ARIC Manuscript Proposal # 1842

PC Reviewed: 9/13/11  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Candidate SNPs and Venous Thromboembolism in African Americans: LITE

b. Abbreviated Title (Length 26 characters): SNPs & VTE in Blacks

2. Writing Group:
   Writing group members: Kazumasa Yamagishi, Weihong Tang, Nathan Pankratz, Mary Cushman, Jim Pankow, Susan Heckbert, Pam Lutsey, Nick Smith, Saonli Basu, Aaron Folsom

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

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
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4. Rationale:
The CHARGE GWAS working group on venous thromboembolism (VTE), led by Weihong Tang, has found several SNPs related to VTE in whites. The genes include Factor V, ABO, Factor 11, and a few others. The GATE study has reported F11 and RGS7 SNPs associated with VTE in a case control study of African Americans (Austin H et al. J Thromb Haemost 2011;9:489-95), and these warrant replication.

One stated aim of the LITE study renewal was to relate VTE SNPs identified by GWAS in whites to VTE in African Americans (n=220). Although statistical power may be limited, we will do this analysis and consider pooling with the few other studies of VTE in African Americans to enhance power.

5. Main Hypothesis/Study Questions:

Do several candidate SNPs related to VTE (from CHARGE and GATE) also associate with VTE 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).

Design: cohort—pooled ARIC and CHS samples (LITE study)

Inclusions: African Americans with SNP data and approval to use DNA. We will not exclude people with prior VTE for this analysis.

SNP data: Measured (or imputed, if necessary and available) SNPs will come from the ARIC GWAS genotyping files. The final set will include the SNPs mentioned above plus a few more identified by the GWAS in whites.

Outcome: validated VTE in LITE

Covariates: baseline age, sex, BMI, smoking, field center, and the first 10 principal components derived from EIGENSTRAT analysis of the AA GWAS data to adjust for population stratification.

Analysis: Examine frequencies of SNPs. Test Hardy-Weinberg equilibrium. Use standard cohort study analysis methods (e.g., Cox models) relating frequencies of risk alleles to occurrence of VTE.

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

8.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.csc.unc.edu/ARIC/search.php](http://www.csc.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)?  

#1535: Genome Wide Association Study (GWAS) for Venous Thromboembolism

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

11.b. If yes, is the proposal  
**x**  A. primarily the result of an ancillary study (list number 1998.03)  
____  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.csc.unc.edu/aric/forms/](http://www.csc.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.