provides a community care planning service that connects caregivers directly to community-based services. Caregivers completed telephone surveys at baseline and 3- and 6-month follow-up. The number of network members engaging in malfeasant (negative) social interactions increased by 0.798 every 3 months (p=0.002). Members engaging in uplifting interactions decreased, especially among intervention participants, by 1.93 every 3 months (p=0.047); urban caregivers reported greater decrease than rural (p=0.006). Participants in intervention group showed a trend for greater decrease in COVID-19 related distress (10-point scale) over time compared to control group (p=0.059); those with more members engaging in uplifting interactions reported lower distress (p=0.017) regardless of intervention status, network size, and rurality.

CONTEXT MATTERS IN DECISION-MAKING: CAREGIVING NETWORKS OF AFRICAN AMERICAN DEMENTIA DYADS
Kalisha Bonds Johnson¹, Fayron Epps², MinKyoung Song³, Karen Lyons⁴, Kenneth Hepburn¹, and Martha Driesnack³, 1. Emory University, Atlanta, Georgia, United States, 2. Emory University, Fairburn, Georgia, United States, 3. Oregon Health & Science University, Portland, Oregon, United States, 4. Boston College, Chestnut Hill, Massachusetts, United States

Limited research explores the contextual and cultural nuances within African American dementia dyads within the United States and how these factors influence decision-making processes. Through a secondary data analysis of semi-structured interviews, we examined decision-making processes in five African American dementia dyads related to how they navigated decisions for the person living with Alzheimer’s disease and related dementias (ADRD) across five unique contexts (e.g., mother with multiple daughters, mother with son and daughter where the son was the “primary” caregiver). Analysis revealed that within dyads, persons living with ADRD were involved in the decision-making processes, but the level of involvement in decision making by the caregiving networks varied across dyads. Understanding the context in which decisions are made (i.e., within the dyad, across multiple family members in a caregiving network) has important implications in clinical practice and research. Interventions should be tailored to reflect these contextual and cultural nuances.

TURNOVER AND DEPRESSIVE SYMPTOMS AMONG MEXICAN AMERICAN CAREGIVERS OF PERSONS LIVING WITH DEMENTIA
Jacqueline Angel¹, Sunshine Rote², and Kyriakos Markides¹, 1. The University of Texas at Austin, Austin, Texas, United States, 2. University of Louisville, Louisville, Kentucky, United States, 3. UTMB, Galveston, Texas, United States

This study explored the role of caregiver background, stressors, and resources for Mexican American caregiver turnover and depressive symptoms. Using two waves of the Hispanic Established Epidemiologic Study of the Elderly (H-EPESE, 2010/2011-2016 N=333) Caregiver Supplement and informed by the sociocultural caregiver stress process model, we estimate logistic and OLS regressions of change in dementia and change in caregiver over five years. Neuropsychiatric expressions were significantly associated with caregiver turnover. Adult children and grandchildren caregivers were more likely to experience caregiver turnover than spouses. While depressive symptoms were relatively low at both waves, there was a greater increase in depressive symptoms occurred for caregivers who completed the interview in Spanish rather than English, which was partially explained by greater perceived stress at baseline. Findings demonstrate the need to provide dementia care supports for Mexican American caregivers, reduce stress for Spanish-speaking caregivers, and support Mexican American grandchildren who unexpectedly become caregivers.

SESSION 3241 (BIOLOGICAL SCIENCES INVITED SYMPOSIUM)

SENESCENCE AND INFLAMMATION
Chair: Marissa Schafer

Cell senescence and inflammation are interconnected mediators of aging and age-related disease. Recent advances in molecular and cellular profiling methods and research models are aiding in our ability to decipher mechanisms through which senescent cells drive inflammatory dysfunction, and inversely, to discover mechanisms through which aging immune cells may drive senescence, inflammation, and pathology. This symposium will feature exciting advances that span the emerging conceptual framework of how senescence and inflammation influence mammalian aging. Dr. Birgit Schilling will discuss the use of advanced mass spectrometric methods for profiling the senescent cell proteome, which reveal new insights into protein pathways and mechanisms of aging and disease. Dr. Matt Yousefzadeh will share how endogenous DNA damage can invoke cellular senescence, which enhances inflammation in both a cell autonomous and non-autonomous manner to drive tissue dysfunction and impact health. Dr. Daniel Tyrrell will discuss discovery of novel population of age-associated CD8 T-cells that enhance local tissue senescence and inflammation, which promote atherosclerosis. Dr. Xu Zhang will share a characterization of senescent cells in skeletal muscle using single-cell RNA-sequencing and the potential recruitment of immune cells by senescent fibroangiogenic progenitors. Dr. Marissa Schafer will discuss cell senescence as a mediator of age-related brain inflammatory cell composition and senescent cell targeting as a strategy to prevent cognitive decline. Importantly, discoveries discussed in this symposium may reveal new avenues for therapeutic development, to ultimately improve human healthspan.

CELL SENESCENCE IS A FEATURE AND MODULATOR OF THE AGED INFLAMMATORY BRAIN CELL LANDSCAPE
Marissa Schafer, Xu Zhang, Chase Carver, Vesselina Pearsall, Elizabeth Atkinson, Benjamin Clarkson,
investigate cell autonomous and non-autonomous effects of wild-type littermates and exhibit the senescent cell burdens repair gene, were utilized. Ercc1-deficient mice age faster than on aging, animal models lacking Ercc1, an important DNA damage and cellular senescence, a DNA damage is also known to induce cellular senescence, a macromolecular damage (including DNA damage) that accumulates in a time-dependent manner. This subpopulation of FAPs did not exhibit elevation in p21 expression exhibit a strong inflammatory phenotype, which is associated with improvements in executive function and spatial learning tasks. Our high-dimensional results reveal dynamic remodeling of the age-dependent brain immune cell landscape and implicate senescent cell targeting as a strategy to counter inflammatory changes and cognitive decline.

SENEGENCE-DERIVED PROTEIN BIOMARKERS DURING AGING AND OSTEOARTHRITIS

Birgit Schilling1, Sandip Patel2, Jacob Rose2, Judith Campisi3, Joanna Bons2, Christina King2, and Charles Schurman2, 1. Buck Institute for Research on Aging, Novato, California, United States, 2. Buck Institute, Novato, California, United States

Aging is a complex biological process associated with progressive loss of physiological function and susceptibility to multiple factors, such as cancer and neurodegeneration. As senescence burden increases with aging and becomes a risk factor for many age-related diseases we are specifically interested in senescence-derived aging signatures. We use cutting-edge proteomic workflows to investigate both the senescence-associated secretory phenotype (SASP) in tissue cultures. We are subsequently examining exosome proteins as well as lipid cargo in plasma from human young (20–26 yrs) and old cohorts and old (60–66 yrs) individuals. We will also present current work assessing senescence markers in cartilage and bone targeting underlying mechanisms and options for intervention for osteoarthritis. Overall, our focus is specifically directed towards senesence-derived biomarkers of aging.

ENDOGENOUS DNA DAMAGE AS A DRIVER OF AGING AND TISSUE DYSFUNCTION

Matt Yousefzadeh, University of Minnesota, Minneapolis, Minnesota, United States

Aging is a complex multifactorial process that enhances stress or impairs the ability to cope with it, whereby increasing the risk of morbidity and mortality. Many factors can contribute to aging, such as macromolecular damage (including DNA damage) that accumulates in a time-dependent manner. DNA damage is also known to induce cellular senescence, a cell fate that is known to play a causal role in aging. To investigate the effects of DNA damage and cellular senescence on aging, animal models lacking Ercc1, an important DNA repair gene, were utilized. Ercc1-deficient mice age faster than wild-type littermates and exhibit the senescent cell burdens that are comparable to that of a naturally aged mouse. To investigate cell autonomous and non-autonomous effects of DNA repair deficiency on senescence and aging, Ercc1 was deleted in mice in a tissue-specific manner. Increased senescent cell burden and dysfunction were present in tissues specifically targeted for Ercc1 deletion. However, enhanced senescence was also present in some non-targeted tissues, suggesting that these occur through cell non-autonomous mechanisms.

AGE-ASSOCIATED GRANZYME K-EXPRESSING CD8+ T-CELLS ENHANCE ATHEROSCLEROSIS IN MICE

Daniel Tyrell1, and Daniel Goldstein2, 1. University of Alabama at Birmingham, Birmingham, Alabama, United States, 2. University of Michigan, Ann Arbor, Michigan, United States

A novel population of age-associated Granzyme K (GZMK)-expressing CD8 T cells was found in mice and humans. These cells enhance local tissue senescence and inflammation and are distinct from central memory and conventional Granzyme B- or Interferon γ-producing effector memory CD8 T cells. It is unknown whether these cells drive chronic disease; thus, we induced atherosclerosis in young (3-mo) and aged (18-mo) wild-type mice via the PCSK9-AAV model and used scRNAseq to demonstrate that this GZMK-CD8 T cell population homes to atherosclerotic lesions exclusively in aged mice. Neutralizing CD8 T cells demonstrates that GZMK-CD8 cells drive age-enhance atherosclerosis. Finally, we transferred GZMK-CD8 cells from different aged donors into young CD8- hosts and demonstrate that GZMK-CD8 cells from aged but not young donors drive atherosclerosis. In conclusion, we identified a novel role for this recently described population of aging-specific GZMK-expressing CD8+ T cells as a critical driver of chronic disease.

IDENTIFICATION AND INVESTIGATION OF SENESCENT CELLS IN SKELETAL MUSCLE AGING

Xu Zhang, Leena Habiballa, Zaira Aversa, Yan Er Ng, Joao Passos, and Nathan LeBrasseur, Mayo Clinic, Rochester, Minnesota, United States

Skeletal muscle aging is marked by the loss and atrophy of resident fibers, and the accumulation of functionally diverse cell types including fibroblasts, adipocytes, and immune cells. Senescent cells amass in multiple tissues with advancing age where they contribute to aging, chronic disease, and physical decline. The role of senescence in mediating muscle aging has become a popular and sometimes contentious topic. However, to date, this concept has not been methodically tested. In this study, we characterized the changes in cell abundance and, importantly, cell-specific transcriptional profiles with skeletal muscle aging using scRNAseq. Interestingly, we identified a small population of p16 positive fibro-adipogenic progenitors (FAPs) which, upon further investigation using immunohistochemical methods, were found to express other senescence markers. This subpopulation of FAPs did not exhibit elevation in p21 levels with age. Instead, terminally differentiated myofibers were the source of the p21 increase. Myofibers with high p21 expression exhibit a strong inflammatory phenotype, which includes activated p53 signaling pathways together with strong cytokine-cytokine receptor interactions. We further identified large amounts of cross-talk between different cell types, suggesting that senescent FAPs and myofibers could contribute to skeletal muscle aging in a paracrine manner. Importantly, these observations in mice were confirmed in human samples, suggesting the strong translational power of these findings.