ARIC Manuscript Proposal #3713

PC Reviewed: 9/8/20	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Microbial Signatures Among Periodontal Profile Classes

b. Abbreviated Title (Length 26 characters): **Bugs, IgG and PPC**

2. Writing Group:
Writing group members:

Julie T. Marchesan, Kevin Moss, Thiago Morelli, Flavia R. Teles, Kimon Divaris, Styner M, Jennifer Webster-Cyriaque, James Beck.

University of North Carolina at Chapel Hill and Flavia Teles, University of Pennsylvania

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

First author:
Name: Julie Marchesan

Address:
3501 Koury Oral Health Sciences Building
385 S. Columbia St., CB 7450
Chapel Hill, NC 27599
Phone: 919-537-3853
E-mail: julie_marchesan@unc.edu

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: Jim Beck

Address:
W.R. Kenan Distinguished Professor
3501 Koury Oral Health Sciences Building
385 S. Columbia St., CB 7450
Chapel Hill, NC 27599

Phone: 919-537-3241
E-mail: James_Beck@unc.edu

3. Timeline: Six months for data analysis and Manuscript Preparation

4. Rationale:
The UNC team has developed a new definition of periodontal disease based on Latent Class Analysis that groups people into mutually exclusive and exhaustive homogenous bins. This new definition of disease called Periodontal Profile Class (PPC) has already been shown to be associated with incident tooth loss (ARIC manuscript 2874) and a variety of other systemic outcomes. In addition, the PPC system exhibits higher heredity scores than more traditional dental classification systems (1). The purpose of this study is to characterize the dental plaque microbiome and systemic antibody signatures of individuals stratified by the PPC System.

5. Main Hypothesis/Study Questions:
We hypothesized that the periodontal profile disease classes would be significantly correlated with higher levels of periodontal pathogens in plaque and higher antibody IgG responses when compared to PPC-I-Health. .

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).

Population:
Our population will be composed of ARIC participants who have a periodontal exam at ARIC visit 4 and who were randomly selected to have both microbial composition of dental plaque and serum antibody levels determined by checkerboard (N=1450).
Outcomes:
The primary outcome is periodontal disease as classified by the PPC-System. We will use the CDC/AAP and WW17 classification systems as secondary analysis. We will test to see if periodontal organisms and systemic antibody levels to periodontal organisms are different for each PPC disease class vs health. We may use Bayesian Information Criterion (BIC) to compare the performance of each model (comparing the different classifications of periodontal disease).
Other variables:
We will use age, sex, race/center, diabetes, BMI, smoking, dental utilization and education as our primary control variables.

Data Analysis:
Microbial counts and antibodies (IgG) will be log transformed to be used as continuous measures for descriptive purposes. They will be dichotomized at the 75^{th} percentile for use in generalized logistic models. We will describe the microbial and IgG loads for eight periodontal organisms. Adjusted Generalized Logit Models will be used because our outcome has multiple classes of disease.

Data analysis will be performed at the UNC School of Dentistry. All data for this manuscript is available. We will not be asking for additional data.

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? ____ 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"? _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)? 3194, 2874, 2891, 2890, 2914, 2889, 2918, 3472, 3278, 1079, 1112

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* _1996.01_____)
___ 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 https://www2.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.

References

(1) Agler CS, Moss K, Philips KH, Marchesan JT, Simancas-Pallares M, Beck JD, Divaris, K. (2019) Biologically Defined or Biologically Informed Traits Are More Heritable Than Clinically Defined Ones: The Case of Oral and Dental Phenotypes. In: Belibasakis G., Hajishengallis G., Bostanci N., Curtis M. (eds) Oral Mucosal Immunity and Microbiome. Advances in Experimental Medicine and Biology, vol 1197. Springer, Cham