

2023 Buck Summer Scholar: Debra Buggs



Hi! My name is Debra Buggs. I am a recent graduate from Oglethorpe University, a private college in Brookhaven, Atlanta. I received my B.S. in Biology with a minor in chemistry. During my last semester at Oglethorpe, I had the chance to participate in two in-class research projects which inspired me to pursue an MD-PhD instead of just an MD. Under the guidance of Dr. Allison Roessler, I studied the spiropyran mechanophore, a force responsive molecule that undergoes a color change when enough force is applied. I wanted to understand how the steric size and electronic properties of substituents affects the mechanochemical activation of spiropyran so that we can control its color change for mechanical purposes. I also did a project under the guidance of Dr. David Katz where I investigated how modulating open and closed chromatin affects health-related phenotypes in the model organism *Caenorhabditis elegans*, a transparent roundworm 1mm in length. I used the *eap-1* gene (H3K9me3 reader) as a tool to open and close sections of chromatin. Because *eap-1* is a K9 antagonist, it modulates the opening of closed (K9) chromatin. Without *eap-1*, closed chromatin that would normally get opened and transcribed stays closed. From this, I could gain a better understanding of the functions those H3K9me3 chromatin sections in a variety of phenotypes such as fertility (brood size assay), sensory ability (chemotaxis), and learning and memory (t-maze assay).

This summer, I got the exciting opportunity to continue to work with *C. elegans* at the Buck Institute for Aging Research in the lab of CSO and Professor Malene Hansen under the guidance of Dr. Hiroshi Ebata, a postdoc in the lab. The research goal of the Hansen lab is to understand the roles of autophagy, our body's cellular recycling system, in aging.

As humans age, we are exposed to many stressors that cause damage to our cellular components. Autophagy acts as a homeostatic mechanism to clear these damaged components from our cells, thereby keeping us healthy. However, over time, waste products can accumulate and eventually render our cells non-functional. In this way, we can think of cellular aging as the balance between the damages we accrue and the rate our bodies are able to clear this damage or waste. Aging has been associated with a decline in the efficiency of autophagy, which can lead to the buildup of cellular debris (e.g., protein aggregates) and eventually lead to age-related diseases such as cancer and Alzheimer's. Thus, it is important to understand the process of autophagy and the mechanisms that underly it.

My project was focused on investigating the role of the autophagy-related (ATG) protein ATG-16 and its WD40 domain. More specifically, I was interested in using this protein as a tool to better understand canonical vs non-canonical autophagy roles through the ATG-16 WD40 domain. Canonical autophagy uses ATG proteins to remove damaged cellular components via lysosomal degradation. However, in non-canonical autophagy, some ATG proteins including ATG-16 and its WD40 domain, can "moonlight" in alternate pathways. To this end, genetically manipulated *C. elegans* with either a deletion of the protein, a deletion of its WD40 domain, or a point mutation within the WD40 domain were characterized in various health and autophagy assays to learn more about the role of ATG-16 and its WD40 domain. Hopefully this research will inform the less well-studied non-canonical roles of ATG proteins and thus better inform interventions for age-related diseases linked to autophagy.