NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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2021 San Diego NSC Pilot Award
Astrocyte Plasticity in the Aging Brain

How did you become interested in aging?
Human average life expectancy from birth has nearly doubled in the last century, but how do our brains adapt to aging? My main interest is to uncover the factors that promote brain aging and cognitive decline, particularly, I am fascinated by the crosstalk between the immune system and astrocytes, and its potential to drive the aging process.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
My proposal focuses on the astrocyte, a glial cell type that regulates neuron function. In Nicola Allen's lab, we recently discovered that aged astrocytes become more inflammatory in the aged cerebellum compared to the cortex. The cerebellum harbors diverse astrocyte sub-types based on their anatomical location and morphology; however, in-depth understanding of their transcriptional heterogeneity is still lacking. My project proposes to profile cerebellar and cortical astrocytes at single-cell resolution in adult and naturally aged mice in order to define the astrocytic sub-sets present in the adult brain and those that dominate regional responses to aging.

What previous research or experience informed the development of this proposal?
The Allen lab and others recently demonstrated that, far from being homogeneous throughout the brain, aged mouse astrocytes undergo regional specialization in aging. In that vein, we found higher perturbation of astrocytes in the cerebellum compared to the cortex, even though the cerebellum is a region less commonly associated with neurodegenerative disease. This raised the question of whether regionally specialized properties of astrocytes (or of astrocyte subsets) contribute to neurodegeneration progression.

What's exciting about your project's potential impact?
The transcriptional analysis of astrocytes at single-cell resolution that we propose will be very impactful for the study of the processes driving brain aging and, given the well-established role of astrocytes in modulating synapses, to inform new strategies to preserve synaptic health in advanced age and in neurodegenerative diseases.

If your project is successful, what is the next step?
We will investigate the transcriptional regulators of regional diversity and intra- region heterogeneity of aged astrocytes and their impact on neurodegeneration.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
SD-NSC has provided economical, technical and intellectual support as well as mentoring to develop this proposal, which will be extremely helpful for future NIH grant applications and for my future career as an independent investigator.