Biomedicine in the New Century
The Yale School of Medicine Bicentennial Symposium

April 28–29, 2011
Mary S. Harkness Auditorium
Yale School of Medicine, New Haven, CT
THURSDAY, APRIL 28

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FRIDAY, APRIL 29

8:25 AM  Carolyn W. Slayman, PhD
Introductory Remarks

8:30 AM  Joseph L. Goldstein, MD
Surviving Starvation: Essential Role of the Ghrelin–Growth Hormone Axis (Part I)
Introduced by Robert J. Alpern, MD

9:20 AM  Michael S. Brown, MD
Surviving Starvation: Essential Role of the Ghrelin–Growth Hormone Axis (Part II)
Introduced by Robert J. Alpern, MD

10:30 AM  Robert J. Lefkowitz, MD
Seven–Transmembrane Receptors
Introduced by Michael Simons, MD

11:20 AM  Susan L. Lindquist, PhD
Tackling Protein Misfolding Diseases
Introduced by Stephen M. Strittmatter, MD, PhD

2:00 PM  Charles L. Sawyers, MD
Overcoming Drug Resistance to Cancer Therapies
Introduced by Thomas J. Lynch, Jr., MD

2:50 PM  Peter S. Kim, PhD
Toward Development of an HIV Vaccine
Introduced by Richard P. Lifton, MD, PhD

3:40 PM  Robert M. Califf, MD
Translational Medicine: Moving from Better Ideas to Better Health
Introduced by Harlan M. Krumholz, MD, SM

4:30 PM  Dean Robert J. Alpern, MD
Closing Remarks
Celebrating 200 Years of History at Yale School of Medicine

Transformation has been a hallmark of Yale School of Medicine since its founding following passage of an Act of Incorporation by the Connecticut Legislature in October 1810. During this watershed academic year of 2010–2011, the School of Medicine is honoring its past, present, and future in myriad ways, and I welcome you to our Bicentennial Symposium, the premier event in our yearlong celebration.

As Yale School of Medicine prepared to celebrate its centennial 100 years ago, the school faced an uncertain future, as was the case with many American medical schools at the time. But Abraham Flexner’s landmark 1910 report on medical education marked a turning point—Flexner deemed the School of Medicine one of only two in New England worthy of continued investment, and Yale energetically advanced on all fronts in the years afterward. In the past, the school has been home to luminaries such as John P. Peters, MD, Dorothy M. Horstmann, MD, Louis S. Goodman, MD, Alfred Gilman, PhD, C.-E.A. Winslow, Dr. PH, Aaron Lerner, MD, PhD, Paul B. Beeson, MD, and George Palade, MD, among many others, and today our faculty is equally distinguished.

It is with great pleasure that I welcome some of the world’s leading thinkers and practitioners in medicine and biomedical science to this forum. We are deeply honored to benefit from their wisdom. I hope that the knowledge you take away from this event enables you to advance your own understanding of, and appreciation for, the interesting times in which we live, learn, and practice our art.

Robert J. Alpern, MD
Eric R. Kandel, MD

On the Persistence of Memory Storage

Eric R. Kandel, MD, is University Professor at Columbia, Fred Kavli Professor and Director, Kavli Institute for Brain Science and a Senior Investigator with the Howard Hughes Medical Institute. A graduate of Harvard College and N.Y.U. School of Medicine, Kandel trained in Neurobiology at the NIH and in Psychiatry at Harvard Medical School. He joined the faculty of the College of Physicians and Surgeons at Columbia University in 1974 as the founding director of the Center for Neurobiology and Behavior. At Columbia Kandel organized the neuroscience curriculum. He is an editor of Principles of Neural Science, the standard textbook in the field. He recently has written a book on the brain for the general public titled In Search of Memory: The Emergence of a New Science of Mind, which won both the L.A. Times and U.S. National Academy of Science Awards for best book in Science and Technology in 2008. A documentary film based on that book also titled In Search of Memory is now showing in the United States.

Eric Kandel's research has been concerned with the molecular mechanisms of memory storage in Aplysia and mice. More recently, he has studied animal models in mice of memory disorders and mental illness. Kandel has received eighteen honorary degrees, is a member of the U.S. National Academy of Sciences as well as the National Science Academies of Austria, Germany and France. He has been recognized with the Albert Lasker Award, the Heineken Award of the Netherlands, the Gairdner Award of Canada, the Harvey Prize and the Wolf Prize of Israel, the National Medal of Science USA and the Nobel Prize for Physiology or Medicine in 2000, which he shared with Paul Greengard and Arvid Carlsson.
Huda Y. Zoghbi, MD

Rett Syndrome: From Genomes to Epigenomes and Neuropsychiatric Conditions

Huda Zoghbi, MD, is Professor of Pediatrics, Neurology, Neuroscience, and Molecular and Human Genetics at Baylor College of Medicine and serves as an Investigator with the Howard Hughes Medical Institute. She is also the Director of the Jan and Dan Duncan Neurological Research Institute at Texas Children’s Hospital.

Zoghbi’s interest is in using the tools of modern genetics to understand the proper development of the brain as well as what goes awry in specific neurodevelopmental and neurodegenerative conditions. She has published seminal work regarding the molecular basis of Rett syndrome and of late-onset neurodegenerative diseases. Dr. Zoghbi is a member of several professional organizations including the NIH Scientific Management Review Board, the McKnight Foundation Neuroscience Board, and the Lasker Jury. Among Dr. Zoghbi’s honors are the E. Mead Johnson Award from Society of Pediatric Research, the IPSEN prize in neuronal plasticity, the Bristol Myers-Squibb Neuroscience Distinguished Achievement Award, and the Vilcek Prize. In 2000 she was elected to the Institute of Medicine, and in 2004 she was elected to the National Academy of Sciences.
Elizabeth H. Blackburn, PhD

Maintaining Chromosome Ends: From Basic Science to Human Health and Disease

Elizabeth H. Blackburn, PhD, Morris Herzstein Professor of Biology and Physiology in the Department of Biochemistry and Biophysics at the University of California, San Francisco, is a leader in the area of telomere and telomerase research. She discovered the molecular nature of telomeres—the ends of eukaryotic chromosomes that serve as protective caps essential for preserving the genetic information—and the ribonucleoprotein enzyme, telomerase. Blackburn and her research team at the University of California, San Francisco, are working with various cells including human cells, with the goal of understanding telomerase and telomere biology.

Blackburn earned her BSc (1970) and MSc (1972) degrees from the University of Melbourne in Australia, and her PhD (1975) from the University of Cambridge in England. She did her postdoctoral work in Molecular and Cellular Biology from 1975 to 1977 at Yale.

In 1978, Blackburn joined the faculty at the University of California at Berkeley in the Department of Molecular Biology. In 1990, she joined the Department of Microbiology and Immunology at UC San Francisco, where she served as Department Chair from 1993 to 1999. Blackburn is currently a faculty member in the Department of Biochemistry and Biophysics at UCSF. She is also a Non-Resident Fellow of the Salk Institute.

Throughout her career, Blackburn has been honored by her peers as the recipient of many prestigious awards. She was elected President of the American Society for Cell Biology for the year 1998. Blackburn is an elected Fellow of the American Academy of Arts and Sciences (1991), the Royal Society of London (1992), the American Academy of Microbiology (1993), and the American Association for the Advancement of Science (2000).

She was elected Foreign Associate of the National Academy of Sciences in 1993, and was elected as a Member of the Institute of Medicine in 2000. She was awarded the Albert Lasker Medical Research Award in Basic Medical Research (2006). In 2007 she was named one of TIME Magazine’s 100 Most influential People and she is the 2008 North American Laureate for L’Oreal-UNESCO For Women in Science.

In 2009, Dr. Blackburn was awarded the Nobel Prize in Physiology or Medicine.
Sir Michael Marmot, PhD
Fair Society, Healthy Lives

Sir Michael Marmot, PhD, has led a research group on health inequalities for the past 30 years. He is Principal Investigator of the Whitehall Studies of British civil servants, investigating explanations for the striking inverse social gradient in morbidity and mortality. He leads the English Longitudinal Study of Ageing (ELSA) and is engaged in several international research efforts on the social determinants of health. He chairs the Department of Health Scientific Reference Group on tackling health inequalities. He was a member of the Royal Commission on Environmental Pollution for six years. He is a Fellow of the Academy of Medical Sciences and an Honorary Fellow of the British Academy. In 2000 he was knighted by Her Majesty The Queen for services to Epidemiology and understanding health inequalities. Internationally acclaimed, Professor Marmot was a Vice President of the Academia Europaea, and is a Foreign Associate Member of the Institute of Medicine (IOM). He was Chair of the Commission on Social Determinants of Health set up by the World Health Organization in 2005: ‘Closing the Gap in a Generation.’ Professor Marmot won the Balzan Prize for Epidemiology in 2004, gave the Harveian Oration in 2006 and won the William B. Graham Prize for Health Services Research in 2008. At the request of the British Government, he conducted a review of health inequalities, which published its report ‘Fair Society, Healthy Lives’ in February 2010. He has now been invited by the Regional Director of WHO Euro to conduct a European review of health inequalities. Sir Michael will be president of the British Medical Association (BMA) 2010-2011.
Phillip A. Sharp, PhD

Roles of RNA in Gene Regulation

Phillip A. Sharp, PhD, is Institute Professor (highest academic rank) at the Massachusetts Institute of Technology and member of the David H. Koch Institute for Integrative Cancer Research. He joined the Center for Cancer Research at the Massachusetts Institute of Technology in 1974 and served as its director for six years, from 1985 to 1991, before taking over as head of the Department of Biology, a position he held for the next eight years. More recently, he was founding director of the McGovern Institute at MIT, a position he held from 2000 to 2004. His research interests have centered on the molecular biology of gene expression relevant to cancer and the mechanisms of RNA splicing. His landmark work in 1977 provided one of the first indications of “discontinuous genes” in mammalian cells. The discovery fundamentally changed scientists’ understanding of gene structure and earned Dr. Sharp the 1993 Nobel Prize in Physiology or Medicine. His lab has now turned its attention to understanding how RNA molecules act as switches to turn genes on and off (RNA interference), a process that could potentially generate a new class of therapeutics. Dr. Sharp has authored over 380 scientific papers. His work has earned him numerous cancer research awards and presidential and national scientific board appointments. He is elected member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences, and the American Philosophical Society. He is also the recipient of the Gairdner Foundation International Award, the Lasker Basic Medical Research Award, the National Medal of Science and the Inaugural Double Helix Medal for Scientific Research from Cold Spring Harbor Laboratory. A native of Kentucky, Dr. Sharp earned a BA degree from Union College, and a PhD in chemistry from the University of Illinois, Champaign-Urbana. He is co-founder of Biogen (now Biogen Idec) and Alnylam Pharmaceuticals Inc.
Harold E. Varmus, MD

Provocative Questions about Cancer

Harold E. Varmus, MD, co-recipient of a Nobel Prize for studies of the genetic basis of cancer, was nominated by President Obama as Director of the National Cancer Institute on May 17, 2010. He began his tenure as NCI Director on July 12, 2010. He previously served as President and Chief Executive Officer of Memorial Sloan-Kettering Cancer Center (MSKCC) and as Director of the National Institutes of Health (NIH).

Much of Varmus’ scientific work was conducted during 23 years as a faculty member at the University of California, San Francisco, Medical School, where he and Dr. J. Michael Bishop and their co-workers demonstrated the cellular origins of the oncogene of a chicken retrovirus. This discovery led to the isolation of many cellular genes that normally control growth and development and are frequently mutated in human cancer. For this work, Bishop and Varmus received many awards, including the 1989 Nobel Prize for Physiology or Medicine. Varmus is also widely recognized for his studies of the replication cycles of retroviruses and hepatitis B viruses, the functions of genes implicated in cancer, and the development of mouse models of human cancer (the focus of much of the work in his laboratory at MSKCC).

In 1993, Varmus was named by President Clinton to serve as the Director of NIH, a position he held until the end of 1999. During his tenure at NIH, he initiated many changes in the conduct of intramural and extramural research programs; recruited new leaders for most of the important positions at NIH; planned three major buildings on the NIH campus, including the Mark O. Hatfield Clinical Research Center; and helped to initiate the five-year doubling of the NIH budget.

At MSKCC, Varmus emphasized opportunities to harness advances in the biological sciences to improve the care of patients with cancer. Under his leadership, the scientific programs were reorganized and enlarged; a new research building, the Mortimer B. Zuckerman Research Center, was constructed; and new graduate training programs were established in chemical biology and computational biology (as part of a new Tri-Institutional Research Program with Rockefeller University and Weill-Cornell Medical College) and in cancer biology (through MSKCC’s first degree-awarding program in the Louis V. Gerstner, Jr. Graduate School of Biomedical Sciences).
In addition, he oversaw the construction of new clinical facilities (for pediatrics, pathology, urology, and surgery) and new centers for breast cancer treatment and imaging (the Evelyn H. Lauder Breast Center and the MSKCC Imaging Center); the founding of a hospital-based program in translational research (the Human Oncology and Pathogenesis Program); and the development of the Tri-Institutional Stem Cell Initiative and the Starr Cancer Consortium, involving five research institutions. To ensure that MSKCC was promoting high-quality cancer care for all citizens of New York and equal opportunities for its employees, he helped to found and oversee a new cancer clinic in central Harlem (the Ralph Lauren Center for Cancer Care and Prevention) and new programs for diversity and gender equity (the Office of Diversity Programs in Clinical Care, Research, and Training and the Women Faculty Affairs Program).

Varmus has authored over 300 scientific papers and five books, including an introduction to the genetic basis of cancer for a general audience and a memoir, *The Art and Politics of Science*, published in 2009. He has been an advisor to the Federal government, pharmaceutical and biotechnology firms, and many academic institutions, and was appointed by President Barack Obama as co-chair of the President’s Council of Advisors on Science and Technology (PCAST). He served on the World Health Organization’s Commission on Macroeconomics and Health from 2000 to 2002; is a co-founder and Chairman of the Board of Directors of the Public Library of Science, a publisher of open-access journals in the biomedical sciences; chaired the Scientific Board of the Grand Challenges in Global Health at the Bill and Melinda Gates Foundation from 2003 to 2008 and now chairs the Foundation’s Global Health Advisory Committee; and is involved in several initiatives to promote science in developing countries, including the Global Science Corps, through the Science Initiatives Group. He was also a member of the Funding Committee of the Empire State Stem Cell Board and serves as co-chair of the Institute of Medicine’s committee on “The U.S. Commitment to Global Health.” He has been a member of the U.S. National Academy of Sciences since 1984 and of the Institute of Medicine since 1991, and has received the National Medal of Science, the Vannevar Bush Award, and several honorary degrees and other prizes, in addition to the Nobel Prize.
A native of Freeport, Long Island, Varmus is the son of Dr. Frank Varmus, a general practitioner, and Beatrice Varmus, a psychiatric social worker. After graduating from Freeport High School, he majored in English literature at Amherst College and earned a master’s degree in English at Harvard University. He is a graduate of Columbia University’s College of Physicians and Surgeons, worked as a medical student in a hospital in India, and served on the medical house staff at Columbia-Presbyterian Medical Center. He began his scientific training as a Public Health Service officer at NIH, where he studied bacterial gene expression with Dr. Ira Pastan, and then trained as a post-doctoral fellow with Dr. Bishop at the University of California, San Francisco.

He is married to Constance Casey, a journalist and gardener, and has two sons, Jacob and Christopher.
Elaine Fuchs, PhD

Skin Stem Cells: Their Biology & Clinical Promise

Elaine Fuchs, PhD, is the Rebecca C. Lancefield Professor in Mammalian Cell Biology and Development at The Rockefeller University. She is also an Investigator, Howard Hughes Medical Institute. Fuchs has published more than 250 papers and is internationally known for her research in skin biology and associated human genetic disorders, which include skin cancers and life-threatening genetic syndromes such as blistering skin disorders. Fuchs’ current research focuses on the molecular mechanisms that underlie how multipotent stem cells respond to external cues, change their program of gene expression, exit their niche and adopt specific lineage fates to make the epidermis, sebaceous glands, and hair follicles of the skin during normal homeostasis and wound-repair. Ultimately through understanding the normal biology of stem cells and their activation, Fuchs hopes to illuminate what goes awry in squamous cell carcinomas and in aging. She is also interested in translating her knowledge of basic stem cell biology to regenerative medicine. Her lecture, titled “Skin Stem Cells: Their Biology and Clinical Promise” will focus on these topics. Fuchs received her PhD in Biochemistry from Princeton University, and after her postdoctoral research at the Massachusetts Institute of Technology, she joined the faculty at the University of Chicago. She stayed there until 2002 when she relocated to The Rockefeller University. Fuchs’ awards and honors include the Presidential Young Investigator Award, the Richard Lounsbery Award from the National Academy of Sciences, the Novartis-Drew Award for Biomedical Research, the Dickson Prize in Medicine, the FASEB Award for Scientific Excellence, the Beering Award and most recently, the National Medal of Science, the L’Oreal-UNESCO Award, the Madison Medal, and the Passano Award. She is a member of the National Academy of Sciences, the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society, and she holds honorary doctorates from Mt. Sinai/New York University School of Medicine and from the University of Illinois, Champaign-Urbana. Fuchs is also a past President of the American Society of Cell Biology and she is currently President of the International Society for Stem Cell Research.
David Baltimore, PhD

MicroRNAs in Inflammation and Cancer

After serving as President of the California Institute of Technology for nine years, David Baltimore, PhD, was appointed President Emeritus and the Robert Andrews Millikan Professor of Biology in 2006. Awarded the Nobel Prize at the age of 37 for research in virology, Baltimore has profoundly influenced national science policy on such issues as recombinant DNA research and the AIDS epidemic. He is an accomplished researcher, educator, administrator, and public advocate for science and engineering and is considered one of the world’s most influential biologists.

Born in New York City, Baltimore became interested in biology during high school when he spent a summer at the Jackson Memorial Laboratory and worked with research biologists on mammalian genetics. He received his BA in Chemistry from Swarthmore College in 1960 and a PhD in 1964 from Rockefeller University, where he returned to serve as President from 1990-91 and faculty member until 1994.

For almost 30 years, Baltimore was a faculty member at Massachusetts Institute of Technology where his early investigations examined the molecular processes underlying the ability of poliovirus to infect cells. This led him to work on other RNA viruses and then to a consideration of how cancer-causing RNA viruses manage to infect and permanently alter a healthy cell. He identified the enzyme reverse transcriptase in the virus particles, thus providing strong evidence for a process of RNA to DNA conversion, the existence of which had been hypothesized some years earlier. Baltimore and Howard Temin (with Renato Dulbecco, for related research) shared the 1975 Nobel Prize in Physiology or Medicine for their discovery, which provided the key to understanding the life-cycle of retroviruses such as HIV. In the following years, he has contributed widely to the understanding of cancer, AIDS and the molecular basis of the immune response. His present research focuses on control of inflammatory and immune responses as well as on the use of gene therapy methods to treat HIV and cancer in a program called “Engineering Immunity”.

Baltimore has several outstanding administrative and public policy achievements to his credit. In the mid-1970s, he played an important role in creating a consensus on national science policy regarding recombinant DNA research. He served as founding director of the Whitehead Institute for Biomedical Research at MIT from 1982 until 1990. An early advocate of federal AIDS research, Baltimore co-chaired the 1986 National Academy of Sciences committee on a National Strategy for AIDS and was appointed in 1996 to head the National Institutes of Health AIDS Vaccine Research Committee. Dr. Baltimore served as a member of the Independent Citizen’s Oversight Committee to the California Institute for Regenerative Medicine until 2007 and on the Board of Directors for both MedImmune until 2007 and for Cellerant until 2008. He currently serves on the Board of the Broad Foundations including the Broad Institute.

He has played an important role in the development of American biotechnology since his involvement in the 1970s in the formation of Collaborative Genetics. He helped found other companies, most recently Calimmune and Immune Design and presently serves on the Board of Directors at several companies including Amgen and Regulus Therapeutics. He is also a Director of the Swiss investment company BB Biotech and a scientific advisor to The Column Group.

Baltimore’s numerous honors include the 1970 Gustave Stern Award in Virology, 1971 Eli Lilly and Co. Award in Microbiology and Immunology, 1999 National Medal of Science, and 2000 Warren Alpert Foundation Prize. He was elected to the National Academy of Sciences in 1974, and is also a fellow of the American Academy of Arts and Sciences, and a foreign member of both the Royal Society of London and the French Academy of Sciences. From 2006 through 2009, he served as President-Elect, President and Chair of the American Association for the Advancement of Science (AAAS). He has published more than 600 peer-reviewed articles.
Surviving Starvation: Essential Role of the Ghrelin–Growth Hormone Axis (Part I)

Joseph L. Goldstein, MD, is currently Chairman of the Department of Molecular Genetics at the University of Texas Southwestern Medical Center at Dallas. In 1985, he was named Regental Professor of the University of Texas. He also holds the Paul J. Thomas Chair in Medicine and the Julie and Louis A. Beecherl Distinguished Chair in Biomedical Science.

Dr. Goldstein and his colleague, Michael S. Brown, MD, discovered the low density lipoprotein (LDL) receptor and worked out how these receptors control cholesterol homeostasis. At the basic level, this work opened the field of receptor-mediated endocytosis, and at the clinical level it helped lay the conceptual groundwork for development of drugs called statins that lower blood LDL-cholesterol and prevent heart attacks. Drs. Goldstein and Brown shared many awards for this work, including the Lasker Award in Basic Medical Research (1985), Nobel Prize in Physiology or Medicine (1985), and National Medal of Science (1988).

In recent work, Drs. Goldstein and Brown discovered the SREBP family of transcription factors and showed how these membrane-bound molecules control the synthesis of cholesterol and fatty acids through a newly described process of Regulated Intramembrane Proteolysis. For this work, Drs. Brown and Goldstein received the Albany Medical Center Prize in Medicine and Biomedical Research (2003).

Dr. Goldstein is currently Chairman of the Albert Lasker Medical Research Awards Jury and is a member of the Boards of Trustees of the Howard Hughes Medical Institute and The Rockefeller University. He also serves on the Scientific Advisory Boards of the Welch Foundation, Memorial Sloan-Kettering Cancer Center, Broad Institute, Scripps Research Institute, and the Massachusetts General Hospital. He is a member of the U.S. National Academy of Sciences and a Foreign Member of the Royal Society.
Surviving Starvation: Essential Role of the Ghrelin–Growth Hormone Axis (Part II)

Michael S. Brown, MD, was born in Brooklyn, New York in 1941. In 1962 he graduated from the College of the University of Pennsylvania and in 1966 from its School of Medicine. He then was a resident in internal medicine at the Massachusetts General Hospital in Boston, where he met Joseph L. Goldstein, MD, a fellow resident. The two established the friendship and mutual respect that led to their long-term scientific collaboration.

Brown spent 1968–71 training in biochemistry at the National Institutes of Health. In 1971, he joined the Department of Internal Medicine at the University of Texas Southwestern Medical School in Dallas where he succeeded in purifying the enzyme HMG CoA Reductase, which participates in cholesterol biosynthesis. He and Goldstein collaborated to elucidate the biochemical and genetic mechanisms that regulate the level of this enzyme. In 1974, the two young scientists discovered that human cells possess on their surfaces a protein that they called the low-density lipoprotein (LDL) receptor. The receptor carries LDL into the cell by a process that they called receptor-mediated endocytosis. Within the cell LDL turns off HMG CoA reductase, stopping cholesterol synthesis. Subjects with familial hypercholesterolemia (one in 500 people) have defective LDL receptors and suffer early heart attacks.

The work of Brown and Goldstein established the first cause of heart attacks that could be traced to the molecular level, providing a strong scientific foundation for the theory that cholesterol-carrying LDL particles are a major cause of heart attacks. Building on their work, scientists in the pharmaceutical industry
developed drugs called statins that inhibit HMG CoA Reductase, increase the activity of LDL receptors, and lower LDL-cholesterol.

In the early 1980s, Brown, Goldstein and their colleagues purified the LDL receptor, isolated its gene, and traced the mutations to the molecular level. As a result, familial hypercholesterolemia is among the best understood of all human genetic diseases.

During the following decade, Brown and Goldstein turned their attention to the feedback process that regulates the genes for the LDL receptor and the enzymes of cholesterol synthesis. They discovered a family of proteins, designated sterol regulatory element binding proteins (SREBPs), that control these genes. The SREBPs also control the process by which the body converts sugars to fats and thus they are important in obesity and diabetes mellitus.

Throughout the 1970s, when their scientific work was most intensive, Brown and Goldstein continued to function as academic physicians, each performing clinical attending rounds on the general medicine wards of Parkland Memorial Hospital.

Brown is married to the former Alice Lapin. They have two daughters, Elizabeth (born 1973) and Sara (born 1977).

Brown currently is Regental Professor at the University of Texas Southwestern Medical School where he holds the W.A. Moncrief Chair and directs the Jonsson Center for Molecular Genetics.

Brown has received honorary degrees from eight institutions. With Goldstein, he has shared 21 major awards, including, in 1985 the Nobel Prize in Medicine or Physiology, in 1988 the National Medal of Science, and in 2003 the Albany Medical Center Prize.
Seven–Transmembrane Receptors

Robert J. Lefkowitz, MD, was born April 15, 1943, in New York City. In 1962 he earned a bachelor’s degree in chemistry from Columbia University, and in 1966 an MD from Columbia University College of Physicians and Surgeons. He completed an internship and residency in general medicine at Columbia-Presbyterian Medical Center. After a clinical and research fellowship at the National Institutes of Health, Lefkowitz completed residency and research and clinical fellowship training in cardiovascular disease at the Massachusetts General Hospital and concurrently served as a teaching fellow and research assistant at Harvard Medical School.

In 1973 Lefkowitz came to the Duke University School of Medicine as an associate professor of medicine and assistant professor of biochemistry. In 1976, he was named an investigator of the Howard Hughes Medical Institute, a position he still holds. By 1977, he was a professor of medicine, and just five years later he was named a James B. Duke Professor of Medicine. He is also currently a professor of biochemistry and of immunology.

Lefkowitz studies receptor biology and signal transduction and is most well known for his detailed characterizations of the sequence, structure, and function of the beta-adrenergic receptor and the proteins required for its regulation. Upon recognizing the sequence and functional homology with the visual protein rhodopsin, Lefkowitz proposed that adrenergic receptors and rhodopsin were related and the first members of a new protein family, the seven transmembrane receptors or G-protein coupled receptors. This superfamily is now known to be the largest, most diverse, and most therapeutically accessible. Lefkowitz is among the...
Robert J. Lefkowitz, MD is one of the most highly cited researchers in the fields of biology, biochemistry, pharmacology, toxicology, and clinical medicine according to Thomson-ISI.

He has served as president of the American Society for Clinical Investigation and of the Association of American Physicians, and on the Council of the USA National Academy of Sciences.

Lefkowitz has received many honors for his work on cellular receptors, including the American Society for Pharmacology and Experimental Therapeutics John J. Abel Award in Pharmacology (1978), the North Carolina Award for Science (1987), the Gairdner Foundation International Award (1988), the Association of American Medical Colleges’ Biomedical Research Award (1990), the American Heart Association Basic Research Prize (1990), the Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Research (1992), the National Academy of Sciences’ Jessie Stevenson Kovalenko Medal (2001), Fred Conrad Koch Award, The Endocrine Society (2001), the 15th Annual Pasarow Cardiovascular Research Award (2002) and honorary doctorates from the Medical College of South Carolina and Mt. Sinai Medical School (both 2004). In 1988, he was inducted into both the National Academy of Sciences and the American Academy of Arts and Sciences, and in 1994, he was elected to the Institute of Medicine of the National Academy of Sciences. In 2006, he was the recipient of the American Heart Association Eugene Braunwald Academic Mentorship Award. In 2007, he received the Albany Medical Center Prize in Medicine and Biomedical Research and The Shaw Prize in Life Science and Medicine. He also received the 2007 National Medal of Science, presented to him by President George W. Bush on Sept. 29, 2008, in a White House ceremony.
Susan L. Lindquist, PhD
Tackling Protein Misfolding Diseases

Susan L. Lindquist, PhD, is a member and former Director of the Whitehead Institute for Biomedical Research, which she guided as the Whitehead Genome Center was transformed into the neighboring Broad Institute. She is also a Howard Hughes Medical Institute Investigator and Professor of Biology at Massachusetts Institute of Technology. She received her PhD in biology from Harvard and was a postdoctoral fellow of the American Cancer Society. She was named the Albert D. Lasker Professor of Medical Sciences in 1999 at the University of Chicago. A pioneer in the study of protein folding, she established that protein homeostasis has profound and completely unexpected effects on normal biology and disease. She found that the chaperone Hsp90 potentiates and buffers the effects of genetic variation, fueling evolutionary mechanisms as diverse as malignant transformation and the emergence of drug resistance. Her work established the molecular basis for protein-based mechanisms of inheritance. More recently she has built tractable genetic models of complex protein misfolding diseases, including Parkinson’s and Huntington’s diseases, which are providing new insights on the underlying pathogenic mechanisms. Dr. Lindquist is an elected member of the National Academy of Sciences and the Institute of Medicine. Her honors also include the Dickson Prize in Medicine, Sigma Xi William Procter Prize for Scientific Achievement, Centennial Medal of the Harvard University Graduate School of Arts and Sciences, Otto-Warburg Prize, Genetics Society of America Medal, the FASEB Excellence in Science Award and most recently the Max Delbrück Medal and the U.S. National Medal of Science.
Charles L. Sawyers, MD
Overcoming Drug Resistance to Cancer Therapies

Charles L. Sawyers, MD, is an Investigator with the Howard Hughes Medical Institute and the inaugural Director of the Human Oncology and Pathogenesis Program (HOPP) at Memorial Sloan-Kettering Cancer Center, where he is building a program of lab-based translational researchers across various clinical disciplines and institutional infrastructure to enhance the application of global genomics tools to clinical trials. Sawyers’ laboratory is currently focused on characterizing signal transduction pathway abnormalities in prostate cancer, with an eye toward translational implications. His research is best demonstrated through his earlier studies of BCR-ABL tyrosine kinase function in chronic myeloid leukemia, his work with Brian Druker and Novartis in the development of the kinase inhibitor imatinib/Gleevec as primary therapy for CML, and his discovery that imatinib resistance is caused by BCR-ABL kinase domain mutations. This discovery led Dr. Sawyers to evaluate second generation Abl kinase inhibitors, such as the dual Src/Abl inhibitor dasatinib, which received fast track approval at the FDA in June 2006 based on his work. Dr. Sawyers’ work in prostate cancer has defined critical signaling pathways for disease initiation and progression through studies in mouse models and human tissues. This preclinical work led to the development of a novel antiandrogen MDV3100, a small molecule inhibitor discovered in collaboration with UCLA chemist Michael Jung, which targets the increased levels of androgen receptor found in hormone refractory disease. Based on impressive clinical results in a phase I/II study, MDV3100 is currently in a phase III registration trial. Dr. Sawyers is past President of the American Society of Clinical Investigation and served on the National Cancer Institute’s Board of Scientific Councilors. He has won numerous honors and awards, including: the Richard and Hinda Rosenthal Foundation Award; the Dorothy Landon Prize from the American Association of Cancer Research; the David A. Karnofsky Award from the American Society of Clinical Oncology; and the 2009 Lasker~DeBakey Clinical Medical Research Award. He is a member of the Institute of Medicine and in 2010 was elected to the National Academy of Sciences.
Peter S. Kim, PhD

Toward Development of an HIV Vaccine

Peter S. Kim, PhD, is a structural biologist known for discovering how proteins cause membranes to fuse, a central feature of all life. He has designed novel compounds that stop membrane fusion by the AIDS virus, thereby preventing it from infecting cells, and has pioneered efforts to develop an HIV vaccine based on similar principles.

Dr. Kim was appointed president of Merck’s Research Laboratories (MRL) in 2003 and is responsible for Merck’s drug and vaccine research and development activities. Previously, Dr. Kim served as MRL’s executive vice president, Research and Development, from 2001 to 2002.

Prior to joining Merck, Dr. Kim was a Professor of Biology at Massachusetts Institute of Technology (MIT). He was also a Member of the Whitehead Institute and an Investigator with the Howard Hughes Medical Institute. Dr. Kim also served as a member of the National Institutes of Health (NIH) AIDS Vaccine Research Committee.

Dr. Kim received his undergraduate education at Cornell University, graduating with distinction in chemistry. He received his PhD in biochemistry from Stanford University. While at Stanford he was a Medical Scientist Training Program Fellow.

His work has earned him numerous awards including the National Academy of Sciences Award in Molecular Biology, the Eli Lilly Award in Biological Chemistry, the Hans Neurath Award of the Protein Society, and the Samsung Foundation Ho-Am Prize in Basic Science.

Dr. Kim currently is a member of the Board of Directors of the Whitehead Institute for Biomedical Research and the Board of Trustees of the Alfred P. Sloan Foundation. He also serves as a member of the Council of the Institute of Medicine.

Dr. Kim was elected a member of the National Academy of Sciences in 1997. He is also an elected member of the Institute of Medicine and the American Academy of Arts and Sciences.
Robert M. Califf, MD

Translational Medicine: Moving from Better Ideas to Better Health

Vice Chancellor for Clinical Research, Director of the Duke Translational Medicine Institute (DTMI), and Professor of Medicine in the Division of Cardiology at the Duke University Medical Center in Durham, North Carolina, Robert M. Califf, MD, leads a multifaceted organization focused on the transformation of how discoveries are translated into improved health outcomes. Prior to his role at DTMI, he was the founding Director, Duke Clinical Research Institute (DCRI), a premier academic research organization. He is the editor-in-chief of *American Heart Journal*, the oldest cardiovascular specialty journal. Born in 1951 in Anderson, South Carolina, Dr. Califf attended high school in Columbia, S.C., where he was a member of the 1969 AAAA South Carolina Championship basketball team. He completed his undergraduate studies at Duke University in 1973, summa cum laude and Phi Beta Kappa. In 1978, he graduated Duke University Medical School, where he was selected for Alpha Omega Alpha. After completing internship and internal medicine residency at the University of California, San Francisco, he returned to Duke for a fellowship in cardiology. He is board-certified in internal medicine (1984) and cardiology (1986), and is a Master of the American College of Cardiology (2006). Considered an international leader in the fields of cardiovascular disease treatment, health outcomes, quality of care, and medical economics, he is the author or coauthor of more than 1,000 peer-reviewed articles. The Institute for Scientific Information acknowledges him as one of the 10 most cited authors in the field of medicine. He also serves as a contributing editor for www.theheart.org, an online information resource for healthcare professionals involved in the diagnosis and management of cardiovascular disease. As the founder and Director of DCRI for a decade, Dr. Califf led many landmark clinical trials in cardiovascular disease. Under his leadership, DCRI grew to an organization of more than 1,000 employees with an annual budget of over $100 million. A leader in clinical research, DCRI collaborates extensively with government agencies, global academic partners, foundations and biotech, pharmaceutical, device, and diagnostics companies to execute clinical trials in
a myriad of therapeutic arenas. He remains actively involved in the leadership, design, and execution of multinational clinical trials. As Director of DTMI, funded in part by an NIH Clinical and Translational Science Award (CTSA), Dr. Califf’s contribution includes service as the first co-chair of the Principal Investigators Steering Committee of the CTSA. He has served on the Cardiorenal Advisory Panel of the U.S. Food and Drug Administration (FDA) and the Pharmaceutical Roundtable of the Institute of Medicine (IOM). He was a member of the IOM committees that recommended Medicare coverage of clinical trials, the removal of ephedra from the market, and on the IOM’s Committee on Identifying and Preventing Medication Errors. He is currently a member of the IOM Forum in Drug Discovery, Development, and Translation and served on the subcommittee of the Science Board of the FDA that recommended sweeping reform of the science base of the FDA in 2008. He was founding director of the coordinating center for the Centers for Education & Research on Therapeutics™ (CERTs), a public/private partnership among the Agency for Healthcare Research and Quality, the FDA, academia, the medical-products industry, and consumer groups. CERTs focuses on research and education to advance and optimize the use of medical products. He currently serves as the co-chair of the Clinical Trials Transformation Initiative (CTTI), a public private partnership focused on improving the clinical trials system and as the Chair of the Clinical Research Forum, an organization of academic health and science system leaders focused on the improvement of the clinical research enterprise. A member of the National Advisory Council on Aging, he also serves on the Secretary’s Advisory Council on Human Research Protections for the U.S. Health and Human Services Department. Dr. Califf is married to Lydia Carpenter, and they have three children—Sharon Califf, a graduate of Elon College; Sam, a graduate student at the University of Colorado-Boulder; and Tom, a graduate of Duke University—and one grandchild. Dr. Califf enjoys time with his family, works at his golf game, listens to music, and remains an ardent supporter of the men’s and women’s basketball programs at Duke.
LEARNING OBJECTIVES  Upon completion of this activity, participants should be able to:
• Identify advancements in biomedical research.
• Discuss the applications of biomedical research in clinical practice.
• Apply the findings from the work of world-renowned researchers to improve the
treatment and care of patients.

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