perform drug screens, requires valid and reliable measures that can be applied in vitro. Christopher Minteer who developed in cellulo epigenetic markers will demonstarte how epigenetic aging changes that can be induced in culture shed light on aging in vivo. Finally, a summarizing discussion will be held by Dr. Morgan Levine, an expert in the field.

A COMPUTATIONAL SOLUTION TO BOLSTER EPIGENETIC CLOCK RELIABILITY FOR CLINICAL TRIALS AND LONGITUDINAL TRACKING

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Epigenetic clocks are widely used aging biomarkers, but they are calculated from methylation data for individual CpGs that can be surprisingly unreliable. We report that technical noise causes six major epigenetic clocks to deviate by 3 to 9 years between replicates. We present a novel computational solution: we perform principal component analysis followed by biological age prediction using principal components, extracting shared age-related changes across CpGs while ignoring noise from individual CpGs. Our novel principal-component versions of six clocks show agreement between most technical replicates within 1 year, and increased stability in short- and long-term longitudinal studies. This requires only one additional step compared to traditional clocks, does not require prior knowledge of CpG reliabilities, and can improve the reliability of any existing or future epigenetic biomarker. The extremely high reliability of principal component epigenetic clocks makes them particularly useful for personalized medicine and clinical trials evaluating novel aging interventions.

DEEP LONGITUDINAL PROTEOMICS PROFILING REVEALS BIOLOGICAL PATHWAYS RESPONDING TO GRF6019 IN TWO AD CLINICAL TRIALS

Benoit Lehallier,[1] Tibor Nanasi,[2] Jonas Hannestad,[2] and Steven Braithwaite,[2] *R&D, Alkahest, California, United States*

Blood has been widely investigated to discover biomarkers and gain insights into the biology of aging and age-related diseases. Its protein composition provides insights into complex biological processes, as proteins are often direct regulators of cellular pathways. In clinical trials, selected proteins have been used as primary and secondary endpoints, but recent methodological developments allow the measurement of thousands of proteins with very high sensitivity and specificity. In two phase 2 clinical trials testing the safety, tolerability, and feasibility of infusions of the plasma fraction GRF6019 in Alzheimer's disease (AD), we measured more than 7000 proteins in plasma over the course of the clinical trials. Differential trajectories analysis revealed groups of proteins and pathways that were responding to GRF6019. Several pathways were relevant to the biology of aging and AD and our study suggests that deep proteomics profiling can inform on specific biological processes responding to treatment in clinical trials.

LONGITUDINAL PROFILING IN PHENOTYPIC METRIC OF AGING: INSIGHTS FROM THE BALTIMORE LONGITUDINAL STUDY OF AGING

Pei-Lun Kuo,[1] Morgan Levine,[2] Jennifer Schrack,[3] Michelle Shardell,[4] and Luigi Ferrucci,[5] *1. National Institute on Aging, National Institute on Aging, Maryland, United States, 2. Yale University, New Haven, Connecticut, United States, 3. Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States, 4. University of Maryland School of Medicine, Baltimore, Maryland, United States, 5. National Institute on Aging, Baltimore, Maryland, United States*

It remains challenging to quantify the pace of aging across lifespan due to lack of comprehensive longitudinal measurements across wide range of age. In Baltimore Longitudinal Study of Aging, we have measured the longitudinal trajectories of more than 30 phenotypes across four pre-identified domain - body composition, energy regulation, homeostatic mechanisms and neurodegeneration/neuroplasticity, among participants with age between 20+ and 90+. We implemented a two-stage approach to summarize the longitudinal trajectories of these phenotypes across four domains into a summarized score. We demonstrated that higher summarized score (denoting for slower longitudinal phenotypic decline) is associated with slower decline in both cognitive and physical functions, across different stages of adulthood. Our results imply that deep longitudinal profiling contains rich information and may potentially replace diseases as an early endpoint in trials targeting at aging. Further, understanding the underpinning of longitudinal phenotypic trajectories may provide clues to the biological mechanisms of aging.

A DNAMCULTURE EPIGENETIC FINGERPRINT RECAPITULATES PHYSIOLOGICAL AGING

Christopher Minteer,[1] Marco Morselli,[2] Margarita Meer,[3] Jian Cao,[4] Sabine Lang,[5] Matteo Pellegrini,[6] Qin Yan,[5] and Morgan Levine,[5] *1. Yale University, Yale University, Connecticut, United States, 2. UCLA, Los Angeles, California, United States, 3. Yale School of Medicine, New Haven, Connecticut, United States, 4. Rutgers University, Rutgers University, New Jersey, United States, 5. Yale University, New Haven, Connecticut, United States, 6. UCLA, UCLA, California, United States*

Aging elicits dramatic changes to DNA methylation (DNAm), however the causes and consequences of such alterations to the epigenome remain unclear. The utility of biomarkers of aging based on DNAm patterns would be greatly enhanced if in vitro models existed that recapitulated physiological phenotypes such that modulation could garnish mechanistic insights. Using DNAm from serially passaged mouse embryonic fibroblasts, we developed a marker of culture aging and asked if culture phenotypes, like exhaustive replication, are epigenetically analogous to physiological aging. Our measure, termed DNAmCULTURE, accurately estimated passage number and was shown to strongly increase with age when examined in multiple tissues. Furthermore, we observed epigenetic alterations indicative of early cultured cells in animals undergoing caloric restriction and in lung and kidney fibroblasts re-programmed to iPSCs. This study identifies culture-derived alterations to the methylome as

physiologically relevant and implicates culture aging as an important feature in known epigenetic aging phenomena.

Session 1020 (Symposium)

AN EXPLORATION ON TRUST

Chair: Elena Portacolone

"Trust is a form of love," explained a study participant. As a form of love, trust nourishes connections and accelerates progress. As a result, the purpose of this session is to reflect upon the notion of trust and examine how trust moves science and social justice forward. Trust must be seen as sustained or broken over multiple generations. Moreover, trust between older adults and medical and social support institutions has profound implications for this historical moment. In the COVID-19 pandemic, trust can be viewed as a facilitator of emergency responses in the State of Washington as noted in Dr. Berridge's paper. On the other hand, distrust and a related sense of abandonment contributes to Black Americans' limited uptake of COVID-19 vaccinations, as noted in Dr. Johnson's work. On a related note, Dr. Perry's work shows that lack of trust over time has led those aging with hemophilia to withdraw from care at different points in their own trajectories. Finally, on a positive note, Dr. Kotwal's work illustrates the role of a peer outreach intervention in facilitating trusting relationships among diverse, low-income older adults which led to sustained reductions, over a 2-year period, in loneliness, barriers to socializing, and depression. This symposium on trust highlights how researchers work, either consciously or unconsciously, within a continuum of trust in their participants' communities. At a broader level, systemic attention to building trust from academia, government, and national advocacy organizations holds the potential to foster meaningful scientific engagement and empowerment of historically marginalized communities.

THE SIGNIFICANCE OF TRUST IN WASHINGTON STATE'S AGING NETWORK COVID RESPONSE

Clara Berridge,[1] Ian Johnson,[2] Callie Freitag,[1] Carolyn Parsey,[1] and Maggie Ramirez,[3] *1. University of Washington, Seattle, Washington, United States, 2. University of Washington, SEATTLE, Washington, United States, 3. University of Washington School of Public Health, Seattle, Washington, United States*

In late summer of 2020, we interviewed 45 senior leaders of social services and health care organizations serving older adults throughout Washington State about service demand, new challenges, and organizational adaptations. These organizations work with people made particularly vulnerable in the pandemic. A significant share reported that half or more of their clients live at or below the poverty line (54%), are people of color (29%), or have limited English language proficiency (20%). The state's aging network leveraged strong partnerships, expertise, and community knowledge to provide trusted essential services to older Washingtonians and their caregivers. The role of trust as an enabler of emergency response and connection in the context of gentrification, the digital divide, employment loss, and language service gaps will be discussed, as will lack of trust as a barrier to service access, particularly for Latinx immigrant and migrant older adults.

A PEER INTERVENTION FACILITATES TRUST AND IMPROVES PSYCHOSOCIAL WELL-BEING IN DIVERSE, LOW-INCOME OLDER ADULTS

Ashwin Kotwal,[1] Shannon Fuller,[1] Janet Myers,[1] Daniel Hill,[2] Soe Han Tha,[1] Alexander Smith,[1] and Carla Perissinotto,[1] *1. University of California San Francisco, University of California San Francisco, California, United States, 2. Curry Senior Center, San Francisco, California, United States*

We evaluate a peer outreach intervention to improve the psychosocial well-being of diverse, low-income older adults. Participants (N=74, Age 58-96 years) were recruited from an urban senior center and matched with peers who were >55 years old, received mental health training, and connected participants with health or social activities. We conducted surveys at baseline and 6-month follow-up for 2 years with validated measures of loneliness, social interaction, barriers to socializing, and depression, and thematically analyzed qualitative, semi-structured interviews conducted among a subset of participants (n=15) and peers (n=6). Participants were 58% male, 18% African-American, 19% Latinx, and 8% Asian. Over 2 years, participants experienced sustained reductions in loneliness ($p=0.015$), depression ($p<0.001$), and barriers to socializing ($p<0.001$). Qualitative interviews detailed the role of longitudinal relationships, program flexibility, and the matching process in facilitating trust, motivation, and improved mood. Results can inform larger efficacy studies and implementation of peer-driven community programs.

CHANGING TIME HORIZONS AND TRUST: EXPERIENCES OF AGING WITH HEMOPHILIA

Tam Perry,[1] and Sara Schwartz,[2] *1. Wayne State University, Detroit, Michigan, United States, 2. University of Southern California, Los Angeles, California, United States*

Trust among those who have experienced a lifetime of medical encounters warrants attention to how trust is both cumulative and complex. This study of a historically isolated cohort incorporates interviews (n=25 older adults/professionals) and focus groups uses a lens of trust to highlight the experiences of those aging with hemophilia, individuals who never expected to age. Understood through the lens of trust, the data show evidence of the absence of safe spaces particularly during the early 80s - blood contamination concerns and homophobia-leading often to social withdrawal. Over time, however, some individuals and families created trusted venues to begin demanding research, treatment and policy change. Advocacy re-engaged the community to organize, educate and advance safety protocols for blood product manufacturing and distribution. This presentation will illuminate how experiences with medical providers, contaminated blood supplies, stigma and uncertain in other spheres of one's life make trust a co-constructed, fragile concept.

FACTORS RELATED TO COVID-19 VACCINE UPTAKE IN BLACK AMERICAN COMMUNITIES

Julene Johnson,[1] Orlando Harris,[2] Carl V. Hill,[3] Peter Lichtenberg,[4] Sahru Keiser,[2] Tam Perry,[4] and Elena Portacolone,[5] *1. University California San Francisco, San Francisco, California, United States, 2. University of California, San Francisco, San Francisco, California, United*