

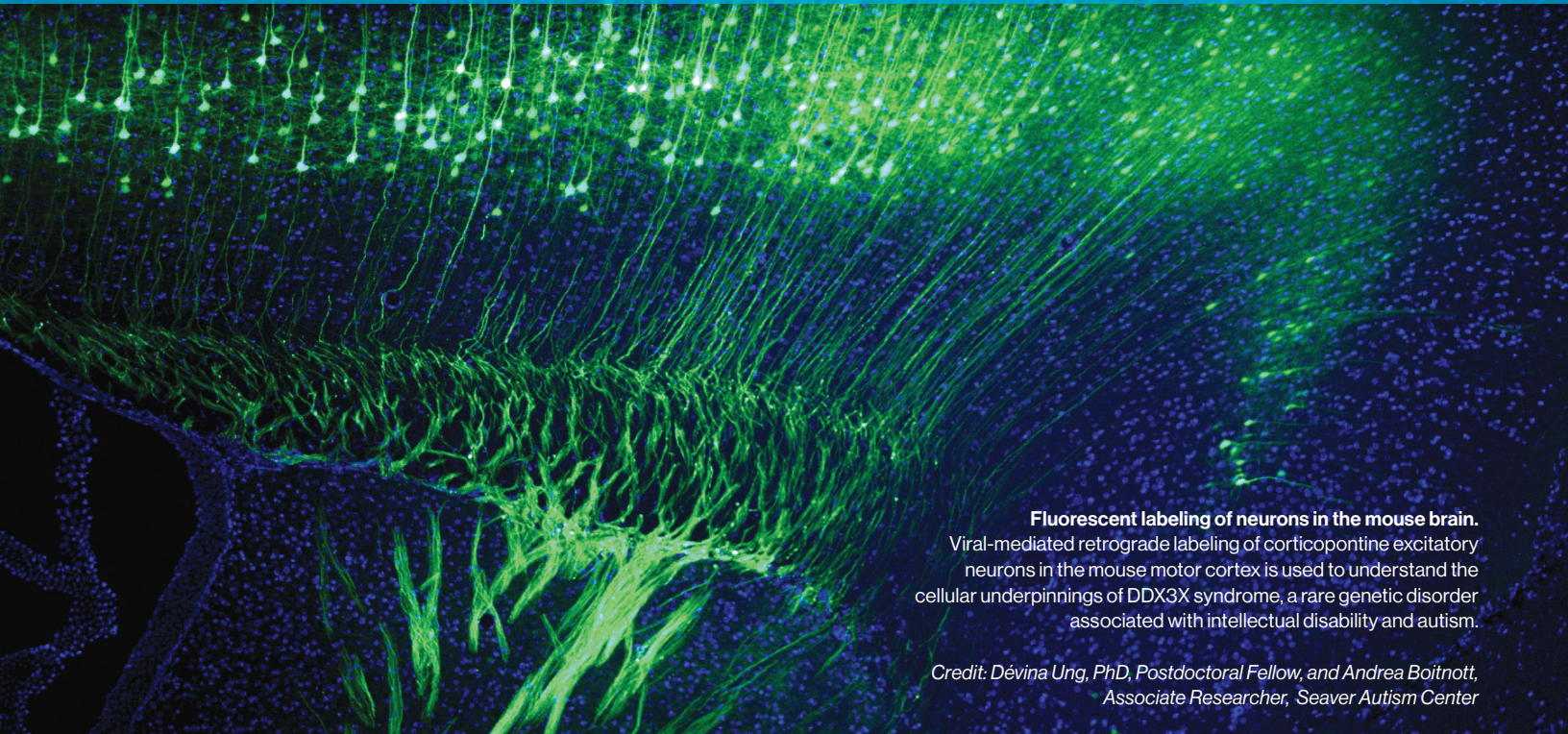


Icahn School
of Medicine at
Mount
Sinai

The Friedman Brain Institute

DIRECTOR'S REPORT | SPRING 2019

mountsinai.org/fbi



Fluorescent labeling of neurons in the mouse brain.

Viral-mediated retrograde labeling of corticopontine excitatory neurons in the mouse motor cortex is used to understand the cellular underpinnings of DDX3X syndrome, a rare genetic disorder associated with intellectual disability and autism.

Credit: Dévina Ung, PhD, Postdoctoral Fellow, and Andrea Boitnott, Associate Researcher, Seaver Autism Center

Seaver Autism Center Celebrates 25 Years

When the Seaver Autism Center for Research and Treatment was founded in 1993, there were few if any institutions of its kind. At the time, there was virtually no publicity or research dedicated to autism, which remained an underdiagnosed, understudied, and enigmatic disorder. The trustees of the Beatrice and Samuel A. Seaver Foundation wanted to establish a center to help individuals and families affected by autism. Mount Sinai took on the challenge.

In 2018, the Seaver Center celebrated 25 years of progress in the fields of autism research, diagnosis, and treatment. The Center works to improve the objective and reliable diagnosis of autism and related disorders, discover its biological causes, and develop and disseminate breakthrough treatments. The Center bridges the gap between new discoveries in basic science and enhanced clinical care, while ensuring that the community is aware of new and improved approaches to caring for young and grown individuals with autism. An interdisciplinary team of more than 40 full-time members—applying epidemiology approaches and new preclinical and clinical tools—is overseeing more than 60 current research projects. The epidemiology program researches large sets of clinical and population data to discover environmental risk factors for autism, such

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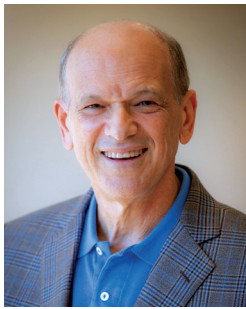
**Top Rankings for
Mount Sinai in
National Institutes of
Health Funding Among
U.S. Medical Schools**

No. 1
Neuroscience
\$31.2 million

No. 6
Psychiatry
\$35.1 million

No. 10
Neurology
\$21.2 million

Blue Ridge Institute for Medical Research data released February 2019 for National Institutes of Health (NIH) funding among U.S. medical schools. Awards received by the Icahn School of Medicine at Mount Sinai during the NIH 2018 fiscal year.



Eric J. Nestler, MD, PhD

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

The neuroscience community at the Icahn School of Medicine at Mount Sinai continues to grow and thrive. We recruited numerous new research and clinical faculty to our constituent departments across the School of Medicine and Mount Sinai Health System. The 2018 National Institutes of Health funding data reflect the national prominence that we are achieving: we are ranked No. 1 in Neuroscience, No. 6 in Psychiatry, and No. 10 in Neurology, with major plans in place to expand research within Neurosurgery, as well. Over recent years, we created several new research centers and clinical programs, and our research findings continue to be published in the world's foremost journals, all as we remain focused on advancing those discoveries into tangible improvements in patient care.

In this issue, we spotlight two recent milestones. Last fall, Mount Sinai's Seaver Center for Autism Research and Treatment celebrated its 25th anniversary. The Seaver Center has become a national and international leader in uncovering genetic and environmental causes of autism and in developing and providing patients with advanced treatments. Mount Sinai also established a new alliance with the Center on Addiction, a world-renowned organization focused on public policy and treatments for addiction. The strategic partnership with our Addiction Institute of Mount Sinai will focus on adolescents, young adults, and their families, and will work to create new, scalable models of care that can be replicated nationally. The Friedman Brain Institute's spectacular progress continues to be powered by the inspired philanthropy of our many supporters as we enter the active phase of Mount Sinai's new capital campaign. Our faculty, trainees, and staff are most grateful for the confidence placed in us to make a difference for people with brain disorders.

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

A New Strategic Alliance to Improve Addiction Treatment

More than 3 million young Americans between the ages of 12 and 25 have an addiction to drugs, and drug overdose deaths in the United States exceed 70,000 each year—more than the total number of U.S. casualties in the Vietnam War over its entire 15-year span. To address this devastating problem, the Addiction Institute of Mount Sinai and the Center on Addiction formed a strategic alliance that will invest in innovative solutions, with a focus on opioid addiction.



Yasmin Hurd, PhD, with Charles J. Neighbors, PhD, MBA, Director of Health Services Research, Center on Addiction.

Together, these entities understand that young people have complex needs that often go unaddressed by the U.S. addiction treatment system, which is designed for adults. Through the collaboration, leading addiction experts will work together to create innovative, scalable models for treatment—which include evidence-based screening, preventive practices, and care specifically tailored to young people with substance use disorders—that can be disseminated nationally.

The Addiction Institute of Mount Sinai seeks to improve patient care, drawing on the extensive clinical footprint of the Mount Sinai Health System and the research strengths in addiction biology of the Icahn School of Medicine at Mount Sinai. The Center on Addiction, founded in 1992 by former U.S. Secretary of Health, Education and Welfare Joseph A. Califano Jr., is an action-oriented nonprofit focused on ending the addiction epidemic. The alliance combines Mount Sinai's outstanding academic and clinical strengths in addiction with the Center on Addiction's 26-year legacy of groundbreaking health service and policy addiction research.

"The Center on Addiction's experience and ability to guide providers in the adoption of evidence-based practices will complement the progressive research being conducted by our experts at the Addiction Institute of Mount Sinai, where we are expanding the biological understanding of addiction and helping to develop new treatments," says Yasmin Hurd, PhD, Ward-Coleman Chair of Translational Neuroscience at the Icahn School of Medicine at Mount Sinai and Director of the Addiction Institute of Mount Sinai. "This collaboration will result in significant breakthroughs that advance

addiction research and care for young people and their families impacted by substance use disorders, which is especially important amid the largest drug epidemic in U.S. history."

Effective treatments that would prevent a lifetime of morbidity for young people are urgently needed and require the creation of new models that will incorporate shared decision-making among patients and care providers regarding medications, patient preferences, the use of technology, psychosocial treatment, and family involvement in care. Scientific advances at Mount Sinai, including advanced neuroimaging modalities and other biological markers that can help to identify individuals at risk, the use of app technologies, and data on non-addictive medications, can help inform and shape new treatment and management interventions.

Ultimately, the mission of this alliance is to promote evidence-based addiction care that is accessible and affordable to everyone to ensure that no family loses a child to substance use.



Making Science Exciting

To commemorate Brain Awareness Week in March, The Friedman Brain Institute, the Center for Excellence in Youth Education, and Mentoring in Neuroscience Discovery at Sinai joined the Dana Foundation in its global efforts to increase public awareness of the progress and benefits of brain research. Among the activities was the Seventh Annual Brain Awareness Fair, which drew nearly 500 participants (see photo), including New York City schoolchildren, along with their parents and teachers, who were able to meet Mount Sinai's top scientists and clinicians who study and treat the brain, play interactive brain games, see how neurosurgeons work, and touch human brain tissue used for research. This Brain Fair is now one of the largest Brain Awareness Week events in the nation.

Thank You, Donors!

Nash Family Supports Circuit Therapeutics The Nash Family has committed a leadership gift as part of the **WE CANNOT WAIT** capital campaign. This remarkable act of philanthropy has enabled the successful launch of our new Center for Advanced Circuit Therapeutics led by Helen S. Mayberg, MD. The Center, which is named for the Nash Family, is investigating novel research into targeting circuits in the brain via surgical deep brain stimulation to treat several neurological and psychiatric conditions such as Parkinson's disease, obsessive-compulsive disorder, and depression. In recognition of this transformational gift, and the family's past spectacular philanthropy to Mount Sinai, the Icahn School of Medicine at Mount Sinai is also pleased to name the Department of Neuroscience for the Nash Family.

Expanding Our Understanding of Cognition Jennifer and Marc Lipschultz have committed to reinforcing our strength in cognitive neuroscience by making an exceptional campaign gift. With transformational new technologies, which, for example, make it possible to record from, and manipulate, specific neurons and circuits in freely moving animals, we are poised to make groundbreaking discoveries that help answer fundamental questions about how we learn, remember, and make decisions and how these processes go awry in many brain diseases. In appreciation for this critical support, we are proud to announce the creation of the Lipschultz Center for Cognitive Neuroscience.

Further Investment in Developing Autism Targets Now in its 26th year, the Seaver Autism Center for Research and Treatment, through its new precision medicine initiative (see page 1 and below), has a goal of delivering new therapies that target individuals with autism who have specific genetic mutations. **Hirschell E. Levine and John Cohen**, Trustees of the Beatrice and Samuel A. Seaver Foundation, recently presented a new gift of more than \$4 million to the Seaver Autism Center at Mount Sinai, a portion of which will be dedicated to this crucial drug discovery effort, as well as to faculty recruitment. We are grateful to the Seaver Foundation for providing tremendous philanthropic support to the Center since its founding.

› SEAVER AUTISM CENTER CELEBRATES 25 YEARS *continued from page 1*

as paternal age, medication exposures, and nutrition. The preclinical program includes research that focuses on the identification of genetic risk factors for autism, as well as stem cells and animal models to uncover the relationship between genetic and environmental risk and the brain changes that lead to autism.

In 2010, the Center co-founded the Autism Sequencing Consortium (ASC), an international collaboration of more than 50 groups. The Consortium launched the largest gene sequencing study of autism, which is a highly heritable disorder. Today, the group is analyzing the genetic data of more than 35,000 individuals to identify autism risk genes. To date, the ASC has identified more than 100 autism-related genes, five of which lead to syndromes that are studied extensively at the Seaver Center: Phelan-McDermid, FOXP1, DDX3X, Helsmoortel-van der Aa (ADNP), and Fragile X syndromes. Compared to a decade ago, when very few autism-causing genes were known, specialists can now identify the genetic cause for autism in roughly 25 percent of individuals who present with the disorder.

To take these gene discoveries and other findings from bench to bedside, the Seaver Center conducts experimental therapeutics and clinical trial studies for children and adults with autism and related disorders. It is currently running five clinical trials, involving more than 100 participants. To measure treatment responses and progress, the clinical staff developed

a biomarkers program that determines objective measures to assess the particular features of each patient's symptoms. All services in the Seaver Center's research studies are provided without charge to eligible participants and can include gold standard diagnostic assessments, such as the Autism Diagnostic Observation Schedule—Second Edition (ADOS-2) and the Autism Diagnostic Interview—Revised (ADI-R).

In 2018, the Seaver Center launched a new precision medicine initiative. With the support of a generous gift from the Seaver Foundation, the Center is building a drug discovery and development platform by using the top gene findings to identify major pathways disrupted in autism. The goal of this initiative is to provide personalized, effective treatment plans for individuals with autism and related disorders.

Educating the next generation of autism experts is also a priority of the Seaver Center, providing training opportunities for medical students, residents, and doctoral students in psychology, neurology, psychiatry, neuroscience, and pediatrics, among other specialties.

As the Center enters its 26th year, the faculty and staff expect to achieve new benchmarks helping individuals with autism, their families, professionals, and the general public to understand the causes of, and available treatments for, autism and related disorders.

2019 Friedman Brain Institute Research Scholars Program

This unique effort, funded entirely through philanthropy, supports innovative and collaborative pilot brain research at Mount Sinai, allowing our most promising researchers to explore bold ideas aimed at driving new diagnostic and therapeutic discoveries.

Fascitelli Research Scholar Award

Hala Harony-Nicolas, PhD

"Implication of the hypothalamic oxytocin system in autism-associated social deficits"

Mount Sinai Research Scholar Award

**Daniel Wacker, PhD, and
Marta Filizola, PhD**

"Empowering structure-based discovery of new medicines to combat the opioid epidemic"

Katz and Martin

Research Scholar Award

**Kristen Brennand, PhD, and
Ian Slaymaker, PhD**

"CRISPR activation screens to identify factors for stem cell maturation"

Nash Family Research Scholar Award

**James Murrough, MD, and
Laurel S. Morris, PhD**

"Brain-computer interface (BCI) technology for neurocircuit-based treatment of depression in humans"

Joseph and Nancy DiSabato Research Scholar Award

**Erin L. Rich, MD, PhD; Kanaka Rajan,
PhD; and Peter H. Rudebeck, PhD**

"Wireless neural recording of social behavior in freely-moving non-human primates"

Satter Research Scholar Award

**Sarah Stanley, PhD, and
Cheuk Ying Tang, PhD**

"Ultrasound as a novel method for neuromodulation"

Richard and Susan Friedman Research Scholar Award

**Henrietta A. Szutorisz, PhD; Yasmin Hurd,
PhD; and Daniel Stein, MD**

"The effects of cannabis on the epigenetic state of human sperm with implications for multigenerational inheritance"

Sundaram Research Scholar Award

Wenfei Han, MD, PhD, and Zhenyu Yue, PhD

"The role of the gut-brain axis in the etiology of Parkinson's disease"

Dyal Research Scholar Award

**Maria de las Mercedes Perez-Rodriguez,
MD, PhD; Julie Spicer, PhD; Daniel Katz,
MD; Joshua Hamburger, MD; Jeffrey Zahn,
MD; Veerie Bergink, MD, PhD; Shanna H.**

Swan, PhD; and Panos Roussos, MD, PhD

"Cerebrospinal fluid (CSF) biomarkers of mother-infant social behavior"

The Scholars represent the departments of Anesthesiology, Perioperative and Pain Medicine; Environmental Medicine and Public Health; Genetics and Genomic Sciences; Medicine; Neuroscience; Obstetrics, Gynecology and Reproductive Science; Pharmacological Sciences; Psychiatry; and Radiology.

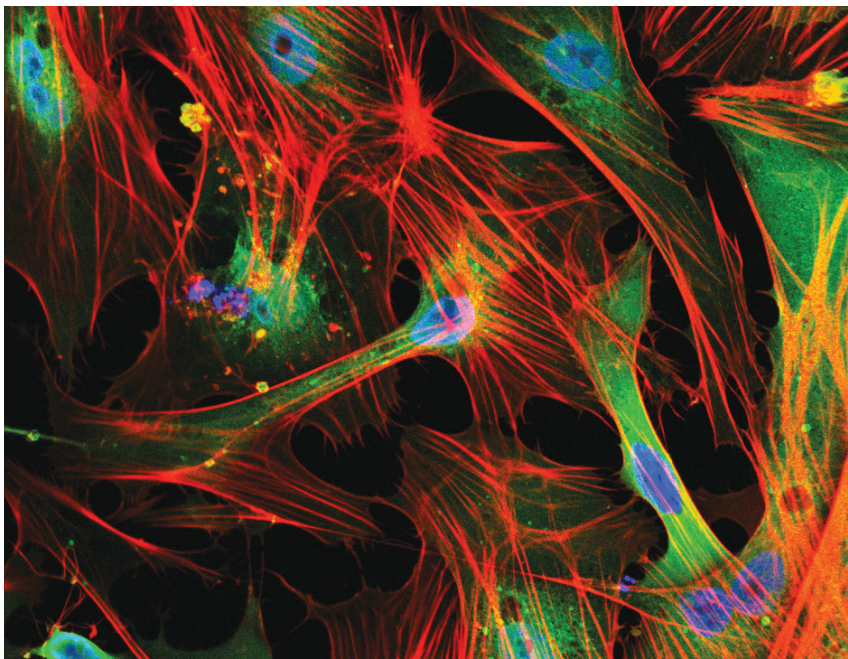


PHOTO ESSAY

When Mechanoregulation Goes Extreme

Human embryonic stem cells over-expressing Plexin-B2 and a mechanoregulator YAP (green) show aberrant morphologies and stress fibers (red). Nuclear staining (blue).

Credit: Chrystian J. Alves, PhD, Postdoctoral Fellow, in the labs of Hongyan Zou, MD, PhD, Associate Professor of Neuroscience, and Neurosurgery; and Roland Friedel, PhD, Assistant Professor of Neuroscience, and Neurosurgery.

