broadly applicable standard biomarkers of systemic chronic inflammation are needed. We tested whether elevated blood levels of the emerging chronic inflammation marker soluble urokinase plasminogen activator receptor (suPAR) were associated with accelerated aging, lower functional capacity, and cognitive decline. We used data from the population-representative longitudinal Dunedin Study (N=875). Plasma suPAR levels were analyzed at ages 38 and 45 years. We performed regression analyses adjusted for sex, smoking, and C-reactive protein. suPAR levels increased from 2.39 ng/mL (SD 0.89) at age 38 to 3.01 (SD 1.03) at age 45 years. Elevated suPAR was associated with accelerated pace of biological aging across multiple organ systems (β 0.28, 95% CI 0.21–0.35), older facial appearance (β 0.16, 95% CI 0.10–0.22), and with structural signs of older brain age (β 0.06, 95% CI -0.00–0.13). Moreover, participants with higher suPAR levels had lower functional capacity (more physical limitations [β 0.24, 95% CI 0.18–0.30]; slower gait speed [β -0.14, 95% CI -0.20; -0.08]) and greater decline in cognitive function (β -0.07, 95% CI -0.13; -0.01) from childhood to adulthood compared to those with lower suPAR levels. Finally, improvements in health habits between age 38 and 45 (smoking cessation or increased physical activity) were associated with less steep increases in suPAR levels over those years. Our findings provide initial support for the utility of suPAR in studying the role of chronic inflammation in accelerated aging and functional decline.

GENE EXPRESSION PROFILING SUGGESTS DOWNREGULATION OF WNT PATHWAY SIGNALING WITH AGING

Allison Kuipers,[1] Cara Nestlerode,[1] Victor Wheeler,[2] Iva Miljkovic,[1] and Joseph Zmuda,[1], *1. University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 2. Tobago Health Studies Office, Upper Scarborough, Tobago, Trinidad and Tobago*

The wingless (Wnt) pathway is involved in many age-related diseases and conditions, including cancer and cardiovascular disease. However, the impact of aging on Wnt pathway signaling remains largely unknown. Therefore, we surveyed peripheral blood expression of 43 Wnt pathway genes and tested for association with age in 369 Afro-Caribbean men recruited from the population of Tobago (mean age 64 years, range 51-89 years). Gene expression was measured in counts per sample, then normalized and background subtracted. All expression counts were transformed to normality after excluding any extreme outliers. Fourteen Wnt genes showed detectable expression in our sample and were examined further for association with age using linear regression both individually and using stepwise selection models to identify independent signals. A Bonferroni-corrected alpha for the 14 tested genes (α=0.0036) was used. Six of the 14 tested genes showed significant univariate correlation with greater age [r (gene): 0.169 (APC), 0.179 (AXIN1), 0.222 (CTNNB1), 0.211 (GSK3b), -0.178 (LEF1), -0.166 (TCF1)]. When combined, expression of four genes was determined to be marginally (P<0.05) independently associated with age (AXIN1, CDH2, CTNNB1, TCF1). After correction for multiple testing, a 10-year greater age was independently associated with 4% greater CTNNB1 expression and 8% lower TCF1 expression respectively (both P<0.0001), and this association accelerated after age ≥60 years (p-interaction 0.01 and 0.07, respectively). Greater expression of CTNNB1 and lower expression of TCF1 may indicate decreased Wnt pathway signaling. These results are the first to suggest that aging may be associated with alterations in Wnt pathway signaling.

GENOME-WIDE LINKAGE ANALYSIS IDENTIFIES A NOVEL LOCUS FOR GRIP STRENGTH: THE LONG LIFE FAMILY STUDY

Adam Santanasto,[1] Mary Wojczynski,[2] Ryan Cvejkus,[3] Bharat Thygarajan,[4] Kaare Christensen,[5] and Joseph Zmuda,[3] *1. University of Pittsburgh, PITTSBURGH, Pennsylvania, United States, 2. Washington University School of Medicine, St Louis, Missouri, United States, 3. University of Pittsburgh, Pittsburgh, Pennsylvania, United States, 4. University of Minnesota, Minneapolis, Minnesota, United States, 5. University of Southern Denmark, Odense C, Syddanmark, Denmark*

Grip strength declines with aging, is an indicator of overall health, and predicts mortality among older adults. Herein, we quantified the genetic contributions to grip strength among 4534 individuals, belonging to 574 families in the Long Life Family Study (age 70.3 ± 15.7, range 24–110 years; 56% women). Grip strength was measured using a handheld dynamometer, and the maximum value of two trials in the stronger hand was used. Quantitative trait linkage analysis was completed using pedigree-based maximum-likelihood methods with logarithm of the odds (LOD) scores >3.0 indicating genome-wide significance. Linkage analysis in the top 10% of families contributing to LOD scores was also performed to allow for heterogeneity among families (HLOD). All analyses were adjusted for age, sex, height and field center. Grip strength was lower per one year of older age (β: -0.34 ± 0.01kg, p <0.01), and overall: 24.3% of men and 19.3% of women had "low" grip strength according to European Working Group on Sarcopenia definitions. Grip strength was highly heritable (h2 = 0.37, p<0.05). We identified a potentially novel locus for grip strength on chromosome 18p (LOD 3.18) with 26 families contributing to this linkage peak (HLOD = 10.94). Deep sequencing of the chromosome 18 region may yield fundamental insight on the biology of muscle weakness with aging, and may help identify novel therapeutic targets for treatment and prevention of this common condition.

INTERACTIONS BETWEEN GENES FROM AGING PATHWAYS SIGNIFICANTLY INFLUENCE RISK OF ALZHEIMER'S DISEASE

Svetlana Ukraintseva,[1] Konstantin Arbeev,[1] Hongzhe Duan,[1] Igor Akushevich,[1] Mary Feitosa,[2] Kaare Christensen,[3] Eric Stallard,[4] and Anatoliy Yashin,[1] *1. Duke University, Durham, North Carolina, United States, 2. Washington University School of Medicine, St Louis, Missouri, United States, 3. University of Southern Denmark, Odense C, Syddanmark, Denmark, 4. Duke University, Biodemography of Aging Research Unit, Durham, North Carolina, United States*

Age is major risk factor for AD; however, relationships between aging and AD are not well understood. Decline in physiological resilience is universal feature of human aging that may also play role in AD. Aging-related pathways (such as IGF-I/P53/mTOR-mediated) that are involved in tissue resilience work in concert to decide outcomes of cell responses to stress/damage, such as survival, apoptosis, autophagy, etc. We hypothesized that interplay among genes in these pathways may influence AD risk as result of epistasis (GxG). We estimated effects of pairwise epistasis between SNPs in 53 genes from respective pathways on AD risk in the LLFS compared with other data (HRS, CHS, LOADFS). We found significant (fdr<0.05) GxG effects on AD risk in older adults across datasets. The SNP rs11765954 in CDK6 gene was involved in top GxG effects on AD in all datasets, when paired with SNPs in BCL2 and PPARGC1A. The CDK6 role in AD could be pleiotropic, depending on its activity in neurons: CDK6 expression is needed for DNA repair and neuronal survival; however, CDK6 overexpression may lead to the cell cycle reentry in postmitotic neurons resulting in apoptosis, which may contribute to neurodegeneration. CDK6 was earlier found to interfere with BCL2 effects on apoptosis, and with PPARGC1A effects on energy metabolism, which might contribute to observed GxG between these genes. We conclude that interactions among genes from biologically connected aging pathways may significantly influence AD risk. Uncovering such GxG effects has a potential to yield new genetic targets for AD prevention/treatment.

INTERGENERATIONAL TRAUMA TRANSMISSION? TEST OF CELLULAR AGING IN MOTHERS EXPOSED TO SEXUAL ABUSE AND THEIR CHILDREN

Laura Etzel,[1] Waylon Hastings,[2] Brooke Mattern,[2] Christine Heim,[3] Jennie Noll,[2] Frank Putnam,[4] Monica Oxford,[5] and Idan Shalev,[2] *1. Penn State University, University Park, Pennsylvania, United States, 2. Pennsylvania State University, University Park, Pennsylvania, United States, 3. Charite Universitatsmedizin Berlin, Berlin, Germany, 4. University of North Carolina, Chapel Hill, North Carolina, United States, 5. University of Washington, Seattle, Washington, United States*

Exposure to maltreatment during childhood can lead to increased risk for poor health outcomes in adulthood. Child maltreatment and later poor health may be linked by premature biological aging. We tested whether childhood sexual abuse (CSA) is associated with telomere length (TL) in adult females. We further tested the hypothesis of intergenerational transmission of trauma by measuring TL in both CSA-exposed and non-exposed mothers and their children. TL was measured in a subset of participants and their children from a prospective-longitudinal cohort study of sexually abused females and a demographically matched comparison group. Linear regression models were used to test for associations between CSA-exposure and age-adjusted TL in females (N=108, mean age 36.3 years). Multilevel linear models were used to test the intergenerational effect of maternal-CSA exposure on age-adjusted TL in their children (N=124 children mean age 10.5 years across 61 mothers). CSA-exposure was not associated with TL in females. Replicating previous work in this area, maternal TL and sex were significant predictors of child TL in all models tested. Longer maternal TL predicted longer TL in children, and female children had longer TL than male children. Maternal-CSA exposure did not predict TL in children. This finding is in line with some previous results on CSA and TL measured in adulthood. Previous significant results associating child maltreatment with shorter TL in adulthood may be capturing a population of individuals exposed to either multiple types of maltreatment or maltreatment in childhood with concurrent TL measurements.

METRICS OF PHENOTYPIC AGING FROM THE ENERGETICS PERSPECTIVE

Pei-Lun Kuo,[1] Michelle Shardell,[2] Jennifer Schrack,[3] Morgan Levine,[4] Eleanor Simonsick,[1] and Luigi Ferrucci[1] *1. National Institute on Aging, Bethesda, Maryland, United States, 2. University of Maryland School of Medicine, Baltimore, Maryland, United States, 3. Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States, 4. Yale University School of Medicine, New Haven, Connecticut, United States*

Identifying the most critical metrics of aging is an ongoing challenge due to a lack of comprehensive measurements and heterogeneity of the aging process. Using the Baltimore Longitudinal Study of Aging, we developed a conceptual framework to identify metrics of aging that capture the hierarchical and temporal relationships between functional aging, phenotypic aging, and biological aging based on four hypothesized domains: energy regulation, body composition, homeostatic mechanisms, and neurodegeneration. Focusing on the energetics domain, we examined trajectories of eight phenotypes using more than 10 years of longitudinal data. The standardized Cronbach's alpha for these variables was 0.80, providing construct validity of our concept. We further implemented item response theory to integrate these phenotypes into a summarized energy score. Linear mixed models were used to assess the cross-sectional and longitudinal associations between the summarized energy score and physical functioning as measured by gait speed and time to walk 400m as quickly as possible (number of participants ~ 811, number of observations ~ 1700). After adjusting for age, sex, weight, and height, a higher summarized energy score was independently associated with faster baseline gait speed (0.13 m/s, p<0.001) and faster 400m time (-35.3 seconds, p<0.001), and longitudinally associated with slower gait speed decline (0.08 m/s/decade, p<0.001) and slower 400m time increase (-37.8 secs/decade, p<0.001). This work demonstrates the utility of our energetics domain-based summarized score. Moving forward, it will be important to clarify relationships between this summarized score and other functional metrics and assess its generalizability to the other cohorts.

NEUTROPHIL-LYMPHOCYTE RATIO AND MORTALITY IN THE LONG LIFE FAMILY STUDY

Sithara Vivek,[1] Bharat Thygarajan,[1] Joanne M. Murabito,[2] Nicole Schupf,[3] Joseph Zmuda,[4] Jonas Mengel-From,[5] and Mary Wojczynski,[6] *1. University of Minnesota, Minneapolis, Minnesota, United States, 2. Boston Medical*