1. Title:
Relationship between LDL-size and response to a high fat meal

2. Writing Group:
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3. Timeline:
Data for this proposal have already been collected, computerized and await further analysis.

4. Rationale:
Circulating plasma LDL particles are typically defined as those between 1.025 and 1.063 g/ml, but there is variability within this class of lipoproteins defined by both diameter and density. Using gradient gel electrophoresis two predominant LDL morphs are detected, a large buoyant particle known as pattern A and a small dense particle known as pattern B. The frequency of pattern B is increased in those with coronary heart disease. Several factors are known to influence LDL-size including menopause and insulin resistance, but a primary determinant is genes. Genetic analyses have determined that LDL-size is influenced by a single gene with a large effect, but the identity of this hypothesized gene remains unknown.

Many of the processes that may influence LDL-size and vice versa (i.e. many processes that LDL-size may influence) are also contributors to the extent and duration of postprandial response. These processes includes the action of lipoprotein lipase, the transfer of lipid among lipoprotein particles and the half-life of circulating apo B-containing particles of hepatic origin. Likewise the extent and duration of postprandial lipemia may influence LDL-size directly. This analysis will determine the relationship between LDL-size and the profile of the post-prandial response in the ARIC study.

5. Main Hypothesis/Issues to be Addressed:
a) The profile of post-prandial triglyceride and retinyl palmitate response will be different among individuals grouped according to LDL-size.

b) The relationship between LDL-size and post-prandial response will be the same in both cases and controls.

c) The relationship between LDL-size and post-prandial response is independent of the well-known relationship between LDL-size and fasting lipid levels.

6. Data Requirements:
Statistical analyses will be done by Eric Boerwinkle.

Data from ARIC Visit 1, the post-prandial lipemia study, and the matched case-control study will be used for this proposed analysis. The necessary variables include: cholesterol, triglycerides (time 0, 1, and 2),
HDL-cholesterol, HDL2-cholesterol, HDL3-cholesterol, LDL-cholesterol, apo AI, apo B, triglycerides in the top fraction (time 0, 1, and 2), retinyl palmitate (time 0, 1, and 2), apo B-48 (time 0, 1, and 2) apo B-100 (time 0, 1, and 2), LDL apo B, Lp(a), hemostatic factors, alcohol consumption, smoking status, physical activity, lipid lower drug use, diabetes status, diabetes medication, hypertension status, race, gender, age, BMI, carotid artery wall thickness, case/control status and matching information (Note, the central lipid laboratory are kept "blind" to this information), ethanol consumption, glucose, and insulin.