DECEMBER 1, 2023 VOL. 05

# THE RESEARCH REVIEW

*School of Medicine Quarterly Newsletter*


IN THIS ISSUE



## NEW NIH AWARDS

### Novel Early Retinal Imaging Biomarkers for Treating Later Spatial Memory Loss in Experimental Alzheimer's Disease

**PI:** *Dr. Bruce Berkowitz- Department of Ophthalmology, Visual and Anatomical Sciences*

Award Number: 1R01AG081981-01

The proposed research is relevant to public health because aging patients remain vulnerable to the devastating dementia associated with Alzheimer's disease, a disease without any treatment options to prevent or delay its trajectory. Accumulating evidence highlights hyperactive neurons in its very beginning stages as an important driver of Alzheimer's disease. Here, we propose new imaging biomarkers of hyperactive neurons in the retina, the most accessible part of the nervous system, to enable very early evaluation of treatment efficacy in patients at risk for Alzheimer's disease.

### Airborne Particulates, Corneal Oxidative Stress and Infection

**PI:** *Dr. Linda Hazlett - Department of Ophthalmology, Visual and Anatomical Sciences*

Award Number: 1R01EY035231-01

PM10 is a global, major toxic air pollutant, but little is known about its corneal effects. Our purpose is to use an in vivo mouse model to test the hypothesis that in the cornea, airborne PM10 triggers ROS, disrupting Nrf2 pathway signaling resulting in inflammation. We predict that this will exacerbate a painful blinding eye condition induced by the pathogen Pseudomonas aeruginosa (P. aeruginosa) and that SKQ1, an antioxidant, will reduce ROS and its sequelae before and/or after infection. We further predict that these data will have human applicability revealed by testing human corneal epithelial cells in culture.

### A novel AR degrader in castrate-resistant prostate cancer

***PI:*** *Dr. Hyeong-Reh C. Kim - Department of Pathology*

Award Number: 1R01CA282040-01

The goal of this application is to test the therapeutic efficacy of novel therapeutic agents for AR protein degradation using autophagy-targeting chimera (AUTOTAC) in castrate-resistant prostate cancer.

## Mechanisms of Motion Detection in Retinal Neural Network

***PI:*** *Dr. Tomomi Ichinose -Department of Ophthalmology, Visual and Anatomical Sciences*

**Award Number: 2R01EY028915-05A1**

Retinal neurons sense diverse types of images, including a direction of a moving object. The mechanisms of sensing the direction by retinal neural networks have been investigated for decades; however, it has not been fully understood. We will test our hypothesis that acetylcholine, a neurotransmitter, contributes to motion prediction to accelerate sensing a moving object.

## Identifying Mechanisms Involved in Hydroxyurea-Mediated Reduction in Vaso-occlusive Adhesive Events in Sickle Cell Disease

***PI:*** *Dr. Jennell White - Department of Pharmacology*

Award Number: 1K01HL165271-01A1

Hydroxyurea (HU) is effective in decreasing the frequency of vaso-occlusive episodes (VOEs) in sickle cell disease (SCD), in part by reducing adhesion receptor expression and red cell-endothelial interactions; however, mechanisms involved are poorly understood. Sickle reticulocytes contribute to VOEs by participating in a series of adhesive events mediated by cell surface adhesion molecules elevated in the SCD microenvironment. This application will determine HU mechanisms that reduce red cell- endothelial interactions that precede VOEs in SCD.

## CXCR4: A potential therapeutic target in HSK

***PI:*** *Dr. Susmit Suvas -Department of Ophthalmology, Visual and Anatomical Sciences*

**Award Number: 1R01EY035540-01**

Herpes stromal keratitis (HSK) occurs due to the growth of blood vessels and accumulation of neutrophils and effector CD4 T cells in the corneal stroma of the HSV-1 infected cornea. The proposed application will study the pleiotropic effects of CXCR4 signaling in promoting the retention of immune cells and hemangiogenesis in HSK.

## Impact of ambient PM2.5 concentrations on fear extinction recall, frontolimbic circuitry, and anxiety in adolescents

***PI:*** *Dr. Clara Zundel - Department of Psychiatry*

Award Number: 1F32MH133274-01A1

Despite the emerging link between air pollution exposure – specifically PM2.5 – and heighted risk of adolescent anxiety, the neurobehavioral mechanisms underlying this association are unknown. The proposed F32 project will be the first to evaluate whether exposure to recent PM2.5 concentrations is associated with poorer extinction recall, lower frontolimbic activation, and higher anxiety symptoms during adolescence, a period of frontolimbic development and psychiatric vulnerability. This project will be an important first step towards identifying mechanisms underlying environmental risk of psychopathology and will lay a critical foundation for early interventions to stem the etiology of anxiety in at-risk pollution-exposed youth.

## Characterizing the relationship between medical mistrust, health behaviors and neighborhood level factors in African American cancer survivors.

***PI:*** *Dr. Ann Schwartz -Department of Oncology*

Award Number: 3U01CA199240-07S1

This project aims to describe the relationship between medical mistrust, health behaviors and health outcomes, in the context of the neighborhood environment in African American cancer survivors. The purpose of this is to better understand how medical mistrust impacts African American cancer survivors to begin developing multilevel interventions.

## Analysis of Cellular Plasticity in White Adipose Tissue.

***PI:*** *Dr. James Granneman-Center for Molecular Medicine and Genetics*

**Award Number: 2R01DK062292-17A1**

The proper function of adipose tissue is essential for metabolic health and depends on close interactions of diverse cell types in the tissue microenvironment. This project will examine how close (micrometer-scale) cellular interactions in adipose tissue regulate the establishment, expansion, and pathophysiological remodeling fat tissues. This analysis will provide new insights into how fat tissue contributes to metabolic heath, and might lead to strategies to combat obesity-related metabolic diseases like diabetes.

## Role of Kidney Microvasculature-Secreted Factors in Neuropilin Signaling in Proximal Tubule During Diabetic Kidney Disease

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

Award Number: 1R21DK136122-01

Diabetes is the leading cause of chronic kidney disease, putting a heavy burden in society despite decades of research and availability of treatments to control blood glucose. Better understanding of the cellular mechanisms occurring early in the diabetic kidney, before renal damage has occurred, will inform the development of effective treatments for diabetic kidney disease. The objective of this proposal is to address this need by studying cell-cell communication between kidney cells, which we believe is interrupted early in the diabetic kidney and results in renal damage.

## Delineating Functional Immunity via Image-Guided PET

***PI:*** *Dr. Nerissa Viola -Department of Oncology*

**Award Number: 4R37CA220482-06**

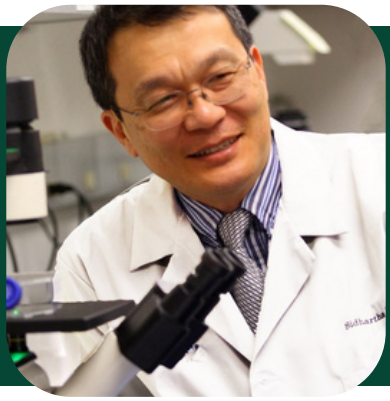
Image-guided delineation of interferon-γ via positron emission tomography (PET) to assess outcomes of cancer immunotherapy has been successfully established. In this proposal, its potential to be a predictive imaging biomarker will be evaluated. Preparation of the radiotracer toward clinical translation to improve clinical decision-making is also proposed.

## Neuroprotection of Remotely Administered Hypothermia on Spleen in Ischemic Stroke

***PI:*** *Dr. Yuchuan Ding - Department of Neurosurgery*

Award Number: 1R21NS132006-01A1

Over one hundred stroke clinical trials have failed to generate a clinically effective neuroprotective treatment, and FDA-approved stroke treatments can be only used on less than 10% of stroke patients. In this proposal we offer the novel theory that the spleen, an important immune system organ, can be manipulated to protect the brain during stroke. We propose to investigate a novel, high risk/high reward technique, Remote Administration of Hypothermia (RAH), that reversibly cools the spleen during the acute phase of stroke to suppress its inflammatory activation, and thereby decrease stroke-induced brain inflammation, which will ultimately limit stroke damage and improve functional outcomes.



## Ferroptosis in knock-in sepiapterin reductase mutation rabbits

***PI:*** *Dr. Sidhartha Tan -Department of Pediatrics*

Award Number: 1R01NS130258-01A1

This proposal investigates the mechanisms of motor deficits of cerebral palsy and congenital tetrahydrobiopterin deficiency, which involve formation of destructive reactive chemical species in early brain injury resulting in cell death. New information about which forms of cell death, how they affect brain cells, and how effective potential therapies are in an animal model of cerebral palsy will be very valuable for future drug development in human studies.

## Mitigating retinitis pigmentosa based on a non-invasive rod energy-landscape biomarker

**PI:** *Dr. Bruce Berkowitz- Department of Ophthalmology, Visual and Anatomical Sciences*

Award Number: 1R01EY034309-01A1

The proposed research is relevant to public health because retinitis pigmentosa is an untreatable cause of blindness. We address a long-standing critical barrier to the translation of experimental findings into the clinic: the absence of non-invasive imaging biomarkers of rod energy-landscape dysfunction for early diagnosis and for predicting treatment benefits. Our proposed studies will address this technology gap with a unique rod energy-landscape biomarker measured from a clinical-relevant imaging modality, optical coherence tomography, in order to enable future transformative bench-to- bedside bridging of treatment to personalize management and clinical treatment of retinitis pigmentosa.

## Investigating the source and the action behind shunt obstruction in the treatment of pediatric hydrocephalus

***PI:*** *Dr. Carolyn Harris -Department of Neurosurgery*

**Award Number: 2R01NS094570-06A1**

Hydrocephalus is a disorder causing excess accumulation of cerebrospinal fluid in the brain, treated by using shunts to divert cerebrospinal fluid out of the cranial cavity. Our team of bioengineers, neurosurgeons, and experts in neurophysiology and biostatistics will identify patient subpopulations which correlate with a high degree of contact between the shunt catheter and tissue; then, we identify the conditions in which cause obstruction by this tissue being mechanically pulled in or biochemically grown in. By studying correlations in the patient population and causations using a benchtop model, we embrace a multi-disciplinary approach that will provide a better understanding of the mechanisms leading to shunt failure so that we can inhibit that response from occuring.

# OTHER NEW AWARDS

**Michigan Prostate SPORE: Biostats Core**
**PI:** *Dr. Elisabeth Heath- Department of Oncology-25W5V*

**Michigan Prostate SPORE: Biostats Core**
**PI:** *Dr. Elisabeth Heath- Department of Oncology-25W5U*

**Anti-Norovirus Protease Inhibitors for Immunocompromised Patients**
**PI:** *Dr. Ladislau Kovari - Department of Biochemistry, Microbiology and Immunology-25W65*

**Michigan Prostate SPORE: Project 2**
**PI:** *Dr. Elisabeth Heath- Department of Oncology-25W5W*

**Aggressive Colorectal Cancer Subtypes and Social Disadvantage in a Racially Diverse Cohort**
**PI:** *Dr. Kristen Purrington - Department of Oncology-25W6F*

**CFF Care Center Grant**
**PI:** *Dr. Zubin Mukadam - Department of Internal Medicine-25W6H*

**Raman Spectrographic: Optical Imaging System (Pneusight) for the Differentiation of Malignant Vs. Normal Tissue**
**PI:** *Dr. Gregory Auner - Department of Surgery-25W6M*

**Mobile Testing For Blood Lead Levels To Combat Lead Exposure**
**PI:** *Dr. Bram Dolcourt - Department of Emergency Medicine-23T8K*

**MDHHS HIV Prevention- Emergency Room Testing**
**PI:** *Dr. Claire Pearson - Department of Emergency Medicine-23T8L*

**MDHHS: Syringe Services Program**
**PI:** *Dr. Andrew King - Department of Emergency Medicine-23T8M*

**Cystic Fibrosis Lung Transplant and Transition Regional Dissemination Network-mini-grant For Quality Improvement**
**PI:** *Dr. Zubin Mukadam - Department of Internal Medicine-25W6J*

**Clinical Psychology Internship Training in Behavioral Health Care for High Need Pediatric Populations**
**PI:** *Dr. Jill Meade - Department of Pediatrics-25W6T*

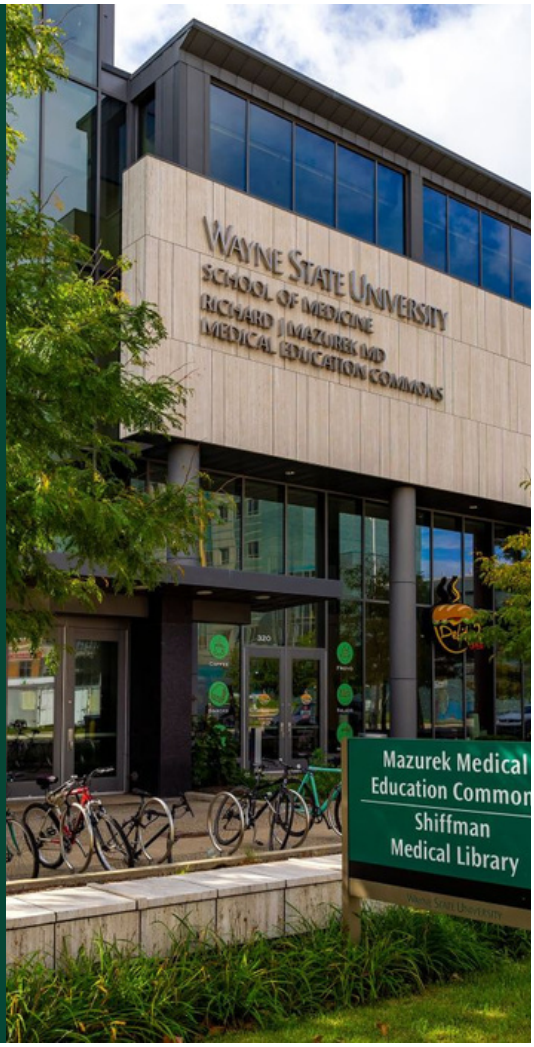
**Frontline Strong Together 2024**
**PI:** *Dr. Alireza Amirsadri - Department of Psychiatry and Behavioral Neurosciences-23T8W*

**Psychiatry Program 2024**
**PI:** *Dr. David Rosenberg - Department of Psychiatry and Behavioral Neurosciences-23T8X*

**Ryan White Part D - Horizons Project**
**PI:** *Dr. Elizabeth Secord - Department of Pediatrics-23T8N*

**Michigan Diabetes Research Center**
**PI:** *Dr. Colleen Buggs-Saxton - Department of Pediatrics-25W6A*

**RNA methyltransferase FTSJ3 regulates ribosome biogenesis in liver cancer: molecular mechanisms and therapeutic potential**
**PI:** *Dr. Zeng-Quan Yang - Department of Oncology-2WES*



# NEW IN RESEARCH NEWS

## Prior Approval Requests for Revisions to an Approved Data Management and Sharing (DMS) Plan Must be Submitted Using the Prior Approval Module

The link to the notice below is remind Principal Investigators that any changes to the Data Management Plan for funded awards subject to the Final NIH Policy for Data Management and Sharing (DMS) Policy requires the PI to submit through the Authorized Organization Representative a formal prior approval request via the Prior Approval Module in ERA Commons as emails or other communications are not acceptable.

## 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 **$183,422,919.

We also compared the number of proposals submitted and the number of awards received through September 2022 to this year; see below for the figures. Approximately 77% of the proposals submitted were awarded.

## Proposals

2022 $500,795,279/647 submitted
2023 $519,138,555/627 submitted

## Awards

2022 $189,425,647/470 awarded
2023 $183,422,919/482 awarded **

***Please note that the September amounts for proposals and awards for 2023 are being verified by OVPR and may increase after that process*