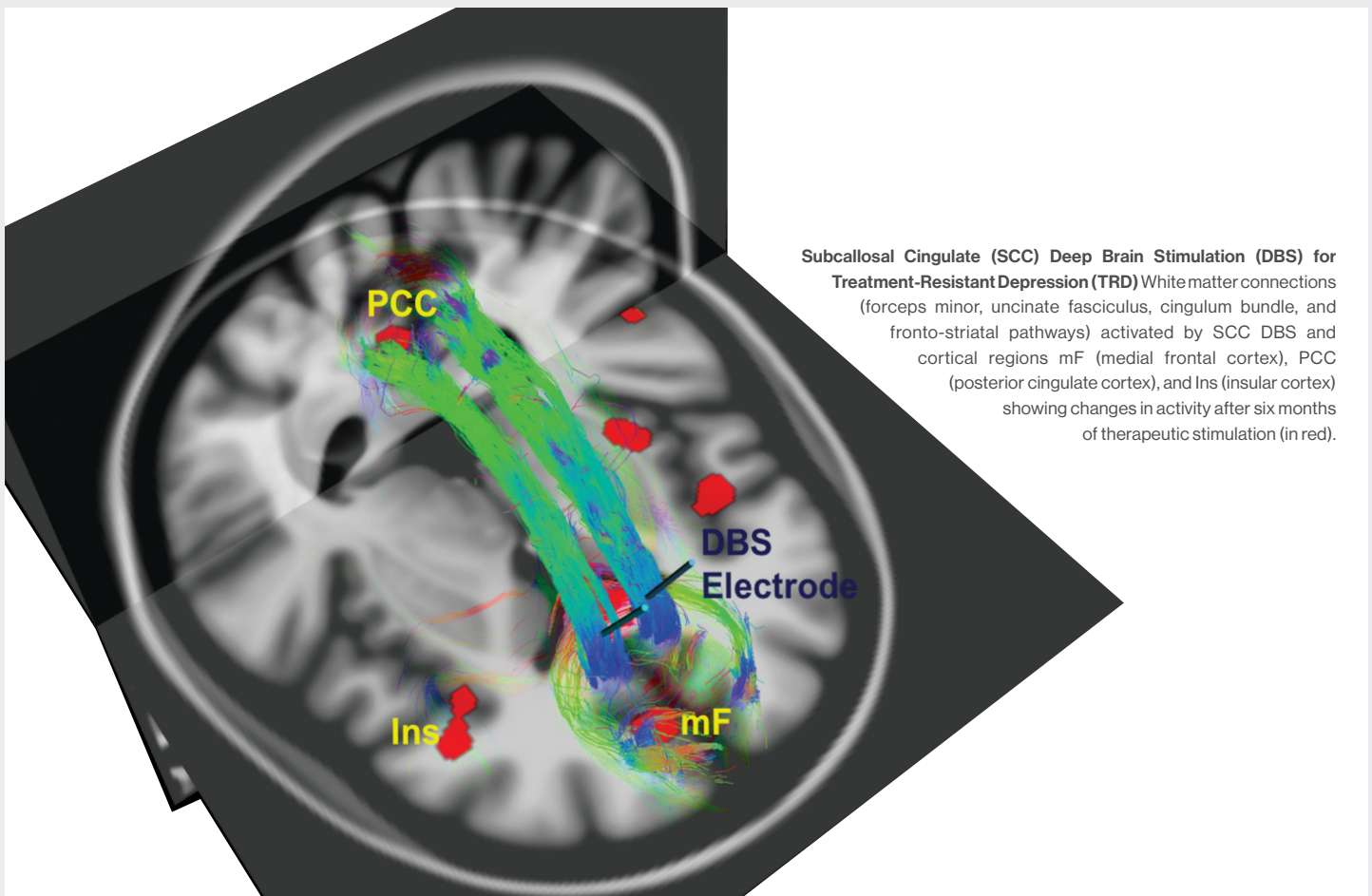




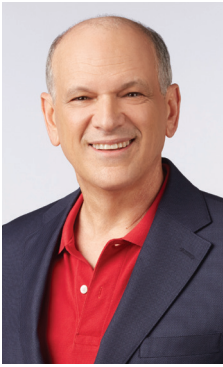
# The Friedman Brain Institute

## Remapping the Boundaries of Neurology, Psychiatry, and Neurosurgery Through the Lens of Brain Circuit Pathology



We are living in a time of rapid technological innovation across neuroscience. Informed by new discoveries in genetics and molecular and cell biology, and powered by novel neuroanatomical, neurochemical, molecular, engineering, and computational tools, we can now watch, listen, interrogate, interpret, and modify brain activity at multiple scales of complexity—from single cells to specified pathways to large-scale neural networks—affecting a wide range of behaviors, including motivation, reward, intention, emotional state, and action. Such advances have further catalyzed a fundamental shift in how we frame our view of the biological constructs of many of our most challenging neurological and psychiatric disorders with a growing emphasis on circuit-level models and treatments.

An exemplar of this cultural shift is deep brain stimulation (DBS)—focal modulation of a specified neural circuit using implanted electrodes—that is being applied to a growing number of severe and often intractable conditions. Approved by the U.S. Food and Drug Administration for Parkinson's disease, dystonia, focal epilepsy, obsessive compulsive disorder (OCD), and Tourette syndrome, it is now being evaluated for major depression, eating disorders, and addiction. Through the lens of brain circuit pathology, Mount Sinai's new Center for Advanced Circuit Therapeutics (C-ACT) is remapping the classical clinical boundaries of neurology, psychiatry, and neurosurgery to refine and extend current applications of DBS. C-ACT was founded and is being led by **Helen S. Mayberg, MD**, who joined the Icahn School of Medicine at Mount Sinai faculty this year.



**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

This issue of The Friedman Brain Institute newsletter highlights the creation of our new Center for Advanced Circuit Therapeutics at the Icahn School of Medicine at Mount Sinai, which is led by Helen S. Mayberg, MD, recruited to Mount Sinai earlier this year. Under her direction, the Center will advance precision surgical treatments for a wide range of neuropsychiatric disorders through the rapid conversion of neuroscience and neuroengineering innovations that correct brain circuit abnormalities to restore mood, as well as motor and cognitive functioning.

Dr. Mayberg will build a cross-disciplinary platform for collaborative translational research that will bring together clinical colleagues in neurology, neurosurgery, and psychiatry with experts from neuroscience, imaging, engineering, bioinformatics, neuroengineering, and computational neuroscience. The goal is to foster the development of new circuit-based strategies and delivery of

state-of-the-art individualized treatments for patients with severe neuropsychiatric disorders.

A close partnership between Dr. Mayberg and Brian H. Kopell, MD, a pioneer of deep brain stimulation and Director of the Center for Neuromodulation within the Department of Neurosurgery at Mount Sinai, will be paramount to the success of the new Center, which will also establish ties with many basic and clinical researchers and clinicians at Mount Sinai. In particular, the Center will work closely with experts from the Movement Disorders Program, the Epilepsy Center, the Mood and Anxiety Disorders Program, the Translational and Molecular Imaging Institute, and many other areas across the Icahn School of Medicine and within the Mount Sinai Health System. This new effort, driven by the Center for Advanced Circuit Therapeutics, promises a revolutionary approach to neuroscience by capturing one of the first precision medicine treatments of neurological and psychiatric disorders.

## 2018 FRIEDMAN BRAIN INSTITUTE RESEARCH SCHOLARS

The Philanthropic Leadership Council of The Friedman Brain Institute is pleased to announce this year's FBI Research Scholars. Funded entirely through philanthropy, the goal of the FBI Research Scholars Program—now in its third year and growing—is to support innovative and collaborative pilot brain research across the Mount Sinai Health System and to offer young pioneers who are venturing into a new area of investigation the freedom to follow their science.

### Fascitelli Research Scholar Award

**Nan Yang, PhD**, Assistant Professor, Neuroscience  
*"Functional annotation of non-coding variants in neuropsychiatric diseases using human neurons"*

### Katz and Martin Research Scholar Award

**Joseph M. Castellano, PhD**, Assistant Professor, Neuroscience, and Neurology  
*"Blood-borne molecules to target Alzheimer's disease pathology"*

### Mount Sinai Research Scholar Award

**Daniela Schiller, PhD**, Associate Professor, Psychiatry, and Neuroscience  
*"The hippocampus maps social space—a novel target for transdiagnostic social dysfunction"*

### Richard and Susan Friedman Research Scholar Award

**Denise J. Cai, PhD**, Assistant Professor, Neuroscience; and  
**Mark G. Baxter, PhD**, Professor, Neuroscience  
*"In vivo imaging of neuronal activity in the nonhuman primate brain with miniature fluorescent microscopes"*

### Nash Family Research Scholar Award

**Drew D. Kiraly, MD, PhD**, Assistant Professor, Psychiatry, and Neuroscience; and  
**Tristan Shuman, PhD**, Assistant Professor, Neuroscience  
*"Interrogation of microbiome effects on nucleus accumbens circuit function in cocaine reward"*

### Joseph and Nancy DiSabato Research Scholar Award

**Ross L. Cagan, PhD**, Professor, Cell, Developmental and Regenerative Biology, Oncological Sciences, and Ophthalmology; and Director, Center for Personalized Cancer Therapeutics; and  
**Arvin Dar, PhD**, Assistant Professor, Oncological Sciences, and Pharmacological Sciences  
*"Exploring functional and therapeutic kinase networks for tauopathies"*

### Mount Sinai Research Scholar Award

**Venetia Zachariou, PhD**, Associate Professor, Neuroscience; and  
**Roger Clem, PhD**, Associate Professor, Neuroscience  
*"Female-specific mechanisms of chronic pain"*

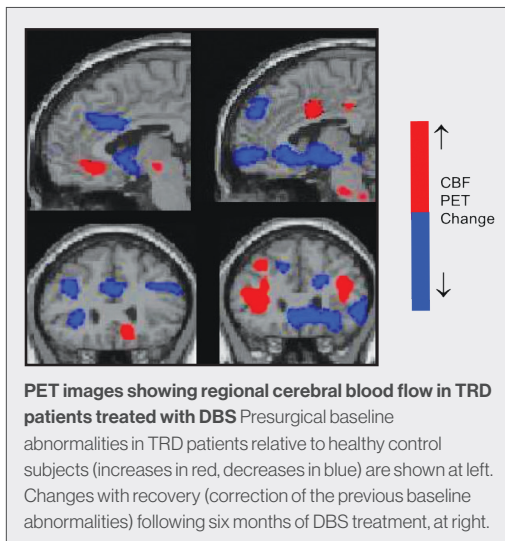
### Sundaram Research Scholar Award

**Inga Peter, PhD**, Professor, Genetics and Genomic Sciences; and  
**Zhenyu Yue, PhD**, Professor, Neurology, and Neuroscience; Aidekman Family Neurological Research Professor; Director, Basic and Translational Research in Movement Disorders  
*"TNF inhibitors as novel therapeutic targets to prevent Parkinson's disease"*

### Mount Sinai Research Scholar Award

**Coro Paisán-Ruiz, PhD**, Assistant Professor, Neurology; and  
**Florence Marlow, PhD**, Associate Professor, Cell, Developmental and Regenerative Biology  
*"Deciphering the functional effects of Parkinsonism-causing genes in the zebrafish nervous system"*

Unlike pharmacological, psychological, or rehabilitative treatments, interventions using neuromodulation posit the importance of anatomical precision, the exact and reliable identification of the optimal stimulation target. Advanced multimodal imaging and invasive and noninvasive electrophysiological recordings, combined with novel behavioral and performance biometric assessments developed with next-generation brain-stimulation devices, will all play an increasingly pivotal role in evaluating these new models of disease pathophysiology.



C-ACT's mission, working closely with the clinical Center for Neuromodulation in Neurosurgery led by **Brian H. Kopell, MD**, is to be a catalytic, multidisciplinary research engine and technology incubator developing and optimizing new neuromodulation-based treatments across the spectrum of disorders noted above. Success will be driven by rapidly translating research innovations to match patients with their optimal treatment, to correct brain circuit abnormalities to restore normal mood, motor, and cognitive functioning, and to maximize long-term outcomes. C-ACT aims to create a culture of precision neuroscience in the domain of surgical interventions for some of our most debilitating brain disorders.

The planned physical structure for C-ACT reflects its interdisciplinary and translational mission and intends to shake up the scientific and clinical status quo. Our blueprint places research laboratories in the patient care environment, encouraging direct interaction of research and clinical personnel and providing unprecedented opportunities for immediate

testing of common disease mechanisms and circuit-tuning strategies.

This research mission is anchored by partnerships across the Icahn School of Medicine at Mount Sinai and the Mount Sinai Health System. In addition to the leadership provided by Drs. Mayberg and Kopell, core C-ACT faculty include **Ki Sueng Choi, PhD**, a biomedical engineer and imaging specialist; **Allison C. Waters, PhD**, a clinical psychologist and brain electrophysiologist; and **Martijn Figeet, MD, PhD**, a

psychiatrist and DBS expert—all new recruits. They will work closely with the Movement Disorders Program, co-headed by **Susan Bressman, MD**, and **Dr. Kopell**; the Epilepsy Center, directed by **Madeline Fields, MD**, and **Lara Marcuse, MD**; and the Mood and Anxiety Disorders Program, led by **James Murrough, MD**.

Additionally, development of a state-of-the-art behavior and performance biometrics platform will use and extend the work of the Institute for Next Generation Healthcare, spearheaded by **Joel Dudley, PhD**, and **David E. Stark, MD**, and including **David F. Putrino, PhD**. New imaging strategies to advance precision surgical targeting and monitoring will also rely on collaborations with Mount Sinai's Translational Molecular Imaging Institute, directed by **Zahi Fayad, PhD**, and its new Advanced Neuroimaging Research Program, led by **Priti Balchandani, PhD**. Finally, C-ACT will leverage fundamental strengths in basic and translational neuroscience within The Friedman Brain Institute.



Ki Sueng Choi, PhD



Martijn Figeet, MD, PhD



Brian H. Kopell, MD



Allison C. Waters, PhD



Helen S. Mayberg, MD

## A New Gift for Seaver Autism Center

Hirschell E. Levine and John Cohen, Trustees of the Beatrice and Samuel Seaver Foundation, announced a \$2.78 million gift to the Seaver Autism Center for Research and Treatment at Mount Sinai to support precision medicine research in autism spectrum disorders (ASD), including rare genetic causes of autism. This most recent gift brings the Seaver Foundation's support of the Center to more than \$50 million as the Seaver Autism Center commemorates its 25th anniversary year as a world leader in research and treatment. This funding will allow the Seaver Autism Center to enhance its focus on precision medicine, including expansion of research programs in ADNP syndrome, FOXP1 syndrome, DDX3X syndrome, and SHANK3 syndrome. Funding will also support the development of a drug discovery and development program, one of the first of its kind in the field of autism.

## Welcoming Helen S. Mayberg, MD

**Helen S. Mayberg, MD**, was recruited to the Icahn School of Medicine at Mount Sinai as the founding Director of the Center for Advanced Circuit Therapeutics. She was named the Mount Sinai Professor in Neurotherapeutics and holds senior faculty appointments in Neurology, Neurosurgery, Psychiatry, and Neuroscience. Dr. Mayberg, a neurologist renowned for her study of brain circuits in depression and for her pioneering deep brain stimulation research—heralded as one of the first hypothesis-driven treatment strategies for a major mental illness—will help Mount Sinai play a leading role globally in devising new and transformational treatments for depression and a host of other severe neuropsychiatric disorders. Immediately prior to joining Mount Sinai, Dr. Mayberg was Professor of Psychiatry, Neurology, and Radiology, and held the inaugural Dorothy C. Fuqua Chair in Psychiatric Neuroimaging and Therapeutics at Emory University School of Medicine. Dr. Mayberg is a member of the National Academy of Medicine and the American Academy of Arts and Sciences.



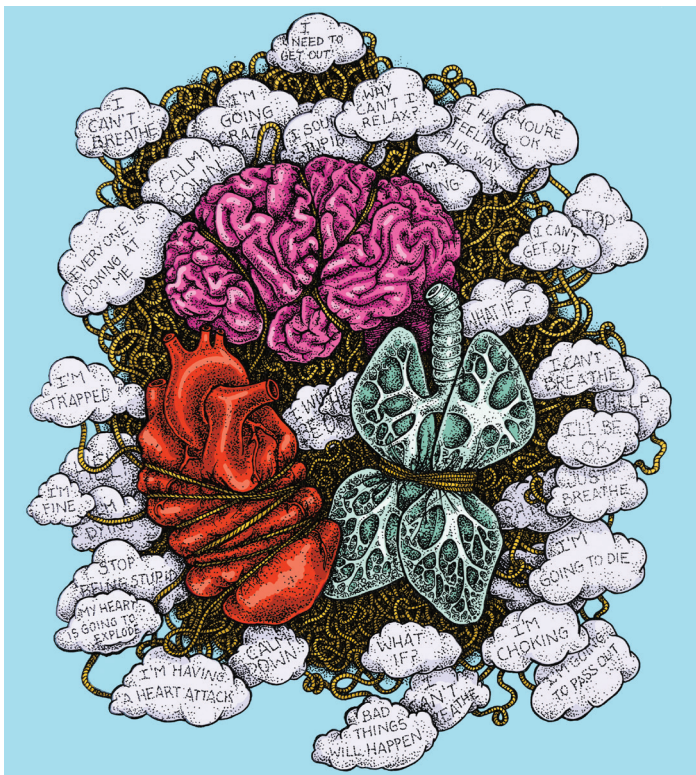


## Honoring Pamela Sklar, MD, PhD

The Mount Sinai community was deeply saddened by the passing in November of Pamela Sklar, MD, PhD, Chair of the Department of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai. Dr. Sklar was both a spectacular scientist who changed the field of psychiatry and a beloved mentor to students and young scientists at Mount Sinai and beyond. With a keen intellect and an unusual force of personality, she led a revolution in the study of the genetic basis of mental illness, showing that hundreds of genes are implicated, and not just a handful, as was previously believed. To honor her extraordinary contributions, the division she once led will now be known as the Pamela Sklar Division of Psychiatric Genomics, and an annual Pamela Sklar Lecture series has been created. The inaugural lecture is being presented on Monday, April 16, as part of a day-long symposium on Advances in Psychiatric Genomics in Dr. Sklar's memory to be held in Goldwurm Auditorium. Please consider a gift to support the Pamela Sklar Annual Lecture at Mount Sinai at <http://giving.mountsinai.org/PamelaSklar>.

## Raising Awareness About Brain Science

In March, The Friedman Brain Institute hosted and supported activities focused on educating students and the public about brain science in fun, interactive ways. The Sixth Annual Brain Awareness Fair delighted more than 450 New York City schoolchildren (see photo) and residents of the East Harlem community. The Fair, organized by Mentoring in Neuroscience Discovery at Sinai and the Center for Excellence in Youth Education, had the support of 100 volunteers. Also an annual highlight is the "Art of the Brain" exhibition, held in a local gallery, that showcases the work of Mount Sinai scientists through their images, photos, and sculptures that celebrate the beauty of the brain, including the "Visual Essay" below.



### VISUAL ESSAY

## Artistic Interpretation of Anxiety Disorder

This image—pen and ink on paper, and digitally colored—was created for the *Neurobiology of Mental Illness* (Oxford University Press) textbook to convey some of the physical and psychological symptoms of anxiety disorder. It was submitted from the newly named Pamela Sklar Division of Psychiatric Genomics, which helps uncover the genomic and epigenomic factors that contribute to the etiology of psychiatric disease, with a focus on schizophrenia and bipolar disorder.

Credit: Jessica S. Johnson, Icahn School of Medicine at Mount Sinai research associate and Laboratory Supervisor, Department of Genetics and Genomic Sciences, Pamela Sklar Division of Psychiatric Genomics

