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.

2025 Summer Scholar Profile: Molly Goldwasser

My name is Molly Goldwasser, and I am a rising senior at the University of Michigan. I am majoring in Biochemistry with a minor in Computer Science. At the University of Michigan, I am a member of Dr. Nils Walter's lab, which aims to uncover the mechanisms behind the vast roles of RNA molecules in the gene expression process to advance therapeutics. Under the guidance of Dr. Adrien Chauvier, I study sequences of bacterial mRNA, called riboswitches, to characterize how they control gene expression in response to specific molecules. I am excited by the application of biomedical research to advance treatments of disease.

At the Buck Institute, I work in the Metabolomics Core, led by Dr. Prasanna Ashok Kumaar. Metabolomics provides a window into the status of a variety of metabolic processes through characterization of the small molecules within a biological sample. Through both internal and external collaborations, the Core has identified metabolic signatures of aging and diseases with its state-of-the-art mass spectrometry technology and data analysis platforms. However, metabolomics is just one type of omics data and can be integrated with other datasets, like proteomics, to provide a more comprehensive view into changes in biological pathways.

My project focused on analyzing lipidomic data, which is still an emerging area of research compared to genomics, proteomics, and metabolomics. Lipids are an important group of molecules involved in energy storage, cell membranes, and signaling. However, studying them is difficult because **lipid analysis is still underdeveloped**—there are no consistent systems for classifying or naming lipids, and the biological roles of many lipid molecules are still unknown. These gaps made it challenging to interpret lipid data and connect it to biological meaning. My work focused on overcoming these challenges to gain a better understanding of the role of lipids in Alzheimer's Disease (AD), a neurodegenerative disease with an unknown pathology.

The APOE gene is strongly associated with AD risk, and different APOE variants (ApoE2, ApoE3 and ApoE4) can either increase or reduce that risk. The Metabolomics Core quantified the relative abundances of different lipids in iPSC-derived-ApoE2, ApoE3 and ApoE4 neurons and pericytes, two brain cell types that help maintain the blood–brain barrier, across different APOE genotypes.
To address the challenge of lipid identification, I first **compiled standard identifiers** for all lipids in the dataset by combining information from several public lipid databases. Because most lipids do not have clear pathway annotations, I then **integrated lipidomics data with proteomics data** to use known protein pathways to help interpret the lipid changes. This approach helped identify **important relationships between proteins and lipids** that varied by APOE genotype.

I also used **computational tools** to classify lipids based on their structural features rather than just broad categories. This gave a more detailed view of lipid patterns and how they changed between cell types and genotypes. My findings suggested that the **APOE genotype influenced lipid metabolism in different ways**, revealing key lipid molecules that might help explain how APOE affects Alzheimer's disease risk.

Overall, my project showed how lipidomics can provide valuable biological insights despite current challenges in the field. While I focused on APOE and AD, expanding this kind of analysis to other biological samples will be important to better understand the role of lipids in health and disease.

2025 Summer Scholar Profile: Suhjin (Angela) Lee

Hello everyone! My name is Suhjin (Angela) Lee, and I am a rising senior at Saint Louis University (SLU) where I am double majoring in health management and bioethics. At SLU, I have been conducting research since my freshman year under the direction of Dr. Uthayashanker Ezekiel. Our lab is interested in understanding how neurodevelopmental processes, such as cell adhesion and motility, are affected in patients with hypotonia, ataxia, developmental delay, and tooth enamel defects syndrome (HADDTS) – a rare neurodevelopmental disorder – through an in-vitro model of patient-derived induced pluripotent stem cells (iPSC) in which we derive neural stem cells and neurons. At the Buck Institute, I was a summer scholar in the laboratory of Dr. Ashley Webb under the mentorship of Dr. José Arevalo. The Webb Lab is interested in understanding how and why hippocampal neurogenesis, the formation of new neurons, declines throughout aging, specifically in the context of neurodegeneration such as Alzheimer's Disease (AD).

This summer, I focused on understanding the role of FOXO3 throughout neurogenesis in Early Onset Alzheimer's Disease (EOAD). EOAD is characterized by an onset of AD at an age of 50 years old or younger and is strongly associated with a genetic mutation in comparison to late onset AD which can be impacted by lifestyle factors. FOXO3 is a transcription factor that has been implicated in cellular and protein homeostasis (proteostasis) and aging in worms and mammals. Within the brain, FOXO3 maintains neurogenesis which declines with age progression, but more drastically in AD patients. By focusing on an EOAD model, we were able to specifically focus on the hallmarks commonly seen in AD, such as a decline in neurogenesis and an increase in protein aggregate accumulation, while also being able to engineer isogenic controls with patient-derived cells that were reverted to the wild-type sequence.

We worked with EOAD-patient derived iPSCs and differentiated them through the process of neurogenesis to obtain neural progenitors, early neurons, and mature neurons. We hypothesized a decline in activated FOXO3 throughout neurogenesis which we tested through Western blots. The second part of my project focused on understanding how FOXO3 regulates protein accumulation throughout neurogenesis. We hypothesized that the levels of protein aggregate accumulation would increase throughout neurogenesis as FOXO3, a gene that plays an integral role in the regulation and autophagy of protein aggregate accumulation, would become less activated. We measured these changes by immunocytochemistry and a protein aggregate assay.

2025 Summer Scholar Profile: Abigail Marciniak

My name is Abigail Marciniak. I am a third-year student at the University of California, Irvine (UCI), where I am majoring in Biomedical Engineering. At UCI, I specialize in immunology research, working under Dr. Abraham Lee and Dr. Anshu Agrawal. As a researcher with Dr. Lee, I generate artificial antigen-presenting cells (aAPCs) capable of immune cell (T cell) activation, utilizing microfluidic technology. These aAPCs have the potential to serve as a powerful form of immunotherapy in the future. The immune system declines with age, so in Dr. Agrawal's lab, we are working to understand dendritic cell (an antigen-presenting immune cell) activity in aging adaptive and innate immunity. At the Buck Institute, I am mentored by postdoctoral researcher Dr. Meiying Wu in the lab of Dr. Chuankai Zhou. The Zhou lab uses the budding yeast Saccharomyces cerevisiae to study protein homeostasis and its role in cellular aging. Although it is a simple single-celled fungi, yeast is a eukaryote with many conserved human biological pathways, making it an ideal model organism. The lab incorporates novel technologies, including microfluidic platforms, to examine aging in yeast.

At the Buck, I quantify changes in yeast replicative lifespan (RLS) in response to varied environmental conditions. RLS, defined as the total number of divisions that yeast undergo during their lifespan, is one of two aging paradigms. Budding occurs every 90 minutes and results in a mother cell and new daughter cell. While studying total lifespan in S. cerevisiae is an excellent model of aging in post-mitotic cells, RLS measurement gives insight into the aging of actively dividing cells and the factors that control longevity. The traditional technique utilized to count yeast RLS is manual microdissection, where a microneedle is used to isolate newly formed daughter cells from the mother cells as budding occurs. However, this process is time consuming and labor intensive. Alternatively, the Zhou lab utilizes microfluidic technology to analyze yeast RLS. This is a high-throughput approach free from the pitfalls of microdissection. Microfluidics (fluid study at the microscale) is a multidisciplinary field integrating physics, chemistry, biology, and engineering. Microfluidic platforms have revolutionized drug discovery, cell biology, medical diagnostics, and yeast studies. In our lab, a complex microfluidic chip with small channels featuring hollow column structures allows us to trap yeast mother cells as media flows continuously through the device. Budding is then captured through time-lapse microscopy imaging.

However, there are limitations to this mechanical trapping approach. While the columns are uniform in size, yeast are not, so not all mother cells are captured. In addition, mother cells are often washed away during analysis, preventing further study. Alongside Dr. Meiying Wu, I am working to develop a novel 3D polymer mesh method of yeast capture that is size independent and compatible with a simpler microfluidic device. The mesh structure is a firm yet malleable surface for S. cerevisiae to grow on. The flexible gel ensures that when daughter cells bud off, the mother cell is pushed into the matrix and is not washed away. This specialized mesh would be applied to the bottom surface of a one-channel microfluidic device (to maintain a constant flow of nutrient-rich media). This method is compatible with imaging and is not limited by yeast size. We will use this approach to study the impact of heavy metal supplementation on yeast RLS, which is highly relevant given the ubiquity of metal supplement use among individuals of all ages.

2025 Summer Scholar Profile: Chaeli Place

My name is Chaeli Place, and I am a rising senior at Northwestern University studying Cell and Developmental Biology with minors in Data Science and German. My research journey started at Northwestern in the lab of Professor Christian P. Petersen, where we use regenerative flatworms called planaria to investigate the process of replacing missing or damaged tissue. My current project involves studying the genes that allow these worms to regenerate their eyes in the correct place and with the proper cellular composition to function properly. This summer at the Buck Institute, Professor Malene Hansen hosted me in her lab, where I worked with Dr. Laurel Koch to study a different type of worm called *C. elegans*. These roundworms are much smaller than planaria and do not regenerate, but they are a great model for studying aging biology. The Hansen Lab investigates a cellular waste recycling process called autophagy, which cells use to prevent waste buildup and recycle raw materials. Cells collect waste in structures called autophagosomes, which are like the trash cans of the cell, and enzymes from another structure called the lysosome then break down the waste into smaller, reusable units. We know that older cells and some diseased cells, such as neurons in neurodegenerative diseases, accumulate waste, drawing a potential link between a decline in autophagy and a decline in health during aging and disease.

Reproductive aging occurs decades before the rest of the body ages, and staying healthy after the end of reproductive years is a prevalent challenge to women's health. The onset of menopause is not just about the end of reproductive years; it is also marked by a significant change in hormones that affects overall health, resulting in not only symptoms like changes in mood or sleep but also an increased risk of more serious health conditions, like osteoporosis, stroke, and even Alzheimer's disease. This decline in overall health occurs on average thirty years before the end of a woman's life. As human lifespan increases yet the onset of menopause is fixed around 50 years of age, women are spending more years at increased risk for disease. During my time in the Hansen Lab, I was asking whether a decline in autophagy in the reproductive system could cause not just a decline in reproductive health but also send signals to the rest of the body that lead to a decline in overall health.

C. elegans allow us to ask questions about how a process like autophagy in one tissue affects other parts of the body and the organism as a whole. My summer project involved studying autophagy in the germline. Autophagy has been studied and characterized in other somatic tissues of *C. elegans*, like the intestine and neurons, and we also know that autophagy in specific tissues like these is required for lifespan extension by various longevity paradigms, indicating that tissue-specific autophagy plays roles in keeping *C. elegans* alive for longer. My research goals were to 1) characterize autophagy in the *C. elegans* germline, asking how it responds to stress and aging, and 2) determine whether germline autophagy is involved in maintaining overall health, asking whether it is required for stress resilience and longevity.

In order to visualize autophagy in the germline, the Hansen Lab developed a new reporter strain with a fluorescently-tagged autophagy protein. When we tag this protein and monitor the animals under a microscope, we can quantify the number of autophagosomes ("trash cans") and extrapolate how much autophagy is occurring. I used this strain to observe germline autophagy for the very first time!

I then was able to use it in various ways to characterize germline autophagy. For example, I counted the number of autophagosomes in response to a mild stress called heat shock, which is subjecting the worms to a higher-than-comfortable temperature. I found that heat shock increases the number of autophagosomes in the germline, indicating that the germline, like other tissues, responds to mild stress through autophagy. I also looked at the effect of reducing autophagy in the germline on the worm's lifespan and ability to withstand heat stress, and the lab will continue studying potential connections between germline autophagy and overall health. Finding such links between germline autophagy and health during aging may inspire interventions in the reproductive system that could extend healthspan beyond reproductive years.

2025 Summer Scholar Profile: Ines Drissi Qeytoni

My name is Ines Drissi Qeytoni, and I am a senior at the University of Rochester majoring in Biomedical Engineering with a minor in Biology. There, I am an undergraduate researcher in the Gorbunova/Seluanov lab studying how PIWI proteins (which help silence transposable elements through small RNA pathways) and PYHIN proteins (which recognize DNA in the cytoplasm and mediate inflammatory responses) affect genome stability in cells and exercise induced inflammation in mice, respectively. I was also part of the Rochester 2023 iGEM team, where we designed a 3D bioprinter capable of printing microbe-laden hydrogels, using an engineered bacteria and yeast hydrogel parallel culture system for the efficient synthesis of plant-derived molecules. At the Buck Institute, I am working in the Ellerby lab under the supervision of Dr. Lisa Ellerby and Dr. Nick Devanney, a postdoctoral fellow. The Ellerby lab is focused on understanding the mechanisms that lead to age-related neurodegenerative diseases, which are diseases that cause progressive damage to the cells in the brain. Understanding these mechanisms is also useful in identifying potential therapeutics for these diseases.

My project focuses on Alzheimer's disease. At the core of this disease is the aggregation of misfolded, small protein fragments called amyloid beta (aβ) in the brain. When clumped together, they form plaques in the brain that affect how neurons communicate and eventually contribute to cell death. Early drug efforts failed to prevent plaque formation and the only approved disease modifying therapies act by clearing existing plaques.

A major genetic risk factor for late onset Alzheimer's is a gene called APOE which has three common versions: ε2, ε3, and ε4. People who inherit two copies of the ε4 version have a ten to fifteen times higher risk of developing Alzheimer's disease. APOE helps transport fats in the brain and affects how aβ is handled. The ε4 version is less efficient at helping clear aβ which contributes to plaque buildup. Research in the Ellerby lab is exploring how metabolic impairment and mitochondrial dysfunction associated with ε4 contributes to this accumulation of aβ.

My project investigates how a small chemical change to the APOE protein (called succinylation) changes how well APOE can do its job. Succinylation is a naturally occurring modification that happens to proteins after they are folded and results from the spontaneous reaction of succinyl CoA (a metabolic molecule from the TCA cycle). Upregulation of succinate in ε4 cells led us hypothesize that succinylation could be upregulated as well. Predicted locations of succinylation in the APOE protein include the area that interacts with lipids and aβ. Therefore, this modification could affect how APOE binds to or clears aβ.

To investigate this, we are using human cell models that differ only in which APOE version they carry and a mouse model of aβ plaque buildup. In both models, we measured succinylation levels as well as localization of succinylation to better understand the link between succinylation and metabolism. These experiments should help us better understand the link between succinylation and Alzheimer's disease which can eventually help guide the development of therapeutics.

2025 Summer Scholar Profile: Yiqiao (Peter) Wang

Hi everyone! My name is Yiqiao (Peter) Wang. I am a rising junior at UCLA double majoring in Molecular, Cell, and Developmental Biology and Music Performance. At UCLA, I work as both a volunteer researcher and lab technician in Dr. John Belperio's lab, which focuses on preventing Chronic Lung Allograft Dysfunction (CLAD), a condition where donor lungs fail after transplant because the host's immune system attacks them. Under the mentorship of Dr. Vyacheslav Palchevskiy, I model immune responses in CLAD in vitro through mixed lymphocyte reactions, where I combine immune cells from two mouse strains to simulate host–donor interactions after a transplant. Just as host immune cells recognize and attack donor cells as foreign, the two strains of mouse immune cells recognize each other and release inflammatory factors. Using this model, I test immunosuppressive drug candidates to see whether they can suppress inflammatory factor secretion, reflecting their potential to protect donor lungs from immune rejection.

At the Buck Institute, I work in Dr. Dan Winer's lab, which explores the intersection of aging and immunity. Under the guidance of Dr. Taylor Valentino, I study how simulated microgravity impacts human immune cell function. Immune dysfunction is a common problem for astronauts returning from space. Understanding how immune cells react and become dysfunctional in microgravity is important because it allows us to understand the role which gravity, a force that is often overlooked due to its omnipresence, plays in supporting the immune system. Furthermore, this research allows us to potentially translate methods capable of rescuing immune dysfunction in microgravity to improve overall immune function under earth's gravity. Previous research in our lab showed that microgravity impairs the cytoskeleton, the protein network that maintains cell shape, movement, and organization. Disruption of the cytoskeleton limits immune cells' ability to travel through the body and fight infection.

Before I joined Dr. Valentino, in collaboration with the Haney lab at UPENN, he identified a gene with strong links to cytoskeletal regulation. They generated monocytes, a type of premature immune cell, lacking this gene. We found that under simulated microgravity, monocytes lacking this cytoskeleton organizer gene die at much higher rates—an effect not seen under Earth's gravity. Knowing the functional importance of this gene to the cytoskeleton, I hypothesized that cells without it will have impaired ability to adjust their shape and reorganize their cellular contents. Those cells are especially vulnerable in simulated microgravity because gravity pulls down on cellular molecules to contribute to their localization, so cells under simulated microgravity may require adaptation genes to reorganize their delocalized molecules. To test this hypothesis, I generated preliminary data, staining neutral and polar lipids, both easy to be observed and known to be compartmentalized, and found that under simulated microgravity they became more evenly distributed, indicating that microgravity has indeed disrupted their localization. Currently, I am identifying the specific pathways through which gravity regulates the cytoskeleton, with the goal of developing treatments to restore immune cell survival in microgravity. Ultimately, I hope these strategies can also be applied to strengthen cytoskeletal and immune function under Earth's gravity.