

## Summer Research Experience

This summer I worked with Dr. Vidya Chandrasekaran looking at the expression and significance of gamma secretase in sympathetic neurons. One of the pathways affected by Alzheimer's disease is the  $\gamma$ -secretase pathway. Mutations in the gene for Presenilins (PSEN1 and PSEN2), the catalytic subunit of  $\gamma$ -secretase, is one of the most common mutations found in familial Alzheimer's patients. It was previously unclear if the function of the  $\gamma$ -secretase complex is conserved in peripheral neurons and if the pathway interacts with BMP signaling to regulate dendritic growth. Therefore, the goal of this study was to understand the role of  $\gamma$ -secretase in BMP-initiated dendritic growth in sympathetic neurons and identify the potential targets of the enzyme complex that might be interacting with BMP-signaling to initiate and maintain dendrites in sympathetic neurons. Using a model system of sympathetic neurons from embryonic rats we ran immunostain and Western Blot analysis finding for the first time that the complex is present in sympathetic neurons, active in the cytoplasm, and localization is unchanged by BMP. Using presenilin siRNA and known  $\gamma$ -secretase inhibitors we found that inhibition of  $\gamma$ -secretase results in a loss of dendrites. Using SMAD antibodies we found that  $\gamma$ -secretase interacts with the BMP signaling pathway downstream of SMAD translocation into the nucleus. Overall this study provided evidence that the  $\gamma$ -secretase complex is required for dendritic growth, suggesting the mutation of presenilin in Alzheimer's disease is associated with the loss of dendrites. Our future directions with this research revolve around determining the targets of  $\gamma$ -secretase in BMP signaling. I am continuing research with Dr. Vidya this semester and plan to take on a full credit of independent research next semester. Overall, the summer research program was an amazing experience for me. At the beginning of the summer I was completely positive that I wanted to go to medical school, but so many things about this opportunity has made me reconsider. It has opened my eyes to a career I hadn't thought to explore and it just felt right. I am so grateful.

