shown to change during aging. Several "clocks" have been developed whereby changes in DNA methylation can be used to predict chronological, and perhaps, biological age. This symposium will focus on recent advances in understanding how and why changes in DNA methylation occur during aging and whether these changes play a causal role in age-related functional declines and disease.

A FUNCTIONAL EPIGENETIC CLOCK FOR RATS

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Evidence from humans suggests that incorporation of phenotypic aging measures in the development of epigenetic clocks leads to more functionally relevant biomarkers. As a result, the aim of this study was to utilize a deeply phenotyped rat cohort—that included data from rotarod, open field, frailty index, and FACS—to generate a novel epigenetic clock. DNA methylation was assessed via reduced representation bisulfite sequencing (RRBS) for n=142 male Fischer rats from NIA aging colony, ranging in age from 1 to 27 months. Phenotypic traits were combined to generate an multi-system aging measure that was then used to train the epigenetic clock. Using an independent validation sample, age-adjusted epigenetic clock measures were associated with numerous traits, including: open field time resting (p=0.005), open field time climbing (p=0.001), body weight (p=0.02), and rotarod max (p=0.04). In moving forward, it will be important to examine cross-species comparisons, longitudinal change, and functional enrichment.

LONGITUDINAL TRAJECTORIES OF EPIGENETIC CLOCKS IN HUMANS AND EFFECTS OF MEDICATION USE

Sara Hagg[1], *1. Karolinska Institutet, Stockholm, Sweden*

We sought to investigate the longitudinal trajectories of the new generation epigenetic clock´s and how medication use is altering the DNA methylation age (DNAmAge). DNA methylation (Illumina 450k and EPIC) was assessed repeatedly up to six times (1992-2014) in whole blood (597 individuals, 1469 samples) from the Swedish Adoption/Twin Study of Aging (SATSA). DNAmAges were generated with the online calculator. Mean age at first measurement was 67 years (58% women). All clocks tested (Horvath, Hannum, Pheno, Grim, Skin&Blood) were correlated with chronological age (ρ=0.62-0.80). The steepest slope was found for Pheno while Horvath had the least steep slope. Correlations between the clocks ranged ρ=0.43-0.75. About 15% of the individuals started statin treatment during the follow-up, which changed the slopes to be less steep. Co-twin control analyses were confirmatory. Different DNAmAges are strongly correlated with each other in a longitudinal perspective. Treatment effects may alter the slopes of the DNAmAges.

EPIGENETIC PREDICTORS OF LIFESPAN AND HEALTHSPAN

Ake T. Lu[1] and Steve Horvath[2], *1. Department of Human Genetics, University of California, Los Angeles, Los Angeles, California, United States, 2. Department of Human Genetics, UCLA, LOS ANGELES, California, United States*

Capturing aspects of biological age, DNA methylation based biomarkers collectively known as "epigenetic clock" can be used to measure the age of any human tissue, cell type, or fluid that contains DNA. Arguably the strongest predictor of lifespan, DNAmGrimAge, is a composite biomarker comprised of DNAm-based surrogates of plasma proteins and a DNAm-based estimate of smoking pack-years. Large-scale validation studies demonstrate that DNAmGrimAge stands out among existing epigenetic clocks when it comes to predicting time-to-death (P=2.0E-75), time-to-coronary heart disease (P=6.2E-24), and its strong relationship with computed tomography measures of fatty liver, and age-at-menopause (P=1.6E-12). DNAm-based estimates of plasma proteins and telomere length (TL) are attractive as well. For example, a DNAm based estimate of Plasminogen Activator Inhibitor 1 strongly relates to multi-morbidity and a DNAm based estimate of TL outperforms actual TL measurements in predicting lifespan. Overall, these epigenetic biomarkers are expected to find many applications including human anti-aging studies.

ROBUST BIOMARKERS OF AGING AND THEIR BIOLOGICAL ORIGIN

Dmitriy Podolskiy,[1] Dmitriy Podolskiy,[1] and Vadim Gladyshev[1], *1. Brigham & Women's Hospital, Boston, Massachusetts, United States*

The biological origin of impressive accuracy of DNA methylation clocks, the most precise currently available biological markers of aging in humans and model animals, remains largely unclear. In addition, they sometimes suffer from uncontrollable precision loss out of sample. To address these two issues, we develop a novel method for constructing robust molecular markers of age based on network analysis of age-dependent omics data. The newly developed robust markers of aging in yeast, fruit fly, mouse and human are nearly free of batch effects and have a transparent biological nature related to tight control of translation-related processes and their disregulation associated with aging.

SESSION 630 (SYMPOSIUM)

HARNESSING THE POWER OF A GERIATRIC EXERCISE NETWORK TO IMPROVE HEALTH: THE VA GEROFIT WAY

Chair: Katherine S. Hall, *Durham Veterans Affairs Health Care System, Durham, North Carolina, United States*
Discussant: Janet Prvu-Bettger, *Duke University School of Medicine, Durham, North Carolina, United States*

The Gerofit Consortium is a clinical and research network that naturally evolved from the dissemination of a VA "Best Practice" exercise and health promotion program for older Veterans. Originally developed in the Durham VA, Gerofit has been disseminated to 15 VA Medical Centers using a successful "collaboratory" team network approach. This group has met regularly (biweekly) for five years; starting with four newly disseminated programs in 2014 and adding 2-3 new programs per year since, following a structured implementation process. We have learned that the sum is much greater than the parts. Each program shares important experiences and contributes to development