ACCELERATING SCIENCE — ADVANCING MEDICINE

The Future of Genetic Medicine is Here

The Supreme Court’s ruling that companies cannot patent human genes, together with Angelina Jolie’s decision to have a preventive double mastectomy based on genetic test results, have ignited public discourse about the robust field of genetic medicine. Ms. Jolie shared with the world the difficult and deeply personal news that she carried the faulty BRCA1 gene that puts her at a much higher risk of developing breast and ovarian cancer. In so doing, she did a tremendous service not just for women, but for all people whose DNA is encoded with risk factors for a range of diseases.

Modern medicine is already able to determine genetic markers for dozens of conditions, including Alzheimer’s disease, Huntington’s disease, cystic fibrosis, certain cancers, and some autism spectrum disorders. At Mount Sinai we are expanding the quest for single-gene markers into the realm of gene networks—those that look at multiple nodes in relation to a particular gene—to more confidently determine an individual’s risk for a certain disease. Network models can also determine how a given person might respond to the range of treatments available.

Harnessing this and other data, our scientists are advancing the domain of personalized medicine by creating therapeutics and protocols that are precisely aligned with a single patient’s DNA. Concurrently, the Mount Sinai Genetic Testing Laboratory and Division of Medical Genetics are on a trajectory of strategic growth. The unit is the leading referral center for clinical genetics and metabolic disorders in the New York metropolitan area, and one of the largest newborn screening referral centers in the United States.

On this strong foundation, Mount Sinai is poised to open a clinical program that would offer whole genome and whole exome sequencing—along with the expert, sensitive analysis that contextualizes this powerful information and helps patients make DNA-based health care decisions.

With the cost of genome sequencing dropping dramatically—from $95,000 in 2001 to $5,600 today—we see expert interpretation as the frontier of an outstanding genomics program. As an American Board of Medical Genetics training site, our scientists and bioinformatic analysts work together with clinical geneticists to train profoundly knowledgeable—and equally sensitive—genetics professionals for work in institutions worldwide.

INNOVATIONS IN EDUCATION

Medical School Admissions for the Twenty-First Century

David Muller, MD, Marietta and Charles C. Morchand Chair in Medical Education and Dean for Medical Education at Icahn School of Medicine at Mount Sinai

Icahn School of Medicine at Mount Sinai has taken a bold step in re-envisioning admission to medical school in order to better prepare gifted medical students from a wide range of backgrounds through its new FlexMed program, which is the first of its kind in the nation.

Starting next fall, half of each medical school class will be guaranteed early acceptance to Mount Sinai during their sophomore year of college without having to take the Medical College Admissions Test (MCAT) or traditional premed coursework. The students will come from majors as diverse as computer science and engineering, the humanities and social sciences, and genetics.

Mount Sinai’s goal is to provide students with the opportunity to become self-directed and lifelong learners, who will have time...
NEW LEADERSHIP

New Era for the Department of Medicine

Barbara Murphy, MD, MB, BAO, BCh, FRCPI, a world-class physician scientist known for her innovative research in transplant immunology, has been named Chair of the Samuel F. Bronfman Department of Medicine at The Mount Sinai Medical Center. Dr. Murphy, the Murray M. Rosenberg Professor of Medicine, is the first woman to serve as Chair of Medicine at an academic medical center in New York City. She has been the department’s acting chair since June 2012, and Chief of Mount Sinai’s Division of Nephrology since 2004.

As Chair, Dr. Murphy oversees 12 divisions and more than 2,000 people. Dr. Murphy’s goal is to “create an environment that challenges current paradigms in clinical care, research, and education in the pursuit of excellence and innovation.”

She says, “The faculty in Mount Sinai’s Department of Medicine—the institution’s largest department—is world renowned. I am honored to take on the challenge of leading this extraordinarily talented team. Together we will continue to provide unsurpassed excellence in all areas, including patient care, research, and education.”

Prior to her appointment, Dr. Murphy also served as the Director of Conduits at Mount Sinai’s Institute for Translational Sciences, and as the Dean of Clinical and Population-Based Research. Having been consistently funded by the National Institutes of Health since 1994, Dr. Murphy’s current focus is on the use of genomics and genetics to investigate outcomes following renal transplantation. She holds one patent for a peptide that inhibits the immune response, and is awaiting approval for another two patents related to biomarkers that predict the development of fibrosis in renal transplants. One of these is a potential predictor for the progression of chronic kidney disease.

After receiving her medical degree from the Royal College of Surgeons in Dublin, Ireland, Dr. Murphy completed her residency, and fellowship in Clinical Nephrology at Beaumont Hospital in Dublin. She moved to the United States to pursue a Nephrology Fellowship in the Renal Division of Brigham and Women’s Hospital, Harvard Medical School in Boston, and was recruited to Mount Sinai as Director of Transplant Nephrology for the Renal Division.

A past president of the American Society of Transplantation, Dr. Murphy also is widely published, and currently serves as Associate Editor for The Clinical Journal of the American Society of Nephrology, and as Consulting Editor for American Journal of Transplantation.

A Robust Program in Immunotherapy

Nina Bhardwaj, MD, PhD, recently joined The Mount Sinai Medical Center as Director of the Immunotherapy Program at The Tisch Cancer Institute. In this role, Dr. Bhardwaj will create a robust program in immunotherapy, with an emphasis on cancer. She plans to develop a recognized vaccine production facility and expand Mount Sinai’s existing immune monitoring core.

Dr. Bhardwaj is known as a leading investigator in the biology of dendritic cells, a class of immune cells in the body that are involved in the early detection of invading pathogens such as bacteria, and have shown potential as a basis for therapeutic vaccines for cancer.

A winner of the Doris Duke Distinguished Clinical Scientist Award and a prestigious Merit Award from the National Institutes of Health, Dr. Bhardwaj was named by Scientific American as one of the top 50 researchers in the country. She is an elected member of the Association of American Physicians.

“My team and I are delighted to have joined The Tisch Cancer Institute. We look forward to working with its outstanding team of investigators to expand the immunotherapy platform for cancers and other chronic illnesses.”

Nina Bhardwaj, MD, PhD, Director of the Immunotherapy Program at The Tisch Cancer Institute

“I am honored to take on the challenge of leading this extraordinarily talented team. Together we will continue to provide unsurpassed excellence in all areas.”

Barbara Murphy, MD, MB, BAO, BCh, FRCPI, Chair of the Samuel F. Bronfman Department of Medicine

Prior to Mount Sinai, Dr. Bhardwaj served as Director of the Tumor Vaccine Program, and Professor of Medicine, Pathology, and Dermatology at NYU Langone Medical Center. She received her MD and PhD degrees from New York University School of Medicine, and completed her internship and residency in internal medicine at Brigham and Women’s Hospital/Harvard Medical School.
NEW LEADERSHIP

At the Forefront of Cancer Genetics

Ramon E. Parsons, MD, PhD, a highly acclaimed researcher in cancer genetics, has joined Icahn School of Medicine at Mount Sinai as the Ward-Coleman Chair in Cancer, and Chair of the Department of Oncological Sciences.

Dr. Parsons succeeds Stuart Aaronson, MD, Jack and Jane B. Aron Professor, whose discoveries in molecular oncology include identifying the first normal function of an oncogene, and its role in growth-factor signaling.

“With an innovative and enthusiastic leader like Dr. Parsons at the helm, Mount Sinai will push the limits of cancer research to discover improved diagnostics and novel treatments,” says Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean of Icahn School of Medicine at Mount Sinai and Executive Vice President for Academic Affairs of The Mount Sinai Medical Center. The author of more than 90 original peer-reviewed articles and the editor of several journals, including Cancer Research, Dr. Parsons’s research is organ-based. He is credited with defining the tumor suppressor gene PTEN that is mutated in cancer and serves as a critical therapeutic target in breast, brain, prostate, and endometrial cancers.

“We are entering a new era in cancer research in which genetics and genomics are playing a central role,” says Dr. Parsons. “Mount Sinai is at the forefront of this movement. I look forward to leading such an accomplished group of researchers, and recruiting additional world-class scientists to the Department of Oncological Sciences.” Dr. Parsons is the recipient of multiple honors, including the American Association for Cancer Research's Outstanding Investigator Award for Breast Cancer Research, and the National Institutes of Health Research Service Award.

Prior to joining Mount Sinai, he was a Professor of Breast Cancer Research, Medicine, Pathology, and Cell Biology in the Institute for Cancer Genetics and in The Herbert Irving Comprehensive Cancer Center at New York-Presbyterian Hospital.

Dr. Parsons served as a Postdoctoral Fellow at the Johns Hopkins University School of Medicine, and received his MD and PhD degrees from the State University of New York at Stony Brook.

Treatment and Prevention of Metabolic Diseases

Andrew Fyfe Stewart, MD, a renowned expert in endocrinology and diabetes research, recently joined The Mount Sinai Medical Center as Director of the Diabetes, Obesity and Metabolism Institute. Under his leadership, Mount Sinai expects to advance translational research into type 1 and type 2 diabetes.

Dr. Stewart concentrates on understanding and developing the means for inducing the replication and regeneration of insulin-producing pancreatic beta cells, the loss of which is linked to both types of diabetes.

During his tenure as Chief of the Division of Endocrinology and Metabolism at the University of Pittsburgh School of Medicine starting in 1997, Dr. Stewart’s group was the first to demonstrate that adult human beta cells can be induced to replicate at substantial rates.

Three of his long-time colleagues from that group have joined him at Mount Sinai: Donald K. Scott, PhD; Adolfo Garcia-Ocaña, PhD; and Rupangi Chhaya Vasavada, PhD. They serve as faculty in the Department of Medicine (Division of Endocrinology, Diabetes and Bone Disease) and as members of the interdisciplinary Diabetes, Obesity, and Metabolism Institute.

“This is an exciting time in science, and my team is thrilled to round out Mount Sinai’s existing diabetes research with our expertise in beta cells,” says Dr. Stewart, the Irene and Dr. Arthur M. Fishberg Professor of Medicine, Director of the Diabetes, Obesity and Metabolism Institute.

Through interdisciplinary, translational research collaborations, the Diabetes, Obesity and Metabolism Institute focuses on understanding the basic mechanisms involved in metabolic diseases, mainly diabetes and obesity, and aims to develop and promote prevention and treatment programs for those conditions. Dr. Stewart will oversee the continued expansion of the Institute through the recruitment of national experts.
Understanding Human Diseases through Next Generation Sequencing

Through the Genomics Core Facility, The Mount Sinai Medical Center’s Icahn Institute for Genomics and Multiscale Biology (IGMB) is making state-of-the-art technologies available to investigators throughout Mount Sinai. The goal is to use next-generation sequencing to carry out cutting-edge basic and translational genomics research to diagnose and cure human diseases.

Mount Sinai’s next-generation sequencing rests upon two platforms from Illumina and Pacific Biosciences.

At full capacity, Illumina sequencing can produce more than 4 billion individual sequences, or “reads,” from DNA samples in less than two weeks. This is suited to sequencing whole human genomes or exomes, counting the abundance of transcripts in RNA, and identifying genome-wide epigenetic signatures.

The Pacific Biosciences platform continuously sequences a single molecule for up to six kilobases, and is well-suited for de-novo sequencing of small genomes and polishing of genomic assemblies for large genomes. DNA samples are sequenced within hours, instead of days.

Within the past several months, the IGMB has begun genomic sequencing on Mount Sinai patients with solid tumor cancers, and patients with diseases in reproductive health, according to Andrew Kasarskis, PhD, Co-Director of the Icahn Institute for Genomics and Multiscale Biology. Each specialty is being analyzed differently, he says, but “Genomic sequencing is giving us the opportunity to look at more precise aspects of disease.”

Eric Schadt, PhD, Director of the Icahn Institute for Genomics and Multiscale Biology, says his team has generated many new insights into the complexity and heterogeneity of solid tumor cancers, in particular, and has begun to fine-tune methods for diagnoses.

The best way to develop personalized cancer therapy and uncover what is happening in a patient’s tumor, he says, is to combine next-generation sequencing with predictive network models. This multilayered approach gives researchers a better understanding of the key driver genes that are mutated, and the signaling pathways that are altered.

A targeted gene panel on a particular patient might show that key signaling genes such as PTEN or HER2 are not mutated, says Dr. Schadt. But “the networks around these genes may be mutated in ways that activate these signaling pathways.”

Genomic researchers believe the clarity and speed at which information is processed will ultimately lead to targeted treatments that are more effective for individual patients.

Using Precision Medicine to Treat Cancer

Investigators at the Icahn Institute for Genomics and Multiscale Biology are rolling out a program based on precision medicine that will create individualized treatments for cancer patients based on unique mutations in their DNA. The program draws upon the expertise of Joel Dudley, PhD, Director of Biomedical Informatics at Icahn School of Medicine at Mount Sinai. He and his colleagues at the Institute will rely on sophisticated algorithms and computer programs that analyze unique mutations in the patient’s DNA.

Within the next few months the team will analyze molecular maps of patients with late-stage cancers of the prostate, head and neck, ovaries, and breast, and patients with hematological cancers, including multiple myeloma. They will see how and where their patients’ genes went awry and gave rise to cancer.

Dr. Dudley says the goal is to “look broadly through the whole genome to create a complete molecular picture of a patient’s cancer.” One possible benefit of this is the ability to select the most optimal therapy for patients based on their unique tumor biology. “You don’t know what drug will be best for individual patients until you look at the whole genome and understand how all the molecular systems in their tumor cells are wired,” he says.

Shortly after the program was launched this spring, Dr. Dudley says the investigators learned that tumors have very unique mutations. They also realized that the non-gene coding regions of a person’s genome are just as important as the genes themselves, because they contain regulatory instructions for the genes. “It is important to sequence the non-gene coding regions because they encode regulatory regions that can influence the response to therapy,” he says.

Collaboration with various Mount Sinai departments is an important part of the process. The Department of Pathology, for example, will collect tumor and blood samples from patients and send them to Mount Sinai’s Genetics Core Facility where they will be sequenced. From there, the samples will be sent to a supercomputer for further analysis and interpretation.

One of the first areas of research will be multiple myeloma, a lymphoid cancer that claims the lives of more than 20,000 Americans each year. Dr. Dudley and his colleagues will work with Sundar Jagannath, MD, Director of the Multiple Myeloma Program at The Tisch Cancer Institute, and Samir Parekh, MD, Assistant Professor of Medicine (Hematology and Oncology), to develop optimal therapeutic strategies to prevent relapse of the disease. The team will use advanced computational techniques to scan thousands of approved drugs to identify those that modulate key molecular drivers of multiple myeloma.

In addition, the team is working in collaboration with investigators at Baylor College of Medicine in Houston, to develop personalized cancer vaccines, and with Ross L. Cagan, PhD, Professor of Developmental and Regenerative Biology at Icahn School of Medicine at Mount Sinai.
Mount Sinai School of Medicine recently was renamed in honor of Carl C. Icahn, Trustee, The Mount Sinai Medical Center, who has generously supported the institution for more than three decades.

The new name—Icahn School of Medicine at Mount Sinai—was bestowed by the Boards of Trustees in recognition of Mr. Icahn’s many years of dedicated service, his leadership in advancing medical science, and his nearly $200 million in lifetime giving to Mount Sinai.

Mr. Icahn’s most recent gift of $150 million is the largest in Mount Sinai’s history, and among the biggest gifts made to a medical school. His previous contributions to Mount Sinai resulted in a state-of-the-art medical school research building on the Mount Sinai campus being named The Icahn Medical Institute.

In addition to renaming the School of Medicine, the Institute for Genomics and Multiscale Biology—one of 14 translational institutes that lie at the heart of Mount Sinai’s strategic plan—was renamed the Icahn Institute for Genomics and Multiscale Biology. Mount Sinai will also be designating a cadre of Icahn Scholars, who will be among the most outstanding scientists across several institutes and departments.

“I am certain that my contributions to Mount Sinai will lead to significant medical breakthroughs in the diagnosis and treatment of disease that will dramatically improve and extend human life.”

Carl C. Icahn, Trustee, The Mount Sinai Medical Center

“Carl Icahn’s support enables our scientists and clinicians to continue pursuing groundbreaking discoveries,” said Kenneth L. Davis, MD, President and Chief Executive Officer of The Mount Sinai Medical Center. “We are honored to bear the Icahn School of Medicine name as we revolutionize health care for Mount Sinai patients and for patients around the world.”

Mr. Icahn, one of America’s most prominent and influential investors, has been a member of the Boards of Trustees, and a Trustee of the School of Medicine, since 2000. His gifts have been, and will continue to be, utilized for general medical research as well as specific research in the burgeoning field of genomics to improve the diagnosis and treatment of disease.

“I have been very impressed with Mount Sinai’s extraordinary achievements to date in scientific discovery, medical education, translational medicine, and patient care,” said Mr. Icahn. “I am certain that my contributions to Mount Sinai will lead to significant medical breakthroughs in the diagnosis and treatment of disease that will dramatically improve and extend human life.”

Mr. Icahn’s most recent giving has supported the Campaign for Mount Sinai, a $1 billion capital campaign that was launched in 2008 and recently surpassed its target well in advance of its scheduled December 2013 conclusion.

“Carl Icahn has been a remarkable supporter of the capital campaign, and as a philanthropist, he is a game-changer for Mount Sinai,” said Peter W. May, Chairman of the Boards of Trustees. “His gift has given us the momentum we need to reach our new goal of $1.3 billion.”
Serial Images of the Prefrontal Cortex and Hippocampus of a Monkey
Taken with an Electron Microscope

Images by Yuko Hara, PhD, Assistant Professor in the Fishberg Department of Neuroscience at Icahn School of Medicine at Mount Sinai

**Monkey Area 46 Neuropil**

*Description:* Three-dimensional reconstruction of dendrites, dendritic spines, and axonal boutons from the monkey prefrontal cortex. Red, transparent orange, yellow, and green structures represent individual dendritic segments with dendritic spines; transparent light blue represents axonal boutons; and dark blue/purple structures inside the dendrites and boutons represent mitochondria.

**Monkey Area 46 Synapses**

*Description:* Three-dimensional reconstruction of synaptic complexes from the monkey prefrontal cortex. Yellow and transparent green structures represent dendritic shafts and spines; transparent light blue and light purple represent axonal boutons; dark blue/purple represent mitochondria; and red patches represent postsynaptic density.

**Hippocampus Neuropil**

*Description:* Three-dimensional reconstruction of dendrites, dendritic spines, and axonal boutons from the monkey hippocampal dentate gyrus. Red, orange, transparent yellow, and transparent green structures represent individual dendritic segments with dendritic spines; transparent blue represents axonal boutons; and dark blue/purple structures inside the dendrites and boutons represent mitochondria.
Mount Sinai and Genisphere LLC to Create a Rapid Allergy Test

The Icahn School of Medicine at Mount Sinai and Genisphere LLC are jointly developing a new, high-throughput allergy test that is expected to characterize patients’ food allergies more accurately and reliably than current testing methods.

Genisphere will work with Hugh A. Sampson, MD, Kurt Hirschhorn Professor of Pediatrics, Dean for Translational Biomedical Research, and Director of the Jaffe Food Allergy Institute at Icahn School of Medicine at Mount Sinai, and his team, to adapt existing allergy tests to the specifications laid out under the agreement. The new peptide bead-based allergy test will avoid reproducibility limitations, and generate food-allergy panels for various allergens.

The partnership with Genisphere, a privately held company in Hatfield, Pa., was established through Mount Sinai’s Blue Mountain Technologies, a program that encourages the commercialization of novel research reagents, diagnostics, and therapeutics based on Icahn School of Medicine at Mount Sinai’s research.

“We look forward to working with Genisphere on these novel assays that should help the clinician better diagnose and counsel food-allergic patients,” says Dr. Sampson, whose research has focused on immunotherapeutic strategies for treating food allergies. Dr. Sampson is the primary investigator on the National Institutes of Health-sponsored Consortium of Food Allergy Research, a group that conducts multicenter trials, observational studies, mechanistic studies, and basic research.

Genisphere is an established life science and diagnostic technology leader specializing in the development of kits and reagents used for the detection of nucleic acids and proteins. The company has scientific and commercial interest in developing biomarker signatures for use in diagnostics and other applications in personalized medicine.

According to Robert Getts, PhD, Chief Science Officer of Genisphere, “We will continue our collaborative partnership with Dr. Sampson and the accomplished scientists at Mount Sinai to adapt the peptide panels into a rapid test that can benefit millions of people who suffer from allergies to various foods.”

Mount Sinai’s Blue Mountain Technologies is part of the institution’s Office of Technology and Business Development (OTBD), which facilitates the transfer of discovery from the laboratory to the marketplace. OTBD evaluates, patents, markets, and licenses new technologies, and negotiates agreements for sponsored research, material transfer, and confidentiality.

Medical School Admissions for the Twenty-First Century (continued from page 1)

to focus on courses in health policy, ethics, genetics, or biostatistics as undergraduates without being encumbered by traditional classes such as organic chemistry or calculus.

The inherent value of a broad and deep undergraduate education encourages creativity and critical thinking, skills that help create the kinds of physicians and scientists we will need in the twenty-first century, says David Muller, MD, Marietta and Charles C. Morchand Chair in Medical Education and Dean for Medical Education at Icahn School of Medicine at Mount Sinai.

Many medical school educators have questioned the usefulness of rigid premed requirements that have not changed much in almost 100 years. They say a traditional premed program encourages aggressive competition for grades that runs counter to what is valued most in medicine: academic and intellectual rigor, creative thinking, teamwork and collaboration, and social conscience. In addition, the MCAT often serves as a barrier of entry to medical school for students who do not do well on standardized tests, or those who cannot afford the high cost of test preparation.

FlexMed is an outgrowth of Mount Sinai’s Humanities and Medicine (HuMed) program, which began in 1987 under the leadership of Nathan Kase, MD, then Dean of the Medical School, and was the first in the nation to offer early assurance of acceptance to sophomores with a background in humanities. HuMed students have performed as well as their peers and are highly represented in clerkship honors, selection to Alpha Omega Alpha, the Gold Humanism Honor Society, scholarly year research participation, first author publications, and community service.

According to Dr. Muller, the metrics and outcomes in medical school, residencies and fellowships, and career paths of FlexMed students will be prospectively tracked in an Institutional Review Board (IRB)-approved longitudinal research study that compares them to their peers. By documenting this in an evidence-based fashion, Mount Sinai leaders hope that FlexMed will serve as a model for premedical preparation, and be duplicated at other schools around the country.
Icahn School of Medicine at Mount Sinai is Home to 14 Translational Research Institutes

THE BLACK FAMILY STEM CELL INSTITUTE
Director: Ihor R. Lemischka, PhD

THE CHARLES BRONFMAN INSTITUTE FOR PERSONALIZED MEDICINE
Director: Erwin P. Bottinger, MD

DIABETES, OBESITY AND METABOLISM INSTITUTE
Director: Andrew Fyfe Stewart, MD

EXPERIMENTAL THERAPEUTICS INSTITUTE
Director: Ravi Iyengar, PhD

THE FRIEDMAN BRAIN INSTITUTE
Director: Eric J. Nestler, MD, PhD

GLOBAL HEALTH AND EMERGING PATHOGENS INSTITUTE
Director: Adolfo García-Sastre, PhD

ICAHN INSTITUTE FOR GENOMICS AND MULTISCALE BIOLOGY
Director: Eric E. Schadt, PhD

IMMUNOLOGY INSTITUTE
Co-Directors: Lloyd F. Mayer, MD; and Sergio A. Lira, MD, PhD

INSTITUTE FOR TRANSLATIONAL EPIDEMIOLOGY
Director: Paolo Boffetta, MD, MPH

THE MINDICH CHILD HEALTH AND DEVELOPMENT INSTITUTE
Director: Bruce D. Gelb, MD

THE RECANATI/MILLER TRANSPLANTATION INSTITUTE
Director: Sander S. Florman, MD

THE TISCH CANCER INSTITUTE
Director: Steven J. Burakoff, MD

TRANSLATIONAL AND MOLECULAR IMAGING INSTITUTE
Director: Zahi A. Fayad, PhD

THE ZENA AND MICHAEL A. WIENER CARDIOVASCULAR INSTITUTE
Director: Valentin Fuster, MD, PhD