



NATHAN SHOCK CENTERS  
OF EXCELLENCE IN THE  
BASIC BIOLOGY OF AGING

## PILOT AWARDEE SPOTLIGHT



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#### 2022 UAB NSC Pilot Award

*Role of chromatin structure in mediating the pathological effects of cardiac aging*

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#### How did you become interested in aging?

Our lab's interest in aging comes from our dedicated research into the impact of epigenetic factors on the development of heart-related diseases. Aging is a significant risk factor for cardiac pathology, as it involves a complex interaction between our genes and the environment, resulting in a gradual decline in heart function. By exploring deeper into these underlying mechanisms, we think we can find some useful insights that might help create new ways to make hearts healthier and improve their overall well-being.

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

Our research studies hearts at different life stages, from early development to old age. We aim to understand how aging affects the heart, a critical organ in our body. We have observed that as the heart gets older, it becomes larger and contains more unhealthy tissue, decreasing its ability to pump blood effectively. Furthermore, we have discovered that older hearts show specific patterns of gene activity that resemble those found in heart failure. Additionally, we have noticed changes in how the genetic material is organized within the heart as it ages, which may be related to the adverse effects of aging. We are now expanding our investigations to better understand the mechanisms behind this reorganization and how it contributes to the detrimental effects of aging on the heart. This newfound knowledge may open up new possibilities for innovative treatments by exploring techniques that modify the structure of the genome, specifically in the context of aging heart diseases.

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

Our in-depth sequencing analysis has uncovered some fascinating insights about aging. We've found that as we age, there's a significant reprogramming of our genes, and this leads to a decrease in factors that are essential for maintaining the 3D structure of the genome. Even more interesting is that our earlier research showed that this reorganization of the genome structure makes it easier for heart failure to occur. These discoveries have piqued our curiosity, and we're now eager to explore the effects of chromatin remodeling in the context of aging.

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

Our research is a pioneering investigation into the cardiac genome in 3D. We aim to get a complete picture of how the structure of the genome organizes and how genes behave within it. We're exploring our data to uncover the parts of the genome that control important genes linked to the natural decline of heart function during aging. This approach is novel, and it should help us pinpoint specific areas of the genome that are strongly tied to the harmful effects of aging on the heart. These areas could be really useful as potential signs of heart issues and as targets for new epigenetic therapies aimed at mitigating the detrimental effects of aging on the heart.

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

After identifying the specific structural features that mediate those changes in gene expression associated with cardiac aging, our next objective is to utilize CRISPR-Cas9 technology to disrupt their organization. This approach will allow us to directly manipulate genome structure and assess its impact on maintaining heart health during senescence.

**How has support from and collaboration with the Nathan Shock Centers helped further this project and/or your research overall?**

Mapping the 3D chromatin structures at various levels of genome organization represents a significant challenge in our project. However, we have successfully accomplished this task through collaboration with the bioinformatics experts from the Comparative Data Analytics Core. Working closely with them, we have established the analysis of our sequencing data and gained valuable insights for interpreting the results. Their expertise and support have greatly facilitated our research process and enhanced our understanding of the obtained findings.