



2025 Summer Scholar Profile: Vivian Chang



My name is Vivian Chang. I am a rising junior at the University of Chicago majoring in Neuroscience and Computational Biology. I am interested in pursuing a PhD and a career in research developing therapies for neurodegenerative diseases and other diseases of aging. I work in Dr. Adam Martersteck's lab, which is part of the Healthy Aging and Alzheimer's Research Care Center (HAARC) at UChicago. The Martersteck Lab studies successful cognitive aging and Alzheimer's disease using advanced neuroimaging techniques and machine learning. There, I am utilizing the MRI analysis software FreeSurfer to investigate morphological differences unique to the brains of successful cognitive agers. This summer at the Buck Institute, I joined Dr. Eric Verdin's lab under the guidance of Dr. Yini Zhang. My project is elucidating

the target and mechanism of the neuroprotective compound P7C3-A20.

While neurodegenerative diseases are increasing in prevalence, we still lack effective disease-modifying therapies. The small molecule P7C3-A20 has shown neuroprotective benefits across multiple neurodegenerative disease models, including Alzheimer's, Parkinson's, and ALS. However, the molecular target of this drug has not been definitively identified, hindering its future therapeutic potential. Our lab has discovered a potential target that plays a key role in the unfolded protein response (UPR), a cellular stress response that is activated by the accumulation of unfolded or misfolded proteins in the endoplasmic reticulum (ER). The ER is a vital organelle in the cell that is involved in protein synthesis and folding, but factors such as genetic mutations and metabolic or environmental stress can disrupt this process, leading to protein misfolding and aggregation. Since protein aggregation is a hallmark of neurodegenerative diseases, targeting the UPR is a promising potential strategy to reduce aggregation and mitigate disease progression.

The goal of my project was to validate the binding of P7C3-A20 to the target compound and to characterize the UPR pathway through which P7C3-A20 exerts its neuroprotective benefits. I validated drug-target binding through the cellular thermal shift assay (CETSA), which measures thermal stabilization of the target protein upon drug binding. In order to characterize the UPR pathway, I conducted cell viability assays by treating cells with P7C3-A20 and subjecting them to ER stress to trigger the UPR. By examining the interaction of P7C3-A20 with its target and how P7C3-A20 rescues cells through the UPR pathway, we hope to define the target and mechanism of the drug and show the benefit of targeting this pathway for future therapeutic development.