NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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2022 UAB NSC Pilot Award
Determining cytotoxic T cell phenotype and function in the aging brain

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How did you become interested in aging?
While I was a graduate student, I was interested in exercise physiology and mitochondria. I happened to join a lab for my PhD research that was in the Department of Gerontology where I examine how blood cell mitochondrial function in older adults correlated with physical function. This was my first exposure to the Biology of Aging, and it has been an interest/fascination of mine since then.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
We know that a person's age is the strongest clinical risk factor for most chronic diseases like cardiovascular disease and neurodegenerative disease (like Alzheimer's disease). Obviously, we can't change a person's age, but we may be able to modify the biological changes that occur as we age. We know that T lymphocytes, the white blood cells of the adaptive immune system, change significantly as we age. We also know that T lymphocytes migrate into the brain during aging where we believe they contribute to damaging brain tissues and structures. We have found a population of T lymphocytes in the brain that we don't know much about, so the question we're trying to answer with this pilot award is simple. Very simply, we want to know why these cells move into the brain and what they are doing once they get there. If they are promoting disease, then we can try to target or remove them as a therapeutic approach.

What previous research or experience informed the development of this proposal?
We have identified that cytotoxic CD8 T cells contribute to atherosclerosis, especially in aging. This is what prompted me to test whether similar mechanisms were occurring in the aging brain because there are some similarities between atherosclerosis and neurodegeneration. One major similarity is that both experience increased vascular cell inflammatory pathway activation which we hypothesize is secreting factors that cause these T cells to home to that site.

What's exciting about your project's potential impact?
To me, it is exciting to potentially uncover new mechanisms of disease since these have potential to become new therapeutic targets. Therapies targeting T cells are increasingly becoming important tools in treatment and management of different cancers. It will be exciting to see whether similar approaches can be applied to other diseases.

If your project is successful, what is the next step?
If we identify the function of these unique T cell populations and how they change with age, then our next goal will be to determine how these functions impact disease in vivo. To test this, we would isolate specific populations of interest and adoptively transfer them into recipient mice to determine whether they are protective or pro-atherogenic in vivo. We could also knock-out specific genes within CD8 T cells to

determine how that modifies their function both in vitro and in vivo.

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

Support from the Nathan Shock Center has been invaluable to many of my projects. The Nathan Shock Center at UAB unifies investigators across campus into a group that shares common goals and interests. I have many contacts within the Nathan Shock Center at UAB that are active collaborators on ongoing research projects, and I also have many colleagues affiliated with other Nathan Shock Centers throughout the country that actively contribute to our ongoing research projects in a collaborative way.