The Highway to the Neuron—Using Myosin Motors to Get There

By Grace Kim, Freshman Neuroscience Major & Spanish Minor

Kelsey Wang is a junior at the University of Southern California, majoring in biology with a minor in Art History and Spanish. Her short term goals also include attending medical school. After taking Molecular Biology her sophomore year, Wang started working in the Arnold Laboratory. Dr. Don Arnold received his PhD from Johns Hopkins and completed his postdoctoral fellowship at Rockefeller University and Harvard. He is a professor of Cell Biology in the Department of Biological Sciences.

Initially, Wang began research to get a taste of what it was like to work in a laboratory and to see whether it was something she wanted to do as a part of her future career. During her first semester in the lab, Wang mostly worked with DNA and rat cortical neurons, using fluorescent protein markers to study the phenotypic expression of a gene. Wang received the Rose Hills Fellowship for her research. More recently, Wang has been working on a research project with Varuzhan Balasanyan, a PhD student in the Arnold Laboratory.

After working in the lab during her first semester, Wang realized she truly had a passion for the research she was conducting. Wang admits, "I really enjoy working in a lab because it gives me an opportunity to work with graduate students as a twenty-year-old and be involved in something my peers usually have never done before." She also notes that working in a lab gives her a sense of responsibility and accomplishment.

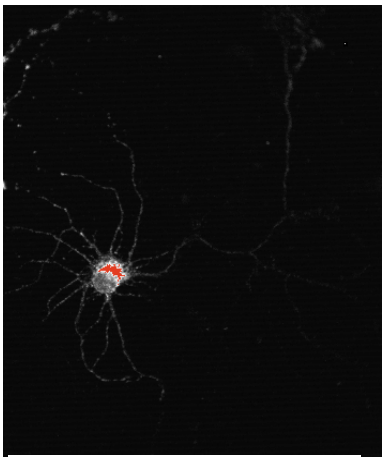
This past summer, Wang, under the guidance of her Primary Investigator, Dr. Don Arnold, began a project on PKD1 – Protein Kinase D1. Protein kinases are molecules that phosphorylate a protein by adding a phosphate group. This usually results in a conformational change in the protein and can activate the protein. PKD1, a specific type of protein kinase, has been shown to be involved in the regulation of various cell-signal pathways. Tommy Lewis, a graduate student in Arnold laboratory, recently published a paper about Myosin 5 and 6 –motor proteins associated with dendritic targeting in neurons. Lewis' studies concluded that PKD1 may be correlated with the mechanism of Myosin motors, which contribute to dendritic targeting.

Wang's goals were to explore the relationship between PKD1 and Myosin motors and to determine whether PKD1 works *through* a myosin-dependent mechanism. Wang received a $1000 stipend through a Provost Fellowship for this project. Lewis had discovered that the Myosin motors localize proteins to just the dendrites. This suggested that the PKD1 mechanism prevents the protein from reaching the axons. In order to determine whether PKD1 and Mysosin motors work together, Wang proposed two hypotheses. First, she hypothesized that blocking Myosin function will inhibit dendritic localization caused by PKD1-CA. Conversely, she also proposed that PKD1-KD will inhibit dendritic localization caused by Myosin.

The experiment was conducted using three different protein kinases. The first type, PKD1-WT (wild type) is the type that appears in normal animals, which causes proteins to localize dendritically. The second type, PKD1-CA (constitutively active) amplifies the effect by overdriving the kinase, which allows for exaggerated effects of the normal PKD1. The last type, PKD1-KD, is a kinase dead form that was used as a control. It does not allow PKD1 to phosphorylate the proteins being transported, thus rendering the cell unable to localize the proteins to a specific compartment. Wang has predicted that if the experiment were successful, then PKD1-CA should result in dendritic localization of the proteins, and PKD1-KD should result in no specific localization.

To test her hypotheses, Wang first used a protein called Transferrin, a protein natural in rats. This was unsuccessful because Transferrin appeared in the proteins *before* the targeting functions for myosin are placed into function. Consequently, Transferrin appeared all throughout the cell and failed to localize to the dendrites.

Thus, she is currently using another protein called Glu-R1. This is known to express later on in the neuron's development and hopefully will produce better results and stronger correlations.



Transferrin Infected Neuron

Although Wang's research on PKD1 does not show immediate cures for a certain disease such as cancer, it nevertheless holds great future implications. Her lab in general as well as her research is involved in developing techniques for observing and analyzing neural cells. This would allow laboratories around the world to utilize the technology that they have created in future experiments to discover even more about neural cells. As Wang and her colleagues continue to uncover information about the neuron, it may lead them to better understand or find cures for diseases that manifest themselves in the nervous system. Wang's research provides a stepping-stone to a greater truth.