



## 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 ( $\text{A}\beta$ ) 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:  $\epsilon 2$ ,  $\epsilon 3$ , and  $\epsilon 4$ . People who inherit two copies of the  $\epsilon 4$  version have a ten to fifteen times higher risk of developing Alzheimer's disease. APOE helps transport fats in the brain and affects how  $\text{A}\beta$  is handled. The  $\epsilon 4$  version is less efficient at helping clear  $\text{A}\beta$  which contributes to plaque buildup. Research in the Ellerby lab is exploring how metabolic impairment and mitochondrial dysfunction associated with  $\epsilon 4$  contributes to this accumulation of  $\text{A}\beta$ .

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  $\epsilon 4$  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  $\text{A}\beta$ . Therefore, this modification could affect how APOE binds to or clears  $\text{A}\beta$ .

To investigate this, we are using human cell models that differ only in which APOE version they carry and a mouse model of  $\text{A}\beta$  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.