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THE RESEARCH REVIEW

School of Medicine Quarterly Newsletter

IN THIS ISSUE

NEW NIH AWARDS

Family mHealth Intervention to Improve Health Outcomes in Black Youth with Type 1 Diabetes: A Multi-Center Randomized Controlled Trial

PI: *Dr. Deborah Ellis- Department of Family Medicine*

Award Number: 1R01MD018583-01

Black adolescents with type 1 diabetes (T1D) face disparities in health outcomes, such as higher risk for elevated blood glucose levels, which can lead to diabetes complications. The proposed study will test a brief, family intervention delivered through mobile health technology intended to optimize family interactions related to diabetes care. If successful, the intervention has the potential to improve health outcomes in a vulnerable population of youth as well as the health of their primary caregivers.

Exercise facilitation of adolescent fear extinction, frontolimbic circuitry, and endocannabinoids

PI: *Dr. Hilary Marusak - Department of Psychiatry & Behavioral Neuroscience*

Award Number: 5U24NS100680-05

Anxiety disorders commonly begin during adolescence, and are characterized by deficits in the ability to inhibit or extinguish pathological fear. Recent research has provided new understanding of how fear is learned and can be regulated in the adolescent brain, and how the endocannabinoid system shapes these processes; however, these advances have not yet translated into improved therapeutic outcomes for adolescents with anxiety. The proposed project will leverage a multi-modal experimental therapeutics approach to test whether a behavioral intervention (i.e., acute exercise) modifies hypothesized targets that are relevant for the pathophysiology and treatment of anxiety in youth.

Mechanisms of polarized protein sorting in AP-1B-deficient epithelia

PI: *Dr. Paulo Caceres - Department of Physiology*

Award Number: 1R35GM150570-01

There are over 150 different epithelia in the body, forming part of organs like the skin, kidney, liver, gastrointestinal tract and structures in the nervous system. Important questions still remain unanswered on how epithelial cells achieve their highly organized architecture, a process known as polarization, which is fundamental to a diverse array of epithelial functions. The objective of this proposal is to bridge this gap in knowledge by uncovering novel intracellular mediators that sort and escort surface proteins on their way to the cell surface and define pathways for epithelial polarization.

Impact of maternal childhood trauma on children's fear neurobiology and internalizing psychopathology risk

PI: Dr. Anais Stenson -Department of Psychiatry & Behavioral Neuroscience

Award Number: 1K01MH130872-01A1

Childhood trauma is an epidemic with lasting effects on physical and mental health, however, the extent to which these effects persist across generations is understudied. The goal of this K01 proposal is to provide critical subject matter and methodological training that will enable the PI to test the hypothesis that maternal childhood trauma history is associated with children's internalizing psychopathology, SNS responsivity, and functional connectivity within fear neurocircuitry. Investigating the impact of maternal childhood trauma on children approaching adolescence is a critical next step towards determining whether intergenerational transmission of trauma increases risk for internalizing psychopathology.

The miR-183/96/182 Cluster in Pseudomonas aeruginosa-induced Keratitis

PI: Dr. Shunbin Xu - Department of Ophthalmology, Visual and Anatomical Sciences

Award Number: 2R01EY026059-06A1

Pseudomonas aeruginosa (PA) keratitis is one of the most rapidly developing and destructive diseases of the cornea and a global cause of visual impairment and blindness. Emergence of antibiotic-resistant bacterial strains poses additional challenges for effective management of the disease and development of alternative treatment is in urgent need. This study will uncover the molecular mechanisms underlying the roles of the miR- 183/96/182 cluster (miR-183C) in PA keratitis and the protective effect of anti-miR-183C against the disease through miR-183C's regulation of corneal sensory nerve function and neuroimmune interaction in both mouse and human.

NEW NSF AWARDS

NSF/BIO-DFG: Cytochrome c oxidase adaptation to hypoxia in systemic vascular cells - From structure to function

PI: *Dr. Lawrence Grossman & Maik Huttemann- Center Molecular Medicine/Genetics*

Award Number: 2329629

Decrease of physiological oxygen level (hypoxia) is one of the most challenging threats that aerobic organisms face, and they accordingly devote considerable resources to counteracting and minimizing the consequent damage. One such recently uncovered mechanism is the reconfiguration of cytochrome c oxidase (COX or complex IV), the final and regulatory electron donor to oxygen of mitochondrial electron transport chain (ETC). We thus aim to investigate the cause and consequences of hypoxia-induced COX subunits in primary cells, and to establish a link to redox sensing and signaling.

I-Corps: Medical Application Game-Generator for Prescription Intelligence Evaluation

PI: *Stephen Farrow - Department of Internal Medicine*

Award Number: 2330404

MAGGIE is automated, customized, health record-interactive, patient-education smart-device intelligent-assistance application that uses two-way physician-patient communication by text message/game play/metaverse patient engagement and wearables/connected remote-patient monitor data curation to rapidly enhance patient health. Patients learn current information on the health teams' disease and medication prescriptions. Patient-demonstrated knowledge and wearable medical device-measured health status are communicated back to the health team to permit timely updates to medication prescriptions.

NEW DOD AWARDS

Developing Therapeutic Approaches Targeting Spiral Ganglion-Cochlear Nucleus Synaptopathy

PI: *Dr. Zhengqing Hu - Department of Otolaryngology*

Award Number: HT9425-23-1-0684

This proposal will develop a novel approach targeting the treatment of auditory synapse defects, an FY22 HRRP focus area. Auditory synapses are neural connections between hearing cells, which are critical for hearing signal transfer from the ear to the brain. Currently, injuries to hearing cells have been extensively investigated. However, central auditory synapse and synaptopathy remains a challenging research area. The objectives of this proposal are to determine the molecular mechanism critical for mouse central auditory synapse integrity and develop therapeutic approaches to treat synaptopathy.

A Novel Strategy Targeting the Metabolic Vulnerability of CRPC

PI: *Dr. Jian Wang - Department of Pathology*

Award Number: HT9425-23-1-0130

A hallmark of aggressive prostate cancer is the excessive metabolism of sugar and lipids, which cancer cells use to generate cellular building blocks to support uncontrolled cell growth, enhance survival, and develop therapeutic resistance. Thus, a promising approach for treating prostate cancer targets the improper metabolism of cancer cell, thereby starving the cells of the building blocks needed to create and maintain tumors. We have discovered a "molecular switch" that blocks the metabolism of sugar and lipids in prostate cancer cells. Our research seeks a better understanding of how this molecular switch alters metabolism and contains the major molecular drivers of prostate cancer cells.

NEW FELLOWSHIPS

The Interplay of Host Genetic Variation and the Gut Microbiome in Crohn's Disease

PI: *Shreya Nirmalan - Center Molecular Medicine/Genetic*

Award Number: 1F30GM151855-01

Crohn's Disease (CD) is an autoimmune disease which leads to chronic inflammation and scarring of the digestive tract. The available treatments involve immunosuppressants and surgery which are costly, with many individuals still experiencing a decreased quality of life. In this proposed research, I aim to characterize the interactions between host genetic variation and the gut microbiome that regulate host gene expression in CD. These studies will provide insight into host-microbiome interactions that modify genetic risk for Crohn's Disease.

ATF4-SCD Axis In Bone Metastatic Prostate Cancer

PI: Alexis Wilson - Department of Pharmacology

Award Number: 1F31CA284576-01

Bone metastatic disease correlates with increased morbidity and mortality in prostate cancer (PCa) patients. Various studies, including our own, have determined that the bone marrow niche plays a supportive role during metastatic progression, which leads to increased tumor cell survival and escape from therapy, but the molecular mechanisms are not fully understood. I propose a multi-faceted approach that includes cell culture and models of lipolysis, in vivo models of intratibial tumor growth, as well as state-of-the-art RNAseq and metabolomics approaches to determine the role of previously unexplored ATF4-SCD axis in regulating tumor metabolism and promoting progression in bone.

OTHER NEW AWARDS

DMC Foundation
PI: *Dr. Stephen Farrow - Department of Internal Medicine*

Oregon Health Science University
PI: *Dr. Lawrence Flaherty - Department of Oncology*

Karmanos Cancer Institute
PI: *Dr. Michael Wilson - Department of Oncology*

Henry Ford Health System
PI: *Dr. Jacob Burmeister - Department of Oncology*

Karmanos Cancer Institute
PI: *Dr. Jennifer Beebe-Dimmer - Department of Oncology*

Karmanos Cancer Institute
PI: *Dr. Mark Greenwald - Department of Psychiatry and Behavioral Neurosciences*

Karmanos Cancer Institute
PI: *Dr. Gen Wu - Department of Oncology*

The Children's Foundation
PI: *Dr. Varun Vohra - Department of Emergency Medicine*

ModernaTX, Inc.
PI: *Dr. Teena Chopra - Department of Internal Medicine*

Cystic Fibrosis Foundation
PI: *Dr. Zubin Mukadam - Department of Internal Medicine*

Mayo Clinic Jacksonville
PI: *Dr. Julie Boerner - Department of Oncology*

Duke University
PI: *Dr. Zeljka Minic - Department of Emergency Medicine*

University of Michigan
PI: *Dr. Joongkyu Park - Department of Pharmacology*

Trustees of Indiana University
PI: *Dr. Xuequn Chen - Department of Physiology*

American Cancer Society
PI: *Dr. Eric Sebzda - Department of Biochemistry, Microbiology and Immunology*

NEW IN RESEARCH NEWS

Notice of Fiscal Policies in Effect for FY 2023

This Notice provides guidance about the NIH Fiscal Operations for Fiscal Year 2023 and implements the Consolidated Appropriations Act, 2023 (Public Law 117-328), signed into law on December 29, 2022.

Sponsored Program Administration Proposal Submission Deadline Policy Effective 1/9/23

All proposals in final form, including all necessary components/documents and necessary approvals, should be submitted via Cayuse to SPA at least three (3) full business days prior to the funding agency's submission deadline to receive comprehensive and proper review. For proposals containing terms and conditions binding upon award, as much lead time as possible should be provided with a minimum of an additional two (2) business days required to ensure proper review.

For more info on NIH updates and things relevant to your research check out the Research Administration Services (RAS) blog here.

SOM RESEARCH FACTS*

The SoM award total at this point for 2023 is $114,991,702 and approximately 72% of the proposals submitted were awarded.

We also compared the number of proposals submitted and the number of awards received through August 2022 to this year, see below for the figures.

Proposals

2022 $456,525.412/588 submitted
2023 $405,413,629/458 submitted

Awards

$114,710,525/354 awarded
$114,991,702/328 awarded

*Per OVPR data