ARIC Manuscript Proposal # 1427

PC Reviewed: 09/09/08 **Status: A** **Priority: 2**
SC Reviewed: _________ **Status: _____** **Priority: ____**

1.a. Full Title: Meta-analysis of genome-wide association data in relation to C-reactive protein (CRP) concentrations in white adults of European descent: CHARGE Consortium

b. Abbreviated Title (Length 26 characters): **CRP, GWAS, meta analysis, CHARGE**

2. Writing Group:
Writing group members:
Vijay Nambi MD
Maja Barbalic PhD
Christie M Ballantyne MD
Eric Boerwinkle PhD
Ron C Hoogeveen PhD
Aaron R Folsom MD
James Pankow PhD
Wei Sun PhD

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

F**irst author**: **Vijay Nambi**
Address: 6565 Fannin Street
STE B 160/MS-A601
Houston, TX 77030

Phone: 713-798-7545 Fax: 713-798-7885
E-mail: vnambi@bcm.tmc.edu

Corresponding/senior author (if different from first author correspondence will be sent to both the first author & the corresponding author):
Address:

Phone: Fax:
E-mail:

3. Timeline: All genotyping is complete. Analysis to begin immediately.

4. Rationale: C-reactive protein (CRP) is a marker of inflammation that has been associated with cardiovascular disease (both coronary heart disease and stroke). High CRP levels have been shown to improve CHD risk prediction and in fact are currently being evaluated as a target for statin therapy. With the availability of genome-wide collection of single nucleotide polymorphisms, it is now possible to identify the genes responsible for inter-individual variation in CRP levels and to, perhaps, contribute to the understanding of mechanisms leading to CHD

5. Main Hypothesis/Study Questions:

Hypothesis: Investigate the association of genome-wide genetic variation with inter-individual variation in CRP levels in adults of European ancestry

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).

General Analysis Approach:
Subjects: European/European-American subjects with CRP levels available
Exposure: 2.5 million HapMap genetic variants identified in CEPH trios
Outcome: CRP levels
Exclusions: those without consent for genetic research, no available CRP levels
Primary statistical approach: Additive linear regression model (1 df) with robust variance estimates adjusted for sex, age
Meta-analysis: all resulting p-values
Validation and Replication: Possible validation genotyping for selected findings; correlation of findings
with those from existing databases
Major Phenotypes to Analyze: CRP levels
Cohorts Included in Analysis: CHS, FHS, Rotterdam, and ARIC

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 personswith a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNAanalysis RES_DNA = “CVD Research” would be used? ____ Yes ____ No

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 CoordinatingCenter must be used, or the file ICTDER03 must be used to exclude those with valueRES_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.
___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)?

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
_ A. primarily the result of an ancillary study (list number*_2006.03 (Stampede, genotyping in Caucasians)))

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.**