

DEAN'S QUARTERLY

Mount
Sinai



MOUNT SINAI
SCHOOL OF
MEDICINE

ACCELERATING SCIENCE – ADVANCING MEDICINE

A Year of New Discoveries and Landmark Anniversaries

We begin 2011 ready for great achievements. This anticipation is grounded in our accomplishments from 2010, which was a year of landmark anniversaries and medical and scientific firsts at Mount Sinai.

At the turn of the twentieth century—when the practice of medical specialization was just emerging—our physician-scientists were developing expertise in novel therapeutic areas and conducting groundbreaking work that resulted in the establishment of four departments: Rehabilitation Medicine, Orthopaedics, Dentistry, and Radiation Oncology.

In organizing around clinical areas, departments such as these established the framework for modern-day academic medicine and translational science, setting the highest standards for all our work today.

We have, for example, taken human stem cells from patients with a rare developmental disorder and developed heart cells with hypertrophic cardiomyopathy. Our investigators have also discovered a new cell-recognition mechanism that helps regulate gene expression in the development of cardiac and muscle tissues. And we have found that immune cells that reside in the brain have a unique origin and are formed shortly after conception. Our aggressive cancer research agenda includes vaccines for treating high-risk hematological malignancies, including leukemia, lymphoma, and myeloma.

Funding from the National Institutes of Health is now more than \$275 million, the highest in Mount Sinai's history, and even during these economically challenging times, we are able to implement our \$2.2 billion strategic plan and to secure major recruitments in all departments. We have also maintained the pace of construction for the Center for Science and Medicine, a 550,000-square-foot facility that, when it opens in 2012, will increase our research capacity by 30 percent.

We believe that our institution is only as great as our graduates, and to that end, we have continued to transform the way we train our medical and basic science students. Much of our medical school curriculum now fully integrates both science and medical education—starting on day one. We have also realigned our basic science training along eight multidisciplinary training areas, a format that takes advantage of our robust research-institute structure and positions our students at the forefront of maturing and emerging disciplines.

With this and more, we look forward to another great year and, indeed, another impressive epoch, at Mount Sinai School of Medicine.



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

DISTINGUISHED BY SERVICE

Bridging Care from Pediatrics to Adult Medicine

The recently appointed chairs of the Departments of Medicine and Pediatrics at Mount Sinai School of Medicine are ushering in a new era of collaboration.

“Children diagnosed with diseases that were previously fatal soon after birth, such as autosomal recessive polycystic kidney disease, now live

into adulthood,” says Lisa M. Satlin, MD, Chair of the Department of Pediatrics and a pediatric nephrologist who collaborates extensively with her colleagues in the Samuel Bronfman Department of Medicine. “This and many other chronic diseases that are diagnosed early in life need to

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be managed as they evolve throughout childhood, adolescence, and adulthood.”

Capitalizing on Mount Sinai’s strength as one of the highest ranked digestive disease programs in the country, Dr. Satlin and Mark W. Babyatsky, MD, Chair of the Samuel Bronfman Department of Medicine, and a gastroenterologist, are focusing on inflammatory bowel disease (IBD) as one of their first areas of collaboration.

Plans are underway to bring together Mount Sinai’s adult and pediatric IBD centers under one roof, facilitating greater collaboration and interaction among physicians as their patients transition from pediatric to internal medicine care.

“By bringing together leaders in gastroenterology in pediatrics and medicine, immunology, and genomics, we hope to identify early risk factors for IBD and use these to develop novel treatment and prevention strategies.”

Research teams that include faculty from Medicine and Pediatrics, as well as Genetics and Genomics Sciences, have identified genes that predispose people to Crohn’s disease, and have helped define the critical role T-cell defects play in the pathogenesis of IBD. They are leading trials of potential new treatment approaches for IBD, and are exploring the origins of IBD through studies of the genomics of the gut.

“By bringing together leaders in gastroenterology in pediatrics and medicine, immunology, and genomics, we hope to identify early risk factors for IBD and use these to develop novel treatment and prevention strategies,” says Dr. Babyatsky.



Top: Mark Babyatsky, MD, Chair of the Samuel Bronfman Department of Medicine
Bottom: Lisa Satlin, MD, Chair of the Department of Pediatrics

Medical Milestones

SPECTRAL COMPUTED TOMOGRAPHY ENHANCES DETECTION OF HIGH-RISK CARDIOVASCULAR DISEASE

A team of Mount Sinai researchers has developed a unique approach to visualizing coronary artery plaques that are vulnerable to rupture. Using spectral computed tomography (CT), the innovative technique stands to revolutionize cardiac imaging in patients by enabling clinicians to obtain a more complete picture of atherosclerotic risk, thereby leading to better and earlier diagnosis of cardiovascular disease.

Led by Zahi A. Fayad, PhD, Professor of Radiology and Medicine and Director of the Translational and Molecular Imaging Institute at Mount Sinai School of Medicine, the team first inserted gold nanoparticles into high-density

lipoproteins (HDLs) and injected the lipoproteins into apolipoprotein E knockout mice. They then used CT to image the gold-HDL, which accumulated inside macrophages in areas of vulnerable plaque in the murine arterial walls.

Because spectral CT allows scientists to identify other materials in addition to gold, Dr. Fayad and his team were able to localize not only the gold-HDL but also calcium deposits and iodine-based contrast material. This novel combination of spectral CT and gold nanoparticles will enhance the diagnosis of high-risk cardiovascular disease by revealing the location and extent of plaque vulnerable to rupture.

Mount Sinai is the first institution to use this

scanner, made by Philips Medical Systems, in a preclinical setting.

“The acquisition of this technology and development of this method will help us improve cardiovascular disease diagnosis in our patients, furthering our commitment to translational research. We look forward to continuing our study of this technology in the clinical setting,” Dr. Fayad says.

To that end, spectral CT technology also may be beneficial in imaging other biological processes and diseases, including cancer, kidney disease, and bowel diseases. The Mount Sinai team plans to continue studying the new scanner in additional animal studies and in humans.

REPROGRAMMED STEM CELLS MAY LEAD TO IMPROVED DIAGNOSIS AND TREATMENT OF CARDIOMYOPATHY

A research team headed by Ihor R. Lemischka, PhD, Director of the Black Family Stem Cell Institute, and Lillian and Henry M. Stratton Professor of Gene and Cell Medicine, and Bruce Gelb, MD, Director of the Child Health and Development Institute, has made an important breakthrough by isolating human stem cells from patients with hypertrophic cardiomyopathy. The tissue culture of these stem cells will enable scientists to develop new diagnostic tools and medications to identify and treat cardiomyopathy at an earlier stage than is currently possible. The results of the team's research were published in the June 9, 2010, issue of *Nature*.

The research involved the use of skin cells from two patients with a genetic disorder known as LEOPARD syndrome. Hypertrophic cardiomyopathy, or thickening of the heart muscle, is experienced by 80 percent of patients with

LEOPARD syndrome and is the most life-threatening aspect of the disorder. The Mount Sinai team took patient skin cells and reprogrammed them to become pluripotent stem cells, which can develop into almost any type of cell in the human body. The researchers then created heart cells that had characteristics of hypertrophic cardiomyopathy.

Scientists know that genetic disorders occur because of a mutation in a protein-signaling pathway called the Ras pathway, but they have been unable to determine precisely how this results in disease-associated problems such as hypertrophic cardiomyopathy. The authors of the *Nature* study concluded that induced pluripotent stem cell-derived heart cells provide the characteristics required to precisely determine the pathology behind these disorders and represent a foundation for studying treatment interventions.



Ihor R. Lemischka, PhD, Director of the Black Family Stem Cell Institute

SCIENTISTS IDENTIFY A NEW MECHANISM BY WHICH DISEASE DEVELOPS

Ming-Ming Zhou, PhD, Professor and Chair, Structural and Chemical Biology, Mount Sinai School of Medicine, and his research team have discovered a new cell signal recognition mechanism involved in the regulation of gene expression during human cardiac and muscle tissue development. This cutting-edge research, published in the July 8, 2010, issue of *Nature*, may help scientists gain insight into the development of muscle and heart disease.

Using a combined structural and molecular biology approach, Dr. Zhou and his team found a new fundamental mechanism in gene transcription through a protein called DPF3b. They

learned that DPF3b recognizes gene-activating chemical marks in these DNA-packing histones very differently than was previously thought. DPF3b plays a critical role in the copying of genes—a crucial part of the transcription process—for muscle growth and heart development.

The results of this research may have important implications in the field of epigenetics and may enable researchers to understand the molecular basis of certain human disorders that result from dysregulation of gene expression. In particular, the research may help scientists uncover some of the molecular origins of abnormal cardiac and skeletal muscle development.



Ming-Ming Zhou, PhD, Professor and Chair, Structural and Chemical Biology

Young Pioneers

MICHAEL RENDL, MD



Michael Rendl, MD, Assistant Professor of Developmental and Regenerative Biology and of Dermatology

Michael Rendl, MD, Assistant Professor of Developmental and Regenerative Biology and of Dermatology, studies stem cell niches, the microenvironment where stem cells reside and receive cues that are essential for tissue growth and regeneration. As the leader of the Rendl Lab at the Black Family Stem Cell Institute, he and his team define the genetic program of stem cell niche cells in the hair follicle, called dermal papilla cells.

Dr. Rendl's dermatologic focus is unique. "No research has addressed how the microenvironment cells talk to stem cells, or looked at stem cell niche cells and the potential they have for hair regeneration," he says.

Since 2008, Dr. Rendl has received several awards for his pioneering work, including a 2010–2015 National Institutes of Health grant to study the cell fate specification of dermal papilla niche cells, two individual 2010–2012 New York State Stem Cell Science grants, and a 2008–2009 Research Career Development Award from the Dermatology Foundation.

Using genetic manipulation in mouse models, Dr. Rendl studies the process by which unspecialized skin fibroblast cells are programmed to become stem cell—activating, specialized dermal papilla niche cells. His lab also is working on dermal papilla niche cells as the preferred source of cells for generating induced pluripotent stem cells. Greater understanding of these processes holds promise for hair loss treatments and regenerative therapies for other tissues.



Randall F. Holcombe, MD, Director of Clinical Cancer Affairs

RANDALL F. HOLCOMBE, MD

Renowned colon cancer expert Randall F. Holcombe, MD, recently joined The Mount Sinai Medical Center as Director of Clinical Cancer Affairs. He also serves as Medical Director of the Ruttenberg Treatment Center, Associate Director for Clinical Affairs at The Tisch Cancer Institute, and Director of Gastrointestinal Medical Oncology for the Division of Hematology/Oncology.

In his role as Director of Clinical Cancer Affairs and Medical Director of the Ruttenberg Treatment Center, Dr. Holcombe will apply his broad experience in basic science and translational research to create a comprehensive, multidisciplinary care center while fostering an environment in which staff can conduct groundbreaking research.

Dr. Holcombe has served as the principal investigator on 127 clinical trials, and he led the team that was the first to describe the selective expression of the LEF1 gene in colon cancer. Most recently, his laboratory has begun examining the clinical effects of a naturally derived compound called resveratrol on the prevention or treatment of colon cancer.

Dedicated to educating and mentoring, Dr. Holcombe commits significant time to training students and

postdoctoral fellows. He has served as a fellowship director for the Accreditation Council for Graduate Medical Education–accredited hematology and oncology fellowship program and on several basic science graduate student thesis committees. His mentorship of undergraduate and medical students and laboratory and clinical fellows was supported through a National Institutes of Health K24 Midcareer Mentoring Award. He also served on the Council of Mentors for the Institute for Clinical and Translational Science at the University of California, Irvine.

After receiving his medical degree from the University of Medicine and Dentistry/New Jersey Medical School in 1983, Dr. Holcombe was a Resident Physician at Brigham and Women's Hospital in Boston and a Clinical Fellow in Medicine, Genetics, and Hematology/Oncology, with additional training in obstetrical hematology, pediatric hematology/oncology, and solid tumor oncology at Harvard Medical School. He also worked at Louisiana State University School of Medicine and the University of California, Irvine Medical Center before joining The Mount Sinai Medical Center.



Sundar Jagannath, MD, Director of the Multiple Myeloma Program

SUNDAR JAGANNATH, MD

Sundar Jagannath, MD, a renowned expert in the research and treatment of multiple myeloma, has joined The Mount Sinai Medical Center as Director of the Multiple Myeloma Program and as Professor of Medicine (Hematology and Medical Oncology) at The Tisch Cancer Institute. In his new role, Dr. Jagannath's goal is to expand Mount Sinai's cutting-edge translational and clinical research to find a cure for multiple myeloma. Such a cure, he feels, is on the horizon in the next decade. Under Dr. Jagannath's guidance, The Tisch Cancer Institute also will have one of the largest bone marrow transplant centers in the country, providing clinical care for a large patient population.

Prior to joining The Mount Sinai Medical Center, Dr. Jagannath served as Chief of the Multiple Myeloma and Transplant Program at St. Vincent's Comprehensive Cancer Center in New York City. The transplant program, which has stored stem cells of more than 300 patients, and the myeloma program, with ongoing clinical trials, have now been integrated into The Tisch Cancer Institute.

Over the past two decades Dr. Jagannath has published more than 180 peer-reviewed articles in top publications, including *Blood*, *Cancer*, *Journal of Clinical Oncology*, and *The New England Journal of Medicine*; has presented more than 150 abstracts; and has authored nearly 30 book chapters. In addition, Dr. Jagannath has received numerous awards for his commitment to multiple myeloma research, including two Humanitarian Awards and the Spirit of Hope Award from the Multiple Myeloma Research Foundation. He also is the Honorary Chairman of Laugh for Life, the foundation's annual fund-raiser.

After receiving his medical degree from Maharaja Sayajirao University of Baroda in India, Dr. Jagannath completed his residency in internal medicine at Bronx-Lebanon Hospital Center in New York and at Harper-Grace Hospital in Detroit, Michigan. He was awarded a fellowship in medical oncology from MD Anderson Hospital and Tumor Institute in Houston, Texas, and later joined the University of Arkansas as Chief of Bone Marrow Transplantation, and then St. Vincent's Comprehensive Cancer Center.

MARSHALL R. POSNER, MD

Marshall R. Posner, MD, has been appointed Medical Director of the Head and Neck Medical Oncology Program and the Cancer Clinical Trials Office at The Mount Sinai Medical Center, where he will provide outpatient and inpatient clinical service and oversee operations that include regulatory and staff management, and protocol review and monitoring.

In his leadership role at The Tisch Cancer Institute, Dr. Posner will conduct clinical and laboratory research focusing on human papilloma virus (HPV), oropharynx cancer, head and neck cancer, skin cancer, and other oncology-related diseases. At Mount Sinai School of Medicine, he holds professorships in the Division of Hematology and Medical Oncology, Department of Medicine, Department of Gene and Cell Medicine, and Department of Otolaryngology.

Dr. Posner's clinical trials in head and neck cancer include:

- A Phase I trial of concurrent chemoradiation/chemo-irradiation with Cetuximab (ERBITUX[®]), Sunitinib, and accelerated radiation in patients with

locally advanced/high-risk/recurrent poor prognosis head and neck cancer

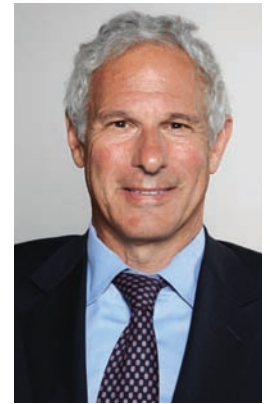
- HPV oral transmission study in partners over time

Other clinical trials in development involve metastatic iodine resistant thyroid cancer, anaplastic thyroid cancer, and reduced radiation therapy in patients with advanced HPV tumors.

Dr. Posner's research in head and neck cancer has been published nearly 200 times in top journals, including *Annals of Oncology*, *Cancer*, *Journal of Clinical Oncology*, and *The New England Journal of Medicine*.

Prior to joining Mount Sinai, Dr. Posner was Medical Director of the Head and Neck Oncology Program and an Associate Professor of Medicine at the Dana-Farber Cancer Institute and the Harvard Medical School.

He received his medical degree from Tufts University School of Medicine, and completed his internship and residency in internal medicine at Boston City Hospital and a fellowship in medical oncology at the Dana-Farber Cancer Institute.



Marshall R. Posner, MD, Medical Director of Head and Neck Medical Oncology Program

Philanthropy

JEAN C. AND JAMES W. CRYSTAL ANNOUNCE \$4.5 MILLION FOR ENDOWED GENOMICS PROFESSORSHIP



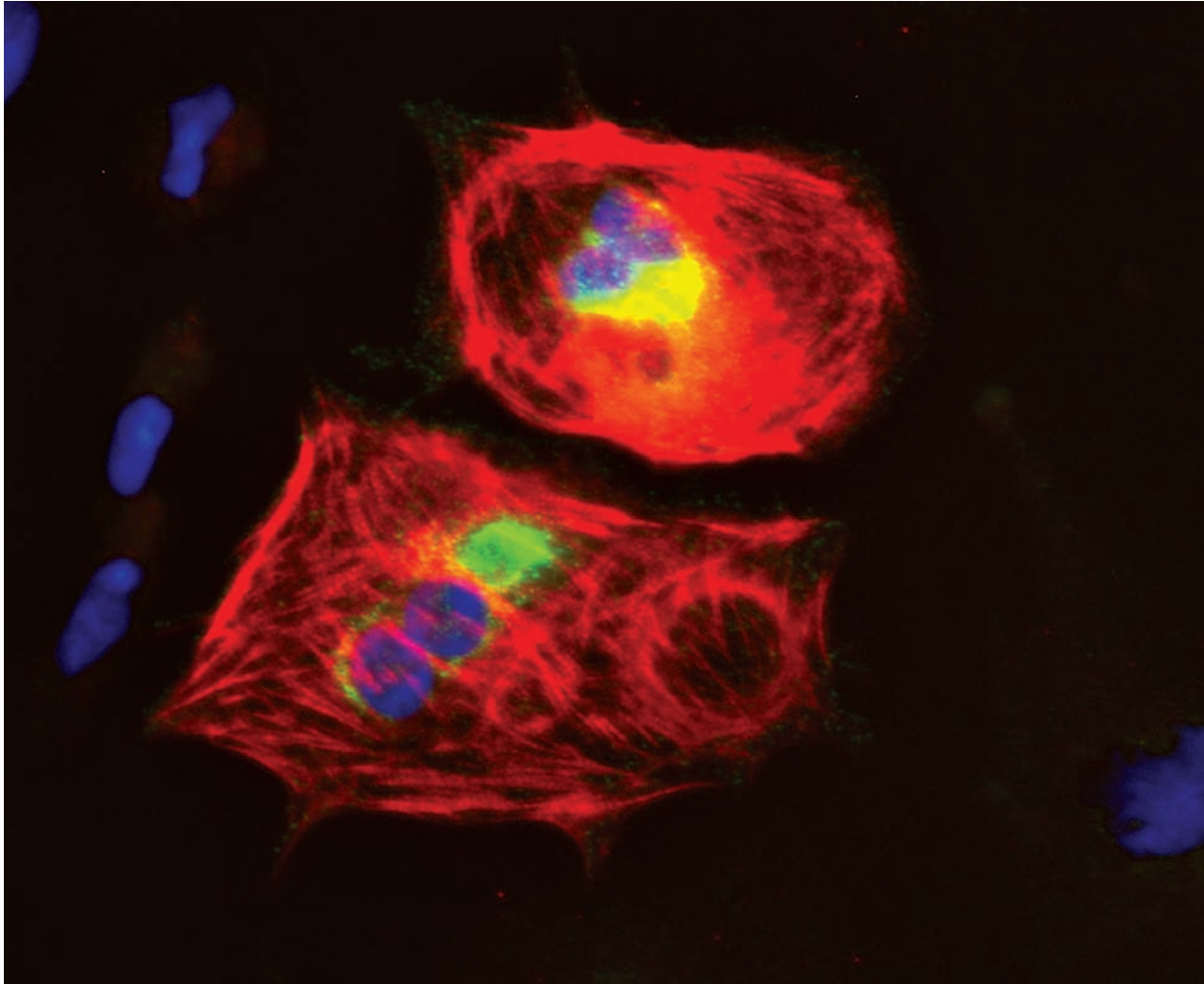
Trustees James W. and Jean C. Crystal

Trustees Jean C. and James W. Crystal, who have supported a variety of initiatives over the years, recently committed to Mount Sinai a gift of \$4.5 million to establish and name an endowed academic professorship for the director of the Genomics Institute at The Mount Sinai Medical Center, to be known as the Jean C. and James W. Crystal Professor of Genomics.

"The support of the Crystals allows Mount Sinai to bring the best talent and leadership on board at the Genomics Institute," says Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean of Mount Sinai School of Medicine. "This will strengthen not only the Genomics Institute but all of the other translational research institutes that will be working in conjunction with it."

"Jean and I believe strongly in the promise of genomics," Mr. Crystal says. "We believe the institute can help unlock many of the medical mysteries we currently face, and we are honored to be a part of that."

The Genomics Institute is a translational research hub focusing on genetics and proteomics for the Mount Sinai community. The institute applies state-of-the-art technologies and expertise to help investigators define genetic risk, identify harmful and protective variants, and explain pathogenic mechanisms in human diseases.



STEM CELLS USED TO CREATE ABNORMAL HEART CELLS

Using the Yamanaka reprogramming method, researchers at Mount Sinai School of Medicine have for the first time taken human stem cells from patients with a rare developmental disorder called LEOPARD syndrome and have developed heart cells with hypertrophic cardiomyopathy. By replicating these diseased heart cells, scientists can develop drug therapies and diagnostic tools to treat cardiomyopathy at earlier stages.

The red color in the two cardiomyocytes pictured above is a marker protein that defines the cells as cardiomyocytes, and the blue color marks the nucleus of the cells.

Photo by Xonia Carvajal-Vergara, PhD, lead author on the stem cell study and former postdoctoral fellow at Mount Sinai School of Medicine

SCIENCE AND MEDICINE IN THE SERVICE OF SOCIETY

Biomedical science matters most when it is translated into tangible benefits for patients. Every day, scientists expand our understanding of the genetic basis and molecular pathways underlying disease. This knowledge ultimately should be translated into highly personalized approaches to diagnosis, treatment, and prevention of disease for individual patients and communities.

As leaders in the education of tomorrow's physicians and scientists, how are we to respond to the expanding scope of twenty-first century research? At every level of our educational mission, we must seamlessly integrate clinical relevance into scientific research, and scientific principles into clinical training.

Historically, medical schools emerged within universities primarily to educate physicians, yet master's and PhD programs centered at medical schools now produce the vast majority of the scientists trained in biological arenas relevant to medicine. All too often, these programs simply coexist, isolated by different curricula and cultures.

If we are to maximize our capacity to affect clinical practice through scientific discovery, however, we need to produce leaders in biomedicine and health care who see themselves as members of large, interactive teams committed to clinically relevant breakthrough science. Clinically oriented medical school courses should become part of the graduate school curriculum, and translational scientists should be part of bedside rounds for physicians in training.

But we can take this one step further. For over a century, the defining mission of medical schools has been to care and advocate for the underserved and to push the envelope of biomedical research. Because of increasing specialization, technological advances, and the competitive nature of research funding, however, most medical schools in the country have had to commit to one primary goal: they are either research oriented or community and public-service oriented.

We need to produce leaders in biomedicine and health care who see themselves as members of large, interactive teams committed to clinically relevant breakthrough science

Teaching tomorrow's physicians and scientists this "hidden curriculum"—that science, service, and advocacy are unrelated—is an injustice both to our students and to our society. These can no longer exist as separate entities if we are to achieve our potential for applied innovation, such as preventing a patient from developing dementia or protecting a community from the environmental risks that will lead to cancer.



Science and service; innovation and advocacy. The National Institutes of Health already has embraced the need to bridge the chasm between the researcher's laboratory bench, the patient's bedside, and the community by setting an expectation for translational research that moves us toward the ultimate goal of better, more accessible care for all. Medical schools must acknowledge the equal importance of these missions if we are to produce leaders who will be agents for change, who will translate the bounty of scientific discovery into improved quality of life in our communities and across the globe. Science is the underpinning of everything we do, but in the absence of service, there is no context for understanding why our scientific breakthroughs matter.

John H. Morrison, PhD, is Dean of Basic Sciences and the Graduate School of Biological Sciences at Mount Sinai School of Medicine in New York City. David Muller, MD, is Dean for Medical Education at Mount Sinai School of Medicine.



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