role of IL-6 in promoting frailty and age-related mitochondrial dysregulation. The human IL-6 (hIL-6) knock-in mouse (TetO-hIL6) was developed utilizing CRISPR/Cas9 technology with transgene donor vector containing a tetracycline response element promoter driving expression of hIL-6 cDNA. Male TetO-hIL6 mice were treated with doxycycline-containing water for six weeks starting at 8 months old. RNAseq analysis of whole blood demonstrated significant upregulation of pro-inflammatory related markers at 6 weeks compared to baseline and upregulated cell proliferation and metabolism pathways. Physical testing of TetO-hIL6 mice before and after hIL-6 induction demonstrated decreased grip strength ($p = 0.003$), decreased running capacity ($p = 0.02$), and 40% increase in falls off of the treadmill ($p = 0.001$). Induced mice also demonstrated decreased basal body temperature ($p < 0.001$). Given the significant dysregulation of metabolism-related genes in RNAseq analysis and changes in basal body temperature following hIL-6 induction, we next performed untargeted metabolomics on plasma from mice at baseline and 6 weeks post-induction to better evaluate metabolic changes associated with hIL-6 elevation. We found changes in key serum metabolites, including circulating adenosine triphosphate (56% reduction, $p = 0.02$), pyruvate (35% reduction, $p = 0.0006$), alpha-ketoglutarate (47% reduction, $p = 0.04$), and succinate (306% increase, $p = 0.001$). The TetO-hIL6 mouse model allows for induction of hIL-6 at various timepoints across the lifespan and demonstrates features of a frailty phenotype.

EFFECTS OF AGE AND SOCIAL ADVERSITY ON IMMUNE CELL POPULATIONS IN A NON-HUMAN PRIMATE MODEL OF HUMAN AGING

Mitchell Sanchez-Rosado,[1] Noah Snyder-Mackler,[2] James Higham,[3] Lauren Brent,[4] Nicole Marzan-Rivera,[5] Melissa Pavez-Fox,[4] Marina Watowich,[6] and Carlos A. Sariol,[1] *1. University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, United States, 2. Arizona State University, Tempe, Arizona, United States, 3. NYU, New York University, New York, United States, 4. University of Exeter, Exeter, England, United Kingdom, 5. UPR-Medical Sciences Campus, UPR-Medical Sciences Campus, Puerto Rico, United States, 6. University of Washington, Tempe, Arizona, United States*

Significant hallmarks of aging are immune function decline and rising cumulative inflammation. These immunosenescent signatures are also found in individuals who experience chronic social adversity, independently of age. However, no studies to date have examined how social adversity alters immune function across the lifespan –data that are essential to identify the molecular routes through which social adversity might lead to increased aging-related disease. Over a two-year period, we investigated how age and social adversity (quantified by low social status) affected immunity. We measured immune cell proportions at baseline and their gene regulation after in vitro stimulation with pathogen molecules that stimulated both Th1 and Th2 immune responses in a population of free-ranging rhesus macaques. We first performed flow cytometry on peripheral whole blood to quantify changes on immune cell proportions across the lifespan (n=235) and in animals of different social statuses (n=141). We found significant decreases in CD20+ B cells and CD3+/CD4+ T cell proportions with age, suggesting diminished antibody production and adaptive immune responses in older individuals. Age-associated increases in CD3+/CD8+, CD3+/CD4+/CD25+ T regulatory cells and CD14-/CD16+/HLA-DR+ non-classical monocytes indicated heightened baseline inflammation in older animals. Social adversity recapitulated the effects of aging in CD14+/CD16-/HLA-DR+ classical monocytes, indicating immune deficits in phagocytosis and pathogen clearance in older and lower status individuals. Using RNA-seq, our stimulations (n=1,320) will allow us to identify molecular immune pathways that are disrupted by age and social adversity, similarities in response between age and adversity, and how the effect of adversity varies across the lifespan.

LOSS OF AWARENESS OR URINARY DYSFUNCTION? INVESTIGATING AMYLOIDOSIS AND URINARY PHYSIOLOGY IN A TRANSGENIC MOUSE

Cara Hardy,[1] Ramalakshmi Ramasamy,[1] Dawn Rosenberg,[1] Philip Scarpa,[1] Xiangyou Hu,[1] George Kuchel,[2] and Phillip Smith,[1] *1. UConn Health, Farmington, Connecticut, United States, 2. University of Connecticut Health, Farmington, Connecticut, United States*

Alzheimer's disease (AD) is a devastating disorder primarily affecting older adults and is the most common neurodegenerative disease in the US. More than one in three AD patients experience AD-associated urinary dysfunction (ADUD), which directly contributes to their institutionalization. While ADUD has been clinically regarded as a result of poor cognitive control over urinary function, the physiology underlying loss of urinary control remains unknown. We hypothesize that amyloidosis in the CNS results in pathologic changes in urinary structure and function. Tg-APP/PS1DE9 mice were used before plaque deposition (4-6 months) and after plaque accumulation (8-10 months) and compared to WT littermates. Behavioral assays (open field testing and voiding spot assays) were performed to assess cortical function. Pressure-flow cystometry was conducted under urethane anesthesia to assess autonomic control of urinary function without cortical influence. Pharmacomyography of bladder strips was used to determine tissue-level changes in the absence of CNS input. In Tg-APP/PS1DE9 mice, plaque accumulation resulted in significant cystometric changes to voiding phase parameters, but not storage phase parameters. Pharmacologic studies showed decreased sensitivity to adrenergic stimulation without change in muscarinic sensitivity. Behavioral assays demonstrated significant differences between transgenic animals and WT in locomotion and voiding spot sizes. We interpret our data to support AD-related pathology of Aβ accumulation results in a distinct urinary phenotype in our model, analogous to the ADUD observed in AD patients. Establishing and verifying models of ADUD may improve the efficacy of treating ADUD and increase quality of life for patients and their caregivers.

METABOLIC ADAPTATIONS TO AEROBIC EXERCISE IN AGED MICE

Tyler Marx, Anastasiia Vasileva, Stephen Hutchison, and Jennifer Stern, *University of Arizona, Tucson, Arizona, United States*