2022 Buck Summer Scholar: Grace Qi

Hi! My name is Grace Qi, and I'm a neuroscience major at Duke University, but I'm originally from Virginia. I have been fascinated with the brain and age-related neurological diseases since starting college and am excited to be working at the Buck Institute this summer! At Duke, I study the role of circadian rhythms in Alzheimer's Disease (AD) in the lab of Dr. Carol Colton. My project has been focused on investigating disruptions in circadian rhythms that occur in various regions of the brain in mouse models of Alzheimer's Disease, with the goal of determining whether such changes contribute to cognitive decline and memory loss. At the Buck Institute, I have been working in Dr. Pankaj Kapahi's lab studying protein trafficking mechanisms in Alzheimer's Disease with fruit flies. Using fruit flies gives me the ability to test a variety of genetic manipulations for their efficacy against age-related diseases like AD. Dr. Kapahi's lab has historically been focused on elucidating how dietary restriction promotes longevity and slows aging. My project was born out of a study that identified a protein called Oxidation Resistance 1 (OXR1) that mediates the effect of dietary restriction on lifespan. Further work determined that this protein plays important roles in protein trafficking mechanisms that could impact neurodegeneration in major diseases like Alzheimer's Disease.

Protein sorting and trafficking within cells is a crucial process that is known to be disrupted in neurodegeneration. Diseases like Alzheimer's Disease and Parkinson's Disease are primarily characterized by proteins that aggregate together due to improper modification or degradation. A major hypothesis in the field is that these protein aggregates (amyloid and tau for Alzheimer's, alpha-synuclein for Parkinson's) disrupt normal neuronal functioning and cause neuronal degeneration that eventually lead to cognitive decline, loss of motor function, or memory loss. Studying the pathways that are responsible for the proper sorting of proteins throughout the cell will give insight into the causes of protein aggregates and neurodegenerative diseases. My project has been focused on a complex called the retromer that is responsible for sorting amyloid precursor protein, the precursor to amyloid aggregates, to its appropriate cellular destination. This pathway is of particular importance since OXR1, the mediator of dietary restriction-induced longevity, has been shown to play roles in regulating the retromer complex and declines with age. Thus, age-related disruptions in OXR1 and retromer sorting could lead to improper trafficking of amyloid precursor protein and neurodegeneration. My results indicate that overexpression of OXR1 in fly models of Alzheimer's Disease protect neurological function with age. These findings indicate that OXR1 and the retromer complex may be valuable targets for therapeutics that could revolutionize the way diseases that involve protein aggregates are diagnosed and treated. I look forward to seeing how this work will continue to expand our view of neurodegeneration towards a treatment for some of the most devastating diseases facing humankind.

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