1.a. Full Title: Association of ApoL1 variants with plasma lipids in African-Americans

b. Abbreviated Title (Length 26 characters): ApoL1 and plasma lipids

2. Writing Group:
   Writing group members:
   Myriam Fornage, Eric Boerwinkle, Tom Mosley, Christie Ballantyne, Ron Hoogeveen, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _MF_ [please confirm with your initials electronically or in writing]

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3. Timeline:
   Dec. 2010

4. Rationale:
   High-density lipoprotein (HDL) constitutes a heterogeneous population of particles with multiple biological functions. In plasma, Apolipoprotein L1 (ApoL1) is associated with large ApoA1-containing HDL particles. The ApoL1-containing HDL subfraction has been shown to play a key role in innate immune defense against some parasite infections. ApoL1 protein levels have been positively associated with plasma triglycerides (TGs) in both normolipidemic and dyslipidemic subjects. Recently,
functional variants of the ApoL1 gene have been identified in African-Americans and have been shown to influence risk of kidney disease in this ethnic group. The association of ApoL1 variants with variation in plasma lipids in this population has not been investigated.

We propose to address the following hypotheses:

5. **Main Hypothesis/Study Questions:**

Variants of the ApoL1 genes (S342G, I384M and delN388) are associated with baseline plasma lipids, including HDL, LDL, and triglycerides in African-Americans.

Variants of the ApoL1 genes are associated with change in plasma lipids, including HDL, LDL, and triglycerides in African-Americans.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

Exclusion: non-fasting at least 8 hrs.

Single SNP and haplotype effects will be evaluated. Linear regression and linear mixed models will be used to evaluate the association of ApoL1 genetic variation with baseline plasma lipids and longitudinal change in lipid levels. Analyses will adjust for age, sex, center, and African ancestry. Further adjustment for BMI, smoking, diabetes status, lipid lowering medication will also be performed.

Sensitivity analyses excluding participants on lipid lowering medication will also be carried out.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes __X__ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? ____ Yes ____ No

(This file ICTDER03 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? __X__ Yes ____ No

b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? __X__ Yes ____ No
9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

___X___ Yes _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)? None.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ___ Yes ___X__ No

11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number* _________)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _________ _________ _________)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire. Agree