SESSION 6510 (SYMPOSIUM)

COGNITIVE AGING: NEW INSIGHTS INTO HOW OUR BRAINS AGE

Chair: Coleen Murphy
Discussant: Saul Villeda

Maintaining quality of life with age is as important as slowing human aging. Slowing cognitive decline will be a critical aspect of keeping older adults healthy as we extend lifespan. To that end, identifying the molecular regulators of neuronal health, including learning and memory, in model systems that can later be applied to humans is an important step. In this symposium, we will hear about work on cognitive decline and its prevention being done in a variety of model systems.

USING C. ELEGANS TO FIND GENES, MECHANISMS, AND DRUGS TO SLOW COGNITIVE DECLINE

Coleen Murphy, *Princeton University, Princeton, New Jersey, United States*

Cognitive decline is one of the most important losses of human quality of life with age. To find new treatments that might slow these declines, it is useful to have short-lived, rapidly aging models in which to identify possible treatments. We found that C. elegans also lose their ability to learn and remember with age, along with other neuronal functions (axon regeneration, motility, etc.), and these declines are staved off by reduction in the insulin signaling pathway, which also extends lifespan. Both the mechanisms that regulate neuronal functions and the mechanisms that slow decline are well conserved evolutionarily, suggesting that we can use worms to identify new genes and compounds that might slow decline. Additionally, we have developed new C. elegans models of Parkinson's and Alzheimer's diseases, and through genetic, genomic, and metabolic studies we have found new approaches that may slow these declines.

REGENERATION AND COGNITION IN AGING

Saul Villeda, *University of California San Francisco, San Francisco, California, United States*

RETROTRANSPOSONS AND BRAIN AGING

Joshua Dubnau, *Stony Book School of Medicine, Stony Brook, New York, United States*

SYSTEMS GENETICS OF COGNITIVE AGING

Adam Hudgins, *Columbia University Irving Medical Center, New York, New York, United States*

SESSION 6515 (SYMPOSIUM)

AGING AND NEURODEGENERATION: NEW APPROACHES TO NEURODEGENERATION AND AGING

Chair: Nancy Bonini

Model organisms like C. elegans and Drosophila are powerful systems to help dissect molecular genetic aspects of complex biological processes. Here we will present a number of biological questions and approaches that have been used to study questions of neural integrity and healthful aging using these systems.

MODULATION OF THE AGING DROSOPHILA BRAIN AND SUSCEPTIBILITY TO NEURODEGENERATION

Nancy Bonini, *University of Pennsylvania, Philadelphia, Pennsylvania, United States*

Human neurodegenerative diseases, like amyotrophic lateral sclerosis, Alzheimer's disease and frontotemporal dementia, are late-onset progressive neurodegenerative disorders for which few cures or treatments are available. To develop new insight, we have been using the model organism Drosophila. We can re-create disease-associated protein toxicity in the fly brain, and then take advantage of the powerful molecular genetic approaches to define pathways and mechanisms. The fly is allowing us to reveal mechanistic understanding that we can then extend to the human condition. These studies have highlighted multiple novel pathways involved in longterm integrity of the brain. Among these processes, we have defined epigenetic pathways critical for longterm brain health. These pathways typically converge on stress pathway players, highlighting that boosting the ability of the nervous system to combat stress may help promote healthful brain aging and resistance to degenerative disease pathways.

NEURONS PUTTING OUT THE TRASH: A NOVEL FACET OF PROTEOSTASIS AND MITOCHONDRIAL QUALITY CONTROL

Monica Driscoll, *Rutgers University, Piscataway, New Jersey, United States*

Toxicity of misfolded proteins and mitochondrial dysfunction are pivotal factors that promote age-associated functional neuronal decline and neurodegenerative disease across species. Although these neurotoxic challenges have long been considered to be cell-intrinsic, considerable evidence now supports that misfolded human disease proteins originating in one neuron can appear in neighboring cells, a phenomenon proposed to promote pathology spread in human neurodegenerative disease. We have found that C. elegans adult neurons that express aggregating proteins can extrude large (~5μM) membrane-surrounded vesicles that can include the aggregated proteins and damaged mitochondria. We speculate that throwing out the trash may correspond to a conserved mechanism that constitutes a fundamental, but formerly unrecognized, branch of neuronal proteostasis and mitochondrial quality control. I will discuss our current understanding of the mechanisms of neuronal trash elimination.

NEURAL CONTROL OF HEALTHY AGING IN DROSOPHILA THROUGH PERCEPTIVE EXPERIENCES

Scott Pletcher, *University of Michigan, Ann Arbor, Michigan, United States*

We will describe how neurosensory circuits relate information about nutrition, danger, and mates to initiate rapid changes health and aging, including evolutionarily conserved neural signaling pathways and molecules that extend organism lifespan. These findings provoke the notion that aging may be considered a complex behavior that is acutely malleable, susceptible to sensory influences, and strictly controlled by coordinated sets of neurons.