Icahn School of Medicine at Mount Sinai

The Friedman Brain Institute

FALL 2016 | DIRECTOR'S REPORT | www.mountsinai.org/fbi

Compassionate Care, Pioneering Research

We are embarking on a new strategic plan for The Friedman Brain Institute (FBI), and for Mount Sinai overall, to guide our growth and investments over the next five to ten years.

The last strategic plan—launched roughly 10 years ago—has resulted in an unprecedented expansion of our neuroscience community through the recruitment of more than 35 basic neuroscientists and many more clinical researchers and clinicians. The dividends are impressive: The Department of Neuroscience is ranked No. 3 in the nation in National Institutes of Health (NIH) funding; Psychiatry is ranked No. 7; and Neurology, No. 11. *U.S. News & World Report* has ranked our clinical neurology and neurosurgery programs No. 12 in the nation. Additionally, Mount Sinai overall is ranked No. 15 in NIH funding, and No. 1 in total research funding per principal investigator by the Association of American Medical Colleges. This latter metric demonstrates the uniquely outstanding quality of our faculty and sets the stage for our future growth.

Our new strategic plan, which is still being finalized and will be presented in 2017, has identified several areas for bold investment, allowing FBI scientists and physicians to further develop comprehensive basic research efforts in several areas of brain disease, with the tangible goal of making demonstrable clinical advances in disease diagnosis and treatment in the next decade.

In this newsletter, we highlight Paul Kenny, PhD, a recent recruit to Mount Sinai and now Chair of Neuroscience and Director of the Experimental Therapeutics Institute, whose own research is paving the way for new treatments for tobacco addiction. We also highlight a groundbreaking innovation in neurosurgery, led by Department Chair Joshua B. Bederson, MD, where simulation of the surgical course through an individual's brain anatomy is transforming neurosurgical care and outcomes.

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Advancing Research Into the Molecular and Cellular Mechanisms Behind Tobacco Addiction

Tobacco smoking is the leading cause of preventable death and disease worldwide, increasing risk for lung, pancreatic, and liver cancer; and heart disease and type 2 diabetes, among other conditions. For the past 10 years, Paul Kenny, PhD, a world authority in the neurobiology of addiction, has focused on understanding the molecular, cellular, and behavioral mechanisms of tobacco addiction and developing novel therapeutics. Dr. Kenny joined the Icahn School of Medicine at Mount Sinai faculty in 2013 as Director of the Experimental Therapeutics Institute. He was named Chair of the Department of Neuroscience in July.

Nicotine, considered the major addictive component of tobacco smoke, acts in the brain by stimulating a group of proteins known as the nicotinic acetylcholine receptors (nAChRs) that are expressed on the surface of specific types of nerve cells. These receptors are

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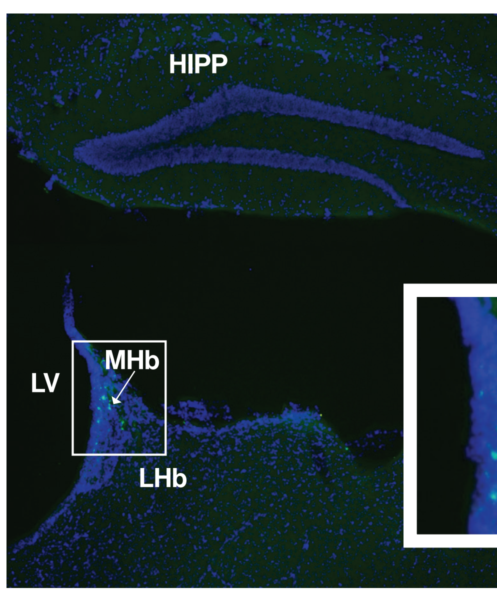
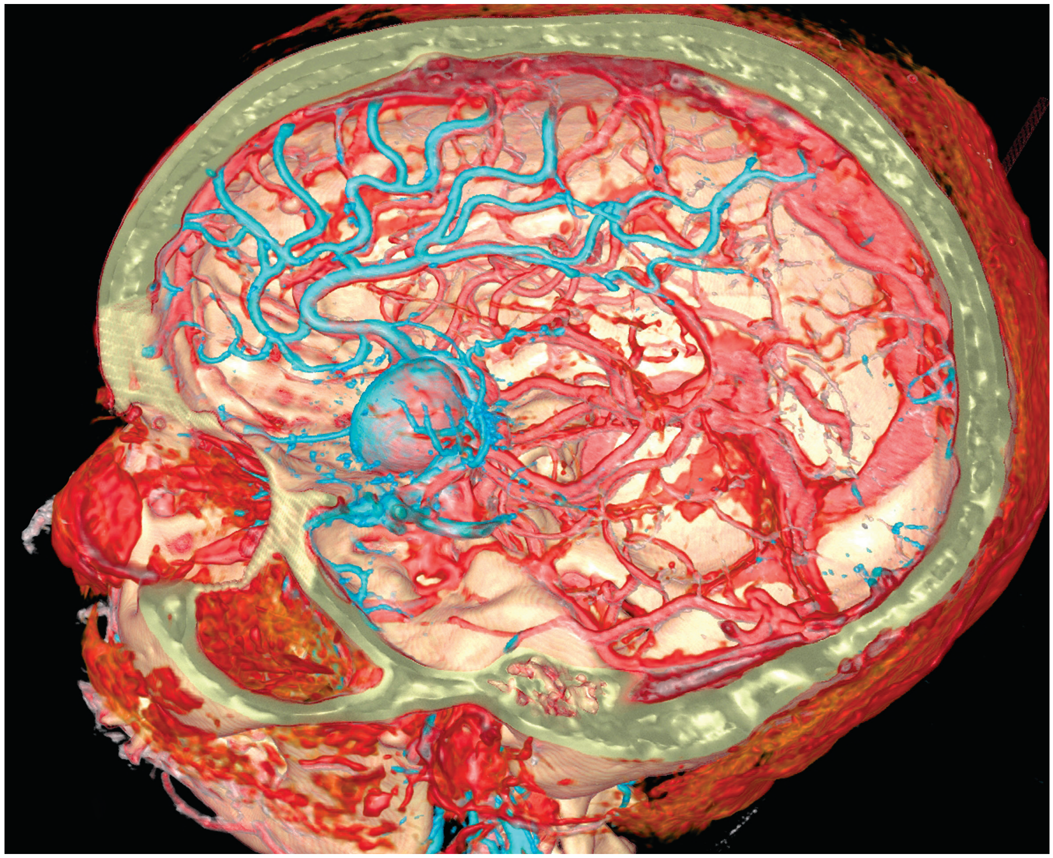


Green fluorescent protein (GFP) expressed from a lentivirus also used to express the α5 nAChR subunit in the medial habenula of α5 subunit knockout mice. (HIPP, hippocampus; LHb, lateral habenula; LV, lateral ventricle; and MHb, medial habenula.) Modified from Fowler et al., *Nature*, 2011.

Higher magnification of the MHb. GFP + DAPI (blue, label of cell nuclei).

Simulation Core: Next-Generation Training in Neurosurgery

The year-old Neurosurgery Simulation Core in the Department of Neurosurgery at Icahn School of Medicine at Mount Sinai has developed and is implementing a number of simulation and modeling technologies that are transforming clinical practice. The group is led by Joshua B. Bederson, MD, Professor and Chair of Neurosurgery, Mount Sinai Health System; and Anthony B. Costa, PhD, Assistant Professor of Neurosurgery.



A patient-specific 3D rendering, generated from a fused CTA, MRI, and a 3D angiogram, which shows a giant carotid-ophthalmic aneurysm, was used for surgical planning. Surgical approach was a left frontal craniotomy with approach to anterior skull base for clipping of the aneurysm.

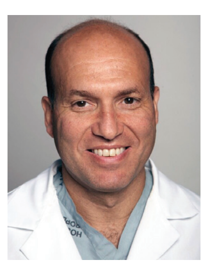
Through basic research and partnerships with industry technology leaders such as Brainlab; Leica; Surgical Theater, LLC; and Synaptive, Mount Sinai's neurosurgeons are using augmented and virtual reality tools during complex brain surgeries, including a world-first implementation of an intraoperative "heads-up" display implemented by Leica called "Captiview." The technique overlays 3D reconstructions of brain fiber tracts, blood vessels, cranial nerves, brain nuclei, bone, and soft tissue that are rendered in the Brainlab platform and projected directly into the surgeon's eye-pieces. The surgeon can program "no-fly zones" and "targets" directly onto the operative field, thereby increasing situational awareness during critical portions of the case.

These same pre- and intraoperative tools are also being integrated into the patient experience. Dr. Bederson has conducted more than 40 "simulation-based consultations," in which an interactive 3D virtual-reality scenario of the patient's specific anatomy and pathology is shared with the patient and family during preoperative consultation. In collaboration with the surgeon, patients can interact with their own models either virtually through a touch-screen interface using virtual-reality goggles, or through a 3D printed model that they can take with them. The Neurosurgery team has found that the enhanced understanding of the patient's condition provided by these tools leads to increased confidence and a better appreciation of surgical alternatives in discussions with family members.

The development of 3D printing technologies is a collaboration with the Mount Sinai Institute for Next Generation Healthcare's Rapid Prototyping Core. In select cases, 3D printing provides pre- and intraoperative planning and surgical rehearsal that cannot be achieved through any other medium. For example, an extensive collaboration between the Simulation and Rapid Prototyping Cores and the Department of Otolaryngology–Head and Neck Surgery has produced a series of preoperative models of skull-base lesions, which are used to plan minimally invasive approaches to the skull base on the model itself and serve as a trial run for the surgery.

Later this year, the 3D printing team, headed by Dr. Costa, will launch the Medical Modeling Core to provide virtual reality and 3D printing services and resources to basic researchers and clinicians at Mount Sinai on a fee-for-service basis, with turnaround times and costs far below what is available on the open market. This general resource will be the first of its kind, catering specifically to the unique modeling requirements of clinicians on a patient-specific basis.

Joshua B. Bederson, MD, owns equity in Surgical Theater, LLC.



Joshua B. Bederson, MD
Co-Director of the Neurosurgery Simulation Core; and Professor and Chair of Neurosurgery, Mount Sinai Health System

Anthony B. Costa, PhD
Director of the Neurosurgery Simulation Core, and Assistant Professor of Neurosurgery

composed of five subunits, with each encoded by its own unique gene. A major breakthrough in the genetics of tobacco addiction was the finding that mutations in the CHRNA5 gene, which expresses one of these subunits, increases vulnerability to tobacco dependence and smoking-associated diseases. (Mount Sinai's Alison Goate, PhD, Director of the Ronald M. Loeb Center for Alzheimer's Disease, was one of the principal scientists to make this discovery.) The CHRNA5 gene encodes the α5 nAChR subunit. This subunit is incorporated into nAChRs in selected types of nerve cells and thereby regulates the actions of nicotine. But precisely how nAChRs containing the high-risk form of the α5 subunit influence vulnerability to tobacco addiction was unknown.

Work in the Kenny Laboratory has shown that α5 subunit-containing nAChRs are expressed (*see figure, page 1*) in a part of the brain called the medial habenula (MHb) and on MHb fibers that project to another brain structure called the interpeduncular nucleus (IPN).

Unexpectedly, α5-containing nAChRs in the MHb-IPN pathway were found to regulate noxious rather than pleasurable effects of nicotine. These findings suggest that people carrying CHRNA5 variants are more likely to smoke, not because they enjoy nicotine more but because they are resistant to aversive effects of the drug. Currently, the Kenny Laboratory is investigating the molecular and cellular mechanisms of nicotine action in the MHb-IPN pathway, exploring the role for this pathway in other neuropsychiatric disorders, and developing novel smoking cessation therapeutics that act by modulating the activity of the MHb-IPN pathway.

The Kenny Laboratory is also investigating the role of molecules contained inside nerve cells that influence addiction and other psychiatric disorders.

The Kenny Laboratory is also investigating the role of molecules contained inside nerve cells that influence addiction and other psychiatric disorders. MicroRNAs are small noncoding regulatory RNAs, meaning they do not make proteins like most other RNAs but instead regulate this process. Dr. Kenny and colleagues were among the first researchers to establish roles for microRNAs in driving drug addiction and schizophrenia, and are currently examining their novel therapeutic potential though the Experimental Therapeutics Institute.

Paul Kenny, PhD
Chair, Department of Neuroscience, and Director, Experimental Therapeutics Institute

The Friedman Brain Institute Research Scholars Partnership

The Philanthropic Leadership Council of The Friedman Brain Institute (FBI) has announced the second round of the FBI Research Scholars Partnership, a pilot grant program for innovative and collaborative brain research. Priority will be given to early- and mid-career faculty who seek collaborations in other disciplines, and to senior scientists undertaking projects outside of their usual investigation area. Successful projects are designed to generate preliminary data needed to secure external funding. Previously awarded Scholars may apply for new projects. Recipients are named "FBI Research Scholars" and receive a one-time grant of up to $50,000. To learn more, email eric.nestler@mssm.edu. Deadline for submission is Monday, October 31.

Introducing a Seminar Series For Postdoctoral Fellows

MSN*seminars* (Mount Sinai Neuroscience *seminars*) is a new seminar series that hosts leading postdoctoral fellows from around the country to present their research and meet with the neuroscience community at Mount Sinai. This new initiative–run by Mount Sinai neuroscience postdocs–aims to promote diversity and give selected postdocs a chance to showcase their work. Speakers who present at MSN*seminars* also meet with faculty and have lunch with Mount Sinai graduate students and postdocs. This series offers an excellent opportunity for senior postdocs to network with colleagues and peers at Mount Sinai.

Nominations (or self-nominations) for the 2016 - 2017 year are now being accepted. Please send an updated CV and abstract describing the candidate's research to MSNseminars@mssm.edu. The MSN*seminars* committee will review the applications and notify the applicant if selected.

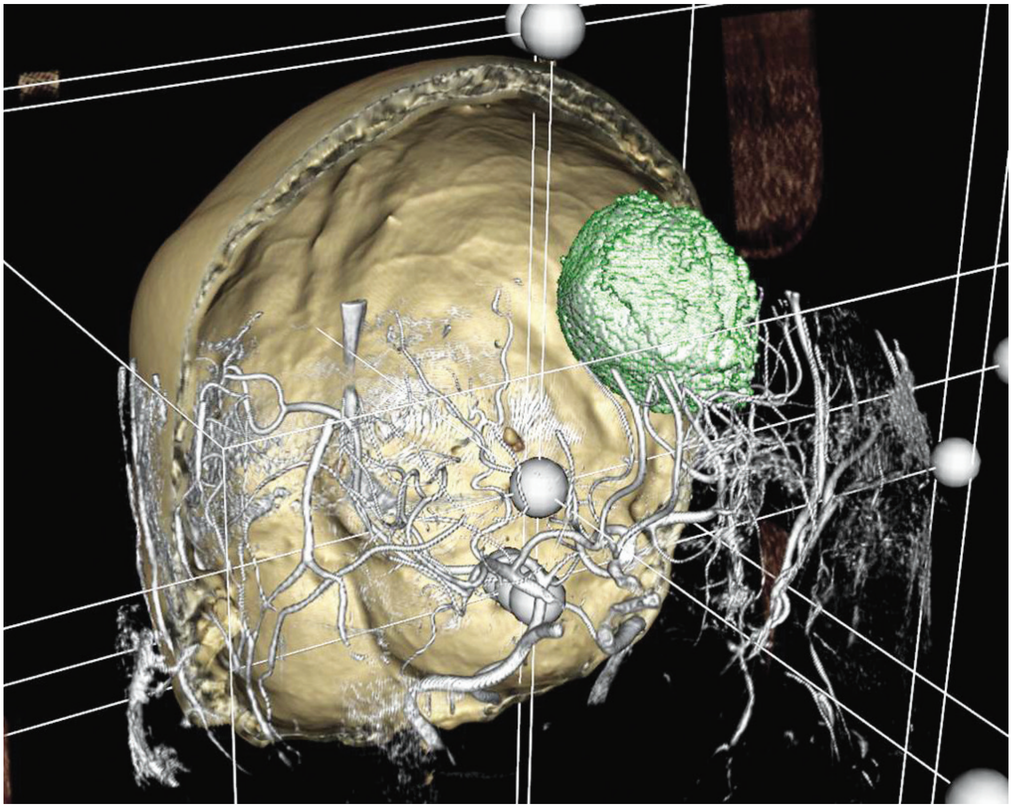
Thank You, Donors!

Philanthropic investment is a catalyst to the work of Mount Sinai physicians, scientists, and educators, allowing for the acceleration of existing studies, the development of even more innovative approaches to scientific inquiry and clinical care, and the training and recruitment of the next generation of medical leaders.

The Friedman Brain Institute is grateful for the partnership of the many individuals and foundations who share its vision for the future of neuroscience. The following gifts, received in the past few months, exemplify the impact of giving:

- **International philanthropists Arminio and Lucyna Fraga's** commitment of $1.2 million established the Cerebrovascular Disease and Stroke Fund in the Department of Neurosurgery to advance the mission of improving global stroke care through the development of a comprehensive stroke program across the Mount Sinai Health System.
- **Friedman Brain Institute Philanthropic Leadership Council member Stuart Katz and his wife Dr. Jane Martin's** most recent gift of more than $1 million will bolster Mount Sinai's ongoing efforts in basic and clinical research in Alzheimer's disease.
- **Neurology faculty member Pedro Pasik, MD,** established the Tauba Pasik, MD Endowment to honor the legacy of his wife, a Neurology Department physician-scientist and educator. The endowment will support an annual Tauba Pasik, MD Memorial Lecture in Neurology, as well as an Award for Teaching Excellence within the Department.
- **Through the Satter Foundation's commitment of $1 million to The Friedman Brain Institute, Ms. Kristen Hertel and Mr. Muneer Satter** continue their commitment to health and human services by supporting research in cognition, an important factor in understanding many neurodegenerative disorders.
- **Following a lifetime of loyalty and generosity to Mount Sinai Beth Israel, Mrs. Betty Yarmon** bequeathed funds through her estate in support of clinical and research efforts in Neurology, Neurosurgery, and Rehabilitation Medicine, with particular focus on Movement Disorders.

PHOTO ESSAY



Advanced Manipulation of Imaging Data in 3D

A multi-component simulation of skull, vasculature, and tumor is segmented from imaging data and displayed interactively using software developed in the Neurosurgery Simulation Core, enabling rapid analysis and visualization of patient neuroanatomical data.

Image by Anthony B. Costa, PhD, Director of the Neurosurgery Simulation Core, and Assistant Professor of Neurosurgery