ARIC Manuscript Proposal # 1750

PC Reviewed: 2/8/11	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: The prevalence of anti-HMGCR autoantibodies in patients with and without statin exposure.

b. Abbreviated Title (Length 26 characters):

2. Writing Group:

Writing group members: Andrew Mammen, Elizabeth Selvin, Joe Coresh, Emma Williams, and others welcome.

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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3. Timeline: We expect these studies to be completed and a manuscript submitted during the 2011 calendar year.

4. Rationale: Antibodies recognizing HMG-CoA reductase (HMGCR) have been found in patients with an autoimmune myopathy, many of whom have been statin-exposed. The prevalence of these autoantibodies in the general population has not been determined.

5. Main Hypothesis/Study Questions: We will determine the prevalence of anti-HMGCR antibodies in a general population of persons with and without statin exposure. This will be the first descriptive epidemiologic study of this novel autoantibody. We will describe the distribution and basic correlates of the presence of anti-HMGCR autoantibodies in the ARIC CARMRI study population.

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).

Overview: Under ancillary study number 2010.10, "waste" serum samples from Dr. Selvin's Glycemic Markers Ancillary Study Pilot Project, which utilized serum samples from the ARIC carotid MRI subsample. The leftover samples are currently being tested by ELISA for the presence of anti-HMGCR autoantibodies. This subsample includes 2032 participants, 792 of whom were on statin therapy. If anti-HMGCR antibodies are detected, we will determine if there is an association between their presence and statin exposure, demographics, cholesterol levels, and other relevant variables.

Study population: ARIC CARMRI participants (2005-06) who had sufficient leftover serum volume to test for anti-HMGCR autoantibodies.

Study design: We will conduct a cross-sectional study of the presence of anti-HMGCR autoantibodies in CARMRI participants, stratified by statin use. First, we will define the distribution and reference range of anti-HMGCR autoantibodies in the CARMRI participants. Second, we will assess the correlates of the presence of anti-HMGCR autoantibodies with a focus on demographics (age, sex, race), lipid levels (total, LDL-, and HDL-cholesterol), the presence of subclinical cardiovascular disease as determined by average internal carotid intima-media wall thickness (IMT), and clinical coronary heart disease (CHD) history (self-reported CHD history at CARMRI, any prior visit or an adjudicated (non-fatal) clinical event or silent MI prior to the date of the CARMRI visit, or silent MI detected at the CARMRI visit). We will make use of data from previous ARIC visits and the annual follow-up telephone calls to determine prior statin use.

Statistical Analysis: We will use multivariable (linear and logistic) regression models to assess the independent association of anti-HMGCR autoantibodies with the above-listed correlates before and after adjustment for demographics. All analyses will be weighted by

the inverse of the sample fractions in the eight sampling strata (four field centers by two IMT groups) using methods for the analysis of complex sample survey design.

7.a. Will the data be used for non-CVD analysis in this manuscript?
X **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 for DNA analysis RES_DNA = "CVD Research" would be used?
X **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?
____ Yes X **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"?
____ 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? X **Yes** **____ No**

11.b. If yes, is the proposal
X **A. primarily the result of an ancillary study (list number*** 2010.10**)**
___ 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.**