NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Jeremy Whitson, PhD

Visiting Assistant Professor of Biology
Davidson College

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Establishment of the Mammalian Lens as a Model System for the Longitudinal Study of Protein Aging via Mass Spectroscopy

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How did you become interested in aging?

I first became interested in aging while studying molecular and cellular biology as an undergraduate at Muskingum University. The idea that we can attribute the physiological effects of aging to quantifiable changes occurring within our cells, which can potentially be slowed or reversed, immediately captured me and I knew that I wanted my career focus to be this topic. I wrote my senior seminar on the molecular and cellular aspects of aging and have worked in the aging field ever since.

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

One thing that happens as we age is that our proteins become damaged by all sorts of different modifications. These modifications can harm the normal functions of our cells and contribute to the decrease in health that is associated with aging. To better understand these modifications and how we might be able to stop or even undo them, I am using pig lenses to determine which modifications accumulate with age. Lenses have a unique structure in which new cells get laid down on top of old cells concentrically, much like rings on a tree. These cells also stop producing new proteins and preserve their old proteins. This means that the deeper into the lens you go, the older the proteins are. By picking apart this structure and seeing which modifications are present and how they change as we go from newer to older layers of cells we can learn more about the aging process.

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

This research combines the expertise I gained from both my graduate research at Case Western Reserve University, which focused on how age-related cataracts form within lenses, and my postdoctoral work at the University of Washington, which focused on the metabolic and proteomic effects of aging and anti-aging drugs in mouse hearts. I have previously published two papers on how aging affects posttranslational modification of proteins as well as a paper on how glutathione levels alter the proteome of the lens. This project is truly the fusion of all the research I have worked on to this point.

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

There are a number of exciting potential impacts of this research. Because the lens's unique structure allows us to study aging longitudinally by obtaining a single endpoint tissue, there is the potential to study aging at the molecular level in many organisms where this was not previously feasible. This has the potential to greatly expand how, and where, biological aging is investigated. Additionally, because we are approaching analyzing posttranslational modifications in a completely unbiased way, we expect to identify modifications previously unassociated with aging; providing new biomarkers and potentially druggable targets and making this research highly translatable.

If your project is successful, what is the next step?
Once we have identified the set of posttranslational modifications that accumulate with age in the lens, we can then begin to test compounds with the potential to slow or reverse these modifications in cultured lenses. Additionally, we can use the techniques we have established to study protein aging in other vertebrate organisms, including wild populations and humans.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
This project truly would not have been possible without the support of the Nathan Shock Centers. Getting access to the world-class expertise of the MacCoss lab to develop new techniques for analyzing posttranslational modifications in the lens allowed me to break new ground and launch a novel research direction. The data we have been able to obtain through this project will result in new grants and collaborations that will be indispensable to my career.