Icahn School of Medicine at Mount Sinai

The Friedman Brain Institute

DIRECTOR'S REPORT | FALL 2019 mountsinai.org/fbi

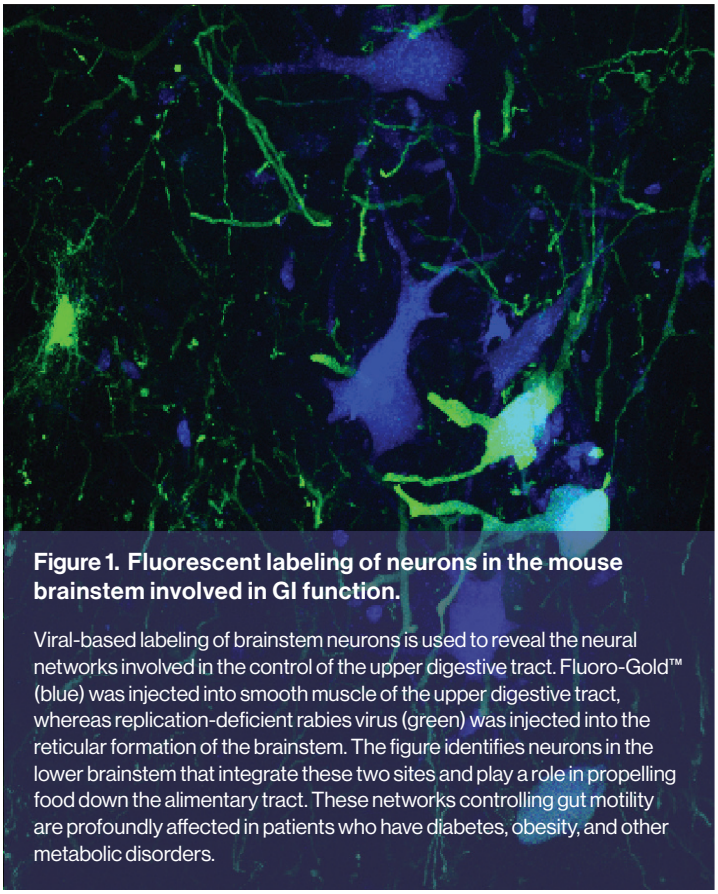

Figure 1. Fluorescent labeling of neurons in the mouse brainstem involved in GI function.

Viral-based labeling of brainstem neurons is used to reveal the neural networks involved in the control of the upper digestive tract. Fluoro-Gold™ (blue) was injected into smooth muscle of the upper digestive tract, whereas replication-deficient rabies virus (green) was injected into the reticular formation of the brainstem. The figure identifies neurons in the lower brainstem that integrate these two sites and play a role in propelling food down the alimentary tract. These networks controlling gut motility are profoundly affected in patients who have diabetes, obesity, and other metabolic disorders.

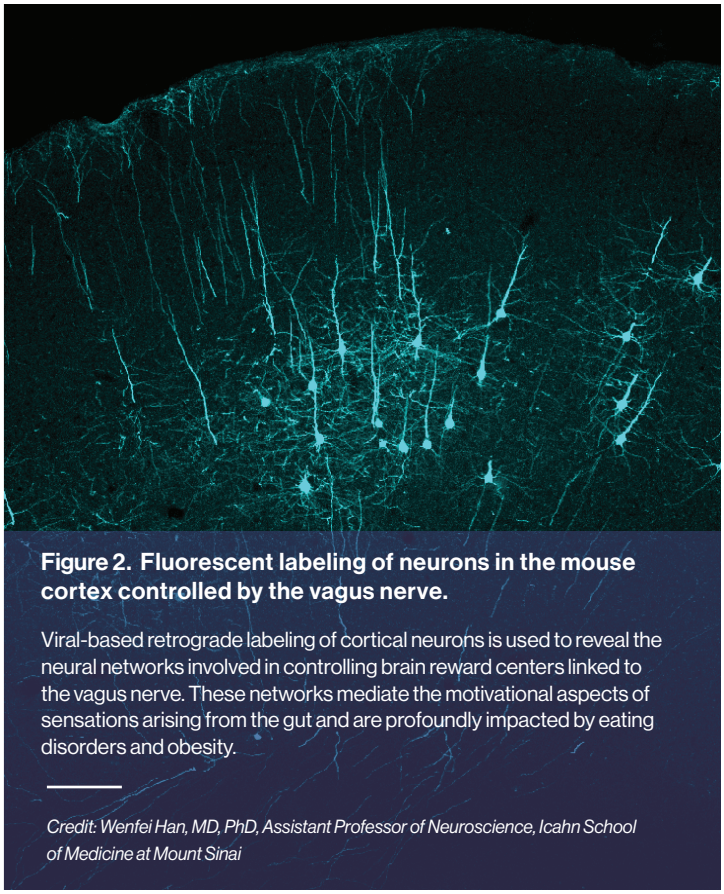

Figure 2. Fluorescent labeling of neurons in the mouse cortex controlled by the vagus nerve.

Viral-based retrograde labeling of cortical neurons is used to reveal the neural networks involved in controlling brain reward centers linked to the vagus nerve. These networks mediate the motivational aspects of sensations arising from the gut and are profoundly impacted by eating disorders and obesity.

Credit: Wenfei Han, MD, PhD, Assistant Professor of Neuroscience, Icahn School of Medicine at Mount Sinai

Uncovering Bidirectional Communication Between the Nervous System and Metabolism

The Icahn School of Medicine at Mount Sinai has been at the forefront of efforts to develop better therapeutic strategies for the hundreds of millions of people worldwide who have diabetes, obesity, or other metabolic or feeding syndromes. While the exact mechanisms remain incompletely understood, it is now widely recognized that the nervous system plays a crucial role in the etiology of metabolic diseases and that peripheral metabolism strongly influences brain function. Today, Mount Sinai investigators, using innovative neurobiological tools, are able to better scrutinize how central and peripheral neural networks interact with visceral organs to regulate body weight and energy homeostasis.

The laboratory of **Christoph Buettner, MD, PhD**, is developing neuroscience-inspired techniques in which specialized molecular probes that emit light in response to neurotransmission are inserted into hepatic and pancreatic cells. The team next uses advanced microscopy to reveal, with unprecedented detail, the biology of altered sympathetic transmission in diabetes and obesity models. Mount Sinai scientists are also engineering novel tools that may, in the future, be employed to restore normal nerve cell activity in metabolic syndrome

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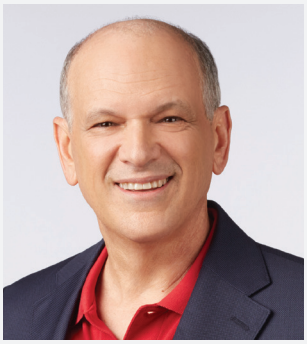
MESSAGE FROM THE DIRECTOR



Eric J. Nestler, MD, PhD
Nash Family Professor of Neuroscience; Director, The Friedman Brain Institute; Dean for Academic and Scientific Affairs, Icahn School of Medicine at Mount Sinai

The brain orchestrates the functioning of all other organs in the body so that an individual can adjust to changing needs of the environment, continuously receiving signals from the rest of the body to enable this top-down control. Knowledge of this bidirectional communication between the brain and these many vital areas, including the immune system, cardiovascular function, the gastrointestinal tract, and peripheral metabolism, is essential for understanding the healthy state of an organism, as well as discerning what goes wrong in disease. Studies of these interactions between the brain and other organs has become a high priority in basic neuroscience, neurology, and psychiatry.

This issue of The Friedman Brain Institute (FBI) newsletter focuses on one such area: the control of feeding and peripheral metabolism. More than 10 percent of the U.S. population has diabetes, and many more are at risk. The National Center for Health Statistics at the U.S. Centers for Disease Control and Prevention has determined that more than 40 percent of U.S. adults are obese. And, while less common, eating disorders, including anorexia nervosa and bulimia, are devastating, life-threatening illnesses that disproportionately affect teenagers and young adults. The FBI, in collaboration with Mount Sinai's Diabetes, Obesity, and Metabolism Institute, is working to advance understanding of these conditions through a highly integrated effort that spans basic molecular-cellular research to human clinical trials.

In future issues, we will present parallel efforts related to other dimensions of the brain-body axis. All of these interactions are key to advancing fundamentally new and more effective treatments for a wide range of neurologic and psychiatric disorders.

http://labs.neuroscience.mssm.edu/project/nestler-lab/ @EricJNestler

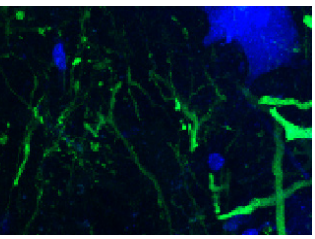
› UNCOVERING BIDIRECTIONAL COMMUNICATION *continued from page 1*

For example, the laboratory of **Sarah Stanley, MBBCh, PhD**, pioneers the use of magnetic fields to remotely modulate the activity of individual cells and neurons. This noninvasive method for controlling neuronal activity has broad research and therapeutic applications, including the potential to normalize autonomic tone in diabetic and obese patients.

Another forward-looking line of research actively pursued at Mount Sinai concerns the role of the gut-brain axis in metabolic disease, namely, the strong links between metabolism and mood and other emotional disorders. **Paul Kenny, PhD**, and colleagues have established a connection between nicotine-sensitive neurons in the brain and the central actions of gut hormones involved in the regulation of blood glucose levels. The functions and neuroanatomical connections of these nicotine-sensitive neurons, and their unanticipated role in controlling energy homeostasis, also constitute a topic of interest for **Jessica Ables, MD, PhD**, and her newly created laboratory. Together, these studies help explain why smokers are significantly more likely to develop type 2 diabetes than nonsmokers, and the interplay between diabetes, depression, and drug abuse, efforts that should lead to the development of novel treatments for these conditions.

Additionally, there are major efforts underway to grasp the importance of the gut microbiome in health and disease. The gut contains roughly the same number of bacteria as human cells in the entire body. The influence of those bacteria on conditions as diverse as depression, drug addiction, and multiple sclerosis is the focus of work in the laboratories of **Drew Kiraly, MD, PhD**; **Ilana Katz Sand, MD**; and **Stephanie Tankou, MD, PhD**.

The vagus nerve is the largest cranial nerve in the vertebrate body and constitutes the core of the gut-brain axis that enables visceral signals to influence brain activity. The laboratory of **Ivan de Araujo, PhD**, who was recruited to Mount Sinai from Yale School of Medicine in 2018, is carrying out studies that reveal a novel, and yet crucial, role for the vagus nerve in controlling motivation and reward. Dr. de Araujo and his team had discovered that the vagus nerve is functionally and anatomically connected to the reward centers of the brain. Mood alterations are



Christoph Buettner, MD, PhD, Professor of Medicine, and Neuroscience

Sarah Stanley, MBBCh, PhD, Assistant Professor of Medicine, and Neuroscience

Paul Kenny, PhD, Professor and Chair of Neuroscience

Jessica Ables, MD, PhD, Assistant Professor of Psychiatry, and Neuroscience

Drew Kiraly, MD, PhD, Assistant Professor of Psychiatry, and Neuroscience

Ilana Katz Sand, MD, Assistant Professor of Neurology

Richard A. Friedman, Co-Chairman, Mount Sinai Health System Boards of Trustees, right, with, from left, benefactors Pamela Nash, Helen Nash, Beth Nash, and Joshua Nash, member, Boards of Trustees, at a reception to unveil the newly named Nash Family Department of Neuroscience.

prevalent, not only in obesity, but also in patients who have severe eating disorders such as anorexia nervosa and bulimia.

Optical and electrophysiological methods are currently being developed in the laboratory to remotely control vagus nerve cells along with other populations of neurons innervating the digestive tract. These approaches may lead to novel opportunities to simultaneously repair metabolic and mood alterations in patients with eating disorders. These efforts add to Mount Sinai's endeavors to employ modern neuro-engineering technologies to improve the lives of metabolic syndrome patients.

Finally, Mount Sinai's Eating and Weight Disorders Center of Excellence within the Department of Psychiatry offers state-of-the-art treatments for individuals with obesity as well as for anorexia nervosa or bulimia. **Tom Hildebrandt, PsyD**, Chief of the Program, and **Robyn Sysko, PhD**, its Director of Research, and their colleagues lead New York City in providing medication, psychological, and surgical treatments for eating and weight disorders, which are notoriously difficult for individuals to conquer.

Stephanie Tankou, MD, PhD, Assistant Professor of Neurology

Ivan de Araujo, PhD, Professor of Neuroscience

Tom Hildebrandt, PsyD, Associate Professor of Psychiatry

Robyn Sysko, PhD, Associate Professor of Psychiatry

Thank You, Donors!

- **Ehrenkranz Family Supports Human Resilience**
  Anne and Joel Ehrenkranz have committed to improving our understanding of human resilience—what determines how individuals will respond in the face of stress or adversity—through their continued philanthropy. The Ehrenkranz Laboratory for the Study for Human Resilience is an integral part of Mount Sinai's Depression and Anxiety Center for Discovery and Treatment, enabling promising research in areas such as depression and post-traumatic stress disorder. Under the leadership of James W. Murrough, MD, PhD, Associate Professor of Psychiatry, and Neuroscience, our talented team of researchers explores mood disorders and resilience from multiple perspectives, with the shared goal of developing new and improved treatment options.

- **Improving Multiple Sclerosis Treatment Through Advanced Neuroscience** **Andrew and Sharon Alper** have committed to supporting our significant expansion of multiple sclerosis (MS) research and related core neuroscience initiatives through a transformational gift to the campaign. The faculty and staff at The Corinne Goldsmith Dickinson Center for Multiple Sclerosis are committed to our patients and optimizing the life-saving labor of our world-renowned specialists in multiple sclerosis and other autoimmune diseases that target the nervous system. In appreciation for this transformational gift, we are proud to announce the creation of the **Alper Neural Stem Cell Center**. This new center will, for example, give us the capacity to generate nerve cells and other types of brain cells from MS patients' skin or blood to study their pathology and use them to screen new treatments. **Kristen Brennand, PhD**, Associate Professor of Genetics and Genomic Sciences, Neuroscience, and Psychiatry, serves as the Center's founding director.

- **Investing in Neuroimaging and Neuropsychology**
  Leroy Schecter, a longtime supporter of Mount Sinai, has made a recent philanthropic investment in both neuroimaging and neuropsychology under The Friedman Brain Institute. The gift will support a recent faculty recruit from Harvard Medical School, **Trey Hedden, PhD**, whose lab focuses on integrating multiple brain markers from neuroimaging to help build a comprehensive picture of how aging and neurodegenerative disease affect the relationship between brain function and cognition at an individual level. Mount Sinai also received one of the inaugural grants from New York State's NYFIRST Program to support Dr. Hedden's recruitment. Additionally, work by **Jane Martin, PhD**, in neuropsychological testing, evaluation, and training will be supported by Mr. Schecter's gift. We are grateful for his continued philanthropic investment and interest in brain research.

2019: **CONFRONTING THE CHALLENGE**

Percentage of **Women in Science** in Departments Affiliated With The Friedman Brain Institute

LEADERSHIP

57% CENTER DIRECTORS

50% INSTITUTE DIRECTORS

FACULTY

54% Assistant Professors

38% Associate Professors

32% Professors

TRAINING

62% Students

56% Postdocs

#DiverseBrains

Graduate Students Make Neuroscience Fun and Accessible

Mentoring in Neuroscience Discovery at Sinai (MiNDS) is a graduate student-run outreach organization determined to make neuroscience education fun and accessible to the East Harlem community. Every year, the MiNDS team organizes a series of activities with the mission of reducing the barrier of entry into Science, Technology, Engineering, and Math (STEM) fields.

MiNDS kicked off the past academic year with its Second Annual Public Lecture, which was led by Yasmin Hurd, PhD, Director of the Addiction Institute of Mount Sinai, and Emily Feinstein, Executive Vice President of the Center on Addiction. The lecture focused on how neuroscience research influences policy surrounding the opioid crisis in the United States.

Committed volunteers among neuroscience graduate students and members of Mount Sinai's postdoctoral community, faculty, and staff drive MiNDS' success. The current leaders of MiNDS include, from left, Joe Simon, Casey Lardner, Carla Golden, and Denise Croote, all pursuing PhDs in Mount Sinai's neuroscience laboratories.

MiNDS also partnered with the Center for Excellence in Youth Education to lead a seven-part introductory neuroscience course at Patrick Henry PS 171. The course began by teaching students about the basic anatomy of a neuron, explained all of the different sensory systems that the brain uses to perceive the world, and concluded with a discussion about several neurologic and psychiatric disorders and the way in which they are studied in the laboratory.

Among the most popular events MiNDS helped host was the Seventh Annual Brain Awareness Fair, which drew more than 600 students, parents, and community members to Mount Sinai to learn about the brain and brain research.

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