CHRD 2022: Abstract & Poster Submission Form

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Presenter Status
- ○ Undergraduate Students
- ◉ Masters Student
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- ○ Residents
- ○ Non-Trainee

Research Category
- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

Role in the project
- ☐ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Title
A DNA methylation signature of frailty and associations with epigenetic age in postmenopausal women

Background

Frailty is a collection of deficiencies in coping with daily life that tends to increase with age, making it a meaningful predictor for disease and mortality in clinical settings. Similarly, epigenetic age (eAge) measured using DNA methylation (DNAm) has been shown to capture the physiological dysregulation that often precedes disease and mortality as we age.

Objective

Since frailty is reportedly highest in postmenopausal women, we wanted to examine whether eAge and whole blood DNAm are associated with frailty-related deficits in the WARMHearts cohort.

Methods

Using the Illumina EPIC microarray for DNAm characterization and a 42 deficits frailty index, we analyzed genome-wide DNAm for frailty-associated loci and compared eAge outputs from the DNAmPhenoAge clock with frailty severity in a case-control study of 56 WARMHearts participants.

Results

We found significant (FDR < 0.05, Δβ > 0.01) changes in DNA methylation at 7 loci including 4 genes. The frailty deficits that most contributed to differential DNAm were blood lipids, body composition, diabetes and self-care. Epigenetic age from the DNAmPhenoAge clock was highly correlated ($r = 0.712$, $p < 0.00001$) with chronological age. Age acceleration, defined as the regularized deviation between chronological and epigenetic age, was marginally higher ($p = 0.0807$, $d = 0.476$) in frail participants. On the other hand, participants with positive age accelerations scored 43% higher in frailty than participants with negative age accelerations ($p = 0.0332$, $d = 0.585$).

Conclusion

Taken together, these results indicate that age acceleration is associated with frailty through a decrease in psychosocial wellness and changes in metabolic systems. Our findings suggest that, while ongoing experiments will be necessary to establish a mechanistic link between epigenetic age acceleration and frailty, we can continue to target physical activity and mental health for folks with a faster rate of aging to reduce frailty-related burdens in later life.

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Authors

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