Session 2440 (Symposium)

NEW FRONTIERS ON CELLULAR SENESCENCE
Chair: Laura Niedernhofer

IDENTIFYING SENESCENT CELLS THAT DRIVE AGING
Laura Niedernhofer, *University of Minnesota, Minneapolis, Minnesota, United States*

Cellular senescence is a potent tumor suppressor mechanism. However, the untoward effect is that the accumulation of senescent cells promotes loss of resilience, aging and age-related diseases. One approach to maintaining the benefits of senescence while preventing the negative consequences is senolytic therapies: drugs that do not prevent senescence, but selectively kill senescent cells. Since virtually any type of cell can become senescent, it is important to identify the lineages of senescent cells that are most potent at driving loss of tissue homeostasis and aging. This will enable honing development of senolytics. We used a genetic approach to drive increased genotoxic stress, a potent inducer of senescence, in a tissue specific manner. The impact of this targeted senescence on different organs and cell types will be discussed, identifying a lead target for senolytics.

SENOLYTICS REDUCE CORONAVIRUS-RELATED MORTALITY IN OLD MICE
Christina Camell, *Institute on the Biology of Aging and Metabolism, University of Minnesota, Province, Minnesota, United States*

The elderly and chronically ill are among groups at the highest risk for morbidity and mortality to several infections, including SARs-CoV-2. Cellular senescence contributes to inflammation, multiple chronic diseases, and age-related dysfunction, but effects on responses to viral infection are unclear. Old mice acutely infected with pathogens that included a SARS-CoV-2-related mouse β-coronavirus experienced increased senescence and inflammation with nearly 100% mortality. Targeting SCs using senolytic drugs before or after pathogen exposure significantly reduced mortality, cellular senescence, and inflammatory markers and increased antiviral antibodies. Thus, reducing the SC burden in diseased or aged individuals should enhance resilience and reduce mortality following viral infection, including SARS-CoV-2.

IMMUNE SURVEILLANCE OF SENESCENT CELLS
Scott Lowe, *Memorial Sloan Kettering Cancer Center & Howard Hughes Medical Institute, New York, New York, United States*

Cellular senescence involves a stable cell cycle arrest and a secretory program that modulates the tissue environment. In cancer, senescence acts as a potent barrier to tumorigenesis and, though many cancers evade senescence during the course of tumor evolution, ionizing radiation and conventional chemotherapy can, to varying degrees, induce senescence in tumor cells leading to potent anticancer effects. Conversely, the aberrant accumulation of senescent cells can reduce regenerative capacity and lead to tissue decline, contributing to tissue pathologies associated with age or the debilitating side-effects of cancer therapy. Our laboratory studies mechanisms of cellular senescence with the ultimate goal of developing strategies to modulate senescence for therapeutic benefit. We have focused on how senescent cells trigger immune surveillance to facilitate their own elimination or, when that fails, how synthetic immune cells (i.e. CAR T cells) can be directed to eliminate senescent cells. Recent advances in understanding senescent cell surveillance by the immune system will be discussed.

CELL SENESCENCE AS A MEDIATOR OF AGE-DEPENDENT BRAIN INFLAMMATION
Marissa Schafer,[1] Xu Zhang,[2] Vesselina Pearsall,[2] and Nathan LeBrasseur,[2] *1. Physiology and Biomedical Engineering, Rochester, Minnesota, United States, 2. Mayo Clinic, Rochester, Minnesota, United States*

Cellular senescence and inflammation are interconnected causes and consequences of tissue aging. Here, we implemented orthogonal approaches to study their interaction in steady-state mature and aged mouse brain. Using single cell sequencing, we identified a putative senescent microglial population, which increased in abundance with age and was characterized by increased expression of p16 and chemotactic senescence associated secretory phenotype (SASP) factors. Using p16-INK-ATTAC transgenic mice to eliminate p16ink4a-positive senescent cells and mass cytometry, we show that p16ink4a-positive cell targeting reduced the abundance of activated inflammatory cells in the aged female brain. Age-dependent declines in executive cognitive function were improved following transgenic p16ink4a-positive cell targeting, and executive function robustly correlated with inflammatory brain cell composition in females. Collectively, our findings demonstrate fundamental differences in the age- and sex-dependent brain inflammatory landscape and implicate p16ink4a-positive senescent cell targeting as a therapeutic strategy to attenuate age-related inflammation and cognitive decline.

Session 2445 (Symposium)

NURSING HOMES AND COVID-19: STAFF EXPERIENCES
Chair: Verena Cimarolli
Co-Chair: Joann Reinhardt
Discussant: Sheryl Zimmerman

Nursing homes (NHs) faced an unprecedented crisis during the rapid spread of COVID-19. This pandemic has had a devastating impact on both NH residents and workers who are often on the frontlines providing hands-on care. These workers are vulnerable to the health risks of COVID-19 due to daily exposure to residents with COVID-19, residence in areas with high infection rates, and challenges specific to low-income workers (e.g. reliance on mass transportation). Research has highlighted the experiences of NH workers during the pandemic to learn how to better support them now and during future pandemics. This symposium will add to this research and present new findings from studies conducted in the United States to capture the unique experiences of NH employees. First, Bryant illustrates specific COVID-19-related challenges that NH frontline workers faced and how these workers' experiences compare to workers in other long-term services and support settings. Reinhardt reports