow at Brigham and Women's Hospital, Turka first became interested in transplantation nephrology and pursued research training in cellular immunology at Brigham in Bernie Carpenter's lab, where he studied human allogeneic immune responses *in vitro*. As a new faculty member at the University of Michigan, Turka first worked in Craig Thompson's lab, where he obtained critical training in molecular immunology and became interested in T cell costimulation, a topic that became a major focus of his research career.

Turka's group was the first to show that blockade of the CD28 T cell costimulatory pathway prevented acute allograft rejection and could induce transplantation tolerance. These studies, done using the soluble fusion protein CTLA4-Ig, helped pave the way for FDA approval of the drug abatacept (Orencia) for the treatment of rheumatoid arthritis and for approval filing of the drug belatacept for treatment of renal transplant recipients. Turka's continued work focused on mechanisms of transplantation tolerance and barriers to achieving it. In partnership with Terry Strom, he demonstrated that T cell tolerance to transplants requires the death of alloreactive T cells, and moreover that calcineurin inhibitors, commonly used as clinical immunosuppressive agents, inhibited this event. This work represented a paradigm shift in the design of clinical trials of tolerance induction. Further studies by Turka of T cell-depleting agents, which also were in clinical use, found that these too were a barrier to tolerance because they led to the post-treatment emergence of alloreactive memory T cells.

Reflecting his broad interests in T cell biology, a substantive body of Turka's

work has focused on pathways that control PI3K metabolism, a key checkpoint in T cell growth and differentiation. His lab discovered that Toll-like receptors expressed on T cells function as direct sensors of inflammation and that, unexpectedly, this T cell–intrinsic function is required for optimal immune responses and protection against pathogens. More recent studies have examined the mechanisms by which the tumor suppressor gene *Pten* exhibits dual, but distinctive, control mechanisms against lymphoma and autoimmunity.

Turka is a former president of the American Society of Transplantation and has served on numerous NIH committees, including a term as chair of the NIAID Board of Scientific Counselors (2002–2007). In 2004 he was appointed as deputy director of the Immune Tolerance Network, and in 2007 he was chosen to serve a five-year term as editor-in-chief of the *Journal of Clinical Investigation*. Among Turka's honors are the Jerome Conn Award for Distinguish Research (University of Michigan, 1993), the American Society of Nephrology Young Investigator Award (1996), and the American Society of Transplantation Established Investigator Award (2005). Turka was elected to membership in the American Society for Clinical Investigation in 1995, the Association of American Physicians in 2003, and the Interurban Clinical Club in 2010.

Philadelphia active members without submitted biographies:

Michael Lisanti

Adam Dicker

PHILADELPHIA EMERITUS MEMBERS BIOGRAPHIES

C. William Balke, MD, FACP

C. William Balke was born in Philadelphia, PA, on November 3, 1949. He earned a BS in biology from Haverford College in 1975 and a BA in philosophy and comparative literature from the University of Pennsylvania in 1977. He graduated from Temple University School of Medicine in 1981 and completed specialty, subspecialty, and research training as follows: three years (1981–1984) of internal medicine training at Johns Hopkins University School of Medicine and the Johns Hopkins Hospital under the

mentorship of Victor A. McKusick, followed by three years (1984–1985 and 1986–1988) of clinical and research cardiology and cardiac electrophysiology training at Harvard University School of Medicine and Brigham and Women's Hospital under division chief Thomas W. Smith and department chair Eugene Braunwald and at the University of Pennsylvania School of Medicine under division chief Mark Josephson. Balke served for one year (1985–1986) as assistant chief of the Osler Medical Service (chief residency) at Johns Hopkins Hospital under department chair John D. Stobo and for three years (1988–1991) as a postdoctoral fellow in molecular physiology in the Department of Physiology at the University of Maryland School of Medicine under the mentorship of W. Gil Wier.

His first academic positions were at the University of Maryland School of Medicine, as assistant professor of medicine in the Division of Cardiology in the Department of Medicine under department chair John A. Kastor (1988) and as assistant professor of physiology in the Department of Physiology under department chair Mordecai P. Blaustein (1991). Over the course of eight years, Balke was promoted to professor of medicine with tenure, chief of cardiology, and the Herbert Berger Professor of Medicine at the University of Maryland School of Medicine. He also concurrently held the position of associate professor of medicine at the Johns Hopkins University School of Medicine. These positions gave Balke the opportunity to pursue his longstanding interests in the physiology of excitable cells. His investigative career is defined by three interrelated themes.

The major focus of his experimental work was the refinement of a quantitative understanding of the regulation of calcium release from the sarcoplasmic reticulum (SR) of cardiac cells by calcium entry via voltage-gated L-type calcium channels. The stochastic relationship of calcium entry with SR calcium release provides a mechanistic understanding of “calcium sparks,” described by his laboratory and others. Throughout his academic career Balke expanded the focus of this work to include investigations of the dysregulation of calcium homeostasis as a mechanism of cardiac dysfunction in animal and clinical models of hypertensive heart disease and heart failure.

A second focus of Balke's research is the discovery and characterization of a novel class of sodium channels that are uniquely permeable to calcium as well as sodium under physiological conditions. The electrophysiological signature of these channels is found in a variety of excitable cells, including cardiac and skeletal muscle and neuronal cells.

Third, Balke has a longstanding commitment to mentored career-development training mechanisms. His research program has provided the platform for mentored experiences for a number of NIH K award (K08, K23, K25, K01) recipients who have gone on to productive careers in academic medicine and industry. In addition, this program has also provided the substrate for several NIH-funded institutional training programs in cardiovascular physiology (NIH T32 awards), integrative physiology (an NIH T32 award), women's health (an NIH K12 award, Building Interdisciplinary Research Careers in Women's Health), and an NIH Roadmap K12 program (UM) for an interdisciplinary training program to prepare junior faculty for successful careers in clinical and translational research. On a national level, Balke has served as chairperson for several NHLBI career development special emphasis panels and study sections, including the Mentored Clinical Scientist Development Program (K08), Mentored Patient-Oriented Research Career Development Program (K23), and Pathway to Independence Award (K99/R00). He was the inaugural chairperson of the NHLBI's institutional T32 study section.

In addition to numerous awards and recognitions for his basic science research, Balke also accumulated senior-level administrative experiences as the senior associate dean of research at the University of Kentucky College of Medicine (2005–2010), associate provost of clinical and translational research at the University of Kentucky (2006–2008), and director of the Clinical Research Services Program at the University of San Francisco Clinical and Translational Science Institute (2010–2014). He is currently a professor of medicine and investigator at the Center for Cardiovascular Research at Washington University School of Medicine and chief of cardiology at the John Cochran Veterans Affairs Medical Center in St. Louis, MO.

Morris J. Birnbaum, MD, PhD

Morris J. Birnbaum was born in Brooklyn, NY, on December 16, 1951. He received his AB and PhD in biological chemistry and his MD from Brown University over the years 1973 through 1978. Following this he worked as an intern and resident at Barnes Hospital at Washington University School of Medicine in St. Louis, MO. He then completed a postdoctoral fellowship under the direction of John Baxter at the University of California, San Francisco, studying the regulation of gene expression by glucocorticoids. He then moved to New York City, where he joined Ora Rosen's laboratory at the Sloan Kettering Institute as a research associate. While in this

position, he succeeded in cloning a cDNA encoding the rat brain glucose transporter protein now known as Glut1.

Birnbaum began his independent career as an assistant professor in the Department of Cellular & Molecular Physiology at Harvard Medical School. Initially, his goal was to understand transcriptional regulation of the *Glut1* gene by insulin and growth factors, largely as a follow-up to his observation that transformation regulates the *Glut1* gene at the transcriptional level. However, several years later Birnbaum cloned the cDNA encoding the insulin-responsive (Glut4) glucose transporter, largely shifting the direction of his lab to insulin action. Birnbaum focused on the mechanism by which Glut4 is retained within an insulin-responsive tissue such as adipocyte and moves to the cell surface in response to hormone. In this context he was active in mapping domains of the glucose transport protein responsible for its unique hormone responsiveness. As the studies of insulin action progressed, Birnbaum turned his attention to the question of the signal transduction pathway that leads from the insulin receptor to Glut4.

In December 1994 Birnbaum moved to the University of Pennsylvania School of Medicine as a Howard Hughes Medical Institute Investigator and the Willard and Rhoda Ware Professor of Diabetes and Metabolic Diseases. While at the University of Pennsylvania, Birnbaum continued his work on insulin action but expanded his approach to include physiological, in vivo models. His focus soon changed to the serine/threonine protein kinase Akt (also known as PKB), which he soon showed by biochemical and genetic evidence to be critical for the actions of insulin. Somewhat frustrated with the limits of biochemical analysis, Birnbaum also implemented *Drosophila* genetics as a research tool in his laboratory and used the fruit fly to demonstrate the role of Akt and insulin signaling in the regulation of cell size. He also established the relevance of this effect to mammalian tissue by demonstrating hypertrophy in pancreatic β cells overexpressing a constitutively active mutant of Akt.

Having established a diabetic phenotype in mice deficient in Akt2, Birnbaum set out to understand the mechanism underlying this deficiency. He studied both glucose and lipid metabolism in liver, establishing the role for Akt isoforms in both processes. He also used isoform specificity in Akt signaling as a tool to probe the precise pathways in the adipocyte. While at the University of Pennsylvania, he received the Stanley Cohen Award for Excellence in Research. He also chaired the Cellular Aspects of Diabetes and Obesity NIH Study Section, served as associate director of the Institute

for Diabetes, Obesity and Metabolism at the University of Pennsylvania, and in 2010 assumed the role of associate dean for Biomedical Research Cores. Birnbaum is currently a professor in the Department of Medicine at the University of Pennsylvania School of Medicine.

Guenther Boden, MD

Guenther Boden was born on January 8, 1935, in Ludwigshafen, Germany. He received an MS degree from the Heidelberg University School of Medicine in 1956, an MD degree in 1959 from the Munich University School of Medicine, and a Dr med degree from the Max Planck Institute for Psychiatry in Munich, Germany, in 1960. From 1960 to 1962 he completed a rotating internship in surgery, medicine, OB/GYN, and psychiatry at city hospitals in Hamburg and Berlin and at the University Hospital in Munich. In 1963 to 1965 he was a postdoctoral fellow in the Department of Biochemistry at the University of Tübingen, and from 1965 to 1967 he was a research fellow in medicine in the EP Joslin Research Laboratory at Harvard Medical School, under the direction of George F. Cahill Jr. During this time he developed a radioimmunoassay for human growth hormone, which he used to study the role of this hormone on glucose and insulin metabolism in pre-diabetic subjects. From 1967 to 1970 he completed a residency in internal medicine at the Rochester General Hospital.

In 1970, Boden joined the Department of Medicine at Temple University School of Medicine under the direction of Sol Sherry, first as assistant professor (1970–1974), then as associate professor (1974–1977). In 1977 he became a full professor of medicine and in 2000 was appointed the Laura H. Carnell Professor of Medicine. From 1978–1987 he was chief of the Section of Diabetes and Metabolism and, from 1987 to 2009, chief of the Section of Endocrinology, Diabetes and Metabolism at Temple University School of Medicine. From 1989 to 2003 he was program director of the NIH-sponsored General Clinical Research Center at Temple University School of Medicine.

During the early part of his career, Boden's scientific interests focused on the pathophysiologic roles of several entero-pancreatic hormones, including secretin, somatostatin, and glucagon. This led to the development of the first radioimmunoassay for the measurement of secretin and the exploration of the physiologic and pathophysiologic role of this hormone, to the introduction of the long-acting analog somatostatin as a useful agent in

the treatment of severe orthostatic hypotension (together with his associated R. Hoeldtke), and to the description of two new syndromes: familial hyperglucagonemia and idiopathic counterregulatory hormone deficiency. More recently his interest has shifted to the pathogenesis of non-insulin-dependent diabetes mellitus and insulin resistance.

Boden was the first to demonstrate that elevated plasma free fatty acid (FFA) levels produced peripheral insulin resistance (findings published in the *Journal of Clinical Investigation*, 1991, 1994, 1995) and that lowering chronically elevated plasma FFA in obese non-diabetic and diabetic patients improved insulin sensitivity. These results have since been widely confirmed and suggest that FFA can account for up to 50% of insulin resistance in obese patients with type 2 diabetes. More recently he has demonstrated that chronic hyperinsulinemia, particularly when associated with hyperglycemia, leads to a large rise in circulating tissue factor procoagulant activity and other blood coagulation factors, providing an explanation for the procoagulant condition known to be present in obese insulin-resistant individuals. His studies have been supported continuously since 1973 by grants from the NIH as well as contributions from the American Diabetes Association.

Boden has served on numerous advisory committees, both federal and private, and has been a member of numerous professional societies, including the American Federation for Clinical Research, the American Society for Clinical Investigation, the Endocrine Society, the American Diabetes Association, and the American College of Physicians. He has received many awards, including the George Thompson Pew Diabetes Research Award in 1986, the Novartis Longstanding Achievement in Diabetes Award in 2005, the AACE Outstanding Clinical Endocrinologist Award in 2012, and the first Sol Sherry Research Award and first Lifetime Achievement Award from Temple University School of Medicine in 2012.

Garrett M. Brodeur, MD

Garrett Brodeur was born in St. Louis, MO in September 1949. He received his BA in Chemistry from St. Louis University in 1971, where he graduated Magna Cum Laude and was inducted into Phi Beta Kappa, as well as the Alpha Sigma Nu Jesuit honor Society. He received his MD from Washington University School of Medicine (WUMS) in 1975, and he received the St. Louis Pediatric Society Award and the Richard S. Brookings

Meritorious Research Award. He completed his Pediatric Residency from 1975-1977 at St. Louis Children's Hospital (SLCH), and then he went to St. Jude Children's Research Hospital in Memphis, TN to complete his Pediatric Hematology-Oncology Fellowship training from 1977-1981. Brodeur returned to WUMS and the Department of Pediatrics at SLCH to do post-doctoral training in molecular biology with Dr. Maynard Olson from 1981-1983. Then he joined the faculty of the Department of Pediatrics at WUMS and SLCH as an Assistant Professor in 1983, and he was promoted to Associate Professor with tenure in 1987. While in St. Louis, he was inducted into Alpha Omega Alpha in 1990. He was also awarded a Junior Faculty Clinical Fellowship from the American Cancer Society, a Basil O'Conner Starter Research Grant from the March of Dimes, a Hartford Foundation Research Fellowship, and a Research Career Development Award from the NIH. He was also awarded his first R01 on the Molecular Genetic Analysis of Human Neuroblastoma for his work on the pathogenesis and clinical significance of *MYCN* amplification and 1p deletion in neuroblastomas. Brodeur then moved to the Children's Hospital of Philadelphia (CHOP) and the University of Pennsylvania (UPenn) in 1993 as a Professor of Pediatrics.

Brodeur was inspired to enter the field of medicine by his father, Dr. Armand E. Brodeur, a pediatric radiologist, but also by his love of science, especially biology and medicine. He became interested in pediatric oncology because of early laboratory and clinical experiences in medical school. He dedicated his career to understanding the molecular pathogenesis of neuroblastoma, one of the most common and deadly of childhood cancers, and developing novel approaches to treatment. He enjoyed making discoveries at the molecular genetic level and determining their clinical significance. One of his earliest and most important discoveries was in 1984 when he determined that amplification of the *MYCN* proto-oncogene occurred in about 22% of neuroblastomas and was a powerful predictor of unfavorable outcome in these patients. This is perhaps the first example of a genomic change that had clinical significance in a human cancer. Currently, neuroblastomas across the civilized world are assessed for amplification of *MYCN* to determine prognosis and select the intensity of therapy.

Brodeur had also identified deletion of the short arm of chromosome 1 as a common feature in neuroblastomas when he was a medical student at WUMS. He analyzed this finding at the cytogenetic and molecular genetic level at WUMS, and he continued this work in more detail at CHOP and UPenn. In 2003, he determined that a gene encoding a novel chromatin re-

modeling protein called CHD5 was frequently deleted in neuroblastomas, and in 2008 he showed that CHD5 was a tumor suppressor gene and likely the target of 1p36 deletions in neuroblastomas, as well as other cancers. He is currently studying the regulation of CHD5 expression, its function as a chromatin remodeling protein, the role that CHD5 plays in normal neural development, and why deletion or inactivation of this gene contributes to malignant transformation in neuroblastomas and in human cancers.

Ever since his initial laboratory experiences in medical school at WUMS, Brodeur had been interested in the role of nerve growth factor (NGF) in the differentiation of normal and malignant neurons. Once TrkA was identified as the NGF receptor, Brodeur began to explore the expression of TrkA and its homologues in neuroblastomas. He found that TrkA was expressed in favorable neuroblastomas and likely contributed to their spontaneous regression or differentiation. Conversely, unfavorable neuroblastomas, especially those with MYCN amplification, overexpressed TrkB, along with its ligand, BDNF. This autocrine survival pathway contributed to invasion, metastasis, angiogenesis and drug resistance. Thus, the unusual behavior of neuroblastomas to spontaneously regress (or differentiate) in some patients, but grow relentlessly despite intensive, multimodality treatment in other patients, could be explained in part by the expression of either TrkA or TrkB. Most of this work was done at CHOP and UPenn, and this led to a decades long search for the optimal TRK inhibitor that might become an integral component of targeted therapy for neuroblastomas, which Brodeur continues to explore. Most recently, Brodeur has been investigating the potential of nanoparticles as vehicles for drug delivery, which he is also actively investigating.

Dr. Brodeur was Chief of the Division of Oncology at CHOP from 1998-2008, and he has been Associate Director of the Abramson Cancer Center at UPenn since 2007. Since coming to CHOP and UPenn, Brodeur has won a number of awards, both locally and on a national/international level. He received the CHOP Mentor Award in 2011 for his role in fostering the career development of a number of young investigators who are currently pursuing successful careers in pediatric oncology. He won the American Society of Clinical Oncology (ASCO) in 2013, and the Advances in Neuroblastoma Research Association (ANRA) Lifetime Achievement Award in 2014. He was only the third recipient of the ANRA Lifetime Achievement Award since 2000. He was elected the President-Elect for the Pediatric Cancer Working Group of the American Association for Cancer Research (AACR), the second person to hold this title.

Steven Daniel Douglas, MD

Steven Daniel Douglas was born in Jamaica, New York, on February 28, 1939. Douglas is a third-generation physician —grandfather Samuel D. Douglas received his MD from University Medical College of New York in 1892, and his father, Albert H. Douglas, received his MD from Cornell University Medical College in 1929 and practiced as a cardiologist. Steven D. Douglas received his AB from Cornell University in 1959 and his MD from Cornell University Medical College in 1963. As a young student he worked with Henry Isenberg on bacterial growth, and as a college and medical student he did studies related to cellular pathology and electron microscopy. He served as an intern and resident at the Mount Sinai Hospital in New York (1963–1964 and 1966–1967) and as a staff associate in the laboratory of Samuel Spicer at the National Institute of Arthritis and Metabolic Diseases (1964–1966). He was an immunology-hematology postdoctoral trainee for the USPHS and worked with Hugh Fudenberg at the University of California, San Francisco (1967–1969). Early in his career Douglas became interested in cellular immunology and host microbe interactions.

In 1969 Douglas joined the faculty of the then-new Mount Sinai School of Medicine as assistant professor, and subsequently associate professor, of medicine in the department of Solomon A. Berson, where he remained until 1973. He became associate professor of medicine and microbiology at the University of Minnesota School of Medicine in 1974 (under Richard Ebert, chair) and professor of medicine and microbiology in 1976. From 1974 to 1980 he was chief of the section of immunology. In 1980 he moved to the University of Pennsylvania as professor of pediatrics and microbiology. From 1980 to 1989 he served as director of the Division of Allergy, Immunology, and Bone Marrow Transplantation at Children's Hospital of Philadelphia. Since 1989 he has served as section chief for immunology in the Division of Allergy, Immunology and Infectious Diseases, and as medical director of the Clinical Immunology Laboratory. Since 1994 he has also served as associate chair of academic affairs in the Department of Pediatrics within the Perelman School of Medicine at the University of Pennsylvania.

Douglas's major studies have included the discovery that pokeweed mitogen stimulates lymphocyte proliferation and differentiation into plasma cells. He was the first to show, using lymphocyte responses to mitogens *in vitro*, that the common variable hypogammaglobulinemia is a genetically

determined disease. He established methods for the isolation and cultivation of human blood monocytes and demonstrated their differentiation into macrophages. He showed that there were changes in membrane topography associated with the interaction between macrophages and immunoglobulin receptors. These studies were important to understanding plasma membrane components and turnover. He was among the first to demonstrate monocyte-derived macrophage infectivity with HIV and the role of macrophages in HIV disease.

Over the last 30 years, Douglas has been a leader in laboratory investigations into cellular immunology and the immunopathology and immunogenesis of HIV/AIDS. He has studied the interaction between HIV and immunology, psychiatric disease, and neurologic disease. He has had continuous funding from the NIH, in the form of R01, IPCP, and U01 grants, to investigate neurokinin-1 and substance P at the basic, translational, and clinical levels. In a phase 1b trial, he showed that Aprepitant, an NK1R antagonist, has important anti-inflammatory properties and is safe for use in HIV-positive subjects. He is the principal investigator of an ongoing U01 study in aviremic HIV-positive subjects administered Aprepitant. He is a core director in the NIMH-funded Penn Mental Health AIDS Research Center and the principal investigator for the Laboratory Biomarkers, Quantitative Pharmacology, Neuroimaging, and Neurobehavioral Characterization Core at Penn. He holds major leadership roles in all of these projects, which are focused on studying the immunologic mechanisms of HIV pathogenesis. He is principal investigator for a newly funded IPCP trial (conducted 2014–2018) on macrophage polarization in neuro-AIDS. He has served as principal investigator for, and had pioneering roles establishing, core laboratories at Penn and the Children's Hospital of Philadelphia, and for the AIDS Clinical Trials Group Network in pediatrics, adolescents, and adults. He has had a major role in the immunology agenda related to HIV/AIDS for the NIH. He is an appointed member of the scientific oversight leadership committee and the laboratory steering committee for the IMPAACT Network, and is a member of the Women's Interagency HIV Study (WIHS) external advisory board. He has served as a member of the NIH Office of AIDS Research external review committee for the Trans-NIH Neuro AIDS Research Program. He has been principal investigator on IPCP (2005–2010), U01 (2009–present), and PO1 (2014–2018) awards.

Douglas is a member of many scientific societies and has served many of these organizations both in relationship to their scientific publications and

in administrative capacities. He was president of the Interurban Clinical Club (1994–1995). He is a past president of the Society for Leukocyte Biology and a member of NIH study sections and the FDA Blood Products Advisory Committee. He has served as a section editor of the *Journal of Leukocyte Biology*, *Clinical Immunology and Immunopathology*, and *Journal of Clinical Microbiology* and as a member of the editorial board of the *Journal of Immunology*. He is the founding editor-in-chief of *Clinical and Diagnostic Laboratory Immunology* (founded in 1994 and published by the American Society of Microbiology). From 1969 to 1974 he was the recipient of a Research Career Development Award from the National Heart and Lung Institute. In 1970 he received the Emil Conason Memorial Award from Mount Sinai School of Medicine, in 1977 he received the XV Annual Redway Award from the Medical Society of the State of New York, and in 1980 he received the William Hammond Award for Distinguished Service from the *New York State Journal of Medicine*. He was the 1997 recipient of the American Society for Microbiology Abbott Award in Clinical and Diagnostic Immunology and the 2000 recipient of the Erwin Neter Award from the Association of Medical Laboratory Immunologists. In 2000 he became an honorary lifetime member of the Society for Leukocyte Biology, in 2003 he was named fellow of the American Association for the Advancement of Science, and in 2012 he was named a member of the Henry Kunkel Society.

He is a member of numerous distinguished medical societies, including the American Society for Clinical Investigation, and is a fellow of the American Academy of Microbiology. He is also member of the Society for Pediatric Research and the American Pediatric Society, and he served as president of the John Morgan Society (1986–1987). From 1987 to 1993 he was chairman of the Veterans Administration Committee for Research Centers of AIDS and HIV Infection, and from 1988 to 1993 he was a member of the Blood Products Advisory Committee of the FDA. He served from 2002 to 2007 on the NIH AIDS, Immunology and Pathogenesis Study Section (chair, 2005–2007). Since 2012 he has been co-chair of the International Union of Basic and Clinical Pharmacology (IUPHARM) subcommittee on tachykinin receptors.

Robert Eisenberg, MD

Robert Eisenberg was born in New York City on August 25, 1944. He received his BA degree in anthropology from Haverford College and his MD

from Stanford Medical School. His clinical training in internal medicine was at the Cornell Medical School/New York Hospital. He specialized in rheumatology as a clinical associate in the US Public Health Service at the Arthritis and Rheumatism Branch of the National Institutes of Health. His research training was completed as a postdoctoral fellow at the Scripps Research Institute in La Jolla, CA.

Eisenberg's first academic job was in the Division of Rheumatology at the University of North Carolina at Chapel Hill, from 1978 to 1995. From 1995 to 2004 he was chief of the Division of Rheumatology at the University of Pennsylvania. He remained at the University of Pennsylvania until 2012, when he retired to emeritus status. He has taken three research sabbaticals: in 1984–1985 at the Institut d'Immunologie in Marseille, France, with Anne-Marie Schmitt-Verhulst; in 2004 at the Institut Pasteur in Paris, France, with Antonio Freitas; and in 2008 at the University of California, Berkeley, with Mark Schlissel.

Eisenberg's career development has been strongly influenced by his mentors and collaborators over the years. As a medical student at Stanford, he spent most of his time in the laboratory of Irving Weissman, where he learned the basics of scientific research and immunology. At the NIH he worked directly with Paul Plotz, where he learned about antibody biochemistry and autoimmunity. At Scripps he was a fellow with Frank Dixon and worked with Argyrios Theofilopoulos, among others. As a faculty member at UNC, his laboratory was strongly interconnected with Philip Cohen, whom Eisenberg also recruited to Penn to continue their interactions.

Eisenberg's research over the years has mainly focused on the mechanisms of autoantibody production and the role of B cells in autoimmunity, interests that stem from his early work in with Paul Plotz. Much of his investigation has utilized mouse models of SLE, such as the MRL/lpr strain, with which he first became acquainted while working with Dixon at Scripps. This work has helped to identify the B cell as a key player in systemic autoimmunity, as a cell in which the genetic etiologies of SLE are directly expressed and that functions normally except in its choice of self-antigens as targets. At Penn he extended this work to the earliest clinical trials of rituximab, an anti-B cell therapy, in people with SLE, and other B cell-related clinical research. His later work focused on the graft-versus-host model of induced murine SLE, the role of Ig receptor editing in the formation of autoantibodies, the KRN model of rheumatoid arthritis in mice, in

vivo imaging of B cells by MRI, and the immune response to flu vaccine of patients treated with rituximab. His research program has been funded mainly by NIH grants for over 30 years, with important participation from private sources such as the Arthritis Foundation, the Lupus Research Institute, the Alliance for Lupus Research, the Kroc Foundation, and the Lupus Foundation. He has published over 190 research papers and reviews.

He has been director of the Rheumatology Training Program at UNC and at Penn. He directed the MD-PHD program at UNC from 1989 to 1995 and was the principal investigator on the rheumatology T32 Training Grant at Penn from 1996 to 1999. He was also principal investigator of the UNC Specialized Center of Research in Systemic Lupus, and was associate director of the Autoimmunity Center of Excellence at Penn from 2000 to 2004. He has extensive experience with grant reviews for the NIH (participation in the Immunological Sciences Study Section, 1985–1989), the Arthritis Foundation, the Lupus Foundation, the Alliance for Lupus Research, the Canadian Arthritis Network, and the Lupus Research Institute, among others. He is a member of the Clinical Immunology Society (website editor, 2010–2013), the American College of Rheumatology, the American Society for Clinical Investigation, the American Association of Immunologists, the Association of American Physicians, the Interurban Clinical Club, the Kunkel Society, the Klemperer Committee, and the Philadelphia Rheumatism Society (president, 2004–2005). He has served on the scientific advisory boards of the Lupus Research Institute and of the American Autoimmune Related Diseases Association, and on the editorial boards of *Arthritis and Rheumatism*, *Infection and Immunity*, the *Journal of Immunology*, the *Journal of Clinical Investigation*, the *Journal of Clinical Immunology*, *Case Reports in Medicine*, *Frontiers in B cell Biology*, *Autoimmunity Reviews*, and *IG News*. He has performed ad hoc grant and manuscript reviews for over 60 different funding agencies or journals. His recognitions include the Burroughs Wellcome Scholar of the Allergy Foundation of America, the Helen Hay Whitney Fellowship, the Senior Investigator Award of the Arthritis Foundation, the Fogarty Senior International Fellowship, the Lady Barbara Colyton Prize in Autoimmunity, and the Master Award of the American College of Rheumatology.

He has served as primary or secondary mentor of 21 postdoctoral fellows and 7 predoctoral trainees over the years. Twenty-seven clinical fellows were trained in the Division of Rheumatology during the period that Eisenberg was chief.

Stephen G. Emerson, MD, PhD

Steve Emerson was born in New York on October 21, 1953, and grew up in Great Neck until 1970, when he left to attend Haverford College. Intending to focus on astrophysics and mathematics, he was drawn into applying the physical sciences to biology by Professor Ariel Loewy, the discoverer of non-muscle actin (the cytoskeleton) and the Factor XIII-mediated isopeptide bond, who invited him to work in his laboratory. Inspired by this experience, Emerson entered the MD-PhD program at Yale University, where he became the first graduate student in the Immunology Program spun out of the Department of Cell Biology, under George Palade. There, working with Robert Cone and Richard Gershon, he identified mouse histocompatibility (H2 and Ia) proteins shed from spleen cells in vesicles (now termed “dendritic exosomes”); at the same time in his clinical experiences he became awestruck by hematopoietic differentiation.

These research and clinical exposures culminated in his commitment to studying the interaction of the immune system with hematopoiesis, which he began in his postdoctoral fellowship, in the laboratory of David Nathan at the Dana-Farber Cancer Institute following internal medicine training at the Massachusetts General Hospital and clinical hematology fellowship at the Brigham and Women’s Hospital. There he used immunological techniques to develop a simple 4-5 log purification of human hematopoietic stem cells, and showed that these purified progenitor stem cells both induced and were the targets of T cell immune responses. Subsequently, in a research laboratory program at the Universities of Michigan and Pennsylvania, Steve’s laboratory continued on the dual interacting themes of hematopoiesis and immune regulation using diverse approaches, including: (1) developing the first stem cell bioreactors; (2) identifying the osteoblast as the local bone marrow niche cell essential for myeloid and lymphoid development, and for hematopoietic proliferation; (3) demonstrating that host dendritic cells were the key trigger cells for graft-versus-host reactivity in stem cell transplantation patients; and (4) identifying a new cell type, the T memory stem cell, that is the long-term reservoir of T cell immune responses.

In parallel with his laboratory’s research contributions, Emerson took on academic leadership positions with gusto, building three singular programs in three institutions. As the Hematology/Oncology Division Chief at the University of Pennsylvania, over thirteen years Steve adumbrated the strong foundation in platelet biology built by Sandy Shattil to build a Divi-

sion that included immunology, molecular genetics, stem cell biology and translational research (including e.g. Craig Thompson, Carl June, David Porter, Barbara Weber, Wafik El-Deiry, Peter Klein) that is now recognized as one of the most vital in the country. In recent years, he has used the same principles of scientific foundations and individual recruitments to build an unprecedented translational Cancer Center at Columbia University. In between, Emerson served as President of his alma mater, Haverford, where he shepherded the school through the aftermath of the 2008 financial crisis and stock market crash while drawing a student body of extraordinary intellectual and personal promise and providing a singular program combining research, praxis and service, e.g. Haverford's Natural Science Division trains more MD-PhD and VMD-PhD students per capita than any other institution in the US.

Over his career Dr. Emerson has served as the Scientific Program Chair of both the American Society of Hematology and the American Society for Blood and Marrow Transplantation, and as the President of the Interurban Clinical Club. He has served for twelve years as a member of NIH study sections, as well as similar review panels for the Leukemia Lymphoma Society and the British Medical Research Council. A member of the American Society for Clinical Investigation and the Association of American Physicians, he has been awarded the Stohlman Prize of the Leukemia and Lymphoma Society, the Wilbur Lucius Cross Medal from Yale University, and Knighthood from the French Legion of Honor. He currently serves as the Clyde Wu Professor of Immunology and Medicine at Columbia, where he directs the Herbert Irving Comprehensive Cancer Center and serves as Associate Dean for Oncology.

Harvey M. Friedman, MD

Harvey Friedman was born in Montreal, Quebec, Canada, on May 29, 1944. He received his BS degree in 1965 and his MD degree in 1969 from McGill University. He did an internship and junior residency from 1969 to 1971 in internal medicine at the Jewish General Hospital in Montreal. He was a fellow in neurovirology at the Wistar Institute in Philadelphia from 1971 to 1973, where he worked under the mentorship of institute director Hilary Koprowski and Donald Gilden, assistant professor of neurology at the University of Pennsylvania (Penn). The theme of the research was virus-host interaction and the role of the immune response in preventing and causing disease. The topic of virus-host interaction has remained

central to Friedman's research throughout his career. From 1973 to 1975 he was a fellow in infectious diseases at Penn. In 1975 he joined the infectious disease faculty in the Department of Medicine, and he has remained at Penn ever since.

During his career, he has played a leadership roll in four major initiatives. Early in his career organ transplant medicine was just taking hold in the USA. During his fellowship in infectious diseases, he saw kidney transplant patients develop serious herpes virus infections, but laboratory facilities to identify a pathogen did not exist on Penn's campus or on most other university campuses at that time. Friedman spent part of his fellowship learning clinical virology, which was an emerging discipline. He went to the California Department of Public Health in Berkeley, CA, under the direction of Edwin Lennette. Friedman then set up a clinical virology laboratory within the Infectious Disease Division of the Children's Hospital of Philadelphia (CHOP), under the mentorship of Stanley Plotkin. The laboratory served as a joint resource for CHOP and the Hospital of the University of Pennsylvania (HUP) for approximately 15 years, until HUP established its own clinical virology laboratory. From 1975 to 1990 Friedman directed the joint laboratory, which offered diagnostic services to hospitals throughout the Philadelphia region. The laboratory continues to thrive and is recognized for its quality and use of cutting-edge technology.

A second aspect of Friedman's career was his time serving as chief of the Infectious Disease Division at Penn (1990–2012). He assumed the leadership role from Rob Roy MacGregor at a time when the HIV epidemic was hitting full stride in the USA. It was also a time when the Penn Health System was expanding by acquiring hospitals in the vicinity. The clinical demands on the division mushroomed, and during his 22 years of leadership the faculty size grew from 8 to 35 members. Very few faculty members left the division during that time. The division developed a reputation locally and nationally for its collegiality and for its excellence in research, teaching, and clinical care.

A third component of Friedman's career is his role as director of the Botswana-UPenn Partnership (BUP) (2001–present). In 2001 Friedman received a request from the Merck Foundation, which had partnered with the Gates Foundation and the Government of Botswana to provide antiretroviral drugs to the citizens of Botswana. The request was to help support the national rollout of the antiretroviral drug program in Botswana. At that time, Botswana did not have a medical school, which was why a need ex-

isted to train local health care providers on HIV treatment. Botswana subsequently formed a medical school, and its first class graduated in October 2014. Penn's involvement in Botswana has continued to grow, first through support from the Merck and Gates foundations, and since 2004, with support from the US Government through the President's Emergency Plan for AIDS Relief (PEPFAR), which funds Penn's role in providing technical advice regarding care for patients with HIV, tuberculosis, and cervical cancer. Currently, BUP has partnerships with the University of Botswana and the Botswana Ministry of Health and employs approximately 170 individuals, mostly citizens of Botswana, to provide clinical care and education and participate in NIH-supported research.

A fourth aspect of Friedman's career is his research, which involves developing a vaccine for genital herpes based on blocking immune evasion properties of herpes simplex virus (HSV). Early in his career, Friedman's laboratory reported that one of the HSV glycoproteins, gC, serves as a complement regulatory protein that binds C3b and inhibits the complement cascade. The discovery of gC as an immune evasion molecule was one of the first reports of a microbial immune evasion molecule. The Friedman laboratory later assigned an immune evasion property to another HSV glycoprotein, gE, which functions as an IgG Fc receptor. The laboratory demonstrated that an antibody molecule can bind via its F(ab')₂ domain to an HSV antigen and that the Fc domain of the same antibody molecule can bind to gE, which blocks activities mediated by the Fc domain such as complement activation and antibody-dependent cellular cytotoxicity. The Friedman laboratory demonstrated that gC and gE are important virulence factors, since in the absence of these glycoproteins the virus is far more susceptible to antibody and complement *in vitro* and *in vivo*. In recent years, efforts by the Friedman laboratory have turned to using gC and gE as immunogens, to induce antibodies that bind to the glycoproteins on the virus envelope or infected cell surface and block their immune evasion properties. The approach is to use gC and gE in combination with other HSV antigens to induce potent humoral and T cell immunity and to prevent the virus from evading the humoral immune response.

Friedman is a member of the Interurban Clinical Club, the American Society for Clinical Investigation, and the Association of American Physicians. He has taken two sabbaticals to Lausanne, Switzerland, to work in Heidi Diggelman's laboratory at the Swiss Institute for Experimental Cancer Research. During his first sabbatical, in 1986, he learned the tools of molecular biology; during the second, in 1993, he learned to appreciate mountain

walks and Swiss wine. Friedman enjoys clinical medicine, teaching house staff and fellows, is gratified by the partnership Penn has developed in Botswana, and hopes that the vaccine studies in his laboratory will lead to clinical trials in humans in the coming years.

Barry Jay Goldstein, MD, PhD

Barry J. Goldstein was born in 1954 in New York City. He received his BS degree with distinction in biochemistry and genetics from Cornell University in 1976. While working in the laboratory of Stanley Zahler, he identified and mapped a *B. subtilis* gene encoding a novel a-keto acid transporter. He graduated with honors from the Medical Scientist Training Program (MD-PhD) of the University of Rochester School of Medicine and Dentistry (1982), where his thesis research on insulin action and metabolism in adipocytes was mentored by J. Nicholas Livingston. Following a medical residency at Strong Memorial Hospital in Rochester, NY (1982–1985), he joined C. Ronald Kahn's group at the Joslin Diabetes Center of Harvard Medical School and the Endocrinology Division of Brigham and Women's Hospital in Boston, where he completed his fellowship training and was specialty board certified in endocrinology (1989). During his postdoctoral research Goldstein cloned the rat insulin receptor cDNA and showed that its novel pattern of tissue-specific alternative mRNA splicing was conserved across species. As an assistant professor at Harvard and a Joslin Research Investigator, he embarked on a characterization of cellular protein tyrosine phosphatases and their regulation of the insulin signaling cascade, a project for which he received continuous funding from the NIH NIDDK between 1991 and 2008. His laboratory was among the first to show at a cellular level that the enzyme PTP1B negatively regulates the tyrosine phosphorylation state of the insulin receptor and its major cellular substrate IRS-1, which has important consequences for downstream insulin action. In 1992 Goldstein was recruited to be director of the Division of Endocrinology, Diabetes and Metabolic Diseases at Jefferson Medical College in Philadelphia and was appointed associate professor of medicine and of biochemistry and molecular pharmacology. He was promoted to full professor at Jefferson in 1997.

Goldstein maintained basic and clinical research programs focused on the mechanisms and regulation of insulin signal transduction, the pathophysiology of insulin-resistant disease states, and vascular abnormalities in diabetes and obesity. During this period his laboratory made a number

of seminal discoveries in the regulation of insulin signaling. While it had been known for years that cellular insulin stimulation elicits a transient burst of intracellular reactive oxygen species (ROS), the mechanism and physiologic significance of this phenomenon were not well understood. Goldstein extended these findings to show that insulin-induced cellular ROS facilitate insulin signal transduction via oxidative inhibition of PTP1B, which requires a reduced thiol moiety for its enzyme activity. His group further provided evidence that a specific NADPH oxidase homolog (Nox4) mediates the generation of cellular ROS by the insulin receptor and, in turn, elicits the oxidative inhibition of PTP1B, thus characterizing at a molecular level a novel mechanistic link in the cellular regulation of insulin signaling. His group also explored the cardiovascular effects of the adipocyte-secreted protein adiponectin. Since adiponectin levels are decreased in obesity, they hypothesized that this adipokine might be involved in vascular dysfunction in insulin-resistant states. They showed that loss of expression of adiponectin in a mouse model induces a primary state of endothelial dysfunction with increased leukocyte-endothelium adhesiveness. Furthermore, his group provided the first evidence that administration of the globular form of the complex adiponectin protein protects the vasculature *in vivo* via increased nitric oxide bioavailability and suppression of leukocyte-endothelium interactions. At a cellular level they also characterized the action of adiponectin *in vitro* to suppress high glucose-induced ROS generation in cultured vascular endothelial cells via cAMP/PKA signaling. Adiponectin was also found to protect against endothelial cell monolayer hyperpermeability that was induced by angiotensin II or tumor necrosis factor- α .

Goldstein served on several NIH grant review panels, including regular memberships on the NIH Endocrinology, Metabolism, Nutrition, and Reproductive Sciences Study Section and the Cellular Aspects of Diabetes and Obesity Study Section and on the grant review committee of the American Diabetes Association. He served as principal investigator of the West Jefferson Medical Center Diabetes Prevention Program. He is a member of the American Society for Clinical Investigation and the Association of American Physicians and is a fellow of the American College of Physicians and the American College of Endocrinology. In 1998 he was elected to the Interurban Clinical Club and later served as a councilor for Philadelphia (2004–2006). He was a member of the board of directors and was president of the Philadelphia Endocrine Society and the Philadelphia chapter of the American Diabetes Association. He was physician secretary for the American Board of Internal Medicine Recertification Program and

the Subspecialty Board Examination in Endocrinology, Diabetes, and Metabolism (1992–2002) and served as an associate editor for the two major journals in his field, the *Journal of Clinical Endocrinology and Metabolism* (2000–2005) and *Diabetes* (2001–2006).

In 2008 Goldstein took on a new role as vice president of clinical research and metabolism at Merck Research Laboratories, where his responsibilities include mid- to late-phase global clinical development of Merck's therapeutics for diabetes and obesity.

Mark I. Greene, MD, PhD

Mark Greene received his MD in 1972 and his PhD in immunochemistry in 1977, both from the University of Manitoba in Canada. Greene also received the FRCP distinction from the Royal College of Physicians in 1976. In 1976 Greene moved to Harvard University, where he was a medical research council fellow. Greene was appointed assistant professor of pathology at Harvard Medical School and University in 1978. In 1980 he rose to associate professor in the Harvard Department of Pathology, where he remained until 1985. Greene also served as a clinical consultant in medicine at the Dana-Farber Cancer Center from 1980 to 1986. In 1984 he was appointed professor of medicine and head of immunology/rheumatology at the New England Medical Center. Greene was recruited to the University of Pennsylvania to head the basic research unit of immunology in 1986. Since 1987 he has also headed fundamental research at Penn's Abramson Cancer Center and in 1993 became vice chair of the Department of Pathology.

Greene's laboratory focuses on the origin, detection, and therapy of breast cancer. His work has deepened our understanding of how the cancer-causing gene called *neu* oncogene causes breast cells to become malignant. Greene and colleagues identified the *neu* oncogene, determined its role in malignancy, and defined the principles that led to the development of the first approved therapy (Herceptin) that targets the proteins of this gene.

By understanding the atomic changes in *neu* that contribute to malignancy, Greene and his team hope to find better ways to disable those changes. Greene and his laboratory have developed small-molecule therapy for tumors caused by members of the *erbB* family that they expect will be administered orally and should have very limited, if any, toxicity. When fully

developed, these therapeutics may be useful in the chronic therapy of certain brain, breast, ovarian, lung, and pancreatic cancers.

They have also developed technology to detect *erbB* oncoproteins that is one-thousand-billion times more sensitive than any currently available technology. This will allow the detection of *neu*-driven breast and ovarian cancer far earlier than before. Greene continues to work on using the detection technology to identify signals important in neurodegenerative disorders and other human diseases for which rapid diagnosis is not possible with current methodology.

Greene discovered how to specifically target and disrupt the homodimeric and heterodimeric kinase receptors that cause human cancers. He discovered that monoclonal antibody-targeted therapy could reverse the malignant properties of *erbB2/neu* oncogene-transformed tumor cells. His work showed that when monoclonal antibodies bound the ectodomain of p185 protein, the kinase activity was diminished and the cells, having lost their driving oncoprotein, underwent reversion to a more normal phenotype. The discovery of a reversal of phenotype established the targeted therapy field because it explained that malignant properties of human cancer cells were not permanent but could be reversed by disabling the oncoproteins.

Greene showed that monoclonal antibodies targeting the ectodomain of the *p185HER2/erb2/neu* protein promoted the internalization of the dimeric kinase complex, leading to its inactivation followed by signaling attenuation, and this specific targeting reversed the malignant properties of tumor cells. He found that antibodies against the ectodomain of *erbB2/neu* promoted receptor internalization, which resulted in the reversal of malignant characteristics of a tumor. His laboratory went on to show that by reversing the malignant features, the now more normalized tumor cells became susceptible to genotoxic signals such as radiotherapy and chemotherapy, which is now the standard way to treat breast cancer in humans. That is, for those tumors that are caused by the *erbB2/HER2/neu* oncogene, monoclonal antibodies to the ectodomain of p185 are administered, followed by genotoxic (chemotherapy and radiation) therapies.

Greene showed that oncogenic *erbB2/neu* as a transgene in animal models induced adenocarcinomas of the breast. Moreover, early targeted monoclonal antibody therapy of p185neu in these female mice could prevent tumor emergence and recurrence. These observations are the basis for the combined tumor adjuvant therapy/targeted therapy approach used today

in humans following tumor resection.

His group also established that the use of two monoclonal antibodies reactive with distinct domains of the erbB2/neu protein led to even more dramatic tumor inhibition. Greene solved the biochemical and structural mechanisms for the more effective inhibition seen with two antibodies. He showed that the antibodies promoted more disabled kinase-dimeric species, leading to more profound reversal of malignant features. The antibodies to two distinct interaction domains caused a more permanent reversal of the malignant properties of human cancer cells.

This work has been recognized as determining a way to treat cancer — that is, to target the oncoprotein causing the specific tumor and then use chemotherapy or radiation therapy. Greene solved both issues by defining the oncoprotein that causes breast cancer, namely p185HER2/erb2/neu, and identifying how to target it with single or combinations of ectodomain-specific monoclonal antibodies.

Greene's studies have formed the foundation for targeted therapy and the basis of personalized cancer therapy that targets HER2/erbB2/neu as well as therapies directed at heteromers of erbB family members (e.g., erbB2/erbB1 and erbB2/erbB3 heteromers). His work has changed the way we treat cancer and has had a great impact on rates of survival from human cancers.

Katherine A. High, MD

Katherine High was born on July 27, 1951, in High Point, North Carolina. She graduated from Harvard College with a degree in chemistry and spent a year working with Kilmer McCully at Massachusetts General Hospital on pathogenesis of homocystinuria before entering medical school at the University of North Carolina (UNC) School of Medicine. She took a one-year break from medical school to return to the chemistry laboratory, where she carried out studies on autoacceleration in the polymerization of vinyl monomers, and then completed medical school and training in internal medicine at UNC hospitals. She trained in hematology at Yale University School of Medicine, working in the laboratory of Edward J. Benz. After a year on staff at Yale, she returned to the UNC faculty in the Department of Medicine.

High began independent research under Harold Roberts, the chief of the UNC–Chapel Hill Division of Hematology/Oncology, and Darrel Stafford, a pioneering molecular biologist. Roberts founded the Comprehensive Hemophilia Treatment Center at UNC, which followed large numbers of patients with clotting factor defects. High capitalized on this, and the recent isolation of the genes encoding Factor IX and other vitamin K–dependent clotting factors, to begin to characterize mutations that cause hemophilia B and deficiencies of Factor X and Factor VII. She used recombinant expression systems to produce large amounts of mutant clotting factor proteins for detailed biochemical studies, an approach that was difficult using plasma-derived proteins, since most clotting factor proteins circulate in very low amounts. She was the first to clone a canine gene, when she isolated the gene encoding canine Factor IX; this paved the way for her identification of the mutation that causes canine hemophilia B. At UNC she began the first studies of gene transfer into canine fibroblasts, a precursor to later work in gene therapy. Her clinical work at UNC focused on the hemophilia population; these were trying years for patients and physicians, as it became clear that virtually all patients with severe hemophilia were HIV infected and that there were no effective drugs to combat the disease.

In 1992 High was recruited to Philadelphia to join the faculty at the University of Pennsylvania and the staff at the Children’s Hospital of Philadelphia. With joint appointments in pediatrics, pathology, and medicine, High pursued her work on the molecular basis of blood coagulation and became involved in studies of gene transfer. In 1997 she published on the correction of the hemophilic mouse model using an AAV vector; she subsequently demonstrated the correction of severe hemophilia in affected dogs by using a similar AAV-based approach. She led the first clinical trial of AAV introduced into human liver, for men with severe hemophilia B. High has been a leader in the development of novel genetic therapies to treat inherited disorders and has been at the forefront of safe and effective clinical translation of genetic therapies for hemophilia. In addition to conducting the first trial in human liver, she also led the first clinical trial in which AAV was introduced into skeletal muscle. In collaboration with Jean Bennett and Albert Maguire, she led the first trial in the US of the introduction of AAV into the subretinal space to treat a form of congenital blindness. Her analysis of problems uncovered in the course of clinical studies, including risk of germline transmission of vector in recipients of donated DNA, and of immune responses to viral vectors, laid the foundation for the expansion of gene therapy.

At the University of Pennsylvania High was the William H. Bennett Professor of Pediatrics. In 2002, she was appointed an investigator of the Howard Hughes Medical Institute. As support for gene therapy began to wane in the wake of several high-profile adverse events, High convinced the leadership of CHOP to establish a center devoted to developing cell and gene therapies for diseases that affect the pediatric population — the result of which is the CHOP Center for Cellular and Molecular Therapeutics. The center recruited outstanding scientists and physicians to continue work on obstacles to successful human gene therapy and to conduct clinical trials when the safety and efficacy data in animals justified these.

High served on NIH study sections in hematology and in genetic disease, on the NHLBI Program Project Grant parent committee, and as a member of the NHLBI advisory council. She served on the board of scientific councilors for the NIH Clinical Center and on the NHLBI Gene Therapy Resource Program steering committee. She was a member of the FDA Cell, Tissue and Gene Therapy Advisory Committee. She is an active member of the American Society of Hematology (and has served on its executive committee) and of the American Society of Gene and Cell Therapy (of which she is a past president).

High is the recipient of a number of awards, including the National Hemophilia Foundation Researcher of the Year Award, and was elected as a American Association for the Advancement of Science fellow for “distinguished contributions in the field of human gene therapy.” She received the Stanley N. Cohen Biomedical Research Award from the University of Pennsylvania, the Distinguished Alumna Award from the University of North Carolina, and a Distinguished Achievement Award from the American Heart Association. She also received the Foundation Fighting Blindness Board of Directors Award and the Outstanding Achievement Award from the American Society of Gene and Cell Therapy. She received the E. Donnell Thomas Award from the American Society of Hematology in 2013.

High has published over 180 scientific articles, including the first reports of AAV-mediated gene transfer into muscle and liver in patients with hemophilia B and into the retina in patients with an inherited retinal disorder that causes blindness in childhood. She is an editor of the hematology textbook *Clinical Hematology*.

High has been elected to honorary societies, including the American Soci-

ety for Clinical Investigation, the Association of American Physicians, the Institute of Medicine of the National Academy of Sciences, and the American Academy of Arts and Sciences. She served on the scientific advisory boards of the Italian Telethon Foundation and of a number of biotech companies, including Bluebird Bio and Alnylam, Inc. She served on the editorial board of the *Journal of Clinical Investigation* and is an associate editor of *Molecular Therapy*. She currently serves on the editorial board of *Blood*.

In 2014 she resigned from Howard Hughes Medical Institute and the Center for Cellular and Molecular Therapeutics at CHOP to devote her time to Spark Therapeutics, which is focused on development of gene-based treatments for serious genetic disease. High is currently president and chief scientific officer of Spark.

Edward Holmes, MD

Edward Holmes was born on January 25, 1941, in Winona, MS. He received the BS degree from Washington and Lee University in 1963 and four years later the MD degree from the University of Pennsylvania School of Medicine. He interned at the Hospital of the University of Pennsylvania (1967–1968) and completed his residency in medicine at Duke University School of Medicine. From 1971 to 1973 he was a fellow in rheumatic and genetic diseases at Duke and from 1973 to 1974 served as chief medical resident. From 1968 to 1970 he worked as a research associate in the division of nephrology of the US Public Health Service, stationed on Staten Island, NY. From 1974 to 1987 he was appointed an investigator of the Howard Hughes Medical Institute. In 1973 he became an associate in medicine at Duke and rose through the ranks to become professor of medicine in 1981, a position he held until 1987. From 1985 to 1991 he was an associate professor of biochemistry, and from 1987 to 1991 he held the title of James B. Wyngaarden Professor of Medicine. He served as chief of the Section of Metabolic and Genetic Diseases in Durham between 1977 and 1983, and as chief of the Division of Metabolism, Endocrinology and Genetics between 1983 and 1991. In 1991 Holmes left Duke to become the Frank Wister Thomas Professor of Medicine at the University of Pennsylvania School of Medicine and chairman of its Department of Medicine. He also held the title of professor of medicine in human genetics and physician in-chief of the Hospital of the University of Pennsylvania.

In January 1999 Holmes returned to Duke University as dean of the School

of Medicine and Walter Kempner Professor in Medicine and Genetics. Holmes was appointed vice chancellor for health sciences and dean of the University of California, San Diego, School of Medicine in the fall of 2000 and served in this role until October 2006. In 2006 he was appointed the executive deputy chairman of the Biomedical Research Council of the Agency for Science, Technology and Research in Singapore, a position he still holds, and the executive chairman of the National Medical Research Council of Singapore, a position he held until 2011. He also holds an appointment as the Lien Ying Chow Professor of Medicine at the Yong Loo Lin School of Medicine of the National University of Singapore. He is currently CEO/president of the Sanford Consortium for Regenerative Medicine, distinguished professor of medicine at the University of California, and emeritus vice chancellor/dean of health sciences at UCSD.

Holmes's interest in basic biomedical research began as a medical student at the University of Pennsylvania. He worked summers and part of one year in the laboratory of Albert I. Winegrad. During this time he developed an interest in the basic mechanisms of the pathogenesis of human disorders. During his fellowship with Bill Kelley at Duke, he studied in depth the biochemistry of disorders of purine metabolism. While at Duke, Wyngaarden and Kelley served to shape his interest in the role of physician-scientists in biomedical research. His research career began with an exploration of the factors that control the rate of purine biosynthesis in eukaryotic cells. His laboratory was the first to demonstrate the molecular basis by which purine ribonucleotides and phosphoribosyl pyrophosphate interact at the level of the allosteric enzyme amidophosphoribosyltransferase to control the rate of purine synthesis in mammalian cells.

Subsequent work in his own laboratory focused on the utility of an intermediate in the purine biosynthetic pathway aminoimidazole carboxamide ribonucleotide to stimulate the rate of purine biosynthesis in intact cells and in organs in vivo. These studies have led to the development of a new class of pharmacologic agents that are currently in clinical trials to treat a variety of cardiovascular disorders. A biopharmaceutical firm on the US West Coast was formed to develop therapeutic agents based on a patent that resulted from these studies. These studies have also inspired in his laboratory a fundamental interest in skeletal muscle biochemistry, and their recent research has focused on the molecular basis of a common inherited defect, deficiency of AMP deaminase activity. They have cloned two genes in this multigene family and demonstrated the molecular basis by which a mutation in the *AMPD1* gene leads to a common inherited metabolic

myopathy that affects 1% to 3% of Caucasian and African Americans. Additional fundamental studies have delineated the molecular basis for muscle-specific expression of this gene and defined a novel mechanism of alternative RNA splicing that may contribute to the phenotype of this common inherited defect. A sabbatical spent at the Massachusetts Institute of Technology in the laboratory of Paul Schimmel afforded Holmes the chance to focus on RNA metabolism. He subsequently identified a novel mechanism by which the 3'-untranslated region of the creatine kinase message exerts its effects on translation.

Holmes has served on the council of advisors for the National Institute for Diabetes, Digestive, and Kidney Diseases of the National Institutes of Health and as chair of the research advisory board of GlaxoSmithKline. He also serves on the Grand Challenges Explorations Innovation grant review panel for the Bill & Melinda Gates Foundation. He has received distinguished alumnus awards from the University of Pennsylvania and Duke University. He has been elected to membership in the American Society for Clinical Investigation and the Association of American Physicians, is a fellow of the American Association for the Advancement of Science, and is a member of the Institute of Medicine of the National Academy of Sciences.

Richard B. Johnston Jr., MD

Richard B. (Dick) Johnston Jr. was born in Atlanta, GA, on August 23, 1935. He attended Atlanta public schools, where his drive for success was focused on athletics. An ACL tear while playing football at Vanderbilt shifted his focus to leadership. At Vanderbilt (1957–1961) he studied philosophy, an early expression of the value he has assigned to the humanities across his lifetime. He stayed at Vanderbilt for medical school (1957–1961) and for 2 years of pediatric residency, then finished his residency at Boston Children's Hospital. After 2 years as a pediatrician in the US Army stationed in Germany, where he furthered his education in European history, architecture, and art, he returned to Vanderbilt for one year as instructor in pediatrics (1966–1967). While there, he made the decision to undertake a research career, based on the fulfillment he had found from publishing five peer-reviewed clinical research articles during his Vanderbilt residency, and he entered a fellowship in immunology at Boston Children's Hospital and Harvard (1967–1970) under the mentorship of Fred Rosen and, on occasion, David Nathan.

His first full-time faculty positions as assistant and associate professor were at the University of Alabama Birmingham (1970–1977), where he developed a pediatric immunology unit with Max Cooper. After a year's sabbatical at Rockefeller with Zanvil Cohn, he assumed the chairmanship of pediatrics at National Jewish Hospital in Denver (now National Jewish Health) and a professorship at the University of Colorado School of Medicine (1977–1986). He took a second Rockefeller sabbatical in 1983–1984 to work with Zanvil Cohn and Carl Nathan. Following his time at National Jewish, he served as chair of pediatrics at Children's Hospital of Philadelphia (CHOP) and University of Pennsylvania (1986–1990), then as medical director of the March of Dimes (1992–1998). In conjunction with the latter role, he transferred his R01 grant to Yale, where he saw immunodeficiency disease patients weekly and served as adjunct professor and chief of the Division of Pediatric Immunology (1992–1998). He then returned to Colorado, to serve as associate dean for research development at the University of Colorado (2001–present) and as executive vice president for academic affairs at National Jewish (2004–2007).

Johnston has published 172 research articles (283 full articles in total) in the areas of complement, neutrophil, and macrophage biology and biochemistry, and immunodeficiency disease; his particular focus has been on complement abnormalities and chronic granulomatous disease. Publications have appeared in the *New England Journal of Medicine* (NEJM; 8 articles), the *Journal of Clinical Investigation* (JCI; 16 articles), the *Journal of Experimental Medicine* (JEM; 10 articles), the *Journal of Biological Chemistry* (JBC; 6 articles), and the *Journal of Immunology* (16 articles). He developed the first quantitative assay of phagocytosis to show that efficient uptake of bacteria requires fixation of C3 to the organism (results published in JEM). He showed that there is an abnormality of alternative pathway complement activation in patients with sickle cell disease that could predispose to invasive pneumococcal disease (published in NEJM). He demonstrated that superoxide anion is involved in bacterial killing through the respiratory burst, and he presented the first evidence suggesting that hydroxyl radical can be generated by mammalian cells (published in JCI). Using a model of immune complex disease he showed that neutrophils (JCI) and monocytes (JEM) vigorously release reactive oxygen metabolites to the outside of the cell, where they could mediate oxidative tissue damage. He described the “priming” of macrophages for enhanced phagocytosis-associated respiratory burst as a fundamental expression of activated macrophages (JEM). He also showed that neutrophils can be primed for enhanced function when stimulated by inflammatory mediators and, thus,

that that this cell type is not an end-stage cell incapable of modification at sites of inflammation, as was previously thought (JEM). In other examples of his research, he published the first evidence that enhanced microbicidal capacity of activated macrophages is directly related to their enhanced respiratory burst (JEM); that multinuclear giant cells function in host defense like large macrophages, exhibiting the same capacity to ingest and kill, using the same oxidative and non-oxidative mechanisms (JEM); and that activation of macrophages increases the respiratory burst by increasing the V_{max} and decreasing the K_m of the oxidant-producing NADPH oxidase (published in JBC).

Johnston has been on the editorial board of five journals and editor-in-chief of *Current Opinion in Pediatrics* (1996–2014). He chaired the FDA Vaccines and Related Biological Products Advisory Committee (1991–1993) and the Howard Hughes Medical Institute selection committee for medical student research fellowships (1995–1997). He has served as reviewer and advisor for the CDC, the NIH (NIAID, NICHD, and NIMH), medical school departments of pediatrics, and other institutions. He was on the committee that established the sub-board of pediatric infectious disease. He served on the Institute of Medicine Board on Health Promotion and Disease Prevention (1994–2001), and he chaired seven Institute of Medicine committees. He currently serves on the medical center affairs committee of the Vanderbilt University Board of Trust.

His honors include membership in the American Association of Immunologists, the American Academy of Pediatrics, the Society for Pediatric Research (president 1980–1981), the American Pediatric Society (APS; president 1996–1997), and the Institute of Medicine (1994). He has received the Commissioner's Special Citation and the Harvey Wiley Medal from the FDA (1994), the John Howland Medal from the APS (the highest award in academic pediatrics, received in 2008), the Godfrey Oakley Award from the National Birth Defects Prevention Network (2012), and the David Rall Medal from the Institute of Medicine (2014). He has been recognized by the establishment of the Richard B. Johnston Jr., MD Research Bridge at the University of Pennsylvania and the Richard B. Johnston Jr., MD Endowed Chair in Pediatrics at CHOP/Penn.

Johnston has been supported in his medical career and in life by his wife, Mary Anne (a medical educator), and his children: Richard III (physician in orthopedic sports medicine), Claiborne (Clay) (physician-scientist and medical school dean), and Kristin (psychologist).

Steven Kelsen, MD

Steven Kelsen was born in Philadelphia Pennsylvania on January 19, 1943. He received a BA degree in Biology from LaSalle College in 1964 and the MD degree from Hahnemann School of Medicine in 1968. This was followed by a residency in internal medicine at the Boston city Hospital (1968-1970); a senior residency at Cornell-New York Medical Center (1970-1971); and a clinical and research fellowship in Pulmonary Medicine at the University of Pennsylvania. Following his research fellowship in 1973, Kelsen was appointed Assistant Professor of Medicine in the Pulmonary Disease division of the University of Pennsylvania and served as director of the pulmonary clinical service at the Philadelphia General Hospital, a University of Pennsylvania affiliate. In 1977, Kelsen moved to Case Western Reserve University in Cleveland with University of Pennsylvania colleagues, Dr. Neil Cherniack and Dr. Murray Altose. In Cleveland, Kelsen directed the pulmonary clinical service at University Hospitals of Cleveland and the pulmonary fellowship training program at Case Western Reserve University. He was appointed Associate Professor of Medicine at Case Western Reserve in 1979 and Professor of Medicine in 1985. In 1987, he moved to Temple University, as Professor of Medicine and Director of the Division of Pulmonary Medicine, a position he held until 1993. Since 1993, Kelsen as directed the research efforts of the pulmonary disease division at Temple.

Kelsen developed his career-long interest in research at the University of Pennsylvania under the mentorship of Dr. Neil Cherniack, a highly imaginative investigator and superb role model. The Cherniack lab was studying the neural and chemical mechanisms which regulate the respiratory response(s) to mechanically loaded breathing. In particular, the efforts of the Cherniack lab were directed toward understanding the contribution of abnormalities in the central regulation of breathing in the setting of obstructive lung disease to the development of hypercapnic respiratory failure. Studies performed during that time with colleagues in the Cherniack lab, including Murry Altose and Musa Haxhiu, led to the development and validation of the airway occlusion pressure, a non-invasivemeasure of the neuromuscular drive to breathe. The occlusion pressure was clinically useful in that it could be used to diagnose central abnormalities in the control breathing in subjects with chronic hypercapnic respiratory failure and to differentiate that group from the group whose hypercapnic respiratory failure resulted from the severity of their lung disease.

Kelsen subsequently developed an interest in the respiratory skeletal musculature, its function in COPD and its contribution to the development of hypercapnic respiratory failure. He demonstrated that under appropriate conditions of mechanical loading, the diaphragm and inspiratory musculature in aggregate could, like other skeletal muscle, develop fatigue. Furthermore, he demonstrated that inspiratory muscle fatigue was accompanied by alterations in the level and pattern of breathing which predispose to CO₂ retention and a heightened sense of dyspnea. Using an animal model of emphysema, he subsequently demonstrated that the respiratory skeletal musculature manifests adaptive changes in muscle ultrastructure which allow their force generating ability to be preserved in the setting of chronic hyperinflation. Adaptive changes in respiratory muscle structure involve addition or subtraction of sarcomeres in series when muscles were chronically lengthened or shortened in the setting of hyperinflation of the thorax. The work on the respiratory muscles was supported by a series of RO1 grants in which he was the PI and by a Program Project grant directed by Dr. Cherniack.

Kelsen's other interest is in airway epithelial cell biology, in particular, the role played by airway epithelial cells in the pathogenesis of obstructive lung disease. In that regard, he described a method to harvest viable airway epithelial cells from living human donors. Using this method, he demonstrated that human airway epithelial cells express both chemokines and cytokines which affect the behavior of lung inflammatory and structural cells and functional chemokine receptors which initiate directed cell migration and proliferation.

Kelsen has received a number of awards including an UpJohn Award for Excellence in Research and an NIH pulmonary Academic Award. He is a member of the American Society for Clinical Investigation and has served as an officer in the American Thoracic Society and the Respiration section of the American Physiological Society. He served as a permanent member of the NIH Respiratory Integrative Biology and Translational Research study section. He has also served as an ad hoc member of the NIH Lung Injury, Repair and Remodeling; Lung Cellular, Molecular, and Immunobiology; and Translational Programs in Lung Disease (PO1) study sections. He has served on the editorial boards of the *American Journal of Respiratory and Critical Care Medicine* and the *American Journal of Physiology: Respiratory Cell and Molecular Physiology*. He reviews for a number of journals including the *Journal of Clinical Investigation*, *American Journal of Respiratory and Critical Care Medicine*, *American J of Respiratory Cell*

and Molecular Biology, New England Journal of Medicine, and the American Journal of Physiology Respiratory Cell and Molecular Physiology.

Michael Alan Levine, MD

Michael Levine was born in New York City on June 11, 1950. He received the AB degree from Rutgers College and the MD degree from Drexel University College of Medicine. From 1976 to 1979 he was intern and resident in medicine at the Johns Hopkins Hospital. The next three years he was a clinical associate in the Metabolic Disease Branch of the National Institute of Arthritis, Metabolism and Digestive Diseases and a fellow in the Combined Endocrinology Training Program at the NIH. From 1981 to 1982 he was a medical staff fellow in genetics and a clinical fellow in the NIH InterInstitute Genetics Training Program. In 1982 Levine joined the Department of Medicine at Johns Hopkins as an assistant professor in the Division of Endocrinology and Metabolism. From 1986 to 1992 he served as associate professor of medicine and pathology and in 1991 was appointed associate professor of environmental health sciences in the Johns Hopkins University School of Hygiene and Public Health. In 1992 Levine was promoted to professor of medicine and pathology in the School of Medicine and professor of environmental health sciences in the School of Hygiene and Public Health.

Levine became the first Lawson Wilkins Professor of Pediatrics at Hopkins with his appointment as director of the Division of Pediatric Endocrinology. In 2003 he left Hopkins to become professor and chair of pediatrics at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University. In 2008 Levine took up his current position as chief of endocrinology and diabetes and director of the Center for Bone Health at the Children's Hospital of Philadelphia (CHOP), where he holds the Lester Baker Endowed Chair in Diabetes. Levine is also professor of pediatrics and medicine at the University of Pennsylvania Perelman School of Medicine.

During his senior year at Rutgers, Levine pursued a project in biochemistry with Robert Niederman, an experience that focused his career in medical research. At Hopkins he was influenced by John Eager Howard. At the NIH he worked in Gerald D. Aurbach's laboratory, where he collaborated with Allen Spiegel during his fellowships in endocrinology and genetics.

Levine's research efforts have been directed toward understanding the molecular pathophysiology of abnormal signal transduction in humans, his accomplishments being concerned with G protein-coupled signal transduction and inherited disorders of parathyroid hormone synthesis and action. To determine the basis for hormone resistance in pseudohypoparathyroidism (PHP), he and Spiegel investigated the hormone receptor adenylyl cyclase complex in cells from these subjects by measuring activity of the guanine nucleotide-binding protein that couples hormone receptors to stimulate adenylyl cyclase (Gas) in erythrocyte membranes. Levine made the observation that levels of Gas, the α chain of the heterotrimeric G protein Gs that couples heptahelical receptors to activate adenylyl cyclase, were reduced in cells from PHP patients who have features of Albright hereditary osteodystrophy (AHO) but were normal in PHP patients who lacked these features. This distinction led to the dichotomization of PHP type 1 into two subtypes, one form with reduced Gas, termed PHP type 1a, and another form with normal Gas, termed PHP type 1b. These early observations enabled biochemical and clinical distinction between these two groups of patients and facilitated future clinical, biochemical, and molecular studies by Levine and other groups.

Over the next 30 years Levine's research in the areas of PHP and G proteins led to the first description of the pattern of inheritance of reduced Gas in patients with PHP type 1a and pseudohypoparathyroidism, which supported the notion of genomic imprinting as the molecular basis for the distinction between these two variants. He also published the first description of a mutation in the *GNAS* gene in patients with PHP type 1a and described the pattern of inheritance of *GNAS* mutations in families with PHP type 1a, which provided further evidence of the role of imprinting in modifying the phenotype of the *GNAS* mutation. Levine's group first demonstrated preferential expression of the maternal *GNAS* allele in normal human thyroid tissue, which confirmed imprinting of *GNAS* in this tissue and provided a basis for understanding the basis for TSH resistance in patients with PHP type 1a. His research group generated an exon I-specific knockout mouse to demonstrate that loss of only Gas, one of at least three proteins generated by the *GNAS* gene, was sufficient to create the PHP type 1a phenotype, including ectopic ossification, and that tissue-specific imprinting of this transcript could explain the unusual pattern of phenotypic changes.

Levine's research group has also characterized the clinical phenotype of AHO, demonstrating that obesity and short stature are features limited to

PHP type 1a and represent the effects of imprinting of *GNAS* on *Gas* expression in the central nervous system. His group's description of growth hormone–releasing hormone (GHRH) resistance and associated growth hormone deficiency in these patients has led to clinical trials of rhGH in patients, the first new approach to treatment of PHP type 1a developed in 25 years.

Levine worked with Eileen Shore, Fred Kaplan, and Michael Whyte to demonstrate that paternal inheritance of *GNAS* mutations could also cause progressive osseous heteroplasia (POH), an observation that further extended the phenotypic variability of *GNAS* mutations and has led to new insights into the molecular controls that regulate development of eutopic and ectopic intramembraneous bone. With Emily Germain-Lee, Levine used the exon 1 knockout mouse to confirm that haploinsufficiency of the *Gas* transcript is sufficient to induce ectopic bone formation, both in the skin and in deeper tissues, thus reproducing the phenotype of AHO and POH.

A second area in which Levine has worked that has direct relevance to the field of bone and mineral metabolism is hypoparathyroidism. Levine and his coworkers were first to show the relationship between hypomethylation of the promoter region of the *PTH* gene and expression of PTH in the parathyroid gland. He subsequently published the first comprehensive molecular genetic analysis of familial hypoparathyroidism, which applied the term “isolated hypoparathyroidism” to patients with non-syndromic genetic hypoparathyroidism.

In ongoing work with collaborators Tom Thacher at Mayo Clinic and Jeffrey Roizen at CHOP, Levine demonstrated that mutations in the *CYP2R* gene, which encodes the principle 25-hydroxylase, are a novel cause of vitamin D–dependent rickets and that polymorphisms in the *CYP2R* gene may account for lower circulating levels of 25(OH)D in many patients. This work is now expanding to other tropical countries and has the potential to explain not only the unanticipated occurrence of rickets in children who are exposed to abundant sunlight, but also the genetic contribution to widespread vitamin D insufficiency in North America and Europe.

Levine is a member of numerous professional societies, including the Endocrine Society, the American Society for Bone and Mineral Research, the American Society for Clinical Investigation, the Association of American Physicians, and the American Pediatric Society. He is a fellow of the Amer-

ican College of Physicians, the American College of Endocrinology, and the American Academy of Pediatrics and an elected member of the Johns Hopkins University Society of Scholars. Levine's honors include the Young Investigator Award from the American Federation for Clinical Research, Eastern Section; the Fuller Albright Award from the American Society for Bone and Mineral Research; and the March of Dimes Basil O'Connor Research Scholar Award. He received the Distinguished Endocrinology Award from the American College of Endocrinology in 2003, and since 2005 has been named as one of America's best doctors. He has served on the editorial board or as an associate editor for *Bone and Mineral* and the *Journal of Clinical Endocrinology and Metabolism*. His research support has come from both private and federal sources.

Willis C. Maddrey, MD

Willis Crocker Maddrey was born on March 29, 1939, in Roanoke Rapids, NC. He received his BS degree from Wake Forest University in 1960 and his MD from the Johns Hopkins University School of Medicine in 1964. He was an intern and then assistant resident on the Osler Medical Service at Johns Hopkins Hospital (1964–1966), after which he served in the United States Public Health Service for two years in Calcutta. On returning to the United States, he served an additional year as assistant resident in medicine at the Johns Hopkins Hospital and was then chief medical resident on the Osler Medical Service there (1969–1970). During 1970–1971 he was a fellow in liver disease at the Yale University School of Medicine, serving under Gerald Klatskin. Maddrey then returned to Johns Hopkins as assistant professor in medicine, where he continued his interest in diseases of the liver and directed the program of liver diseases. In 1975 his interests turned toward administration, and he became assistant dean for postdoctoral programs and faculty development at Johns Hopkins. He became an associate professor of medicine in 1975 and then served as a professor of medicine from 1980 to 1982. From 1979 to 1982 he served as associate director of the department of medicine under Victor McKusick, who was chairman of the department at the time.

In 1982 Maddrey moved to Philadelphia as Magee Professor of Medicine and chairman of the department of medicine at Jefferson Medical College. In 1990 he moved to the Southwestern Medical Center of the University of Texas in Dallas as vice president of clinical affairs. He subsequently served as executive vice president (1993–2001) and was in charge of the clini-

cal programs. He is a professor of internal medicine and, since 2001, has served as assistant to the president at UT Southwestern.

Maddrey's research interest has continued to be in various areas of liver disease. He has made significant contributions related to chronic hepatitis (viral and autoimmune), alcohol-induced liver disease (corticosteroid therapy), liver transplants, and the management of complications of cirrhosis. He has also studied the effects of keto-analogs of essential amino acids in portal-systemic encephalopathy. In collaboration with John Cameron, he developed a new treatment for Budd-Chiari syndrome.

From 1972 to 1982 Maddrey was associate editor of *Medicine*. He has served on the editorial boards of other journals, including *Viewpoints on Digestive Diseases*, *Gastroenterology*, and *Transplantation Science*, and as associate editor of *Hepatology*.

Maddrey is a member of the American Society for Clinical Investigation, the American Gastroenterological Association, the American Federation for Clinical Research, the American Clinical and Climatological Association, and the American Association for the Study of Liver Diseases (president, 1981). He is a master of the American College of Physicians (since 1993) and served as its president in 1992–1993. He is a member of the Southern Society for Clinical Investigation and a fellow of the Royal College of Physicians.

Maddrey was awarded the George Stuart Outstanding Teacher Award at Johns Hopkins (1970) and the Christian R. and Mary F. Lindback Award for distinguished teaching in the clinical sciences at Jefferson Medical College (1986). He received the Distinguished Service Citation from Wake Forest University in 1991. In 1998 he was awarded the Distinguished Educator Award by the American Gastroenterological Association. He was named the Adelyn and Edmund M. Hoffman Distinguished Chair in Medical Science at UT Southwestern, a position that he still holds, and was awarded the Arnold N. and Carol S. Ablon Professorship in Biomedical Science. He was awarded the Distinguished Service Award from the American Association for the Study of Liver Diseases in 2000, and the Distinguished Alumnus Award from the Johns Hopkins University School of Medicine in 2008.

Eric Grant Neilson, MD

Eric Neilson was born in Brooklyn, NY, on September 14, 1949. He received his BS degree *magna cum laude* from Denison University in 1971, his MD degree *magna cum laude* from the University of Alabama in Birmingham in 1975, and a BA degree with honors from the University of Pennsylvania in 1987. From 1975 to 1980 he served as an intern, resident, and nephrology fellow at the Hospital of the University of Pennsylvania, and then was appointed assistant professor of medicine (1980–1987), associate professor of medicine with tenure (1987–1991), professor of medicine and pediatrics (1991–1998), the C. Mahlon Kline Professor of Medicine and Pediatrics (1993–1998), chief of the Renal-Electrolyte and Hypertension Division (1988–1998), and director of the Penn Center for Kidney and Hypertensive Diseases (1996–1998), all at the University of Pennsylvania School of Medicine. From 1998 to 2010 he served as the Hugh Jackson Morgan Professor of Medicine and Cell and Developmental Biology and chairman of the Department of Medicine, and since 2010 he has served as the Thomas Fearn Frist, Sr. Professor of Medicine, both at the Vanderbilt University School of Medicine.

Neilson has had a life-long interest in diseases of the kidney. He received his early training in cellular immunology with S. Michael Phillips and in basement membrane biology with Nicholas Kefalides at the University of Pennsylvania; he received career mentorship from Arnold Relman, Alfred P. Fishman, Laurence E. Earley, Edward Holmes, and William Kelley at the University of Pennsylvania, and later from Harry Jacobson at Vanderbilt University. His early experimental work involved mapping the immunogenetic mechanisms and subpopulation interactions that form the nephritogenic T and B cell responses in interstitial nephritis, which is the final common pathway to end-stage renal disease. His laboratory later turned to the problem of cell fate of fibroblasts in tissue fibrosis. His group cloned fibroblast-specific protein 1 (FSP1) and, with this protein, showed that fibroblasts derive locally from tissue epithelia and endothelia via epithelial-mesenchymal transition (EMT) and endothelial-mesenchymal transition (EndoMT), respectively. This work also advanced thinking about the role of EMT in cancer metastasis. In other areas, his group identified the antigen involved in anti-tubular basement membrane nephritis (anti-TBM), first expressed the epitopes of the Goodpasture antigen, and provided a biochemical explanation for isoform switching of basement membrane collagen protomers, which fails in Alport syndrome. Neilson's laboratory has also had a long interest in the molecular and signaling mechanisms

that lead to cellular hypertrophy of tubular epithelia. Finally, Neilson transformed the Department of Medicine at Vanderbilt into a large and successful research enterprise. As a national leader for the development of physician-scientists in internal medicine, he has been a tireless advocate for including more science in the practice of clinical medicine.

Neilson previously served as chairman of the NIH Pathology A Study Section (1990–1992) and on the Advisory Council of the NIDDK (1997–2000), is a member of the American Society for Clinical Investigation (joined in 1986), the Association of American Physicians (1992), the Interurban Clinical Club (1994; councilor, 1996), the Association of Subspecialty Professors (founding president, 1994), the Association of Professors of Medicine (1998; chairman of the research committee and board of directors, 1999–2002), and the American Clinical and Climatological Association (2001). He is a past member of the scientific advisory boards of BioStratum and NephroGenex, Inc., and the holder of two patents.

Neilson is a past recipient of the Hugh J. Dempsey Award (the dean's award for highest academic achievement in medical school, received 1975), a clinician-scientist award from the American Heart Association (1980), and an Established Investigator Award from the American Heart Association (1985). The American Society of Nephrology granted Neilson the Young Investigator Award (1987), the President's Medal (1994), and the John P. Peters Award (2005), and he presented the society's inaugural Barry M. Brenner Lecture (2001). In 1991 he received an NIH MERIT Award, the A. N. Richards Distinguished Achievement Award from the University of Pennsylvania School of Medicine (1998), and the Distinguished Professor Award from the Association of Subspecialty Professors (2003; now renamed the Eric G. Neilson, MD Distinguished Professor Award). In 2006 Neilson received the Distinguished Alumnus Award from the University of Alabama Medical Alumni Association and the Robert H. Williams, MD Distinguished Chair of Medicine Award (2010) from the Association of Professors of Medicine. In 2002 he co-edited *Immunologic Renal Disease*, 2nd edition, with William Couser, and since 2007 he has been editor-in-chief of the *Journal of the American Society of Nephrology*. In 2010 he served as associate editor of *Schrier's Diseases of the Kidney*, 9th edition (co-edited with Schrier, Coffman, Molitoris, and Falk).

Richard Pestell, MD, PhD

Richard Pestell completed his MD (1981) and PhD, and received his oncology and endocrinology training, in Australia. As recipient of the Royal Australian College of Physicians Winthrop and Neil Hamilton Fairley awards (1991–1994) he continued research at Harvard University and was a clinical fellow at Massachusetts General Hospital. From 2002 he served as chairman of the Department of Oncology, the Charlotte Gragnani Endowed Chair, director of the Lombardi Cancer Center, and associate vice president of Georgetown University Medical Center. From 2005 he has been director of the Sidney Kimmel Cancer Center and associate dean and vice president of oncology services at Thomas Jefferson University and Hospital in Philadelphia. The Jefferson Cancer Network includes 22 hospitals in the USA Northeast. He is a past president of INCTR USA and was the founding director of the Delaware Valley Institute for Clinical and Translational Science (founded in 2008). He is married and has two sons.

Pestell has authored more than 575 published works, including 340 original publications and book chapters and more than 180 published abstracts. His papers have been published in journals such as *Cell*, *Science*, *Nature Medicine*, *Molecular Cell*, and *EMBO J*. His work is highly cited (22,000 citations, h-index of 69). In March 2002 he was ranked first in the world for increase in total scientific impact in biology and first in the world for biochemistry (ISI). Pestell receives funding from six NIH R01 grants and is named principal investigator for the Kimmel Cancer Core Center grant.

He has received a number of awards for his scientific discoveries in breast and prostate cancer: he is a member of the American Society for Clinical Investigation and a fellow of the Royal Society of Medicine; received the Irma T. Hirschl Weil Caulier Career Scientist Award; was named the Diane Belfer Faculty Scholar in Cancer Research and the Gragnani Endowed Chair; received the Pfeiffer Award, the Harrison award (the highest award of the Australian Endocrine Society), the R. D. Wright medal, the Komen Light of Life Award, and an honorary doctorate degree; and was the Raine Distinguished Professor. Pestell serves as a reviewer for 11 funding agencies and has been an active member of NIH study sections (R01, SPORES, cancer centers, program projects). He serves as scientific advisory board member for seven NCI-designated cancer centers and for many funding agencies. Pestell has been a reviewer for 18 scientific journals, has served on editorial boards of six journals, and has founded two biotechnology companies.

Pestell's major contributions to research include the discovery that cyclins are direct transcriptional targets of oncogenic and tumor suppressor signals and that cyclin expression is rate-limiting for oncogene-induced tumor growth in vivo. His laboratory established this as a general mechanism of oncogenic signaling and showed that the cyclins physically interact with nuclear receptors and tumor suppressors and thus are potential novel targets for cancer therapies.

Pestell was the first to show that nuclear receptors are acetylated, and that acetylation is rate limiting in hormone signaling and growth control and may be a new target for cancer therapy. He demonstrated that acetylation is a general mechanism conserved among nuclear receptors and affects diverse biological processes. His laboratory pioneered the application of tissue-specific inducible transgenics and the development of gene-targeted and transgenic mice, which provide a superior model of human cancer. He holds a patent for light-activated gene therapy, which allows for single-cell targeting of a payload and can be applied to all genes in the human genome.

Roger J. Pomerantz, MD

Rodger Pomerantz was born in New York City on March 17, 1957. He received his BA in biochemistry at the Johns Hopkins University (1978) and his MD at the Johns Hopkins School of Medicine (1982). He completed his internal medicine internship and residency training, and his subspecialty clinical and research training in infectious diseases and virology at the Massachusetts General Hospital (M.G.H.) of the Harvard Medical School (1982 -1988), and was selected and served as the chief medical resident at the M.G.H (1988).

Pomerantz's post-doctoral research training in Molecular Retrovirology was obtained at both the Harvard Medical School and the Whitehead Institute of the Massachusetts Institute of Technology (M.I.T.), in the laboratory of Nobel Laureate, Dr. David Baltimore (1988 -1990). Dr. Pomerantz is Board Certified in both Internal Medicine and Infectious Diseases.

He was an endowed, tenured professor of medicine, biochemistry and Molecular pharmacology, chief of infectious diseases, and the founding director and chair of the Institute for Human Virology and Biodefense at the Thomas Jefferson University and Medical School in Philadelphia (1990-2005).

Dr. Pomerantz has published over 300 articles in the scientific literature and presented well over 200 invited lectures, nationally and internationally, concentrating on the clinical research, molecular pathogenesis and especially latency of human immunodeficiency virus (HIV) and other pathogenic human viruses. In 2010, Dr. Pomerantz was recruited to and joined Merck Research Laboratories (MRL), Merck & Co., Inc., as global head of the infectious diseases franchise and senior vice president, in charge of all anti-viral, anti-bacterial, anti-fungal and anti-parasitic agents, including global strategy. In summary, over his career, Dr. Pomerantz has led the development of 8 drugs, for HIV, HCV, and MDR-TB, which have been approved and launched worldwide

Reed E. Pyeritz, MD, PhD

Reed Edwin Pyeritz was born in Pittsburgh, PA, on November 2, 1947. As the first member of his extended family to attend college, he studied chemistry at the University of Delaware and was awarded a BS with distinction in 1968. He received the Alexander Taylor Award as the outstanding senior man. He then attended Harvard Medical School on an NSF Graduate Research Fellowship, where he received an MS and PhD (1972) from the Department of Biological Chemistry, with Charles Thomas as his dissertation advisor. His work focused on the organization of repeated sequences in eukaryotic DNA. He developed an interest in human genetics and pursued medical training specifically to become a medical geneticist. He received his MD from Harvard in 1975 and was one of the first two graduates of the Medical Scientist Training Program there. He completed two years of internal medicine training at the Peter Bent Brigham Hospital and a senior residency at the Johns Hopkins Hospital under Victor McKusick. He joined the faculty at the Johns Hopkins University School of Medicine in 1978 and rose to the position of professor of medicine and pediatrics.

During his 16 years in Baltimore, Pyeritz directed the Medical Genetics Clinic and developed a life-long interest in heritable disorders of connective tissue, especially Marfan syndrome and other disorders that affect the arterial system. The pleiotropy characteristic of many conditions proved a fertile reason to collaborate, and together with colleagues from 17 different academic departments at Hopkins, he published results from clinical studies of numerous conditions. In the early 1990s, a combination of biochemical, immunohistological, linkage, and sequencing studies, conducted with David Hollister, Lynn Sakai, Clair Francomano, and Hal Dietz, a pediat-

ric cardiology fellow, culminated in the identification of the microfibrillar protein fibrillin-1 as central to the etiology of Marfan syndrome and of mutations in *FBNI* as causative.

Another interest during these years was the economics of clinical genetics services. In collaboration with Barbara Bernhardt and his wife, Jane Tumpson, he documented the labor-intensive nature of the provision of comprehensive services and showed that clinical income from cognitive activities alone could not support the multidisciplinary teams required to provide the services. Additionally, he developed an interest in biomedical ethics, which led to two activities. First, he founded the medical ethics consultation service at the Johns Hopkins Hospital and chaired its ethics committee; this allowed him to study the many ways that ethical issues impact the emergence and application of genetic technologies. Second, when recruited from Hopkins in 1993, he became the clinical director of the Center for Medical Genetics. For personal and professional reasons, Pyeritz accepted the position of director of the Institute of Human Genetics at what later became the Allegheny University of the Health Sciences, based in both Pittsburgh and Philadelphia. He developed a clinical program there that provided consultative and laboratory services for genetic issues that spanned preconception to maturity.

In 2000 he was recruited to become chief of the Division of Medical Genetics at the University of Pennsylvania School of Medicine. There he continued to focus his research on Marfan syndrome and expanded the clinical and research scope to all familial arteriopathies. Pyeritz founded the Hereditary Hemorrhagic Telangiectasia Center at Penn, which was designated a “Center of Excellence” by the HHT Foundation International and continues to be one of the busiest programs in the nation. In 2007 Pyeritz and Barbara Bernhardt were awarded a P50 grant from the National Human Genome Research Institute to establish a Center for Excellence in Ethical, Legal and Social Implications Research. The focus of the center was to address genetic uncertainty — specifically, to address the problem that, although analysis of the human genome has become increasingly precise, use of the information has often led to more questions than answers. He and his colleagues across six schools at Penn have written extensively on the introduction of cytogenomic arrays, cell-free DNA analysis of fetal DNA in maternal serum, and whole exome and whole genome sequencing. Topics have included intellectual property, informed consent, economic comparisons of molecular versus clinical screening, the duty to recontact, patient concerns about unfair discrimination, direct-to-consumer genetic

testing, and health professional readiness to offer genetic and genomic testing. A sabbatical at the Brocher Foundation in Hermance, Switzerland, was central to Pyeritz's progress in many of these topics. He is a co-editor of the standard reference text in his field, *Emery and Rimoin's Principles and Practice of Medical Genetics*. He has authored over 500 contributions to the medical and scientific literature. Pyeritz served in the Medical Corps of the US Army Reserve and was on active duty as a lieutenant colonel during Operation Desert Storm.

Pyeritz has worked extensively with disease-focused volunteer support groups. He founded the National Marfan Foundation in the early 1980s and continues to serve on its professional advisory board. He serves in a similar capacity with the Canadian Marfan Association and the John Ritter Foundation and directs the Montalcino Aortic Consortium. He has served on the editorial boards of the *New England Journal of Medicine*, *Circulation*, the *Journal of the American College of Cardiology*, and *JAMA* and is a corresponding editor for *Human Mutation*. He has served on numerous study sections for the NIH, the FDA, and the March of Dimes. He now serves on the Secretary's Advisory Committee for Human Research Protections of the US Department of Health and Human Services. Pyeritz was a founder of the American College of Medical Genetics and served as its second president. Currently he is the secretary-treasurer of the ACMG Foundation. He has served as the president of the Association of Professors of Human and Medical Genetics and on the board of directors of the American Society of Human Genetics. He has been elected to the American Society for Clinical Investigation and the Association of American Physicians and is a fellow of the American College of Physicians, the American Association for the Advancement of Science, and the College of Physicians of Philadelphia.

Angara Koneti Rao, MD

Angara Koneti Rao was born in Madras (Chennai) in India on December 22, 1950. He obtained a premedical degree from Hindu College of Delhi University in 1968 and the MBBS degree from the All India Institute of Medical Sciences in New Delhi in 1973. In 1974 Rao came to Philadelphia, where he was an intern in internal medicine at Albert Einstein Medical Center (1974–1975) and a medical resident at Thomas Jefferson University (1975–1977). He was a fellow in hematology-oncology at Temple University School of Medicine (1977–1978) and at the Cardeza Foundation for Hematologic Research of Jefferson University (1978–1979), where he worked

with Scott Murphy on platelet adenine nucleotides metabolism. In 1979 he joined the faculty at Temple as an instructor in medicine (hematology-oncology) and the Thrombosis Research Center to initiate his independent laboratory. In 1980 Rao became an assistant professor of medicine and director of the special clinical studies laboratory of the Thrombosis Research Center. In 1984 he was promoted to associate professor with tenure, and he became professor of medicine in 1991. He was also appointed to the rank of professor of pathology (1992), professor of pharmacology (2002), and professor of thrombosis research (2003), all at Temple. In 2010 he became the Sol Sherry Professor of Medicine.

Rao served as the associate dean for the Temple MD-PhD program from 2001 to 2005. In 2005 he became the director of the Sol Sherry Thrombosis Research Center and chief of the hematology section.

Rao's major research interest since 1979 has been in the area of platelets and the molecular mechanisms of inherited disorders of platelet function. Patients with these disorders are widely encountered, and in the vast majority the underlying mechanisms are unknown. His interest in platelets started initially through his interaction with Stefan Niewiarowski and grew during his work with Holm Holmsen, who was a mentor and collaborator from 1979 to 1985 on studies of platelet defects. The thrombosis center provided an outstanding environment to collaborate with investigators such as Sol Sherry, Robert Colman, Peter Walsh, and J Bryan Smith. Rao's studies provided the first descriptions of human deficiencies in key platelet signaling proteins, including phospholipase C- β 2, GTP binding protein G α q, and protein kinase C- θ . He was among the first to apply platelet expression profiling to studies of human platelet dysfunction. These studies established that transcription factor RUNX1 regulates platelet/megakaryocyte proteins, myosin light chain, platelet factor 4, 12-lipoxygenase, and protein kinase C- θ . His research has been supported since the 1980s by grants from the NIH and other foundations.

Rao has had a wide range of research interests, including in antithrombotic therapy, sickle cell disease, and cardiopulmonary bypass. He spearheaded an early collaborative study with Robert Colman on experimental human Rocky Mountain spotted fever; these studies documented the activation of platelets and coagulation in very early disease. The results of this study, published in the *New England Journal of Medicine*, strengthened his interest in clinical research.

He served on the executive and steering committees of the multicenter NIH-funded Thrombolysis in Myocardial Infarction (TIMI) Trial–Phase I in the 1980s and was one of the first investigators to demonstrate systemic fibrinogenolysis with administration of tissue plasminogen activator. Rao's recent studies have focused on the alterations in tissue factor and coagulation mechanisms in hyperinsulinemia, hyperglycemia, and diabetes mellitus.

Rao was elected to the Interurban Clinical Club in 1997 and served as its president in 2004. He is a member of the American Society for Clinical Investigation and a fellow of the American College of Physicians, the Society of Vascular Biology and Medicine, the Molecular Medicine Society, and the American Heart Association council on thrombosis. He has served on several committees at Temple and for other organizations, including the NIH, the American Society of Hematology, and the International Society of Thrombosis and Haemostasis (ISTH). Rao has chaired the ISTH platelet committee and served as an elected member of the scientific and standardization committee of ISTH.

Rao has served as the principal editor for USA of the journal *Platelets* since 1989 and as guest editor for *Seminars in Thrombosis and Hemostasis* and *Hematology/Oncology Clinics*. He has been a member of the editorial boards of the *Journal of Cardiovascular Pharmacology and Therapeutics*, *Vascular Medicine, Clinical and Translational Science*, and *HemOnc Today* and is a contributing faculty member of the *F1000Prime*.

Rao has received several awards, including an NIH Academic Award in Vascular Diseases (1992), an Investigator Recognition Award from ISTH for his contributions to the field of hemostasis and thrombosis (1997), a Temple University Faculty Research Award (2001), a Distinguished Career Award from the South Asian Society for Atherosclerosis and Thrombosis (2006), and a Mario Toppo Distinguished Scientist Award from the Association of Scientists of Indian Origin in America (2009). Rao has been recognized as an accomplished clinician and listed as one of the Best Doctors in America and as a Philadelphia Top Doctor by *Philadelphia* magazine.

Sanford Jack Shattil, MD

Sanford Shattil was born in 1943 in Chicago, IL. He was awarded the AB degree by the University of Illinois in 1965 and the MD degree by the University of Illinois College of Medicine three years later. From 1968 to 1970

he was intern and assistant resident in medicine on the Second and Fourth (Harvard) Medical Services at Boston City Hospital. In 1970–1971 he was a research fellow at the Thorndike Memorial Laboratory and, for the following two years, he completed his military service at the US Public Health Service (USPHS) Hospital in San Francisco. During that time he was a clinical instructor in medicine at the University of California, San Francisco, promoted in 1973 to assistant clinical professor. From 1971 to 1973 he served as chief of the hematology service in the Department of Medicine at the USPHS Hospital. In 1973 he joined the faculty of the University of Pennsylvania School of Medicine as an associate in medicine. He rose through the ranks, serving as assistant professor (1974–1979); associate professor of medicine, pathology, and laboratory medicine (1979–1982); and professor of medicine, pathology, and laboratory medicine (1985–1995). From 1995 to 2004 he worked as professor of vascular biology and cell biology at Scripps Research Institute in La Jolla, CA. In 2004 he joined the faculty of the University of California, San Diego, as professor of medicine, and in 2011 he was promoted to distinguished professor of medicine. From 1973 to 1981 Shattil was chief of the hematology-oncology service for the University of Pennsylvania Medical Service at the Philadelphia VA Hospital, and from 1977 to 1979 he was assistant chief of medicine there. At the Hospital of the University of Pennsylvania, Shattil served as director of the Coagulation and Thrombosis Laboratory in the Department of Pathology and Laboratory Medicine (1981–1986) and as chief of the Hematology-Oncology Division in the Department of Medicine (1985–1992). From 2004 to 2014, he served as chief of the Hematology-Oncology Division in the Department of Medicine at UCSD. Since 2008 he has served as director of the Hematology-Oncology Fellowship Training Program at UCSD.

Shattil became interested in biomedical research while working, during his college years, in the laboratory of Sheldon Berger at the Evanston Hospital and Northwestern University. His formal training occurred during an NIH-funded hematology fellowship at the Thorndike Laboratory. His prime mentor was Richard Cooper, but the stellar team of hematologists, including Jandl, DesForges, Bunn, Aster, Abramson, and Castle also had an important influence. While at the Thorndike Laboratory, Shattil characterized changes in red cell membrane lipids during maturation of the reticulocyte. This introduction to membrane research focused his long-term interest onto the area of blood cell membrane structure and function. His emphasis shifted in 1973 to the platelet and, later, to the role of integrin adhesion receptors in hemostasis, thrombosis, vascular biology, develop-

ment, and neoplasia.

His most significant contributions relate to several thematic areas: activation-induced changes in platelet surface membrane structures, with particular emphasis on the platelet fibrinogen receptor (integrin α IIb β 3); alterations of the platelet membrane in disease states; relationships between platelet adhesion and signaling; and the role of integrin signaling in wider aspects of human biology. Shattil and his colleagues developed a murine monoclonal antibody that is specific for the fibrinogen receptor on activated platelets but that fails to bind to resting cells. This antibody inhibits fibrinogen binding and, conversely, fibrinogen-inhibited antibody binding. Binding of the antibody to activated platelets is inhibited by a tetrapeptide (RGDS) that is present in a number of extracellular matrix proteins, including fibrinogen. This antibody contains an “RGD-like” RYD sequence in one of its hypervariable regions. Shattil took advantage of the novel properties of this antibody by developing a recombinant version of it to explore changes in β 3 integrins during activation of blood and vascular cells as well as the intracellular signaling pathways responsible for “inside-out” integrin signaling.

Shattil has adapted basic research techniques to the study of patients in an attempt to characterize mechanisms of platelet dysfunction in disease. For example, he demonstrated that high concentrations of penicillin inhibit platelet function *in vitro* by impairing the interaction of agonists and von Willebrand factor with their receptors on the platelet. He developed a technique to detect activated platelets in whole blood that takes advantage of the specificity of activation-dependent monoclonal antibodies with the sensitivity of flow cytometry. The advantage over previous methods is that platelets are examined directly and no washing steps are required. This permits the direct detection of circulating activated platelets in thrombotic disorders and facilitates the evaluation of anti-platelet drugs.

In addition to their roles in cell adhesion, integrin receptors can also function to transmit extracellular cues into the cell, much like “conventional” agonist receptors, growth factor receptors, and cytokine receptors. Thus, integrins are involved in bidirectional signaling across the plasma membrane. Shattil’s work has elucidated mechanisms and consequences of bidirectional integrin signaling in human platelets and in benign and malignant cells in several model systems, including zebrafish and mice.

Shattil has received both the Investigator Recognition Award (1989) and

the Distinguished Career Award (1999) from the International Society of Thrombosis and Hemostasis, as well as the Henry M. Stratton Medal from the American Society of Hematology for sustained contributions to the field (2010). In 2010 he was the Sol Sherry Distinguished Lecturer of the American Heart Association. He has been a member of numerous professional societies, including the American Society of Hematology (secretary, 1979–1983), the American Society for Cell Biology, the American Federation for Clinical Research, the American Society for Clinical Investigation, the Association of American Physicians, the American Heart Association, and the International Society of Thrombosis and Hemostasis. He has held editorial positions for numerous journals, including *Blood* (editor-in-chief), *Proceedings of the Society for Experimental Biology and Medicine*, the *Journal of Clinical Investigation*, and the *British Journal of Haematology*. His grant support has come primarily from the NIH. He has served on the NIH hematology study section and on numerous other advisory bodies, both private and public.

Scott Waldman, MD, PhD

Scott Waldman was born in Brooklyn, NY, on October 22, 1953. He received a BS in biology from the University at Albany, New York, in 1975, followed by a PhD in anatomy from Thomas Jefferson University in Philadelphia in 1979. He pursued postdoctoral training in clinical pharmacology in the laboratory of Ferid Murad (Nobel Laureate in Physiology or Medicine, 1998) at the University of Virginia, Charlottesville, from 1979 to 1981. He continued his postdoctoral training in clinical pharmacology in the Murad laboratory at Stanford University from 1981 to 1983. He enrolled in medical school at Stanford in 1983, where he completed specialty training in internal medicine and subspecialty training in clinical pharmacology in 1990. During his years in medical school (1983–1987), he held a position as a principal investigator at the Palo Alto VA Medical Center in a research laboratory fully funded by an NIH MERIT Award. This funding was competitively renewed contemporaneously with his house staff training in medicine, from 1987 to 1990. Upon completing clinical training at Stanford, Waldman assumed a position as assistant professor in the division of clinical pharmacology in the Department of Medicine at Thomas Jefferson University. He became director of the Jefferson Clinical Research Unit in 1991 and director of the division of clinical pharmacology in 1997 and was appointed the Samuel M. V. Hamilton Chair in Medicine in 1998. In 2005 Waldman led the initiative to expand the division into the first

Department of Pharmacology and Experimental Therapeutics at Jefferson and became its inaugural chair.

In his research Waldman has focused on a translational program of bench-to-bedside discovery and development in the field of GI oncology. He discovered the translational importance of compartmentalization of the membrane receptor GUCY2C normally in apical membranes of intestinal epithelial cells and its universal overexpression in primary and metastatic colorectal tumors. These studies resulted in the application of GUCY2C as a key prognostic and predictive molecular marker for managing patients with colorectal cancer. Furthermore, he led the field in identifying GUCY2C as a key tumor suppressor whose dysfunction universally contributes to the initiation and progression of colorectal tumorigenesis. These observations were the basis for the hypothesis that colorectal cancer initiates as a disease of paracrine hormone insufficiency that results in the silencing of GUCY2C signaling. The correlative therapeutic hypothesis suggests that oral hormone replacement therapy can prevent or treat colorectal cancer, a paradigm that is currently being tested in clinical trials. Moreover, Waldman has defined the utility of GUCY2C as a novel vaccine candidate for the secondary prevention of colorectal cancer recurrence; as a result of these observations, he recently received funding for human testing. Together, this body of work has produced over 200 publications, more than 20 awarded patents, and more than 30 pending patent applications in the field of targeted diagnosis, treatment, and prevention of GI malignancies.

Waldman has received many awards and honors, including the PhRMA Foundation Award in Excellence in Clinical Pharmacology and the Henry Elliott Award from the American Society for Clinical Pharmacology and Therapeutics. He is editor-in-chief of *Clinical Pharmacology and Therapeutics* (2006–2017) and served as inaugural senior editor for *Biomarkers in Medicine* (2007–2012) and deputy editor-in-chief of *Clinical and Translational Science* (2007–2012). He is a past president of the American Society for Clinical Pharmacology and Therapeutics, a past regent of the American College of Clinical Pharmacology, and a past officer of the American Board of Clinical Pharmacology. He has served on, and chaired, numerous national and international peer-review panels and scientific boards. He is an editor and author of the successful textbook *Pharmacology and Therapeutics: Principles to Practice*.

James B. Wyngaarden, MD

James B. Wyngaarden was born in East Grand Rapids, Michigan, on October 19, 1922. He became an internationally recognized authority on the regulation of purine biosynthesis and the genetics of gout, and a national advisor on various aspects of the administration of biomedical research, becoming the 12th NIH director on April 30, 1982, a position he held until July 1989. Immediately prior to his appointment, he was professor and chairman of the department of medicine at Duke University School of Medicine, a position he had held since 1967.

From 1953 to 1954, he was a research associate in the Laboratory of Chemical Pharmacology of the then National Heart Institute, and from 1954 to 1956, he was a clinical associate at the then National Institute of Arthritis and Metabolic Diseases. After leaving in 1956 to become associate professor at the Duke University School of Medicine, he continued an association with NIH. He has held grants from several NIH components. Dr. Wyngaarden has been active on various NIH study groups, evaluation committees, and review panels over the years, including a term with the board of scientific counselors of the then NIAMD (1971-1974). He also served as a consultant to the NIH as a member of study sections (1958-1960; 1967-1969).

He has also served as advisor to the broader scientific community as a member of the National Academy of Sciences since 1974, and was active from 1975 to 1982 on an NAS committee set up to study the Nation's overall need for biomedical and behavioral researchers; consultant for the President's Office of Science and Technology (1966-1972), a member of the President's Science Advisory Committee (1972-1973), and a member of the U.S. Atomic Energy Commission's Advisory Committee on Biology and Medicine.

Wyngaarden is the coauthor of *Cecil Textbook of Medicine*. In collaboration with former NIH director, Dr. Fredrickson, and others, he edited *The Metabolic Basis of Inherited Disease*. The original work was published in 1960. He attended Calvin College and Western Michigan University in 1943-1944. In 1948 he graduated first in his class from the University of Michigan Medical School.

Wyngaarden trained in internal medicine at the Massachusetts General Hospital and did postdoctoral work at the Public Health Research Institute of the City of New York, under the direction of Dr. DeWitt Stetten, Jr.,

former NIGMS director. After serving as research associate at NIH from 1953 to 1956, he went to Duke and in 1959 became director of the medical research training program there as well as associate professor of medicine and biochemistry. In 1961 he became professor of medicine and associate professor of biochemistry.

In 1963 and 1964, he was a visiting scientist at the Institute de Biologie-Physiocochemie in Paris. Shortly after his return to this country, he left Duke to become professor and chairman of the department of medicine and professor of biochemistry at the University of Pennsylvania. He returned to Duke in 1967.

Dr. Wyngaarden has received many honorary degrees: University of Michigan (D.Sc., 1980), Medical College of Ohio (D.Sc., 1984), University of Illinois at Chicago (D.Sc., 1985), George Washington University (D.Sc., 1986), and Tel Aviv University (Ph.D., 1987). He is a diplomate of the American Board of Internal Medicine. He has served on editorial boards of numerous professional publications.

Wyngaarden is a member of a number of professional societies including the NAS Institute of Medicine, the American Academy of Arts and Sciences, the American Society for Clinical Investigation, and is a past president of the Association of American Physicians. He is a fellow of the Royal College of Physicians of London and was elected to the Royal Academy of Sciences of Sweden in 1987.

Philadelphia emeritus members without submitted biographies:

Jean Bennett

Robert Coleman

Nancy Cooke

Allen Schreiber

Steven Shapiro

Judith Swain

James Hoxie

William Kelley

Peter Walsh

INDEX

- Abraham, 94
Abrams, 140, 449
Agre, 154
Aiello, 93
Al-Awqati, 365
Alper, 205
Andrews, 64, 208
Arany, 450
Armstrong, 94
Artman, 366
Askenase, 294
Ausiello, 271
Austen, 63, 210
Avruch, 271
Balke, 140, 472
Barker, 5, 57
Barouch, 94
Barry, 57, 297
Bartlett, 156
Basson, 63, 65, 87, 140, 368
Beatty, 95
Bender, 63, 140, 298
Bennett, 522
Benz Jr, 63, 212
Berliner, 64, 299
Bertino, 301
Birnbaum, 474
Bjornsson, 95
Blaser, 370
Blumberg, 63, 65, 215
Bochner, 157
Bockenstedt, 64, 92, 273
Boden, 476
Bogan, 275
Bondy, 67
Boyer, 303
Braunwald, 218
Brenner, 220
Brentjens, 95, 343
Broadus, 63, 305
Brodeur, 477
Bucala, 307
Bunn, 63, 222
Cabot, 5, 11
Cahill, 271
Calderwood, 225
Camac, 5, 28
Cannon, 448
Cantley, 63, 309
Cappola, A.R., 64, 452
Cappola, T.P., 454
Carey, 227
Casadevall, 345
Castle, 76
Chen, 347
Chess, 63, 372
Chin, L., 64, 373
Chin, W.W., ix, 87, 91, 229
Chodosh, 456
Christian, vii, 375
Christy, 448
Clark, 134
Cohen, A., 271
Cohen, D.E., 190, 191
Cohen, L.S., 310
Cole, 5, 52
Coleman, 63, 522
Conner, 5, 29
Cooke, 522
Cotsarelis, 458
Cox, A., 94
Cox, R.P., 377
Craft, 341
Cristofanilli, 459
Cronstein, 378
Crow, 380

Crowley, 232
Dannenberg, 364
Davies, 383
Deming, 448
Desir, i, 136
Dexter, 77
Deykin, 233
Diamond, 385
Dicker, 472
Donowitz, 63, 160
Douglas, 480
Dranoff, 193
Drazen, 63, 234
Duffy, ix, 63, 67, 133, 312
Dzau, 236
Edelson, 341
Edsall, viii, 5, 35
Eisenberg, 482
El-Deiry, ix, 63, 65, 85, 135, 140, 461
Elias, 63, 341
Emerson, C.P., 5, 54
Emerson, S.G., 63, 85, 140, 485
Engle, 194
Epstein, i, ix, 63, 92, 133, 135, 464
Fasano, 271
Fearon, 190
Feinberg, 162
Felig, 313
Fikrig, 277
Finch, 341
Finland, 76
Fisher, 63, 386
Flier, 239
Forget, 63, 316
Forrest Jr, x, 63, 65, 88, 135, 318
Frenette, 349
Fried, 388
Friedman, 486
Futcher, vii, 5, 6, 50
Germino, 92
Gershengorn, 390
Gill, 280
Glickman, 392
Glimcher, 64, 241
Goldman, 394
Goldstein, B.J., 140, 489
Goldstein, D.R., 95, 282
Gorelick, 321
Greene, 491
Griffin, 63, 163
Haase, 93
Hajjar, 395
Halene, 95
Ham, 76
Hampson, v, 65
Harvey, vii, 11
Hazzard, 165
Hempstead, 64, 397
Hendrix, 63
Henske, 64, 140, 195
Herman, 134
Herold, 278
Hiatt, 242
High, 64, 493
Hirsch, 448
Hirschhorn, 63, 399
Hock, 93
Holmes, 496
Horwitz, 341
Hostetter, 323
Hoxie, 522
Insogna, 341
Isselbacher, 63, 244
Jacob, 134
James, 5, 27
Janeway, C., 76
Janeway, T.C., 5, 32
Johns, 67
Johnston Jr., 498
Joiner, 325
Jonas, 64, 140, 284
Joslin, 5, 16
Kahn, 271
Kantor, 327
Kappas, 448
Karsenty, 401
Kasper, 271
Kazmierczak, i, 64, 133, 286

Keefer, 76
 Kelley, 63, 522
 Kelly, 5, 42
 Kelsen, 501
 Kessler, 404
 Kieff, 246
 King, 140, 154
 Kitsis, 63, 140, 448
 Koretzky, 406
 Kronenberg, 271
 Lambert, vii, 5, 25
 Landry, i, 136, 408
 Landsberg, 248
 Lazarus, 63, 169
 Lee, 93
 Levine, M.A., 503
 Levine, R.L., 140, 193, 351
 Levitsky, 140, 154
 Levy, 140, 197
 Lichtenstein, 190
 Lieberman, 64, 250
 Liggett, 170
 Lisanti, 472
 Locke, viii, 5, 18
 Loeb, 409
 London, 448
 Longcope, 5, 45
 Lord, 5, 20
 Loscalzo, i, ix, 75, 136, 252
 Lowell, 92
 Lowenstein, 93, 171
 Luster, 199
 MacDonald, 64, 172
 MacRae, 201
 Maddrey, 506
 Malawista, 63
 Mammen, 95
 Mani, A., 94
 Marbán, 175
 Marcus, 63, 65, 410
 Marks, A.R., 415
 Marks, P.A., 63, 413
 Martin, 255
 Marx, 93
 McDonald, 140
 McCrae, 5, 6, 56
 McKhann, 63, 176
 Meara, 5, 31
 Mendelsohn, 92
 Miller, 179
 Minot, 76
 Mulrow, 341
 Murphy, 64, 352
 Nagel, 448
 Nathan, 417
 Nathanson, 329
 Neel, 418
 Neilson, 508
 New, 421
 Noble, 140, 330
 Orange, 95
 Orlowski, 134
 Osler, v, vii, 3, 6, 7, 59, 67, 75, 81, 84,
 91, 97, 133
 Parks, 448
 Parmacek, i, 466
 Pestell, 140, 510
 Philips, 423
 Pollak, 202
 Pomerantz, 511
 Pomper, 143
 Potts, 63, 256
 Powe, 180
 Powell, 145
 Pratt, 5, 22
 Pyeritz, 512
 Rafii, 92
 Rao, 63, 85, 140, 514
 Ray, 147
 Reichlin, 271
 Reynolds, 331
 Riesman, vii, 5, 43
 Rosen, 63, 65, 92, 141, 149
 Rosenberg, 341
 Rosenblatt, 257
 Ross, Richard, 63, 190
 Ross, Robert, 190
 Rossetti, 92

Roth, 190
 Rubin, 271
 Russell, 93
 Rustgi, 92
 Sailer, 5, 44
 Samuels, 425
 Sawyers, 427
 Scadden, 141, 260
 Scheinberg, 428
 Scheuer, 429
 Schreiber, 522
 Sears, ix, 63-5, 83,140, 182
 Selleri, 94
 Shafritz, 63, 431
 Shannon, i, 63, 136, 140, 469
 Shapiro, S., 522
 Shapiro, T.A., 64, 184
 Sharpe, 205
 Shattil, 516
 Shipp, 205
 Shulman, 333
 Simons, 141, 288
 Skolnik, 141, 448
 Steere, Jr, 262
 Stegmaier, 95
 Stengel, 5, 34
 Stewart, 341
 Stobo, 190
 Stossel, 63, 264
 Straud, vii
 Strauss, 76
 Strom, 265
 Suchy, 337
 Surks, 433
 Swain, 522
 Sykes, 63-5, 87, 141, 435
 Sylvaster, 190
 Tacket, 64, 186
 Tardiff, 364
 Thayer, 5, 48
 Their, 338
 Thio, 64, 151
 Tileston, 5, 24
 Tomaselli, 190
 Tomer, 354
 Turka, 470
 Velculescu, 93, 152
 Waldman, 63, 519
 Walser, 190
 Walsh, 522
 Wang, 355
 Weinsaft, 94
 Weisfeldt, i, 63, 136, 188
 Weiss, H.J., 437
 Weiss, 76
 Weissleder, 267
 Weissmann, 67, 439
 Weksler, B.B., 63, 442
 Weksler, M.E., 444
 Wells, 94
 Werner, 64
 Wesemann, 95
 Wilkins, 76
 William, 448
 Wolchok, 357
 Wolkoff, 446
 Wyngaarden, 521
 Wysolmerski, 63, 65, 93, 140-1, 290
 Young, 292
 Zaidi, M., ix, 135, 140-1, 359
 Zaidi, S., 134
 Zakim, 448
 Zaret, 340
 Zeidel, i, 63, 135-6, 140-1, 269
 Zhou, 205
 Zon, 204

