Garrison Lab

Neuropeptides, signaling molecules that facilitate communication between distant cells and tissues in the body, are widely distributed in brain areas responsible for learning and memory processes where they are primarily neuroprotective. Recent studies have shown that neuropeptide signaling may play a crucial role in cognitive resilience and frailty in Alzheimer's disease (AD), the most common cause of dementia in the elderly. AD is characterized by age-related cognitive decline, accumulation of amyloid-β plaques and tau tangles, and synapse loss. However, the relationship between neuropathology and cognitive symptoms is not straightforward, prompting investigations into neuropeptide signatures in AD brain compared to age-matched controls. Global neuropeptidomics analysis of human brain cortex synaptosomes has revealed distinct profiles of neuropeptides in AD, suggesting that dysregulation of neuropeptide signaling systems may be associated with severe cognitive deficits. Importantly, reproductive aging has been associated with increased risks of age-related diseases, including AD. We are interested in understanding how reproductive aging in females influences AD. To explore this connection, we are developing a novel model system to test the germline flux model, which proposes that changes in reproductive capacity over time may influence post-reproductive healthspan. This model suggests that the decline in ovarian function and associated hormonal changes during reproductive aging could impact neuropeptide signaling and cognitive function, potentially contributing to AD pathogenesis. Currently, our ability to address how reproductive aging effects post-reproductive healthspan is limited in most model organisms. This is largely attributed to the stress related to mating, that results in death prior to their post-reproductive lifespan. Here, we propose to build a model system that circumvents male induced demise and allows us to empirically test the role germline flux has on post- reproductive healthspan in *C. elegans*. By empirically test how germline flux affects post-reproductive healthspan and AD risk, we hope to gain new insights into the complex relationship between reproductive aging and neurodegenerative disease.