INTERNAL MEDICINE
COLLEGE OF MEDICINE

SUMMER RESEARCH OPPORTUNITIES FOR UNDERGRADUATE students

FOR APPLICATION YEAR: 2026

PROJECT TITLE: The role of the unfolded protein response pathway in microbiome-associated abdominal aortic aneurysm

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Project Description

This research project is focused on the pathogenesis of abdominal aortic aneurysms (AAA), particularly examining the role of the gut microbiome-derived metabolite trimethylamine-N-oxide (TMAO) in exacerbating AAA progression. The project aims to determine the mechanisms through which TMAO induces vascular smooth muscle cell (VSMC) dysfunction focusing on the role of the PKR-like ER kinase (PERK) signaling pathway in the context of AAA.

Area of the Research:
The project addresses the increasing incidence and mortality associated with AAA, investigating the relation between TMAO levels and AAA progression through VSMC dysfunction and endoplasmic reticulum (ER) stress signaling pathways. It will focus on the role of the PKR-like ER kinase (PERK) signaling pathway in mediating TMAO's effects on VSMCs within the context of AAA.

Research Tasks the Student Will Be Performing:
Students will conduct in vitro experiments to assess the impact of TMAO on human aortic vascular smooth muscle cells (HAVSMCs), including evaluating apoptosis and autophagy signaling pathways. They will also participate in animal studies, including the use of genetically modified mouse models to examine the effects of VSMC-specific PERK deletion on AAA progression. Students will also analyze data from single-cell RNA sequencing to characterize VSMC responses to TMAO and PERK signaling, and assist in the preparation and analysis of tissue samples for histological and protein expression assessments related to AAA progression. Key to these experiments will be collaboration with team members to document findings and contribute

to the preparation of manuscripts for publication.

Training that the Mentor Will Provide to the UPRISE Student:
Hands-on training in molecular biology techniques, including cell culture, RNA sequencing, and Western blot analysis; guidance on animal models relevant to cardiovascular research and understanding surgical techniques for aneurysm induction in mice; and mentorship in data analysis, including statistical methods for evaluating experimental results and interpreting gene expression profiles. There will be opportunities for professional development, including presenting research findings at lab meetings and potentially at national conferences.

Specific Requirements That the Mentor Expects the Student to Meet:
Commitment to maintaining ethical standards in research, particularly in animal studies, and active participation in laboratory meetings, training sessions, and discussions on research progress. The mentee will utilize effective communication skills for collaborating with lab members and presenting findings and will develop a foundational understanding of cardiovascular biology or related areas, which may be assessed through a preliminary meeting or application process. This project represents an innovative approach to understanding AAA pathogenesis and could provide insights into potential therapeutic targets, significantly impacting clinical practice and patient outcomes.