1. Title:
Diabetes and Lp(a)

2. Writing Group:
(lead) S.A. Brown, E. Boerwinkle, W. Patsch
Field Center Representative: Aaron Folsom
Project Officer Representative: Paul Sorlie

3. Timeline:
Initial data examination can be performed immediately.

4. Rationale:
Lp(a) represents a broad class of particles which contains apoB-100-apo(a) as the protein moiety. A positive relationship exists between apo(a) size, Lp(a) density and, possibly, Lp(a) pathogenicity in humans. Apo(a) is known to be heavily glycosylated (308 by weight) and its heterogeneity in size and charge may be affected by changes in the carbohydrate composition. The majority of the Lp(a) particles consists of a cholesteryl ester-rich core. However in the postprandial state, apoB-100-apo(a) was found to be associated with triglyceride-rich lipoproteins.

Lp(a) levels have been described in a number of clinical studies in diabetic subjects. One cross-sectional study has shown median Lp(a) concentrations twice as high in insulin dependent patients with microalbuminuria as in those patients without microalbuminuria. Additional data for elevated Lp(a) levels in insulin-dependent patients were reported in both black and white children. Increased levels of Lp(a) were associated with hyperglycemia. In addition, Lp(a) levels may be influenced by dietary control in diabetic subjects.

It would therefore be of interest to investigate the influence of carbohydrate control on Lp(a) levels in ARIC participants. ARIC participants with either high glucose or insulin levels will be identified and the relationship to Lp(a) will be ascertained. We propose to examine the following questions related to Lp(a) and diabetes: 1) are elevated levels of Lp(a) in ARIC participants associated with family history of diabetes; 2) does dietary therapy for diabetes influence Lp(a) levels; and 3) do oral anti-diabetic medications effect Lp(a).

We would like to discuss Lp(a) in relationship to glucose control in the ARIC cohort and examine effects of medical history, dietary therapy and medication regimens which greatly exceeds the scope of manuscript 125. We propose to use endogenous insulin levels to verify or supplement the glucose data as indicators of carbohydrate control. We will not report associations and interactions of endogenous insulin levels.
5. Main Hypothesis/Issues to be Addressed:
1) What is the association of Lp(a) to carbohydrate control as defined by serum glucose levels?
2) Are elevated levels of Lp(a) in ARIC participants associated with family history of diabetes?
3) What are the associations of dietary therapy for diabetes on Lp(a)?
4) What are the associations of oral antidiabetic medications on Lp(a)?
5) What are the associations of insulin on Lp(a)?

6. Data Requirements:
Data analysis will be performed at the Baylor College of Medicine, Department of Medicine. Variables required are: all plasma lipid measurements, glucose, insulin, hemostasis data, Lp(a) phenotype data, medical history, body mass index, medication use, reproductive history, diabetes, blood pressure, smoking status, alcohol consumption, physical activity, gender, race, age, field center, and average and maximum far wall thickness at the common and internal carotid artery and its bifurcation.