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1. Full title: Lipoprotein lipase gene variation predicts the occurrence of atherosclerosis, PAD and Incident CHD.
   Abbreviated title: LPL, Atherosclerosis, PAD and CHD

2. Writing group:
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3. Timeline:
   Measurement of LPL gene variation is nearly complete. Analyses will be carried out during March and April with a first draft of the paper in May.

4. Rationale:
   Lipoprotein lipase (LPL) is the rate-limiting enzyme in the lipolysis of triglyceride-rich lipoproteins. Multiple studies have now shown that the Asn291Ser mutation and Ser447Stop truncation mutations are associated with altered HDL-cholesterol and triglyceride levels and the occurrence of CHD in cross-sectional case-control studies. The Framingham study has reported that LPL DNA variation is associated with the onset of incident CHD. We propose to examine the association of these two LPL polymorphisms with carotid artery wall thickness, PAD, and incident CHD using the ARIC study's 3-group, CRS, African-American, PAD and CHD supplement case-control groups.

5. Main Issues/Hypotheses to be Addressed:
   a. Ability of the Asn291 Ser mutation and Ser447Stop truncation mutations 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.
   b. Ability of the Asn291Ser mutation and Ser447Stop truncation mutations to predict PAD case status (as measured by a reduced ankle-arm index), both
individually and after considering the predictive ability of traditional risk factors.
c. Ability of the Asn291 Ser mutation and Ser447Stop truncation mutations to predict incident CHD case status, both individually and after considering the predictive ability of traditional risk factors.

6. Data:
ARIC’s 3-group, CRS, African-American, PAD and CHD supplement case-control groups 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 Q analysis of carotid artery wall thickness and PAD. Independent variables include, but are not limited to the LPL polymorphisms and the vector of traditional risk factors, such as age, sex, BMI, plasma lipids, hypertension status, etc.