

2023 Buck Summer Scholar: Sydney Becker



My name is Sydney Becker, and I am an incoming third year undergraduate student at the University of California, Davis, majoring in biochemistry and molecular biology. I intend to pursue a PhD in biochemistry and conduct research focused on the development of novel therapeutics that will address age-related diseases. At Davis, I work in Dr. Justin Siegel's lab where my experience largely includes *de novo* enzyme design and SNP analysis focused on designing, testing, and implementing *de novo* enzymes. The lab's overarching goals include using computational and wet lab approaches to improve human health, food industries, and combat climate change. Moreover, I have also worked under the supervision of Dr. Angela Gelli, whose lab is focused on resolving the mechanisms of neuroinfections in the brain. In the Gelli Lab, I elucidated a possible cooperative action between two proteins during *Cryptococcus neoformans* penetration that may play a mechanistic role in blood-brain barrier penetration and infection. This summer, I joined Dr. Eric Verdin's laboratory under Postdoctoral Fellow Dr. Génesis Vega Hormazabal and PhD candidate Christina Alexandru. The Verdin Lab studies the intersection between the immune system and metabolism to try to better understand the causes and mechanisms of inflammation during aging.

My project focused specifically on understanding the processes behind brain aging and neurodegeneration via the blood-brain barrier. The blood-brain barrier is a thin layer of cells that repairs the central nervous system of the brain from the vascular system, maintaining critical brain homeostasis. While essential molecules, ions, and cells are allowed to pass between the CNS and vascular system, the brain is protected against daily fluctuations in body metabolism, pathogens, and disease. Changes in the blood-brain barrier have been characterized during pathogenesis and aging, including a "leaky" blood-brain barrier, which is a state where the blood-brain barrier can no longer prevent molecules, ions, and cells from going between the body and brain. This has been correlated with the presence of senescent cells, but limited studies have elucidated potential mechanisms responsible for this physiological phenomenon. Also of importance to BBB health is the coenzyme NAD⁺, involved in a number of metabolic processes. While NAD⁺ levels have been shown to decline with age, contributing to neurodegenerative diseases and cancer, the cause of this decrease is unknown.

My project studied the multifaceted enzyme CD38, one of the primary consumers of NAD⁺ in mammalian cells. CD38 is likely responsible for driving the decline in NAD⁺ levels and has been shown to increase with age - but the mechanistic explanation for this remains unclear. To understand the role of CD38 on NAD⁺ decline in the brain, we must first understand how CD38 levels are changing in the brain during aging. We must also understand if the decline of NAD⁺ within the BBB can be associated with other aging-related phenomena such as the infiltration of cytokines and chemokines into the brain. Knowing the mechanism behind NAD⁺ changes and the associated "leaky" blood-brain barrier will bring us one step closer to developing therapies to address neurodegenerative diseases and other age-associated changes in the brain.