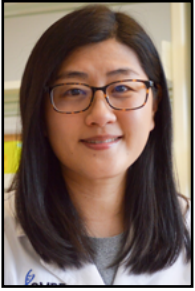




NATHAN SHOCK CENTERS
OF EXCELLENCE IN THE
BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT



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Oklahoma Medical Research Foundation

2021 UW NSC Pilot Award

Age-dependent phosphoproteomic changes in heart failure with preserved ejection fraction

How did you become interested in aging?

I became interested in aging during my PhD training in Dr. Merry Lindsey's lab in UT Health San Antonio. At the time, the lab mainly focused on investigating the roles of matrix metalloproteinases (MMPs) in extracellular matrix (ECM) remodeling after myocardial infarction. After my rotation, I got to decide whether to work on a myocardial infarction project like the rest of the lab or to start a new project and study the role of MMP-9 and ECM remodeling in cardiac aging. After looking into the literatures, I was surprised by how little was known regarding the molecular mechanisms of cardiac aging. Knowing the aging expertise and resources available at the Barshop Institute at UT Health San Antonio, I decided to start a project to study the role of MMP-9 in cardiac aging.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?

Aging significantly increases the risk of heart failure (HF), especially heart failure with preserved ejection fraction (HFpEF). HFpEF is an emerging health problem with high morbidity and mortality and there are currently no effective treatments for HFpEF. This study aims to understand why the aging heart is more prone to HFpEF pathogenesis. This will facilitate the development of new therapy for HFpEF.

What previous research or experience informed the development of this proposal?

Our previous studies demonstrated that the heart undergoes proteomic remodeling, at both protein abundance and post-translational modification levels, during aging. Using an experimental mouse model of HFpEF that combines metabolic stress and hypertensive stress, our pilot study showed that old mice developed exacerbated cardiac dysfunction upon HFpEF development. This study will investigate how advanced age impacts the proteomic remodeling in the heart during HFpEF development.

What's exciting about your project's potential impact?

This study investigates the impacts of normal aging on HFpEF pathogenesis in a preclinical HFpEF model. The results of this study will reveal whether aging amplifies proteomic and phospho-proteomic changes during HFpEF development to exacerbate HFpEF progression. This information will improve our understanding on the mechanism by which aging predisposes the heart to increase susceptibility to HFpEF. The results will also facilitate the identification of novel therapeutic targets for HFpEF in older adults, who are most at risk for the disease.

If your project is successful, what is the next step?

Once we identified the age-dependent proteomic and phosphoproteomic changes during HFpEF progression, we will perform pathway analysis to identify upstream regulators of these changes. We will then test if targeting these upstream regulators will ameliorate HFpEF progression.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?

The support from UW Nathan Shock Center is instrumental to this project. The Protein Phenotypes of Aging Core at University of Washington Nathan Shock Center provided state-of-the-art technologies for proteomic and phosphoproteomic analyses for this project. The results will provide the basis for the identification of age-dependent regulators of HFpEF development, which will be further investigated in our future studies.