ARIC Manuscript Proposal # 1411

PC Reviewed: 07/30/08 **Status: A** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Meta-analysis of genome-wide association data in relation to circulating monocyte chemoattractant protein-1 concentrations in white adults of European descent: CHARGE Consortium

b. Abbreviated Title (Length 26 characters): Mcp1 Meta-analysis of GWAS data in Whites

2. Writing Group:
Ron C. Hoogeveen, Alanna Morisson, Christie Ballantyne, Maja Barbalic, Gerardo Heiss Josef Coresh, plus authors from other cohorts

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __EB__ **[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).

Name: Christie Ballantyne
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3. Timeline: All genotyping is complete. Analyses to begin immediately.

4. Rationale: Monocyte chemoattractant protein-1 (MCP-1) has been suggested to play a key role in atherosclerosis, peripheral arterial disease and coronary heart disease (CHD) (Hoogeveen et al 2005). MCP-1 is a member of the CC chemokine family and acts through promoting recruitment of inflammatory cells. MCP-1 concentration is heritable and a recent report found significant linkage to MCP 1(Dupuis J et al 2005). 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 MCP-1 concentration and to contribute to the understanding of mechanisms leading to CHD.

5. Main Hypothesis/Study Questions: Investigate the association of genome-wide genetic variation with inter-individual variation in MCP-1 concentrations 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 MCP-1 data available

Exposure: 2.5 million HapMap genetic variants identified in CEPH trios

Outcome: MCP-1 concentration

Exclusions: those without consent for genetic research

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: MCP-1 concentration

Cohorts Included in Analysis: CHS, FHS, Rotterdam, and ARIC

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

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. ___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

_X_ A. primarily the result of an ancillary study (list number* _2006.03_)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

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.

Reference

Hoogeveen RC, Morrison A, Boerwinkle E, Miles JS, Rhodes CE, Sharrett AR, Ballantyne CM. Plasma MCP-1 level and risk for peripheral arterial disease and incident coronary heart disease: Atherosclerosis Risk in Communities study.
Atherosclerosis. 2005 Dec;183(2):301-7.

Dupuis J, Larson MG, Vasan RS, Massaro JM, Wilson PW, Lipinska I, Corey D, Vita JA, Keaney JF Jr, Benjamin EJ: Genome scan of systemic biomarkers of vascular inflammation in the Framingham Heart Study: evidence for susceptibility loci on 1q. Atherosclerosis 2005, 182:307-314.