NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Jason Vevea, PhD

Assistant Member
St. Jude Children's Research Hospital

2023 JAX NSC Pilot Awardee

Investigating the age and sex dependent molecular changes in synaptic vesicles

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How did you become interested in aging?
I think aging is something everyone is interested in. We all lose loved ones to age and the diseases that come with age. These diseases are not only horrible for the individual but can take an incredible toll on the family psyche. From a monetary perspective, these diseases cause financial hardship on immediate loved ones and society as a whole. It is a huge unmet need.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
I view those diseases as preventable if we had better knowledge of the molecular nature of aging. I would like to contribute to that goal. Simple as that. Specifically, I am interested in neurodegenerative diseases and their associated dementias. I believe underlying organelle dysfunction contributes to and drives these diseases. I am particularly interested in the synaptic vesicle and how they age.

What previous research or experience informed the development of this proposal?
During my graduate training in Liza Pon's lab, I was fortunate to work on a project that, for the first time, directly implicated mitochondria as cellular aging factors. Since then, I have always wanted to isolate and molecularly interrogate critical organelles like mitochondria and, in neurons, synaptic vesicles. This proposal benefits greatly from a new synaptic vesicle rapid immunoisolation technique developed in the lab of my postdoc advisor Ed Chapman, by a talented graduate student Mazdak Bradberry.

What's exciting about your project's potential impact?
For the first time, we will have a molecular view of the synaptic vesicle (proteome, lipidome) as a function of age and sex. It has been historically difficult/impossible to isolate synaptic vesicles with this type of purity. Moreover, no one has attempted an experiment like this with 6 age timepoints, from both males and females. This proposal goes even further by isolating synaptic vesicles from a menopause mouse model. If there are any changes in the synaptic vesicle proteome or lipidome that change with age or sex, we will see it. This is the first step to understanding why age and sex are the main risk factors for degenerative diseases.

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

We will have a catalog of molecular differences based on age and sex and we will begin to follow up on these leads. This process will determine which changes are benign, and which changes are associated with, or drive, aging related diseases.

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

This support has been indispensable. As a new Principal Investigator, gaining immediate access to aged animals and tapping into the expertise from Jackson Labs has been pivotal in catapulting my lab's research efforts forward from the outset.