ARIC Manuscript Proposal # 1860

PC Reviewed: 10/11/11	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: A gene-centric association study of activated partial thromboplastin time (aPTT): the ARIC Study (for CARe-VTE R01, PI: Weihong Tang)

b. Abbreviated Title (Length 26 characters): CARe IBC SNPs and aPTT

2. Writing Group:

Writing group members: Weihong Tang, Mary Cushman, James Pankow, Saonli Basu, Nena Matijevic and Aaron Folsom (other coauthors from ARIC and LITE are welcome)

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

First author: Weihong Tang

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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).

Name: **Aaron Folsom**
Address:

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3. Timeline: Begin 10/2011

4. Rationale:

I have received an R01 award from NIH, titled "Genetic Epidemiological Study of Venous Thromboembolism and Hemostatic Factors" (R01 HL095603), which aims to utilize the CARe candidate gene resources to understand the genetic determinants of VTE

in LITE and coagulation intermediate phenotypes in CARe cohorts including ARIC. The project period is 8/20/09-5/31/13. Activated partial thromboplastin time (aPTT) is one of the intermediate phenotypes proposed in the R01 and it is only available in ARIC among CARe cohorts. Therefore, it does not belong to CARe (aPTT data was not submitted to CARe). This MS proposal serves to cover the analysis of aPTT proposed in this R01. The ARIC ancillary study ID# for this R01 is 2008.08.

5. Main Hypothesis/Study Questions:

Genetic variants in cardiovascular-related candidate genes are associated with aPTT, the functional index of coagulation pathway.

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: Cross-sectional analysis for aPTT in ARIC. Both Caucasians and African Americans will be included and analyzed separately.

Inclusions: all participants with CARe IBC SNP data and approval to use DNA.

SNP data: CARe IBC SNPs in ARIC.

Outcome: plasma levels of aPTT in ARIC.

Covariates: Basic adjustment includes baseline age, sex, and field center. Principal components derived from EIGENSTRAT analysis of GWAS data will be added if the outcome variable is influenced by population stratification. BMI, smoking, and diabetes will be additionally adjusted for in secondary analyses.

Analysis: Analysis will be stratified by race. Examine frequencies of SNPs. Test Hardy-Weinberg equilibrium. Linear regression models will be used to relate frequencies (dosages) of alleles to aPTT levels.

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

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.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)?

#1438: Genome-wide Association Study of Activated Partial Thromboplastin Time (aPTT) and Protein C – the ARIC Study

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 and 2008.08**)**

___ 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.

Yes.