1.a. Full Title:

b. Abbreviated Title (Length 26 characters):
Exome chip analysis in the International COPD Genetics Network (ICGC)

2. Writing Group:
Writing group members: Michael Cho, Bing Yu, Alanna Morrison, Stephanie London

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

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4. Rationale:
Genome-wide genetic association analyses in COPD predominantly address Common, mostly regulatory variants. However, coding variants account for a disproportionate share of associations relative to their content in the genome, and have more easily interpreted
5. **Main Hypothesis/Study Questions:**

Exome array analysis will identify novel risk variants for COPD.

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).**

   a. Phenotypes: COPD, as defined in the recent ICGC case control paper: pre-bronchodilator FEV1 < 80% predicted with FEV1/FVC < 0.7 (GOLD criteria). Controls have FEV1 >= 80% predicted and FEV1/FVC >= 0.7

   b. Covariates: Age, sex, pack-years, and ever smoking.


   d. Genetic variation: Exome chip, referenced to hg19.

   e. Analysis method:

      i. Logistic regression using an additive model. If the Firth method is available, it should be done as a secondary analysis.

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 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

   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](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)?
   MS#2131 London Meta-analysis of exome chip variants and pulmonary function in the CHARGE consortium

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/](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/](http://publicaccess.nih.gov/) are posted in [http://www.csc..unc.edu/aric/index.php](http://www.csc..unc.edu/aric/index.php), under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit_process_journals.htm](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.