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TITLE: Epigenetic Changes and Clinicopathological Characterization of Prostate Cancer from Patients of African Ancestry

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CONTRACTING ORGANIZATION: University of Southern California, Los Angeles, CA

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Prostate cancer is the most common non-skin cancer and the second leading cause of cancer death amongst men in United States. Prostate cancer heath disparities are largely coming from ethnic differences. In particular, men of African ancestry have higher risk of prostate cancer and progression is more aggressive than men of European ancestry. However, the factors and underlying mechanisms that lead to those ethnicity-related disparities are not yet fully understood. Prostate tumor molecular subtypes are defined by genetic alterations and it is reported that prostate molecular subtypes are associated with disease prognosis. However, molecular mechanisms, which are related to aggressiveness of prostate tumors in each prostate tumor molecular subtype, are not clear. Epigenetics enable us to unravel the hidden molecular mechanisms of gene regulation, which can give rise to heterogeneous tumor phenotypes that include aggressiveness of prostate cancer. The proposed study will investigate epigenetic changes linked to aggressive prostate tumors from men of African ancestry by generating new genome-wide epigenome datasets from metastatic and primary prostate tumors and performing multivariate statistical analyses. Moreover, integrating multi-omic datasets, this study will identify key epigenetic changes that are found in aggressive prostate tumors of each prostate tumor molecular subtype. Novel findings and newly uncovered biology of aggressive prostate cancer from the proposed study will facilitate developing biomarkers and treatments for aggressive prostate tumors from men of African ancestry. Moreover, the proposed study will accelerate the development of improved targeted therapeutic tools in the field and further providing benefits to prostate cancer patients.

15. SUBJECT TERMS

None listed.

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1. INTRODUCTION

Prostate cancer heath disparities are largely coming from ethnic differences. In particular, men of African ancestry have higher risk of prostate cancer and progression is more aggressive than men of European ancestry. However, the factors and underlying mechanisms that lead to those ethnicity-related disparities are not yet fully understood. Studies on identifying epigenetic alterations in aggressive prostate cancer from men of African ancestry are lacking. As far as we know, all epigenetic studies on prostate tumors from men of African ancestry are promoter-centric. However, activities of distal regulatory elements such as enhancers are altered in prostate cancer and their activities are more dynamic across individuals than promoters. Therefore, studies on epigenetic changes of enhancers are greatly needed to understand aggressive prostate cancers from men of African ancestry. In this study, we proposed to profile global DNA methylation including both promoters and enhancers in prostate tumors from men of African ancestry to identify DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry (Aim 1). Moreover, integrating multi-omic datasets of prostate tumors, we proposed to identify and characterize key epigenetic alterations associated with aggressive prostate tumor molecular subtypes (Aim 2). By performing cutting-edge bioinformatic and statistical analyses using the datasets, we have been characterizing key epigenetic alterations linked to aggressive prostate tumor from men of African ancestry. Successful completion of this study will identify key epigenetic alterations linked to aggressive prostate molecular subtypes and characterize prostate tumor molecular subtypes, enlightening novel molecular mechanisms of aggressive prostate tumors.

2. KEYWORDS

Epigenetic alterations
DNA methylation
Aggressive prostate cancer
African ancestry
Racial Disparities
Bioinformatics
Molecular Biology

3. ACCOMPLISHMENTS

What were the major goals of the project?

Our major goals of the project for this funded period (Year 2: 9/30/2022 - 9/29/2023) were to profile global DNA methylation from prostate tumors obtained from men of African ancestry to identify DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry and to identify key epigenetic alterations associated with aggressive prostate tumor molecular subtypes, analyzing multi-omic datasets. As we outlined in the statement of work (SOW), we performed the proposed tasks. Aim 1 was delayed due to unexpected challenges (e.g. COVID-19), but to compensate, we put lots of efforts into Aim 2 for this funded period. Please see the below table that includes all of tasks proposed and target completion, completion dates and % of completion.

Specific Aim 1: Identify DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry			
Major Task 1: Profile global DNA methylation in 50 metastatic and 50 primary prostate tumors from men of African ancestry	**Target Completion Date**	**Completion Date**	**% Completion**
Subtask 1: Obtain IRB/HRPO approval to use prostate tumor tissues*	12/31/21	10/6/22	100%
Subtask 2: Collect and assess prostate tumor tissues	12/31/22	N/A	50%
Subtask 3: Obtain clinicopathological datasets	12/31/22	N/A	40%
Subtask 4: Profile global DNA methylation from prostate tumor tissues	12/31/23	N/A	30%
Major Task 2: Identify and characterize DNA methylation sites that are differentially methylated between metastatic and primary prostate tumors from men of African ancestry	**Target Completion Date**	**Completion Date**	**% Completion**
Subtask 1: Identify differentially methylated sites between metastatic and primary tumor tissues, building multivariate statistical regression models, associating clinicopathological datasets with DNA methylation datasets	3/31/24	N/A	20%
Subtask 2: Process functional genomic datasets to annotate identified differentially methylated sites	3/31/24	N/A	10%
Subtask 3: Identify and characterize DNA methylation sites that are linked to aggressive prostate tumors in men of African ancestry	9/30/24	N/A	N/A

Specific Aim 2: Identify key epigenetic alterations associated with aggressive prostate tumor molecular subtypes, integrating multi-omic datasets

Major Task 1: identify genes that are linked to aggressive prostate tumor molecular subtypes that are defined by genetic alterations, using matched DNA-seq and RNA-seq datasets obtained from TCGA and ORIEN	**Target Completion Date**	**Completion Date**	**% Completion**
Subtask 1: Process matched DNA-seq and RNA-seq datasets	11/30/22	8/31/23	100%
Subtask 2: Identify prostate tumor molecular subtypes of each dataset	5/31/23	N/A	80%
Subtask 3: Using clinical information of de-identified prostate tumor samples, Perform multivariate statistical analyses to identify genes linked to aggressive prostate tumors of each molecular subtype	3/31/24	N/A	10%
Major Task 2: Identify key epigenetic alterations that control the expression of genes linked to aggressive prostate tumor molecular subtypes	**Target Completion Date**	**Completion Date**	**% Completion**
Subtask 1: Process multi-platform epigenomic datasets	9/30/23	N/A	90%
Subtask 2: Perform integrative analyses to identify key epigenetic alterations linked to prostate tumor molecular subtypes	9/30/24	N/A	N/A

What was accomplished under these goals?

Specific Aim 1. We have been profiling DNA methylomes of prostate tumor tissue samples from men of African ancestry. To identify DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry, we started analyzing newly generated datasets. For example, we compared DNA methylation levels between normal and prostate tumor samples and identified CpG sites which were hypermethylated specifically in tumor samples. We also found that DNA methylation patterns were heterogeneous among tumor tissue samples (Figure 1). Integrating with clinicopathological information, we are currently in the processing of analyzing these sites to identify CpG sites that are statistically significantly associated with aggressive tumor type, generating more datasets.

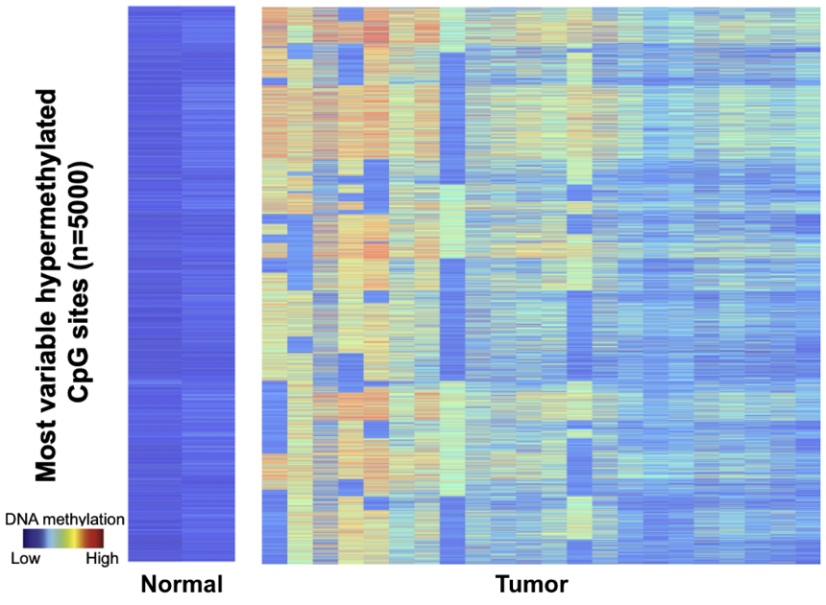


Figure 1. Heterogeneous DNA methylation patterns are observed among tumor samples. After profiling DNA methylomes of prostate tumor tissue samples we identified hypermethylated CpG sites in prostate tumor samples compared to normal prostate samples. Distinct DNA methylation patterns are observed among tumor samples.

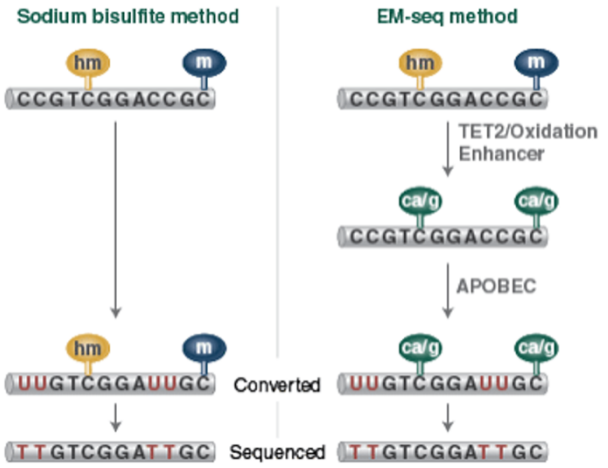


Figure 2. Workflow of two whole genome methylation sequencing methods. Using sequencing, we can now profile whole genome DNA methylation. First method of whole genome methylation sequencing is to use bisulfite. Second method is to use enzymes which allow to distinguish differentially methylated CpG sites.

Moreover, we noted that there are better methods to measure global DNA methylation levels. For example, Illumina developed a newer version of EPIC array which now can cover 935,000 CpG sites. Furthermore, we found that whole genome methylation sequencing allows to measure DNA methylation levels of all of CpG sites genome-wide. Whole genome methylation sequencing can be performed using sodium bisulfite method or enzymatic-methyl sequencing method (Figure 2). We optimized protocols and established the bioinformatic workflow for both bisulfite sequencing and enzymatic methyl sequencing using prostate tumor tissue samples (Figure 3). Example whole genome bisulfite sequencing datasets generated using prostate tumor tissue samples are shown in Figure 4. We found that *HEXA* promoter region is differentially methylated between tumor samples.

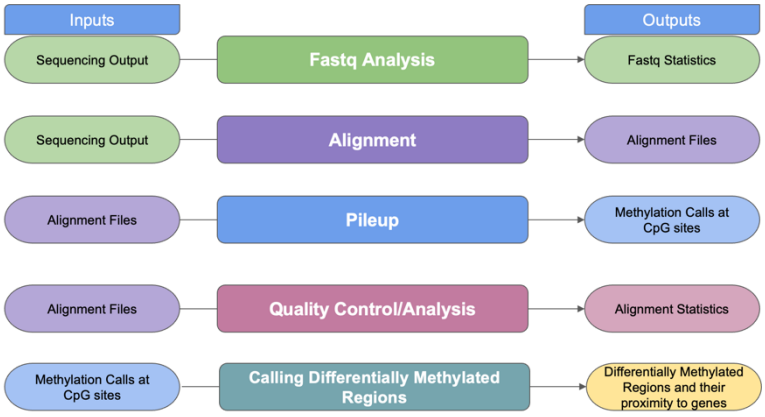


Figure 3. Bioinformatic workflow for whole genome methylation sequencing. We established the bioinformatic workflow to process whole genome methylation sequencing that includes fastq QC analysis, alignment to genome (bisulfite/methylome), pileup, QC after mapping and counting to normalize signals, and differentially methylated region calling steps.

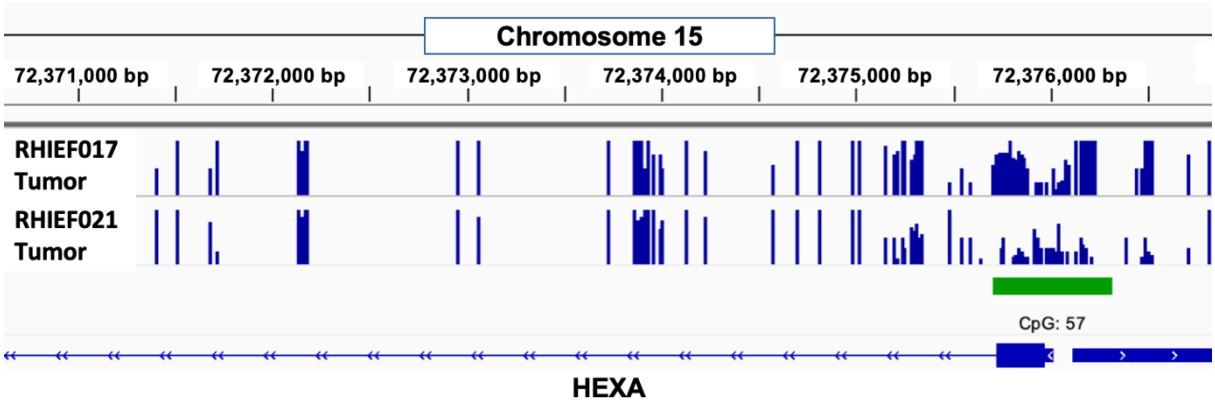
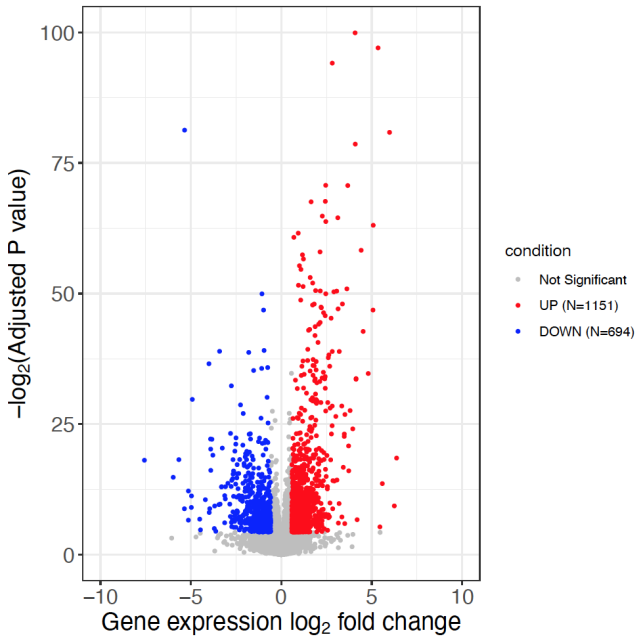


Figure 4. Example whole genome bisulfite sequencing data generated in-house. We found that *HEXA* gene promoter is differentially methylated among prostate tumor samples.

Specific Aim 2. We also analyzed DNA-seq and RNA-seq datasets of prostate tumor tissue samples. We determined molecular subtypes of the tissue samples using TMPRSS2-ETS fusions and somatic mutations of SPOP, FOXA1, IDH1, and other genetically altered genes. We have also started performing ancestry analyses to define alterations linked to aggressive prostate tumors from men of African ancestry. For example, we analyzed RNA-seq datasets from the Cancer Genome Atlas (TCGA) consortium and compared gene expression profiles between prostate tumor tissues from White men vs Black men. We identified thousands of genes that are differentially expressed between groups (Figure 5). We are currently performing ancestry analysis using genetic variants along with prostate cancer risk variants to determine key genes that are statistically significantly associated with aggressive prostate cancer from men of African ancestry.

Figure 5. Volcano plot showing differentially expressed genes among prostate tumor samples with different ancestries. Using TCGA RNA-seq data, we identified genes that are differentially expressed between prostate tumor tissue samples from men of European ancestry and prostate tumor tissue samples from men of African ancestry.



Moreover, we searched and read over twenty published manuscripts, which reported studies of DNA, RNA, and DNA methylation analysis of prostate tumors from African ancestry. We organized datasets and published a review manuscript. For example, we made a list of CpG sites that were dysregulated in prostate tumors from African ancestry (Table).

Table. Studies that compared DNA methylation features of prostate tumors between African Ancestry and European Ancestry prostate cancer patients.

PubMed ID	Name	Sample	Total Cohort Size	Cohort Details	Method	Genes Examined	Key Findings
33374332	Barry et al., 2020	FFPE tissue	89	43 AA and 46 EA	Pyrosequencing	*MYC*	Strong association for *MYC* DNA methylation at one CpG site, but no CpG locations studied were observed to be significantly differentially methylated
25864488	Devaney et al., 2015	Radical prostatectomy tissue	6	3 AA and 3 EA	Human Methylation450 BeadChip arrays and pyrosequencing	*ABCG5, ACOT7, MST1R, SPTB, SHANK2, SNRPN, WDR70*	Hypermethylation of *SNRPN, MST1R, ABCG5* in AA relative to EA
15800905	Enokida et al., 2005	Radical prostatectomy tissue	121	44 AA and 77 EA	Methylation specific PCR	*GSTP1*	No significant differences between races
20606036	Kwabi-Addo et al., 2010	Radical prostatectomy tissue	100	39 AA and 67 EA	Methylation specific PCR	*GSTP1, AR, RARB, SPARC, TIMP3, NKX2-5*	Differential methylation of *RARB, SPARC, TIMP3*, and *NKX2-5* between AA and EA patients No significant differences in methylation of *GSTP1* between AA and EA patients
26902887	Rubicz et al., 2019	FFPE tissue	76	76 AA and 476 EA**	Human Methylation450 BeadChip arrays	450,000 CpG sites throughout the genome	Hypermethylation of *STOX7, SNRPN, TIMP3*, and *PMEPA1* in AA relative to EA with no corresponding changes in mRNA levels

PubMed ID	Name	Sample	Total Cohort Size	Cohort Details	Method	Genes Examined	Key Findings
24694733	Sharad et al, 2014	Radical prostatectomy tissue	77	35 AA and 42 EA	COMPARE-MS (methylated-DNA precipitation and methylation specific restriction enzymes) followed by qPCR	*PMEPA1, GSTP1*	Hypermethylation of *PMEPA1* in AA relative to EA No significant difference in hypermethylation of *GSTP1* between AA and EA
12692786	Woodson et al., 2004	FFPE tissue	111	47 AA and 67 EA	Methylation specific PCR	*GSTP1, CD44, E-cadherin*	No significant difference in hypermethylation of *GSTP1* between AA and EA Hypermethylation of *CD44*, higher frequency amongst AA patients relative to EA patients No differential methylation of *E-cadherin*

Please see the below table that includes the summary of experiments results for each aim/task/subtask.

Specific Aim 1: Identify DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry	
Major Task 1: Profile global DNA methylation in 50 metastatic and 50 primary prostate tumors from men of African ancestry	**Summary of experiments results**
Subtask 1: Obtain IRB/HRPO approval to use prostate tumor tissues*	IRB is finally approved.
Subtask 2: Collect and assess prostate tumor tissues	We started obtaining high-quality prostate tumor tissue samples from the USC Institute of Urology. To increase the sample size and expedite the completion of the proposed aims, we also contacted our collaborator Dr. Sara Falzarano, a Pathologist of the University of Florida (UF). We started obtaining prostate tumor tissue samples from UF.
Subtask 3: Obtain clinicopathological datasets	We have been obtaining clinicopathological datasets matched to the collected prostate tissue samples from the USC Institute of Urology and UF.

Subtask 4: Profile global DNA methylation from prostate tumor tissues	New and better methods to profile global DNA methylomes were developed, and we optimized the workflow to generate high quality data. We measured DNA methylation levels from the obtained samples.
Major Task 2: Identify and characterize DNA methylation sites that are differentially methylated between metastatic and primary prostate tumors from men of African ancestry	**Summary of experiments results**
Subtask 1: Identify differentially methylated sites between metastatic and primary tumor tissues, building multivariate statistical regression models, associating clinicopathological datasets with DNA methylation datasets	We installed bioinformatic and statistical software program needed to perform DNA methylation and integrative analyses. We started analyzing the DNA methylation datasets generated in-house.
Subtask 2: Process functional genomic datasets to annotate identified differentially methylated sites	We started processing functional genomic datasets (e.g. ChIP-seq datasets) including ones generated from prostate cells donated from men of African ancestry.
Subtask 3: Identify and characterize DNA methylation sites that are linked to aggressive prostate tumors in men of African ancestry	N/A for this funded period

Specific Aim 2: Identify key epigenetic alterations associated with aggressive prostate tumor molecular subtypes, integrating multi-omic datasets	
Major Task 1: identify genes that are linked to aggressive prostate tumor molecular subtypes that are defined by genetic alterations, using matched DNA-seq and RNA-seq datasets obtained from TCGA and ORIEN	**Summary of experiments results**
Subtask 1: Process matched DNA-seq and RNA-seq datasets	We completed processing DNA-seq and RNA-seq datasets obtained from the Cancer Genome Atlas (TCGA) and the Oncology Research Information Exchange Network (ORIEN) databases. We also noted that dbGaP database includes additional DNA-seq and RNA-seq datasets for prostate cancer (e.g. phs001648). We also contacted dbGaP and obtained and processed these datasets. We published a manuscript that summarizes key molecular

	signatures linked to prostate cancer patients from African ancestry.
Subtask 2: Identify prostate tumor molecular subtypes of each dataset	We analyzed DNA-seq and RNA-seq data for prostate tumor tissue samples. By performing data analysis, we determined molecular subtypes (e.g. TMPRSS2-ERG fusion, SPOP mutation status) of the tissue samples. We are in the process of performing ancestry analysis to compare self-reporting ethnicity information with the ancestry information obtained from genetic variant analysis from DNA-seq and RNA-seq datasets.
Subtask 3: Using clinical information of de-identified prostate tumor samples, perform multivariate statistical analyses to identify genes linked to aggressive prostate tumors of each molecular subtype	We started installing and testing software programs to perform multivariate statistical analyses.
Major Task 2: Identify key epigenetic alterations that control the expression of genes linked to aggressive prostate tumor molecular subtypes	**Summary of experiments results**
Subtask 1: Process multi-platform epigenomic datasets	We collected different types of epigenomic datasets (e.g. ChIP-seq, ATAC-seq, DNase-seq, Hi-C, Micro-C) generated from prostate cancer cells. We established bioinformatic pipelines to process these multi-platform epigenomic datasets. We started processing and analyzing these datasets, identifying prostate cancer-specific enhancers and enhancer-promoter loops.
Subtask 2: Perform integrative analyses to identify key epigenetic alterations linked to prostate tumor molecular subtypes	N/A for this funded period

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

Dr. Rhie was able to develop her career and profession during this funded period. For example, Dr. Rhie attended several trainings and workshops including the Gordon Research Conference, the National Cancer Institute Professional Development Workshop, and the American Society of Human Genetics Annual Meeting. Dr. Rhie also presented findings of this project in several meetings, conferences, and classes. Dr. Rhie served as a grant reviewer for several study sections of the National Institute of Health, Wright Foundation, and Mathers Foundation. Dr. Rhie served as a reviewer for Nature Communication, Cell Reports, and Nature Cancer. Dr. Rhie honed her mentoring skills by training graduate, undergraduate, and postbac students. Her students also attended conferences and conferences and presented research at these meetings, developing their professional career.

How were the results disseminated to communities of interest?

Dr. Rhie has been afforded several speaking engagements to disseminate research stemming from this grant, including USC Department of Biochemistry and Molecular Medicine Annual Retreat, USC Norris Comprehensive Cancer Center Translational Research Conference, and Genitourinary Disease Research Affinity Group meetings. Dr. Rhie also attended the Gordon Research Conference, the National Cancer Institute Professional Development Workshop, and the American Society of Human Genetics Annual meeting and presented her research to communities. Moreover, she participated in the cancer outreach programs held by USC Norris Comprehensive Cancer Center and the CaRE2 Florida-California Health Equity Center. As the USC Norris Comprehensive Cancer Center Diversity, Equity, and Inclusion Council Committee member, she has been participating in various activities to promote diversity workforce and to reduce cancer racial disparities.

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

Overall plans and goals of this project will remain the same. We plan to continue performing the proposed research to accomplish the goals. We will continue analyzing global DNA methylation profiles of prostate tumors from men of African ancestry. We will put more efforts into identifying key DNA methylation sites that are linked to aggressive prostate tumors from men of African ancestry. We will continue characterizing genes as well as signaling pathways that are linked to aggressive prostate tumor molecular subtypes that are defined by genetic alterations by integrating multi-omic datasets.

4. IMPACT

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

During this funded period, Dr. Rhie was able to accelerate investigating prostate cancer epigenomics with her research team members. The recruited talented graduate students and a lab technician enabled us to perform the research proposed to be on the track. Although there was a delay of performing wet lab experiments due to COVID-19, we tried to catch up for this funded project period. We were able to optimize ways to profile global DNA methylation. We started generating and analyzing DNA methylation profiles of prostate tumor tissues collected from men of African ancestry. We found differentially methylated regions between tumor samples, and we are currently in the process of analyzing datasets to identify key epigenetic alterations linked to aggressive prostate cancer, writing manuscripts. We found that prostate tumor samples from men of African ancestry are mostly lack of ERG fusion and expression. We are currently studying whether the molecular subtype difference is related to aggressiveness of the disease. Analyzing different omics datasets generated in-house as well as other researchers, we are hoping to identify epigenetic alterations linked to aggressive prostate molecular subtypes to further reduce cancer health disparities. The newly datasets, analyses, and research findings will be a useful resource to the prostate cancer, health disparity, and epigenetics research community. Our long-term goals are to understand the molecular mechanisms underlying aggressive prostate cancer from men of African ancestry. Identified key epigenetic alterations of aggressive prostate cancer will be potential biomarkers and therapeutic targets. Successful completion of the proposed study will accelerate the development of improved targeted therapeutic tools in the field and further providing benefits to prostate cancer patients.

What was the impact on other disciplines?
Noting to Report

What was the impact on technology transfer?
Noting to Report

What was the impact on society beyond science and technology?
Nothing to Report

5. CHANGES/PROBLEMS TO REPORT

Year 1 was very severely affected due to COVID-19, so we could not perform the proposed research on time. We nearly returned to a state of normalcy for this funded period, Year 2, but lab members were sick and had to be out of the lab for several weeks due to the spread of COVID-19 during this funded period. Due to this, there was a delay in obtaining tissue samples and conducting wet lab experiments. A newly hired postdoc abruptly left the lab without completing the assigned tasks, citing the rising cost of living in Los Angeles. Hiring of a talented postdoc who fits into the lab has been very challenging. Moreover, the minimum salary and stipend rates for USC Keck School of Medicine postdoctoral scholars increased significantly this year. While we will continue to make efforts to hire talented postdocs, we will try to expedite the proposed research with graduate students and lab technicians.

No significant changes to Vertebrate Animal(s)

No significant changes to Human Subjects

No significant changes in use of biohazards and/or select agents

6. PRODUCTS

Presentations:

Characterization of nucleosome positioning and DNA methylation signatures from prostate cancer cells from diverse ethnic groups using NOMe-EM-seq Gonzalez-Smith L, Stevens C, Lee Y, Wu Z, Nelson-Moore E, Rhie SK *American Society of Human Genetics (ASHG) Annual Meeting October* 26, 2022; Los Angeles, CA, USA

Using 3D Epigenomic Maps to Understand Functions of Risk Genetic Variants Rhie SK *University Southern California Center for Genetic Epidemiology Seminar* November 16, 2022; Los Angeles, CA, USA

Characterizing DNA methylation signatures in prostate tumors to understand health disparities in Black and White men Rhie SK *CaRE2 Connects with the Community* January 11, 2023; Gainesville, FL, USA

Genomic and Other Omics Databases for Cancer Biomarker Discovery Rhie SK *University of Southern California Norris Comprehensive Cancer Center Translational Research Conference* March 10, 2023; Los Angeles, CA, USA

Characterizing the DNA Methylome of Prostate Adenocarcinoma using Targeted DNA Methylation Sequencing Stevens C, Gonzalez-Smith L, Nelson-Moore E, Rhie SK *University Southern California Department of Biochemistry & Molecular Medicine retreat* March 12, 2023; Oxnard, CA, USA

Methyl-Micro-C: Simultaneous characterization of DNA methylation state and chromatin structure in prostate cancer Gonzalez-Smith L, Cao H, Stevens C, Nelson-Moore E, Wu Z, Rhie SK *USC Department of Biochemistry & Molecular Medicine Retreat* March 12-13, 2023; Oxnard, CA, USA

Elucidate chromatin structure landscape difference associated with racial disparities in prostate cancer Wu Z, Lee B, Nelson-Moore E, Rhie SK *USC Department of Biochemistry & Molecular Medicine Retreat* March 12-13, 2023; Oxnard, CA, USA

Characterizing Transcriptional Regulatory Networks of Prostate Tumor Subtypes Rhie SK *University of Southern California Norris Comprehensive Cancer Center Genitourinary Disease Research Affinity Group* May 25, 2023; Los Angeles, CA, USA

The effect of epigenetic alterations on the 3D epigenome and replication timing of prostate cancer Cao H, Gonzalez-Smith L, Wu Z, Lee B, Yang S, Lee B, Rhie SK *Gordon Research Conference Chromosome Biology From Cellular, Molecular and Physical Perspectives* June 25-30, 2023; Barga, LU, Italy

The effect of epigenetic alterations on the 3D epigenome and replication timing of prostate cancer Cao H, Gonzalez-Smith L, Wu Z, Lee B, Yang S, Lee B, Rhie SK *National Cancer Institute (NCI) Professional Development Workshop* Aug 3-4 2023; Rockville, MD, USA

Publications:

Genomic, epigenomic, and transcriptomic signatures of prostate cancer between African American and European American patients Stevens C, Hightower A, Buxbam S, Falzarano S, Rhie SK *Frontiers in Oncology* 2023 13:1079037 doi:10.3389/fonc.2023.1079037

Evidence of Novel Susceptibility Variants for Prostate Cancer and a Multiancestry Polygenic Risk Score Associated with Aggressive Disease in Men of African Ancestry Chen F, Madduri RK, Rodriguez AA, Darst BF, Chou A, Sheng X, Wang A, Shen J, Saunders EJ, Rhie SK, et al *Eur Urol* 2023 S0302-2838(23)02561-7. doi: 10.1016/j.eururo.2023.01.022

Websites:

https://sites.usc.edu/rhielab/

No inventions, patents, or licenses

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Suhn K. Rhie, PhD
Project Role:	PI
Research Identifier (e.g. ORCID ID):	0000-0002-5522-5296
Nearest person month worked:	2
Contribution to Project:	Dr. Rhie has performed data analyses and supervised the study.
Funding Support:	N/A

Name:	Leonardo Gonzalez-Smith, BS
Project Role:	Lab Technician
Research Identifier (e.g. ORCID ID):	0000-0002-7585-6407
Nearest person month worked:	2
Contribution to Project:	Mr. Gonzalez-Smith has collected and assessed prostate tumor tissue samples and worked on wet lab experiments.
Funding Support:	N/A

Name:	Claire Stevens, BS
Project Role:	Graduate Student
Research Identifier (e.g. ORCID ID):	0000-0003-2695-0410
Nearest person month worked:	5
Contribution to Project:	Ms. Stevens has assisted performing DNA methylation profiling and performed data analyses.
Funding Support:	N/A

Name:	Zexun Wu, BS
Project Role:	Graduate Student
Research Identifier (e.g. ORCID ID):	0000-0003-2566-1326
Nearest person month worked:	3
Contribution to Project:	Mr. Wu has performed multi-omic data analyses to reduce prostate cancer racial disparities.
Funding Support:	N/A

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

Nothing to Report

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

Not Applicable