ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #: 491

1.a Full title: E Selectin S128R Polymorphism and the Occurrence of Atherosclerosis and Incident CHD.
1.b. Abbreviated title: E selectin, Atherosclerosis and CHD
2. Writing group:
   Lead: Eric Boerwinkle
   Address: Human Genetics Center
   University of Texas - Houston Health Science Center
   PO Box 20334
   Houston, TX 77225
   Phone: 713-500-9816 Fax: 713-500-0900

   Shih-Jen Hwang     Christie Ballantyne     Richey Sharrett     Lou Smith

Time line: Data collection is complete; analysis and manuscript preparation remain.

Rational: E-selectin is expressed on vascular endothelium, and is involved in the process of leukocyte migration into inflammatory cites. We have previously shown that elevated plasma Eselectin levels are associated with increased carotid artery wall thickness. An amino acid substitution in E-selectin at codon 128 (S 128R) has been reported to alter ligand binding and to be associated with early onset CHD.

Main issues / Hypotheses to be addressed: Ability of the S 128R polymorphism to predict carotid artery disease: case status (as measured by wall thickness), both individually and after considering the predictive ability of traditional risk factors. Note: Inclusion of the Black supplement should permit adequately powered analyses in both Blacks and Whites for this hypothesis.
Ability of the S 128R polymorphism to predict PAD case status (as measured by wall thickness), both individually and after considering the predictive ability of traditional risk factors.
Ability of the S 128R polymorphism to predict incident CHD case status, both individually and after considering the predictive ability of traditional risk factors.
Data: The simultaneous batch minus the MRI cases will be used for these analyses. The primary dependent variable is incident CHD case status. However, the results from incident CHD status will be compared to those obtained from the analysis of carotid artery wall thickness and PAD. Independent variables include, but are not limited to the E-selectin polymorphism and the vector of traditional risk factors, such as age, sex, BMI,
plasma lipids, hypertension status, etc.