SPRING 2010

DEAN'S QUARTERLY

Mount Sinai
MSSM
MOUNT SINAI SCHOOL OF MEDICINE

ACCELERATING SCIENCE, ADVANCING MEDICINE

Genomics: The Threshold of Medical Transformation

A revolution is occurring in biology as new technologies and computational analyses increase our ability to determine how genes influence development, evolution, physiology, and disease. With these advancements, we can analyze genome sequences, understand regulatory mechanisms, and identify disease-causing and -predisposing genes, as well as their protein and metabolite alterations.

Dennis S. Charney, MD, is the Anne and Joel Ehrenkranz Dean of Mount Sinai School of Medicine and the Executive Vice President for Academic Affairs of The Mount Sinai Medical Center.

To learn more, visit www.mountsinai.org/Charney

Translation of these findings will lead to greater understanding of disease pathogenesis, improved diagnostics, and new therapeutics. One of six technology-based institutes in Mount Sinai's strategic plan, the Genomics Institute is a collaborative research and analytical engine that will support the work of all 15 of our research institutes.

Under the direction of Robert J. Desnick, MD, PhD, who is also Chair for the Department of Genetics and Genomic Sciences, ongoing research is directed toward understanding how newly identified genes and their encoded proteins are regulated in different organs and at different times of the life cycle. Investigations are also determining how genes and proteins work to mediate complex biological processes: from heart function to metabolism to higher brain activity, in both health and disease.

Since virtually all human diseases have genetic underpinnings, it is anticipated that genome-based technologies will facilitate their identification. These breakthroughs will transform medicine as we know it by establishing definitive diagnostic tests and improved treatments. Eventually, work in this area will lead to cures and preventive strategies.

Translational medicine has been synonymous with Mount Sinai since the founding of our Hospital in the mid-19th century, when our doctors turned to their microscopes to better understand the conditions they encountered in their patients. With profound relevance and applications to nearly every medical subspecialty, genomics has opened up a previously unthinkable frontier in translational medicine.

The next decade will witness the fruits of this revolution. Personalized medicine will mature as the identification and validation of pharmacogenetic variants, biomarkers of disease severity and progression, and personalized therapeutics become a reality.

INSIDE THIS ISSUE

DISTINGUISHED BY SERVICE

Mount Sinai School of Medicine received the 2009 Spencer Foreman Award for Outstanding Community Service, an annual honor given to only one institution by the Association of American Medical Colleges (AAMC).

The award recognizes exceptional medical school programs that exceed the traditional role of academic medicine and successfully meet the needs of communities underserved by the current health care system. David Muller, MD, Dean for Medical Education, and Gary Butts, MD, Director of the Center for Multicultural and Community Affairs and Associate Dean for Diversity, Policy, Programs, and Community Affairs, accepted the award on November 7 during a dinner at the AAMC annual conference in Boston.

CONTINUED ON PAGE 2

Medical Milestones

Mount Sinai physicians were the first in the country to perform a nonsurgical procedure using sutures to tie off a left atrial appendage (LAA), which can be the source of blood clots leading to stroke in patients with atrial fibrillation (AFib). AFib is the most common sustained heart-rhythm disorder in the United States.

The procedure was performed on a 78-year-old patient by Vivek Y. Reddy, MD, Director of the Cardiac Arrhythmia Service at Mount Sinai Heart, and his colleague, Srinivas R. Dukkipati, MD, Director of Mount Sinai's Experimental Electrophysiology Laboratories. With the patient under general anesthesia, the physicians guided two catheters into the patient's heart to seal the LAA with a pre-tied suture loop. The technique is a safe alternative to drug therapies, such as the blood thinner warfarin (Coumadin), which can have serious side effects, as well as to open-heart surgery and more invasive implant surgery.

Drs. Reddy and Dukkipati joined Mount Sinai in 2009 to focus on building the institution's services for heart-rhythm disorders. They had been performing preclinical testing of the nonsurgical LAA device, and this procedure represents its first application in people in the United States.

Vivek Y. Reddy, MD (RIGHT), and Srinivas R. Dukkipati, MD (LEFT), were first in the country to perform a nonsurgical procedure using sutures to tie off a left atrial appendage, which can be the source of blood clots leading to stroke in patients with atrial fibrillation.

Approximately six million U.S. adults have been diagnosed with AFib, a condition characterized by a rapid and irregular heartbeat that can cause serious complications, including stroke and early death. Patients who take warfarin must rigorously manage the drug's level in their blood. In eliminating the need to take warfarin, the LAA procedure can reduce the need for frequent medical visits.

Says Dr. Reddy, "This nonsurgical procedure could lead to a permanent means of protecting against stroke in patients with AFib who are ineligible for long-term warfarin anticoagulation therapy," says Dr. Reddy.

DISTINGUISHED SERVICE CONTINUED FROM PAGE 1

Lauren Steele (right), a second-year medical student, visits with Jacqueline Beale, an East Harlem resident, as part of Mount Sinai's Longitudinal Clinical Experience. Mount Sinai School of Medicine received the Spencer Foreman Award for Outstanding Community Service from the Association of American Medical Colleges and was commended for its community programs, including Visiting Doctors.

The award honors medical schools that demonstrate a broad-based, continuing commitment to community service through innovative programs and initiatives that reflect a true partnership with the community. Within these criteria, AAMC commended many of Mount Sinai's programs, including those that address adolescent health, care for the homebound, and assistance for the uninsured. It also noted the Center for Multicultural and Community Affairs, which is one of only 13 federally funded Centers for Excellence for Minority Health.

> The award recognizes exceptional medical school programs that exceed the traditional role of academic medicine and successfully meet the needs of communities underserved by the current health care system.

In addition, the School of Medicine was recognized for incorporating educational opportunities into outreach and community initiatives. These programs have strong leadership support—the School of Medicine helps fill in financial gaps when philanthropic support wanes, which is significant considering that the Medical Center provides more than $75 million in uncompensated care every year.

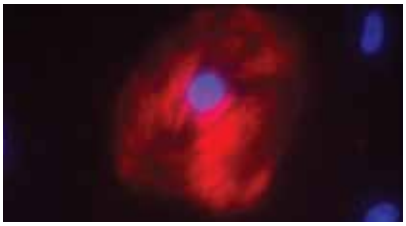
The Spencer Foreman Award was renamed in 2007 to honor Spencer "Spike" Foreman, MD, who established the award in 1993 while serving as Chair of the AAMC.

USING STEM CELLS TO TREAT NOONAN SYNDROME

Noonan and related syndromes are genetic diseases caused by mutations in several genes that encode proteins that cells use to signal from the outer membrane to the nucleus. The disorder affects more than 100,000 people in the United States and leads to short stature, heart problems, mental retardation, and an altered facial appearance. Researchers at Mount Sinai then asked: what if we could alter this signaling to change the outcome and prevent disease?

That question led to a unique collaboration involving experts in stem cell biology and molecular cardiology. Ihor Lemischka, PhD, Director of The Black Family Stem Cell Institute, has teamed up with Bruce Gelb, MD, Director of the Center for Molecular Cardiology and Director of the Child Health and Development Institute, to examine how stem cells generated from cultured skin cells malfunction, leading to developmental disorders, and whether cellular development can be coaxed to function more normally.

"The process for reprogramming human skin cells into stem cells is quite new," says Dr. Lemischka. "We hope to gain a window into early stem cell differentiation and how that leads to Noonan syndrome. Knowing when and where things go wrong during stem cell differentiation could provide us with fundamental insights into biological processes and the pathogeneses of these syndromes."



A cardiomyocyte derived from LEOPARD patient-induced pluripotent stem cells.

"This project represents the success of the multidisciplinary, collaborative environment that Mount Sinai fosters," says Dr. Gelb. "Individually, neither Dr. Lemischka nor I would have undertaken this project. Working together, our research teams are poised to make great progress."

SEARCHING FOR THE GENES BEHIND AUTISM

Mount Sinai will participate in a national, multicenter American Recovery and Reinvestment Act grant totaling $21 million that will investigate the genetic causes of autism spectrum disorders (ASDs), neurodevelopment disorders that affect an estimated 6 out of every 1,000 children ages above the age of 3.

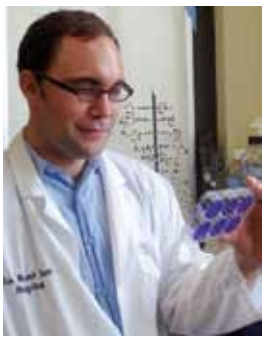
Mount Sinai will receive a total of $1.2 million to conduct high-throughput sequencing—a new high-tech methodology—to pinpoint the genes responsible for the illness. Joseph Buxbaum, PhD, Professor of Psychiatry, Neuroscience, and Genetics and Genomic Sciences, will lead the investigation at Mount Sinai.

The goal is to first sequence 1,000 genes among 1,000 autism cases and compare the findings to 1,000 controls. Subsequently, Dr. Buxbaum and colleagues plan to replicate the top findings among a larger cohort of 9,000 samples.

"Autism appears to have a number of rare, independent mutations," explains Dr. Buxbaum. "These mutations make it a challenge to identify the genetic sources of autism. However, if we can identify these genes, then we can create mouse models with the same genetic mutations and start to develop therapies to treat this condition and we have already developed a few such models. So, while this study is about gene discovery, it is really more about creating novel therapeutics for aspects of autism spectrum disorders that have no treatment."

Young Pioneers

BENJAMIN R. TENOEVER, PHD



Benjamin R. tenOever, PhD

Benjamin R. tenOever, PhD, Assistant Professor in the Department of Microbiology at Mount Sinai School of Medicine, studies cellular response to RNA virus infections—the genetic interactions that occur within cells attacked by a virus—as well as processes that render cells resistant to infection, in the hope of reducing the global burden from such pathogens.

His work was noticed. In January, Dr. tenOever was one of 100 young scientists in the nation to receive the Presidential Early Career Award for Scientists and Engineers and to be recognized by President Barack Obama at a White House reception. The award is the highest honor bestowed by the country on young professionals in the early stages of their research careers.

The award includes a total of $1 million over the next five years for Dr. tenOever's research from the U.S. government. Half of this grant comes from the U.S. Department of Defense, the federal agency that nominated him.

Nominees are chosen each year by nine federal departments and agencies. Selections are based on two criteria: pursuit of innovative research at the frontiers of science and technology and a commitment to community service.

"I think presidential recognition reflects the priority Mount Sinai School of Medicine, and its microbiology department, place on discoveries that have immediate impact on human health," says Dr. tenOever.

This is not the first time Dr. tenOever's research has earned accolades. Last year, he was selected as a Pew Scholar in the Biomedical Sciences, an honor that acknowledges and supports promising young investigators in advancing human health.

Sander S. Florman, MD

SANDER S. FLORMAN, MD

Sander S. Florman, MD, returns to Mount Sinai as the new Director of the Mount Sinai Recanati/Miller Transplantation Institute.

A leader in multi-organ and abdominal transplantation and complex hepatobiliary surgery, Dr. Florman helped direct the efforts to rebuild Tulane University Hospital's transplant program after the devastation of Hurricane Katrina in New Orleans in 2005. At the time, Dr. Florman served as the Director of Liver and Intestine Transplantation at Tulane and later served as the Director of the Tulane Abdominal Transplant Institute as well as the Director of Transplantation at Childrens Hospital of New Orleans.

Dr. Florman's clinical interests include pediatric and adult deceased and live-donor organ transplantation for liver, kidney, pancreas, and intestine. Dr. Florman has published more than 80 manuscripts and 9 book chapters and is active in the transplant community, serving on many committees and boards.

After earning his medical degree at the University of Louisville, Dr. Florman went to Tulane University to pursue his general surgery training. He then spent one year at the Liver Transplant Lab at Mount Sinai investigating the effects of brain death and ischemia/reperfusion injury in liver transplantation. Dr. Florman returned to Tulane to complete his residency in surgery. After his residency, he returned to Mount Sinai to complete a fellowship in multi-organ transplantation and hepatobiliary surgery. He then took a faculty position at Mount Sinai before returning to New Orleans to join the Tulane Transplant Team.

Yvonne Saenger, MD

YVONNE SAENGER, MD

Yvonne Saenger, MD, Assistant Professor of Medicine (Hematology and Medical Oncology) and of Dermatology, will be studying immunotherapy for melanoma in mouse models in the laboratory, with a focus on the role of dendritic cells. She will also be focusing on melanoma immunotherapy in her clinical practice.

Dr. Saenger previously studied cancer vaccines at Johns Hopkins University in Baltimore and recently presented a study of listeria vaccination against pancreas cancer at the annual meeting of the American Association for Cancer Research.

Trained at Memorial Sloan Kettering Cancer Center, Dr. Saenger focused on melanoma during her fellowship and developed a project demonstrating that monoclonal antibodies can work synergistically with vaccines in the treatment of melanoma in mice. She recently published her findings in Cancer Research.

Dr. Saenger became interested in tumor immunology when at Columbia College of Physicians and Surgeons, where she received her medical degree and completed an internal medicine residency.

Yaron Tomer, MD

YARON TOMER, MD

Yaron Tomer, MD, has joined the Department of Medicine as the Vice Chair of Research. In the past five years, the department's research program has grown considerably, rising from a rank of 23 to 14 among all departments of medicine in the nation in funding from the National Institutes of Health (NIH). The Department also received a significant number of American Recovery and Reinvestment Act grants from the NIH in recent months, totaling over $9.5 million.

Dr. Tomer is responsible for the continued growth of the Department's research programs, including identifying of new funding opportunities, fostering the careers of young and established researchers, facilitating collaboration, and expanding new initiatives.

This position is a return home for Dr. Tomer, who graduated from the Department of Medicine's residency program and completed a fellowship in endocrinology and metabolism at Mount Sinai. After completion of his fellowship Dr. Tomer joined the full-time faculty of the Division of Endocrinology at Mount Sinai as an Assistant Professor, and in 2003, he was named Associate Professor in the Department of Medicine.

From 2005 to May 2009 Dr. Tomer was a Professor of Medicine in the Division of Endocrinology and Metabolism at the University of Cincinnati.

His research focuses on the mechanisms leading to the development of autoimmune thyroiditis and type 1 diabetes. He mapped key susceptibility genes for autoimmune thyroid diseases and identified novel mechanisms by which they cause disease. In addition, he is studying the effects of environmental factors, such as infection, and epigenetics, on the development of thyroid autoimmunity.

SUSAN P. AND RICHARD A. FRIEDMAN ANNOUNCE $20 MILLION CAMPAIGN GIFT TO BRAIN INSTITUTE

Richard A. Friedman, an active member of the Board of Trustees since 2001, and his wife, Susan, recently committed to a transformational gift of $20 million—with a pledge to garner more support—to the Brain Institute at The Mount Sinai Medical Center. In honor of their commitment, the Institute will now be called the Friedman Brain Institute (FBI).

The $20 million gift allows Mount Sinai to expand its groundbreaking scientific and clinical research in such areas as Alzheimer's disease, addiction, schizophrenia, depression, and autism spectrum disorders.

With the Friedmans' support, the Institute will be able to recruit 20 to 25 additional neuroscientists, explained Eric J. Nestler, MD, PhD, Nash Family Professor of Neuroscience and Director of the Friedman Brain Institute. The gift will also enable the FBI to occupy two floors within the 10-story Center for Science and Medicine, a 450,000-square-foot facility scheduled for completion in 2012.

> Mount Sinai is an established leader in the neurosciences. The magnanimous support of Richard and Susan Friedman will allow Mount Sinai to continue making significant advancements in this complex field, for the benefit of patients worldwide.
>
> — KENNETH L. DAVIS, MD
> *President and CEO, The Mount Sinai Medical Center*

The Friedmans' gift is among the largest in Mount Sinai's history, and reflects their longstanding commitment to neuroscience research at Mount Sinai. Mr. and Mrs. Friedman have committed more than $22 million to Mount Sinai since 1987, and they have supported a range of activities, from the annual fund to a variety of events. The couple chaired the Crystal Ball in 2006, and Mr. Friedman serves as co-chair of the Trustee Development Committee and is a member of the Trustee Executive Committee.

"Susan and I value our role as philanthropists greatly," said Mr. Friedman, who is co-chair of the Board's Development Committee and a member of both the Executive and Investments committees. "Part of that role includes becoming active partners for the charitable causes that we support."

Noting that Richard Friedman will co-chair the FBI Philanthropic Leadership Committee, Dr. Nestler said, "I am humbled and honored by Susan and Richard Friedman's incredibly strong support and commitment to the Brain Institute. This gift gives us the unique opportunity to build on Mount Sinai's established strengths in the neurosciences to develop a truly transformative basic to clinical neuroscience research program that will be one of the best in the world."

Mount Sinai expects to leverage the Friedmans' leadership gift to raise an additional $50 million in support of FBI initiatives. These contributions will position the FBI to reach the $100 million fundraising goal established in the Medical Center's strategic plan several years ago.

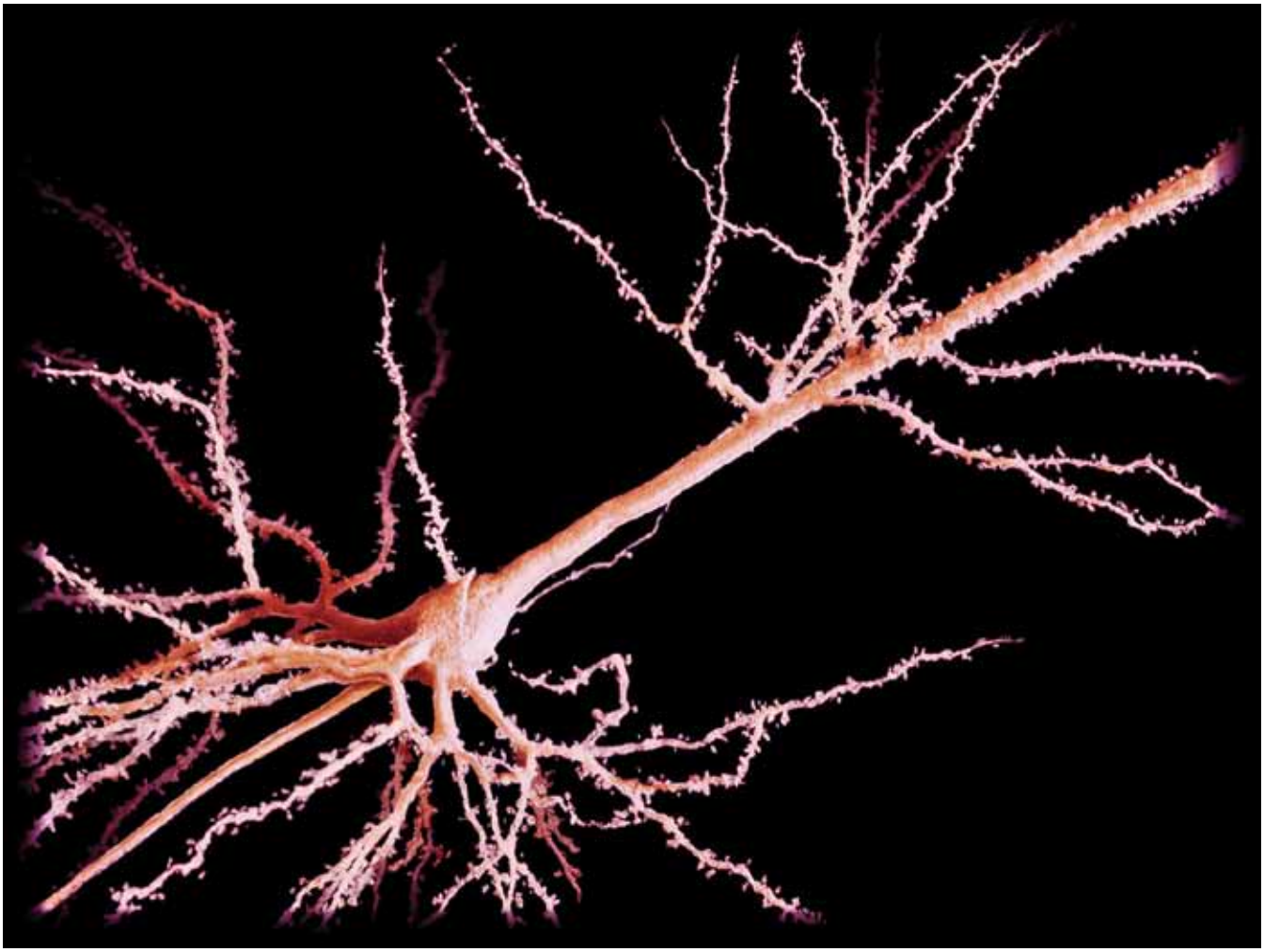
Susan and Richard A. Friedman

Mr. Friedman, who serves as Managing Director at Goldman Sachs, explained that the gift builds on a strong legacy of his company's support for Mount Sinai. "This gift isn't just a commitment from our family, but part of a larger connection between two of New York's most respected institutions," he said, pointing to a decades-long relationship between Goldman Sachs and the Medical Center. Former Mount Sinai Board Chair Gustave L. Levy, who oversaw the creation of Mount Sinai School of Medicine and the most ambitious expansion of Mount Sinai up to now, served as Senior Partner at Goldman Sachs.

But the connection goes back even further, since the very founding of the firm. Bernard Sachs, MD, the Mount Sinai physician who contributed to the discovery of Tay-Sachs disease, was the brother of Harry Sachs, a founder of Goldman Sachs.

Kenneth L. Davis, MD, President and CEO of The Mount Sinai Medical Center, praised the Friedmans' generosity and their desire to perpetuate the Mount Sinai–Goldman Sachs partnership. "Mount Sinai is an established leader in the neurosciences. The magnanimous support of Richard and Susan Friedman will allow Mount Sinai to continue making significant advancements in this complex field, for the benefit of patients worldwide."

Trustee and Chair of The Campaign for Mount Sinai James S. Tisch added, "A leadership commitment like this one allows Mount Sinai to move forward with the ambitious plans set forth in its strategic plan. Richard and Susan are exactly the kind of partners that Mount Sinai needs during this exciting time."



BRIDGES WITHIN THE BRAIN

A pyramidal neuron, pictured above, has been filled with dye and reconstructed through computerized microscopy. This neuron is in the brain's prefrontal cortex—the cortical region responsible for the highest level of cognitive functions. The branches are dendrites, and the numerous small extensions on each dendrite are called spines. These spines receive inputs from other neurons, and these inputs are modified by learning. At least 30 percent of these spines are lost with aging, contributing to age-related cognitive impairment.

To learn more, visit www.mountsinai.org/Morrison

PHOTO: John H. Morrison, PhD
Dean of Basic Sciences and the Graduate School of Biological Sciences
Professor of Neuroscience

PRIMARY CARE PARITY

In the national health care debate, access to care is frequently equated with insurance coverage. But coverage alone is not the cure. Patients need good primary care physicians to rely on, and as a nation, we need many more of them.

Paul Klotman, MD

Numerous studies show that the availability of primary care physicians correlates with better health outcomes and lower health care costs. It is also well documented that in the United States, the supply of primary care physicians is far below that of nations with better health care outcomes and lower costs.

To promote primary care as a career choice, more action is needed from government as well as the institutions and regulatory bodies responsible for medical training.

Congress needs to retain provisions in proposed bills that would reduce the income disparity between primary care physicians and specialists. Reimbursement should be aligned to the time spent with, and quality of care provided to, patients—rather than to the number of procedures and tests performed.

To make the field immediately more attractive, Congress should expand currently limited debt-relief programs to include all graduates pursuing careers in primary care.

As President Obama has emphasized, health care reform needs to include incentives that encourage use of electronic medical records and creation of medical homes focused on coordinated, quality care with care teams that include nurses, physician assistants, and others. Such improvements would reduce the administrative burden on primary care physicians while providing them greater job satisfaction and more time for patients.

To further foster growth, physician training must be reevaluated. Medical schools and residency programs need to highlight primary care as a valued and respected career choice and provide the knowledge and experience contemporary primary care medicine demands.

The current medical resident training structure was developed a century ago, when patients received most of their care as inpatients. Today, all but the most acutely ill are treated in the outpatient setting.

New curricula focused on the divergent demands of inpatient and outpatient medicine are required. Attractive outpatient curricula would enhance primary care training in team leadership skills, cost-effective care, preventive medicine, and chronic disease management. This would also establish parity between primary care and other areas including specialty practices and academic pursuits. To achieve this, legislators need to create more residency spots by lifting restrictive caps, making access to internal medicine residency less intense and thus more attractive.

> Patients need good primary care physicians to rely on, and as a nation, we need many more of them.
>
> — PAUL KLOTMAN, MD
> *Chairman of the Department of Medicine, Mount Sinai School of Medicine*

At all stages of training, future primary care doctors spend far more time learning treatment techniques than they do mastering prevention strategies—those proven to improve outcomes and reduce costs. Curricula that help all aspiring physicians master preventive medicine are needed.

As we continue to debate health care reform, it is essential to voice the fact that access to care relies on more than insurance. Ensuring that our most promising physicians-in-training are attracted to, and properly trained in, primary care medicine will give patients the access they need to doctors capable of delivering the highest quality care.

To learn more, visit www.mountsinai.org/Klotman.
Paul Klotman, MD, is Chairman of the Samuel Bronfman Department of Medicine at Mount Sinai School of Medicine.
This commentary was first published in *The New York Times* on September 30, 2009.

The Mount Sinai Medical Center
One Gustave L. Levy Place, Box 1107
New York, NY 10029-6574