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TITLE: Epigenetic Aging in TMPRSS2 Fusion-Negative African American Prostate Cancer

PRINCIPAL INVESTIGATOR: Dr. Christopher C Coss

CONTRACTING ORGANIZATION: The Ohio State University, Columbus, OH

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Dr. Christopher Coss

E-Mail:

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COLUMBUS OH 43210-1016

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14. ABSTRACT

There is strong evidence that altered signaling via the vitamin D receptor (VDR) makes a significant contribution to AA PCa in the absence of the oncogenic actions of TMPRSS2:ERG fusion events. We have now undertaken the first integrative genomic analyses of the VDR cistrome-transcriptome in the context of health disparities using EA and AA cell models. These analyses lend strong evidence to the concept that the VDR is a significantly more potent transcriptional regulator in non-malignant AA prostate epithelial cells than EA cells, and that altered expression of the BAZ1A/SMARCA5 chromatin remodeling complex distorts VDR actions. We therefore propose to study how altered BAZ1A/SMARCA5-VDR interactions impact the circadian rhythm and lead to increased epigenetic aging in AA TMPRSS2 fusion negative PCa. ***We hypothesize*** that *TMPRSS2* fusion negative PCa arises more frequently in AA men due to altered VDR transcriptional control of protein coding and non-protein coding genes that are significantly enriched for anti-inflammatory and circadian rhythm pathways. Disrupted VDR signaling arises through two mechanisms, **i**. reduced expression of the BAZ1A/SMARCA5 chromatin remodeling complex, and **ii**. Elevated miRNA expression targeting the same networks. The combined impact directly and indirectly lead to changes in CpG methylation at sites that are important for the control of epigenetic aging.

15. SUBJECT TERMS
None listed.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER**	**19a. NAME OF RESPONSIBLE PERSON** USAMRDC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
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Introduction

We hypothesize that *TMPRSS2* fusion negative PCa arises more frequently in African American (AA) men arises due to altered VDR transcriptional control of protein coding and non-protein coding genes that are significantly enriched for anti-inflammatory and circadian rhythm pathways. Disrupted VDR signaling arises through two mechanisms, **i**. reduced expression of the BAZ1A/SMARCA5 chromatin remodeling complex, and **ii**. Elevated miRNA expression targeting the same networks. The combined impact directly and indirectly lead to changes in CpG methylation at sites that are important for the control of epigenetic aging. BAZ1A/SMARCA5 tumor expression, and serum microRNA expression can both be exploited to predict status and progression in *TMPRSS2* fusion negative PCa in African American men. This hypothesis is investigated in three ***Specific Aims***, namely, 1. To define BAZ1A/SMARCA5 functional control of VDR cistrome-transcriptome relationships; 2. To test functional links between VDR and regulation of the epigenetic clock; 3. To measure associations between vitamin D and VDR-regulated miRNA in PCa patient cohorts. We predict the **Impact** of our innovative proposal is to addressa molecular mechanism that is at the intersection of biological and psychosocial causes of PCa health disparities, namely that VDR signaling is mechanistically linked with regulation of the epigenetic clock and disruption is a cancer driver. Defining VDR genomic functions and its control of epigenetic aging will lead to new diagnostic and therapeutic insight into the biological basis of AA PCa. Ultimately, these approaches will be exploited by therapeutic approaches to slow epigenetic aging.

Keywords

Prostate cancer, epigenetics, health disparities, vitamin D signaling, BAZ1A/SMARCA5

Accomplishments

***Major research goals*.**

Specific Aim 1: To define BAZ1A/SMARCA5 functional control of VDR cistrome-transcriptome relationships and how this relates to AR signaling.

Specific Aim 2: To test functional links between VDR and regulation of the epigenetic clock to test how this relates to apparent epigenetic aging in African American prostate cancer.

Specific Aim 3: To measure associations between vitamin D and VDR-regulated miRNA in PCa patient cohorts using tumor and control serum samples from African men, as well as African American tumor and control samples.

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.

1. Major Activities.

Unfortunately, there has been modest productivity during this reporting period due to the challenges of moving institutes for both Dr. Campbell (from Ohio State to Cedar-Sinai Medical Center) and Dr. Yates (from Tuskegee to University to Johns Hopkins School of Medicine) (see *actual and anticipated problems*).

Progress has been made as follows;

***Specific Aim 1**: To define BAZ1A/SMARCA5 functional control of VDR cistrome-transcriptome relationships and how this relates to AR signaling*.

We have begun to explore how BAZ1A and SMARCA5 impact androgen receptor signaling in African American (AA) and European American (EA) PCa. Specifically, we utilized EA and AA non-malignant prostate and PCa cell models with confirmed genomic ancestry and defined the basal and dihydrotestosterone (DHT)-regulated AR and H3K27ac cistromes using CUT&RUN and integrated these data with publicly available genomic counterparts (**Figure 1**).

The DHT-dependent AR and H3K27ac cistromes significantly overlapped within AA cells and EA cells but there was significantly less overlap between AA and EA cells. For example, H3K27ac distributions were frequent (~15-20k sites) in each of non-malignant AA RC43N and EA HPr1AR, and malignant RC43T and LNCaP, and the significance of the overlaps were comparable for basal and DHT treated cells, but this was not significantly impacted by ancestry. By contrast the AR cistrome was highly DHT-dependent, with ~2k sites notably in LNCaP and RC43T, which very significantly overlapped with H3K27ac in the same cells but significantly less so across cells. Thus, although the H3K27ac cistrome was comparable across cells, the overlap with AR was driven by genomic ancestry.

These findings identified that the shared AR and H3K27ac cistromes are driven by genomic ancestry, and that reduced expression of SMARCA5 and other components of the cBAF complex are significant in AA and advanced PCa, and impact AR signaling. Our future directions are focused on how

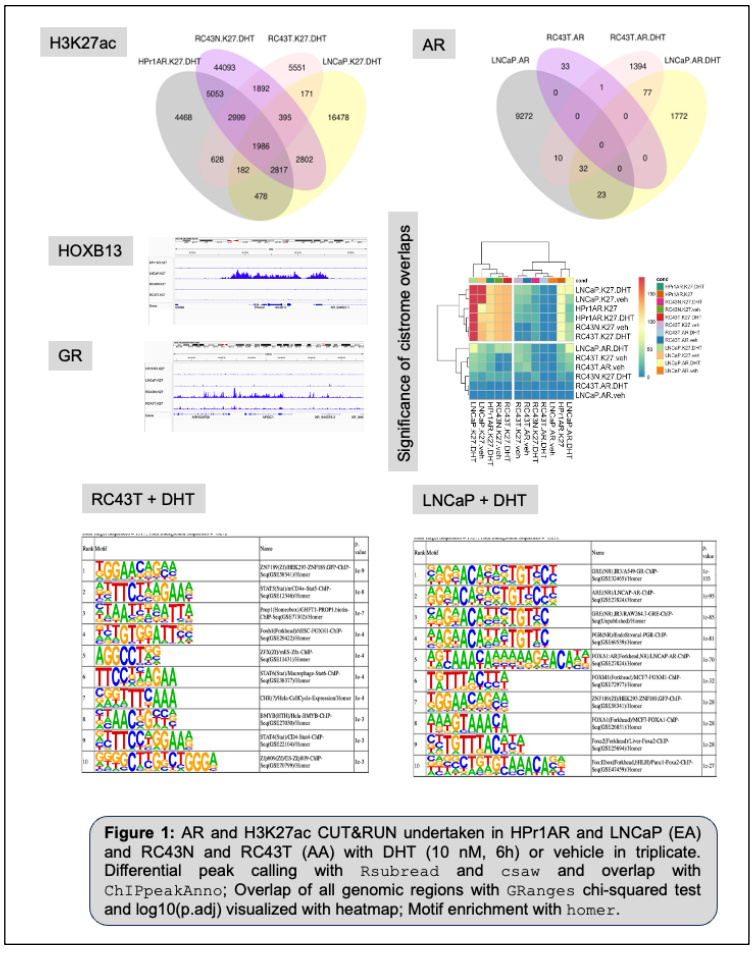

Figure 1: AR and H3K27ac CUT&RUN undertaken in HPr1AR and LNCaP (EA) and RC43N and RC43T (AA) with DHT (10 nM, 6h) or vehicle in triplicate. Differential peak calling with `Rsubread` and `csaw` and overlap with `ChIPpeakAnno`; Overlap of all genomic regions with `GRanges` chi-squared test and log10(p.adj) visualized with heatmap; Motif enrichment with `homer`.

SMARCA5 expression disrupts the balance between transcription factor functions, such as for the AR and other transcription factors, and effective DNA repair.

In parallel, we have also focused our energies on developing cell clones with stably-expressing CRISPR-activation and -repression domains (see *actual and anticipated problems*). The table below summarizes progress over the last six months to establish these vital reagents. In **Figure 2** we show how SMARCA5 is modulated by CRISPR-activation in RC77T cells.

Cell Line clone	Lost during move to Cedars	Current Status
LNCaP-dCas9-VP64	Yes	Currently in puromycin selection.
LNCaP-dCas9-KRAB	Yes	Have cells selected and frozen again. Confirmed dCas9 expression by western blotting (WB)
RC43T- dCas9-VP64	Yes	Generated RC43T cells. Confirmed dCas9 expression by WB
RC43T- dCas9-VP64-SA1	Generated after move	Generated stable cell line and checked SMARCA5 expression by WB (figure 1)
RC43T- dCas9-VP64-SA2	Generated after move	Generated stable cell line and checked SMARCA5 expression by WB (figure 1)
RC43T- dCas9-VP64-SA2	Generated after move	Generated stable cell line and checked SMARCA5 expression by WB (figure 1)
RC43T- dCas9-VP64-BAZ1A	Yes	In process of hygromycin selection for BAZ1A overexpression
RC77N- dCas9-VP64	Yes	Have cells selected and frozen again. Confirmed dCas9 expression by WB
RC77N- dCas9-VP64-SA1	Generated after move	Generated stable cell line. Confirmation by WB pending
RC77N- dCas9-VP64-SA2	Generated after move	Generated stable cell line. Confirmation by WB pending
RC77N- dCas9-VP64-SA3	Generated after move	Generated stable cell line. Confirmation by WB pending
RC77N-dCas9-VP64-BAZ1A	Yes	Generated stable cell line. Confirmation by WB pending
RC77T- dCas9-VP64	Yes	Generated stable cell line. Confirmed by WB (Figure 2)
RC77T- dCas9-VP64-SA1	Generated after move	Generated stable cell line. Confirmed by WB (Figure 2)
RC77T- dCas9-VP64-SA2	Generated after move	Generated stable cell line. Confirmed by WB (Figure 2)
RC77T- dCas9-VP64-SA3	Generated after move	Generated stable cell line. Confirmed by WB (Figure 2)
RC77T-dCas9-VP64-BAZ1A	Yes	Generated stable cell line. Confirmation by WB pending (Figure 2)

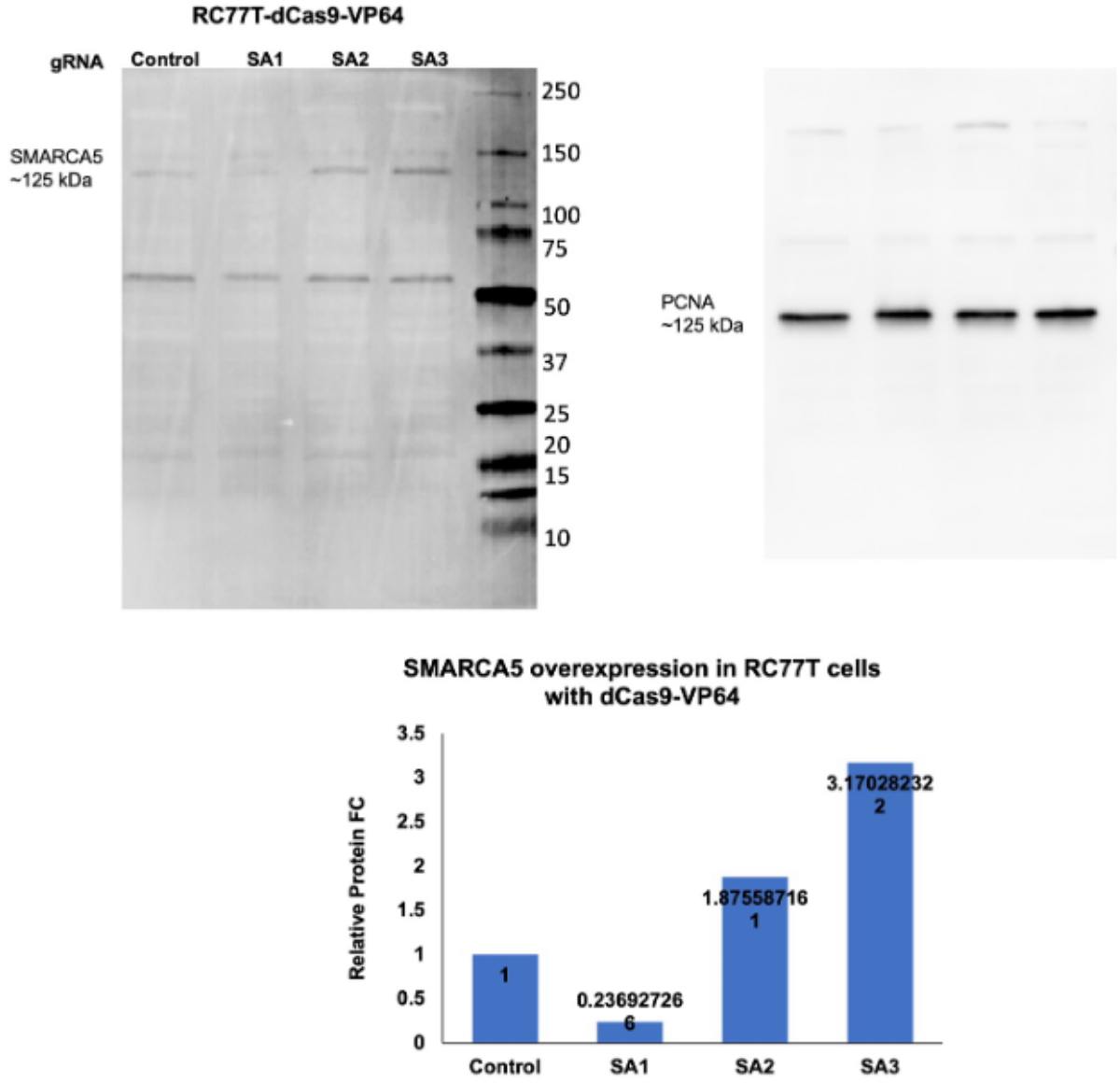

Figure 2: RC77T AA PCa stably expressing dCas9-VP64 were further transduced with three gRNAs encoding plasmids (SA1, SA2, SA3) and selected with hygromycin. Western blot was carried out to measure change in expression of SMARCA5. Saw modest increase in SMARCA5 in SA1 and SA3.

***Specific Aim 2**: To test functional links between VDR and regulation of the epigenetic clock to test how this relates to apparent epigenetic aging in African American prostate cancer.*

There has been no significant progress on this specific aim.

***Specific Aim 3**: To measure associations between vitamin D and VDR-regulated miRNA in PCa patient cohorts using tumor and control serum samples from African men, as well as African American tumor and control samples.*

Measurement of the concentration of serum vitamin D (25(OH)vitamin D3, ng/ml) has been undertaken in 185 Nigerian PCa patients in collaboration with Dr. Solomon Rotimi, Covenent University, Nigeria. The data are currently being analyzed and associated with patient outcomes.

We are still optimizing antibodies for IHC for markers VDR, BAZ1A and SMARCA5 in a Tissue microarray comprised of tumors from African American and European American patients. Protein expression will be associated with tumor characteristics such as Gleason Score and other pathological parameters. Each marker will be scored for intensity of staining and subcellular localization utilizing g Leica SC2 Aperio whole cell imaging algorithm. We will perform both univariate and multi-variant analysis to determine the correlation of expression of each marker with clinical-pathological features of prostate disease, such as race, age, and Gleason grade. Cox proportional hazard models will be used to measure differences in survival outcomes adjusting for covariates significantly associated with outcome of interest (e.g. age and pathological criteria).

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."

Throughout the year, whilst the groups were moving and the logistics of the new grant structure were secured, the groups at Tuskegee/Johns Hopkins University and Ohio State/Cedars-Sinai have continued to meet every two weeks by teams and this has allowed various members of the groups, both junior and more senior, to share knowledge and insights.

Ohio State/Cedars-Sinai

A post-doctoral researcher, Dr. Shahid Hussain, was supported at OSU and has moved to Cedars-Sinai with Dr. Campbell. He has continued to work in a very focused manner in this project and has submitted abstracts from this work, as well as fellowships, for example to the Prostate Cancer Foundation (unfunded) and the Tower Research Program (under review).

In the previous period another post-doc, Dr. Debasis Nayak was recruited to the project, and he completed preliminary studies for SA2. He has now secured a faculty position in India and started there in the Spring of 2023.

Ms. Hedieh Jafari was also working on the grant and did not move to Cedars-Sinai, and instead stayed at Ohio State where she was recruited into a successful leukemia research group in the Cancer Center.

Tuskegee University Group:

Dr. Isra Elhussin successfully defended her PhD in Fall 2022 and also moved with Dr. Clayton Yates to Johns Hopkins University. She has continued to present the work at various meetings on prostate cancer.

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.

At both Cedars-Sinai Medical Center (***MJC***) and Johns Hopkins School of Medicine (***CY***) there are well-established and prominent interactions with advocate groups for African American cancer patients generally and specifically prostate cancer. For example, at Cedars-Sinai Medical Center, ***Zul Surani*** is the Director, Community Outreach and Engagement program in the Cancer Research Center for Health Equity Team. The Health Equity team work closely with various partners in Southern California including ***Pastor Rhonda Holbert***, CEO and founder of Celebrate Life Cancer Ministry – a well-known African American, interfaith-based, cancer organization from South Los Angeles, that offers services to people from all backgrounds (www.celebratelifecm.org). Another important group who work closely with Cedars-Sinai is the Men's Cancer Health Network (https://themenscancernetwork.com/) led by Freddie Muse Jr, who is a prostate cancer survivor.

Recently, ***MJC*** worked with the ***ZS*** as well as with ***Christina Elston***, a Communications Specialist at Cedars-Sinai, to undertake publicity for our recent publication on the vitamin D receptor function in African American prostate cancer (PMID: 37082578), and is illustrative of how ***ZS*** and the Health Equity Team engage with the local and wider community This was highlighted multiple times as follows;

April 18, 2023: Onco'Zine – Study details genetic differences in cellular processing of Vitamin D;

April 20, 2023: Enlace Judio – ¿Vitamina D y cáncer de próstata?;

April 24, 2023: The ASCO Post – Vitamin D deficiencies may lead to health disparities in Black patients with prostate cancer (Picked up in 3 outlets, including *Technology Networks*);

April 24, 2023: OncLive – Study: Vitamin D may play a role in prostate cancer disparities;

April 25, 2023: MedicalNewsToday – Is vitamin D the reason behind higher prostate cancer rates among Black men?;

May 1, 2023: AACI Update – Study: Vitamin D may play a role in prostate cancer disparities;

June 3, 2023: Finding Genius Podcast – Do vitamin D and genomic ancestry affect cancer cells.

19th September 2023: ***MJC*** participated in a Virtual Panel with Blackdoctors.org: "What's Next for Prostate Cancer: Clinical Trials & Preventive Health Care"

November 4th 2023: ***MJC*** participated in *Pastor Holbert*'s support group for cancer patients, and specifically spoke about Vitamin D Deficiency and Men.

In parallel ***CY***, who is the John R. Lewis Professor of Pathology at Johns Hopkins School of Medicine, has an established international reputation in the arena of investigating prostate cancer health disparities and working with patient advocate groups. ***CY*** also has a prominent role in the AACR Health Disparities and ACS prostate Cancer Research symposiums, serves on the AACR MICR council, and was the Chair, 2022-2023. He continues to draw upon these experiences to distribute findings through local programs, such as the JHU Schaufeld Program which focuses on African American men with prostate cancer in Baltimore area.

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.

Cedars-Sinai:

Dr. Shahid Hussain will complete the BAZ1A/SMARCA5-dependent genomic studies in SA1 as well as to continue to work on SA2.

Dr. Campbell will continue to undertake the bioinformatic analyses of ChIP-Seq, ATAC-Seq and RNA-Seq.

Dr. Hussain and Dr. Campbell will also focus their energies on SA2.

Johns Hopkins University School of Medicine:

Dr. Isra Elhussin will continue the analyses of BAZ1A/SMARCA5 in PCa samples including using nanostring approaches in primary samples as part of SA3, as well as IHC.

Dr. Yates and Dr. Campbell will continue to liaise with Dr. Solomon O. Rotimi (Covenant University, Nigeria) to complete the analyses of vitamin D3 serum levels and relate this to clinical outcome as part of SA3.

4. **IMPACT:** D*escribe 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).

Dr. Campbell and Dr. Yates have continued to work together on research projects and the writing of key reviews. For example, the primary work from SA1 was published (see section 6) (#2) as well as a review on the topic (#3) and a book chapter. These publications highlight to the scientific community that the vitamin D receptor functions in a significantly different manner in the genome of prostate cells from African American men, compared to European American men. This adds to an emerging literature that strongly suggests that the functions of transcription factors are profoundly influenced by genomic ancestry. They have also extended this work into parallel projects in prostate cancer and health disparities (#1, #3).

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.

These studies have examined how genomic ancestry shapes nuclear receptor signaling by applying proteogenomic approaches in African American and European American prostate cells and clinical cohorts of PCa patients. These studies focused on the VDR, given its associations with AA PCa, and included developing methods to calculate weighted VDR cistrome-transcriptome relationships, and test how these were significantly shaped by African genomic ancestry as a result of changes in components of the BAF complex. More recently, H3K27ac and AR cistromes have been measured and revealed distinct differences, which also demonstrate the distinctiveness of the epigenome between EA and AA PCa cells. Therefore, these studies add to others focused on how genomic ancestry impacts transcription factor interactions.

We reason that these studies will contribute to expanding efforts to increase understanding of the unique cancer-driver events that shape the epigenome in AA PCa. These knowledge gaps are demonstrable. For example, as of May 2023, there were ~130,000 publications in PubMed with the word "Prostate" in the title, but not containing either "Black" or "African" in the abstract, whereas search terms including "Black" or "African" resulted in ~1000 publications, representing less than 1% of the literature. Similar analyses in Gene Expression Omnibus (GEO) indicates that volume of genomic data available from cells of African genomic ancestry represents ~ 0.1% of all the studies focused on prostate cells. Given that health disparities in PCa remains a stubborn health challenge across the US and other countries, this suggests this is a persistent, impactful and deleterious knowledge gap.

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:*

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.

Nothing to report

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.

On Feb 1st the PI, Dr. Campbell, left The Ohio State University and joined Cedars-Sinai Medical Center. The post-doc Dr. Shahid Hussain who had been working on the grant also moved in April 2023 to Cedars-Sinai to continue working on the project.

In late November 2022 Dr. Campbell began to prepare for lab move and the transfer of grants so as to minimize the amount of time the grant was inactive, and that research was held up. The first formal communication between Campbell/OSU and CDMRP was Dec 1st 2022, and as of the date of writing of this report (Dec 1st 2023) the award modifications have not been finalized. This has not been ideal.

A new PI at Ohio State has been identified (Dr. Chris C Coss), who is a colleague of Dr. Campbell, and has shared interests in nuclear receptor signaling. However, the fdelay in restructuring the award in a timely manner has a significant impact on Dr. Clayton Yates and his team at Johns Hopkins University, as his team are focused most directly on SA3, and the funds to purse this aim have been held up making progress more challenging. However, within recent weeks it appears the issues of grant restructuring have been resolved and it seems reasonable to believe that this will be achieved within coming weeks and research can then accelerate again.

Another challenge is that the move of the two investigators to new host institutes (OSU to Cedars-Sinai, and Tuskegee to Johns Hopkins University) inevitably impacted productivity. For example, in the case of Dr. Campbell, there was essentially a five-month gap between freezing cells down in Ohio, packing, moving and getting cells growing again Los Angeles. This was exacerbated by a leak of liquid nitrogen from the frozen cell dewer, and these included several of the prostate cancer cell lines that had been stably transfected with generated with CRISPR activating and repressing complexes. However, Dr. Shahid Hussain, who moved with Dr. Campbell, is now growing the cells and re-making the clones of cells with CRISPR domains to control expression of SMARCA5 and BAZ1A.

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 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).*

1: Gray JS, Wani SA, Hussain S, Huang P, Nayak D, Long MD, **Yates C**, Clinton SK, Bennet CE, Coss CC, **Campbell MJ**. The MYC axis in advanced prostate cancer is impacted through concurrent targeting of ERβ and AR using a novel ERβ-selective ligand alongside Enzalutamide. ***bioRxiv*** [Preprint]. 2023 Nov 17:2023.11.15.567282. doi: 10.1101/2023.11.15.567282. PMID: 38014010; PMCID:
PMC10680693.

2: Siddappa M, Hussain S, Wani SA, White J, Tang H, Gray JS, Jafari H, Wu HC, Long MD, Elhussin I, Karanam B, Wang H, Morgan R, Hardiman G, Adelani IB, Rotimi SO, Murphy AR, Nonn L, Davis MB, Kittles RA, Hughes Halbert C, Sucheston-Campbell LE, **Yates C**, **Campbell MJ**. African American Prostate Cancer Displays Quantitatively Distinct Vitamin D Receptor Cistrome-transcriptome Relationships Regulated by BAZ1A. ***Cancer Res Commun***. 2023 Apr 18;3(4):621-639. doi: 10.1158/2767-9764.CRC-22-0389. PMID: 37082578; PMCID: PMC10112383.

3: White JA, Kaninjing ET, Adeniji KA, Jibrin P, Obafunwa JO, Ogo CN, Mohammed F, Popoola A, Fatiregun OA, Oluwole OP, Karanam B, Elhussin I, Ambs S, Tang W, Davis M, Polak P, **Campbell MJ**, Brignole KR, Rotimi SO, Dean-Colomb W, Odedina FT, Martin DN, **Yates C**. Whole-exome Sequencing of Nigerian Prostate Tumors from the Prostate Cancer Transatlantic Consortium (CaPTC) Reveals DNA Repair Genes Associated with African Ancestry. ***Cancer Res Commun***. 2022 Sep 16;2(9):1005-1016. doi: 10.1158/2767-9764.CRC-22-0136. PMID: 36922933; PMCID: PMC10010347.

4: Hussain S, **Yates C**, **Campbell MJ**. Vitamin D and Systems Biology. ***Nutrients***. 2022 Dec 7;14(24):5197. doi: 10.3390/nu14245197. PMID: 36558356; PMCID:PMC9782494.

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).*

1: Nonn L, Krieger K, **Yates C**, **Campbell MJ**. Vitamin D and prostate cancer. ***Feldman and Pike's Vitamin D***. 5th Edition - October 28, 2023 Editors: Martin Hewison, Roger Bouillon, Edward Giovannucci, David Goltzman, Mark Meyer B., JoEllen Welsh. Publisher Elsevier

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.*

Nothing to report

- **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: Moray Campbell
Project Role: PI
Researcher Identifier (e.g. ORCID ID): 0000-0002-3355-0928
Nearest person month worked: 1.2

Contribution to Project: Supervised Shahid Hussain (post-doc); Coordinated with Dr. Clayton Yates (JHU) to through regular communication (e.g. Zoom lab meetings) and led genomic analyses of cells
Funding Support: Cedars-Sinai Medical Center

Name: Shahid Hussain
Project Role: Post-doc
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 12

Contribution to Project: Shahid has begun to re-establish the CRISPR activation and repression system for BAZ1A and SMARCA5, and make stable clones in cell lines several of which were lost in the move.
Funding Support: Cedars-Sinai Medical Center

Name: Clayton Yates
Project Role: co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1

Contribution to Project: Lead on clinical analyses of vitamin D signaling in tumor samples
Funding Support: Johns Hopkins University

Name: Isra Elhussin
Project Role: Post-docs
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 12

Contribution to Project: Assisting with genomic analyses of relevant publicly available resources
Funding Support: Johns Hopkins University

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.

Nothing to report

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: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) should be updated and submitted with attachments.*

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*