2023 Buck Summer Scholar: Olivia Wilson

My name is Olivia Wilson, and I am a rising senior majoring in Cell and Molecular Neuroscience at Scripps College, in Claremont, California. At Scripps, I work in Dr. Melissa Coleman's lab investigating the neural circuitry underlying female zebra finch song preference formation and maintenance, with an emphasis on the role of dopamine in these mechanisms. The lab performs song preference behavioral assays on zebra finches treated with dopamine agonists and uses immunohistochemistry to examine the brains of paired versus unpaired finches. At the Buck Institute for Research on Aging this past summer, I worked with Sudipta Bar, a postdoctoral fellow in Dr. Pankaj Kapahi's lab. The lab is focused on investigating the potential of dietary restriction to slow age-related diseases and extend lifespan, as well as the nutrient-signaling pathways that underlie these benefits. Specifically, my project aimed to characterize the role of several gene candidates in a *Drosophila melanogaster* model of tauopathy, with applications to the study of Alzheimer's Disease (AD), one well-known tauopathy disease.

Tauopathies are a diverse class of diseases that involve the abnormal changes to tau proteins, resulting in toxic aggregations and cellular dysfunction. Tau proteins are critical for the structural integrity and proper functioning of neurons, the cells in the brain responsible for complex information processing, communication, and behavior generation. Neurons, like other cell types, can maintain their structural integrity because of the function of a cytoskeleton, a network of protein filaments and fibers within the cell acting like a vertebrate's skeleton. One type of protein filament composing this dynamic cytoskeletal network consist of microtubules, which are long tubular structures made up of neatly arranged subunits critical for neuron shape, structure, and the movement of substances around the cell. These microtubules are stabilized by tau proteins, which are subject to dysfunction in the context of neurodegenerative disease producing aberrant neuronal communication and eventually neuron death. In the Kapahi Lab, I studied a transgenic model of tauopathy in fruit flies, wherein mutant human tau proteins are expressed, causing neurodegenerative phenotypes that largely recapitulate characteristics of Alzheimer's disease. Specifically, my project sought to identify promising gene candidates with a role in the pathogenesis of complex and poorly understood tauopathies.

I first examined the effect of silencing these gene candidates on the lifespan and healthspan of normal flies, then characterized whether the silencing of these individual genes influenced neurodegenerative disease phenotypes in transgenic tau fly populations. My work revealed that silencing a gene central to a highly conserved inflammatory response can increase lifespan in flies, indicating that reducing this inflammatory pathway may be neuroprotective.

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