ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #022

1. Title (length 26):
Lp(a) Polymorphs

2. Writing Group (list individual with lead first):
(lead) J.W. Gaubatz, J.D. Morrisett, W. Patsch et al.

3. Timeline:
All analysis have been performed and a rough draft of the paper has been written.

4. Rationale:
Apo(a) is a human apolipoprotein that occurs in several Mr polymorphs. Utermann et al resolved six polymorphs allegedly resulting from six alleles at a single locus. This study also suggested that these alleles determine the plasma concentration of apoLp(a). Dr. Morrisett and coworkers have greatly refined the methodology to separate and quantify apo(a) polymorphs. They can identify 11 (eleven) polymorphys distinguished by their apparent molecular weight in sodium dodecylsulfate polyacrylamide gels. The purpose of this study is to report the improved resolution of apo(a) molecular weight polymorphs, the abundance of the resulting phenotypes, and to analyze their mode of inheritance. There is intense scientific interest in the relationship of apo(a) and its polymorphs to plasm lipid transport and CHD. In fact, the Lipid Working Group of ARIC recommended to include apo(a) phenotyping in cases and controls.

5. Main Hypothesis:
1. Description of apo(a) polymorphs.
2. Apo(a) phenotypes are not the result of simple Mendelian inheritance. This is tested in family studies. In addition, the frequency of apo(a) phenotypes observed in populations is compared with the frequency predicted from simple Mendelian inheritance.

6. Data (variables, time window, source, inclusions/exclusions):
Apo(a) phenotypes were determined in local families and some 600 random ARIC samples. It should be stressed that ARIC samples were used because Lp(a) concentrations were available for these samples. Analyses were performed in the aliquots reserved for Lp(a) measurements. Furthermore, the source of samples was not critical for our analyses and any other population or set of samples could have been used to answer our questions. However, for completeness of data presentation, we would need a description of the subjects used with respect to age, sex, and race. For this purpose, we would send to the Coordinating Center the ARIC-ID numbers of samples used. No further analyses or service by the Coordinating Center would be necessary. For completeness, we also would like to include correlation of apo(a) phenotypes with lipids and apolipoproteins. As expected and previously published by us and others for Lp(a), we found very weak correlations with plasma apoB levels ($r = 0.090$, $p < 0.05$), plasma cholesterol ($r = 0.158$, $p < 0.001$), and triglyceride ($r = -0.091$, $p < 0.05$) in the specimens used for analysis.