ARIC Manuscript Proposal # 1817

PC Reviewed: 7/12/11	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Endogenous Hormones, Nutritional Biomarkers and Prostate Cancer Collaborative Group: Pooled study of circulating biomarkers and prostate cancer

b. Abbreviated Title (Length 26 characters): Biomarkers & prostate cancer

2. Writing Group: The proposal is for a pooled analysis of existing prospective cohort data. Writing group members will include Naomi Allen, Tim Key, Paul Appleby, authors from the other prospective cohort studies that are participating in the pooled effort, including ARIC. Corinne Joshu and Elizabeth Platz will represent ARIC.

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

First author: Naomi Allen
Address: Cancer Epidemiology Unit
University of Oxford
Richard Doll Building
Roosevelt Drive
Oxford OX3 7LF, UK

Phone: +44(0) 1865 289 600 Fax: +44(0) 1865 289 610
E-mail: naomi.allen@ceu.ox.ac.uk

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: Corinne Joshu
Address: Johns Hopkins Bloomberg School of Public Health
Department of Epidemiology
615 N. Wolfe St.
Baltimore, MD 21230
Phone: 443 287 3821 Fax: 410 614 2632
E-mail: cjoshu@jhsph.edu

3. Timeline: We anticipate it will take 12 months from receipt of the data to submission of a manuscript to the ARIC Publications Committee.

4. Rationale: From the protocol provided by Dr. Allen (see attached):
"The Endogenous Hormones and Prostate Cancer Collaborative Group (EHPCCG) was established in 2004, with the aim of bringing together the worldwide prospective data and conducting collaborative re-analyses on the relationship between circulating sex

hormones, insulin-like growth factors (IGFs) and prostate cancer risk. The first results were published in 2008, based on almost 4,000 cases of prostate cancer from 18 studies. For sex hormones there were no significant associations with prostate cancer risk (EHPCCG, 2008a) but there was a clear increase in risk with increasing serum concentrations of IGF-I (EHPCCG, 2008b).

We would now like to update the information on sex hormones and IGFs, as there are about 2,000 more cases of prostate cancer available worldwide. We would also like to include new data on nutritional biomarkers, and there are between 2,000 and 6,000 cases for whom data on circulating fatty acids, carotenoids and tocopherols, other vitamins, selenium and other nutrients are available (please see the summary table on page 2). The aim of this pooling project is to provide a unified analysis of the published worldwide prospective data to further our understanding of the relationships of endogenous hormones and nutritional biomarkers with the risk of prostate cancer. For most biomarkers there will be sufficient statistical power to analyse the associations subdivided by disease aggressiveness and other patient characteristics."

Dr. Allen asked ARIC to provide data on fasting serum glucose, insulin, and cholesterol on ARIC participants with and without prostate cancer. The request is for already published ARIC data: Tande AJ, Platz EA, Folsom AR. The metabolic syndrome is associated with reduced risk of prostate cancer. Am J Epidemiol. 2006 Dec 1;164(11):1094-102. Epub 2006 Sep 12. PubMed PMID: 16968859. That paper included glucose, insulin, and HDL cholesterol.

5. Main Hypothesis/Study Questions: To evaluate the association of fasting serum measures of glucose, insulin, and cholesterol with prostate cancer in a pooled analysis of prospective cohort studies.
The request is for existing biomarker data only; no laboratory work will be performed.

Statistical analysis of the pooled data will be performed at Oxford. If approved, Dr. Joshu will work with the ARIC coordinating center to determine the best method for providing Oxford with the relevant ARIC data, and to assure that all ARIC protocols are followed, and forms (i.e. Data Distribution if necessary) are complete.

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: Prospective cohort study from which the Oxford group will select all of the cases and sample 3 controls matched to each case (matching factors: age at recruitment, date of recruitment, race, time of blood draw, smoking status).

Inclusion/Exclusion:
Exclude:

1) Women

2) Men with a cancer diagnosis at baseline (aside from non-melanoma skin cancer)

3) Men without data on glucose, insulin, and HDL cholesterol at Visit 1

Exposures: Visit 1 serum glucose, insulin, and HDL cholesterol concentrations

Outcome: Prostate cancer diagnosed through 2006 (Tande et al. paper included cases through 2000)

Other variables of interest: Other covariates requested are:
· Date of birth
· Date of blood collection
· Time of blood collection
· Fasting status at blood collection / time since last meal
· Use of medications on day of blood collection
· Height
· Weight
· Waist and hip circumferences
· Smoking
· Alcohol
· Educational status
· Marital status
· Race

Analysis: ARIC data will be pooled with data from other cohorts. Associations between biomarkers and prostate cancer will be estimated using conditional logistic regression. Details are described in the attached proposal.

Project Specific Limitations: Information on stage and grade of prostate cancer is not uniformly available in ARIC, thus biomarker associations with aggressive vs non-aggressive disease will not be performed. We will provide Visit 1 concentrations (which is parallel to the other studies, which are mostly nested case-control, and as not to interfere with manuscript proposals #1520, #1791, and #1792); a single measure of these biomarkers may not reflect the men's usual levels.

7.a. Will the data be used for non-CVD analysis in this manuscript?

X Yes

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?

(This file ICTDER03 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

X Yes

8.a. Will the DNA data be used in this manuscript?

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"?

NA

8.c. If yes, is the author aware that the participants with RES_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?

NA

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

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)?

1078 - Metabolic Syndrome and Prostate Cancer Incidence (Tande et al. paper is published)

1153 - Circulating caveolin-1 levels and prostate cancer incidence

1520 - Statins, cholesterol, and prostate cancer in the Atherosclerosis Risk in Communities (ARIC) study

1545 - HbA1c and Cancer Risk in the Atherosclerosis Risk in Communities (ARIC) Study

1791 - The natural history of diabetes in relation to the natural history of cancer.

1792 - The influence of obesity, diabetes, and associated metabolic perturbations on cancer risk.

1797 - The Association of AHA Ideal Cardiovascular Health with Cancer Incidence: The ARIC study

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?

X Yes

11.b. If yes, is the proposal

X___ A. primarily the result of an ancillary study (list number* 1995.04 Cancer Study (Cancer) Folsom, A.**)**

__ 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/

12. 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.

References

EHPCCG (2008a). Endogenous sex hormones and prostate cancer: a collaborative analysis of 18 prospective studies. *J Natl Cancer Inst,* 100: 170-183

EHPCCG (2008b). Insulin-like growth factors, their binding proteins, and prostate cancer risk: analysis of individual patient data from 12 prospective studies. *Ann Intern Med,* 149: 461-71, W83-8