aging, the functionality of stem cells declines, contributing to tissue decline. This symposium will focus on the mechanisms underlying stem cell aging in various compartments, including muscle, brain and the hematopoietic system.

**GENETIC, EPigenetic, AND METABOLIC MAINTENANCE OF NEURAL STEM CELLS DURING AGING**

**Ashley Webb, Brown University, Providence, Rhode Island, United States**

Tight metabolic regulation is essential to maintain stem cell homeostasis and support healthy aging. With age, metabolic alterations cause neural stem cell (NSC) dysfunction and are associated with a decline in neurogenesis, but the underlying mechanisms are not known. Aged stem cells display defects in the autophagy-lysosomal pathway that may disrupt mitochondrial dynamics, resulting in metabolic disruptions that alter self-renewal and differentiation potential. We have used genomic and functional approaches to investigate the metabolic mechanisms that support NSCs throughout aging. We found that mitochondrial and mitophagy gene networks as well as mitophagy dynamics are differentially regulated between the quiescent and activated states and become dysregulated with age. This work provides new insight into the metabolic regulation of NSCs and may lead to strategies to enhance neurogenesis in the context of aging and neurodegenerative disease.

**INTERVENTIONS TO DRIVE IMPROVED FUNCTIONAL POTENTIAL OF AGED OR DYSFUNCTIONAL HEMATOPOIETIC STEM CELLS**

**Isabel Beerman,1 Le Zong,2 Mayuri Tanaka-Yano,3 Hagai Yanai,2 and Ferda Tekan-Turhan,2 1. NIA, Baltimore, Maryland, United States, 2. NIA / NIH, Baltimore, Maryland, United States, 3. NIA/NIH, Baltimore, Maryland, United States**

Stem cell dysfunction is a hallmark of aging, associated with the decline of physical and cognitive abilities of humans and other mammals. Therefore, it has become an active area of research within the aging and stem cell fields, and various techniques have been employed to mitigate the decline of stem cell function both in vitro and in vivo. We have examined changes in the hematopoietic system after interventions and show modest, but positive effects on the aged system as well as the aged stem cells.

**STEM CELLS IN TISSUE MAINTENANCE AND REPAIR**

**Amy Wagers, Harvard University, Cambridge, Massachusetts, United States**

**SESSION 6555 (SYMPOSIUM)**

**MODEL ORGANISMS: GRANDEUR IN THE DIVERSITY OF AGING ORGANISMS**

**Chair: Anne Brunet**

Aging is a complex process that converts vigorous and healthy individuals into frail and decrepit ones, with increased susceptibility to a constellation of diseases. Human aging is influenced by many factors, including genetics, environment, lifestyle, sex, and socio-economic status. While aspects of aging can be studied directly in humans, discovering the causative factors that modulate this process often requires interventions and modeling. Traditional models will likely continue to provide a wealth of translatable information. Studying ‘extremophiles’ has exciting potential for providing new concepts that could be implemented for lifespan regulation. The development of new experimental models uniquely tailored to aging studies is also an essential step. This symposium will discuss African killifish, planarian, naked mole rats, and domestic dogs as new models for aging and exceptional longevity and rejuvenation. The iteration between new models and humans could be particularly helpful in delineating strategies to promote healthy aging and extend the disease-free portion of life.

**DEVELOPMENT OF THE AFRICAN KILLIFISH AS A NEW MODEL TO STUDY AGING AND SUSPENDED ANIMATION**

**Anne Brunet, Stanford School of Medicine, Stanford, California, United States**

We have pioneered a new model organism for aging research, the naturally short-lived African killifish Nothobranchius furzeri. The African killifish lives in ephemeral pools of water in Africa, and has evolved a short life cycle adapted to this habitat. Its embryos can also resist drought until the next wet season in a state of ‘suspected life’. In laboratory conditions, the African killifish has a maximal lifespan of about 4-6 months, and is, so far, the shortest-lived vertebrate that can be bred in captivity. We have successfully transformed this natural short-lived vertebrate into a usable model organism for aging research, including de novo assembly of the genome and CRISPR-Cas9 mediated genome-editing. Our goal is to use this model to discover new principles underlying aging, longevity, and ‘suspended animation’ in vertebrates.

**EXTREME LONGEVITY MECHANISMS IN THE NAKED MOLE RAT**

**Shelley Buffenstein**

**COMPANION DOGS TO TEST LONGEVITY INTERVENTIONS**

**Matt Kaeberlein, University of Washington, Seattle, Washington, United States**

**PLANARIA: A MODEL FOR IMMORTALITY**

**Alejandro Sanchez Alvarado**

**SESSION 6560 (SYMPOSIUM)**

**REGULATION OF AUTOPHAGY IN AGING AND DISEASE**

**Chair: Malene Hansen**

The cytosolic recycling process of autophagy plays an important role in many age-related diseases and has been directly linked to aging, including in the nematode C. elegans.
where autophagy appears beneficially induced in many conserved longevity models. As a critical process to ensure cellular homeostasis, autophagy is regulated at multiple levels, yet it remains a challenge in the field to understand how the regulation of autophagy is integrated at the cellular and molecular level to ensure health- and lifespan benefits. I will here discuss our progress on understanding the different molecular mechanisms employed by cells and organisms to regulate autophagy in response to stressors such as aging and disease.

REGULATION OF AUTOPHAGY IN AGING AND DISEASE
Malene Hansen, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, California, United States

The cytosolic recycling process of autophagy plays an important role in many age-related diseases and has been directly linked to aging, including in the nematode C. elegans where autophagy appears beneficially induced in many conserved longevity models. As a critical process to ensure cellular homeostasis, autophagy is regulated at multiple levels, yet it remains a challenge in the field to understand how the regulation of autophagy is integrated at the cellular and molecular level to ensure health- and lifespan benefits. I will here discuss our progress on understanding the different molecular mechanisms employed by cells and organisms to regulate autophagy in response to stressors such as aging and disease.

DISCOVERY OF NOVEL REGULATORS OF AUTOPHAGY IN ANIMALS
Eric Baehrecke, UMass Medical School, Worcester, Massachusetts, United States

The clearance of organelles by autophagy is important for cell health, and defects in this process have been associated with age-associated degenerative disorders. Ubiquitination of proteins enables their recognition by cargo receptors that facilitate the delivery of both protein aggregates and organelles to forming autophagosomes for degradation. We have investigated developmentally programmed autophagy to identify novel regulators of organelle clearance. We identified an Atg7-independent autophagy program that is required for cell size reduction and clearance of mitochondria. We have used this system to screen for new factors regulate ubiquitin-dependent autophagy and clearance of organelles. We screened a collection of putative ubiquitin binding domain encoding genes, and identified the novel gene Vps13D. Vps13D is an essential gene that is necessary for autophagy, mitochondrial size, mitochondrial clearance, and is associated with human movement disorders. We have used genetics and biochemistry to identify factors that link Vps13D, mitochondrial biology and autophagy.

AUTOPHAGY AND IMMUNITY
Vojo Deretic

LYSOSOMES AND CANCER
Rushika Perera

SESSION 7000 (SYMPOSIUM)

3D TEAM CARE MANAGEMENT TRIAL FOR COGNITIVELY VULNERABLE OLDER ADULTS: WHO PARTICIPATES AND HOW DOES THE TEAM WORK?
Chair: Richard Fortinsky Discussant: Caroline Stephens
Community-dwelling older adults often experience cognitive symptoms, and three common conditions that contribute to changes in cognition are dementia, depression and delirium. Despite the clinical inter-connectedness among these medical conditions, hereafter referred to collectively as cognitive vulnerability, little is known about the potential for success of clinical interventions that simultaneously address these conditions. From the perspective of older adults with cognitive vulnerability and their families, hospital admissions and emergency department (ED) visits are disorienting and often lead to declines in functional capacity and well-being, and significant family distress, threatening continued independent living. In this Symposium, we present details about an ongoing clinical trial testing a novel in-home, multidisciplinary team care management intervention for older adults with cognitive vulnerability and their families. This care management intervention led by nurse practitioners, called the 3D Team care model, aims to help reduce ED visits and hospitalizations and achieve other health-related outcomes. The first presentation will provide study background and design features as well as characteristics of study participants. The next two presentations by the 3D Team nurse practitioners will provide details about how the multidisciplinary team works, and how each team member provides interventions intended to address risk factors for adverse health outcomes. The fourth presentation by the 3D Team community health educator will explain how needs related to social determinants of health are addressed. The Discussant will place this clinical trial within the broader context of multidisciplinary team care for older adults with cognitive vulnerability led by nurse practitioners trained in geropsychiatry.

3D TEAM CARE MANAGEMENT TRIAL: STUDY DESIGN FEATURES AND PARTICIPANT CHARACTERISTICS
Richard Fortinsky, University of Connecticut, Farmington, Connecticut, United States

This clinical trial was designed in partnership with a Medicare Advantage (MA) plan, with the goal of comparing two care management approaches for its MA policyholders age ≥65 living with cognitive vulnerability. To test the efficacy of the 3D Team, we are using a randomized design, with the comparison group receiving telephonic care management currently offered to MA members. In this presentation, detailed aspects of the study design, characteristics of the study population, and patterns of 3D team referrals will be explained. To date, 390 older adults and 306 informal caregivers are enrolled in the trial toward a recruitment goal of 576 older adults and 380 caregivers. Among older adults, 40% have depression only, 23% have dementia only, and the rest have more than one of these conditions and/or delirium. Most common referrals by 3D Team nurse practitioners are