# 2024 Summer Scholar Profile: Sriram Selvakumaran

My name is Sriram Selvakumaran, I am a third-year student at the University of California San Diego, majoring in Molecular Cell Biology with a minor in Chemistry. I aim to pursue a career in research by obtaining a PhD focusing on the molecular basis of aging, with the goal of developing interventions to improve health span. I work as an undergraduate researcher in Dr Chengbiao Wu's lab, where I study Alzheimer's disease (AD). AD is a neurodegenerative disorder characterized by cognitive decline, with certain genetic mutations serving as prominent risk factors. One such gene is RIN3, and my research focuses on elucidating the mechanism by which RIN3 mutations contribute to AD by utilizing mice that overexpress the RIN3 gene.

As part of the Summer Scholars Program, I worked in Dr. Ashley Webb's lab. The Webb lab focuses on studying the aging brain, particularly the hypothalamus. Often referred to as the brain's master regulator, the hypothalamus controls body homeostasis and survival-related behaviors such as sleep, circadian rhythms, reproduction, hormonal control, and food regulation. The lab previously identified gene expression changes in the individual cell types of the hypothalamus with age and is now interested in investigating the different phenotypes these aging cells exhibit, the mechanisms driving the expression differences, and potential interventions to improve the activity of the aging neurons.

This summer, I collaborated with Dr. Kaitlyn Hajdarovic, a postdoctoral researcher in the Webb lab, to explore the underlying mechanisms driving age-related changes in neuronal subtypes within the hypothalamus. This research is crucial for developing therapeutics that could potentially rejuvenate aging cells. Typically, researchers rely on animal models or human induced pluripotent stem cell (iPSC) models to study these questions, but these models often fall short in accurately replicating aging phenotypes. To address this, we are advancing direct reprogramming technology to create *in vitro* models of aging hypothalamic neurons. This technique involves converting one cell type into another using transcription factors known as pioneer factors. A key aspect of my summer research was validating whether our reprogrammed neurons exhibit aging characteristics. With age, cells generally display increased DNA damage, mitochondrial dysfunction, nuclear protein damage, and heightened expression of inflammatory molecules. To assess these markers, I employed quantitative PCR to analyze indicators of nuclear protein damage, inflammation, and mitochondrial dysfunction, alongside the Comet assay to measure DNA damage. This approach enabled us to confirm whether the reprogrammed neurons retained aged traits.