



LONG SCHOOL OF MEDICINE **OFFICE FOR RESEARCH**

The LSOM Office for Research joins forces with UT Health San Antonio Institutes and the Department of Medicine to support collaborative research

Basic and clinical research is the cornerstone of the Long School of Medicine's mission. In alignment with the LSOM strategic initiatives, the LSOM Office for Research has partnered with Institutional leaders to support inclusive, collaborative, and multidisciplinary research projects with Multi-PI pilot funding. These allocated funds are to support competitive pilot projects that we expect will generate extramural grant awards.

Multi-PI Awards At a Glance

Five research teams granted up to
\$75,000 for one year!

- **Jeremy Tanner, MPH, MD and Yaxia Yuan, PhD**
- **Swati Banerjee, PhD and Yidong Bai, PhD**
- **Kumar Sharma, MD and Bernard Fongang, PhD**
- **Katsumi Kitagawa, PhD and Siyuan Zheng, PhD**
- **Shangang Zhao, PhD and Xianlin Han, PhD**

Special Thanks to Our Collaborative Partners!



BREAKTHROUGH RESEARCH AIMS TO UNLOCK POTENTIAL TREATMENT FOR A SEVERE NEURODEVELOPMENTAL DISORDER



Jeremey Tanner and Yaxia Yuan plan to make significant strides towards developing therapeutic options for a severe neurodevelopmental disorder known as congenital contractures of the limbs and face, hypotonia, and developmental delay (CLIFAHDD). His team aims to discover potential drug candidates that can modulate sodium leak channel (NALCN) activity and bring hope to children affected by this debilitating condition. The NALCN ion channel is responsible for maintaining the resting membrane potential in neurons and regulating pacemaking activity in excitable cells. However, *de novo* gain-of-function mutations in NALCN disrupt its normal functioning, leading to the onset of CLIFAHDD.



Currently, there are no approved treatments available for this disorder. The team's commitment to unraveling the complexities of NALCN activity modulation represents a beacon of hope for families grappling with the challenges posed by CLIFAHDD.

NOVEL ROLE OF TPPP PROTEINS IN MITOCHONDRIA LINKED TO PARKINSON'S DISEASE AND RELATED DISORDERS



Swati Banerjee and Yidong Bai have developed a new fly (*Drosophila*) model relevant to Parkinson's disease (PD) through a mutation in a *Drosophila* homolog of human Tubulin Polymerization Promoting Proteins (TPPP) named *Ringer*, which has been linked to PD and Lewy Body Dementia. The *Ringer* mutant flies exhibit severe locomotor disabilities, progressive neurodegeneration, and mitochondrial damage similar to those observed in PD and related neurodegenerative disorders.

The team plans to use various scientific techniques to uncover the role of *Ringer*/TPPP in maintaining mitochondrial health. This will provide unprecedented insights into the pathogenic mechanisms underlying PD and related disorders that can lead to the identification of therapeutic targets. Drs. Banerjee and Bai anticipate that this pilot award will help them secure additional funding from organizations such as the NIH, American Parkinson's Disease Association, and the Michael J. Fox Foundation, allowing them to further expand their research that will have clinical implications.



Novel Link Between Chronic Kidney Disease and Cognitive Decline



Kumar Sharma and Bernard Fongang are utilizing cutting-edge spatial metabolomics with cognitive testing and tissue analysis to elucidate the mechanism underlying cognitive impairment in chronic kidney disease (CKD).

The collaborative team developed aims to investigate how CKD affects cognitive function by examining changes in tryptophan catabolism, as tryptophan breakdown through the kynurenine pathway, has been implicated in cognitive decline. Alterations in tryptophan metabolism have been observed in both CKD patients and the animal model, suggesting the involvement of this pathway in cognitive impairment. These groundbreaking findings may lead to pilot clinical trials using a specific enzyme inhibitor to improve the quality of life for CKD patients.

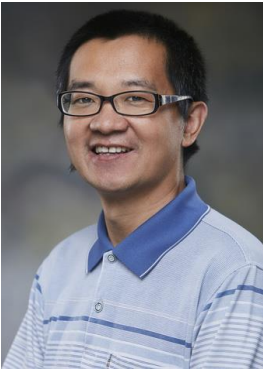


Investigating the Role of Whole Genome Doubling in Aneuploidy Formation and Survival



Katsumi Kitagawa and Siyuan Zheng are conducting groundbreaking research on the role of whole genome doubling (WGD) in the formation and survival of neuploidy, a common chromosomal abnormality in cancer cells. Previous studies have shown that WGD promotes chromosomal mis-segregation, instability, and aneuploidy. On the other hand, the deleterious alterations in Aneuploid tumors can impose significant pressure for cells to double their genomes presumably to buffer detrimental effects.

The team aims to identify and catalog WGD driver genes, validate candidates like *STK11* in lung adenocarcinoma, and investigate the molecular mechanisms of tetraploid formation caused by driver gene loss. Successful outcomes could advance our understanding of cancer development and enable targeted therapies.



Novel Lipid Class and Protein Hold Promise for Alzheimer's Disease Treatment

Shangang Zhao and *Xianlin Han* have made significant advancements in understanding the involvement of lipid metabolism in neurodegenerative diseases, particularly Alzheimer's disease (AD). Their research has focused on a previously unknown lipid class called lysophosphatidylethanolamine (LPE), which shows a strong correlation with the onset and severity of AD. To explore the role of LPE in AD progression, the team has successfully characterized a new secreting protein called J18, found in high concentrations in the salivary glands of mice and humans. Notably, J18 displays a unique regulation pattern, increasing during metabolically healthy states like fasting and calorie restriction, while decreasing with aging and obesity—known risk factors for AD. This intriguing pattern suggests the significance of J18 and its interaction with LPE in the development of AD. The team hypothesizes that J18-accessible LPE represents a novel lipid class crucial for AD development and proposes targeting J18 as a promising therapeutic strategy. Dr. Zhao and his team aim to uncover the precise mechanisms underlying the J18-LPE interaction, with the goal of translating these findings into effective therapeutic interventions for AD.



Office for Research
Long School of Medicine

The LSOM Office for Research supports Joe R. and Teresa Lozano Long School of Medicine faculty and trainees to achieve their research goals. We provide programs and services to support strategic research areas from the lab bench to the bedside.



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