METHODS USED IN 'ALDH2*2 ASSOCIATION WITH LONGEVITY AND REDUCED RISK OF COGNITIVE DECLINE IN JAPANESE-AMERICAN MEN'

Anubhav Nikunj Singh Sachan,[1] Steven Edland,[1] Julia Chosy,[2] Lenore Launer,[3] Sudha Seshadri,[4] and Lon White,[2] *1. University of California San Diego, La Jolla, California, United States, 2. Pacific Health Research and Education Institute, Honolulu, Hawaii, United States, 3. National Institute on Aging, Bethesda, Maryland, United States, 4. UT Health San Antonio, San Antonio, Texas, United States*

ALDH2*2 is a loss of function mutation common in East Asian populations associated with facial flushing on exposure to alcohol and increased risk of certain cancers. Conversely, absence of the ALDH2*2 mutation is associated with increased risk of hypertension and cerebral microbleeds, and two recent studies report a higher frequency of ALDH2*2 alleles in nonagenarians compared to population control samples. We used survival analysis to investigate the association between ALDH2*2 and risk of cognitive impairment and death after controlling for midlife alcohol consumption and other covariates. Participants are 621 Japanese-American men (72 to 92) enrolled in the Honolulu Asia Aging Study (HAAS) and assessed for cognitive impairment for up to 20 years. Impairment was defined as crossing below a threshold score of 74 on the Cognitive Assessment Screening Instrument (CASI). Age at death was determined by Hawaii state death certificate. Ounces of ethyl alcohol consumed per month was assessed by structured interview (number, frequency, and type of beverage) conducted 25 years prior to baseline cognitive assessment. Persons heterozygous for the ALDH2*2 variant have reduced risk of cognitive impairment and reduced risk of death, compared to homozygote non-carriers. Covarying by alcohol exposure had no effect on observed associations. This study replicates previous findings associating ALDH2*2 with longevity, and provides evidence the protective effect extends to cognition. This poster details the statistical analysis carried out to obtain these results.

MTOR INHIBITION ALTERS MIRNA PROFILE IN CULTURED BONE MARROW MESENCHYMAL STEM CELLS

Lisa Stukenborg,[1] Manali Potnis,[2] and Christian Sell,[1] *1. Drexel University College of Medicine, Philadelphia, Pennsylvania, United States, 2. Drexel University, PHILADELPHIA, Pennsylvania, United States*

Progressive decline in adult stem cell function is a feature of aged tissues and contributes to multiple age-related diseases. Of particular interest are bone marrow mesenchymal stem cells, also known as bone marrow stromal cells (BMSCs), which are multipotent, and have significant therapeutic potential for age-related disease. BMSCs isolated from older individuals show decreased differentiation and characteristics of cell senescence. We and others find that inhibition of the mTOR pathway prevents senescence and extends BMSC proliferation. We have examined miRNA profiles in rapamycin-treated BMSCs to identify miRNAs that may be needed to maintain "stemness" and facilitate differentiation in this population in undifferentiated cell populations. The analysis reveals a distinct miRNA profile induced by rapamycin associated with enhanced differentiation capacity.

PLASMA BIOMARKERS OF ANGIOGENESIS RELATED TO SMALL VESSEL BRAIN DISEASE IN SPRINT

Nicholas Pajewski,[1] Fanny Elahi,[2] Joachim Ix,[3] Ilya Nasrallah,[4] Jason Hinman,[5] Lenore Launer,[6] Jeff Williamson,[1] and Donna Wilcock,[7] *1. Wake Forest School of Medicine, Winston-Salem, North Carolina, United States, 2. University of California San Francisco, San Francisco, California, United States, 3. University of California San Diego, La Jolla, California, United States, 4. University of Pennslyvania, Philadelphia, Pennsylvania, United States, 5. David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, United States, 6. National Institute on Aging, Bethesda, Maryland, United States, 7. University of Kentucky, Lexington, Kentucky, United States*

Meta-analyses incorporating the Systolic Blood Pressure Intervention Trial (SPRINT) have shown a reduced incidence of dementia with blood pressure lowering. However, mechanistic explanations for this effect are lacking, apart from slowed progression of cerebral white matter lesions (WML). Here we examine possible biomarkers of angiogenesis related to small vessel brain disease including bFGF, FLT1, PLGF, TIE-2, VEGF, VEGF-C, and VEGF-D. The biomarkers were assayed in plasma at baseline and during follow-up (median follow-up = 3.8 years) in a subgroup of participants 60 to 89 years old from SPRINT (N=517). We modeled changes in each biomarker using robust linear mixed models accounting for treatment group, time since randomization, and kidney function. Participants were 69.8 ± 7.1 (standard deviation) years of age, 42.1% female, with a mean systolic blood pressure (SBP) of 138.2 ± 17.0 mm Hg. At baseline, none of the biomarkers were associated with WML lesion volume or total brain volumes adjusting for age (all $p>0.05$), while FLT1, PLGF, and TIE-2 were negatively associated with frontal gray matter cerebral blood flow (partial correlations of -0.11, -0.10, and -0.12 respectively, all $p<0.05$). For both intensive (target SBP<120 mm Hg) and standard (target SBP<140 m Hg) blood pressure control, mean levels for the majority of biomarkers increased during follow-up, with the exceptions of TIE-2 (decreased over follow-up) and VEGF-D (no change). We did not observe significant between-group differences for the change in these plasma biomarkers of angiogenesis comparing intensive to standard blood pressure treatment.

SIRTUIN-1 ISOFORMS DIFFERENTIALLY REGULATE MITOCHONDRIAL FUNCTION

Xiaomin Zhang,[1] Fathima Ameer,[2] Jasmine Crane,[2] Gohar Azhar,[2] and Jeanne Wei,[2] *1. University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States, 2. UAMS, UAMS, Arkansas, United States*

Alternative splicing generates multiple distinct isoforms that increase transcriptome and proteome diversity. Alternatively spliced isoforms may lose part of the protein domain and have different intracellular localization as well as distinct functions. The main form of the SIRT1 (SIRT1v1) protein contains 11 exons. We have identified two new isoforms, SIRT1v2 (lost 2 exons), and SIRT1v3 (lost 3 exons), but their effect on mitochondrial gene expression has not been reported. To study the effect of the three SIRT1 isoforms on mitochondrial gene expression