Ver. 04.24.24

Actively seeking match	Eligible Career Level	Academic Level Required by PI	Special Eligibility Requirements	PI Name	Department/ Divison	Title	Project Abstract	Grant Funding Date(s)	NIH Award Number	Project End Date
Yes	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees	Graduate Student and higher	No special training/skills required.	Erika Bach	Biochemistry and Molecular Pharmacology	Somatic control of germline differentiation in spermatogenesis	The broad, long-term objectives of this proposal are to characterize soma-germline interactions during adult spermatogenesis. The proposal will utilize biochemistry, site-directed mutagenesis in cultured cells and immunofluorescence, genetics, RNA interference, targeted protein degradation and rescue assays in the adult Drosophila testis to determine how a secreted, conserved, immunoglobulin (Ig) domain protein maintains the blood-testis barrier (BTB) in somatic support cells of adult testes. We will capitalize upon the powerful genetics available in Drosophila, as well as the ability to unequivocally identify the niche, germline stem cells (GSCs), spermatogonia and somatic support cells in the Drosophila testis. This proposal is supported by unpublished results demonstrating that (1) the secreted protein is expressed in somatic cells of the testis and is required for spermatogonial differentiation and for robust expression of a BTB domain protein; (2) the only known receptor for the secreted protein is a neuronal adhesion protein that is not expressed or required in the adult testis, indicating that another receptor is involved; (3) another receptor with high homology to known one is expressed in somatic membranes in the adult testis and its depletion leads to phenotypes similar to loss of the secreted protein; (4) this other receptor is required for maintenance of the blood-brain-barrier during development, suggesting a conserved barrier function. Aim 1 centers on using in vitro assays (cell-cell aggregation, affinity purification followed by mass spectrometry, structure-function analysis) to determine how the secreted ligand and receptor interact in cultured cells and on employing in vivo assays (split-GFP reconstitution and deGradFP-dependent protein degradation with genetic "add back") to test whether these interactions occur in the adult testis. The Aim 2 is focused on determining whether the permeability barrier function of the BTB is compromised in testes lacking the ligand or receptor. These experiments are designed to reveal mechanistic insights into how the BTB domain is maintained in adults. The studies in this proposal will increase the knowledge base about signals that maintain spermatogenesis during adult stages and will foster new avenues of research into mechanisms and treatments for age-related male infertility.	not specified	R03	not specified
Yes	Not specified	Not specified	Not specified	Narjes Razavian	not specified	SCH: Dementia Early Detection for Under-represented Populations via Fair Multimodal Self-Supervised Learning	not specified	not specified	R01AG085617	not specified
Yes	Graduate student	Graduate student	None	Leonardo Trasande	Pediatrics and Population Health	Assessing the Impact of Ambient Heat Exposure on Child and Caregiver Mental Health within the Community Context	Climate change poses a severe risk to pediatric mental health via increased and prolonged heat exposure.1 Multiple studies have linked increased ambient temperatures to elevated pediatric mental health-related emergency department visits. 2 3 To protect children from the health impacts of heat, we need to characterize better how ambient temperature influences their and their caregiver's mental health within the larger context of the social environment. To address this, my project will investigate the Patient-Reported Outcomes Measurement Information System (PROMIS) item bank for depression and anxiety and determine which subpopulations are most susceptible to the harmful impacts of heat using data from the NIH ECHO program. Then I will use census-tract-level data to assess the distribution of protective factors against heat within the child's environment.	not specified	5UH3OD023305	not specified
Yes	Graduate student,Post Doctoral trainees,Junior Faculty	Graduate student,Post Doctoral trainees,Junior Faculty	Advanced statistical analysis skills; experience working with large datasets	Brian Elbel	INTERNAL MEDICINE/MEDICINE	The Influence of Sugary Beverage Taxes on Fast Food Restaurant Purchases: An Evaluation Using National Sales Data	This project will examine the impact of taxes on sugar sweetened beverages (SSBs) utilizing detailed sales data from one of the largest fast food retailers in the U.S. Taxes on SSBs are one of the most promising solutions to reduce population-wide consumption of these unhealthful beverages and, consequently, their contribution to obesity and the health challenges of cardiovascular disease, diabetes and cancer. SSB taxes have reduced purchasing and consumption of SSBs in settings such as supermarkets and other food stores across the seven U.S. cities that have implemented them. However, fast food restaurants are also a key source of SSBs -- more than a third of U.S. adults consume fast food on any given day, often including an SSB, and a single beverage at a fast food restaurant contains more than the recommended daily allowance of calories from added sugars in just one serving – and have not been studied. The central hypothesis is that SSB taxes will reduce purchase of SSBs at fast food restaurants, with a greater impact in lower-income census tracts, despite less than complete "pass-through" of the tax to the consumer by the fast food restaurants. Using detailed sales data and appropriate comparison groups from multiple communities, the study estimates the influence of SSB tax policies in a detailed and causal way for several years after taxes are implemented. The model is a difference-in-difference approach, taking advantage of the fact that some locations implemented taxes and (most) others did not. The study will look at sales in localities that are similar at baseline (before taxes) and determine how they diverge after a tax is implemented. This is the first study to rigorously examine SSB taxes across the U.S. in a longitudinal manner, including thousands of retail locations for Taco Bell and hundreds of millions of purchases. The national scale of the data and multiple restaurants within each city that implemented a tax will allow estimation of whether effects of taxes differ by community income, critical to understanding health disparities and the regressive nature of SSB taxes. The specific aims are: Aim 1: Determine the change in price paid in fast food restaurants as a result of SSB taxes (i.e., effective "pass-through"). Aim 2: Determine the change in beverage calories purchased per customer order as a result of SSB taxes. Aim 3: Determine how neighborhood characteristics, such as the income of the area in which a restaurant is located, influence both pass-through and beverage calories purchased in response to SSB taxes.	2/1/2022	R01HL157191	1/31/2026
Yes	Not specified	Not specified	Not specified	Mara McAdams Demarco	SURGERY	Structural Racism, Resilience, and Premature Cognitive Aging in End-stage Renal Disease	Only 13% of the 780,000 adults living with end-stage renal disease (ESRD) have normal cognitive function. We found that 14.0% of ESRD patients aged 35-49 experience severe cognitive impairment and 2.9% have a co- occurring functional dependence suggestive of Alzheimer's disease and related dementia (AD/ADRD). After dialysis initiation older (≥65) patients experience a 21-25% lifetime risk of AD/ADRD. Younger ESRD patients experience premature cognitive aging requiring the study of cognition and AD/ADRD across the lifespan. Black ESRD patients are more than twice as likely to develop cognitive impairment and 70%-78% more likely to be diagnosed with AD/ADRD; this disparity is comparable to a 10 year increase in age. While systemic racism is a known contributor to health disparities in community-dwelling older adults, its impact on cognitive aging among ESRD patients is understudied. Measurement of systemic racism (i.e., structural, institutional, and interpersonal) is crucial to identifying ESRD patients who are at risk of premature cognitive aging and those who are resilient in the face of racism. Elucidating mechanisms by which systemic racism impacts cognitive aging will lead to interventions and policies that may prevent the devastation of AD/ADRD for 234,000 Black ESRD patients. We seek to address a National Institute on Aging (NIA) goal (RFA-MD-21-004): "To elucidate whether and how mechanisms connecting structural racism to aging-relevant outcomes, including cognition and AD/ADRD, operate on multiple levels." ESRD patients are the ideal population to elucidate these mechanisms: 1) 30% of patients are Black; 2) 87% experience premature cognitive aging; 3) all enroll in a national registry and 65% in Medicare for measurement of institutional racism. For all adult ESRD patients in the national registry/Medicare database, we will glean 23 indicators of structural racism from publicly available data and identify 3 indicators of institutional racism. Then, we will link these data to our ongoing, NIA-funded, multi-center, prospective cohort study (FAIR, n=5,275) of aging and ESRD to fully characterize systemic racism (lifecourse structural racism, institutional racism, and interpersonal racism). This is the oldest (>12 years) ESRD cohort study that includes longitudinal measures global and domain specific cognitive function. The National Kidney Foundation, Alzheimer's Association, and a local community advisory board will guide the design and interpretation of the following aims: 1) To estimate the impact of structural and institutional racism on incident AD/ADRD; 2) To quantify the contributions of lifecourse systemic racism on cognitive impairment and decline; and 3) To test whether resilience to systemic racism protects against cognitive impairment and decline. By taking a lifecourse approach and engaging community, family, and patient stakeholders in all phases of our study, we will identify feasible targets for improving resilience in the face of systemic racism. These potential targets for interventions and policies to counter structural racism will likely generalize to other populations with chronic diseases.	7/15/2022	R01AG077888	3/31/2027
Yes	Graduate student	Graduate student	Research experience, basic data analysis skills, qualitative data collection skills	Charles Neighbors	INTERNAL MEDICINE/MEDICINE	Organizational factors associated with quality of care for opioid use disorders among transition-age adults in Medicaid	Transition-age (TA) adulthood—between ages 18 to 25—is a distinct and critical developmental period where unique biological, psychological, and social changes are occurring. Brain development continues into the latter part of this period, with neurological structures associated with reward sensitivity and self-regulation continuing to form. Social roles are in flux, with reduced parental monitoring and shifts in societal expectations that presage lifetime functioning at the personal, familial, and community levels. Substance use disorders (SUD) and mental health conditions are more prevalent in this age group than at other ages, 14.4% and 29.4% respectively in 2019. Effective treatment at this age has the potential for large long-term payoffs. Over the past decade, there has been a large rise in the prevalence of opioid use disorders (OUD) among TA adults. Yet, the treatment system for OUD performs poorly for TA adults: they are less likely to obtain scientifically supported treatment and more likely to leave treatment early. Although the most efficacious treatment for OUD is pharmacotherapy, naturalistic studies demonstrate that there are large gaps in receipt of medications for opioid use disorder (MOUD), low adherence to these medications, and poor outcomes for most TA adults who enter treatment. Few current studies of quality in OUD treatment programs account for individual, organizational, and contextual factors that vary over time. In particular, variation in the quality of treatment programs occurs within the complex interplay of social and ecological factors related to communities, treatment programs, and characteristics of the patient. Specifically, social determinants of health, such as poverty and racial/ethnic disparities, create added barriers to obtaining and sustaining scientifically supported treatments. A better understanding of the program characteristics associated with higher quality care for TA adults with OUD will inform organizational changes, payer incentives, and government policies to improve treatment for this poorly served population. Because of rapid organizational changes caused by the COVID-19 public health emergency, there is an opportunity to explore whether new forms of SUD treatment delivery—telehealth, liberalization in provision of pharmacotherapy—lead to improved treatment engagement and outcomes for TA adults. The proposed longitudinal study will combine data from multiple sources, including Medicaid and a state registry of SUD treatment episodes, to examine three aspects of OUD treatment quality for approximately 65,000 TA adults entering treatment for OUD between 2012 and 2025: 1) access to MOUD; 2) adherence to pharmacotherapy and retention in treatment; and 3) adverse events (e.g., overdoses). To guide our study, we propose a conceptual model that draws from the Donabedian quality of care framework (Organizational Structure>Clinical Process>Outcome) and from social ecology to examine program quality of OUD treatment for TA adults while accounting for individual and community level factors associated with the ability of these programs to deliver care.	4/15/2023	1R01DA057267	2/28/2028

Yes	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees,Junior Faculty	Prefer post-doctoral trainees and junior faculty, would consider very strong post-bacc graduates or graduate students.	No specific certifications are required but the person would have to be interested in substance use research and/or research at the intersection of housing/homelessness and health and they would have to be a strong writer.	Kelly Doran	EMERGENCY MEDICINE	Implementation of Overdose Prevention Practices in Permanent Supportive Housing	Permanent supportive housing (PSH), the gold standard intervention for ending chronic homelessness, has expanded rapidly across the U.S. in recent years and is likely to continue expanding as homelessness increases in the wake of the COVID-19 pandemic. Due to a confluence of individual and environmental risk factors, PSH tenants face heightened risk for overdose (OD). While evidence-based practices (EBPs) to prevent OD exist, they have not been broadly implemented in PSH settings. We propose to address this significant research to practice gap by tailoring a set of evidence-based OD prevention practices for PSH settings, then studying their implementation in 20 PSH buildings in New York. We will test a package of implementation strategies that includes an implementation toolkit, tenant-staff implementation champion dyads, limited practice facilitation, and learning collaboratives. The project will be conducted in partnership with the Corporation for Supportive Housing, a national organization that advances solutions to improve PSH through education, practice, and policy. Aim 1 is to adapt evidence-based OD prevention practices for PSH, using key stakeholder focus groups, and develop a PSH OD Prevention Toolkit to guide implementation. In this preparation phase we will adapt an existing package of EBPs in consideration of the unique environmental characteristics of PSH and will prepare for implementation. Aim 2 is to evaluate implementation of evidence- based OD prevention practices across diverse PSH buildings and effectiveness on PSH tenant outcomes in a stepped wedge trial. In this Hybrid Type 3 effectiveness-implementation study, the primary implementation outcome is PSH building adoption of the OD prevention EBPs. We will additionally examine secondary implementation outcomes, tenant clinical outcomes, and implementation sustainment. Aim 3 is to explore multilevel factors influencing implementation—including barriers and facilitators—and refine dissemination and implementation frameworks for housing settings, using qualitative interviews with PSH staff. The research draws from the EPIS (Exploration, Preparation, Implementation, Sustainment) implementation framework and Rhodes' Risk Environment Framework. The research will inform implementation frameworks and strategies by examining application of EPIS for PSH and testing novel housing-relevant implementation strategies including staff-tenant implementation champion dyads. Findings from this PSH-focused research are expected to be more broadly applicable to other types of housing and settings serving people experiencing homelessness. The multidisciplinary investigator team will work with a Stakeholder Advisory Board to maximize impact of the research, which has been designed to inform local and national programmatic and policy interventions. Changes in the epidemiology of the U.S. OD crisis highlight the need for concerted efforts to reduce the disparate burden of ODs faced by particularly marginalized populations.	3/29/2023	R01DA054976	3/31/2027
Yes	Post Baccalaureate Graduate	Post Baccalaureate Graduate	Development of a career development plan in clinical-translational research for my research coordinator. We are applying for a Diversity Grant through NIH, and would appreciate support.	Anli Liu	NEUROLOGY	Hippocampal-Neocortical Interactions During Naturalistic Learning	Episodic memories are representations of our personal past, anchored to time and space. Episodic memory impairments in neurological disorders like epilepsy, traumatic brain injury, and Alzheimer's Disease significantly limit patients' ability to work and live independently. In everyday life, the brain must process the continuous present to form discrete memories of the past. This ability to parse experience into meaningful chunks, termed event segmentation, is foundational to human episodic memory. Functional neuroimaging studies suggest that the hippocampus and a posterior cortical network demonstrate a simultaneous increase in activity at event boundaries and endings, but the neural events supporting this demarcation are unknown. Numerous rodent studies suggest that neural oscillations—particularly theta, gamma, and sharp-wave ripple (SWR) activity—coordinate hippocampal-neocortical interactions at these critical junctures. Our long-term goal is to discover how the brain organizes and consolidates continuous experience under naturalistic circumstances. The objective of this proposal is to measure the hippocampal-neocortical dynamics at key moments in episodic memory. Our central hypothesis is that the hippocampus plays a critical role in segmenting and consolidating information delivered from the neocortex, via enhanced theta-gamma activity at event boundaries and increased SWR rate during post-viewing rest. To test these main hypotheses, we will obtain intracranial EEG (iEEG) recordings from epilepsy patients undergoing invasive monitoring for surgical treatment. Subjects will view a series of short films that possess a narrative structure and sequence, then will be asked to recall selected content. Upon successful completion of this project, we will accomplish the following aims: Aim 1. To measure the relative contributions of hippocampus and PMN to event segmentation during film viewing. Aim 2. To measure the hippocampal contribution to memory consolidation during post- viewing rest. Aim 3. To test the necessity of the hippocampus for event segmentation through electrical stimulation (ES). This proposal represents a significant advance from prior work in the cognitive neuroscience of memory by using iEEG to determine the hippocampal-neocortical oscillations involved in remembering naturalistic events. This project is innovative in concept and method because of (1) the use of short films to investigate human episodic memory; (2) the translation of key neurophysiological findings in rodent memory to human episodic memory; and (3) establishing the necessity of the hippocampus in event segmentation and memory performance through ES. Our findings will advance mechanism-guided approaches to the assessment and remediation of memory dysfunction in neuropsychiatric disorders such as epilepsy and traumatic brain injury.	4/10/2023	R01NS127954	3/31/2028
Yes	Not specified	Not specified	Not specified	lama Nazzal	INTERNAL MEDICINE/MEDICINE	Gut-kidney axis in enteric hyperoxaluria	In the United States, more than 200,000 patients are estimated to suffer from enteric hyperoxaluria (EH). EH affects patients with malabsorptive gastrointestinal diseases and is well-known to cause recurrent nephrolithiasis. Therapies for EH are limited and only partially mitigate hyperoxaluria. Several gut bacteria can degrade oxalate and likely play an essential role in protecting against hyperoxaluria. The role that these oxalate-degrading bacteria, collectively referred to as the oxalobiome, play in the pathophysiology of EH has not been elucidated. We developed a novel computational method to perform the first comprehensive study of human oxalate-degrading microbes. We defined their individual contributions to overall oxalate degradation in vivo in healthy and inflammatory bowel disease (IBD) population, a population at risk for EH. Our data showed that IBD patients have a reduction in the function of the oxalobiome associated with higher levels of fecal oxalate, suggesting that this population might benefit from the restoration of the oxalobiome. Hence, this proposal's scientific premise is that the microbiome is an important determinant of urinary oxalate (UOx) levels and that with greater knowledge of the oxalobiome's biology, we can manipulate it to prevent EH and kidney stones. Our overall hypothesis is that the oxalobiome function determines UOx. As a corollary, we hypothesize that the microbiome can be therapeutically targeted to reduce hyperoxaluria and the risk of kidney stones. To test this hypothesis, we propose studies that leverage our expertise in conducting microbiome trials and microbiome functional analyses in addition to our experience in performing humanizations. Our first aim is to analyze associations of oxalobiome alterations with UOx levels in patients with EH. We will place healthy and EH subjects on controlled diets before and after inducing their oxalobiome with daily oxalate supplementation to analyze the oxalobiome structure, using metagenomic sequencing, and function, using metatranscriptomic sequencing. We will identify the oxalobiome members with the highest oxalate metabolic activity in healthy and EH subjects, and those whose absence is associated with the development of hyperoxaluria. Global analysis of the microbiome dynamics and networks will allow us to identify bacterial taxa that are associated with lower UOx in EH and healthy adults. Our second aim is to determine whether human-to-mouse transfer of whole and enriched oxalobiome communities results in reduced urinary oxalate. For this aim, we will develop an EH IBD mouse model and perform human-to-mouse transfer of whole and enriched oxalobiome communities to evaluate its effects on UOx. Deciphering the oxalobiome function in EH, using recently developed technologies, in conjunction with our targeted computational methods, and then testing our hypotheses in mouse models, will permit us to develop promising microbiological approaches to control hyperoxaluria in EH.	9/6/2021	R01DK129675	5/31/2026
Yes	Not specified	Not specified	Not specified	Marie Bragg	INTERNAL MEDICINE/MEDICINE/Population Health/ Health Policy	Examining the Mechanisms Underlying the Influence of Facebook Food Advertisements on Adolescents' Eating Behaviors: Randomized Controlled Trials - Resubmission - 1	Poor diet and excess weight during adolescence predicts excess weight and diet-related cancers during adulthood, yet there is little research on the risk factors that contribute to weight gain among adolescents. The National Academy of Medicine identifies exposure to food advertisements (ads) as a major predictor of poor diet among children (<12 years of age) because studies have shown that children who are exposed to food ads consume more calories than children who are exposed to non-food ads. The few food ad studies that have included adolescents (13–17 years of age) found associations between self-reported exposure to television (TV) food ads and poor diet, but we do not know which mechanisms explain this relationship. It is also well established that food companies promote their least healthy products to Black consumers more than White consumers and perceive Black youth as trendsetters. But it is not known whether seeing racially congruent ads (i.e., the person in the ad and the viewer are the same race) places Black adolescents at higher risk of poor diet relative to Whites. Finally, most food ad research is based on TV ads, but food companies are increasingly targeting adolescents on social media. And no social media food ad studies have focused on racially targeted ads. Addressing these gaps is important because adolescence is a critical period for adopting nutritious eating habits that can prevent future diet-related cancers. The overall objective of our three studies is to identify the extent to which exposure to Facebook food ads increases the number of calories purchased and consumed by Black and White adolescents. Guided by strong preliminary data, we will test three aims: 1) To evaluate the extent to which exposure to racially congruent vs. incongruent Facebook food ads causes Black vs. White adolescents to purchase more calories for a snack; 2) To determine the extent to which exposure to many vs. few "likes" on Facebook food ads causes Black and White adolescents to purchase more calories for a snack; and 3) To test the degree to which visual attention to unhealthy foods, racially congruent people, and/or "likes" in Facebook ads explains the relationship between ad exposure and calorie intake. To address the first and second aims, we will conduct two randomized online experiments. Under the third aim, we will conduct a within-subjects lab study using eye-tracking technology. We hypothesize that exposure to racially congruent Facebook food ads will increase the number of calories purchased and consumed by adolescents. We also predict that Black adolescents who attend to Black people in food ads will consume more calories than those who attend to other ad features. This innovative work will examine actual purchases and caloric intake; use novel tools (e.g., Facebook "reaction" buttons) to examine ad preferences; and use a state-of-the-art eye-tracking computer with discreet cameras. The proposed research will increase our mechanistic knowledge of communication tools that influence adolescents' dietary behaviors and could inform cancer prevention interventions that aim to improve adolescents' diets using effective ad techniques.	7/1/2021	5R01CA248441	6/30/2026
Yes	Graduate student	Graduate student	None anticipated at the moment	Thaddeus Tarpey	ANESTHESIOLOGY	EPPIC-Net DCC	The Data Coordinating Center (DCC) of the Early Phase Pain Investigation Clinical Network (EPPIC-Net) will be the data and biospecimen manager for pain research within the HEAL Partnership. As such, it will host, manage, standardize, curate, and provide a sharing platform for data and biospecimens for HEAL initiatives, such as the Acute to Chronic Pain Signature initiative and the BACPAC, in addition to EPPIC-Net studies. The DCC will develop and maintain a databank for depositing pre-clinical, clinical, neuroimaging, microbiome, genomics, and other omics biomarker data, will link these data with a repository for biological samples, and will create a platform for teams to work together to analyze and interpret data. Further, the DCC will provide leadership in the statistical design and analysis of EPPIC-Net studies, and will deploy advanced systems and processes for data collection, management, quality assurance, and reporting. The DCC will create, sustain, and continually advance a robust organization for the rapid design, implementation, and performance of high- quality rigorous Phase II clinical trials to test promising therapeutics for pain. The proposed DCC brings together experts from statistics, clinical trials design and simulation, data management, neuroimaging, bioinformatics, genomics, and radiology, and leverages decades of experience instituting and running large data sharing consortia and data coordinating centers. Our aims are to further the goals of EPPIC-Net and the HEAL initiative through: 1) Integration of the DCC within the EPPIC-Net structure and facilitation of the alliance with HEAL partners; 2) Provision of biostatistical expertise, support, and leadership to EPPIC-Net studies; 3) Provision of legacy and de novo secure data storage and comprehensive data management for EPPIC-Net studies; 4) Institution of a pain-related expandable biospecimen repository; and 5) Establishment of the EPPIC- Net DataExchange and BiospecimenExchange to foster the development of non-addictive treatments for pain. The DCC will be structured around four cores: 1) an Administrative Core; 2) a Statistical Core; 3) a Data Core; and 4) a Biospecimen Core. This DCC will work with the EPPIC-Net Clinical Coordinating Center (CCC) and with the Specialized Clinical Centers (SCC, a hub and its spokes/clinics) to educate clinicians and staff in good clinical trial practices for reproducibility of research, and to train them in the data management system and procedures employed in the network. The DCC will provide sites with user-friendly dashboards to monitor their own performance and will promote collegial and supportive relationships with the sites' personnel to cultivate rigorous and enthusiastic engagement in the conduct of the studies. The DCC will use state-of-the-art concepts and techniques in the acquisition, transfer, storing, management, standardization, linking, and curation of the clinical and biomarker data to launch and maintain the EPPIC Exchange encompassing the DataExchange, and the BiospecimenExchange. The EPPIC Exchange represents the final product delivered by the DCC -- a resource with capability for continual growth, that will be shared by the pain research community.	9/30/2019	5U24NS113844	8/31/2024

Yes	Not specified	Not specified	Not specified	Tanya Sippy	PSYCHIATRY	Dissecting the Synaptic and Cellular Actions of Dopamine in Vivo	The neuromodulator dopamine is critical for motivating, performing, and reinforcing goal-directed behaviors, and deficits in dopamine signaling are common in neuropsychiatric disorders like depression, obsessive-compulsive disorder, addiction and Parkinson's disease. Central to our understanding of dopamine function is the notion that phasic increases and decreases in extracellular dopamine levels in the striatum modulate striatal output to modify behavior on short and long timescales. For instance, phasic elevations in striatal dopamine elicited by salient stimuli and reward-predicting cues have been proposed to promote arousal, facilitate action initiation and increase motivation to work on timescales of seconds to minutes, but also to modify future actions and behavioral decisions on longer timescales extending to days. This raises a fundamental question: How does dopamine modulate the activity of striatal neurons to exert its influence on behavior? Experiments in vitro have revealed a myriad of molecular targets sensitive to modulation by dopamine. However, the net effects of these changes on striatal output in vivo remain unknown. One reason is that few methods are capable of dissecting dopamine's cell type-specific neuromodulatory effects on synaptic strength, somatic excitability and network dynamics in the awake, behaving brain. This proposal aims to fill this gap in knowledge using in vivo whole-cell electrophysiology and two-photon microscopy, focusing initially on the neuromodulatory effects occurring on timescales of seconds to minutes. Informed by our published and preliminary data with these techniques, we will test the hypothesis that phasic dopamine transients reflecting positive and negative reward prediction errors promote the activation of striatal projection neurons expressing D1- and D2-type dopamine receptors (D1-SPNs and D2-SPNs), respectively, via a combination of intrinsic and synaptic short-term plasticity mechanisms. To do so, we will harness our ability to record sub-threshold membrane potential dynamics in vivo to reveal how behaviorally- and optogenetically-evoked dopamine transients alter the intrinsic excitability of D1- and D2-SPNs (Aim 1) and the potency of excitatory synapses impinging on them (Aim 2). In Aim 3, we will employ calcium imaging to uncover the short-term influence of phasic dopamine transients on striatal output. Together, our experiments will provide crucial mechanistic insights into the modulatory actions of dopamine in vivo, shedding light on a key link between dopamine release and behavioral modifications, and paving the way for novel therapeutic interventions aimed at treating neuropsychiatric disorders.	7/8/2022	5R01MH130658	4/30/2027
Yes	Post Doctoral trainees	Post Doctoral trainees	Not specified	Chiara Giannarelli	INTERNAL MEDICINE/MEDICINE	Dissecting the role of CD8+ T cells in atherosclerosis	Atherosclerotic cardiovascular disease (ACVD) is the leading cause of mortality and disability worldwide, even in optimally treated patients. While the impact of many immune cell types on atherosclerosis is well- established, the contribution of CD8+ T cells to the disease pathology remains to be further elucidated. In previous work using unbiased single-cell (sc) analyses to study the immune composition of human atherosclerotic plaques we found new dysregulations tissue resident memory (TRM) CD8+ T cells associated with clinical CV outcomes. CD8+ T cell infiltrates have been described in both early and advanced human atherosclerotic plaques and their cytotoxic effector functions contribute to plaque progression in mice. However, information on how CD8+ T cells contribute to atherosclerotic plaque vulnerability and cardiovascular (CV) events is limited and remains to be fully understood. In preliminary sc studies, we identified the transcriptional regulator Zeb 2 as a top candidate master regulator of plaque CD8+ T cell proatherogenic alterations. We hypothesize that Zeb2 is a key driver of the activation and cytotoxicity of effector TRM CD8+ T cells in atherosclerotic plaques and that these alterations contribute to disease progression and plaque vulnerability. We also contend that its downregulation is implicated in the reprogramming of PD-1+ TRM CD8+ T cells found in plaques of patients with recent stroke. We propose two independent aims to study the role of Zeb2 in plaque vulnerability and CV events. In Aim 1, we will dissect the Zeb2-mediated activation of plaque TRM CD8+ T cells and determine their association with plaque vulnerability at pathology. In this Aim we will also determine the effect of Zeb2 deficiency selectively in activated TRM CD8+ on atherosclerosis in mice. In Aim 2, we will identify how Zeb2 mediates TRM CD8+ T cell dysregulations of adverse CV outcomes and determine how Zeb2 downregulation in all CD8+ T cell affect their exhaustion reprogramming and whether these alterations contribute to plaque size and vulnerability in vivo. These studies will address important gaps in knowledge in CD8+ T cell biology in atherosclerosis, and will tackle previously unappreciated cellular and molecular mechanisms associated with plaque rupture/erosion that may contribute to clinical CV outcomes. We foresee that this information may help guide the future design of precise, molecularly targeted immunotherapies to prevent CV outcomes in patients with carotid and coronary disease.	6/2/2023	R01HL153712	5/31/2025
Yes	Junior Faculty	Junior Faculty	CITI human subjects research training. Would prefer someone with skills in qualitative research, interviewing and data collection.	Macey Levan	SURGERY	Development of a Robust Strategy for Living Kidney Donor Follow-up and Engagement	Developing a Robust Strategy for Living Donor Follow-up and Engagement There are more than 150,00 living kidney donors in the US, and the number of new donors is increasing yearly. Understanding the risks and sequelae of donation is a practical requirement for expanding live donor kidney transplantation and an ethical requirement for supporting informed consent and honoring an altruistic act. This requires the collection of granular follow-up data in donors, and a comparison to healthy non-donors. To date, national efforts at kidney donor follow-up and long-term engagement have failed. As a living kidney donor myself, I am intimately aware of the profound and systemic failures in post-donation surveillance from both the donor-level and the health system-level. In 2013 a national policy mandating transplant centers meet standards for living donor follow-up was implemented, yet this policy has proven nearly impossible for transplant centers, with fewer than 50% successful in meeting the mandate. Continued engagement with transplant centers not only allows a better scientific understanding of the implications of donation, but also allows careful surveillance of donors to identify early physiologic changes (such as hypertension) and intervene before these become major adverse outcomes. Furthermore, a proper healthy non-donor cohort has never been successfully captured and studied. To improve this ongoing failure, in 2017 we launched a pilot Living Donor Collective (LDC) at 10 kidney transplant centers, centralized though the Scientific Registry of Transplant Recipients (SRTR). In an effort to improve living donor follow-up in a systematic, scientific manner that can be disseminated to centers across the country, we will take the important first steps of evaluating how the 10 pilot transplant centers and the SRTR implemented the LDC and use this information to plan the next iteration of this important endeavor. Since only 10 centers participated in the pilot, out of 273 transplant centers in the US, it is critical to understand barriers to implementation across a wide spectrum of transplant center characteristics. Guided by an implementation science framework and a mixed methods approach, we aim: (1) to understand LDC implementation among pilot centers and SRTR, (2) conduct a formative evaluation and assess transplant center readiness and capacity for participation in the LDC across the US, and (3) create an implementation strategy to refine and expand the LDC. This study will provide a comprehensive understanding of implementation challenges, successes, and failures of a centralized program for living donor follow-up. This provides the foundation for all U.S. transplant centers to participate, solves a historically unsolvable and embarrassing health system challenge, and is necessary to prepare a future R01 to develop and implement centralized living donor follow-up nationally.	8/15/2022	1R03DK132222	7/31/2024
Yes	Undergraduate,Post Baccalaureate Graduate,Graduate student	Undergraduate Post Baccalaureate Graduate,Graduate student	Comfortable working with racial and ethnic minoritized populations, qualitative analysis skills are preferred but not mandatory.	Ayana Jordan	PSYCHIATRY	Culturally Response Integrated Harm Reduction Services for Black and Latinx People Who use Drugs	This study is part of the NIH's Helping to End Addiction Long-term (HEAL) initiative to speed scientific solutions to the national opioid public health crisis. The NIH HEAL Initiative bolsters research across NIH to improve treatment for opioid misuse and addiction. Over 100,000 people died from drug overdoses in 2021, underscoring the need for urgent action. While the rates of overdose deaths among White people have begun to plateau, there has been a drastic surge in deaths among racial/ethnic minoritized individuals. There are also stark disparities from other substance use, including stimulants among Black and Latinx people who use drugs (PWUD). While effective treatment exists for problematic substance use, along with harm reduction (HR) services that decrease substance-related harms, studies demonstrate that racial/ethnic minoritized people are less likely to have access to these services. They not only experience more negative consequences related to substance misuse but are also less likely to receive HR services or be retained in evidence-based treatment such as MAT. To tackle these unique problems, we created an integrated harm reduction intervention (IHRI) to be mobile and flexible to the needs of Black and Latinx PWUD. This culturally responsive IHRI will employ a HR care coordinator that can assess vulnerabilities in the social determinants of health (SDOH) and link people to needed services. Data from community partners who operate HR services and serve largely Black and Latinx PWUD suggests that participants who receive HR services have significant improvements in health and engagement. Yet, systemic barriers to additional social services NOT directly related to substance use persist, which often influence health outcomes and quality of life. Thus, offering a low barrier, geographically distributed, culturally informed HR intervention in historically excluded communities may prove a highly disseminable strategy, for improving access to HR services and MAT. We plan to evaluate the efficacy of this integrated HR intervention (by providing legal, housing and mental health treatment support, along with linkage to MAT) on participant retention and engagement of HR services among n=200 Black and Latinx PWUD compared to services as usual in two mobile Community Harm Reduction Organizations. The escalating overdose death rates among Black and Latinx PWUD is a serious public health. The focus on health disparities in addiction is of high priority to NIDA and may prove a useful model for decreasing harm and broadening MAT access for Black and Latinx PWUD, who have been historically excluded these services in traditional settings.	9/30/2022	1R01DA057651	9/29/2025
Yes	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees,Junior Faculty	Prefer post-doctoral trainees and junior faculty, would consider very strong post-bacc graduates or graduate students.	No specific certifications are required but the person would have to be interested in substance use research and/or research at the intersection of housing/homelessness and health and they would have to be a strong writer.	Kelly Doran	EMERGENCY MEDICINE	Crisis Response, Durable Lessons: A Mixed Methods Examination of a Large-Scale Hoteling Intervention for People Experiencing Homelessness During the COVID-19 Pandemic	Over 1.4 million people experience homelessness in the U.S. each year. A large body of evidence has demonstrated the bidirectional relationship between homelessness and substance use (SU), and overdose is the leading cause of death among people experiencing homelessness. The COVID-19 pandemic has greatly exacerbated the existing and overlapping crises of homelessness and SU. Localities across the U.S. have taken drastic steps to mitigate risk of COVID-19 among their homeless populations—including mass movement of tens of thousands of homeless individuals to hotels—but there has not yet been research on how these efforts have affected SU. We propose to conduct community-partnered, mixed methods research to examine SU and related health impacts of a large-scale initiative to place people experiencing homelessness into commercial hotels during the COVID-19 pandemic. The proposal leverages a natural experiment in New York City, where 9,500 homeless individuals were moved to hotels during the pandemic. Aim 1 is to explore how SU behaviors and treatment access changed for people experiencing homelessness who were placed into hotels during the COVID-19 pandemic, using in-depth interviews with homeless services clients and staff. Aim 2 is to examine effects of hotel placement on SU-related and other health care outcomes using a difference-in- differences approach with linked homeless services and Medicaid data. Aim 3 is to understand effects of hotel placement on SU-related outcomes and to identify strengths, gaps, and best practices to inform future efforts, using merged findings from Aims 1 and 2 as well as a national environmental scan of COVID-19 hotel strategies relevant to SU disorders. The research will be conducted by a transdisciplinary investigator team in partnership with the NYC Department of Social Services and Project Renewal, Inc., a nonprofit homeless and health services provider. The research team will work together with a Stakeholder Advisory Board that includes individuals with lived experience of homelessness to maximize the practical impact of the research, which has been designed to inform local and national programmatic and policy interventions. The study will identify challenges, assets, and innovations with durable lessons for the future that will be critical not only to prepare for future pandemics, but also to inform future programs and policies to better respond to the overlapping crises of homelessness and substance use disorder. This research is especially important as the pandemic is expected to bring with it large increases in homelessness, as well as worsening SU and overdose nationally. The pandemic has spurred communities to rapidly change how they address homelessness, including by permanently converting unused hotels for long-term shelter and housing. It is therefore critically important to understand the benefits and potential unintended consequences—and how to best mitigate them—of such initiatives. We have a unique, time-limited opportunity to study this topic of large national importance.	8/15/2022	R01DA054956	6/30/2027

Yes	Graduate student,Post Doctoral trainees,Junior Faculty	Graduate student,Post Doctoral trainees,Junior Faculty	Advanced data analysis; advanced statistics	Brian Elbel	INTERNAL MEDICINE/MEDICINE	COVID-19 Vaccinations and School / Community Resources: Children's Longitudinal Health and Education Outcomes Using Linked Administrative Data	PROJECT SUMMARY/ABSTRACT This research will examine how significant disruptions to children's health, education and overall well-being during the COVID-19 pandemic created lasting influence on health, development and social trajectories through the lifecourse, and the risk for long-term health outcomes. Effects of the pandemic are unevenly distributed amongst children, particularly with respect to race/ethnicity and income, and are anticipated to both reflect and exacerbate the already wide health disparities in the United States. As vaccines continue to roll out, inequality in access to and take up of vaccinations could compound the disparate outcomes. New York City (NYC), where the 1 million public school children are majority Black or Hispanic (66%) and 74% are low-income, is an ideal place to situate this research. In the health domain, changes in diet and physical activity and missed healthcare may increase incidence and exacerbation of chronic diseases like obesity, asthma and diabetes. The pandemic generated stress and anxiety, with fewer of the usual mental health services supports available, posing risk for new and more severe health problems. Even after schools fully return to in-person learning, the educational consequences are expected to be protracted – including declines in academic achievement (test scores), increases in chronic absenteeism, repeating grades, or high school dropout. The research leverages the NYC Student Population Health Registry (SPHR), a uniquely inclusive, longitudinal database of all NYC public school students, created jointly by the NYC Department of Health and Mental Hygiene and NYC Department of Education to examine these and other outcomes. SPHR links multiple municipal data sources at the child-level, allowing us to examine the influence of the COVID pandemic on myriad outcomes. The impact of variation in child-level, classroom-level and school-level vaccination rates will be important to understand, and it is expected that neighborhood and school characteristics (income, vaccination sites, emergency food resources, open space) will mitigate (or exacerbate) sustained impacts. Identifying sources of resilience, at either the individual or neighborhood level, is a public health priority. The specific aims are: • Aim 1: With a focus on disparities, determine health and education changes among children 2-4 years after pandemic onset compared to pre-pandemic using a new, comprehensive and powerful set of linked child-level administrative data. • Aim 2: Determine how child-level, school-level and neighborhood-level COVID vaccination rates influence the course of the COVID pandemic, with a focus on disparities. • Aim 3: Determine the role of neighborhood and school resources in exacerbating or mitigating health and educational disparities due to the COVID pandemic.	9/22/2021	U01NR020443	6/30/2026
Yes				Shukti Chakravarti	OPHTHALMOLOGY	Cellular and genetic defects in keratoconus	Keratoconus (KC), a common corneal dystrophy that affects young people, causes progressive thinning, scarring and loss of corneal shape, which can ultimately lead to loss of vision. Crosslinking of collagens in the cornea can stiffen and delay its weakening, but severe cases require corneal transplantation. Although KC has a strong *genetic* component, its etiology is complex, polygenic and multifactorial. There is an urgent need to understand its etiology for developing early diagnosis and treatment strategies for KC. To address this, our competitive renewal application focuses on identifying *cellular defects* , biomarkers and the *genetic* causes of KC. Beyond obvious familial KC, the vast majority are isolated where disease likely results from rare pathogenic coding sequence variants and genome-wide common noncoding variants that increase one's susceptibility. Elucidating the underlying *genetic defects* in these "isolated KC" requires a range of biological evidence. Our recent studies and preliminary data provide this biological foundation for the current proposal. First, by whole- exome sequencing of KC families, we identified rare pathogenic variants in genes related to cell stress, cytoskeleton and extrac*ellular* matrix (ECM), which are now prioritized as candidate genes and networks for the isolated KC studies. Second, our transcriptomic and proteomic characterizations of KC and control donor corneas identified significant dysregulation in the NRF2-antioxidant program that is crucial for corneal cell survival and its functions. Finally, we developed corneal cell culture models that mimic key KC features, from oxidative stress to ECM insufficiency, and assays to measure these. We further developed the first cornea organoids from human induced pluripotent stem cells that will allow functional studies of genes and therapeutic agents in a physiological, cornea-like setting and in organoid-derived epithelial and stromal cell cultures. Importantly, this approach will yield cell culture disease models from *genetic* ally defined patient blood cells. These cell culture disease surrogates are particularly important, as there are no animal models that can capture the polygenic complexity of KC. In Aim 1 we will assess potential NRF2-regulated antioxidants as tear fluid biomarkers for KC, and investigate this network in corneal cell cultures. In Aim 2 we will identify rare pathogenic variants and common noncoding variants that increase disease susceptibility in isolated KC cases using the 1000Genome and the UK Biobank databases as controls. In Aim 3 we will functionally test the concept that a rare pathogenic variant (e.g., our published c.G12982A HSPG2), will cause *cellular* disease surrogates when CRISPR-edited into cells derived from KC individuals with high polygenic and not controls with low polygenic scores. Our findings will lead to potential anti-oxidant biomarkers, development of NRF2- activators for KC treatments, *genetic* ally defined KC cell culture models and insights into the complex *genetic* architecture of KC. Our studies are highly relevant to the goals of the NEI in understanding the complex *genetic* s of eye diseases, treatments and reversing vision loss.	6/10/2016	R01EY026104	1/31/2027
Yes	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees,Junior Faculty	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees,Junior Faculty	Analytical Chemistry, Biochemistry, Statistical Analysis with R. Training available in my group.	Jose Aleman	NYU LONG ISLAND SCHOOL OF MEDICINE	Biogenesis of Atherogenic Lipoproteins	BIOSTATISTICS AND BIOINFORMATICS CORE (CORE 1) The Biostatistics and Bioinformatics Core (Core 1; C1) will provide data management and analytical competencies to all projects (P1–P3) and cores (C2, C3, and the Administrative Core). C1 personnel will work closely with the other project and core leaders to support study design, data collection, management, data curation, statistical analysis, interpretation, and publication of the study outcomes. C1 will play a crucial role in creating data collection instruments and managing data in REDCap systems to ensure proper data validation. C1 personnel will also create standardized requirements and scripts to perform regular data quality checks, develop a formal data sharing protocol, and oversee the data request and distribution. The biostatistics personnel from C1 were actively involved in producing each project protocol, including sample size and power analysis. We will work with each project leader to provide state-of-the-art statistical and bioinformatics collaboration and consultation throughout the study and use novel methodologies to analyze and interpret data. We will use a high-performance computing cluster with 90 compute nodes to run all bioinformatics analyses. As an integral part of the PPG, all C1 members will attend all the PPG's monthly meetings and focus on analyzing and interpreting data generated by the projects and other cores. C1 will also educate the junior members of the PPG on biostatistics and bioinformatics methods and techniques.	5/1/2023	P01HL160470-01A1	4/30/2028
Yes	Not specified	Not specified	Not specified	Hong Sun	PUBLIC HEALTH & PREV MEDICINE	ALKBH5 and nickel-induced lung carcinogenesis	Nickel compounds are well-established human carcinogens. Epidemiological studies have reported an increased incidence of *lung* and nasal cancer following long-term exposure to nickel compounds due to either environmental or occupational exposure. Growing evidence indicates that alterations of the epigenetic landscape, including DNA methylation and histone modification, are important mechanisms in *nickel-induced lung carcinogenesis* . However, the impact of nickel exposure on the epitranscriptome and the potential role of RNA modification in nickel *carcinogenesis* have never been explored. Our preliminary studies discovered that human bronchial epithelial cells exposed to nickel compounds exhibited reduced mRNA stability of maternally expressed gene 3 (MEG3), an imprinted gene that was downregulated in many types of tumors and a strong driver for *nickel-induced* malignant transformation. In addition, nickel upregulated m6A demethylase *ALKBH5* mRNA and protein expression that coincided with MEG3 RNA destabilization, suggesting *ALKBH5* may contribute to cell transformation via modulating global- or gene-specific m6A abundance. Moreover, knockdown of *ALKBH5* completely abolished MEG3 degradation in nickel-exposed cells, suggesting that RNA methylation may play a role in protecting MEG3 stability. However, it is not clear how nickel upregulates *ALKBH5* as well as whether increased *ALKBH5* mediates *nickel-induced* cell transformation. Additionally, how m6A abundance modulates MEG3 RNA stability remains largely unknown. Therefore, in this application, two specific aims were proposed to address the key events in *nickel-induced* MEG3 destabilization. The first aim will address whether increased *ALKBH5* is sufficient to induce malignant transformation in vitro. The second aim will target the potential upstream regulators and downstream effectors that mediate *nickel-induced ALKBH5* expression and MEG3 destabilization. To the best of our knowledge, this is the first proposal to tackle the impact of environmental nickel exposure on the changes of m6A enzymes as well as transcriptome-wide or gene-specific m6A methylation profiles. Success of this proposal will facilitate our understanding of how nickel targets RNA modification enzymes or RNA binding proteins to initiate or promote *lung* tumor formation, and further identify new aspects of m6A enzymes as a prognostic biomarkers or therapeutic targets to improve clinical outcomes of *lung* cancer patients.	12/10/2022	R21ES034811	11/30/2024
Yes	Post Baccalaureate, Graduate,Post Doctoral trainees	Post Baccalaureate Graduate,Post Doctoral trainees	Molecular techniques such as ELISA, Western blot. The candidate will be trained by my laboratory's members on the more sophisticated technologies (exosomes) specific to the R01.	Carla Nasca	PSYCHIATRY	A translational approach for novel mechanisms of epigenetic regulation in treatment responses: toward a precision medicine model	Treatment resistant depression (TRD) is a leading cause of illness and disability worldwide; there is a dearth of new mechanistic models for the development of better therapeutic strategies. Studies to date showed that administration of LAC, a pivotal mitochondrial metabolite, leads to a rapid and persistent antidepressant-like response by increasing histone acetyltransferases (HATs) activity and the related expression of a key inhibitor of glutamate release mGlu2 receptor in circuits implicated in TRD. Furthermore, LAC levels are decreased in clinical phenotypes of TRD. The objective of this application is to understand the role of central and peripheral LAC-related mitochondrial metabolism in the regulation of TMS responses in phenotypes of TRD. We will also use computational algorithm and statistical clustering to ascertain the role of the novel biomarkers of TMS responses in the trajectories of functional connectivity, and how these pathways are modified by sex. This contribution will advance our understanding of cellular and molecular mechanisms of mitochondrial metabolism for TMS responses in phenotypes of TRD, and identify sex-differences in these mechanisms.	12/14/2022	R01MH128311	12/31/2026

Yes	Undergraduate,Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees	Undergraduate, Post Baccalaureate Graduate,Graduate student Post Doctoral trainees	None	Damian Ekiert	ANATOMY/CELL BIOLOGY	Structural characterization of MCE transport systems from Mycobacterium tuberculosis	Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is one of the deadliest pathogens on the planet, and for decades, TB has been the leading cause of death due to infectious disease. The cell envelope of Mtb forms a notoriously tough barrier around the cell, protecting the bacterium from harsh agents in the environment such as antibiotics and host immune responses. At the same time, Mtb imports nutrients from the host cell, such as cholesterol, across the cell envelope. Transport of lipids, metabolites and nutrients across the cell envelope, between the inner and outer membranes is critical for building and maintaining the cell envelope itself, and for import of key factors required for bacterial growth. Therefore, the transport systems that facilitate this trafficking are critical for allowing Mtb to survive and thrive in its intracellular niche, most typically macrophages in the lungs. The MCE (Mammalian Cell Entry) family of proteins are transport systems that have been implicated as virulence factors in Mtb, and are an expanded protein family in mycobacteria compared with other double-membraned bacteria. In Mtb, several lines of evidence suggest that MCE systems are important for importing nutrients such as cholesterol and fatty acids. Recent work on E. coli MCE systems has shown that these are multi-protein complexes anchored in the inner membrane of double-membraned bacteria, and may play an important role in the maintenance of outer membrane integrity, raising the possibility that this may also be a role that MCE proteins play in Mtb. The structure and mechanisms of the highly complex MCE systems in Mtb remain unknown, and studying these is critical for understanding how MCE systems work, what their substrates are, and how they may be linked to virulence. This proposal is focused on biochemical and structural characterization of MCE transport systems from Mtb and the non-pathogenic model, Mycobacterium smegmatis. Using single particle cryo-EM, mass spectrometry, biochemical and functional assays, we aim to study the structure and function of endogenous Mtb MCE systems, decipher which protein subunits come together to form complexes and define protein-protein interactions that are important for the systems to assemble and function. The results of this work will provide important insights into the structure and function of the large, multi-protein MCE complexes in the Mtb cell envelope, and how they influence replication and virulence in the host.	2/3/2023	R01AI174646	1/31/2028
Yes	Not specified	Not specified	Not specified	Tanya Sippy	PSYCHIATRY	Sensory Plasticity in the Auditory Striatum as an Impetus for Action Control	The ability to translate sensory experiences into action is essential for our survival. Despite its importance in health and disease, we know remarkably little about how we assign meaning to and use sensory stimuli to guide behavior. The dorsal striatum is thought to be particularly important for the formation of sensorimotor associations during reinforcement learning due to the dopaminergic inputs it receives, as well as a diverse array of cortical and subcortical inputs. There are two cell types that make up the two output pathways of the dorsal striatum, direct pathway striatal projection neurons (dSPNs) and indirect pathway striatal neurons (iSPNs). While much work has focused on how these pathways might function to initiate movements, very little is known about how sensory learning influences the neuronal activity of these neurons and what effect this has on behavior. The experiments that make up this proposal provide a framework for understanding how sensory input shapes the activity of dSPNs and iSPNs in the dorsal striatum. In this proposal, we focus on a specific part of the dorsal striatum known as the auditory striatum (AudStr), that receives dense auditory inputs. We hypothesize that auditory sensorimotor learning enables the formation of cue-specific ensembles that correlate with and predict motor output. We expect that these changes will be primarily driven by synaptic plasticity of inputs that converge onto SPNs, rather than changes to their intrinsic excitability. We will perform two independent, inter-related aims to test this hypothesis. We will train mice on a task that requires them to associate a 'go' cue with a specified action to receive a reward, and to suppress this action in response to a 'no-go' cue. In Aim 1, we will employ longitudinal calcium imaging of AudStr neurons to characterize the outputs of these neurons to cues before and after learning. In Aim 2, we will explore the cellular mechanisms underlying anticipated changes in population activity that results from learning, and aim to demonstrate the importance of synaptic plasticity in the AudStr to this process. In both aims we will employ methods that enable us to identify neurons as dSPNs and iSPNs. This is crucial because a major outstanding question in this field is whether these cell types play opposing or complementary roles in producing appropriate motor responses. Overall, this work will lay the groundwork for a new conceptual model for understanding how sensory learning influences striatal activity to control behavior.	3/1/2022	5R01NS126391	2/28/2027
Yes	Undergraduate,Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees,Junior Faculty	Undergraduate, Post Baccalaureate Graduate, Graduate student,Post Doctoral trainees,Junior Faculty	We can train people, but molecular biology skills are useful!	Liam Holt	PATHOLOGY	Cancer under pressure: Mechanisms of adaptation to compressive stress	Physical pressure is fundamentally important for *cancer* biology, but its effects remain poorly *under*stood. When solid tumors grow confined within surrounding tissue, they build up *compressive stress*. Given that cells evolved to function in a stable mechanical environment, even slight changes in pressure perturb physiology. Normal cells and early stage *cancer* cells stop growing when pressure builds up. In contrast, in advanced *cancer*, compression can change cellular behavior to drive migration of *cancer* cells to other organs or confer resistance to chemo- therapy. This difference implies that *cancer* cells somehow adapt to physical pressure. A lack of tools has slowed progress in *under*standing the relationships between compression, the physical properties of cells, and *cancer* behavior. We developed two new technologies to overcome this limitation: First, we created a gene that enables cells to produce a steady supply of fluorescent nanoparticles that act as tell-tales for shifts in intracellular physical properties. Second, we developed microfluidic devices to control *compressive stress*, either quickly or slowly, while maintaining a constant chemical environment. We will combine these innovations to test the overarching hypothesis that mutations that confer resistance to mechanical compression enable pancreatic *cancer* cells to adapt to their high-pressure environment and drive their oncogenic evolution. Aim 1: We will determine how compression differentially impacts wildtype and mutant pancreatic cells. We will use GEM nanoparticles to quantify the physical response to pressure and test the hypothesis that oncogenic mutations alter both the physical and physiological response to pressure. Aim 2: We will determine the effects of compression on phase separation. We will investigate the hypothesis that decreased cell volume *under* pressure leads to in- creased phase separation of *stress* granules. We will evaluate molecular crowding as a mechanism for these effects. We will determine the importance of *stress* granule formation for mechanical *adaptation* and drug re- sistance. Aim 3: We will determine genetic *mechanisms* of pressure *adaptation*. We will follow up on pre- liminary mutants that confer resistance to compression, using a CRISPR modifier screen to determine mecha- nisms of *adaptation*. We will overexpress known oncogenes to find further *adaptation* pathways. Our innovative combination of genetic nanoparticles and microfluidic approaches, and our expertise that bridges biophysics, mechancbiology and cell biology make us uniquely qualified to connect compression, the physicochemical properties of cells, and *cancer* physiology. Our studies promise to reveal key network pertur- bations essential to *cancer* cell growth and survival *under* pressure. *Under*standing these adaptive *mechanisms* promises to suggest treatments that exploit the aberrant mechanical properties of tumors caused by high com- pressive *stress*.	5/31/2019	R37CA240765	5/31/2024
Yes	Post Baccalaureate Graduate,Graduate student,Post Doctoral trainees	Post Baccalaureate Graduate, Graduate student,Post Doctoral trainees	Beneficial to have some analytic skills, programming experience and/or neuroimaging experience but not cirtical	Candace Raio	PSYCHIATRY	Neural and affective mechanisms underlying prospective self-control costs	*Self-control* failures are a universal challenge for healthy and clinical populations. Recent theoretical and empirical work suggests these failures may arise from excessive cognitive *costs* associated with exercising control. However, traditional *self-control* paradigms do not provide a methodological platform to quantify these *costs*. Further, we know little about the *neural* basis of *self-control costs* nor how these representations change under different classes of psychological stress, which is a major risk factor for *self-control* failure. To address this, we developed a novel decision-making task that measures how much individuals will pay to restrict access to tempting rewards that may derail their long-term goals and lead to *self-control* failure (precommitment). Here, we aim to use an expanded and refined version of this newly validated tool to examine neurocomputational and *affective mechanisms underlying prospective self-control costs* and how they relate to real-world *self-control* failures. In Aim 1, we seek to identify the computational, motivational and cognitive mechanism that gives rise to *self-control costs*. We will model the cost function for *self-control*, test how this metric relates to cognitive constructs typically implicated in *self-control* in the literature and disentangle the motivational mechanism *underlying* the use of precommitment. In Aim 2 we seek to characterize the *neural* correlates of *self-control costs*, track how activity within these regions dynamically fluctuate depending on the feature of food stimuli participants focus on and identify *neural* mediators and connectivity patterns stemming from these *costs*. In Aim 3, we seek to examine how different classes of stressor type (physiological, social, or lifetime stress) shapes the behavioral and *neural* representations of *self-control costs*. Characterizing individuals' *self-control* cost function and how these *costs* are represented in the brain will allow for a more direct test of how stress exposure affects decisions to use *self-control* and may lead to potential interventions that can buffer individuals from the effects of stress on such decisions.	04/31/2023	R01MH130532	03/31/2028
Yes	Post Baccalaureate Graduate,Post Doctoral trainees	Post Baccalaureate Graduate,Post Doctoral trainees	data analysis, programming	Eric Sigmund	RADIATION-DIAGNOSTIC/ONCOLOGY	Advanced Diffusion Imaging for Management of Renal Cancer: Oncologic Control and Renal Functional Reserve	*Renal* cancer is a source of severe mortality and morbidity, not only due to the primary malignancy but also due to loss of *renal* function (sometimes leading to chronic kidney disease) after partial nephrectomy. Methods to noninvasively monitor *renal* function and predict its robustness against this decline of function are therefore in high demand. *Diffusion*-weighted MRI is well poised to play this role as an adjunct to *renal* cancer patients' existing clinical MR workup. Our group has been at the forefront of research into *advanced renal diffusion* MRI contrast, including methods to separate microstructure from microcirculation (intravoxel incoherent motion (IVIM)) and assess microscopic anisotropy (*diffusion* tensor *imaging* (DTI)). A recent comprehensive approach (REFMAP) collects these contrasts jointly, allowing assessment of microstructural and microcirculation anisotropy. We propose to apply this composite dataset both to classify aggressiveness of the primary *renal* lesion and to assess and predict post-surgical *renal* function. IVIM-MRI will be performed to characterize the aggressiveness of the primary lesion. The REFMAP-MRI protocol will be used to evaluate *renal* cancer patients before surgery and at 1 year follow up, in comparison with standard clinical workup (measured glomerular filtration rate, proteinuria). Cross-sectional correlation will validate the markers of the REFMAP-MRI technique as probes of *renal* function, and those baseline values predicting which patients experience *renal* function decline will be identified.	7/7/2020	R01CA245671	4/30/2025
Yes	Post Baccalaureate Graduate	Post Baccalaureate Graduate	Diligent, hard-working, and responsible individuals. Strong motivation in neuroscience related research. Responsibilities involved: subject recruitment, cognition testing, imaging studies, data collection and management, etc.	Yu-Shin Ding	RADIATION-DIAGN	Brain Effects of Lifetime Racial/Ethnic Discrimination on the LC-NE Function and the Risk for Alzheimer's Disease	Despite the fact that global population is racially and ethnically diverse, there remain substantial gaps in the scientific literature regarding the impact of Alzheimer's disease (AD) risk among blacks; e.g., limited studies investigate health disparities and blacks have been underrepresented in many prominent U.S. AD biomarker studies and clinical trials. By 2050, 42% of the nation's older adults will be minorities. This demographic shift will represent a critical challenge to older blacks, as current evidence suggests that they may be at greater risk of developing AD; with 2-3 times higher prevalence rate. Although it's been difficult to explain why AD disproportionately affects blacks, evidence from limited studies suggested that possible race-dependent biological mechanisms may contribute to different expression of AD. Overall, these results indicate that the current ATN biomarkers for AD (i.e., amyloid (A), tau (T), and neuro-degeneration (N)) may not fully account for health disparities in AD risk and may lead to under-diagnosis of AD among blacks. Degeneration of the locus coeruleus (LC) is an ubiquitous feature of AD and postmortem studies suggest that loss of LC neurons better predicts the onset and severity of symptoms of AD than Aß/neurofibrillary tangles or cell loss in any other brain region. We have previously demonstrate the vulnerability of the LC to aging and stress, and our preliminary data shows faster LCnorepinephrine (NE) functional decline among blacks, possibly related to lifetime experience of discrimination. This study will test whether loss of LC-NE function better predict cognitive decline than current ATN biomarkers. This innovative study represents a novel approach to racial dependent strategies for diagnosis and therapeutical interventions in AD.	6/29/2023	R01AG072644	7/1/2026

Yes	Graduate student,Post Doctoral trainees	Graduate student,Post Doctoral trainees	Ability to work well independently and collaboratively on complex tasks and to lead junior staff in the conduct of research. Commitment to issues of diversity, equity, and inclusion	Alan Mendelsohn	PEDIATRICS	Mitigating Adverse Effects of COVID-19 through Preventive Interventions for Families with Young Children Living in Poverty: Linking Data from 3 Cities with Diverse Risks and Exposures	Public health disasters, such as COVID-19, have disproportionate consequences on low-income and racial- ethnic minority communities through pathways that likely exacerbate disparities associated with poverty and racism, and act over extended periods. Young children are vulnerable to deleterious effects of the pandemic on psychosocial development but have received less attention and resources. Preventive interventions focused on relational health (e.g., positive and structuring parenting practices, parent-child relationship quality) have been shown to address the adverse consequences of poverty for young children. However, such interventions have yet to be tested during a public health disaster, much less one with potentially compounding effects on poverty- related and racial/ethnic disparities. The current application provides a unique opportunity to determine whether healthcare- and community-based interventions initially targeting pathways of adversity for families with young children living in poverty can prevent widening of disparities in the context of COVID-19. We propose to examine these critical issues by pooling and harmonizing seven data sets across four studies (including three NICHD R01 awards) in: 1) three very different cities (New York City, Pittsburgh, PA and Flint, MI); 2) that include low-income, Black and Latinx families; 3) involve trials of scalable preventive relational health interventions delivered in early childhood (primarily birth to 3 years), the majority with a randomized design; and 4) assess families longitudinally with multiple informants/methods to assess family socioeconomic risk, parent-child relational health, and child psychosocial development, as well as exposure and experiences linked to COVID-19, through the preschool or early school age period. Thus, the current application examines the consequences of COVID-19 for already-vulnerable families' relational health and child psychosocial development, the potential protective role of relational health interventions in attenuating emerging COVID-19- related disparities, and the variation in these effects across timing of intervention pre- and post-COVID-19 onset, experience, and exposure to the pandemic, and pre-existing family-related risk. Findings will address complex drivers of health disparities and our ability to utilize population-scalable, preventive parenting interventions to promote children's healthy psychosocial development in the context of both the COVID-19 pandemic and future public health disasters, with implications across the life course. In addition to determining the degree to which preventive interventions buffer adverse consequences on parents and children, the extensive questions that can be addressed by combining and harmonizing across these rich data sets, promise to offer the field critical information about how our most vulnerable families are faring following the pandemic. This proposal directly addresses NICHD priorities for studying "developmentally informed strategies to mitigate health disparities" of the COVID-19 pandemic on children and families.	8/9/2022	R01HD109187	7/31/2027
Yes	Graduate student,Post Doctoral trainees	Graduate student,Post Doctoral trainees	Programming experience in python and R; bioinformatics experience; statistics and machine learning; high dimensional data visualization	Jonas Schluter	MICROBIOLOGY/IMMUN/VIROLOGY	The unleashed microbiome of cancer patients as a discovery platform for rational microbiome engineering	*The* human gut *microbiome* is associated with a range of diseases, and may positively or negatively affect *the* success of *the* rapies. However, *the* causal directions between *the* human gut *microbiome* and host health are seldomly clear due to a lack of feasible controlled experiments in humans. High resolution, high frequency temporal data of paired *microbiome* and physiological measurement, and rich metadata of potential confounders, allow *the* application of causal inference frameworks. Such data can be mined for potential *microbiome* drivers of host health, especially if both *the microbiome* and host physiology are perturbed during *the* time courses. We have recently published a vast longitudinal *microbiome* set from *cancer patients* undergoing severe perturbation of *the* ir immune system. Concurrently, *the* se *patients* experience dramatic shifts in *the ir* gut ecosystem. We here propose to unlock this data and build a *discovery platform* for *microbiome* causality, towards *rational microbiome engineering*. We will develop a new machine-learning technique that enables rapid exploration of our data through effective visualization and a web-based interface. We will develop a new method to identify gut microbial competitor species of common pathogens, which are systematically missed by existing approaches but are representing *the* most promising targets for *microbiome engineering*. Finally, we will elucidate *the* bidirectional interplay between human- targeted medications and *the* gut *microbiome*. For this, we will leverage our large data set of paired *microbiome* and host immune cell trajectories. This will validate recent in vitro results indicating that human-targeted medications may influence gut ecology using in situ data, and it will identify potential gut *microbiome* modulation of pharmacokinetics.	7/26/2022	DP2Act AI164318	7/31/2026
Yes	Post Doctoral trainees	Post Doctoral trainees	Not specified	Tanya Spruill	INTERNAL MEDICI	Telephone-based mindfulness training to reduce BP in Black women with hypertension in the Jackson Heart Study	Black women experience disproportionately high rates of hypertension compared to women of other racial and ethnic groups, and their blood pressure (BP) control rates are well below targets despite high levels of awareness and treatment. There is an urgent need for effective nonpharmacological strategies beyond lifestyle behavior change to improve hypertension and cardiovascular disease (CVD) outcomes in this understudied population. Chronic psychosocial stress is associated with hypertension and CVD. Black women are exposed to both race- and gender-based stressors and may employ coping strategies (e.g., emotion suppression, self- care postponement) that increase vulnerability to stress. While many stressful events and circumstances cannot be avoided, adaptive coping can mitigate adverse effects of stress exposure. Mindfulness-based cognitive therapy (MBCT) is an evidence-based program that teaches meditation practices and cognitive strategies to reduce perceived stress and negative emotions. Qualitative research supports the cultural relevance of mindfulness interventions for Black women but clinical trial evidence in this population is limited. Further, the burdensome nature of traditional in-person MBCT poses a significant barrier to participation. We have adapted MBCT for delivery to small groups by telephone (MBCT-T) and our preliminary data support the feasibility, acceptability and effects of the intervention. We propose an RCT to evaluate effects of MBCT-T on BP and psychological outcomes in Black women with uncontrolled hypertension in the Jackson Heart Study (JHS) - a longitudinal cohort study designed to investigate the causes of CVD in Blacks. A sample of 300 female JHS participants with uncontrolled hypertension will be enrolled and randomized to MBCT-T or telephone-based support groups (TSG), an active comparison condition. Both programs involve 8 weekly group-based phone sessions. The primary outcome is home (HBP), a better predictor of CVD risk than clinic BP, measured for 7 days at baseline and 3- and 6-month follow-up with validated wireless devices. Secondary outcomes are perceived stress and depressive symptoms. Measures of chronic stress, coping, resilience and potential psychological, social and behavioral mediators of intervention effects will be assessed. Data from the three prior JHS exams and 20 years of annual follow-up data will also be used to characterize long-term levels of psychosocial factors that may help to explain variability in treatment response. The specific aims are to: (1) Test the hypothesis that MBCT-T will be associated with greater 6-month reductions in systolic BP vs. TSG; (2) Test the hypothesis that MBCT-T will be associated with greater 6-month reductions in perceived stress and depressive symptoms vs. TSG; and (3) Explore potential mediators and moderators of intervention effects on BP and secondary outcomes. Findings will advance understanding of stress, coping and effects of mindfulness training in Black women. If effective, this scalable psychosocial intervention has the potential to positively impact hypertension and other health outcomes among Black women in the JHS cohort and beyond.	3/23/2023	R01MD016402	3/31/2027
Yes	Post Baccalaureate Graduate,Graduate student	Post Baccalaureate Graduate,Graduate student	Not specified	Antoinette Schoenthaler	INTERNAL MEDICI	Do no digital harm? A multilevel evaluation of technology-facilitated team care on the patient-provider relationship in health disparity populations	Patient-provider relationships characterized by high levels of commitment and trust are central to delivering high quality care for improved hypertension (HTN)-related outcomes. Unfortunately, health disparity populations are least likely to be in patient-provider relationships characterized by high levels of commitment and trust leading to negative affective, behavioral and physiological patient outcomes including heightened anxiety during the interaction, medication non-adherence, and poor blood pressure (BP) control. COVID-19 not only highlighted these social inequities but also led to a rapid change of our health system – from mainly in-person to telehealth visits. While telehealth has shown great promise in improving the clinical management of HTN, its impact on patient-provider relationships is unclear. Some evidence suggests telehealth could strengthen these relationships through improved access to the care team, but its technical and interpersonal drawbacks may reduce commitment and trust. To address these gaps, this proposal will leverage the infrastructure established by our NIMHD-funded R01, which will support 10 primary care clinics in the integration of technology-facilitated team care (herein called ALTA) to improve medication adherence and BP control in health disparity populations. ALTA enhances standard in-person and telehealth visits with opportunities for patients and providers to interact via secure messaging through the electronic health record (EHR) and patient portals. While a central premise of ALTA is that it will build clinic capacity to deliver equitable, high-quality care to health disparity populations, it was not designed to evaluate the impact of healthcare technologies on patient- provider relationships. Guided by the multilevel NIMHD research framework, the proposed study will employ a mixed methods study design that links four data sources to rigorously evaluate the multilevel impacts of ALTA on relationship commitment (primary outcome), patient-provider trust (secondary outcome) and patient health outcomes (tertiary outcomes) across 10 primary care clinics and 700 patients with uncontrolled HTN (Aims 1 and 2). Our evaluation strategy will combine cognitive, affective and behavioral measures of the patient-provider relationship and patient outcomes to create a multifaceted view of how individual perceptions and actions of the partners change when ALTA is introduced. Specifically, validated self-report measures (e.g., State Anxiety Inventory) will be augmented by automated text analysis of audiotaped interactions and secure messaging using natural language processing techniques, and EHR-extracted data on clinic and home BP readings and medication adherence (i.e., pharmacy records). Aim 3 will explore potential contextual factors (e.g., equity; digital literacy; communication modality) that influence the relationship between ALTA and the interpersonal and patient-level outcomes using self-report and EHR-derived measures. Aim 4 will use the human centered design approach to systematically gather feedback from clinic stakeholders to identify best practices for effective technology-facilitated patient-provider relationships.	7/11/2023	R01MD018018	1/31/2028
Yes	Post Doctoral trainees	Post Doctoral trainees	Not specified	Devin Mann	INTERNAL MEDICI	Do no digital harm? A multilevel evaluation of technology-facilitated team care on the patient-provider relationship in health disparity populations	Uncontrolled type 2 diabetes (T2D) is a major health problem in the US that constitutes a significant cause of morbidity and mortality, particularly in vulnerable populations who continue to suffer disproportionately higher rates of complications. Despite the significant physical and psychosocial impact T2D has on patients' behavioral, functional and clinical outcomes; much of clinical practice continues to neglect patients' perspective of their T2D giving preference to the physiological aspects of the disease. However, without incorporation of patients' perspective of their health and functional status into diabetes care, achievement of the outcomes desired by patients and primary care providers (PCP) will be unattainable. To address this gap, we will use the Technology Acceptance Model and Capability-Opportunity-Motivation Model of Behavior to evaluate the efficacy of a technology-based patient-reported outcome (PRO) system, the Modern Journal System, for management of T2D [MJS DIABETES]. MJS is an innovative mobile platform that utilizes text-messaging to capture PRO data in real-time, enhance patient engagement through data-driven feedback and motivational messages, and creates dynamic data visualizations of the PRO data that can be shared through printed reports, and integrated into the electronic health record (EHR). Using a mixed-methods design, we will conduct this study in two phases: 1) A formative phase, using the evidence-based user- centered design approach; and 2) a clinical-efficacy phase. The formative phase will use qualitative methods to: a) adapt MJS DIABETES to the needs of PCP and patients with T2D; b) integrate MJS DIABETES into the EHR system, primary care practice as well as the lives of patients with T2D; and c) evaluate the usability of MJS DIABETES in a subset of T2D patients and PCPs in order to optimize the tool's performance and workflow integration. For the clinical efficacy phase, we will evaluate in a randomized control trial, the efficacy of MJS DIABETES versus Usual Care (UC) on reduction HbA1c at 12-months, among 282 patients with T2D who receive care in safety-net practices. Patients randomized to the intervention arm will be enrolled in MJS DIABETES where they will receive and respond to PROs via text message, receive data-driven feedback and motivational messages based on patterns of their PROs, and journal reports over the 12-month study. PCPs will have access to reports of patients' PRO data through the MJS-EHR interface, which can be viewed during visits with the patient or asynchronously to track patient PROs between visits. Patients randomized to the UC arm will receive standard T2D treatment recommendations, as determined by their PCP. The primary outcome will be mean reduction in HbA1c from baseline to 12 months. Secondary outcomes will include changes in: a) patient adherence to self-care behaviors (e.g., lifestyle and medication recommendations); and b) theoretical mediators of diabetes knowledge, self-efficacy, outcomes expectations, and patient-provider communication. Regardless of group assignment, all outcome data will be assessed at baseline, 3- 6-, 9- and 12-months.	6/28/2023	R01HS026522	5/31/2028

Yes	Post Doctoral trainees	Post Doctoral trainees	Not specified	Devin Mann	INTERNAL MEDICI	Do no digital harm? A multilevel evaluation of technology-facilitated team care on the patient-provider relationship in health disparity populations	Latinx adults experience a disproportionate burden of cardiovascular disease in the United States, driven in part by structural barriers to accessing and utilizing care. Latinx patients are at risk for hypertension (HTN), and are less likely to be able to access necessary care to manage this condition. Digital health tools such as remote patient monitoring (RPM) have potential to improve the care of Latinx patients with HTN by enabling more frequent and tailored monitoring of blood pressure, providing additional health information, empowering patients, and enhancing care decision-making without disrupting patients' daily lives. However, there are significant disparities in the access and use of these digital tools, as well as challenges to equitable and sustainable implementation. To mitigate these disparities, there is urgent need to identify methods to equip and facilitate the implementation of RPM for diverse populations and address social, structural, and digital determinants of health to make RPM care more appropriate for diverse patient needs. Community health workers (CHWs) are specifically trained to address social and structural determinants of health to help patients manage health conditions, provide culturally and contextually competent support, and navigate complex health systems; "tech- enabled" CHWs have potential to be catalysts for improved RPM use for Latinx patients. Our team – comprised of leaders of RPM implementation and infrastructure, CHW training, informatics, digital health, quantitative and qualitative study design, data analytics, and health disparities research – seeks to determine if the addition of RPM-enabled CHWs provided with specific training and EHR support tools can improve HTN control and reduce inequities among Latinx patients with uncontrolled HTN. Specifically, we seek to: 1) develop adapted community health worker remote patient monitoring training modules ("CHW RPM") and electronic health record support tools ("CHW RPM-EHR") guided by the CFIR model to enhance the management of hypertension in Latinx patients; 2) evaluate the effectiveness of RPM-enabled CHWs compared to standard of care RPM hypertension management on blood pressure reduction among 300 Latinx patients with uncontrolled hypertension; and 3) apply Proctor's Implementation Outcomes Framework (IOF) to evaluate the implementation of the RPM-enabled CHWs for HTN management, and examine adoption, acceptability, fidelity, cost, sustainability, and equity as mechanisms of implementation effectiveness. The primary outcome will be improvements in HTN management at 12 months. We will utilize a mixed methods approach – including EHR-based data review, patient surveys, in- depth interviews with PCPs, RNS, CHWs, and patients – novel consensus-building, user-centered design and agile development techniques, and theory-driven implementation assessment frameworks to assess the intervention. This research will help inform RPM implementation for our diverse patient population, as well as offer larger insights into to the opportunities and challenges of using CHWs to expand access to RPM to Latinx patients and ultimately improve health equity.	7/21/2023	R01HL165427	1/31/2028
Yes	Post Doctoral trainees,Junior Faculty	Post Doctoral trainees,Junior Faculty	Those interested should have a Ph.D. in one of the following areas: Public Health, Clinical neuropsychology, Neuroscience, Epidemiology (Neuro-epidemiology, Social epidemiology, etc.), or a related field. Applicants should be highly motivated, with exceptional communication skills, and a strong internal drive to learn one on one	Omonigho Bubu	PSYCHIATRY	Using a Health Disparity Research Framework to examine mechanisms linking Obstructive Sleep Apnea with higher Alzheimer's disease risk in older Blacks/African-Americans	Blacks/African-Americans (blacks) have two times the risk of developing Alzheimer's disease (AD) compared to non-Hispanic whites (whites), in part attributable to the higher prevalence of vascular risk factors. Examining other risk factors and delineating pathological mechanisms associated with this higher AD-risk in older blacks is a critical initial step needed to optimize patient care paradigms. Obstructive sleep apnea (OSA) is one such risk factor. Notably, blacks have a higher burden of OSA with excessive daytime sleepiness (EDS), which is associated with longitudinal amyloid-PET uptake. OSA is associated with decreased non rapid eye movement (NREM) slow wave sleep/activity (SWS/SWA) and increased inflammation, both of which affect amyloid and tau pathology. NREM SWS/SWA and inflammation are also associated with changes in cognition in late-life, and are more burdensome in blacks. The current proposal will utilize a health disparities research framework related to aging to: (i) investigate within and between race effects of OSA on AD pathology. (ii) Identify decreased NREM SWS/SWA and increased inflammation as potential intermediate mechanisms linking OSA and AD. (iii) Examine whether socio-structural determinants of health (SDOH) can help explain racial heterogeneity in OSA- AD outcomes. Our neurodegeneration, central hypothesis is that black OSA subjects will exhibit higher tau and greater as well as reduced NREM SWS/SWA and increased inflammation compared to white OSA subjects, in the context of amyloid burden. Furthermore, we hypothesize SDOH (i.e., environmental, socio- structural, and behavioral factors) and vascular risk will mediate racial heterogeneity in OSA-AD outcomes. We will test our central hypothesis in a sample of 300 community-dwelling cognitively normal (CN) subjects; ages 55-85 matched on race (2:1), age and sex, and balanced by education, income and BMI. Subjects will include 150 controls (100 blacks & 50 whites), and 150 newly diagnosed OSA subjects with EDS (100 blacks & 50 whites). This proposal will recruit from the community, 125 new black subjects [80 OSA and 45 controls] and leverage existing data and resources in 175 (75 blacks [20 OSA and 55 controls] & 100 whites [50 OSA and 50 controls]) community-dwelling CN subjects with similar eligibility criteria, from NYU Alzheimer's Disease Research Center and two-affiliated ongoing NIH supported R01 studies (R01AG056031 and R01AG056531). Subjects will undergo 2 nights of at-home sleep monitoring for OSA, followed by 5 days of actigraphy and sleep logs. Clinical visits will include full clinical evaluation, neuropsychological tests and clinical labs on visit 1; 1 night of nocturnal polysomnography (NPSG) recording on visit 2; neuroimaging measures of vascular burden, amyloid (18F- florbetaben) and tau (18F-PI2620) PET-MRI on visits 3 and 4 respectively, at baseline and at 2.5 years follow-up. Importantly, we will prioritize acquisition of SDOH data to elucidate disease mechanisms to aid future discovery of novel AD prevention targets e.g. targeting stress management, inflammation and sleep quality in OSA.	5/19/2023	R01AG082278	4/30/2028
Yes	Post Doctoral trainees,Junior Faculty	Post Doctoral trainees,Junior Faculty	Those interested should have a Ph.D. in one of the following areas: Public Health, Clinical neuropsychology, Neuroscience, Epidemiology (Neuro-epidemiology, Social epidemiology, etc.), or a related field. Applicants should be highly motivated, with exceptional communication skills, and a strong internal drive to learn one on one	Omonigho Bubu	PSYCHIATRY	Treatment of OSA on sleep-dependent memory and blood biomarkers in blacks	Growing evidence suggests that obstructive sleep apnea (OSA) patients have cognitive impairments as well as increases in Alzheimer's disease (AD) biomarkers such as amyloid beta and tau. Positive airway pressure (PAP) therapy is an effective treatment for OSA but is often limited by suboptimal adherence. Anecdotal evidence show both short and long-term adequate OSA treatment improving attention, psychomotor speed, memory and executive function deficits associated with OSA. However, there is scarcity of data regarding the impact of OSA treatment among blacks on neurocognitive outcomes, despite having a disproportionate burden of OSA and AD, as well as a traditionally low treatment adherence. In this innovative hypothesis-driven study, we will address inadequate adherence to OSA treatment in blacks with "personalized multi-modal OSA treatment", tailored to reduce health risks in minoritized communities by offering any combination of PAP, oral appliance therapy (OAT) and positional therapy, as well as address individual and system-level barriers through no-cost enrollment, personalized educational/instructional use, and real-time adherence monitoring that results in an effective reduction in AHI. Using a pre-and-post treatment design, we will examine the personalized multi-modal OSA treatment effect on within-subject changes on i) blood-based biomarkers of neurodegeneration (Aim 1), ii) sleep-dependent spatial navigational memory and functional magnetic resonance imaging (fMRI) (Aim 2), and iii) examine whether adequate sustained reductions in AHI at 12 months (effective AHI<15) are associated with sustained improvement in global cognition, standard declarative memory, attention and processing speed tests (Aim 3). Our central hypothesis is that the degree of effective AHI reduction by our personalized multi-modal OSA treatment will predict: 1. the longitudinal change in overnight plasma NfL; 2. the longitudinal change in brain circuit activity and spatial navigational memory improvement and 3. the degree of sustained improvements in sleep and cognitive performance at 12-months.We will leverage the success of our Sleep Disparity Workgroup in recruiting from minoritized communities, and the collaboration with affiliated sleep clinics and test our central hypothesis in a sample of 60 newly diagnosed moderate-to-severe OSA black subjects ages 45-75. Subjects will undergo full clinical evaluation, neuropsychological tests and clinical labs. Prior to and after 3-months of personalized multi-modal OSA treatment, all subjects will undergo a night of in-lab polysomnography with a pre-sleep and post-sleep blood draw and spatial navigational memory test in the MR scanner. A 12-month follow- up will also assess the effect of sustained improvements in sleep on changes in cognitive performance. Importantly, we will acquire and explore identifying socio-structural determinants of health (SDOH) factors that are associated with sustained treatment adherence to inform both clinical and public health practices targeting inadequate adherence and impact of OSA treatment on cognition in blacks.	8/18/2023	RF1AG083975	8/31/2026
Yes	Graduate student,Post Doctoral trainees	Graduate student,Post Doctoral trainees	We are looking for a self-driven, creative, and interactive individual who is motivated to acquire new skills and work with an interdisciplinary team. The ideal candidate would have a degree in software engineering, computer science, or equivalent. Good	Ricardo Lattanzi	RADIATION-DIAGN	Cloud MR: an Open-Source Software Framework to Democratize MRI Training and Research	Cloud MR: an open-source software framework to democratize MRI training and research This project is a competing continuation of our project entitled Novel Software Tools for Rational Design and Assessment of MR Coils, which yielded seminal advances in understanding radiofrequency coil performance at high and ultra-high field. It also delivered novel computational tools for rapid coil simulation using Integral Equation techniques, and introduced the ultimate intrinsic transmit efficiency as an absolute metric for transmit coil performance. Our continuing project will integrate these advances into the development of Cloud MR, a comprehensive framework to simulate all aspects of the MRI experiment. By means of an intuitive web-based user interface, Cloud MR will allow the development of RF coils, pulse sequences and image reconstruction methods within an interconnected simulation environment that will enable users to optimize them jointly or individually. We will introduce the first web-based tool for modeling and simulation of flexible RF coils, as well as an innovative tool for pulse sequence development based on a Sequence Description Language. We will train a convolutional neural network for the removal of Gibbs artifacts using synthetic brain images generated with Cloud MR. The overall goal is to provide to anyone with an internet connection a powerful, innovative, comprehensive open-source tool for MRI research and training. By providing a virtual simulation environment to test new technology and optimize clinical protocols without operating an actual MR scanner, Cloud MR will reduce the carbon footprint of MRI. Cloud MR will also allow to generate realistic synthetic MR datasets to train neural networks, without the need to access actual patients' data. We will distribute all software freely and fully documented, including tutorials and examples that could be used to demonstrate physics and engineering concepts in undergraduate and graduate courses.	12/30/2022	R01EB024536	11/30/2026
Yes	High School	High School	Reading and understanding scientific journals, clear and concise writing, making/creating figures for scientific dissemination, honesty and integrity	Yvonne Lui	RADIATION-DIAGNOSTIC/ONCOLOGY	Diffusion MRI Model Parameter Estimation to Study Brain Microstructure as it Relates to Cognitive Status in Mild Traumatic Brain Injury	Mild Traumatic Brain Injury (MTBI) is a major public health problem with U.S. annual incidence of over 2 million. We propose to use an innovative paradigm in bicompartment diffusion MRI model parameter estimation to study the dynamic longitudinal microstructural changes that occur after MTBI and to investigate the link between white matter injury, cortical volume loss and cognitive outcome. Our preliminary findings suggest diffusion-based biophysical parameters of axon integrity including intra-axonal diffusivity (Da) and axonal water fraction (f) can detect microstructure changes in MTBI and provide more biophysically relevant information compared with traditional, empirical measures of Diffusion Tensor Imaging (DTI). We will employ a rotationally invariant formalism and parameter estimation scheme for the so-called "Standard Model" of diffusion in white matter which unifies previous attempts of multi-compartment white matter modeling over the past decade, now a widely accepted benchmark for multi-compartment modeling of diffusion in the brain. We will further incorporate spherical tensor encoding (STE) and spherical kurtosis (SK) to increase the precision in axon-specific microstructure parameters central to this project and use an optimized and clinically feasible protocol for this translational project. The proposed work is expected to bridge the gap between macroscopic and microstructural alterations relevant to cognitive status after injury, revealing the dynamic structural changes occurring after injury and pointing to imaging biomarkers most relevant to cognitive outcome. By concentrating on cognitive outcome, we will address one of the main barriers to predicting outcome in MTBI which is heterogeneity of clinical status. The results of this work are expected to be significant from both scientific and clinical perspectives by 1) advancing basic knowledge of injury in an impactful way, 2) discovering biophysically meaningful imaging biomarkers relevant to cognitive status in MTBI, and 3) mechanistically linking microstructural and macrostructural brain alterations, in three respective specific aims. This will provide a means toward quantitative tracking of injury and recovery specific to the cognitive domain, and tracking of efficacy of targeted cognitive therapeutic strategies such as cognitive rehabilitation and integrated behavioral health treatment in patients with MTBI.	7/31/2023	R01NS119767	7/31/2025

Yes	Undergraduate, Post Baccalaureate Graduate,Graduate student	Undergraduate, Post Baccalaureate Graduate,Graduate student	Our ideal candidate would be a trainee interested in developing and testing a culturally centered diabetes prevention intervention tailored for Spanish-speaking older adults	Jeannette Beasley	INTERNAL MEDICINE/MEDICINE	BRinging the Diabetes Prevention Program to GEriatric Populations (BRIDGE)	Over 24 million Americans are ≥65 years and have prediabetes. Prediabetes can be addressed using a public health approach: among the 20% of participants in the Diabetes Prevention Program (DPP) who were ages 60 and over, the diet and physical activity intervention conferred a 71% risk reduction of diabetes after an average follow-up of 3 years. The population of older adults is projected to more than double from 52.5 million in 2019 to ~100 million by 2060, and if projections hold, about half (48.3%) will have prediabetes. The proposed study will compare a DPP program Tailored for Older Adults and delivered via Telehealth (DPP-TOAT arm) to an in person DPP tailored for older adults (DPP arm) using a randomized, controlled trial design (n=230). Our preliminary data suggests DPP-TOAT is a feasible and acceptable way to deliver the DPP to older adults, and this will be the first study to compare the effectiveness and implementation of two strategies (telehealth versus in-person) to deliver a tailored DPP for the unique needs of the growing population of older adults. Eligible patients will be recruited through electronic health records (Epic and MyChart) and randomized to the 12-month DPP-TOAT or the in-person DPP program. The primary effectiveness outcome will be 6-month weight loss and implementation outcome will be attendance. We will use a pragmatic approach in order to inform future studies conducted in community-based and rural settings. Findings will inform best practices in the delivery of an evidence-based intervention that could reach the 24+ million adults aged 65 and over with prediabetes.	11/28/2022	R01 DK127916	11/30/2026
Yes	Graduate student,Post Doctoral trainees	Graduate student,Post Doctoral trainees	Immunology Microbiology Willing to work in BSL3	Chiara Giannarelli	INTERNAL MEDICINE/MEDICINE	Not Specified	not specified	not specified	not specified	not specified
Yes	Junior Faculty	Junior Faculty	Preferably someone with Clinical Decision Support, Informatics, Behavioral Economics, and/or Design experience.	Safiya Richards	INTERNAL MEDICINE/MEDICINE	EHR Nudges: Optimizing a Clinical Decision Support System for Evidence-Based Statin Medication Prescribing to Reduce the Risk of Cardiovascular Disease	Statins reduce the risk of major adverse cardiovascular events and mortality. However, providers fail to prescribe statin therapy for about half of patients meeting guideline criteria for initiation. The electronic health record (EHR) creates opportunities to develop clinical decision support systems (CDSSs) to support cardiovascular disease (CVD) risk recognition, assessment, and management. However, low provider adoption has limited the clinical impact of CDSSs designed to improve guideline-concordant statin prescribing. Integrating insights from behavioral economics into CDSS design represents a novel approach to improving adoption by minimizing key barriers - provider time and cognitive load burden. Behavioral economics studies the effects of psychological, social, cognitive, and emotional factors on the decisions of individuals and uses nudges to influence behavior at a largely unconscious level. Nudges are defined as positive reinforcement and indirect suggestions which have a non-forced effect on decision-making. For example, “opt-out” options for organ donation consent lead to striking differences in enrollment. Nudges represent an exciting and novel approach to developing CDSSs that minimize provider burden and are, therefore, more efficient, scalable, and impactful (i.e., optimized). The overall objective of this proposal is to develop and optimize a CDSS, including several nudges, to increase guideline-concordant statin prescribing for CVD risk (Nudge-CVD-CDSS). We use an innovative, engineering-inspired multiphase optimization strategy (MOST) framework to arrive at an intervention that is not just efficacious or effective but efficient and scalable. Several potential intervention components (EHR-nudges) will be developed, usability tested, revised, and evaluated. A randomized trial using a specialized design will evaluate the individual and combined effects of nudges. We will seek the combination of nudges that maximizes impact on guideline-concordant statin prescribing while minimizing provider time and cognitive load burden. Specific Aims: 1) To develop, based on a conceptual model of the prescribing process, a set of potential intervention components (EHR-nudges) to promote and support AHA/ACC guideline-concordant statin prescribing, 2) To revise potential intervention components through iterative usability testing, including real-time measures of provider time and cognitive load burden and 3) To use a randomized trial with a specialized design to identify which EHR-nudges, or combinations of nudges, contribute most efficiently to AHA/ACC guideline-concordant statin prescribing. The proposed work is significant in its efforts to develop an effective, efficient, and scalable intervention to improve guideline- concordant care for CVD risk management. It is innovative in its use of insights from behavioral economics and the MOST framework to optimize a CDSS by balancing clinical impact with provider time and cognitive load burden. Achieving the project’s objectives will advance the science of CDSS design and development.	12/11/2023	R01HL171292	12/31/2028
Yes	Graduate student,Post Doctoral trainees,Junior Faculty	Graduate student,Post Doctoral trainees,Junior Faculty	Laboratory basic/translational research	Mahmood Hussain	INTERNAL MEDICINE/MEDICINE	Biogenesis and Catabolism of Atherogenic Lipoproteins	More people die of cardiovascular disease (CVD) than any other disease worldwide. Our proposal focuses on the biogenesis and catabolism of atherogenic apoB- containing lipoproteins (apoB-Lps), which are major risk factors for CVD. ApoB-Lps comprise both cholesterol and triglycerides (TGs). Whereas reducing cholesterol is well established to reduce atherosclerosis, it remains to be convincingly determined whether decreasing levels of TGs or the apoB-Lps that carry TGs will decrease CVD. Blocking secretion of apoB-Lps by the liver reduces levels of cholesterol-rich apoB-Lps, such as LDL and its TG-rich precursor VLDL. Unfortunately, such approaches have led to hepatosteatosis. However, human genetic mutation and animal studies demonstrate that reduced liver secretion of TGs does not invariably cause steatosis. By characterizing novel factors and pathways regulating liver apoB-Lp production, intravascular lipolysis, and adipose TG retention and mobilization, we will identify unique targets to reduce circulating apoB- Lps, their infiltration into the artery wall, and atherosclerosis. We will define basic mechanisms in cells and in new rodent models and then correlate our discoveries with human data, emphasizing a translational and transfomative approach. Our overall goals are to: 1) identify new processes and factors regulating circulating TG and FA levels, 2) investigate the lipidation and intracellular transport of apoB in hepatocytes, and 3) study how different apoB-Lps interact with cells and ultimately catalyze atherogenesis. This application comprises three projects (P1–P3) that have integrated work from three established investigators of apoB-Lp metabolism and atherosclerosis. P1 will investigate the role of adipose MTP and FIT2 in regulating adipose lipolysis, circulating lipids, hepatic apoB-Lp production, and atherosclerosis. P2 will study two poorly characterized proteins in the liver, KLHL12 and FIT2, which control hepatic apoB-Lp lipid-loading and secretion, and the composition of atherogenic apoB-Lps. P3 will study how TG-rich apoB-Lps interact with the vascular wall, and specifically determine the role of the N-terminal region of apoB on lipid uptake and transcytosis of apoB-Lps by vascular ECs and their links to atherosclerosis. The PPG has an administrative core and three scientific cores (C1–C3). The Administrative Core will oversee the overall PPG function and finances. To assist P1–P3, C1 will provide biostatistics and bioinformatics support, C2 will perform lipidomics and proteomics on apoB-Lps and tissues and provide human samples, and C3 will perform state-of-the-art atherosclerosis assays. Our studies will generate novel mouse models invaluable to understand the factors that regulate lipid metabolism and atherosclerosis, identify new therapeutic targets, and better define how high circulating levels of atherogenic apoB-Lps and other factors contribute to atherogenesis. Dissecting pathways that regulate the production and atherogenicity of apoB- Lps promises to reveal novel approaches to reduce CVD. This requires the integration of reseach in our three projects, as experiments in each require assistance from the others and core resources.	4/28/2023	P01HL160470	1/30/2028