NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Melissa Harris, PhD
Associate Professor

Nunaya Polycarp
PhD Student

University of Alabama at Birmingham

2023 UAB NSC Pilot Awardees

Investigating the potential of the small molecule RT175 in regulating mitochondrial function to impact aging

How did you become interested in aging?

Melissa: During my postdoc at the National Human Genome Research Institute I began developing my research program looking at biological mechanisms that negatively affect stem cell populations. My lab at UAB studies melanocyte stem cells in the hair and loss of melanocyte stem cells causes gray hair. Everyone past their 40's will likely agree, begrudgingly, that the process of hair graying is one of the most visible aging phenotypes in humans. Thus, it was a natural step for me to think scientifically about using melanocyte stem cells to address questions about aging in stem cells.

Polycarp: I became interested in aging because, in today's world, there's a collective desire to delay or avoid the visible and biological signs of aging, even though it is an inevitable part of life! What fascinates me is that aging no longer strictly follows a chronological timeline; its effects are increasingly seen across all stages of life, including in younger individuals, often with significant adverse implications. My interest lies in exploring the biological mechanisms of aging using stem cells as tool. Stem cell research is a great revolution in modern science and stem cells are a tractable target for the future of medical health care.

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

It is known that healthy mitochondria are key to healthy aging. For this project we are interested in evaluating a small molecule for its ability to improve mitochondrial function with the hopes we could use this small molecule to improve human healthspan.

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

Using our melanocyte stem cell and hair graying model, we discovered that treatment with this small molecule prevents stem cell depletion in mice. While preventing or reversing gray hair is something we find pretty cool (and attractive to a lot of humans), we were interested in understanding how this small molecule was really working. Fortuitously, when we studied this small molecule on cells we found an interesting change in mitochondrial gene expression and connected with the UAB NSC Mitometabolism Core to investigate the role of these mitochondrial changes further. We do not yet know if these mitochondrial changes are the key mechanism to prevent stem cell depletion, but this is a question we hope to answer through this research.

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

While we focus on melanocyte stem cells, improving mitochondrial function is universally important in many cell and tissue types. Understanding how this small molecule elicits these mitochondrial changes may also reveal mechanisms important in regulating mitochondrial biology and novel targets for pro-longevity interventions.

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

When we first started studying the small molecule, we were focused primarily on stem cell function and not longevity or healthspan. In future studies, we would like to address the potential of this small molecule for both, and particularly in mammalian systems.

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

Melissa: Before starting this project, I admit that my lab did not have any real expertise in mitochondrial biology or longevity assays. Working with the UAB NSC Cores has broadened the ability of my lab to delve into scientific disciplines that we would not have otherwise. This UAB NSC Pilot has also provided a unique opportunity for my graduate student, Nunaya Polycarp, to gain formal experience in biology of aging with experts in the field. Nowadays it is difficult to be an expert in everything, but having multidisciplinary resources, like the NSCs, has helped us increase the impact and relevance of our work.

Polycarp: The Nathan Shock Centers cultivate a collaborative environment that fosters innovation, and participating in this research with the UAB NSC has enabled me to integrate diverse approaches to address critical challenges in aging research and make meaningful contributions to the broader scientific community. Through my involvement, I have developed essential research skills that extend beyond the conventional practices of our lab (like western blotting for mitochondrial proteins and Seahorse assays). This experience has ignited in me a deeper passion for discovery, as every new insight fuels my drive to explore further and continuously expand my knowledge in the field.