Massachusetts, United States, 6. University of Minnesota, Minneapolis, Minnesota, United States

The Long Life Family Study (LLFS) has longitudinally measured key aging phenotypes on 4,953 participants (539 pedigrees) in the USA and Denmark selected for exceptional familial longevity. On average, both generations of the LLFS sample are healthier than average for their age/sex, for many phenotypes. However, the pedigrees are heterogeneous, with different families showing familial clustering of protection for different phenotypes. Linkage analyses identified extremely strong genetic linkage peaks for many cross-sectional as well as longitudinal trajectory rates of change phenotypes. These peaks are NOT explained by GWAS SNPs (either measured or imputed). Pedigree specific HLODs and preliminary deep sequencing suggests that these peaks are driven by rare, protective variants running in selected pedigrees. Whole Genome Sequencing, a third longitudinal visit, and extensive OMICs (transcriptomics, epigenomics, metabolomics and proteomics) will help us resolve the mechanisms behind these protective genetically linked variants, and could illuminate new biology and enable new therapeutics.

OMICS OF LONG-LIVED MAMMALS AND LINKS TO HUMAN CENTENARIANS

Gregory Tombline,[1] Jonathan Gigas,[1] Matthew Simon,[1] Yousin Suh,[2] Andrei Seluanov,[1] and Vera Gorbunova,[1] *1. University of Rochester, Rochester, New York, United States, 2. Columbia University, New York, New York, United States*

Mammalian species differ up to 100-fold in their aging rates and maximum lifespans. Long-lived mammals appear to possess traits that extend lifespan and healthspan. Pro-longevity mechanisms are complex traits afforded by connections between metabolism and protein functions that are unlikely to be predicted by genomic approaches alone. Thus, metabolomics and proteomics studies are required to understand the mechanisms of longevity. Sirtuin 6 will be presented as an example of a protein that evolved enhanced enzymatic function in long-lived species and also demonstrates enhanced activity and unique alleles in human centenarians. Proteome analysis reveal several longevity related proteins such as Cip1/p21, FOXO3, TOP2A, AKT1, RICTOR, INSR and SIRT6 harboring PTM sites that preferentially appear in either short- or long-lived species. The prospects of enhancing life expectancy and healthspan of humans by altering metabolism and proteoforms with drugs that mimic changes observed in long-lived species will be discussed.

IDENTIFYING TRANSLATIONAL LONGEVITY TARGETS WITH GENETICALLY MEDIATED TRANSCRIPTOME-WIDE ASSOCIATION STUDIES

Daniel Evans,[1] Steven Cummings,[1] and Nicholas Schork,[2], *1. California Pacific Medical Center, San Francisco, California, United States, 2. Translational Genomics Research Institute, Phoenix, Arizona, United States*

We hypothesized that trait associations with genetically mediated gene expression could be used to screen for genes that are good candidates for translational studies of longevity. We compiled a collection of genetically-mediated transcriptome-wide association studies using 33 traits and outcomes from large-scale, publicly-available GWAS meta-analysis results. The traits/outcomes were grouped within eight categories (aging, anthropometric, cardiovascular, inflammation, lung function, metabolic, musculoskeletal, and neurological). To test the utility of this approach, we examined trait associations with the drug target of statins, and we correctly identified known therapeutic effects and adverse events of statins. Specifically addressing the hypothesis, we examined a collection of candidate longevity-associated genes and identified one gene associated with lifespan that appears to also be associated with protection from atrial fibrillation and hearing impairment without being associated with adverse events. This screening approach can be used to prioritize gene targets for longevity translational efforts.

EFFECT OF LONGEVITY GENETIC VARIANTS ON THE MOLECULAR AGING RATE

Paola Sebastiani,[1] Anastasia Gurinovich,[1] Zeyuan Song,[1] William Zhang,[2] Stefano Monti,[1] Sofiya Millman,[2] Nir Barzilai,[2] and Thomas Perls,[3], *1. Boston University, Boston, Massachusetts, United States, 2. Albert Einstein College of Medicine, Bronx, New York, United States, 3. Boston University School of Medicine, Boston, Massachusetts, United States*

We conducted a genome-wide association study of 1317 centenarians from the New England Centenarian Study and 2885 controls using >9M genetic variants. The most significantly associated variants were correlated to 4131 serum proteins in 224 study participants. The genetic and protein associations were replicated in a genome-wide association study of 480 centenarians and ~800 controls of Ashkenazy Jewish descent and a proteomic scan of approximately 1000 participants of the same study. The analysis replicated a protein signature associated with APOE genotypes and confirmed strong overexpression of BIRC2 ($p < 5E\text{-}16$) and underexpression of APOB in carriers of the APOE2 allele ($p< 0.05$). The analysis also discovered and replicated associations between longevity variants and slower changes of protein biomarkers of aging, including a novel protein signature of rs2184061 (CDKN2a/CDKN2B in chromosome 9). The analyses show that longevity variants correlate with proteome signatures that could be manipulated to discover healthy aging targets.

SESSION 7695 (SYMPOSIUM)

POLICY SERIES: INTERDISCIPLINARY PUBLIC POLICY DISCUSSION

Chair: Brian Lindberg

Discussant: Linda Harootyan

Aging and health care public policy in Washington can be driven and influenced by the work of GSA researchers, educators, and practitioners from across the nation. This session will examine and explore public policy priorities from an interdisciplinary perspective and consider opportunities for communicating these policies with key policymakers. This session is an interdisciplinary look at policy issues in aging with the speakers representing views from the six sections of GSA. This session, organized by the GSA Public Policy Committee, will provide both GSA section leadership and attendees an opportunity to have an open