ARIC Manuscript Proposal #3656

PC Reviewed: 7/14/20	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Prevalence of clonal hematopoiesis amongst Individuals with HIV in comparison to population prevalence of clonal hematopoiesis from the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Prevalence of Clonal Hematopoiesis amongst Individuals with HIV

2. Writing Group:

Writing group members: Alexander G. Bick, Konstantin Popadin, Christian W. Thorball, Md Mesbah Uddin, Markella Zanni, Christie M. Ballantyne, Steven Grinspoon, Pradeep Natarajan, Jacques Fellay

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

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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 propose to perform analyses as described below and submit a brief research letter describing our findings within 1-3 month of P&P approval.

4. Rationale:

Coronary atherosclerosis is a major source of morbidity in individuals with HIV. While HIV influences atherosclerosis through inflammation, the specific biological mechanisms underlying this association are incompletely understood. Clonal hematopoiesis of indeterminate potential (CHIP), the age-related expansion of hematopoietic cells with leukemogenic mutations in the absence of detectable malignancy, is associated with accelerated atherosclerosis mediated by inflammation. Whether CHIP is more prevalent amongst individuals with HIV is unknown

5. Main Hypothesis/Study Questions:

We hypothesize that individuals with HIV have higher rates of clonal hematopoiesis than the general 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).

Study design.
We have previously identified CHIP in a multi-ethnic sample of 600 individuals with HIV who had available exome sequences from the Swiss HIV Cohort Study, aged 21-83. We have previously identified CHIP in a set of 8111 individuals with available exome sequences from ARIC, aged 44-84, which will be used as population controls. As CHIP prevalence is strongly age dependent, we performed a 1:5 case/control propensity matching on age, sex and self-reported ethnicity. Univariate Pearson's chi-square test and multi-variate logistic regression tested the association between HIV status and CHIP prevalence. Multi-variate models were adjusted for age, sex, self-reported ethnicity and smoking status.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes __x__ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The 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 current derived consent file ICTDER05 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/mantrack/maintain/search/dtSearch.html

___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)? There are no related manuscript proposals in ARIC currently.

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 https://sites.cscc.unc.edu/aric/approved-ancillary-studies

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.