ARIC Manuscript Proposal # 1379r

PC Reviewed: 6/18/19 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: GWAS of kidney function traits and chronic kidney disease

b. Abbreviated Title (Length 26 characters): GWAS of kidney function and CKD

2. Writing Group:
Writing group members: Zhi Yu, Adrienne Tin, Josef Coresh, Anna Kottgen and others welcome.

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _ZY_ **[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: Data analysis to start immediately. The manuscript will be completed by the Scr GWAS consortium.

4. Rationale:
This is an addendum to the ARIC Manuscript Proposal #1379 (GWAS of kidney function traits and chronic kidney disease). In this project, the ARIC Study has contributed GWAS results to meta-analyses carried out in the CKDGen Consortium. Recently, Dr. Kuokkanen

(mikko.kuokkanen@thl.fi) from the University of Helsinki has initiated the meta-analysis of GWAS of serum creatinine project. We proposed that the ARIC study participates in this project.

5. Main Hypothesis/Study Questions: GWAS for serum creatinine can identify variants that are associated with creatinine metabolism.

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: GWAS

Phenotype: serum creatinine

Exclusion: 1. age ≤ 18
2. pregnant
3. eGFR ≤ 60 (CKD-EPI)
4. cystatin-C > 1.2 mg/l
5. one of the close relative pairs (defined as pi_hat > 0.20)

Other variables: age at time of creatinine measurement**,** principal components to control population stratification, center, diabetes, hypertension.

Given that creatinine is the end product of muscle metabolism, which may differ by age and sex, we will conduct four GWAS stratified analysis by age (< 50 years and ≥ 50 years) and sex (men and women). The GWAS summary statistics will be uploaded for meta-analysis.

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 ICTDER 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)?

1379 GWAS of kidney function traits and chronic kidney disease

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

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number* _____)

___ 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/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes __X__ No.