WINTER 2009

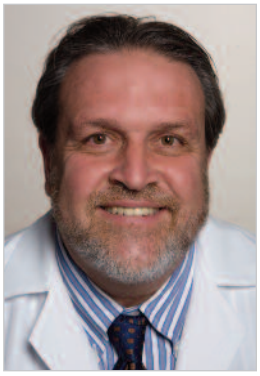
DEAN'S QUARTERLY

Mount Sinai
MSSM
MOUNT SINAI SCHOOL OF MEDICINE

ACCELERATING SCIENCE – ADVANCING MEDICINE

Rethinking Medical Education

In 2008, after years of planning, Mount Sinai School of Medicine embarked on a major transformation of its curriculum, a dramatic re-thinking of how we train physicians and scientists to advance medicine in the 21st century.



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

At the undergraduate level we created—and continue to develop—dynamic courses and programs that embody our institution's commitment to translational medicine. We are also transforming our curriculum to support the early integration of science and clinical medicine.

Two new curricular components are already in place—the Individual Scholarly Project and Independent Research Experience (INSPIRE) and the Longitudinal Clinical Experience (LCE). INSPIRE provides students with up to six months of protected time to undertake meaningful and mentored scholarship, and LCE gradually introduces first-year students to a panel of chronically ill patients that they will follow—with the guidance of a clinical preceptor—throughout medical school.

Later this year, you will receive a publication that details our new educational approach and curricular changes.

At our Graduate School of Biological Sciences, first-year predoctoral students can apply to our new Training Program in Translational Basic Research. Working with basic science and clinical mentors, a cadre of students will take special courses and participate in research dedicated to translational science. They will join mentors on clinical rounds, and learn about intellectual property and commercialization through our Office of Technology and Business Development. Upon completion of the two-year program, students will be awarded a Certificate in Translational Basic Science.

Mount Sinai's goal is to provide medical and graduate students with an exemplary education in translational science. Building on a long tradition of medical and scientific firsts, the physicians and scientists we train will continue to anticipate the future of medicine and deliver the breakthrough science needed to improve health outcomes and save and extend millions of lives.

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

HONORED FOR SERVICE AND DEDICATION

The Mount Sinai Medical Center was presented with the Humanitarian and Public Service Emmy Award during a ceremony at the National Health Science Summit at Rockefeller Center's legendary Rainbow Room on November 7.

The award was given by the National Academy of Television Arts & Sciences in recognition of Mount Sinai's ongoing commitment to advancing medical research and improving public health. Mount Sinai is the first and only academic medical center in the country to receive this Emmy Award. Previous award recipients include The Aspen Institute, The Metropolitan Museum of Art, and Partnership for a Drug-Free America.

Accepting the award, Kenneth L. Davis, MD, President and CEO of the Medical Center, thanked everyone and reflected upon the institution's history and core values of caring for all individuals regardless of racial or socioeconomic backgrounds.

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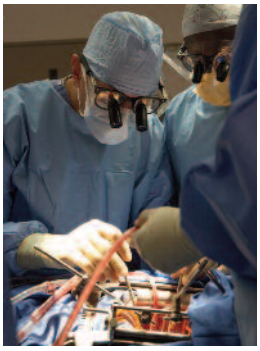
INSIDE THIS ISSUE

REPAIR MORE HEART VALVES — DR. ADAMS EXPLAINS



David H. Adams, MD

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

David H. Adams, MD, is a "superspecialist" in mitral valve repair—90 percent of his patients have mitral valve disease, and he and his team perform about 300 valve repair surgeries a year.

Dr. Adams is the Program Director of Mount Sinai's Mitral Valve Repair Reference Center—one of the most successful mitral valve repair reference programs in the country—and is the Marie-Josée and Henry R. Kravis Professor and Chairman of Cardiothoracic Surgery at Mount Sinai.

Two percent of the US population has mitral valve disease, resulting in 100,000 operations every year—roughly half of which involve repair and half which involve artificial replacement using a metal or animal valve. Dr. Adams wants to change that equation so more patients undergo repair, which provides better outcomes.

Replacement comes with several risks: bioprosthetic valves calcify and wear out over time; mechanical valves require lifelong anticoagulation with inherent increased risks of bleeding and thromboembolism. This is why the major guidelines for valve intervention all recommend mitral valve repair whenever feasible.

"Mitral valve repair is more technically challenging and focuses on rebuilding the patient's own damaged tissue," Dr. Adams says. The benefit to the patient, however, is measured in lower mortality and stroke rates evident as early as five years after surgery. Yet despite recognition of the benefits of valve repair over replacement, "one in three patients operated on in the United States continues to undergo replacement of a potentially repairable valve," says Dr. Adams.

To help change this equation, Dr. Adams was recently appointed to chair a Society of Thoracic Surgeons Task Force that will work toward improving mitral valve repair adoption and educating the medical professional community about repair procedures.

Dr. Adams and his team gave over 30 national and international invited lectures on their philosophy and results with mitral valve repair over the past year. The Mitral Valve Repair Reference Center also boasts one of the largest video libraries of mitral valve repair ever assembled.

HONORED FOR SERVICE AND DEDICATION (CONTINUED)

FROM LEFT: Journalist Charlie Rose (LEFT) with Valentin Fuster, MD, PhD, Director of Mount Sinai Heart, after presenting Dr. Fuster with the Global Prevention Prize; Dennis S. Charney, MD, leads a panel discussion on Pioneers of Modern Medicine; Kenneth L. Davis, MD, President and CEO of The Mount Sinai Medical Center (LEFT), accepts the Humanitarian and Public Service Award from presenter and basketball legend Magic Johnson at the National Health Science Summit.

"This started 155 years ago, about a group of people who had the vision to do the right thing," Dr. Davis said. Mount Sinai sits on "the fault line of the richest and poorest zip codes," he added. However, "no matter how hard economic times might be, we will continue to stand by our core values."

During the Summit, Mount Sinai Heart and its director, Valentin Fuster, MD, PhD, received the first annual Global Prevention Prize. The Global Prevention Prize, sponsored by US Preventive Medicine, acknowledges achievements that improve the quality and longevity of patients' lives as well as help advance a culture of prevention. Dr. Fuster was honored for his work around the globe in treating and preventing cardiovascular disease and for revolutionizing cardiac care both in the United States and in developing countries.

The award was presented to Dr. Fuster by journalist and PBS television talk show host Charlie Rose, who commended Dr. Fuster and Mount Sinai Heart for working to "change not just the way we live, but the way our children will live."
"I am honored to receive The Global Prevention Prize and grateful to US Preventive Medicine for such a recognition," said Dr. Fuster. "Cardiovascular disease is the number-one killer throughout the world. In just the United States, the cost of treating cardiovascular disease doubled from about $150 billion a decade ago to about $300 billion in 2005. This trend will continue unless we aggressively focus on preventing heart disease and promoting healthy living."

To see more of the award presentation and the National Health Science Summit awards ceremony and panels, visit http://www.mountsinai.org /Summit

GRANT WILL CREATE NEW SYSTEMS BIOLOGY CENTER

The National Institute of General Medical Sciences (NIGMS), a division of the National Institutes of Health, gave Mount Sinai a five-year, $13.3 million grant to support the creation of the new Systems Biology Center New York, the only NIGMS-funded facility of its kind in the state.

Led by Ravi Iyengar, PhD, Professor and Chair of Pharmacology and Systems Therapeutics, and Professor of Oncological Sciences and of Psychiatry, the Center brings together a team of experts in biomedicine, mathematics, engineering, and computer science from the Courant Institute of Mathematical Sciences, New York University; the State University of New York at Stony Brook; the City College of New York; Columbia University, College of Physicians; and the IBM Thomas J. Watson Research Laboratory.

"Medicine is heavily driven by clinical studies and observations. At the Center, we want to ask deeper scientific questions, such as, 'If cells begin to behave a certain way, what happens to the tissues?' or 'How does one organ system communicate with another?'" says Dr. Iyengar. "These questions sound simple, but the answers are complex. They could help us understand why people develop disease, who is at risk, and what we can do to possibly prevent illness. What we learn will help us personalize medicine even more."

The Center will study the heart and brain, and how diseases affect these organs. The researchers will conduct benchside studies using animal models to assess activity at the cellular and tissue levels. They will also investigate how drugs impact disease progression.

Ravi Iyengar, PhD

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

MOUNT SINAI LEADS NATION'S LARGEST HEALTH STUDY

A team of researchers headed by Dr. Philip Landrigan, MD, Chair of the Mount Sinai Department of Community and Preventive Medicine, has begun knocking on doors in Queens to recruit 4,000 pregnant women or women who intend to soon become pregnant to participate in the National Children's Study (NCS).

The $3 billion NCS, authorized by Congress in 2000, is the largest longitudinal study of human health undertaken in American history, with the goal of following 100,000 children from before birth through age 21 to document how environmental and genetic factors influence their health and development. Ultimately, the study will expand to 105 counties nationwide, including Manhattan, Brooklyn, and Nassau in New York and Passaic, Middlesex, Warren, and Monroe in New Jersey.

"By following children from before birth and examining factors such as family history, environmental quality, and exposure to chemicals, we can develop guidelines that in the future may reduce childhood illnesses such as asthma, autism, and diabetes," says Dr. Landrigan.

Participants receive free prenatal and postnatal medical screenings and referrals if health issues are detected by NCS investigators. Eligibility in the study is not affected by previous health conditions or immigration status.

Philip Landrigan, MD

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

Young Pioneers

ON THE PATH TO A CURE FOR TYPE 1 DIABETES

Brian D. Brown, PhD, Assistant Professor of Genetics and Genomic Sciences, did not necessarily view himself as a pathfinder, but the National Institute of Diabetes and Digestive and Kidney Diseases did—Dr. Brown received the Diabetes Pathfinder Award, a new, five-year federal grant that supports creative new investigators with innovative research projects focused on type 1 diabetes, a disease that affects more than 300,000 Americans. Dr. Brown received $2.5 million.

Dr. Brown and his team work in the field of gene transfer and gene therapy to induce immunologic tolerance. "Your body has mechanisms for naturally maintaining tolerance and preventing autoimmunities," Dr. Brown says. "These mechanisms break down in type 1 diabetes patients. The idea is to develop a vaccination that puts the antigen—in this case, insulin—into a pathway to boost the immune system's tolerance and reduce the chance that the immune system is going to respond against this antigen."

Brian D. Brown, PhD

Dr. Brown and his colleagues will determine if they can target the vaccine to specific cell types that have a physiologic role in maintaining immunologic tolerance. Then they will assess whether their approach can induce tolerance to insulin. Finally, they will use a mouse model of diabetes to evaluate the effectiveness of the vaccine. The hope is to change the future of type 1 diabetes care: health care providers could screen at-risk patients based on family history, and then perform a genetic blood test to determine the likelihood of developing type 1 diabetes before administering the vaccine.

To learn more, visit www.mountsinai.org/PathfinderAward/Brown

Eric A. Rose, MD

ERIC A. ROSE, MD

Eric A. Rose, MD, has been named Chairman of the Department of Health Policy at Mount Sinai Medical Center and Associate Director for Clinical Outcomes at Mount Sinai Heart.

Dr. Rose is a world-renowned surgeon and scientist who performed the first successful pediatric heart transplant, changing the course of medical history. He also organized and led the first trial to conclusively demonstrate that long-term use of mechanical circulatory support devices prolongs and enhances life in non-transplantable, end-stage heart disease patients.

A pioneer of medicine in many ways, Dr. Rose has been involved in grants totaling more than $25 million in funding and is the recipient of prestigious awards, including the John Jay Award and the Allen O. Whipple Memorial Award in surgery. Dr. Rose was Surgeon-in-Chief and Chair of the Department of Surgery at New York–Presbyterian Hospital/Columbia University Medical Center for 13 years, and is a past President of the International Society for Heart and Lung Transplantation.

The Mount Sinai Medical Center is honored to welcome a clinician of such stature and expertise into two vitally important roles with the Department of Health Policy and Mount Sinai Heart.

Eric J. Nestler, MD, PhD

ERIC J. NESTLER, MD, PHD

Eric J. Nestler, MD, PhD, was recently appointed Director of the Mount Sinai Brain Institute, Nash Family Professor of Neuroscience, and Chair of the Department of Neuroscience.

Dr. Nestler is a renowned neuroscientist, molecular biologist, and psychiatrist whose work focuses on how the brain responds and adapts to harmful experiences. He has made great strides in developing molecular and animal model techniques to unravel the reward and motivation pathways in the brain. Dr. Nestler will lead research on the role of neural repair in diseases that cause structural nerve cell damage, such as Alzheimer's disease, Parkinson's disease, Lou Gehrig's disease, and multiple sclerosis. He will examine how the brain's potential for neuronal regeneration may help treat psychiatric disorders and addiction.

Dr. Nestler earned his medical and postdoctorate degrees at Yale University School of Medicine, and completed his residency training at McClean Hospital. On the Yale faculty he was Director of the Abraham Ribicoff Research Facilities and of the Division of Molecular Psychiatry. Later, he served as Chairman of the Department of Psychiatry at the University of Texas Southwestern Medical Center at Dallas. Dr. Nestler was elected to the Institute of Medicine in 1998 and to the American Academy of Arts and Sciences in 2005.

Peter L. Elkin, MD

PETER L. ELKIN, MD

Peter L. Elkin, MD, has joined us as Vice President of Biomedical and Translational Informatics, Vice Chairman of the Department of Medicine for Biomedical Informatics, and Director of the Center for Biomedical Informatics.

A leader in biomedical informatics, Dr. Elkin is renowned for building biomedical data infrastructure systems and protocols that have transformed research and clinical care. At Mount Sinai, he will develop a program to integrate data collected in Mount Sinai's genomics and proteomics laboratories and will establish electronic quality-monitoring systems.

Dr. Elkin has been credited with starting the field of concept-based indexing and fully automated electronic quality monitoring. Among many other accomplishments, he has created and implemented bioinformatics standards for data storage and exchange. He has been elected to Mastership by the American College of Physicians and is the index recipient of the Homer R. Warner Award for outstanding contributions to the field of medical informatics.

After earning his medical degree from New York Medical College, Dr. Elkin completed an internal medicine residency at the Lahey Clinic and a National Institutes of Health–sponsored fellowship in medical informatics at Harvard Medical School and Massachusetts General Hospital.

Dr. Elkin spent the past 12 years at the Mayo Clinic College of Medicine. As Professor of Medicine and Director of the Biomedical Informatics Research Collaborative there, he did much to advance the emerging field of biomedical informatics, making significant contributions toward improvements in research and clinical care.

SUPPORTING THE FUTURE

The Wiener family lays the groundwork for groundbreaking research

Mount Sinai Trustee Michael A. Wiener and his wife, Zena, have committed $5 million to The Mount Sinai Medical Center to establish The Wiener Family Cardiovascular Research Laboratories. Mount Sinai celebrated the gift with a reception in the Atran-Berg Building last fall that was attended by faculty, trustees, and supporters. The reception also included tours of the laboratory space.

The Wieners' gift will fund scientific research that focuses on unraveling the basic mechanisms of heart failure, the discovery of new genes associated with the development of heart failure, and the clinical use of gene therapy to treat patients afflicted with heart failure and other cardiovascular diseases.

The science conducted within the new Wiener Family Cardiovascular Research Laboratories will fall under the umbrella of Mount Sinai's Cardiovascular Research Center and contribute to investigations already in progress. Under the leadership of Roger J. Hajjar, MD, the Arthur and Janet C. Ross Professor of Medicine, the Center is exploring the molecular mechanisms of cardiovascular disease and translating basic findings to novel therapies and diagnostic techniques. Dr. Hajjar pioneered the study of gene therapy for congestive heart failure at Harvard Medical School before joining Mount Sinai in 2006.

"The creation of The Wiener Family Cardiovascular Research Laboratories will allow for more discovery at the basic level and help advance research to the clinical trial phase," Dr. Hajjar says.

Five million Americans have congestive heart failure. There are approximately 500,000 new cases and 280,000 deaths every year. Dr. Hajjar's lab is looking at both gene-based and regenerative therapies. The gene-based therapies focus on replacing defunct genes causing disease with functional genes.

"We identified that calcium-cycling abnormalities within a cardiac cell of a patient with heart failure are related to a deficiency of SERCA2a, an important transporter," Dr. Hajjar says. "This discovery allowed us to focus on developing tools and delivery methods to restore SERCA2a to normal levels and improve cardiac function and the quality of life for patients with this debilitating disease."

> There are things going on now at Mount Sinai that will make a difference six months, a year, five years down the line.
>
> — Michael A. Wiener

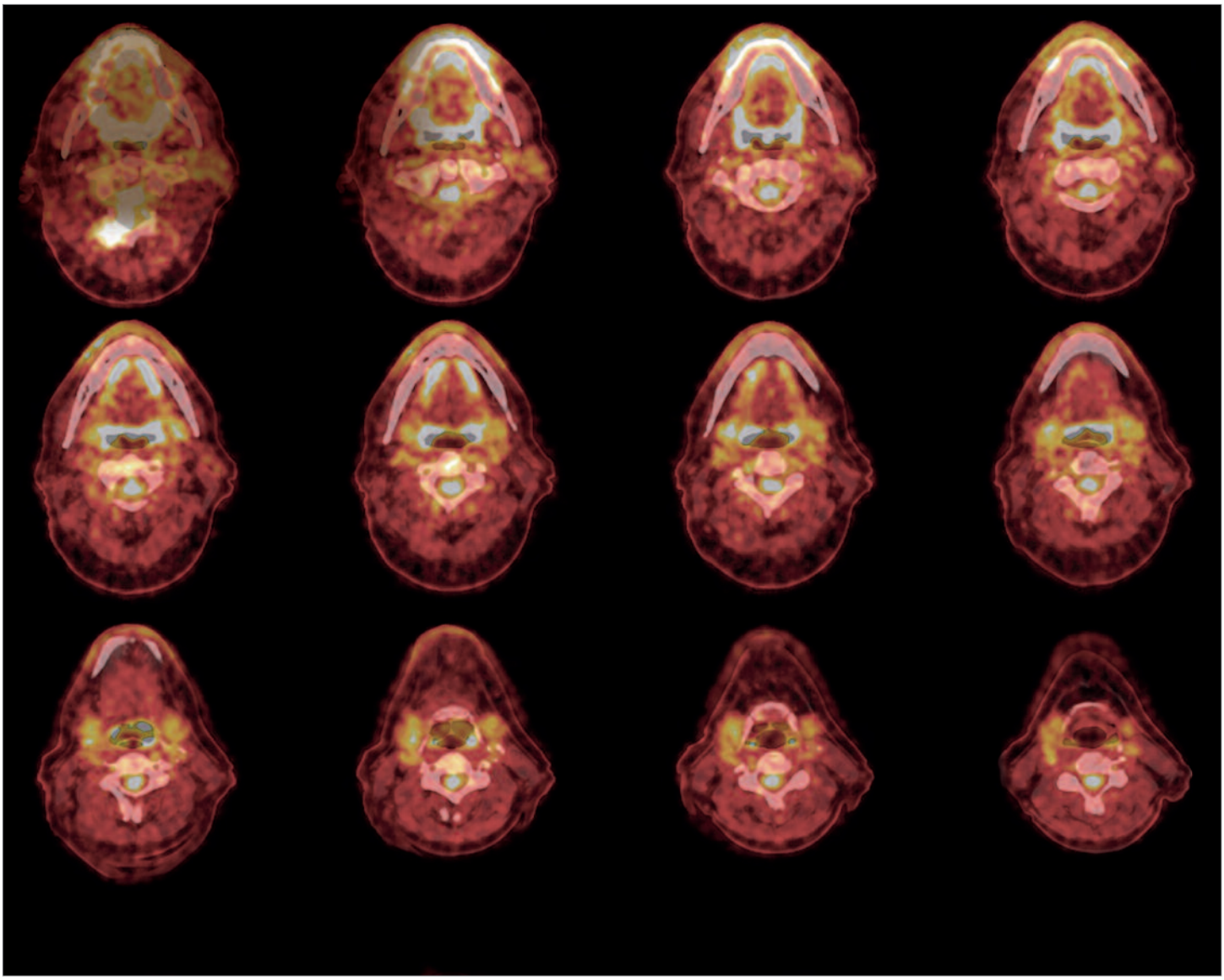
This breakthrough gene treatment is delivered directly to the patient's heart muscle during a routine outpatient catheterization procedure. Patients who received the genetically targeted enzyme replacement therapy, called MYDICAR®, showed significant improvement. Mount Sinai and 12 other US medical institutions are currently enrolling patients for a phase two clinical trial, Calcium Up-Regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease (CUPID Trial).

LEFT TO RIGHT: Roger J. Hajjar, MD; Michael A. Wiener, and Zena Wiener

Recent developments in regenerative research have also shown promising results. "The heart was thought not to have regenerative capacity, but instead it has been found to contain endogenous stem cells that can repair damaged tissue," says Dr. Hajjar.

"We discovered that we can induce pleuripotency stem cells or embryonic stem cell–like cells from skin biopsies using specific factors and then make any type of specific organ cell. That has opened up the way for potentially new diagnostic tools—you can now take a skin sample from a patient and try to understand what happens to their heart cells or their coronary vessels. You can also take those same skin cells and induce cardiac cells to repopulate the damaged area. It is a very exciting time for both gene and cell-based therapies in cardiology."

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



POSITRON EMISSION TOMOGRAPHY IMAGES FROM A PATIENT WITH CARDIOVASCULAR DISEASE

Positron emission tomography images from a patient with cardiovascular disease. The images show inflammation in the carotid arteries due to atherosclerosis. These images are used to detect the disease and to monitor the treatment response. This technique relies on the use of a sugar analogue (FDG) to evaluate the level of inflammation, a marker of high-risk atherosclerotic plaques in the arteries, and is an example of the innovative work performed at Mount Sinai and the Translational and Molecular Imaging Institute.

PHOTO BY: Zahi A. Fayad, PhD,
Professor of Radiology and Medicine (Cardiology),
Interim Director of the Translational and Molecular Imaging Institute,
Director and Founder of the Eva and Morris Feld Imaging Science Laboratories, and
Director of Cardiovascular Imaging Research at the Mount Sinai School of Medicine
and Mount Sinai Medical Center

WORTH THE RISK

Public policy must change to encourage development of breakthrough drugs

Advances in biology, genetics, and molecular biology are creating a watershed moment in medical science. Those of us at the leading edge of research in the life sciences, especially at academic medical institutions, see extraordinary opportunities.

Kenneth L. Davis, MD, President and Chief Executive Officer of The Mount Sinai Medical Center

Yet, from the perspective of those on the front line of these discoveries, there is an enormous disconnect today between the potential of biomedical research coming out of large academic medical centers and the effort needed to translate that science into real, breakthrough drugs.

The problem isn't that pharmaceutical companies don't have large research programs or don't devote enough capital to research. Rather, the core of the problem resides within a pharmaceutical industry that, through no fault of its own, has become increasingly risk averse in its business model. There are several reasons:

• The cost of product development is skyrocketing. The expense of generating new molecules and then proving them efficacious and safe is becoming almost prohibitive, even without factoring in the very real possibility of failure.

• Existing patent law does not recognize the extended time it takes for drug discovery and development. Generic-drug makers are successfully able to challenge new drugs at a relatively early stage in their marketing cycles.

• It has become safer to develop analogues of existing compounds than to develop new compounds with novel mechanisms. A successful business model has been for companies to focus on creating and then marketing their own brand within various categories or reconfiguring formulations based on already approved drugs.

One need not look far to see the impact of these trends. In 2007, the Food and Drug Administration approved the fewest number of drugs of novel mechanism in nearly a quarter century. The new drugs that are introduced tend to be for indications that offer the largest market share rather than for the most severe human diseases. Drug companies are developing additional drugs for conditions such as allergies, erectile dysfunction, and insomnia that mirror existing pills.

In doing so, they neglect tackling harder challenges that may now be solvable with advances in research. However, the risks in developing truly novel compounds, particularly for very serious diseases, are enormous. Consequently, drug companies can find it safer to take on lifestyle rather than life-threatening conditions, particularly when prototype compounds for those conditions have already been approved. It is safer to invest in marketing than in drug development.

To correct the situation, federal legislation to encourage risk taking and discourage risk avoidance is needed. We should establish longer patent life for truly novel compounds and those offering significantly fewer side effects than approved compounds. Enhanced patent protection should be available for drugs that target diseases that are especially burdensome to the health care system, such as diabetes and Alzheimer's disease.

We should also consider tax disincentives to discourage the kind of direct-to-consumer advertising that supports the mass-market lifestyle approach to driving sales. At the same time, we should consider tax breaks to encourage the development of drugs for life-threatening diseases by providing higher write-offs to lower the cost of failure.

Far too many critics of the pharmaceutical industry concentrate on the size of its profits rather than the effectiveness of its business model. The question is whether the drug companies deliver what the medical establishment needs to extend and enhance the quality of human life, cure and prevent disease, and produce new forms of treatment. If the goal is to reform the pharmaceutical industry, it is essential that we understand how its business model is flawed, why the industry does what it does, and what regulation and reform could do to shift its priorities.

This article is excerpted from an essay by Kenneth L. Davis, MD published in *Modern Healthcare* on July 7, 2008. To read the full article, reprinted with permission, visit www.mountsinai.org /KennethDavis/ModernHealthcare.

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