Online Proceedings

Poster Session 3

MGH 241, Easel 152

2:30 PM to 4:00 PM

Screening for Genes Regulating Recovery from Adult Reproductive Diapause in *C. elegans*

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Mentor: Nikolay Burnaevskiy, Pathology
Mentor: Matt Kaeberlein, Pathology

The process of aging brings about susceptibility to disease and death, but its mechanisms are still poorly understood. Dietary restriction is a potent approach to slow down the aging process, which has shown efficacy in multiple species, including the roundworm, *Caenorhabditis elegans,* a popular model organism for aging studies. Specifically, pre-reproductive adult *C. elegans* subjected to starvation enter a state of adult reproductive diapause (ARD), which preserves their lifespan and reproductive potential. Intriguingly, diapaused animals show signs of age-related deterioration upon prolonged starvation, but exhibit dramatic morphological improvements and have normal lifespans following return to feeding. However, the mechanisms regulating this lifespan preservation and apparent rejuvenation are not known. In this project, we aim to identify the genes responsible for the recovery during diapause exit. For that purpose, we used an RNA interference (RNAi)-based screen to inactivate individual genes during exit from diapause and analyzed the resulting phenotypes. Our current results reveal many regulators of metabolism and cellular homeostasis as crucial mediators of post-diapause recovery. Further studies based on these findings will discover the critical steps required for post-diapause tissue rejuvenation and preservation of longevity.

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Characterizing Age-Related Structural Changes during Adult Reproductive Diapause of *C. elegans*

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Mentor: Nikolay Burnaevskiy, Pathology
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It is known that dietary restriction is a positive intervention in aging. Its efficiency was demonstrated in multiple species suggesting that dietary restriction acts through conserved mechanisms that are not well understood. Specifically, in *Caenorhabditis elegans* (*C. elegans*), dietary restriction can extend lifespan well beyond that of their fed counterparts. Remarkably, it has been found that upon starvation young adult *C. elegans* enter a state of adult reproductive diapause (ARD) that allows a full lifespan preservation. We aim to characterize the mechanism by which lifespan can be preserved and extended in the diapaused animals. To this end we will investigate whether ARD animals experience typical age-related changes during prolonged starvation and whether they are reset upon diapause exit. Through fluorescent microscopy, we intend to distinctively characterize phenotypic differences of the cytoskeleton and nuclear morphology between ARD individuals and their fed counterparts. We expect these age-related markers either remain intact throughout the diapause state, or repaired upon diapause exit. This will further allow a better understanding of aging as wells the mechanisms of lifespan and healthspan preservation.

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Analysis of Proteostasis During *C. Elegans* Adult Reproductive Diapause

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Mentor: Matt Kaeberlein, Pathology

Aging is a phenomenon that brings about the onset of disease and eventually death. One of the hallmarks of aging is the decline in proteome maintenance that can lead to the accumulation of misfolded proteins. In extreme cases, protein misfolding can induce such devastating neurodegenerative diseases such as Huntington's disease and Alzheimer's for which very limited treatment is currently available. It has been observed previously that dietary restriction is a method that increases lifespan and delays the loss of function caused by age-associated pathologies. Specifically, complete food removal leads to robust increase in longevity in the roundworm *Caenhorbabditis elegans*, a popular model organism for aging research. Remarkably, when pre-reproductive adult worms are subjected to starvation, they enter a condition known as adult reproductive diapause (ARD). Upon reintroduction to food

after prolonged starvation, ARD worms experience a pronounced morphological recovery and have normal lifespan. To understand how diapaused animals preserve this rejuvenation potential and normal lifespan we aim to analyze how proteome quality is maintained during the diapause. We hypothesize that proteome quality is either well maintained during the diapause or is restored back to youthful state upon exit from the diapause. To discriminate between these possibilities, we use *C. elegans* models of proteotoxicity wherein toxic protein species produced in muscle cells induce paralysis with age. By analyzing the accumulation of insoluble protein aggregates and motility during and after the diapause we will gain a better understanding of the physiological aspects of the ARD state. These insights will be useful in developing novel approaches to counter age-associated pathologies.