

METABOLISM INSTITUTE

ACCELERATING
SCIENCE

ADVANCING
MEDICINE



MOUNT SINAI
SCHOOL OF
MEDICINE

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PASSION

Fierce Competition

Fierce Cooperation

We intend to create a research environment
that encourages collaboration and rewards
work that challenges conventional wisdom.

— DENNIS S. CHARNEY, MD

MESSAGE FROM THE DEAN



DENNIS S. CHARNEY, MD

The Anne and Joel Ehrenkranz Dean of Mount Sinai School of Medicine
and Executive Vice President for Academic Affairs of The Mount Sinai
Medical Center

Where Does the Future Happen?

I am very proud to introduce Mount Sinai School of Medicine's vision for its twelve translational research institutes. These institutes embody our mission as a leader in basic and clinical research and lie at the heart of the larger strategic plan for The Mount Sinai Medical Center.

Translational medicine has been synonymous with Mount Sinai since the founding of the Hospital in the mid-nineteenth century, when our doctors turned to their microscopes to better understand the conditions they had just encountered in their patients.

The halls of our medical school are lined with portraits of Mount Sinai pioneers who first described clinically complex disorders, including Crohn's disease, Churg-Strauss disease, Tay-Sachs disease, and Brill's disease.

This passion for patient-focused research inspired another generation of physicians, who created Mount Sinai School of Medicine. Today, we are building upon this legacy with a research model that moves beyond the conventional departmental structure that typically governs medical schools.

Our plan originated in 2005, when I invited over 100 of Mount Sinai's leading researchers to form twenty-two working groups that would address our future. Together, we agreed that Mount Sinai had an unparalleled opportunity to transform itself into an even more powerful translational medical institution.

The basic infrastructure of The Mount Sinai Medical Center, a medical school embedded in a hospital, is tailor made for collaborative projects that can progress rapidly, unencumbered by a complex bureaucracy. In fact, Mount Sinai is unique among academic medical centers in not being accountable to either a university administration or a governmental organization.

During two years of intense study and discussion, we identified areas of research where Mount Sinai can truly be a world leader. This analysis formed the basis of the twelve research institutes that you will learn more about in subsequent chapters.

Each institute is designed to facilitate breakthrough science. We intend to create a research environment that encourages collaboration and rewards work that challenges conventional wisdom. Scientists from different departments and disciplines will be provided the intellectual freedom, the physical space, and the financial support they need to pursue their best ideas. Further, these research institutes will be characterized by organizational flexibility in order to maximize our capacity to respond quickly to scientific advances.

As the medical sociologist Rogers Hollingsworth observes, the most successful scientists possess “high cognitive complexity,” which gives them the capacity to see important relationships among disparate fields of knowledge. Both the physical design and intellectual atmosphere of our institutes reflect this insight, by encouraging the constant and open exchange of ideas. I believe we have greatly increased the potential for major discoveries at Mount Sinai by designing our research model to reflect Hollingsworth’s findings.

Seven of our institutes are disease oriented, focusing on the brain, cancer, child health and development, the heart, immunology, metabolism, and emerging pathogens.

Five institutes will complement and advance the work of the disease-oriented institutes: experimental therapeutics, molecular imaging, personalized medicine, stem cell research, and disease prevention and public health.

Our decision to target areas where Mount Sinai can excel also governs research priorities within the institutes, which build upon established clinical and research strengths, the expertise of our new recruits, our unique location at the intersection of New York’s most and least affluent zip codes, and our long-standing commitment to all of the communities that Mount Sinai serves.

Above all, Mount Sinai will continue to encourage and support the bold thinking and disciplined science that can fundamentally

change the face of medicine. Heart and brain researchers, for example, are working toward restoring tissue and repairing functions thought to have been lost forever. Experts in children's health are uncovering the genetic and environmental underpinnings of asthma, the primary cause of school absenteeism in New York City. Diabetes researchers are unraveling the complex web of factors that contributes to a national health crisis. Cancer investigators are using new knowledge of stem cells to fundamentally transform the fight against one of the leading causes of death worldwide.

These and myriad other investigations will take place on a campus invigorated by the new Center for Science and Medicine, which is designed to promote translational research. This 450,000-foot facility will house six full floors of laboratory space built to encourage scientists to share ideas and findings on an informal basis.

The Center will also be home to our cancer clinics and labs, and our new imaging center. This will facilitate communication between researchers and their clinical partners and will enable patients and doctors to take full advantage of the latest technologies. Overall, the Center for Science and Medicine, scheduled to open in 2012, will increase our research capacity by 30 percent.

Mount Sinai School of Medicine is a magnet for visionary scientists and clinicians, and I am honored to be working with such a passionate and productive group of colleagues.

VISION

Rigorous Thinking

Revolutionary Medicine

Many discoveries are now within our grasp, including those that will increase the plasticity of the human brain, rejuvenate damaged heart tissue, and protect society from devastating pandemics.

— KENNETH L. DAVIS, MD

MESSAGE FROM THE PRESIDENT AND CEO



KENNETH L. DAVIS, MD
President and Chief Executive Officer of The Mount Sinai Medical
Center and the Gustave L. Levy Distinguished Professorship

A Portrait of the Future

We are living at a watershed moment in medical science. The elaboration of the human genome has created a revolution in biology that is equivalent to the revolution in physics that occurred in the early years of the twentieth century. Between 1890 and 1920 a sequence of basic discoveries set the stage for nuclear energy, transistors, and rapid communication, transforming life to such an extent that someone living a century ago could not have imagined the world of today.

The current revolution in the biomedical sciences reflects an increased understanding of how genes are controlled and how proteins are made and can be changed, and it presents unprecedented opportunities for the development of new classes of drugs and diagnostic tools. Armed with such new innovations, the medical profession can treat and cure some of the most serious diseases and conditions known to humanity, improving outcomes and extending millions of lives.

Those of us at the leading edge of research in the life sciences, especially at academic medical institutions, see extraordinary opportunities before us every day. I am particularly proud that The Mount Sinai Medical Center has both the intellectual and financial resources to deliver on these opportunities.

Our new institute structure, as envisioned by my colleague Dennis Charney, will accelerate the pace of breakthrough ideas. We have carefully chosen the areas of research in which we can excel, and we have recruited world-renowned scientists and clinicians to join our distinguished faculty. Many discoveries are now within our grasp, including those that will increase the plasticity of the human brain, rejuvenate damaged heart tissue, and protect society from devastating pandemics.

Financially, The Mount Sinai Medical Center is in sound condition, giving us the capacity to recruit world-renowned talent, support young scientists, build new facilities, and fund novel ideas.

Furthermore, successful translational medicine, by its very nature, promises to increase intellectual property and royalties, hospital revenues from new treatments and therapeutics, National Institutes of Health funding, and future philanthropy.

Our success and our stability as an academic medical institution reflect both the wisdom of the institute plan and the strength of the entire Mount Sinai team. Thanks to their efforts and foresight, we have every reason to be optimistic about the future of Mount Sinai and the future of medical science.

Breaking Ground

Building Greatness

The creation of twelve translational
research institutes is a bold move forward and a
natural evolution of Mount Sinai's legacy.

— PETER W. MAY

MESSAGE FROM THE CHAIR



PETER W. MAY
Chair of the Boards of Trustees

Building the Right Place at the Right Time

For over 150 years, Mount Sinai physicians have advanced science, and accelerated the pace at which research breakthroughs have been developed into novel therapies that benefit our patients. The creation of twelve translational research institutes is a bold move forward and a natural evolution of Mount Sinai's legacy.

Today, the revolution in the biological sciences is opening new avenues for investigation and even greater opportunities to improve patient care. At this critical moment, Mount Sinai is ideally positioned to shape the future of medicine.

Our endowment has grown to \$1.1 billion. This important measure of stability reflects both sound financial management and the long-term generosity of so many of our supporters.

Last year alone, Mount Sinai raised a record \$147 million in philanthropy, and soon we will launch a \$1 billion capital campaign to fuel Mount Sinai's comprehensive strategic plan. Many of the families responsible for our extraordinary growth are continuing a tradition that dates to the founding of the Hospital in the nineteenth century.

We are about to break ground for the new Center for Science and Medicine, a state-of-the-art facility that will serve as a focal point for our translational research efforts. The Center will include six full floors of laboratory space and will house all of Mount Sinai's cancer-related research, clinics, and advanced imaging technologies. With almost a half million square feet of space, the Center will increase our overall research capacity by a full 30 percent.

Recently, The Mount Sinai Hospital and Mount Sinai School of Medicine received an "A"-category rating from Moody's Investors Service. This is a tremendous achievement and represents the fruition of all of our financial improvement efforts. Among our particular strengths, Moody's praises our "focused and driven management team committed to financial success."

Of course, the most important component of Mount Sinai's growth is the superb quality of our scientists and physicians. Over the past two years, Mount Sinai has recruited scores of world-renowned researchers and clinicians who have chosen an environment that offers the freedom to explore new avenues of inquiry and the opportunity for cross-disciplinary collaboration.

As Board Chair, I am proud that Mount Sinai is in a position to fully support the unified vision of Dr. Davis and Dr. Charney, and encourage the work of so many remarkable medical pioneers.

THE CENTER FOR SCIENCE AND MEDICINE

The new Center for Science and Medicine will be a state-of-the-art, modern facility that will house both clinical care and basic research programs. Designed to increase interaction and collaboration among faculty and staff practicing a variety of disciplines, the building will feature wide open spaces, significant laboratory and clinical care space, as well as a roof lounge.



Construction for the Center for Science and Medicine is scheduled to begin in 2008 and is expected to take approximately three to four years. The 450,000-square-foot facility will increase Mount Sinai School of Medicine's research capacity by about a third.



METABOLISM INSTITUTE

Derek LeRoith, MD, PhD

Director

Life
in the
balance.

The Metabolism Institute was created in response to urgent and chronic health care needs of people with diabetes and obesity. The problems posed by these conditions are especially evident at The Mount Sinai Hospital, where approximately one-third of patients are diagnosed with diabetes. This chronic condition is also reaching epic proportions in our neighboring communities of East and Central Harlem and is on the rise worldwide. Underlying this epidemic is a complex relationship among metabolism, lifestyle, and genetics. Never before has the need been as urgent and the opportunity as great for breakthroughs in research and treatment.

The development and promotion of obesity- and diabetes-prevention programs are key areas of translational research in the Metabolism Institute.



Patient Populations

The Mount Sinai Medical Center straddles two communities that share an inverse relationship between income and obesity and diabetes rates. In East Harlem, which is primarily Hispanic and where many people live below the poverty level, obesity and diabetes rates are estimated to be about eight times higher than in the Upper East Side, which is largely Caucasian and affluent. Consequently, complications of stroke, cardiovascular diseases, cancer, kidney failure, and leg amputation occur more often and strike at an earlier age in the East Harlem community than in the Upper East Side.

Type 2 diabetes no longer affects just those in mid- and late-life; increasingly, this condition, along with obesity, appears in young adults, adolescents, and even children. Therefore, research aimed at helping people of all ages is part of the Metabolism Institute's strategic plan.

Many of those hit hardest by the dual epidemics of obesity and diabetes can least afford treatment, so when they finally come to the hospital, they often require the most extensive care. Thus, there is an urgent need to put effective prevention strategies into place that can benefit an entire community, perhaps even an entire generation, and potentially reduce health care costs associated with the treatment of these chronic conditions. The development and promotion of obesity- and diabetes-prevention programs are key areas of translational research in the Metabolism Institute.

Building on Existing Research

The Metabolism Institute emerged from the Department of Medicine's Division of Endocrinology, Diabetes, and Bone Disease. Among its first recruits was a diabetes epidemiologist with experience in clinical trial design. The Institute, while still recruiting, is currently collaborating with clinical investigators in many other departmental programs, including:

- *The Diabetes Center of Excellence, a New York State-funded program in the Department of Health Policy;*
- *The Metabolic Monitoring Program in the Department of Psychiatry, which tracks patients taking antipsychotic drugs;*
- *The Division of Experimental Diabetes and Aging in the Department of Geriatrics and Adult Development;*

- *The Neurobiology of Aging Laboratory in the Department of Neuroscience;*
- *The Division of Adolescent Health in the Department of Pediatrics;*
- *The Division of Transplantation in the Department of Surgery;*
- *The Program for Inherited Metabolic Diseases in the Department of Genetics and Genomic Sciences; and*
- *Mount Sinai Heart, which includes the Department of Medicine's Division of Cardiology as well as the Department of Cardiothoracic Surgery.*

Target Areas for the Metabolism Institute

Epidemiology of Obesity and Type 2 Diabetes

The epidemiology program is focused on identifying risk factors and protective factors for obesity and type 2 diabetes, including dietary, environmental, and behavioral variables, and on studying the interactions within the diverse populations that Mount Sinai serves.

Mount Sinai's catchment area offers opportunities for epidemiologic and genetic studies among ethnically diverse populations that few other academic medical centers in the world can claim.

This program has reported findings about the limited availability of fresh produce in the East Harlem neighborhood and has partnered with community members to initiate change.

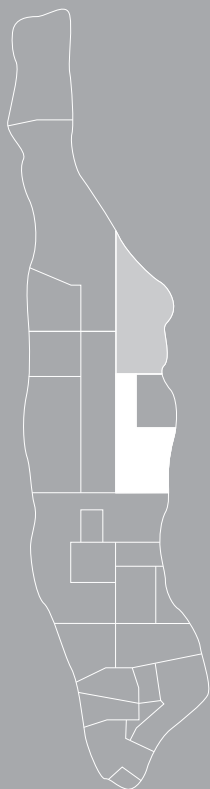


Furthermore, newly recruited faculty with expertise in epidemiology and clinical study design are providing guidance for expanding ongoing efforts, such as the Department of Health Policy's New York Center of Excellence Harlem Diabetes Program. This program has reported findings about the limited availability of fresh produce in the East Harlem neighborhood and has partnered with community members to initiate change, such as bringing a green market to the community and advocating for fresher, more nutritional foods at local stores. Ongoing collaboration with the Metabolism Institute will enable the Health Policy faculty to further expand its programs.

Genetics of Metabolic Disorders

The genetics of metabolic disorders program works to identify the critical genetic factors that increase or decrease the risks for various aspects of obesity and type 2 diabetes. Studies in this program are investigating genetic contributions to comorbid conditions such as kidney failure, given that only a subset of diabetics succumb to kidney failure.

MANHATTAN
New York City



OBSESITY



31%

EAST HARLEM



7%

UPPER EAST SIDE

DIABETES



15%

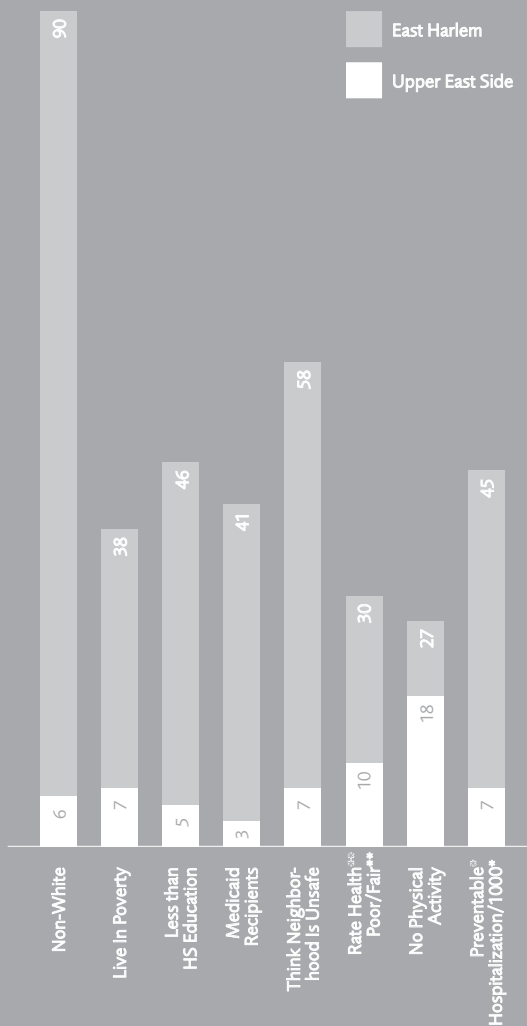
EAST HARLEM



2%

UPPER EAST SIDE

MOUNT SINAI SERVES
THE POPULATIONS WITH
NEW YORK CITY'S HIGHEST
AND LOWEST RATES OF
OBESITY AND DIABETES.



FAULT LINE (NUMBERS IN PERCENTS)

*EH has highest rate in NYC

** EH has highest rate in Manhattan

In the long term, this program will also look for hereditary factors that influence individual responses to new therapies for diabetes or obesity.

These studies apply in-depth, genome-wide scanning techniques, first to find informative polymorphisms and ultimately to identify candidate disease genes. Success requires large numbers of patients and controls, and sizeable numbers of families with and without the diseases. When candidate genes are found, the research will then move into cellular or animal – primarily rodent – models of the putatively defective genes.

Pathophysiology of Metabolic Disorders

The program in pathophysiology is researching and identifying the mechanisms that underlie these metabolic diseases. “One of the areas that’s really very hot, and that surprised us, is the role the hypothalamus plays not just on appetite but on the function of tissues like the fat cell, the liver, the muscle, the pancreas, all of which are important for obesity in type 2 diabetes,” says Derek LeRoith, MD, PhD, Director of the Metabolism Institute, the Lillian and Henry M. Stratton Professor of Molecular Medicine, and Chief of the Division of Endocrinology, Diabetes, and Bone Disease. “For a long time we focused on the pancreas, the liver, the muscle, and the fat cell, but now we are focusing on how the gut plays an important role and how the brain is probably very critical in controlling all of these systems.”

The Institute is also partnering with Helen Vlassara, MD, Director of the Division of Experimental Diabetes and Aging, and the Mount Sinai Professor in Diabetes and Aging, and her team to study issues surrounding diabetes and aging. “Our research has focused on the AGEs, the advanced glycation end products,” says Dr. Vlassara. “Underneath all chronic diseases is a dominating oxidative process that makes us slowly decline. We used to call it aging, normal aging. In fact, we are learning that there is no such thing. But younger people do acquire a lot of diseases, including diabetes, which used to be the companion of old age. This has made us tremendously interested in the concept of health-span as opposed to life span.”

The Institute is also investigating conditions such as progressive liver disease, non-alcoholic hepatosteatosis (NASH), and other specific disorders that frequently accompany obesity and diabetes. In the case of obesity, investigations will range from behavioral studies, such as on

eating disorders, to cellular studies for understanding abnormal rates of adipogenesis. In diabetes, investigations cover topics such as insulin secretory dysfunction and defects in insulin action. This research will use both human tissue biopsy specimens and animal models.

These studies require core facilities such as nuclear magnetic resonance (NMR) spectroscopy as well as magnetic resonance imaging (MRI) and computed tomography (CT) scanning and therefore will be done in collaboration with members of the Translational and Molecular Imaging Institute.

Translational Research on Metabolic Disorders and Treatments

Discoveries made at the bench will be introduced into the clinical arena, first by investigating their utility in a clinical research setting and then in clinical trials for such common disorders as childhood/adolescent obesity and type 2 diabetes; obesity and NASH; and type 2 diabetes and complications, such as cardiovascular disease and kidney failure.

As an example, Mount Sinai neuroscientists working with an already approved drug have evidence suggesting that the drug may be useful in treating obesity. Under the umbrella of the Metabolism Institute, they will collaborate with clinicians from the Division of Endocrinology, Diabetes, and Bone Disease to study a cohort of obese patients in a weight-reduction clinic, examining the feasibility of testing the drug in patients in the clinic.

As another example of interdisciplinary translational research, researchers in the Metabolism Institute are collaborating with faculty in Surgery to build a program in pancreatic islet-cell transplantation. Development of islet-cell transplantation strategies for treating type 1 diabetes has been under way for several years. However, it is increasingly apparent that people with type 2 disease also undergo pancreatic islet-cell shutdown over time. Given the epidemic proportions of type 2 diabetes and the decrease in age of disease onset, there is a need for creating a long-term treatment, such as islet-cell transplantation, which now seems a viable strategy for halting disease progression. The Metabolism Institute is developing a program to address this.

Extramural Collaborations

Some research in metabolism may be best served by joining forces with groups outside Mount Sinai. A prime example involves a joint effort with investigators at the State University of New York at Stony Brook. This basic research on rodent metabolism is leveraging a well-established facility for rodent metabolic studies at Stony Brook and exceptional computational strength at Mount Sinai.

The Metabolism Institute has also partnered with pharmaceutical companies to create a training program for endocrinology clinicians in key aspects of clinical drug testing. This allows a large number of endocrinologists to more quickly acquire critical expertise in the design and execution of clinical trial studies.

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