NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Sarah Hopp, PhD

Assistant Professor
UT Health San Antonio

2022 San Antonio NSC Pilot Awardee

Investigating the role of microglial sialylation in aging and ADRD

How did you become interested in aging?
Aging is the largest risk factor for Alzheimer's disease, and as I learned about Alzheimer's disease I realized that many processes involved in brain aging could set the stage for the pathogenesis and progression of Alzheimer's disease and related dementias. During my graduate training at Ohio State University with Gary Wenk I became particularly interested in how brain aging affected brain immune cells (microglia), and how microglia dysfunction in aging could influence development of age-related neurodegenerative disorders like Alzheimer's disease. I have been studying microglia and interested in their changes during aging ever since.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
We observed changes in specific sugars (sialic acids) present on the surface of brain immune cells (microglia) in patients with Alzheimer's disease and other dementias. We were curious if appearance of these sugars was a feature of brain aging, or related to the buildup of plaques and tangles that happens specifically in neurodegenerative diseases like Alzheimer's disease. We were also curious how these different sugars could affect the function of brain immune cells. Aging brain immune cells are worse at debris cleanup than young brain immune cells, so we also wanted to investigate whether the appearance of these sialic acid sugars could influence debris removal by brain immune cells.

What previous research or experience informed the development of this proposal?
As I mentioned before, aging brain immune cells (microglia) are worse at debris cleanup than young brain immune cells. Previous research had shown that one cause of this decline in debris cleanup was increased levels of a type of receptor called a "Siglec" that can detect a specific type of sugar (sialic acid) and reduce microglia debris removal processes. Some Siglec receptors contain genetic mutations that increase or decrease risk for Alzheimer's disease. Previous research has focused on these Siglec sugar receptors, but I was interested in knowing if the sialic acid sugars themselves were changing during aging and Alzheimer's disease.

NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Sarah Hopp, PhD

Assistant Professor
UT Health San Antonio

2022 San Antonio NSC Pilot Awardee

Investigating the role of microglial sialylation in aging and ADRD

What's exciting about your project's potential impact?
Identifying processes that influence our brain's cleanup crew has really exciting implications for developing targeted therapies that could enhance the dwindling debris removal that we know happens in aging that could contribute to Alzheimer's disease and related dementias.

If your project is successful, what is the next step?
We want to manipulate levels of sialic acid sugars on microglia in mouse models of aging and neurodegenerative diseases using manipulation of different genes. Using these tools, we would be able to understand specifically how these sialic acid sugars on microglia influence complex processes such as memory and development of plaques and tangles in Alzheimer's disease and related dementias.

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 allowed us to perform experiments on a wider array of human postmortem brain samples from aging brains with several different neurodegenerative diseases.