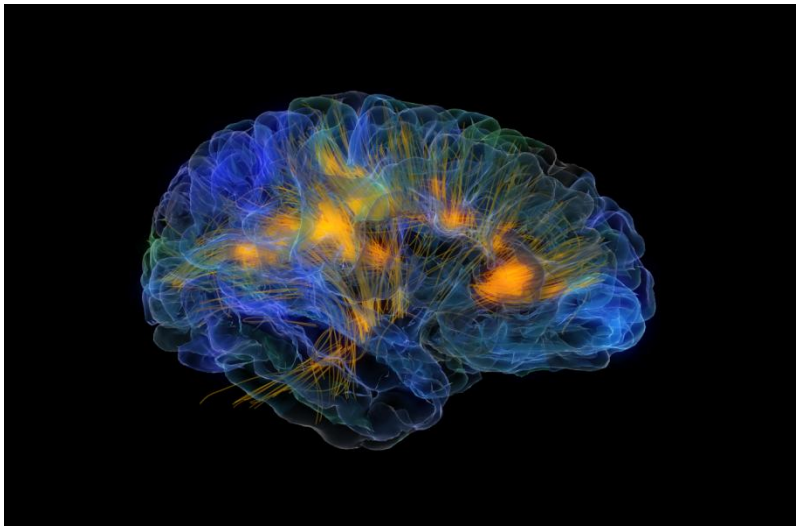


I grew up in a family of biologists. My parents work at a biomedical research institute, and my sister is currently pursuing an MD. I've been immersed in the wonderful world of proteins, signaling pathways, and gene expression, but I never really understood the dinner table discussions about "the interactions between β-catenin and PTEN pathways," and other esoteric jargon. Frequently I found myself Googling "What is beta cat neen neen?", but even then, I never understood the Wikipedia pages I'd click on. Landing a summer position shadowing at a research lab and enrolling in biology both my freshman year, I felt that I finally had the opportunity to follow my family's footsteps.

Next summer, I had an internship lined up at the University of Kansas Medical Center (KUMC) department, but first, my family and I went to China to visit relatives as usual. I always enjoyed spending time with each of them, but in particular I loved seeing my grandma. She was the one who always knew exactly how I liked my noodles: stir fried noodles with green onions and soy sauce. However, this trip was very different from our past visits. Upon walking into the familiar apartment, instead of the usual enthusiastic Chinese my grandma greeted us with, we were met with harsh, questioning tones. I didn't quite understand what was happening, since my grandma had a heavy rural accent, but I learned later that she didn't recognize us! In our hotel,

my father explained to me that my grandma was recently diagnosed with Alzheimer's disease. I knew what Alzheimer's did, but being personally affected by it, seeing a mother not know her son, honestly terrified me. What other disease can steal your memories, your identity?

Upon returning to Kansas and starting my internship, I had the opportunity to use high-tech microscopes, grow my own cells, and test the effects various drugs had on those cells. Everything was fascinating to me: I could see the direct impact a tiny drop of chemicals had on the growth and health of these cells, and I could do so using amazing machines that were larger than me. However, with the thoughts of my grandma in mind, I knew I wanted to contribute to science in a different way. Inspired, I filled out the application for a research internship at the National Institutes of Health (NIH) and applied specifically to the National Institute of Neurological Disorders and Stroke (NINDS). I was thrilled to find I was accepted.

At the NIH, I was immersed in the research experience, unlike at KUMC. After an initial training period, I was more or less performing procedures independently. This summer, I had a specific project with an end goal, which would actually contribute to the work of my supervisor, which was very different compared to the rather introductory nature of what I did at KU. I worked almost 50 hours a week, growing, examining, and imaging the axons of neurons to identify a specific link to neurodegenerative disorders, including Alzheimer's. I helped define a method to quantify the distribution and density of lysosomes in distal axons, which helped set a foundation for comparison for my supervisor to continue on. My work didn't just stop when I left the lab though; each night I'd study a bit from a textbook I borrowed from my mentor titled *Fundamental Neuroscience.* After I built up knowledge on the workings of the nervous system most pertinent to what I was doing in the lab, I started reading a seemingly endless stream of scientific articles supplied by my supervisor. These papers were the densest reading I've ever

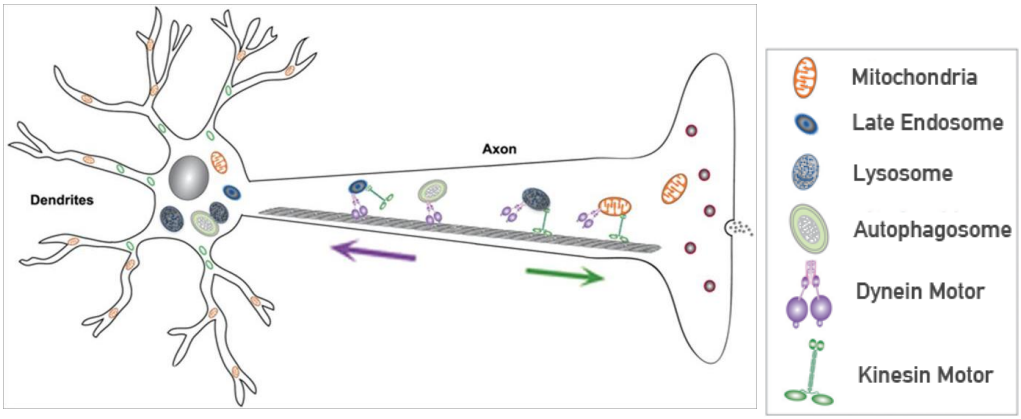
encountered, and even with the information I learned from the textbook, it took me much longer to read and comprehend a full article than what I felt it should. However, in the process, I picked up a great deal of knowledge relevant to my specific project.

If I were to give any advice to other high-schoolers, it would be to show initiative and find opportunities to do what they're interested in. Advanced scientific research can only be done in labs with proper equipment, and the best way to understand a subject is to become immersed in it. With the help of trained researchers, learning about procedures and protocols would be infinitely easier that trying to pick up knowledge through reading textbooks. A quick Google search yielded many different summer internship opportunities around the nation. As long as one is doing as much as one can to further their ambitions, then he or she should succeed.

After my last summer, I became more interested in neuroscience and the pathology of neurodegenerative diseases. After my summer with the NIH, I realized that the depth of knowledge humans have accumulated about the human body is immense, but we still don't have enough knowledge to cure or treat all diseases. I was given the amazing opportunity to investigate a specific branch of information. In the future, I'd like to be able to add to the mass collection of knowledge.

Nerve cells, also called neurons, are the cells in the nervous system responsible for transmitting and processing information throughout the body. Neurons have a unique shape compared to other cells: they have a cell body, where the majority of organelles, or cellular components, are located, dendrites, which are short extensions branching off the cell body, and

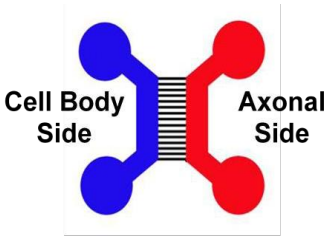
an axon, a very long extension branching off the cell body.

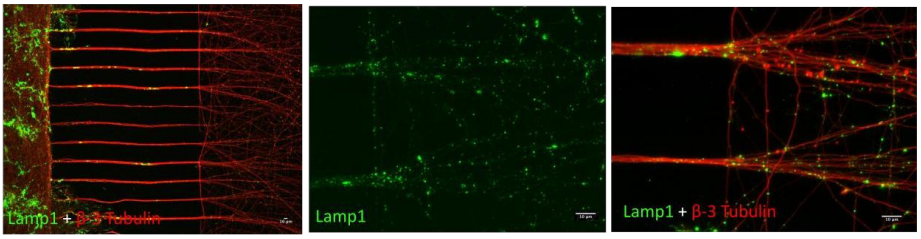


Since most of the cellular organelles are concentrated in the cell body, the transport of certain intracellular organelles and/or material, including ‘waste’ proteins, along the long axons is critical for a cell’s function and health. These ‘waste’ proteins and damaged organelles are required to be removed or self-cleaned, or else they will affect neuronal function and health. Recently, scientists have found that certain neurodegenerative diseases, like Alzheimer’s Disease (AD), Parkinson’s Disease (PD), and Amyotrophic Lateral Sclerosis (ALS), are linked to defects in the degradation process. Lysosomes are the main cellular organelle that degrades this waste and are mainly located in the cell body; lysosome-like organelles have actually been found in axons. However, the molecular content, distribution, and trafficking patterns of lysosome-like organelles, and their impact on axonal function in distal axons remain largely unknown.

In my research, I specifically studied lysosomal distribution in distal axons, or the parts of the axons that were further away from the cell body. I did so using microfluidic chambers which are devices that allow the physical separation of the cell body and the axons. Microfluidic chambers consist of two chambers connected by microgrooves which separate axons from cell

bodies. Neurons are plated in the cell body chamber. Microgrooves length (450 µm) assures that axons and not dendrites are passing into the axonal compartment.





In the image above, one can see a low magnification immunostaining image of a DIV7 (days in vitro, or cultured for 7 days before fixation) microfluidic neuronal culture (left). The red represent the cytoskeleton of the neuron, and the green represent lysosomal organelles. The middle and rightmost images are higher magnification images of the axonal compartment, co-immunostained for Lamp1 (middle) and neuronal marker β-3 Tubulin (right). Without the use of these microfluidic chambers, signal from glial cells, which are “helper cells” in the nervous system, and signal from dendrites will interfere with the desired signal from lysosomes within axons. Furthermore, I took time-lapse videos of living neurons to observe the movements of lysosomes in distal axons, specifically the directionality of the movements of the lysosomes. I saw that lysosomes moved both toward the cell, which is the expected result, and also away from the cell body, toward distal axons. I also detected active lysosomal enzymes in distal axons, which implies that lysosomes are active in degrading materials in these axons.

Altogether, my research actually suggests that lysosomes are mobile, and can be recruited to degrade waste in neurons' axons, instead of staying within the neuronal cell body. Defects in lysosomal either transport or function may lead to accumulation of "waste" proteins in axons as seen in neuronal disorders. This study established a solid foundation to further investigate the role of lysosomes in distal axons under healthy and stress conditions associated with axonal degeneration. If we better understand the mechanisms behind lysosomal movement and distribution in axons, we can develop better therapeutic strategies in treating major neurodegenerative diseases, such as AD, PD, and ALS.