2023 Buck Summer Scholar: Kaya Ceyhan

My name is Kaya Ceyhan, and I recently graduated from Ohio State University, where I minored in Molecular Genetics and minored in History. I am interested in combating neurodegeneration through a career in medicine and research. I worked in Dr. Nicolas Wein's lab at Nationwide Children's Hospital in Columbus, Ohio, during my undergraduate. In the Wein lab, I focused on assessing the efficacy of AAV gene therapy vectors for rare neurodegenerative disorders such as Duchenne Muscular Dystrophy.This summer at the Buck Institute, I worked in the Newman lab. The Newman lab seeks to leverage small molecule metabolites for therapeutic development in age-related diseases. Cells utilize ketone bodies as an alternative energy source when glucose levels are low, however, ketone bodies have numerous non-energetic functions that have not been fully explored. The long-term mission of the lab is to develop therapeutics which leverage endogenous metabolism to increase functionality and independence in older adults.

During the summer, I had the opportunity to work on two separate projects. The first project focused on establishing a detailed timeline of changes in the insoluble protein compartment (insolublome) in the mouse brain following administration of a ketogenic therapeutic. In neurodegenerative diseases, loss of protein homeostasis (proteostasis) is a key hallmark. Previous research in the lab has discovered that the ketone body beta-hydroxybutyrate (BHB) can regulate protein solubility in the brain, targeting proteins related to neurodegenerative diseases. However, while evidence of the change is robust, further investigation is needed to clarify a timeline of what happens in the brain insolublome. To deliver BHB, we orally administer a ketone ester that is cleaved to produce ketone bodies, including BHB, without any change to dietary composition. Looking across the treatment timeline in the insolublome, we investigated overall changes in protein concentration as well as proteins associated with neurodegenerative diseases like Alzheimer's disease. By analyzing the effects on the overall insolublome and specific proteins over a more detailed timeline following ketone administration, further steps can be made toward developing ketogenic therapies for neurodegenerative diseases.

Furthermore, I also looked at the role immune response plays in contributing to Delirium. Delirium is a sudden and severe change in brain function that leads to confusion, altered consciousness, and cognitive impairment. The immune system, particularly its inflammatory response, has been identified as a significant player in the onset and progression of Delirium. Elevated levels of certain cytokines, which are proteins that mediate and regulate immune and inflammatory responses, have been linked to the development of delirium in both clinical and pre-clinical settings. Through my project at the Newman lab, I have sought to characterize the effects of cytokines on delirium-like symptoms in mice. By focusing on the intricate relationship between the immune system and brain function, we aim to pinpoint specific inflammatory markers associated with Delirium. Better characterizing specific factors in immune response is vital to better understanding the causes and potential treatments for Delirium.

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