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VASCULAR DISEASE

GENOME-WIDE ASSOCIATION OF CORONARY ARTERY DISEASE

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Session Title: Biomarkers and Vascular Disease 3 Abstract Category: Vascular Biology/Atherosclerosis/Thrombosis/Endothelium Presentation Number: 1272-340

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Background: Coronary heart disease is the leading cause of death in the United States, with atherosclerosis of the coronary arteries being the major underlying etiology. Patients with atherosclerotic coronary artery disease (CAD) are more likely to suffer a myocardial infarction or sudden cardiac death. CAD is heritable, but our knowledge of the genetics underlying CAD is incomplete. To further determine the genetic etiology of anatomic CAD, we are performing a genome-wide association study of anatomic coronary artery disease in an ethnically and racially diverse subject population. Our preliminary dataset consists of 650 cardiac catheterization patients.

Methods: A CAD burden index was calculated for each subject based on severity and location of their coronary lesions. Data were generating using the Affymetrix SNP array 6.0 platform for 900,000 SNPs. Extensive quality controls tests were performed to ensure the integrity of the data, including Eigenstrat methods to correct for population substructure. We tested for association using linear regression using the PLINK software package, and included smoking, cholesterol, blood pressure, age, sex, and two vectors describing the population substructure of the sample.

Results: We detected strong association (p < 0.00001) on 14 different chromosomes, in 10 different genes. Among these are the largely uncharacterized PRUNE homologue gene on chromosome 1 (p-value = 8 x 10-7) and citron (rho-interacting, serine/threonin kinase 21) gene on chromosome 12.

Conclusions: These data provide promising results that may lead to further insights into the genetics of anatomic coronary artery disease. Expansion of our dataset is ongoing.