

## ACCELERATING SCIENCE, ADVANCING MEDICINE

### Becoming an Engine of Discovery

I am pleased to outline the strategic plan for the Center for Discovery and Innovation (CDI) at The Mount Sinai Medical Center. This entity, designed to capitalize on the unprecedented opportunities of 21st century biomedicine, will bring together some 30 renowned translational scientists, many of whom are successful drug developers and patent-holders already, with the charge of translating discovery into therapeutics and generating new intellectual property.

Under the direction of a senior leader with international stature in translational medicine and the successful development of therapeutic interventions, the CDI discovery group will identify the most promising research within all of Mount Sinai's disease-focused institutes with the goal of illuminating new disease targets and the molecules that treat those targets.

This new era of growth will span years and will require great institutional commitment and investment, and the results will be breathtaking. The CDI is structured to focus on five areas that represent the most pressing global disease burden: cardiovascular disease, cancer, neurological disorders, immune disorders, and virology/vaccines. To explore these areas in the greatest depth and breadth possible, we will expand the facilities and capabilities of our

Experimental Therapeutics Institute in five key areas: small-molecule drug discovery, monoclonal antibodies and purified proteins, high-content screening/RNAi, induced pluripotent stem cells, and systems pharmacology and network analysis facilities.

The success of the CDI enterprise and the scientists it recruits and supports will ultimately be measured by the discoveries made, and the applications developed, to predict, prevent, and treat disease. I look forward to sharing with you the progress and results of CDI throughout the coming years.

*See the Drug Discovery Roadmap on page 2.*



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](http://www.mountsinai.org/Charney)

### 5 CORE FACILITIES OF THE EXPERIMENTAL THERAPEUTICS INSTITUTE (ETI)

Small-molecule drug discovery

Monoclonal antibodies and purified proteins

High-content screening/RNAi

Induced pluripotent stem cells

Systems pharmacology and network analysis

### DISEASE FOCUS AREAS OF ETI CORE FACILITIES

CARDIOVASCULAR DISEASE  
CANCER  
NEUROLOGICAL DISORDERS  
IMMUNE DISORDERS  
VIROLOGY/VACCINES

#### INSIDE THIS ISSUE

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#### ■ DISTINGUISHED BY SERVICE

### Department of Rehabilitation Medicine Anniversary

In 1910, The Mount Sinai Medical Center established one of the nation's first departments devoted to rehabilitating patients with disabling injuries and medical conditions. Today, the Department of Rehabilitation Medicine is consistently ranked one of the best in the nation by *U.S. News & World Report* in its annual Best Hospitals survey. The Department commemorated its 100th anniversary in November.

Kristjan T. Ragnarsson, MD, Lucy G. Moses Professor and Chair of the Department of Rehabilitation Medicine, and Wayne A. Gordon, PhD, the Jack Nash Professor of Rehabilitation Medicine, and an Associate Director of the Department of Rehabilitation Medicine, lead an interdisciplinary team of professionals.

*Continued on page 2*

## ■ ACCELERATING SCIENCE

### The Drug Discovery Roadmap

Mount Sinai and other academic medical centers are the new engines of research and discovery for the pharmaceutical industry.

#### BASIC SCIENCE RESEARCH

Scientists pursue basic research questions in the laboratory to understand the fundamental mechanisms of molecular, cell, and systems biology.

#### THE CENTER FOR DISCOVERY AND INNOVATION (CDI)

#### TRANSLATIONAL SCIENCE

Scientists use animal models and human patients to explore disease mechanics.

#### DISCOVERY OF POTENTIAL NOVEL THERAPEUTICS

Scientists collaborate with research staff in ETI core facilities to develop new molecules with the goal of creating new therapies, including mAbs, small molecules, and biologics.

*Industry partnerships with biotech and pharmaceutical companies begin to form.*

*Industry partners assist in the final steps of therapy discovery to determine safety and efficacy, and to incorporate therapy into medical practice.*

#### PHASE 1 FDA SAFETY TRIALS

Researchers test new treatments for safety and, in some cases, efficacy in humans through standard FDA trials.

#### PIVOTAL FDA CLINICAL TRIALS

Physician-scientists conduct large-scale, well-controlled efficacy trials in order to gain FDA approval.

#### MEDICAL PRACTICE IS CHANGED

The new therapy becomes available to patients. Large-scale effectiveness trials are conducted in patients with more complicated diseases to guide medical practice.

## ■ MEDICAL MILESTONES

### A New Alternative to Open Heart Surgery

Three leading physicians at Mount Sinai Heart have performed the first U.S.-based percutaneous implantation of a novel device that replaces a diseased aortic heart valve, providing a viable treatment for patients too elderly or high risk to undergo open heart surgery. The device, the Medtronic CoreValve® Transcatheter Aortic Valve Prosthesis, treats severe aortic stenosis with a catheter-based technology that does not require an incision in the chest or the use of a heart lung machine.

David H. Adams, MD, Marie-Josée and Henry R. Kravis Professor and Chair of the Department of Cardiothoracic Surgery; Samin K. Sharma, MD, the Zena and Michael A. Wiener Professor and Director of the Cardiac Catheterization Laboratory; and Annapoorna S. Kini, MD, Associate Professor and Associate Director of the Cardiac Catheterization Laboratory, have begun using the CoreValve System as part of the FDA's Pivotal Clinical trial. Dr. Adams is the trial's national Co-Principal Investigator.

"We think more than 70 percent of patients receiving the CoreValve will survive more than two years," says Dr. Sharma, whose estimates are based on the 13,000 devices that have been implanted in patients throughout Europe since 2007.

David H. Adams, MD (LEFT), and Samin K. Sharma, MD (RIGHT), with the CoreValve device.

Approximately 100,000 people in the United States are diagnosed with severe aortic stenosis each year, but one-third of them do not qualify for surgery due to their advanced age, the fact that they've suffered a stroke, or have lung disease. In the past, physicians have relied on a balloon procedure to open the heart valve, but this has proven to be a temporary fix, with results lasting up to nine months before the symptoms return. Dr. Sharma says the balloon procedure can be performed only a few times before it actually begins to weaken the patient's heart valve.

Implantation of the CoreValve, a self-expanding stent measuring slightly more than three centimeters, is guided over a wire and a catheter placed in a peripheral artery through the diseased aortic valve, and once it expands in this position, the new aortic valve begins functioning immediately.



## ■ DISTINGUISHED BY SERVICE

### Department of Rehabilitation Medicine Anniversary, *continued from page 1*

The department has become a world-renowned center of excellence providing comprehensive rehabilitation for patients with spinal cord injury, brain injury, stroke, limb amputations, multiple traumas, and joint replacement surgery. It is the only federally designated Model System of Care facility in New York State for spinal cord injury and traumatic brain injury (TBI). Among its many research accomplishments is the development of an assessment tool for diagnosing subtle brain damage, and an intervention to address impairment of executive function, such as goal-setting, problem-solving, and planning abilities in patients with traumatic brain injury.

Thousands of patients have reclaimed their lives through care and support from Mount Sinai practitioners. Notable examples include ABC News Reporter Robert Woodruff, who in 2006 sustained TBI after being hit by a roadside bomb while on assignment in Iraq, and Dennis Byrd, a former New York Jets football player who broke his neck during a game in 1992, and now can walk on his own.

## RESEARCH FRONTIERS

# \$17.2 Million Grant for Research on Immune Modeling and Experimentation

Mount Sinai School of Medicine recently received a five-year, \$17.2 million grant from the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIH), to improve the collection and computation of data used to study immunology and infectious diseases.



Stuart C. Sealfon, MD

This is the second round of funding that MSSM's Program for Research on Immune Modeling and Experimentation (PRIME) has received since 2005, when the program—directed by Stuart C. Sealfon, MD, Glickenhau Professor and Chair of the Department of Neurology—was awarded \$16.8 million.

“We are trying to change the paradigm of how research is done, especially research in immunology and infectious diseases,” says Dr. Sealfon. “Our goal is to combine large amounts of information from different sources to reach conclusions and accelerate the discovery process.”

Integrating mathematical approaches into research that ultimately has an impact on patient care is particularly vital in the complicated realm of infectious disease, according to Dr. Sealfon.

PRIME will conduct large-scale experiments as a way to validate mathematical models and test their predictions. The PRIME team includes colleagues at Yale University, Princeton University, Ohio State University, The BioAnalytics Group, LLC, a New Jersey-based data analysis and management company, and Contur AB, a Swedish research software company. Dr. Sealfon says the NIH funding is an outgrowth of U.S. government concerns over managing the potential threat of bioterrorism.

# New Discovery into the Origins of Brain Cells



Miriam Merad, MD, PhD

Miriam Merad, MD, PhD, Associate Professor of Gene and Cell Medicine at Mount Sinai School of Medicine, and her team of researchers at The Mount Sinai Medical Center have made a significant discovery that microglia, the small, immune cells that reside in the central nervous system, have a unique origin, and are formed shortly after conception. Microglia had been thought to develop at birth, and originate at the same time as macrophages, the body's other immune cells. The findings were published in *Science* in November.

The study resolves a longstanding controversy about the origin of microglia cells, and has the potential to lead to new treatments for diseases of the nervous system. Microglia protect vulnerable brain tissue from infection and metabolic injury. They clear out debris and dead cells, reducing inflammation when infectious agents enter the brain. “They are very important in maintaining brain integrity, which may be why they develop so early,” says Dr. Merad.

Studies suggest that defective microglia that increase with age may lead to the release of inflammatory substances that contribute to the development of neurodegenerative diseases, such as Alzheimer's and Parkinson's, and autoimmune disorders, such as multiple sclerosis.

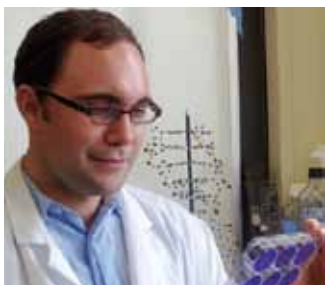
“Now that we know that microglia originate in early embryos, we should, in theory, be able to generate microglia from embryonic stem cells and inject them into a degenerated brain,” says Dr. Merad. “This study shows why it is so important to be able to conduct research with embryonic stem cells.”

Translating these discoveries into clinically relevant treatments for neurodegenerative diseases will be the next phase of research.

## YOUNG PIONEERS

# Benjamin R. tenOever, PhD, Receives Award

Benjamin R. tenOever, PhD, Assistant Professor of Microbiology, Mount Sinai School of Medicine, was recently honored with the American Society for Microbiology's 2010 Interscience Conference



Benjamin R. tenOever, PhD

on Antimicrobial Agents and Chemotherapy (ICAAC) Young Investigator Award for his work in understanding small RNAs and their potential antiviral roles.

Dr. tenOever's research focuses on two unique aspects of small RNAs, called microRNAs, that exist in all the cells of the body. One aspect of his research is based on the idea of utilizing these microRNAs in an antiviral capacity to generate novel strategies for vaccine design. The second focus is based on engineering recombinant viruses that can be used for therapeutic purposes. “We

were the first to demonstrate that a subset of viruses can be designed to produce custom-made small RNAs,” says Dr. tenOever.

At the most basic level, Dr. tenOever's work centers on RNAs that are only 20 nucleotides in length, which are naturally present in cells, but can also be synthesized and artificially introduced. “In a nutshell, we can generate a novel vaccine by exploiting the cell's microRNA profile, or take a very harmless virus and engineering it so that it now encodes small RNAs that will essentially attack another virus

of our choice,” he says.

A 2008 Pew Scholar, Dr. tenOever has also received the Presidential Early Career in Science Award, the highest honor given by the United States government to outstanding scientists and engineers who are beginning their careers. His research has been published in more than a dozen journals, including *Cell*, *Science* and *Nature Biotechnology*. The Young Investigator Award recognizes an early-career scientist for research excellence in microbiology and infectious diseases.



Michael J. Goldstein, MD

## Michael J. Goldstein, MD, FACS

Michael J. Goldstein, MD, FACS, a renowned transplant surgeon, who specializes in high-risk procedures that improve patient access to transplantation, has been appointed

Associate Professor of Surgery and Director of Kidney and Pancreas Transplantation at The Mount Sinai Medical Center.

One of Dr. Goldstein's areas of expertise is operating on patients with high immunologic risk, and helping them to overcome organ

rejection through the use of advanced immunosuppressant drug regimens. He also performs procedures that maximize the use of organs that might otherwise have been less than optimal for transplantation.

Dr. Goldstein's innovative technique for minimally invasive kidney transplantation utilizes a small, two-inch incision, which minimizes pain, accelerates patient recovery, and reduces hospital stay.

In addition to his work at Mount Sinai, Dr. Goldstein is Medical Director of the New York Organ Donor Network, a nonprofit organization that works to improve the quality

and the number of organs available for transplant in the Greater New York area. He is also the Vice Chair of the United Network for Organ Sharing's Organ Availability Committee, and is on the Medical Directors Council of the Association of Organ Procurement Organizations.

Dr. Goldstein serves as a medical advisor to the National Kidney Foundation of Greater New York and to pharmaceutical and biotechnical companies.

Prior to joining Mount Sinai, Dr. Goldstein was an Assistant Attending Surgeon and an Assistant Professor at New York Presbyterian Hospital, Columbia University Medical Center.



Robert Maki, MD, PhD

## Robert Maki, MD, PhD

Robert Maki, MD, PhD, a leading sarcoma cancer researcher, has joined The Mount Sinai Medical Center as the Chief of Pediatric Hematology/Oncology Division, and Medical Director of the Sarcoma Cancer Program at The Tisch Cancer Institute.

Dr. Maki is credited with making significant contributions to the understanding and targeting of soft-tissue and bone sarcomas, of which there are more than 50 types. His expertise in novel therapies for treatment has led him to investigate new drugs to attack molecular targets.

At The Tisch Cancer Institute, Dr. Maki's responsibilities include the expansion of basic and translational sarcoma cancer research programs. Working closely with his colleagues in the Division of Hematology and

Medical Oncology, and in the Department of Orthopaedics, he will deliver personalized treatments to sarcoma patients, and develop novel therapeutics in this population. This collaboration will offer comprehensive specialty care to adult and pediatric patients with sarcoma, and build a portfolio of translational clinical trials to improve the outcome of patients with this aggressive cancer.

Dr. Maki will help expand the breadth of the pediatric clinical program in Hematology/Oncology, focusing on soft-tissue and bone sarcomas, adolescent cancer care, and transitioning pediatric cancer patients to adult care.

Prior to joining Mount Sinai, Dr. Maki was an Associate Professor of Medicine at the Weill Cornell Medical College, and Co-Director of the Adult Sarcoma Program at Memorial Sloan-Kettering Cancer Center.

## Kenneth Rosenzweig, MD



Kenneth Rosenzweig, MD

Kenneth Rosenzweig, MD, a respected physician-scientist who specializes in the treatment of lung cancer and malignant mesothelioma, has been appointed Chair of the Department of Radiation Oncology at Mount Sinai School

of Medicine. Dr. Rosenzweig has developed innovative methods for delivering precise doses of radiation to lung tumors during key points in the respiration cycle. His work enables physicians to safely increase the radiation dose, shorten treatment, spare healthy tissue, and improve the outcome in people receiving radiation.

A groundbreaking researcher in radiation therapy, Dr. Rosenzweig was the principal investigator for a critical-dose escalation study that established the maximum tolerated dose of radiation that can be safely delivered. He has published more than 70 articles in scientific journals, and has authored numerous textbook chapters, including one in *Principles and Practice of Oncology*, the leading textbook of cancer medicine.

In his new position, Dr. Rosenzweig will continue the innovative research in radiation oncology that engaged him at Memorial Sloan-Kettering Cancer Center, where he worked as a radiation oncologist from 1997 to 2010. He will be part of a multidisciplinary team of top surgeons, radiologists, and researchers at Mount Sinai who are using earlier diagnoses and

less invasive surgery to give patients with lung cancer higher cure rates and faster recovery times.

An accomplished educator, Dr. Rosenzweig was named "Teacher of the Year" by the Association of Residents in Radiation Oncology. He has served as a consultant to the International Atomic Energy Association, and on many professional committees, including the Radiation Therapy Oncology Group (RTOG) Lung Committee, the RTOG Data Monitoring Committee, and the National Cancer Institute Clinical Trials Evaluation Panel.

Dr. Rosenzweig completed his residency at the Joint Center for Radiation Therapy at Harvard Medical School.

## ■ PHILANTHROPY

# Zweigs Pledge \$5 Million to Center for Living Donation

Barbara and Martin Zweig, PhD, recently committed to a \$5 million leadership gift to the Recanati/Miller Transplant Institute (RMTI) to support an ambitious new center and establish an endowed professorship.

The center will be named the Zweig Family Center for Living Donation in their honor, and will focus on providing the best in medical, surgical, and psychological care to living kidney and liver donors. The Sidney J. Zweig Professor of Medicine will play a key role in advancing the knowledge and practice of transplantation.

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“Living organ donors are giving the most a person can give. The Zweig Family Center for Living Donation will honor that gift by providing exceptional care.”

— MARTIN ZWEIG, PhD

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“This gift will allow us to provide dedicated care and specialized services for these incredible people who actually give a piece of their own liver or one of their own kidneys to save another person’s life,” says Sander Florman, MD, the Alfred and Florence Gross Professor of Surgery and Director of the Recanati/Miller Transplant Institute. Currently, there is a critical shortage of organs, both nationally and within the New York region.



Martin Zweig, PhD, and Barbara Zweig

“Living organ donors are giving the most a person can give,” says Dr. Zweig. “The Zweig Family Center for Living Donation will honor that gift by providing exceptional care. Barbara and I are happy to be a part of this important, innovative new center.”

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## ■ PATIENT-CENTERED CARE

# A Focus on Living Donors

The recently named Zweig Family Center for Living Donation at the Recanati/Miller Transplantation Institute (RMTI), is the first major multi-organ program in the nation to address the unique physical and psychological concerns of living donors. Emphasis is placed on meeting each patient’s unique pre-, peri-, and post-transplant needs by providing a wide range of treatments and services throughout the transplant process, including counseling, support groups, yoga, nutrition counseling, and patient education on donation and overall health.

Pre-donation care is focused on evaluating the donor and educating

him or her about the risks and benefits of donation. During the inpatient and recovery phase, the staff focuses on safety, advocacy,



Dianne LaPointe Rudow, DNP

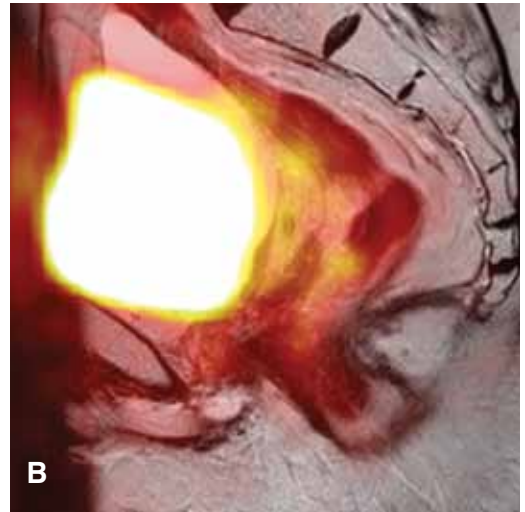
psychological support, and monitoring for complications. In post-recovery, patients are taught how to maintain their health and receive long-term monitoring.

Dianne LaPointe Rudow, DNP, a leading advocate for living donors, is the center’s director. She helped develop national and New York State standards for donor care while serving on the board of directors of the Organ Procurement and Transplantation Network/United Network for Organ Sharing (UNOS), and at the New York Center for Liver Transplantation.

In addition to Dr. LaPointe Rudow there is a multidisciplinary team of

transplantation experts, including Marcelo Facciuto, MD, and Juan Pablo Rocca, MD. Dr. Facciuto, who was named Surgical Director of Living Donor Liver Transplantation, has broad surgical experience with end-stage liver disease and hepatocellular carcinoma. Dr. Rocca, the Associate Director of fellowship training at Mount Sinai, serves as Surgical Director of Living Donor Kidney Transplantation. The center has dedicated resources to ensure that donor safety is paramount. The gift from the Zweig family will also include the renovation of four patient hospital rooms specifically for the care of donors.

## Prostate Cancer Imaging



Whole-body Philips MR/PET images show a 69-year-old man with prostate cancer and persistent hypermetabolism in (A): the left lateral resection area; and (B): near the base of the penile bulb. (C) This image appears to show the recurrence of a suspicious looking tumor.

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To learn more, visit [www.mountsinai.org/tmii](http://www.mountsinai.org/tmii)

PHOTO: Zahi A. Fayad, PhD, is Director of the Translational and Molecular Imaging Institute; Professor of Radiology and Medicine (Cardiology); Director and Founder, the Eva and Morris Feld Imaging Science Laboratories; and Director, Cardiovascular Imaging Research.

## A National Call to Action: Reduce Barriers to Mental Health Care

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.

In the aftermath of the Tucson, Arizona, shootings, much has been said about the role mental illness might have played in this tragedy. Such discourse is understandable, but unfortunately it has tended to reinforce, rather than challenge, misconceptions about mental illness.

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**“Given the prevalence and burden of mental illness, funding is both inadequate and disproportionately low compared to that for heart disease, stroke, and cancer.”**

— Wayne Goodman, MD and  
Dennis S. Charney, MD

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One is that mental illness leads inexorably to violence. Outwardly directed violence is rare among the majority of people with a mental illness. In fact, individuals with a mental disorder are much more likely to harm themselves or be victims of violence. In only a small minority, such as those with an unstable psychotic disorder that is accompanied by paranoia and “command” auditory hallucinations, is violent behavior elevated.

Unwittingly, the media may be perpetuating another myth: that people with mental illness appear abnormal. The demonic smirk and haunting countenance of the alleged shooter are ubiquitous and, for many, may become the archetypal face of severe mental illness. However, mental illness is faceless—invisible, yet pervasive. It does not discriminate by gender, race, or socioeconomic status. In the vast majority of cases, it is no more recognizable on the surface than diabetes.

Finally, the spotlight on Tucson could deepen the already profound stigma associated with mental illness. Negative attitudes are felt by those with mental illness, their families, and the public alike. Stigma makes people more reluctant to seek help, or to offer it. The events in Tucson should not

be allowed to magnify negative attitudes toward mental illness.

It is unfortunate that at this critical juncture, the gap between the need for mental health services and resources to fund them is large and growing. As local and state governments struggle to balance budgets, mental health services are often first on the chopping block. One result of this reduction is the expanding number of people with mental illnesses who are incarcerated, rather than in treatment programs, for predominantly nonviolent crimes—situations that might have been prevented by better psychiatric management in the first place.

Given the prevalence and burden of mental illness, funding is both inadequate and disproportionately low compared to that for heart disease, stroke, and cancer. If this trend is not reversed, even those who do seek help may not be able to find or afford it—and those who would benefit from outreach may never be identified and treated. The Mental Health Parity and Addiction Equity Act, which lifted some restrictions and guaranteed coverage in certain circumstances, is a step in the right direction, but there are loopholes that will still leave many uninsured.

Increased funding directed at research into risk factors—both behavioral and genetic—would also help us develop the tools that could detect mental illness early and accurately. As with other medical diseases, early intervention may change the trajectory of mental illness.

What happened in Tucson exposed fault lines in our mental health care system, but we must not let it lead to mixed or erroneous messages about mental illness. Instead we must use it as a call to action to strengthen our mental health system.

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To learn more, visit [www.mountsinai.org/Commentaries](http://www.mountsinai.org/Commentaries). Wayne K. Goodman, MD, is Professor and Chair of the Department of Psychiatry at The Mount Sinai Medical Center, and Dennis S. Charney, MD, is Dean of Mount Sinai School of Medicine. This commentary was first published in *The New York Times* on February 22, 2011.



Wayne Goodman, MD



Dennis S. Charney, MD