The Friedman Brain Institute Announces 2020 FBI Research Scholars

On behalf of the Philanthropic Leadership Council of The Friedman Brain Institute, we are pleased to announce the 2020 recipients of The FBI Research Scholars Awards.

Karen Strauss Cook Research Scholar

Ana Pereira, MD
Assistant Professor, Neurology

John F Crary, MD, PhD
Professor, Pathology

Single cell mapping of tau pathology in the degenerating human brain

Tau pathology characterizes a spectrum of "tauopathies". There is a critical need to better understand the association between neuropathology in these disorders and molecular mechanisms regulating cell death. We will perform single-cell RNA sequencing and multiplex immunofluorescence microscopy across tauopathies, generating a catalog of abnormal cellular signatures. Then, we will make personalized iPSC-derived cellular models from the same donors, enabling mechanistic validation in a cell-type specific manner. The study will identify potential divergent and convergent mechanisms of tau-mediated neurodegeneration in human brain tissues from our unique dataset of single-cell transcriptomic signatures.

Joseph and Nancy DiSabato Research Scholar Award

Minghui Wang, PhD
Assistant Professor, Genetics and Genomic Sciences

Aiqun Li, PhD
Senior Scientist, Genetics and Genomic Sciences

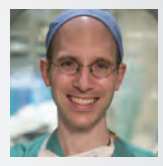
Multiplex identification of novel microglia targets of alzheimer's disease using CRISPRa and scRNA-seq

Accumulating evidence has implicated a potential causal role of microglial/immune response dysfunction in the pathogenesis of Alzheimer's disease (AD). Yet, the underlying mechanism and functional role of microglia risk genes in AD remain elusive. We perform multi-scale integrative network analysis of large-scale multi-omics data of AD and control brains and find a network of microglial/immune response pathway genes highly associated with AD pathology. Building on these findings, we intend to develop a systems genetic screen platform integrating networking modeling, stem cell technology, CRISPR gene editing, and single-cell sequencing analyses, with an aim to discover critical key drivers of the dysfunctional microglia network in AD.

Dyal Research Scholar Award

Kanaka Rajan, PhD
Assistant Professor, Neuroscience

Neha Dangayach, MD
Neurocritical Care Fellowship Director, Neurosurgery and Neurology



Eric K Oermann, MD
Instructor, Neurosurgery

Unlocking critical care data to predict catastrophic clinical events using artificial intelligence

Extended stays in neurosurgical intensive care units (NSICUs) are associated with an increased risk of catastrophic outcomes such as delirium, seizures, and secondary brain injury. However, the accurate prediction of such impending catastrophic outcomes is notoriously difficult. Availability of extensive time-series measurements from patients in the NSICU, with no additional burden to them, presents an incredible opportunity to uncover predictive features from such data. With support from the FBI Pilot Award, we propose to develop a transformative new artificial intelligence (AI)-based tool to discover from time-series patient data the signals predicting upcoming catastrophic clinical outcomes before they occur. Systematic, real-time inference and visualization of predictive signals from patient data will inform individualized care to improve the outcomes of critically ill neurology and neurosurgery patients.

Fascitelli Research Scholar Award

Silvia De Rubeis, PhD
Assistant Professor, Psychiatry

Zhuhao Wu, PhD
Assistant Professor, Cell, Developmental & Regenerative Biology

Capture the cellular and molecular drivers of cortical development in DDX3X syndrome

In a new collaboration, the De Rubeis and Wu labs will study the cellular and circuitry mechanisms underlying DDX3X syndrome, a rare genetic condition associated with intellectual disability and autism spectrum disorder. The researchers will explore how cortical projection neurons develop in a novel mouse model of DDX3X syndrome using a combination of whole-brain tracing of cortical projections, circuit mapping, and molecular profiling. This study aims at opening new horizons for understanding and treating DDX3X syndrome.

Katz / Martin Scholar Award

Lotje Dorothee de Witte, MD, PhD
Assistant Professor, Psychiatry

Viviana Simon, MD, PhD
Professor, Microbiology and Medicine

Dissecting the mechanisms driving microgliosis in primary human microglia cells

Emerging evidence suggests that microglial cells play a critical role in neurodegenerative disorders. An increased number of microglia cells ("microgliosis") is observed in neurodegenerative disorders. The cause and clinical consequences of microgliosis remain, however, elusive. Our project will build on our findings that HIV infection leads to rapid expansion of primary microglial cells isolated from human post-mortem brain tissues. By studying how HIV rewires microglia cells, we will gain a better understanding of the molecular mechanisms controlling microglia proliferation at the single cell level and create novel tools to study proliferation and clonal expansion of human microglia.

Lipschultz Scholar Award

Abha Karki Rajbhandari, PhD
Assistant Professor, Neuroscience and Psychiatry

Ivan de Araujo, PhD
Professor, Neuroscience

Regulation of PTSD via neuropeptidergic signaling in the brain-vagus-body axis

While most PTSD research focuses on understanding fear and stress regulation via the central nervous system, a much less studied area is the biological mechanisms underlying the brain and body interactions in these processes. The current FBI Scholars grant proposal establishes an inter-departmental multidisciplinary collaboration between Dr. Abha Karki Rajbhandari and Dr. Ivan de Araujo, experts in models of stress and fear disorders and brain/peripheral circuit mapping, respectively, to understand autonomic mechanisms that regulate traumatic fear via the 'brain-vagus-body' axis. The results from this proposal can be harnessed to develop novel therapeutics for fear and stress related-psychiatric conditions including, but not limited to, PTSD.

Mount Sinai Research Scholar

Roger Clem, PhD
Associate Professor, Neuroscience

Paul Slesinger, PhD
Professor, Neuroscience

Neuropeptide signaling by prefrontal interneurons in fear memory encoding

Memory encoding figures prominently in both cognitive and emotional disorders, but its cellular basis remains poorly understood. We recently established that the recruitment of a prefrontal network underlying fear memory depends on inhibitory neurons that express the "marker" neuropeptide somatostatin. With the aid of Miniscope technology and cell-based neurotransmitter fluorescent reporters (CNiFERs), our project will test whether these neurons signal during fear learning through an unconventional mechanism, the release of somatostatin and its binding to G protein-coupled receptors. This could ultimately help establish novel therapeutic interventions for memory-related disorders.

Nash Family Research Scholar Award

Allison Waters, PhD
Assistant Professor, Psychiatry and Neuroscience

James Murrough, MD
Associate Professor, Psychiatry and Neuroscience

Helen Mayberg, MD
Professor, Neurosurgery, Neurology, Neuroscience and Psychiatry

Ketamine plus deep brain stimulation for severe treatment-resistant depression: identifying synergistic brain mechanisms to advance novel treatment discovery

Treatment resistant depression (TRD) represents a severe and disabling condition characterized by significant functional impairment, non-response to conventional antidepressants, and a high risk for suicide. Complementary mechanisms of action are attributed to successful treatment of TRD with deep brain stimulation (DBS) or ketamine. The proposed research will test if an EEG-derived biomarker of the antidepressant response to DBS also predicts outcomes following ketamine treatment. Results will provide critical rationale for a novel treatment approach that enhances DBS efficacy with a combined ketamine-DBS approach.

Satter Research Scholar Award

Dolores Malaspina, MD, MS, MSPH
Professor, Psychiatry, Neuroscience, Genetics and Genomic Sciences

Yuen Ping Toco Chui
Associate Professor, Ophthalmology

Psychosis insights from ocular imaging

Schizophrenia is a disabling neurodevelopmental disorder typically diagnosed in the late teens or early twenties, defined by psychotic symptoms, such as hallucinations and delusions, and socio-emotional deficits. The syndrome is caused by different types of underlying brain abnormalities, but it is treated as a single disorder because we lack an inexpensive and rapid technology to determine the pathology for individual cases. However, the eye, which develops as an outgrowth of the brain in fetal life, can be rapidly imaged using sophisticated optical imaging technologies that can measure neurons, axons, glia, microvasculature, myelination, and immune function. This study will test the use of ocular imaging for research and clinical treatment in schizophrenia, obtaining state of the art ocular imaging for schizophrenia cases and controls. The results will be examined with respect to the subjects' individual gut microbiome composition, circulating inflammatory cytokines and magnetic spectroscopic (MRS) brain images.

Shah Research Scholar Award

Tristan Shuman, PhD
Assistant Professor, Neuroscience

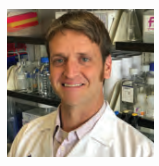
Yasmin Hurd, PhD
Professor, Neuroscience and Psychiatry

Neural circuit mechanisms driving therapeutic effects of CBD in epileptic mice

Cannabidiol (CBD) is a cannabis extract that has become a popular drug for self-medication and has recently been shown to be an effective treatment for certain genetic forms of childhood epilepsy. Despite its immense popularity, very little is known about how CBD alters the brain to produce its effects. In this proposal, we will administer CBD to control and epileptic mice running through a virtual reality environment and record brain activity with high-density electrodes in order to better understand how CBD rescues seizures and cognitive deficits in epilepsy.

Sundaram Research Scholar Award

Bojan Losic, PhD
Associate Professor, Genetics and Genomic Sciences



Alex Charney, MD
Assistant Professor, Psychiatry, Genetics and Genomic Sciences, Neuroscience and Neurosurgery

Navneet Dogra, PhD
Assistant Professor, Genetics and Genomic Sciences and Pathology

Live brain profiling via blood derived exosomal small RNA

A scalable, inexpensive technique is urgently needed to profile the complex biological activity of a living human brain and facilitate remote sensing in the treatment of neuropsychiatric disorders. This project will use the Living Brain Project to catalog peripheral exosomal small RNA signatures and associated ribonucleoproteins that are brain specific.

Zhao Research Scholar Award

Coro Paisán-Ruiz, PhD
Associate Professor, Neurology, Psychiatry and Genetics and Genomic Sciences

Joanna Jen, MD, PhD
Professor, Neurology, Neurosurgery and Otolaryngology

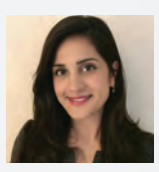
Robert Sebra, PhD
Associate Professor, Genetics and Genomic Sciences

Mapping the genomic landscape of episodic ataxias.

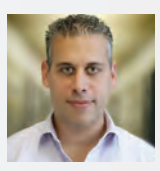
Episodic ataxia (EA) is a hereditary movement disorder characterized by recurrent episodes of incoordination and imbalance. Despite the mapping of 8 loci and the identification of mutations in 5 genes, the genetic causes are unknown for an estimated 40-50% of the patients and are suspected to involve changes in the noncoding regions of the genome. For this project, we have clinically characterized two EA kindreds with no mutations in the known EA or ataxia genes and aim to perform single molecule real time sequencing to identify large dynamic repeat expansions and complex DNA structural variations that may be pathogenic.

Richard and Susan Friedman Research Scholar Award

Manish Jha, MBBS
Assistant Professor, Psychiatry and Neuroscience



Priti Balchandani, PhD
Associate Professor, Diagnostic, Molecular and Interventional Radiology and Neuroscience



Scott Russo, PhD
Professor, Neuroscience and Psychiatry

James Murrough, MD
Associate Professor, Psychiatry and Neuroscience

Using high-field neuroimaging to unlock the therapeutic potential of orexin antagonists for depressed patients with anger and irritability

Irritability affects one in two adults with depression, worsens quality of life, and increases risk for suicide. Yet, there are no treatments currently available that specifically target irritability. Preclinical studies have identified the habenula as a key brain region modulating aggression, a common behavioral manifestation of irritability. Hence, we propose to characterize the role of habenula in the neural circuitry of irritability in humans using ultra-high field neuroimaging, and to generate pilot data demonstrating the potential of orexin antagonists as a novel treatment for irritability.

Icahn School of Medicine at **Mount Sinai**