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Epigenetic Age and Depressive Symptoms in African American Women with Cardiometabolic Conditions

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OBJECTIVES/GOALS: To examine the relationship between epigenetic age acceleration (EAA) and depressive symptoms in a cohort of African American women (AAW) with cardiometabolic conditions (CMC) including hypertension, diabetes, obesity; and to explore clinical phenotypes of depressive symptoms in this population. METHODS/STUDY POPULATION: This secondary analysis utilized genomic and longitudinal clinical data from AAW in the InterGEN cohort (n = 250). EWAS data was used to estimate EAA based on the Horvath method, which incorporates the DNA methylation statuses at 353 specific CpG sites and regresses this epigenetic age on chronological age to determine EAA. Pearson's correlations and linear regression will be used to examine the relationship between EAA and depressive symptoms and a linear mixed model will investigate this relationship over four time points during a two-year period. Clinical phenotyping of depressive symptoms will be explored using a cluster analysis. RESULTS/ANTICIPATED RESULTS: Analysis is underway and will be complete by the time of presentation. We hypothesize that higher EAA will associate with higher depressive symptoms and poorer trajectories over time. We expect that this relationship may be meditated by the presence of CMCs. Exploratory analysis of clinical phenotyping is expected to provide descriptive evidence with respect to specific depressive symptoms or clusters which are most associated with EAA and CMCs. These results will address several gaps. To our knowledge, this is the first study to examine the relationship of EAA and depressive symptoms considering the role of CMC, in a historically understudied population with disproportionate risk. DISCUSSION/SIGNIFICANCE OF IMPACT: Depression limits life quality and quantity and is highly comorbid in CMC. AAW have high risk of comorbidity, and this study furthers knowledge of depression and aging with a clinically accessible marker and aids recognition of a heterogenous phenotype in an undertreated population.

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Establishment of Screening Methods for G6DP Deficiency – Translational and Clinical Applications

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OBJECTIVES/GOALS: To develop feasible screening methods for activity of the enzyme Glucose-6-phosphate dehydrogenase (G6PD) with point of care applicability. METHODS/STUDY POPULATION: Current knowledge establishes the relevance of G6PD as a critical therapeutic determinant for effective antimalarial therapy due to the occurrence of mutations that lead to post-treatment severe adverse effects. We present our findings on development of cost effective point-of-care screening methodologies to ascertain G6PD deficiency. RESULTS/ANTICIPATED RESULTS: Using Patient Cohort Explorer and data from the Department of Pathology, we established the prevalence of G6PD deficiency at the University of Mississippi Medical Center, Jackson, MS as high as 11.8% (African-American males in all population, n = 2518). Next, for selection of potential target groups, we set up a protocol for recruitment of volunteers based on ethnic background, parental ethnicity, and medical history. G6PD activity was evaluated using point of care methods [Trinity Biotech test or CareSTART Biosensor], and Gold Standard quantitative spectrophotometric assay (LabCorp). Determinations in >20 subjects have showed comparable concordance. If used with a conservative interpretation of the signal, the Trinity Biotech test showed superior potential for use in the field relative to the CareSTART Biosensor. DISCUSSION/SIGNIFICANCE OF IMPACT: We established the prevalence of G6PD deficiency in our medical center. We have also setup tests for point-of-care assessment of G6PD. Pending evaluation of the relative tests performance, we will be in position to screen individuals and select them for a prospective clinical trial to evaluate the safety of antimalarial agents on scope of G6PD deficiency.

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European Ancestry as a Risk Factor for Atrial Fibrillation in Puerto Rican Hispanics

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OBJECTIVES/GOALS: Atrial fibrillation (AF) not only is the most common sustained cardiac arrhythmia in clinical practice placing patients at increased risk for thromboembolic events. Hispanics despite having a higher risk factor burden for developing AF have a lower overall incidence and prevalence of AF when compared to Non-HispanicWhites (NHW). European ancestry in the African American population was found to be an independent predictor for developing AF. Consequently, we have decided to evaluate if European ancestry is an independent risk factor for Puerto Rican Hispanics(PRH) METHODS/STUDY POPULATION: This project is a secondary analysis of a Puerto Rican population sample (n = 250) fromThePharmacogenetics of Warfarin in Puerto Ricans StudyandAGenomic Approach for Clopidogrel in CaribbeanHispanics; and1000GenomeProject to establish a control group of healthy PRH population. We will evaluate the presence of 111 known single nucleotide polymorphisms(SNP)associated with AF Europeans and determine the frequency in PRH population sample.Using admixture informatic markers (AIM) analysis will determine the percentage of admixture. Statistical analysis will include the use of Pearson Product-MomentCoefficient correlation analysis and multivariate regression. For admixture will use Maximum LikelihoodEstimation Markov Chain Monte Carlo models RESULTS/ANTICIPATED RESULTS: We anticipate that higher-frequency of AF associated European SNPs and overall higher percentage of European admixture will be associated with atrial fibrillation in PRH patients. DISCUSSION/SIGNIFICANCE OF IMPACT: The expected outcomes for this study are to identify the frequency of known genetic loci associated with AF Europeans and validate their use PRH population for machine learning risk factor models.

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