The Friedman Brain Institute Announces 2022 FBI Research Scholars

On behalf of the Philanthropic Leadership Council of The Friedman Brain Institute, we are pleased to announce the 2022 recipients of the FBI Research Scholars Awards.

Karen Strauss Cook Research Scholar Award

Cameron S McAlpine, PhD
Assistant Professor, Medicine and Cardiology

Sleep mediates monocyte recruitment to the cerebral vasculature in tauopathy and Alzheimer's disease

Humans should spend a third of their life asleep, yet we are becoming increasingly sleep-deprived. Clinical evidence has long established that sleep disruption is associated with tauopathy, dementia, and Alzheimer's disease. Despite these associations, the biological underpinnings that link sleep with neurodegenerative diseases are poorly understood. We are studying how sleep alters the immune system and inflammatory pathways to shape neurodegenerative pathology. We will test how sleep influences the production of immune cells in the bone marrow and their transit to the brain's vasculature to mediate neurovascular inflammation and neurodegeneration. Together, our findings will identify how the immune system connects sleep to tauopathy and Alzheimer's disease.

Ram Sundaram Research Scholar Award

Rebecca M Brown, MD, PhD
Assistant Professor, Neurology

Nicholas David Gulati, MD, PhD
Assistant Professor, Dermatology

Diphencyprone Immunotherapy in Cutaneous Neurofibromas Associated with NF1

Neurofibromatosis type 1 (NF1) is the most common genetic tumor predisposition syndrome, affecting up to 1 in 2500 individuals, or ~3400 children and adults in New York City. Mutation in the NF1 gene leads to the growth of benign tumors known as neurofibromas along large nerves and in the skin. Cutaneous neurofibromas begin to appear in late childhood and they never spontaneously resolve, resulting in a tumor burden that can sometimes reach the tens of thousands. They are disfiguring and can be painful or itchy, leading to loss of confidence, anxiety, and depression. Currently, the only treatment is surgery or laser therapy, however, only a limited number of tumors can be simultaneously removed, recovery can be painful, and there is significant risk of regrowth. There is a strong need for noninvasive topical treatments for cutaneous neurofibromas. Diphencyprone (DPCP) is a topical immunotherapy that works by activating immune cells within the region of application. DPCP has previously been used to eliminate warts, restore hair growth in idiopathic baldness (alopecia areata), and treat malignant melanoma. We are planning a phase 1 clinical trial for DPCP in adult patients with NF1 and 4-20 symptomatic/bothersome cutaneous neurofibromas with a goal accrual of 40 patients. Outcomes include safety, tumor regression, immune activation measures, and quality of life.

Ross Family Research Scholar Award

Philipp Mews, PhD
Instructor, Neuroscience

Marine Salery, PhD
Instructor, Neuroscience

Spatial Transcriptomics to Illuminate Neuronal Circuit Function in Memory

Experiences modulate transcriptional landscapes across brain regions and cell types to adapt future behavior. Both rapid and lasting changes in gene expression are thought to support neuronal plasticity during learning and memory encoding. However, current approaches to studying gene expression involve tissue dissection and cannot preserve the spatial organization of neural circuits, limiting our ability to explore the anatomical distribution of gene responses in the brain. In this project, we will implement cutting-edge spatial transcriptomics technology, which will allow us to uncover gene networks underlying neural plasticity-related gene networks. We will describe changes in gene regulation across brain regions and nuclei involved in different learning and memory paradigms. By capitalizing on our expertise in the brain-wide mapping of neuronal ensembles, we will integrate the concept of transcriptional priming to model gene regulation across activated cell populations in memory encoding and retrieval. This project will ultimately help us uncover new clinical targets for treating memory-related disorders.

Fascitelli Research Scholar Award

Laura Berner, PhD
Assistant Professor, Psychiatry

Laurel Morris, PhD
Assistant Professor, Psychiatry

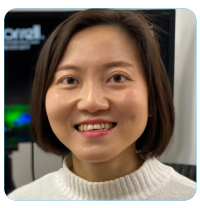
Priti Balchandani, PhD
Professor, Diagnostic, Molecular and Interventional Radiology, Neuroscience and Psychiatry

Using a Novel, Non-Invasive Measure of Dopamine to Test a Model of Control in Bulimia Nervosa

Bulimia nervosa (BN) is associated with high rates of disability and premature death, but surprisingly little is known about the neurobiological factors that maintain the disorder's hallmark symptoms: eating and purging episodes that feel out of control. This study combines a non-invasive proxy measure of dopamine in the brain, called neuromelanin-sensitive MRI, with behavior on a neuroeconomic task to test a novel model of compromised control in BN. Results will clarify links among BN symptoms, midbrain dopamine function, and changes in the perceived cost of expending mental effort on control after eating starts. As such, this project will identify potential neuromolecular and decision-making targets for new treatments.

Nash Family Research Scholar Award

Thomas B Hildebrandt, PsyD
Professor, Psychiatry



Wenfei Han, MD
Assistant Professor, Neuroscience

Characterizing the Vagal Nerve influence on Food Avoidance in Anorexia Nervosa

The defining criteria of anorexia nervosa is a persistent food avoidance in the context of aversion to feeling fat. Recent work by our lab discovered that this reflexive avoidance and difficulty overcoming this avoidance is a function of disgust, an aversive emotion characterized by alteration of gastric rhythm and specific facial expression (nose curl, frown). We will extend this work to test whether noninvasive manipulation of the vagus nerve, which strictly controls gastric rhythm and provides nutrient information from digestion to the brain, can alter this aversive food response in patients with anorexia nervosa. Specifically, we will examine the comparative impact of stimulating the left auricular pathway (gastric rhythm) or the right auricular pathway (gastric feedback) on disgust (facial expression), gastric rhythm, and laboratory feeding.

Lipschultz Research Scholar Award

Dolores Hambardzumyan, PhD, MBA
Associate Professor, Oncological Sciences and Neurosurgery

Hongyan Zou, MD, PhD
Professor, Neurosurgery and Neuroscience

Lineage tracing of tumor hypoxia in primary and recurrent GEM (genetically engineered mouse) model of GBM (glioblastoma)

Normal tissues require regular supply of oxygen and nutrients to maintain viability. These processes are achieved through a functional blood supply, which is impaired in tumors, leading to the formation of micro-regional areas within the tumor characterized by glucose and energy deprivation and oxygen deficiency- referred to as hypoxic regions. Tumor hypoxia is linked to poor outcomes for cancer patients, including glioblastoma (GBM), a highly lethal primary brain tumor. Hypoxic tumor cells are better equipped to resist therapy and spawn tumor recurrence. However, the trajectory of hypoxic cells during GBM progression and their contribution to GBM recurrence post-therapy remains not well understood. This FBI Scholar award will provide a crucial seed fund to study the mechanisms of tumor hypoxia and hypoxic memory in GBM by deploying hypoxia-sensitive reporter systems with lineage tracing capability in genetically engineered mouse (GEM) models of GBM.

Jane Martin and Stuart Katz Research Scholar Award

Xiang Xu, PhD
Professor, Diagnostic, Molecular and Interventional Radiology

Trey Hedden, PhD
Director, Neuroimaging and Biomarker Research in Aging and Alzheimer's Disease at Mount Sinai

In vivo measurement of Aβ in preclinical Alzheimer's Disease by saturation transfer MRI

Alzheimer's disease (AD) is related to pathophysiological processes many years prior to the clinical onset of symptoms, including the hallmark accumulation of beta-amyloid (A-β) plaques. A-β burden is an important biomarker for identifying individuals at high risk of clinical progression and evaluating treatment efficacy. A-beta burden can be measured with radiotracers using positron emission tomography (PET). However, the use of radioactive PET tracers is expensive, involves relatively low resolution, and inhibits frequent measurements, which are necessary in tracking longitudinal changes and monitoring treatment effects. In this project, we will evaluate the feasibility of supplementing and/or replacing the amyloid PET measurement with a newly developed MRI method that is sensitive to pathological aggregates, such as A-β.

Joseph and Nancy DiSabato Research Scholar Award

Lazar Fleysher, PhD
Instructor, Diagnostic, Molecular and Interventional Radiology

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

Sodium MRI as a novel biomarker for Alzheimer's disease.

Alzheimer's disease is a progressive neurodegenerative disorder which typically starts as a mild memory loss and then progresses to disrupt language and cognitive brain function.

Currently available methods of monitoring the disease progression are either invasive or detect unrecoverable cell death. We believe that our novel ultrahigh field (7 Tesla) sodium brain imaging method could allow the detection of cell distress at an earlier stage non-invasively.

The main idea of our approach is logically simple: the disease development leads to an accumulation of sodium inside the brain cells. This accumulation is a slow process and precedes the cell death. In this project we attempt to detect the intracellular sodium accumulation using non-invasive sodium magnetic resonance imaging.

If successful, such a technique could be used as a screening tool or a disease progression monitoring method which will facilitate treatment planning and early detection.

Richard and Susan Friedman Research Scholar Award

Emily Bernstein, PhD
Professor, Oncological Sciences and Dermatology

Joel Blanchard, PhD
Assistant Professor, Neuroscience and Cell, Developmental & Regenerative Biology

Modeling the distinct steps of melanoma brain metastasis in the dish.

The brain is a common site of metastasis for multiple cancers and is associated with poor survival. Melanoma brain metastases (MBMs) occur in ~60% of metastatic melanoma patients and up to 90% at autopsy, illustrating melanoma's striking ability to access and colonize the brain. Recent genomic sequencing studies revealed an enrichment of mutations the gene ARID2, in MBMs. However, how these mutations influence brain metastasis remain unclear. Here, we will investigate the hypothesis that ARID2 alterations confer an advantage to crossing the blood-brain barrier (BBB) and/or colonizing the brain using cutting-edge iPSC-based models of the human blood-brain barrier. These studies will provide mechanistic insight into how cancer cells enter and colonize the human brain that will open new avenues for prevention and earlier diagnosis.

Icahn School of Medicine at Mount Sinai