A New Capital Campaign Underway for 2017

Anticipating the future of medicine takes a village. At the Icahn School of Medicine at Mount Sinai, our village is an extraordinarily talented community of researchers and physicians who are busy laying the groundwork for our 2017 capital campaign. Through a robust exchange of knowledge and ideas, hundreds of faculty members and more than 100 external advisors are helping to create a roadmap that will guide us over the next five years in prioritizing commitments and making investments in research and education that could ultimately change the practice of medicine.

What will Mount Sinai’s new capital campaign look like? Judging from our last strategic plan in 2008, it will focus on areas of medicine that we plan to develop further, as well as those that are just beginning to emerge. Our vision will unfold from the ground up in a process that requires creativity, innovation, and entrepreneurial spirit.

Our last campaign, which exceeded our goal of $1.5 billion, was a game changer for the Icahn School of Medicine, resulting in the establishment of 16 multidisciplinary research institutes that increased collaboration and eliminated unnecessary silos. The strategic plan led to dramatic increases in our National Institutes of Health portfolio, which is now ranked No. 15 in the United States in overall dollars. Mount Sinai this year ranked No. 1 in microbiology, No. 3 in neuroscience and pharmacology, and No. 8 in genetics.

The creation of the Leon and Norma Hess Center for Science and Medicine, which increased Mount Sinai’s research space capacity by nearly 30 percent when it opened at the end of 2012, also arose from our last strategic plan. The Hess Center houses laboratories dedicated to research in cancer, the brain, heart disease, and genetics and multiscale biology.

As we embrace change once again, we have harnessed some of the best minds in science to help us chart a course that will ultimately improve human health. To fulfill this mission, our village must anticipate the future. We are limited only by our collective imagination.

Resilience Study Focuses on What Keeps People Healthy

Resilient adults who carry a mutated gene for a severe childhood disease but fail to develop it themselves may provide researchers with a promising avenue of investigation for developing new cures, according to scientists Eric Schadt, PhD, and Stephen Friend, MD, PhD, at the Icahn School of Medicine at Mount Sinai.

Leading a proof-of-concept study that appeared online in the April 11, 2016, issue of Nature Biotechnology, Drs. Schadt and Friend screened 589,506 individuals worldwide and identified thirteen who were healthy despite harboring mutations for eight Mendelian conditions, including cystic fibrosis and Smith-Lemli-Opitz syndrome. Dr. Schadt is the Jean C. and James W. Crystal Professor of Genomics and Director of the Icahn Institute for Genomics and Multiscale Biology. Dr. Friend, President and Co-Founder of Sage Bionetworks, is a Professor of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai.

Mendelian disorders—caused by a mutation at a single point in a person's genetic code—are rare but devastating. Very few treatments for these gene-destroying mutations are available and most of them relieve symptoms rather than provide a biological cure.

“Most genomic studies focus on finding the cause of a disease, but we see tremendous opportunity in figuring out what keeps people healthy,” says Dr. Schadt. “Millions of years of evolution have produced far more protective mechanisms than we currently understand. Characterizing the intricacies of our genomes will ultimately reveal elements that could promote health in ways we haven’t even imagined.”

Through a global collaboration that employed...
Public-Private Collaboration to Accelerate Cancer Discoveries

The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai and three additional leading U.S. academic institutions recently established a pioneering research consortium to accelerate the discovery of new treatments for cancer.

In addition, the global biopharmaceutical company Celgene Corp. paid $50 million to enter into four public-private collaboration agreements with each member of the new consortium for the option of developing and commercializing novel cancer therapeutics arising from their efforts. Celgene paid $12.5 million each to Mount Sinai, The Abramson Cancer Center at the University of Pennsylvania, The Herbert Irving Comprehensive Cancer Center at Columbia University Medical Center, and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Over the next 10 years, the academic cancer centers intend to present multiple high-impact research programs to Celgene with the goal of developing new life-saving therapeutics. Subject to Celgene’s decision to opt-in and license the resulting technologies, each program has the potential to be valued at hundreds of millions of dollars.

“This is a paradigm-shifting collaboration that further strengthens our innovative ecosystem,” says Bob Hugin, Executive Chairman of Celgene Corp. “We remain firmly committed to driving critical advances in cancer and believe the tremendous expertise of our collaboration partner institutions will be invaluable in identifying new therapies for cancer patients.”

The magnitude of the multi-institutional consortium and agreements will support the rapid delivery of disease-altering treatments to clinicians and ultimately benefit cancer patients, global health care systems, and society. Collectively, the four academic medical centers care for more than 50,000 new cancer patients each year and have nearly 800 faculty members involved in clinical care and basic and clinical cancer research. They are among the sixty-nine institutions designated as Cancer Centers by the National Cancer Institute (NCI), serving as the backbone of NCI’s research in the war on cancer.

Erik Lium, PhD, Senior Vice President of Mount Sinai Innovation Partners, who leads Mount Sinai’s development and commercialization division, helped spearhead the collaboration agreement. “This consortium allows the institutions to leverage their synergistic and individual strengths in research and patient care to accelerate the discoveries of new treatments for cancer,” he says.

Mount Sinai Unveils a Novel Platform for Characterizing Cancer

A novel method of characterizing prostate cancer that uses computer vision and artificial intelligence to help determine the best course of treatment for each patient is being rolled out this summer by the Lillian and Henry M. Stratton-Hans Popper Department of Pathology at the Icahn School of Medicine at Mount Sinai.

The platform, called Precise Medical Diagnosis™, or Precise MD, has been under development at Mount Sinai for more than three years by a team of physicians, scientists, mathematicians, engineers, and programmers. The proprietary diagnostic system creates detailed, specific data about the patient’s cancer cells using multispectral fluorescent imaging to evaluate biomarker status and architectural patterns and then sophisticated computer analytics to combine and create predictive models.

“Our goal is to improve the way we stratify patients into treatment groups,” says Gerardo Fernandez, MD, Associate Professor of Pathology, and Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai and Director of Precise MD. “By refining the treatment, we can save patients from unnecessary treatments and help improve the entire health care system.”

By combining multiple data sources, the new platform provides a view of cancer that is far more comprehensive than can be seen using conventional microscopes. Ultimately, this multilayered approach to analyzing and characterizing an individual’s prostate cancer may be used by pathologists as a more sophisticated alternative to a traditional grading system such as the Gleason Score, which has been used since the 1960s to guide a patient’s treatment options and establish his prognosis.

“Cancer diagnoses are based on pattern recognition. But pattern recognition is imprecise,” says Carlos Cordon-Cardo, MD, PhD, the Irene Heinz Given and John LaPorte Given Professor and Chair of the Department of Pathology at the Mount Sinai Health System. “We have created a Systems Pathology approach that integrates the patient’s electronic health records, phenotype, and genotype and overcomes the limitations of earlier technologies. This is truly the next generation in personalized medicine.”

Mount Sinai’s Department of Pathology processes more than 80 million tests a year, making it the largest department of its kind in the country.

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Reversing Cardiac Fibrosis Through Gene Targeting in Heart Failure

A matricellular protein, CCN5, has for the first time been found to reverse established cardiac fibrosis in heart failure models, according to research led by Roger J. Hajjar, MD, Professor of Medicine and Director of the Cardiovascular Research Center at the Icahn School of Medicine at Mount Sinai.

Dr. Hajjar collaborated with Woo Jin Park, PhD, Professor of Life Sciences at the Gwangju Institute of Science and Technology (GIST), South Korea, in a study that appeared online in the March 28, 2016, edition of the Journal of American College of Cardiology (JACC).

The study was funded by the National Institutes of Health and the government of South Korea.

“For the first time, we have demonstrated the ability to reverse cardiac fibrosis in heart failure models by targeting a specific gene,” says Dr. Hajjar. “Our findings demonstrate that CCN5 may provide a novel platform for the development of targeted anti-cardiac fibrosis therapies, which could benefit many patients with previously untreatable heart failure.”

Cardiac fibrosis occurs when healthy cardiac cells are replaced with fibrous connective tissue that causes scarring and stiffer, less compliant cardiac muscle. It is found to be an independent predictor for the progression of heart failure, which accounts for approximately 450,000 deaths per year in the United States. There are no effective cardiac fibrosis therapies currently available.

In earlier research, Dr. Hajjar found that CCN5 is significantly lower in the myocardium of patients with severe heart failure. In the most recent study, his team discovered the reversal of cardiac fibrosis eight weeks after transferring CCN5 to experimental animal models. The researchers used trichrome staining and analysis of myofibroblast contents before and after CCN5 gene transfer to clearly show the reversal.

“We may be able to deliver the CCN5 secreted protein itself rather than the CCN5 gene in the form of recombinant virus or stem cells that are engineered to express CCN5,” says Dr. Park. “The efficacy of these alternative approaches has yet to be tested, but they certainly deserve serious consideration.”

New Research Shows Depression May Be a Circuit-Level Disorder

New findings from the Icahn School of Medicine at Mount Sinai suggest that depression may be comprised of small changes affecting multiple genes located in several interconnected brain regions, rather than large changes that take place in a small subset of genes, which has been the long-held view.

Lead researcher Rosemary C. Bagot, PhD, a postdoctoral researcher in the Nestler Laboratory of Molecular Psychiatry at Mount Sinai, says the in vivo study was the “first to identify and validate the gene networks across brain circuits. It showed that manipulating their activity alters the activity of brain cells and, ultimately, depression behavior.” She adds, “Depression may reflect fundamental changes in the architecture of gene networks.”

The study, which appeared online in the May 12, 2016, issue of Neuron, relied on bioinformatics and big data to uncover patterns that were then tested in mouse models.

The scientists identified three specific genes that regulated the gene networks. Manipulating these “master regulator” genes could make the mice either susceptible or resilient to chronic stress. The scientists found a key role for the ventral hippocampus in making the mice susceptible to depression, whereas the prefrontal cortex was important in making the mice resilient.

“We took information about coordinated gene networks involved in depression and then manipulated these networks within animals to conclusively show that the networks regulated depression-like behavior,” says Dr. Bagot.

The search for a new, more effective class of drugs for depression is an important element in the research. “Virtually all of the drugs that are currently in use were identified more than 60 years ago, and many patients do not respond well to them,” says Eric J. Nestler, MD, PhD, Nash Family Professor of Neuroscience and Director of The Friedman Brain Institute at the Icahn School of Medicine at Mount Sinai. Through these discoveries, the team hopes to identify small molecules that may lead to new treatments for depression.

Says Dr. Nestler, “The study’s findings suggest that we need drugs that alter the way clusters of genes function within brain circuits.

Depression is a circuit-level disorder and needs to be understood and treated at that level.”
Artificial Pancreas Technology Helps Manage Type 1 Diabetes

Research underway at the Icahn School of Medicine at Mount Sinai is revolutionizing the management of type 1 diabetes by using novel technology that serves as an artificial pancreas and automatically enables patients to achieve more stable glucose levels 24 hours a day.

Led by Carol Levy, MD, Associate Professor of Medicine (Endocrinology, Diabetes and Bone Disease), the Icahn School of Medicine is one of nine U.S. and European sites participating in the research and sharing a $12.7 million grant from the National Institutes of Health. Dr. Levy is one of the study’s lead investigators.

The InControl AP (Artificial Pancreas) system, developed at the University of Virginia, runs a software algorithm on a smartphone that communicates with a standard insulin pump and an implanted glucose sensor that identify and maintain a personalized blood-glucose range for each patient.

The system monitors and controls the patient’s blood-glucose levels to avert nighttime hypoglycemia and ensure a goal glucose level in the morning. The application takes into account variables that include meals, physical activity, sleep, and stress.

The Artificial Pancreas system runs an algorithm on a smartphone that communicates with an insulin pump and an implanted glucose sensor.

The 240-patient trial, starting enrollment this summer, will run for three years and compare the InControl AP system to a control of a standard insulin pump to assess how well blood-sugar levels are controlled and whether the risk of hypoglycemia is reduced. This will be one of the largest long-term clinical trials of an artificial pancreas ever to be done in the home setting.

The new study builds on research conducted at Mount Sinai in 2014-2015. In collaboration with the University of Virginia and the Mayo Clinic, that study followed ten patients with type 1 diabetes for five days and was the first outpatient study of an AP system in New York State.

“That initial study showed that patients achieved stable glucose levels during the night and that the AP system led to improved blood-sugar control throughout the next day, as well,” says Dr. Levy.

A second study conducted by Dr. Levy’s team in November 2015 was done in partnership with the Rensselaer Polytechnic Institute, Stanford University, and the Barbara Davis Center for Diabetes at the University of Colorado. This study observed outpatient participants over three days while they wore another AP system throughout the day and night. Dr. Levy, who has type 1 diabetes herself, says that if the system is approved by the U.S. Food and Drug Administration, it is likely to be used widely because it is user-friendly and regulates only a single hormone: insulin. Other, more complex, systems are currently under development.

New Era for Ventricular Assist Device Surgery

A new, less invasive approach to the implantation of the HeartMate 11 left ventricular assist device (LVAD) shows promising results in advanced heart failure patients, according to research by Anelechi Anyanwu, MD, Professor and Vice Chairman of the Department of Cardiovascular Surgery.

LVAD technology, which takes over the function of a failing heart’s damaged left ventricle, is used for patients with severe heart failure, powering the heart to pump and helping to circulate blood through the body. It can serve as a bridge-to-transplant therapy for patients awaiting a heart transplant or as a destination therapy for those patients in need of permanent support to extend their survival.

Dr. Anyanwu’s pioneering sternum-sparing technique for routine HeartMate 11 implants uses a left subcostal incision to create a pocket for the LVAD and to access the left ventricular apex, and a right minithoracotomy to access the ascending aorta. The procedure carries a lower incidence of bleeding, respiratory morbidity, and right ventricular failure than the standard approach of median sternotomy.

“While tremendous success has been achieved with LVADs, their use is still associated with significant comorbidity, which may be related to several factors, including the need for extensive surgical dissection, a large pump, and a large-diameter percutaneous lead,” says Dr. Anyanwu. “Their long-term durability is not guaranteed, with some patients requiring reoperations for device exchange, which may result in significant morbidity and mortality.”

The new minimally invasive approach avoids sternotomy and may make it safer to perform heart transplantation and allow for faster mobilization and healing of critically ill patients undergoing LVAD surgery, he says.

Mount Sinai has one of the largest LVAD programs in the United States, successfully implanting more than 50 patients each year.

In other news, Dr. Anyanwu is participating in a 60-center clinical trial that is testing the efficacy of a new, smaller LVAD—MOMENTUM 3, which is designed to be more compatible with human biology and provides patients with a small pulse.
Marta Filizola, PhD

“Our goal is to empower students with the skills they need to make a difference in today’s world.”

Marta Filizola, PhD, an expert in computational biophysics, recently was named Dean of the Graduate School of Biomedical Sciences at the Icahn School of Medicine at Mount Sinai.

As the new Dean, Dr. Filizola says she plans to fully integrate quantitative methods, immersive learning strategies, and digital technologies into the current biomedical education model and to foster collaboration among disciplines to maximize scientific innovation.

Recognized as an innovative researcher and a strong advisor and mentor to students and trainees at all levels, Dr. Filizola will oversee the academic and administrative functions of all PhD and Master’s programs, as well as the Office of Postdoctoral Affairs.

“Our goal is to empower students with the skills they need to make a difference in today’s world,” says Dr. Filizola, Professor of Structural and Chemical Biology with secondary appointments in Neuroscience, and Pharmacology and Systems Therapeutics.

Dr. Filizola plans to incorporate more computational thinking into the Graduate School program. This is made possible by Mount Sinai’s significant investment for the past five years in computational resources and the recruitment of both faculty and students with backgrounds in math, physics, chemistry, computer science, and engineering.

The Icahn School of Medicine is in a unique position to prepare students for a wide range of careers, including those with nonacademic trajectories, she says. “We need to train our students so they can succeed in whichever career path they choose, whether in academia, industry, or even finance, should they decide to do that.”

One of the few female investigators specializing in computational biophysics, Dr. Filizola is extremely motivated to increase the participation of women and minorities in quantitative sciences.

As Dean, Dr. Filizola will continue to lead her own research programs that focus on developing painkillers that are less addictive than opioids, and novel therapeutics for the treatment of renal, hematologic, neoplastic, bone, and fibrotic diseases. Her laboratory is active in five research projects funded by the National Institute on Drug Abuse; the National Institute of Mental Health; and the National Heart, Lung, and Blood Institute.

Bart Barlogie, MD, PhD

“We have a unique opportunity to move the field forward with our understanding of the underlying mechanisms that cause cells to become malignant.”

Bart Barlogie, MD, PhD, a world-renowned physician who introduced the first curative therapy for multiple myeloma, a multi-drug regimen known as Total Therapy, has joined The Tisch Cancer Institute of the Mount Sinai Health System as Director of Research in the Multiple Myeloma Program.

Dr. Barlogie works with the program’s leader, Sundar Jagannath, MD, Professor of Medicine (Hematology and Medical Oncology), to develop new therapies to treat the disease, which is characterized by cancerous plasma cells that form in the bone marrow and crowd out normal, blood-forming cells. Their collaboration helps make Mount Sinai the nation’s premier myeloma program. About 26,850 new cases of the disease occur in the United States each year, according to the American Cancer Society.

“I’m dedicating my efforts toward improvement of patients with high-risk myeloma in whom we have made only negligible progress, as opposed to the 85 percent of patients presenting with genomically defined low-risk disease where we have a cure expectation of about 50 percent,” says Dr. Barlogie, who served for twenty-six years as Director of the Myeloma Institute for Research & Therapy at the University of Arkansas for Medical Sciences (UAMS), an institute he founded.

By collaborating with Dr. Jagannath, he says, “We have a unique opportunity to move the field forward with our understanding of the underlying mechanisms that cause cells to become malignant.”

The physicians will work with colleagues in the Department of Genomic Sciences and Department of Immunology to identify suitable drugs that target gene mutations found in bone marrow samples taken from patients. Mount Sinai offers a unique opportunity to advance the team’s knowledge due to the depth and breadth of its basic science research, says Dr. Barlogie.

Dr. Barlogie’s scientific career has focused on biological and therapeutic research, including chemotherapy, immunotherapy, and hematopoietic stem cell transplantation. He developed the first effective salvage regimen (VAD) for melphalan-prednisone refractory myeloma, introduced autologous transplantation for myeloma, and identified thalidomide as a first-in-class novel agent for the treatment of myeloma. Together with John Shaughnessy, Jr., PhD, who also recently joined the Mount Sinai Health System, Dr. Barlogie developed gene expression profiling to identify molecular subclasses of myeloma and established a highly predictive risk model.
Advancing the Department of Family Medicine and Community Health

Alfred B. Engelberg and his wife, Gail May Engelberg, recently made a $4 million gift to the Department of Family Medicine and Community Health at the Icahn School of Medicine at Mount Sinai to help fund the expansion of residency education.

The school's newly named Alfred and Gail Engelberg Department of Family Medicine and Community Health is dedicated to advancing education, research, and patient care in underserved communities. Its mission is to ensure outstanding primary care educational experiences for students, residents, and other trainees in both outpatient and inpatient settings, using a family practice model.

“Alfred and Gail are longtime advocates of family medicine,” says Neil Calman, MD, Professor and Chair of Family Medicine and Community Health, Mount Sinai Health System. “I am very grateful for their longstanding support. We’re delighted to be able to offer this training experience to the next generation of family physicians.”

Dr. Calman, who serves as President and Chief Executive Officer of the Institute for Family Health—one of the largest community health centers in New York State, with 27 locations—says the donation will specifically support the family medicine residency program, a federal initiative to provide direct payments to federally qualified health centers for the training of primary care physicians. “Our program is particularly exciting because it combines outpatient training in health centers with inpatient training at The Mount Sinai Hospital,” he says.

A co-founder of the Institute for Family Health, Dr. Calman has provided medical care to underserved populations throughout New York State since 1985.

Says Mr. Engelberg, “Mount Sinai is the only academic medical center in Manhattan to recognize that training family physicians who are capable of providing high-quality and low-cost care in urban neighborhoods is essential to the health and well-being of New York City. We are proud to support this effort.”

Kenneth L. Davis, MD, President and Chief Executive Officer of the Mount Sinai Health System, says, “The development of primary care is an essential part of the emerging model of population health care. This gift will have an enormous positive effect on our ability to address the shortage of primary care physicians and serve communities across the country.

Resilience Study Focuses on What Keeps People Healthy (continued from page 1)

In its initial phase this summer, Precise MD will offer a test used to analyze patients who have had prostatectomies at the Milton and Carroll Petrie Department of Urology at the Icahn School of Medicine to help determine which of them will likely have a recurrence of cancer and may need additional therapy such as chemotherapy.

A second, higher-impact test will follow in 2017, which will be used to characterize prostate cancer in newly diagnosed patients. At that time, Dr. Cordon-Cardo says all prostate cancer patients at Mount Sinai will have the option to receive this test.

In addition to the current efforts in prostate cancer, Precise MD is also applying its computer vision and machine learning tools to better characterize breast cancer. The new platform could eventually be used to characterize many disease states, including melanoma, lung, and colon cancers, and chronic conditions such as inflammatory bowel disease.

As part of the development efforts in breast cancer, Dr. Fernandez’s team is gathering between one and two petabytes of data for its archive and is employing the latest technologies in deep learning and neural networks to analyze data that is not visible to the human eye. “We expect to find features that we don’t even know exist at this point,” says Dr. Fernandez.
Top Three Winners in The Friedman Brain Institute’s Call-for-Images Competition

**First Place**
*Image by Candice Chapouly, PhD, Department of Neurology*
*Icahn School of Medicine at Mount Sinai*

**Title:** Reactive Astrocyte Cluster Containment of Activated Leukocytes  
**Description:** IL-1β reactive human astrocytes (red) are co-cultured with human activated CD3+ leukocytes (green). After twenty-four hours of co-culture, the inflammatory cells become surrounded by dense rings of astrocytes with thin, elongated processes. This in vitro model helps us to understand how circulating leukocytes breach the astrocytic barrier in inflammatory disease.

**Second Place**
*Image by Joshua B. Bederson, MD; Anthony B. Costa, PhD; Jillian Beroza, Department of Neurosurgery*
*Icahn School of Medicine at Mount Sinai*

**Title:** Close-up View of a Benign Tumor  
**Description:** A 3D patient-specific rendering generated from a fused CTA & MRI. The tumor is in close proximity to the ventricles, carotid arteries, and optic chiasm.

**Third Place**
*Image by Alan Seifert, PhD, Translational and Molecular Imaging Institute*
*Icahn School of Medicine at Mount Sinai*

**Title:** Human Brainstem in Six Shades Colormap  
**Description:** Nine axial slices through the human brainstem. The anatomical right side of each image is displayed in Fiji’s “6 shades” colormap, and the left side is displayed in standard grayscale and overlaid with segmentations from Duvernoy’s Atlas.
Icahn School of Medicine at Mount Sinai is Home to the Following Multidisciplinary Institutes

The Arnhold Global Health Institute
The Friedman Brain Institute
Global Health and Emerging Pathogens Institute
Icahn Institute for Genomics and Multiscale Biology
Immunology Institute
Institute for Advanced Medicine
Institute for Critical Care Medicine
Institute for Health Care Delivery Science
Institute for Medical Education

The Black Family Stem Cell Institute

The Charles Bronfman Institute for Personalized Medicine

Clinical Diabetes Institute

Diabetes, Obesity and Metabolism Institute

Ear Institute

Experimental Therapeutics Institute

The Joseph F. Cullman, Jr. Institute for Patient Experience
Institute for Translational Epidemiology
The Mindich Child Health and Development Institute

The Mirken Family Clinical Neuroscience Institute

Mount Sinai Head and Neck Institute
Mount Sinai Institute for Liver Medicine

Mount Sinai Institute of Technology
Mount Sinai–National Jewish Health Respiratory Institute
Primary Care Institute

The Recanati/Miller Transplantation Institute
The Tisch Cancer Institute

Translational and Molecular Imaging Institute

The Zena and Michael A. Wiener Cardiovascular Institute