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TITLE: Identifying DNA Methylation Features that Underlie Prostate Cancer Disparities

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14. ABSTRACT In the U.S., African Americans (AA) are more likely to be diagnosed with prostate cancer than European American (EA), and after diagnosis, AA men are more likely to die from prostate cancer than EA men. We hypothesize that differences in DNA methylation patterns across ethnic groups may contribute to prostate cancer disparities. Our objective is to conduct a genome-wide study of methylation patterns in prostate tumors and adjacent normal tissue derived from both AA and EA individuals. We will determine if DNA methylation patterns in prostate tissue (both cancerous and normal tissue) differ between AA and EA individuals. We will also identify methylation features that differ between tumor and normal tissue. Using this information, we can then determine if methylation events that accompany prostate cancer development differ between ethnic groups. In addition, we will attempt to determine if these epigenetic differences are driven by genetic and environmental factors that vary by ethnicity. Developing an understanding of these differences is a critical and necessary step towards understanding and addressing prostate cancer disparities. Features identified here can be used in future studies of disparities to better characterize the prostate cancer phenotype in diverse populations.					
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1. INTRODUCTION:

In the U.S., there are pronounced racial disparities in prostate cancer incidence and mortality. We hypothesize that the methylation features in prostate tissue (both cancerous and normal) differ between AA and EA men and that the methylation events that accompany prostate cancer development differ between ethnic groups. Our goals are to identify methylation features that vary by ethnicity and to identify ethnicity-specific methylation features of prostate cancer that could contribute to the racial disparities that exist in the U.S.

2. KEYWORDS:

Disparities, prostate cancer, DNA methylation, SNP

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

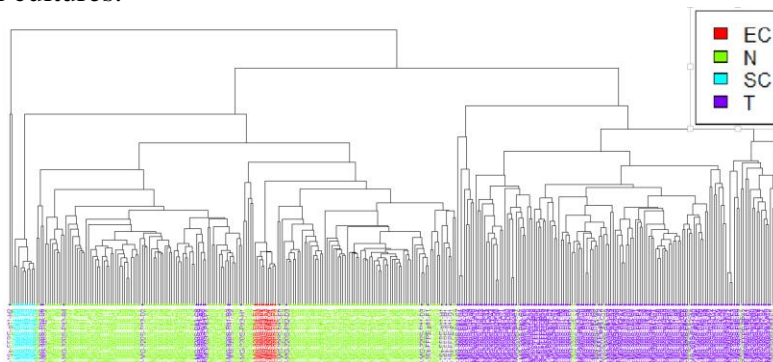
Process Aims: Generate genome-wide methylation and SNP Profiles
Primary Aim #1: Determine if methylation profiles differ by race/ancestry
Primary Aim #2: Identify ethnicity-specific markers of prostate cancer
Primary Aim #3: Identify methylation Quantitative Trait Loci

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

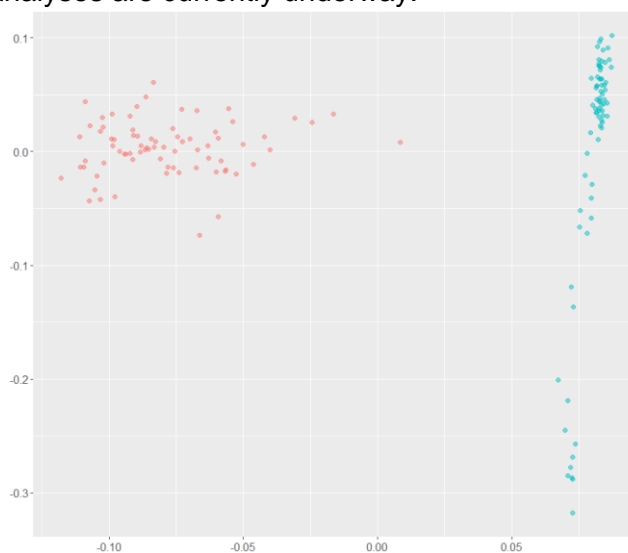
Process Aims: All tasks related to the process aims are complete. We have generated DNA methylation data on ~850,000 CpG sites for all 300 tissue samples (150 cancer and 150 normal). We have also completed the generation data for ~1 million SNP for 150 subjects. The data quality was excellent for the vast majority of samples, CpG sites, and SNPs.

Primary Aims 1 and 2: My group is currently in the processes of characterizing differences in DNA methylation profiles between cancer and normal tissues and between different ancestry groups. In the image we observe clear clustering by tumor (T, purple) and normal (N, green) status. In addition, our results show that PrEC cultures (EC) clearly cluster within the “normal” prostate samples, suggesting these cell lines highly similar to prostate epithelial cells in vivo (which is useful knowledge for further use of these cells for the purposes of understanding our results). SCs are prostate stromal cell cultures.



For Aim 1, generation of methylation features (task 1) is complete. Association analysis (task 2) is underway. For aim 2, task 1 (regression analysis) and task 2 (ROC analyses) are underway.

Primary Aim 3: my group is currently in the process of (1) identifying prostate mQTLs, (2) characterizing how mQTLs differ by ancestry and cancer status, and (3) determining which prostate susceptibility variants appear to be mQTLs in the prostate. Principal components analysis of SNP data (task 1) shows clear clustering of African American (red) and European American (blue) groups. Task 2, mQTL analyses are currently underway.



What opportunities for training and professional development has the project provided?

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

One PhD student (Dayana Delgado) and one MD-PhD student (Meytal Chernoff) are using the data generated in this project in their dissertation research. They are working one-on-one with Dr. Pierce (PI) who is their advisor. Dayana Delgado has also presented her preliminary results as a poster at the Susan G. Komen Graduate Training Program in Breast Cancer Disparities Annual Training Meeting.

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Dayana Delgado (a PhD student) presented preliminary results from this project as a poster at the Susan G. Komen Graduate Training Program in Breast Cancer Disparities Annual Training Meeting (November 2018). Title: “Genome-wide differentially methylated regions in benign prostate cancer tissue of African American and European American men”

What do you plan to do during the next reporting period to accomplish the goals?

If this is the final report, state “Nothing to Report.”

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Nothing to Report

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- transfer of results to entities in government or industry;
- instances where the research has led to the initiation of a start-up company; or
- adoption of new practices.

Nothing to Report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

- 5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:*

Nothing to Report

Changes in approach and reasons for change

Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Actual or anticipated problems or delays and actions or plans to resolve them

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to Report

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”*

- **Publications, conference papers, and presentations**

Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as*

noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Poster presentation at the Susan G. Komen Graduate Training Program in Breast Cancer Disparities Annual Training Meeting (November 2018).
Presenter: Dayana Delgado (PhD student)
Title: “Genome-wide differentially methylated regions in benign prostate cancer tissue of African American and European American men”

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

*Name: Mary Smith
Project Role: Graduate Student
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: 5*

Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.

Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)

Name: Brandon Pierce	No Change
Name: Donald Vander Griend	No Change
Name: Lin Chen	No Change
Name: Marc Gillard	No Change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Brandon Pierce

Closed

R01 ES023834

NIH/NIEHS

Genetics of arsenic metabolism: fine-mapping and rare variant analysis

6/6/14-3/31/18

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*

- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *N/A*

QUAD CHARTS: *N/A*

9. APPENDICES: *N/A*