ARIC Manuscript Proposal #3032

PC Reviewed: 8/8/17       Status: _____       Priority: 2
SC Reviewed: _______       Status: _____       Priority: _____

1.a. Full Title: ARIC participation in large scale meta-analysis of pulmonary function

b. Abbreviated Title (Length 26 characters): Large-scale analysis of PFTs

2. Writing Group: Stephanie London, Annah Wyss and there is room for one additional ARIC investigator (Kari North or her designate)
   Writing group members:

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

First author:    Stephanie London
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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:    Stephanie London
    Address: as above

    Phone: 919-541-5772       Fax: 
    E-mail: london2@niehs.nih.gov

3. Timeline: We are invited to participate if we can either provide results files by August 10 to participate in the discovery analysis or else by end of August to participate in the follow-up of significant loci. The lead authors on this paper have an exceedingly aggressive time line for this paper because the UK Biobank data have been publically released.

4. Rationale: CHARGE meta-analysis of PFTS (ARIC MS proposal #2397) will be completed soon. Our UK collaborators who participated in replication by looking up our results in a smaller version of the UK Biobank data are doing a new meta-analysis that will include over 320,000
UK Biobank individuals, all SpiroMeta studies and some others. They are willing to take the results that we have already generated for the CHARGE 1000G meta-analysis so that no new analysis needs to be done.

5. **Main Hypothesis/Study Questions:** Identify novel loci for publication function in ever large samples sizes.

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). I have pasted in the document sent by our colleagues leading this analysis:


**Contributing Studies**

**UK Biobank:** approx. 336k individuals of European ancestry and ~16k individuals of non-European ancestry with good lung function data.

**SpiroMeta:** data from 22 studies, with either HRC or 1000Genomes imputed data. Total sample size approx. 88k.

**CHARGE:** We also propose to utilise data from the 1000 Genomes analyses from CHARGE studies. These include analyses in ~60k European Ancestry and ~30k non-European ancestry individuals. *We are requesting the already completed study-level data from CHARGE cohorts, so no further analyses would be required by contributing studies.*

**Proposed Analyses**

We intend to undertake our main discovery analyses using individuals of European Ancestry only. For our identified signals, we intend to utilise non-European individuals from CHARGE and UK Biobank to 1. Examine whether there is heterogeneity in effects across different ancestries 2. Provide an overall meta-analysis result in all ancestries, for signals where there is no evidence of heterogeneity.

**Publication of results**

We aim to submit the results of these analyses to bioRxiv alongside submission to a journal. We shall not deposit/submit any results including the CHARGE data, without prior approval from CHARGE members.

b. **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 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.csc.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)?  #2397

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.csc.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.csc.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.