Background: Endothelial dysfunction and subsequent inflammation contribute to the development of vascular cognitive impairment (VCI). Soluble intercellular adhesion molecule-1 (sICAM-1) is upregulated in endothelial dysfunction and promotes an inflammatory response; however, the relationship between sICAM-1 and VCI remains equivocal. Objective: To determine whether sICAM-1 contributes to the prediction of VCI. Methods: Community-dwelling older adults (n=172) from the "Cohort of Obesity, Sarcopenia and Frailty of Older Mexican Adults" (COSFOMA) study were identified as VCI or controls using standard neuropsychological evaluations and neuroimaging. sICAM-1 was quantified using ELISA, and multivariate logistic regression determined the association between sICAM-1 and VCI. Results: 31 VCI cases were identified. sICAM-1 was higher in VCI [VCI: 450.7 (241.6) ng/ml vs. Control: 296.9 (140.9) ng/ml]. sICAM-1 concentrations above the 90th percentile (464.1 ng/mL) was associated with VCI group membership in all models [OR = 6.9 (95% CI: 1.1- 42.2)]. The final saturated model explained 64% of the variance in VCI group membership. Conclusion: High concentrations of sICAM-1 are independently associated with VCI group membership. Efforts to further characterize the relationship between indices of endothelial dysfunction and pathological changes to the aging brain should be further pursued.

SINGLE-CELL TRANSCRIPTOMICS OF AGING MOUSE ISLET REVEALS AGE-RELATED RECRUITMENT OF ISLET-RESIDENT MACROPHAGE

Jia Nie,[1] and Nicolas Musi[2], *1. University of Texas Health Science Center Barshop Aging Institute, San Antonio, Texas, United States, 2. Barshop Institute for Longevity and Aging Studies, University of Texas Health Science Center, San Antonio, Texas, United States*

Type 2 diabetes (T2D) prevalence increases with age. The notion of inevitable progression of T2D has been challenged by reports of remission in some human T2D cases; however, this remission is dependent on islet function reserve. To elucidate the molecular mechanisms driving islet cell dysfunction, it is necessary to understand islet cell composition, diversity, and function throughout the lifespan. We generated a single-cell transcriptomic atlas of healthy islets isolated from young (5 weeks old), middle-aged (12 months old), and older-aged (25 months old) mice. Cell clustering identified 13 initial cell clusters that were further sub-clustered. This single-cell RNAseq profile showed that each cell type/group has different markers and functional characteristics and that age causes a remarkable shift in islet cell composition, diversity, and number. By comparing macrophages from young and old mice, we also found that aged islets contain a higher number of islet-resident macrophages. Overall, this single-cell islet atlas covers nearly all cells in the normal islet and allows a comprehensive exploration of all transcriptional states throughout the lifespan.

ASSESSING THE RELATIONSHIP BETWEEN SERUM IGF-1 AND ADIPOSITY BY AGE IN THE LONG LIFE FAMILY STUDY

Rehab A. Sherlala,[1] Candace M. Kammerer,[2] Allison L. Kuipers,[3] Mary K. Wojczynski,[4] Svetlana Ukraintseva,[5] Mary Feitosa,[6] Jonas Mengel-From,[7] and Ryan Minster[1], *1. University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 2. Department of Human Genetics University of Pittsburgh; Pittsburgh, Pennsylvania, United States, 3. Department of Epidemiology University of Pittsburgh; Pittsburgh, Pennsylvania, United States, 4. Department of Genetics Washington University in St. Louis, Saint Louis, Missouri, United States, 5. Duke University, Durham, North Carolina, United States, 6. Washington University School of Medicine, St Louis, Missouri, United States, 7. University of Southern Denmark, Odense C, Denmark, Denmark*

Serum levels of insulin-like growth factor 1 (IGF-1) and measures of adiposity, such as body mass index (BMI), are associated with susceptibility to age-related diseases. Previous reports of the relationship between IGF-1 and BMI ranged from positive to negative to no relationship, perhaps because previous reports studied different age cohorts. Using data on 4270 participants (aged 24-110 years) from the Long Life Family Study, we investigated the relationship between IGF-1 and BMI overall and by age groups. IGF-1 and BMI were positively correlated in the total sample (β=0.161, r2= 0.0038, p=1.8-05). However, further analyses revealed that the relationship between IGF-1 and BMI varied by age quartile: in the 1st quartile (24-58yo) the relationship was negative (β=–0.204, r2= 0.011, p=0.0008); in the 2nd quartile (59-66yo) the relationship was negative but non-significant (β=–0.069, r2= 0.0012, p=0.28); in the 3rd quartile (67-86yo) the relationship was positive but non-significant (β=0.106, r2= 0.002, p=0.13); and in the 4th quartile (87-110yo) the relationship was positive (β=0.388, r2= 0.019, p=1.2–05). This pattern did not differ by sex. We also detected a similar age-related pattern between IGF-1 and BMI using an independent dataset (NHANES III), comprising 2550 men and women aged 20-90 years. Our results may clarify some of the inconsistency in previous literature about the relationship between IGF-1 and BMI. Additional studies of IGF-1 and adiposity measures are needed to better understand the underlying mechanisms involved.

FASTING-MIMICKING DIET REDUCES RISK FACTORS FOR AGING-RELATED DISEASES IN PRECLINICAL AND CLINICAL STUDIES

Sebastian Brandhorst[1], *1. University of Southern California, Los Angeles, California, United States*

Prolonged fasting promotes stress resistance, but its effects on longevity are poorly understood. Calorie restriction or major dietary composition changes can have profound effects on healthy aging but the inability of many subjects to adhere to chronic and extreme diets together with the potential of adverse effects limit their application. Fasting-mimicking diets (FMDs) are effective in increasing health and lifespan, possibly by inducing stem cell-based regeneration, or as therapies in mouse models of a variety of diseases. FMDs reduce cancer incidence/progression, modulate the immune response, reduce immuno-senescence, ameliorate or reverse disease progression of multiple sclerosis, Type I and Type II diabetes, and reverse inflammatory bowel disease pathology. In a randomized clinical trial, markers/risk factors for metabolic syndrome and other age-related diseases were favorably impacted after completion of 3 FMD cycles. These effects were larger in participants at risk for age-related diseases.