

ACCELERATING SCIENCE—ADVANCING MEDICINE

Personalized and Precision Medicine

Two years ago in this space, I discussed the incredible promise of genomic medicine. Today, I am pleased to outline the advancements Mount Sinai has made in building a truly outstanding genomics enterprise—one that will make personalized medicine an everyday reality and answer the call of a new global imperative: Precision medicine.

Eric E. Schadt, PhD, a world leader in the use of computational biology in genomics, was named Director of the Institute of Genomics and Multiscale Biology, the Jean C. and James W. Crystal Professor of Genomics, and Chair of the Department of Genetics and Genomic Sciences. He and his team are renowned for integrating and modeling vast quantities of molecular data so they can see things that others cannot, and identify targets for precise and individualized therapeutic intervention.

Carlos Cordon-Cardo, MD, PhD, who is internationally acclaimed for groundbreaking research in experimental pathology and molecular oncology, joined as Chair of the Department of Pathology. Kumar Chatani arrived as Senior Vice President for Information Technology and Chief Information Officer. He is directing the rollout of the Epic electronic medical record (EMR) system for improved patient care, and

has greatly enhanced scientific research based on comprehensive de-identified medical information. Patricia Kovatch, our new Associate Dean for Scientific Computing, is already building Minerva, a supercomputer named after the Roman goddess of wisdom, medicine, and science.

Together with Erwin P. Bottinger, MD, Director of the Charles R. Bronfman Institute for Personalized Medicine, this great group will accelerate the advancement of genomic medicine. They have the powerful machines needed to collect, bank, and mine internet-scale biomedical data from EMRs, the more than 20,000 individuals enrolled in Mount Sinai's landmark Biobank Program, and other major collaborative efforts.

With all of this, Mount Sinai will make significant contributions to precision medicine, which, according to the National Academies, brings with it the urgent need for a modern taxonomy of disease, one that is based on molecular biology



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.

rather than primarily symptoms, imaging studies, and microscopic examination of diseased tissues and cells.

With crucial molecular insights, modern medicine will authorize the most comprehensive revision ever to the *International Statistical Classification of Diseases and Related Health Problems*, which has guided health care for well over a century, and chart a new course for the centuries to come.

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

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■ DISTINGUISHED BY SERVICE

ABC News Spotlights Mount Sinai's Global Health Program



Mount Sinai physicians Anu Anandaraja, MD, MPH, left, and Sigrid Hahn, MD, MPH, work with community health workers in Mozambique. PHOTO COURTESY ABC NEWS NIGHTLINE

Teaching health care workers how to improve care for local citizens in two impoverished African countries, the republics of Liberia and Mozambique, is an ongoing effort for several Mount Sinai physicians whose work was featured on ABC's *Nightline*.

In the first segment of a two-part series, *Nightline* anchor Cynthia McFadden traveled to the John F. Kennedy (JFK) Medical Center in Monrovia, Liberia, to observe Andy Sechler, MD, a fourth-year resident in Internal Medicine and Pediatrics, and Torian Easterling, MD, a fifth-year resident in Preventive Medicine, both part of the Mount Sinai

Continued on page 2

■ MEDICAL MILESTONES

Advancing Treatment for Multiple Myeloma

One of the great success stories in cancer research has been in the area of multiple myeloma, where the life expectancy and quality of life of those with this cancer of the bone marrow is steadily improving. A vast number of new treatment options have transformed multiple myeloma from a terminal disease into a chronic one that can be managed on a long-term basis.

Under the leadership of Sundar Jagannath, MD, Director of the Multiple Myeloma Program and Professor of Medicine (Hematology and Medical Oncology), The Tisch Cancer Institute at The Mount Sinai Medical Center now runs the largest multiple myeloma program in New York City. Approximately 80 patients are enrolled in 23 clinical trials. Two of the trials are studying the use of vaccines in different patient populations—those with pre-multiple myeloma, characterized by excess protein but a low level of plasma cells, and those whose disease is in remission.

“Mount Sinai has taken a multidisciplinary approach to treating multiple myeloma,

and works closely with the Bone Marrow Transplantation Service, and the departments of Cardiology, Rheumatology, Nephrology, and Pathology, among others,” says Dr. Jagannath. “We are part of the fabric of Mount Sinai.”

Mount Sinai also works closely with the Multiple Myeloma Research Foundation, the nonprofit organization that supports innovative treatments for the disease. Together they are carrying out the genomic sequencing of 1,000 newly diagnosed multiple myeloma patients.

Physicians in the program gain a tremendous amount of clinical knowledge through the trials, which in turn, offer patients the unique opportunity to live longer, healthier lives.

“Now that people with multiple myeloma are living longer, they have to be surrounded by multidisciplinary care,” says Steven J. Burakoff, MD, Director of the Tisch Cancer Institute, Professor of Oncological Sciences, and Professor of Medicine, Hematology, and Medical Oncology. “Mount Sinai has the ideal setting.



Sundar Jagannath, MD

There are new drugs that have to be evaluated in clinical trials. Dr. Jagannath, a great clinician and investigator, has been an integral part of these trials.”

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ABC News Spotlights Mount Sinai’s Global Health Program, *continued from page 1*

Global Health program, care for patients. JFK Medical Center, a gift from the U.S. government in the 1960s, is a bare-bones medical facility that had no electricity and running water just five years ago.

This was the doctors’ second trip to Liberia through HEARTT (Health Education And Relief Through Teaching), a program that enlists the support of physicians from Mount Sinai and nearly 20 other top U.S. medical schools. The American doctors stay for approximately one month to teach Liberian health care workers—physicians, nurses, and birth attendants—how to improve care for their patients. The segment aired last November.

“Our main goal isn’t to provide primary care,” says Dr. Sechler. “It’s to train their people to do this. When someone says, ‘I appreciate what you taught me, and I’m a better doctor for it,’ that’s rewarding.”



In the *Nightline* segment on Mozambique, which aired last December, correspondent Juju Chang traveled to the remote perimeter of Gorongosa National Park with two Mount Sinai physicians. Anu Anandaraja, MD, MPH, is Director of the Global Health Training Program and Assistant Professor of Pediatrics and Medical Education, and Sigrid Hahn, MD, MPH, is Associate Director of the Global Health Training Program, and Assistant Professor in the Department of Emergency Medicine.

Roughly 225,000 people live in the buffer area around Gorongosa that was decimated by war. Mount Sinai is working with the nonprofit Gorongosa Restoration Project and the government of Mozambique as part of a comprehensive effort to restore the park’s once-abundant wildlife and ecosystem, and improve the health of nearby residents, many of whom suffer from diarrhea, malaria, and HIV, which often prove deadly.

“It is estimated that one-third of these deaths could be avoided if the people weren’t malnourished,” says Dr. Anandaraja. “Our emphasis is on building local health care capacity by building a health care workforce.”

Three times a year, she, Dr. Hahn, and Mount Sinai residents and medical students visit Mozambique to train local community health workers to recognize and treat illness, and to help get people to the nearest medical facility, which can be hours away on foot.

They also teach traditional birth attendants about neonatal care, family planning, and the danger signs to look for in infants and young children.

Torian Easterling, MD, left, and Andy Sechler, MD, teach Liberian health care workers how to ensure that newborns are breathing properly. PHOTO COURTESY ABC NEWS NIGHTLINE

RESEARCH FRONTIERS

Mount Sinai Opens Center for Health Equity and Community Research

Mount Sinai School of Medicine recently created the Center for Health Equity and Community Engaged Research (CHECER) to conduct research that improves the health of vulnerable and underserved populations in New York City. CHECER will operate within the Department of Health Evidence and Policy and maintain a multidisciplinary focus by drawing upon Mount Sinai's groundbreaking translational research in cancer, metabolic disease, cardiovascular disease, maternal-child health, emergency medicine, and pediatrics.

"This is the place where we come together to understand and eliminate health disparities, and work with community members and leaders to improve local health," says Carol Horowitz, MD, MPH, Associate Professor of Medicine, and Health Evidence and Policy, and Co-Director of CHECER.

According to Nina Bickell, MD, MPH, Associate Professor of Medicine, and Health Evidence and Policy, and Co-Director of CHECER, "There are ways to improve the health of vulnerable populations, but the system is not helping them as it should."

One example of such a failure became apparent when Mount Sinai researchers found that breast cancer survival rates among women in New York State were lower among low-income Latinas and African Americans than white women, even when they had received early screenings and appropriate surgeries. "We found there was a system failure," says Dr. Bickell. "Surgeons thought they had ordered follow-up treatments but the women weren't getting them." Dr. Bickell is now working with hospitals to close that loop.

Another glaring inequity is the higher rate of depressive symptoms among African-American and Latina postpartum mothers in East Harlem. Elizabeth Howell, MD, MPP, Associate Professor of Obstetrics, Gynecology



FROM LEFT: Co-Directors of the Center for Health Equity and Community Engaged Research (CHECER), Nina Bickell, MD, MPH, and Carol Horowitz, MD, MPH; and Associate Director Elizabeth Howell, MD, MPP

and Reproductive Science, and Health Evidence and Policy, and Associate Director of CHECER, has been working with psychiatrists, psychologists, and social workers to establish educational programs that have successfully reduced depression among these women.

The center will look for novel strategies to conduct clinical trials among vulnerable populations that traditionally have had very low participation. "We are developing trials people want to be in, and we have really robust recruitment," says Dr. Horowitz. The ultimate goal, she adds, is to create change that is sustainable long after the trials are over, and that will influence health, health systems, and social policies.

YOUNG PIONEERS

Uncovering Clues to Early Stent Thrombosis

Researchers at Mount Sinai School of Medicine helped identify four gene variants and six clinical factors that contribute to early stent thrombosis (ST). The findings were published in the October 26, 2011, *Journal of the American Medical Association*.

"Our research indicates that early stent thrombosis is strongly related to the ineffectiveness of the blood thinner clopidogrel in certain patients," said the study's first co-author Jean-Sébastien Hulot, MD, PhD, Associate Professor of Medicine (Cardiology) and Director of Pharmacogenomics and Personalized Therapeutics at the Cardiovascular Research Center at Mount Sinai School of Medicine.

The study was conducted in partnership with the Institut de Cardiologie at Pitié-Salpêtrière University Hospital in Paris, France. Researchers evaluated the DNA of 123 patients who had undergone percutaneous coronary intervention,

and developed early ST while being treated with a dual antiplatelet therapy of aspirin and clopidogrel. A web registry of patients in France, known as ONline ASSistance for Stent



Jean-Sébastien Hulot, MD, PhD

Thrombosis (ONASSIST), provided the patient information. Investigators compared the DNA results to those of 246 coronary patients without early ST. They found that CYP2C19*2, which is commonly associated with loss of enzyme function, was highly prevalent in individuals presenting with early ST, as was the ABCB1 3435T variant. Yet both were infrequent in the control group. Significantly, two other variants, CYP2C19*17 and ITGB3, were prevalent in the control group but not in the early ST group, indicating a protective effect.

Separately, the research team also discovered six clinical factors—among them, a low dose of clopidogrel in combination with the use of a proton pump inhibitor drug—that also increased early ST risk. From the data, they developed, for the first time, a comprehensive clinical and genomic score to identify patients at risk for early ST.

■ NEW FACES

Jagat Narula, MD, PhD



Jagat Narula, MD, PhD, an internationally acclaimed physician-scientist in clinical cardiovascular medicine and imaging, has joined Mount Sinai School of Medicine as Philip J. and Harriet L. Goodhart Professor of Medicine (Cardiology), and Associate Dean for Global Health. Dr. Narula also was named Director of the Cardiovascular Imaging Program at the Zena and Michael A. Wiener Cardiovascular Institute and the

Marie Josée and Henry R. Kravis Center for Cardiovascular Health. He plans to develop a cardiovascular imaging program, and a center at Mount Sinai for global prevention of cardiovascular diseases.

Dr. Narula's groundbreaking research helped establish imaging strategies to identify patients susceptible to heart attacks and those likely to develop symptomatic heart failure.

He has published extensively in major basic science and clinical journals, including *Science*, *Nature Medicine*, *PNAS*, *The New England Journal of Medicine*, and *The Lancet*, and is actively involved in population-based heart attack prevention programs, including the Heart Attack Prevention Program for You (HAPPY). Dr. Narula is the Editor-in-Chief of the *Journal of the American College of Cardiology: Cardiovascular Imaging* and the Editor-in-Chief of *Global Heart*, the official journal of the World Heart Federation. He was recently named Editor-in-Chief of Friedberg's *Diseases of the Heart*. A renowned mentor, Dr. Narula was recently honored with the American College of Cardiology's Gifted Educator Award for 2012.

Ila R. Singh, MD, PhD



Ila R. Singh, MD, PhD, a basic scientist whose work in retrovirology has garnered international recognition, has joined Mount Sinai School of Medicine as Professor and Vice Chair of Clinical Pathology in the Department of Pathology.

Widely respected for her academic rigor and in-depth analyses, Dr. Singh has become a leader in the research of XMRV, a novel retrovirus. Her seminal paper on the role of

XMRV in chronic fatigue syndrome was the largest and most meticulously performed study on the subject. Dr. Singh is now researching genome-wide approaches to better diagnosis and treatment of this disease in collaboration with Eric E. Schadt, PhD, Director of the Institute for Genomics and Multiscale Biology, and Chair of the Department of Genetics and Genomic Sciences at The Mount Sinai Medical Center.

Dr. Singh has run National Institutes of Health-funded research laboratories for more than 12 years, and has trained undergraduates, graduate students, post-doctoral fellows, and residents. In 2008, she joined the University of Utah and ARUP Laboratories as Medical Director and Associate Professor of Pathology.

After receiving her medical degree from the University of Bombay, Dr. Singh completed her residency in Clinical Pathology at Columbia University School of Medicine, and received her PhD from Yale University's School of Medicine. She served as a Jane Coffin Childs Fellow at Stanford University School of Medicine.

Janina Longtine, MD



Janina Longtine, MD, a nationally recognized leader in molecular pathology and diagnostics, has joined The Mount Sinai Medical Center as Professor and Vice Chair of Molecular Pathology and Genetics in the Department of Pathology.

Known for her commitment to translational research and mentoring, Dr. Longtine served as Chief of Molecular Diagnostics at Harvard Medical School, and in 2004,

spearheaded a collaborative effort to bring online the first diagnostic assay for targeted drug therapy for lung carcinoma (the EGFR mutation analysis for "Gefitinib"). The partnership among Brigham and Women's Hospital (BWH), Massachusetts General Hospital and the Laboratory for Molecular Medicine set a precedent for the proactive role of the pathologist in translating molecular pathogenesis into effective therapies for patients.

Dr. Longtine was the founding Program Director of the Harvard Medical School Molecular Genetic Pathology Fellowship. Recently, she served as Co-Director of The Personalized Cancer Medicine Partnership, a collaboration between the Dana-Farber Cancer Institute and the Brigham and Women's Hospital to help realize the promise of "personalized medicine" for every patient seeking cancer care. In addition, she is highly valued for her clinical expertise in hematopathology and has led a core laboratory supporting clinical research in acute lymphoblastic leukemias. In 2010, Dr. Longtine was recognized by the BWH Physicians' Organization with its prestigious Clinical Innovation Award.

Harshwardhan M. Thaker, MD, PhD



Harshwardhan M. Thaker, MD, PhD, a renowned specialist in fetal/placental pathology and mechanisms of cancer, has joined The Mount Sinai Medical Center as Professor and Vice Chair of the Department of Pathology. Dr. Thaker's expertise as a diagnostician and administrative leader will enable him to assume a key role at Mount Sinai.

For nearly seven years, Dr. Thaker was director of the Tissue and Tumor Bank at Columbia University College of Physicians and Surgeons, a core facility of the Herbert Irving comprehensive Cancer Center, which he developed into a state-of-the-art repository that attracted funding from the National Cancer Institute. Dr. Thaker transformed the facility, creating encrypted databases that provided detailed pathological information about each sample with links to clinical databases, and downstream molecular genetic applications.

At Columbia, Dr. Thaker engineered many operational improvements in the Pediatric Pathology service. By forging clinical partnerships, he improved utilization of the service and increased clinical volumes. His research collaborations led to numerous publications and grants.

Prior to his arrival at Mount Sinai, Dr. Thaker had been Director of the Perinatal Pathology and Pediatric Autopsy Service at the University of Utah's ARUP Laboratories, and the Primary Children's Medical Center of the Intermountain Health Care, where he helped create centralized services throughout the state.

A \$10 Million Gift for Food Allergy Research

Philanthropist David H. Koch recently donated \$10 million to the Jaffe Food Allergy Institute at The Mount Sinai Medical Center, to create the David H. and Julia Koch Research Program in Food Allergy Therapeutics. The program will serve as a hub for drug discovery related to food allergies, and build upon the promising work already under way at Mount Sinai. The additional recruitment of leading scientists will help establish a robust team dedicated to food allergy therapeutics. Mr. Koch is Executive Vice President of Koch Industries, and a major advocate for medical research. The gift represents one of the largest donations ever made to the Jaffe Food Allergy Institute.

Hugh A. Sampson, MD, Director of the Jaffe Food Allergy Institute, said Mr. Koch's gift strengthens Mount Sinai's position as a global leader in food allergy therapeutics. "Right now, the only recourse for patients who have

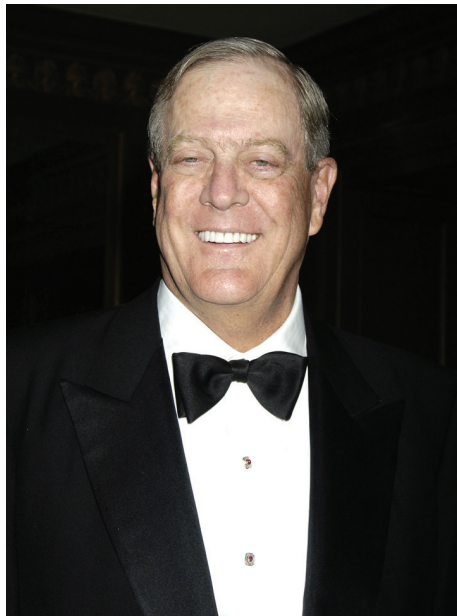
"My hope is that in the not-too-distant future, children who suffer from life-threatening food allergies will have their lives transformed from the therapies that originated here."

— DAVID H. KOCH

food allergies is to avoid those foods," said Dr. Sampson. "This program has the potential to deliver the first therapies and cures for food allergy."

Kenneth L. Davis, MD, President and Chief Executive Officer of The Mount Sinai Medical Center, said, "Breakthrough therapeutics such as these will change the face of children's health. Mr. Koch's visionary philanthropy brings us one step closer to that goal."

According to Mr. Koch, future therapies can significantly improve children's lives. "This is an



David H. Koch

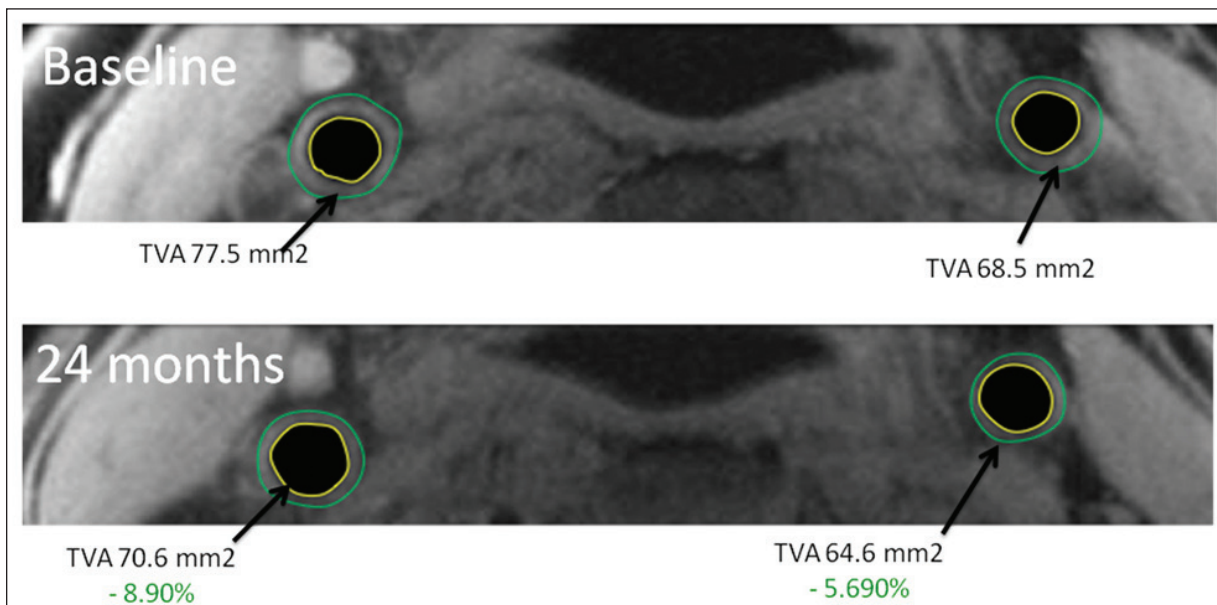


Hugh A. Sampson, MD

exhilarating time for science and medicine in food allergy, and Dr. Sampson and his team are the best at what they do. But the most exciting discoveries are yet to come," Mr. Koch said. "My hope is that in the not-too-distant future, children who suffer from life-threatening food allergies will have their lives transformed from the therapies that originated here."

Imaging Studies Determine the Efficacy of Heart Drugs

Sample MRI images from a patient at baseline and treated with dalcetrapib 600 mg for 24 months showing regression in Total Vessel Area (TVA)



TVA Average % change in carotid artery - 7.39% @ 24 months vs. baseline

In the September 12, 2011, issue of *The Lancet*, researchers from Mount Sinai School of Medicine showed that noninvasive imaging techniques were able to analyze the inflammation and progression of plaque in artery walls, and determine whether dalcetrapib, a new treatment for atherosclerosis was working. The study used positron-emission tomography (PET)/computed tomography (CT) and magnetic resonance imaging (MRI) to examine 130 patients over a 24-month period, and took place at 10 sites in the United States and Canada.

According to the team's lead researcher, Zahi A. Fayad, PhD, Professor of Radiology, and Medicine (Cardiology), and Director of the Translational and Molecular Imaging Institute at Mount Sinai School of Medicine: "After six months we were able to demonstrate that the drug had reduced the size of the inflammation, which gave us confidence that it was working."

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

How Not to Fix the ‘Doc Fix’

The Balanced Budget Act of 1997 was written in another time and, though very successful, produced a legacy for Medicare that 15 years later can have a calamitous impact on doctors and hospitals.

The sustainable growth rate (SGR) formula for Medicare—adopted as a footnote in the Balanced Budget Act—has been a ticking time bomb. The SGR pegs Medicare physician payments to the nation’s gross domestic product (GDP), rather than to the actual costs of running a medical practice. It was developed as a way to control federal spending on doctors, but the formula did not anticipate that Medicare patients would increase their use of physician services—which, for preventive and maintenance health, is desirable. So Medicare spending on doctors has grown faster than the overall economy, which is exactly what the SGR sought to avoid.

As such, year after year the SGR formula proposes to cut Medicare physician payments to align them with the GDP, but at the last minute, the realignment is averted and the spending gap grows ever larger. This year’s potential cut is a Draconian 27.4 percent. Reductions of this magnitude would be impossible for physicians to absorb and would, in turn, jeopardize their ability to provide care to Medicare beneficiaries.

Since 2002, Congress has avoided these cuts through a series of so-called “doc fixes” that stop reductions from going into effect. Now, with partisan bickering driving policy, this year’s doc fix is in jeopardy, and the proposed solution could be even worse than the problem it is trying to fix.

To pay for the doc fix, the U.S. House of Representatives has proposed cutting Medicare payments for hospital outpatient clinic evaluation and management (E/M) services. This idea stems from the misguided notion that hospitals should be able to provide the same services at the same costs as physicians do in their offices. It disregards significant hospital costs such as for caring for the uninsured and underinsured, having 24-hour standby and emergency facilities, and treating patients with more severe conditions.

The purported solution also fails to realize the vast differences in clinical billing regulations between hospitals and offices. Hospitals must accept a single fee that often includes multiple items and procedures that are essential to good care. Offices bill these items separately, with a lower fee for the primary consultation, but additional bills for necessary related costs such as imaging or certain drugs.

Nearly one-third of the proposed hospital cuts would impact just 6 percent of hospitals—America’s teaching institutions.

Hospitals already lose money treating Medicare patients, and under this doc fix, they would stand to lose another \$6.8 billion over 10 years. Hospital payments would be reduced by almost 75 percent—to about \$15 per visit. It is absurd to think this begins to cover costs for comprehensive E/M care. Medicare beneficiaries in underserved communities who rely on hospital-based clinics for care would be particularly impacted as these community resources are forced to close. Nearly one-third of the proposed hospital cuts would impact just 6 percent of hospitals—America’s teaching institutions.

It is time for this shell game to stop. You cannot help physicians—or patients—by hurting the hospitals where they train and work, or by pitting doctors and hospitals against one another. Other solutions for the doc fix must be found.

Kenneth L. Davis, MD, is President and CEO of The Mount Sinai Medical Center in New York City.



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THE CHARLES R. BRONFMAN INSTITUTE
FOR PERSONALIZED MEDICINE

Director: Erwin P. Bottinger, MD

CHILD HEALTH AND DEVELOPMENT INSTITUTE

Director: Bruce D. Gelb, MD

DISEASE PREVENTION AND PUBLIC HEALTH INSTITUTE

Director: Paolo Boffetta, MD, MPH

EXPERIMENTAL THERAPEUTICS INSTITUTE

Director: Srinivas Iyengar, PhD

THE FRIEDMAN BRAIN INSTITUTE

Director: Eric J. Nestler, MD, PhD

GLOBAL HEALTH AND EMERGING PATHOGENS INSTITUTE

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