2022 Buck Summer Scholar: Brennen Keuchel

Hello, my name is Brennen Keuchel, and I am a rising senior at Vanderbilt University in Nashville, Tennessee, studying Human Development and Molecular and Cellular Biology. At Vanderbilt, I was introduced to the world of aging research in the lab of Dr. Kris Burkewitz, where I am currently conducting research into age-related changes in neurons. Specifically, I am studying changes in a sub-cellular structure called the endoplasmic reticulum, which is essential for communication and protein folding in a cell. Dysregulation of these functions has been associated with neurodegenerative disease. My experiences in the Burkewitz lab have inspired me to pursue a career in research in the biology of aging. Leading up to this past summer, I wanted an experience where I could be exposed to the diversity of aging research and make meaningful contributions to a scientific project. Luckily, I was given an opportunity at the Buck Institute this summer in the lab of Dr. Malene Hansen to study the interrelation between age and the cellular recycling process known as autophagy.

Although most cellular entities (proteins, organelles, etc.) function properly during youth, many will slowly lose their ability to function over time. When a dysfunctional entity interacts with the rest of the cellular environment, it can cause a multitude of detrimental effects, potentially leading to disease. To alleviate the accumulating dysfunction that might ensue, cells have evolved to undergo autophagy. In this process, the dysfunctional entities are isolated from the rest of the cell in a structure called the autophagosome, broken down to their molecular components, and even reused to create new and fully functional entities.

My project is focused on deciphering how a protein (p62/SQSTM-1 in humans) that helps recruit cellular components for autophagy can promote healthy aging. In the model organism *Caenorhabditis elegans*, a transparent roundworm around 1mm in length, a genetically manipulated *C. elegans* strain was created with extra copies of the gene coding for our p62 protein (called SQST-1 in *C. elegans*). This strain, which is able to generate more copies of the SQST-1 protein, shows an increased lifespan as well as increases in both the number and size of autophagosomes in neurons.

However, we do not know how the specific proteins involved in autophagy are affected by SQST-1 overexpression. If we can understand the specific autophagic activities that SQST-1 modifies when it is overexpressed, we may be able to design more specific and effective therapeutics in the future that can target those specific mechanisms.

To establish this understanding, I employed genetic crosses between the SQST-1 overexpression strain and other *C. elegans* strains with fluorescent tags on autophagy proteins that SQST-1 interacts with. I then compared how the localization and intensity of the fluorescent autophagy proteins change in response to SQST-1 overexpression. I am excited to generate new data that informs our understanding of longevity and contributes to the research at the Buck!

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