



Compassionate Care, Pioneering Research

The Friedman Brain Institute (FBI) has made major strides since it was founded in 2008 and is now one of the leading brain research enterprises nationally and internationally.

Over this period, we have recruited more than 60 basic and clinical neuroscience research faculty, along with a large number of faculty throughout the clinical specialties. Our National Institutes of Health funding has grown accordingly: the Department of Neuroscience is now ranked No. 3 in the nation, followed by Psychiatry, at No. 6, and Neurology, at No. 18. We are developing a new strategic plan to guide the further growth and strengthening of the FBI over the next five to ten years. Ultimately, our success will be

judged based on the ability of our scientists and physicians to develop new treatments for a range of brain and spinal cord disorders.

In this Director's Report, we spotlight the following recent efforts:

- Our leadership role in PsychENCODE, a national effort to define the epigenomic basis of psychiatric disorders;
- Innovative research by Don Des Jarlais, PhD, on HIV and drug abuse, which takes advantage of the unique breadth of the

Mount Sinai Health System;

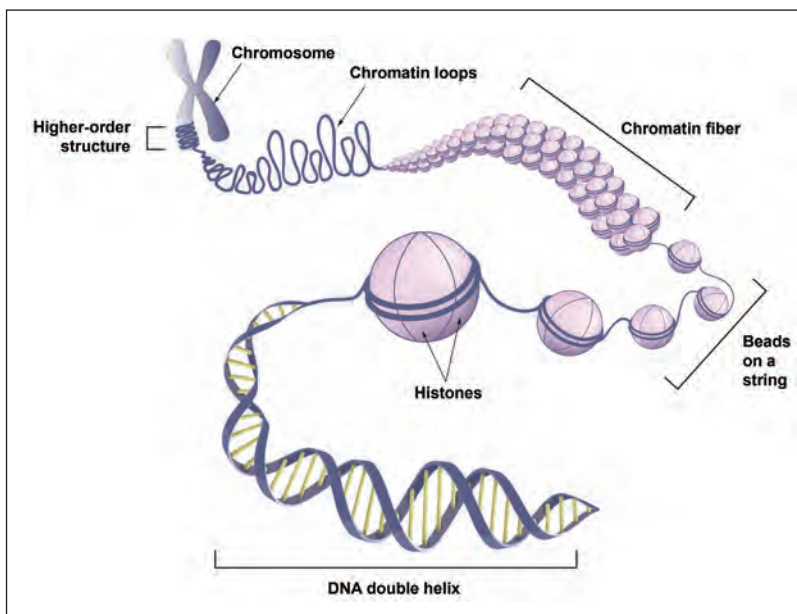
- Our commitment to address issues of diversity in the neurosciences (*#DiverseBrains*), and
- The announcement of the inaugural recipients of our FBI Research Scholars Partnership, funded through generous philanthropy.



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ADVANCING GENOME UNDERSTANDING

PsychENCODE Established at Mount Sinai



Chromatin structure The figure shows the DNA double helix wrapped around octamers of histone proteins to form "beads on a string," which are then further compacted; the most condensed form is recognizable as a chromosome. Chromatin loops bring distant segments of DNA into close proximity. Figure created by Veronica Szarejko

A formidable challenge for brain scientists is reflected by the fact that greater than 98 percent of our DNA is "noncoding" (not translated into protein), but nonetheless thought to be critically important for human health and disease, including psychiatric and neurological disorders. However, it is extremely difficult to ascribe function to noncoding DNA because the sequence itself offers very few clues on potential importance for cognition and behavior.

Therefore, the National Institutes of Health (NIH) recently launched a national consortium called PsychENCODE (Psych + Encyclopedia of DNA Elements), involving multiple institutions and investigators, aimed at understanding genome organization and function in the normal and diseased human brain. The Mount Sinai team, led by Schahram Akbarian, MD, PhD, and Pamela Sklar, MD, PhD, is mapping multiple types of histone marks (including H3 trimethyl-lysine 9 or H3 acetyl-lysine 27) in more than 600 brains collected by several U.S. brain banks across a very wide age range and including subjects diagnosed with schizophrenia or bipolar disorder. Among the brain banks is Mount Sinai's brain collection at the James J. Peters VA Medical Center in New York City, directed by Harry Haroutunian, PhD. Histones provide the backbone of chromatin (nuclear contents), and chemical modifications

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Ending HIV Among People Who Inject Drugs: From Intractable Epidemic to Solvable Challenge

Since the first cases of AIDS among people who inject drugs were observed in late 1981, AIDS has become the most important threat to the health of this population. Significantly, it also has forced the public health community to develop transformative approaches for addressing the individual and social harms associated with addictive disorders.

Don Des Jarlais, PhD, Professor of Psychiatry, and Preventive Medicine, at the Icahn School of Medicine at Mount Sinai, has been at the forefront of research on HIV/AIDS among drug users since his initial National Institutes of Health grant in 1985. It was this “Risk Factors” grant that led to the fundamental understanding that HIV is transmitted through sharing injection equipment as well as sexual intercourse. He and colleagues also identified the conditions for rapid transmission of HIV among drug users.

The first Risk Factors grant, which studies the HIV epidemic among drug users in New York City, has been funded consistently for more than three decades. The current grant focuses on “Getting Close to Zero” for new HIV infections—essentially ending the HIV

epidemic among people in the metropolitan New York area who use drugs. This grant also provides a complete history of the world’s largest HIV epidemic among people who use drugs.

With the potential for ending HIV epidemics among the drug-using population, Dr. Des Jarlais is also conducting research on reducing initiation into using drugs by injection. He recently received a National Institute on Drug Abuse “Avant Garde” award to study “Combined Prevention to Reduce Initiation into Injecting Drug Use.” What was once viewed as an intractable epidemic is evolving into a solvable challenge.

Additionally, Dr. Des Jarlais has led international research on HIV in addiction, which includes the first studies showing that it was possible to prevent HIV epidemics among these individuals by initiating early intervention, establishing close ties between people who use drugs and health care workers, and providing good access to sterile needles. He has conducted studies in more than 20 countries, with current large

studies under way in Eastern Europe and Southeast Asia.

Dr. Des Jarlais has also been active in policy development. He is a former Commissioner of the National Commission on AIDS, and has served on the New York City Commission on HIV and AIDS, the New York State Ending the HIV Epidemic Task Force, and the Scientific Advisory Board for the United States President’s Emergency Plan for AIDS Relief (PEPFAR). Dr. Des Jarlais remains a frequent consultant to the U.S. Centers for Disease Control and Prevention, the National Institute on Drug Abuse, the World Health Organization, and the United Nations’ UNAIDS. He has been a strong advocate for policies that are based on scientific evidence and that respect the human rights of individuals who use drugs.



Don Des Jarlais, PhD
Professor of Psychiatry,
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› PsychENCODE Established at Mount Sinai *continued from page 1*

of histones help define the functional architecture of the genome (for example, active gene promoters, enhancers, and repressed genes). See figure on Page 1. The vast amounts of data (many terabytes) generated by PsychENCODE will flow into databases accessible to scientists worldwide, and are expected to dramatically accelerate mechanistic insights linking genome sequence to epigenetic modifications to brain function in health and disease.

The vibrant research environment associated with PsychENCODE, including the unique accumulation of technical know-how on ways to optimally process chromatin from human brain tissue, has provided a critical incubator for many Mount Sinai investigators to launch their own epigenetic research programs to further enhance the methods and approaches put forward in PsychENCODE. This has resulted in additional NIH and VA grants awarded to Mount Sinai for research on a wide range of brain diseases.

Signature approaches of Mount Sinai’s team, which have been receiving widespread

recognition in the field, include the mapping of histone modifications and other epigenomic profiles in specific cell types of the brain by sorting and separating brain cell nuclei using cell-type specific antibodies for immunotagging and fluorescence-activated sorting. The team also pioneered mapping the 3D structure of chromatin in human brain through a recent finding that much of the genome packaged inside the cell nucleus is arranged in chromosomal loops (see figure), and that this organization is a very important part of human biology.

Ultimately, the epigenetic landscapes mapped by PsychENCODE could be viewed as molecular bridges that link both genetic material and the environment to brain function and human behavior. From this perspective, this pioneering work is critical to harness the powerful tools of modern genome medicine for a better understanding of the molecular underpinnings of psychiatric and neurological disease as a prerequisite to developing better diagnostic tools, and novel and more effective evidence-based therapies.



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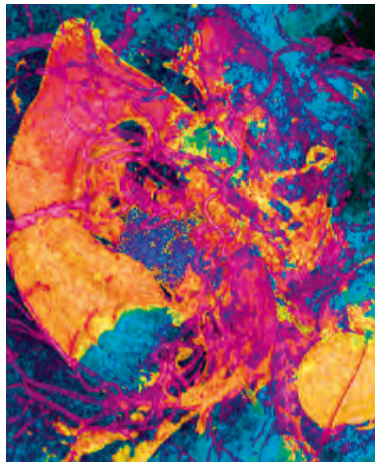
Brain Awareness Week

The Fourth Annual Mount Sinai Brain Awareness Fair

To commemorate Brain Awareness Week, March 14 - March 20, The Friedman Brain Institute joins The Dana Foundation, a private philanthropic organization that supports brain research through grants, publications, and educational programs, in its global efforts to increase public awareness of the progress and benefits of brain research. Mount Sinai's Fourth Annual Brain Awareness Fair for local students, parents, and the public is a highlight of the week-long activities. The fair features educational hands-on activities and demonstrations by Icahn School of Medicine at Mount Sinai faculty, who will also lead discussions that disprove common "Brain Myths." *Hosted by Mentoring in Neuroscience Discovery at Sinai (MiNDS), with support from The Friedman Brain Institute, and the Center for Excellence in Youth Education (CEYE) at Mount Sinai.*

The Art of the Brain

The Art of the Brain is an exhibition of photographs that celebrates the beauty of the brain as seen through the eyes of Mount Sinai scientists. They were created with the aid of advanced imaging technology, allowing researchers to gain a better understanding of how the brain works, with the ultimate goal of accelerating the development of new treatments for brain disorders. The event, first sponsored three years ago by The Friedman Brain Institute to commemorate Brain Awareness Week, has grown in popularity each year. This year's exhibit will feature a variety of images, including the "Close-Up View of a Benign Brain Tumor," pictured here, which will be on display at two locations: Mount Sinai Beth Israel and the Grady Alexis Gallery in Manhattan.



Close-up View of a Benign Brain Tumor

A 3D patient-specific rendering generated from a fused CTA and MRI

Image by Joshua B. Bederson, MD; Anthony B. Costa, PhD; Steven Philemond, MPH; and Jillian Beroza, Department of Neurosurgery

Advancing the Study of Vascular Malformations in Children

Alejandro Berenstein, MD, Director of the Pediatric Cerebrovascular Program at the Icahn School of Medicine at Mount Sinai and Director of the Hyman Newman Institute of Neurology and Neurosurgery, is leading efforts to study vascular malformations of the brain, central nervous system, head, and neck in pediatric patients. Vascular malformations are a complex group of lesions that can result in high morbidity and mortality, yet researchers face significant limitations in developing new treatments because of a lack of reliable and reproducible testing models.

Dr. Berenstein and his team have succeeded in developing tissue-engineered models of in vitro channels, lymphatic channels, and combinations of arterial and venous channels, as well as canine models of aneurysms. Two recent gifts totaling \$1 million from The Zimin Foundation will allow for additional development of testing models to address venous and lymphatic malformations and also provide a platform for researchers to promote awareness of vascular malformations throughout the Mount Sinai Health System.

FBI Research Scholars Named

The Philanthropic Leadership Council of The Friedman Brain Institute is pleased to announce the inaugural class of FBI Research Scholars who will receive pilot grants through the new FBI Research Scholars Partnership:

Richard and Susan Friedman Research Scholar Award:

Junqian (Gordon) Xu, PhD, Assistant Professor of Radiology, and Neuroscience

Paula Croxson, D.Phil, Assistant Professor of Neuroscience, and Psychiatry

"Exploring the functional and metabolic imaging features of neuroplasticity in brainstem and spinal cord"

Nash Family Research Scholar Award:

Roland Friedel, PhD, Assistant Professor of Neuroscience, and Neurosurgery

Hongyan (Jenny) Zou, MD, PhD, Associate Professor of Neurosurgery, and Neuroscience

"Utilizing methylation reporter to assay locus-specific methylation dynamics in glioblastoma"

Rosen Family Research Scholar Award:

Ian Maze, PhD, Assistant Professor of Pharmacology and Systems Therapeutics, and Neuroscience

"Function of a novel 'reader' of neuronal chromatin in Trisomy 21-associated Alzheimer's disease"

Elizabeth and Michael Fascitelli Research Scholar Award:

Reymundo Lozano, MD, Assistant Professor of Psychiatry, Genetics and Genomic Sciences, and Pediatrics

"FOXP1 variants and a new syndromic form of autism spectrum disorder (ASD)"

Saint-Amand Research Scholar Award:

John Crary, MD, PhD, Associate Professor of Pathology, and Neuroscience

Jason Fuller, Biomolecular Engineer

Russell Hanson, Assistant Professor, Genetics and Genomic Sciences

"Aptamer-based bioactuators for early diagnosis of Alzheimer's disease"

Funded entirely through philanthropy, the goal of the program is to encourage innovative brain research and to offer young pioneers who are venturing into a new area of investigation the freedom to follow their science.

#DiverseBrains: Promoting Diversity in Neuroscience



Among leading faculty from the Icahn School of Medicine at Mount Sinai participating in a recent panel discussion on Diversity in Neuroscience were: Sandra K. Masur, PhD, left photo; Reginald Miller, DVM, middle photo; and Stephen Krieger, MD, left, and Yasmin Hurd, PhD, second from left, right photo. Also on the panel were Barbara Juarez, graduate student, and Elizabeth Heller, PhD, postdoctoral fellow.

A lot has been written recently about diversity issues in science. Compared with two decades ago, women are now well represented (approximately 50 percent) among medical and graduate students, postdoctoral fellows, and assistant professors. However, despite these gains, we still have a small number of senior women faculty and far fewer faculty from under-represented minority groups—at Mount Sinai and nationwide. Recent studies continue to document implicit biases in the scientific workplace, and there have been several widely publicized cases of bad

behavior at other institutions that went unaddressed for years. Moreover, concerns remain around quality-of-life issues and obstacles to faculty retention and promotion that affect everyone.

To address these challenges, The Friedman Brain Institute launched a year-long initiative to formulate positive steps by which we can make progress in these areas. The FBI cannot solve societal issues, but we can serve as a smaller focus group and demonstrate the kinds of tangible actions that lead to real improvements.

For more information on our activities—which to date have included a Town Hall meeting, workshops, panel discussions, and lectures by renowned national authorities from other institutions—and to comment, please go to: neuroscience.mssm.edu/diversityinneuroscience/ or [#DiverseBrains](https://twitter.com/DiverseBrains), where a lively discussion continues. One of the important lessons is that talking about gender and race bias is often uncomfortable and awkward, and that's okay. Only by crafting an environment where these issues can be discussed openly will we be able to make progress.

PHOTO ESSAY

Reactive Astrocytes Cluster to Contain Activated Leukocytes

Human astrocytes (red), one of the brain's cellular components, are placed together with leukocytes (green), cells that are involved in protecting the body against foreign invaders. The cells are placed in conditions that mimic a disease state. After one day, the astrocytes form dense rings to surround leukocytes, providing novel insight into how the brain responds to inflammation and infection. Blue indicates cell nuclei.

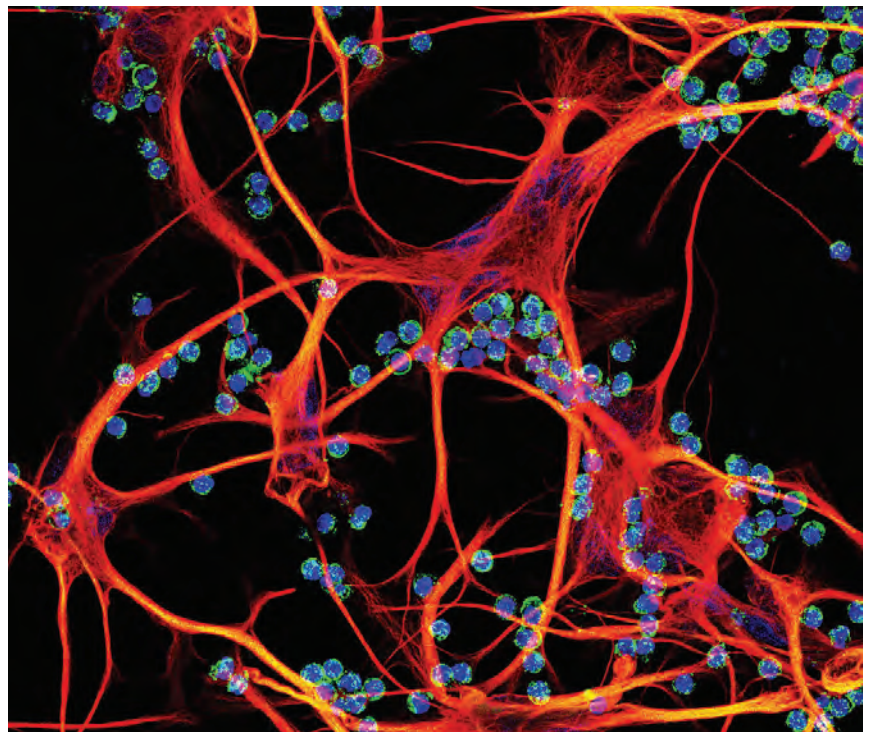


Image by Candice Chapouly, PhD, from the laboratory of Gareth John, PhD, Professor of Neurology