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14. ABSTRACT

Objective: Systemic low-grade inflammation is a prostate cancer risk factor in men of African descent, and correlates with West African ancestry, genetic susceptibility, a distinct tumor biology, and aggressive disease. Our overall objective is to understand these relationships with a view to informing prevention and therapeutic strategies.

Impact: Our study will be the first to explore the relationship between systemic/chronic inflammation, ancestry, and tumor biology as a cause of disease progression in men of African descent. Creating an understanding of how the interaction between chronic inflammation and tumor biology affects prostate cancer progression in a high-risk population, like African-American men, offers the opportunity to the develop improved prevention and therapeutic strategies using anti-inflammatory drugs and immune modulators to decrease the disease burden among all men

15. SUBJECT TERMS
Cancer, Prostate Cancer, Oncology

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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Men of African descent experience a disproportionately high prostate cancer mortality. We and others have shown that prostate tumors in African-Americans harbor a distinct immune-inflammation signature. Low-grade inflammation has been described as a prostate cancer risk factor that is associated with aggressive disease. We also reported that regular aspirin use reduces the risk of aggressive prostate cancer and disease recurrence in these men. We further validated this finding in the prospective Southern Community Cohort Study by showing that aspirin use at time of recruitment associates with a reduced prostate cancer mortality on follow-up among the African-American men in this cohort. Together, the observations suggest that a low-grade chronic inflammation related to either ancestral or tumor biological factors, or to the neighborhood environment in which men live, could be a driver of prostate cancer mortality in men with African ancestry. We therefore proposed to examine whether a systemic low-grade inflammation is a prostate cancer risk factor in men of African descent and correlates with West African ancestry, genetic susceptibility, a distinct tumor biology, and aggressive disease. Our research aims included the analysis of a systemic immune-inflammation signature in men of African ancestry that relates to prostate cancer. We also proposed to assess the genetic and ancestral basis of prostate cancer-associated inflammation using a genome-wide association approach. Furthermore, in partnership with our Co-PI, Dr. Clayton Yates at Tuskegee University now Johns Hopkins University, we aimed to determine the prevalence and origin of an immune-inflammation signature in prostate tumors of Nigerian men and compare our findings with African-American and European-American men from the NCI-Maryland cohort. Also not described in the original proposal, but added to the research, we also investigated the role of the neighborhood environment in inducing the systemic immune-inflammation signature in men of African ancestry. Census-tract linked neighborhood characteristics became available to us for the NCI-Maryland cohort after we started the research for the award.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

African-American, Africa, ancestry, biomarker, blood, case control study, chromatin, cyclooxygenase, disease progression, DNA, genetic variation, genomics, immunity, inflammation, mutation, RNA, risk factor, fatty acid, tumor biology, transcriptome, urine, whole exome sequencing.

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.

Aim 1. Determine if there is a unique immune-inflammation signature in men of African ancestry that relates to prostate cancer.

Goal/Tasks: All goals were met with the publication of the final manuscript in 2023.

Aim 2. Assess the genetic and ancestral basis of prostate cancer-associated inflammation using a genome-wide association approach.

Goal/Tasks: Preparation of a manuscript and revisions for publication.

Aim 3. Determine the prevalence and origin of an immune-inflammation signature in tumors of men of African and European ancestry.

Goal/Tasks: Preparation of manuscripts and revisions for publication.

The award is managed as a collaborative research study that involves two lead investigators, Dr. Stefan Ambs at the National Cancer Institute/NIH, and Dr. Clayton Yates who moved from Tuskegee University to his new position as a Professor of Pathology/Oncology at Johns Hopkins University. Dr. Ambs' group has the lead on the projects described under Aims 1 & 2, whereas Dr. Yates' group has the lead on the projects described under Aim 3. The experimental parts for Aims 1-3, as described in the SOW, have been completed. For Aim 1, all tasks have been completed. For Aim 2, the remaining tasks are preparation and submission of a manuscript for acceptance in a peer-reviewed journal. For Aim 3, Major Tasks 1 & 2, all what is left is data analysis and manuscript preparation. A manuscript with genomics data has been published.

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.

Specific Aim 1: Measure 97 markers in plasma/serum or urine and examine their association with prostate cancer (PCa), genetic ancestry, family history, and lifestyle factors.	**Timeline**	**Site 1** NCI	**Site 2** TU
Major Task 1: Measurement of 92 immune-inflammation markers, lipopolysaccharide, and Omega-3 fatty acids, respectively, in plasma/serum, and three metabolites of cyclooxygenases - PGE-M, thromboxane B2 and prostacyclin - in urine.	Months		
Subtask 1: Prepare plasma/serum and urine samples for shipment • Obtain IRB approval and MTAs covering the NCI-Maryland and NCI-Ghana Prostate studies and the two study sites, NCI and University of Tuskegee. • Receive (Ambs) and aliquot plasma/serum samples from 1650 cases (150 samples from Nigerian PCa cases) and 1650 controls (150 samples from Nigerian men) and ship to Olink (Watertown MA), Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research (Frederick, MD), and OmegaQuant LLC (Sioux Falls, SD). Also, aliquot urine samples from the NCI-Maryland Prostate Cancer Case-Control study (n = 1800) and ship to the Eicosanoid Core Laboratory at Vanderbilt University (Nashville, TN).	1-8	Ambs, Cook, Dorsey, Minas	Yates
Subtask 2: Measure plasma/serum and urine markers and build a database • Measurement of 92 inflammation-related and immune-modulatory analytes at Olink; lipopolysaccharide at Leidos Biomedical Research Inc.; three metabolites of cyclooxygenases, PGE-M, thromboxane B2 and prostacyclin at Eicosanoid Core Laboratory, Vanderbilt University; and Omega-3 fatty acids at OmegaQuant LLC. Obtain measurement data and create a database for analysis with a statistical software.	8-16(24)	Ambs, Dorsey, Minas	
Major Task 2: Statistical analysis			
Using statistical software packages (e.g. SAS or STATA), assess association of markers with prostate cancer, genetic ancestry, family history, and lifestyle factors using unconditional logistic regression models and additional analysis tools as described under Methods in the Project Narrative.	12-18	Ambs, Cook, Minas, Butler	
Major Task 3: Preparation of manuscript and revisions			

Progress with Specific Aim 1

We completed all tasks related to **Specific Aim 1.** All goals were met. In last year's report, we described research findings from two manuscripts that were under review with *Nature Communications* and *JAMA Network Open*. Both manuscripts have since been accepted for publication by these journals and have been published (PMID: 37468456;36662526) – see appendices for their pdfs. The publication in

Nature Communications entitled “Circulating trans fatty acids are associated with prostate cancer in Ghanaian and American men” analyzed the circulating fatty acid dataset, generated under subtask 2, and evaluated how circulating fatty acid levels relate to prostate cancer (PMID: 37468456). The key findings are summarized as follows (abstract below):

The association between fatty acids and prostate cancer remains poorly explored in African-descent populations. Here, we analyze 24 circulating fatty acids in 2934 men, including 1431 prostate cancer cases and 1503 population controls from Ghana and the United States, using CLIA-certified mass spectrometry-based assays. We investigate their associations with population groups (Ghanaian, African American, European American men), lifestyle factors, the fatty acid desaturase (FADS) genetic locus, and prostate cancer. Blood levels of circulating fatty acids vary significantly between the three population groups, particularly trans, omega-3 and omega-6 fatty acids. FADS1/2 germline genetic variants and lifestyle factors explain some of the variation in fatty acid levels, with the FADS1/2 locus showing population-specific associations, suggesting differences in their control by germline genetic factors. All trans fatty acids, namely elaidic, palmitelaidic, and linoelaidic acids, associated with an increase in the odds of developing prostate cancer, independent of ancestry, geographic location, or potential confounders.

The publication in *JAMA Network Open* entitled “Association of neighborhood deprivation with prostate cancer and immune markers in African American and European American men” incorporated the circulating immune marker dataset, generated under subtask 2, and evaluated how neighborhood deprivation may influence their levels as an indicators of immune function changes in an adverse environment (PMID: 36662526). This publication also evaluated the contribution of neighborhood deprivation to the excessive burden of prostate cancer among African American men (abstract below):

Importance: Neighborhood factors may contribute to the excessive burden of prostate cancer among African American (AA) men.
Objective: Examine associations between neighborhood deprivation, circulating immune-oncology markers, and prostate cancer among diverse men.
Design: Case-control study with National Death Index follow up through December 31, 2019.
Setting: Between 2005-2015, cases were recruited at the Baltimore Veterans Affairs and University of Maryland Medical Centers; controls through the Maryland Motor Vehicle Administration database.
Participants: Cases (n = 769, 405 AA, 364 EA men) and age- and race-frequency matched population controls (n = 1,023, 479 AA, and 544 EA men). The median survival follow up was 8.4 years with 246 deaths among cases.
Exposure: 2000 Census-tract neighborhood deprivation index as standardized score.
Main Outcomes and Measures: Primary outcomes included prostate cancer, all-cause mortality, and disease-specific mortality. Secondary outcomes included the National Comprehensive Cancer Network risk score and serum proteomes for 82 immune-oncology markers with pathway annotation.
Results: Among 884 AA and 908 EA men, the mean age at recruitment was 64 and 66 years, respectively. In the multivariable logistic regression analysis [odds ratio (OR), 95% confidence interval (CI)] with individual socioeconomic status (SES) adjustment, neighborhood deprivation was associated with 55% increased odds of prostate cancer among AA men (1.55, 1.33-1.81), but

did not associate with the disease among EA men. Residing in the most deprived neighborhoods corresponded to 88% higher disease odds (1.88, 1.30-2.75, quintile (Q) 5 vs. Q1) among all men and an about 3-fold increase among AA men (3.58, 1.72-7.45), but no association among EA men. In Cox regression analyses (hazard ratio (HR), 95% CI), SES-adjusted neighborhood deprivation was associated with an increased all-cause mortality only among AA men (1.28, 1.08-1.53) whereas it was associated with metastatic disease and a 50% increased hazard of a prostate cancer-specific death among all men (1.50, 1.07-2.09). In analyses restricted to controls, neighborhood deprivation was associated with increased activity scores of serum proteome-defined chemotaxis, inflammation, and tumor immunity suppression.
Conclusion and Relevance: A deprived neighborhood may predispose AA men to prostate cancer and a related mortality, potentially through its effects on systemic immune function and inflammation.

In a follow-up to this study, Catherine Pichardo assessed whether neighborhood gentrification may have effects similar to neighborhood deprivation in an investigation entitled "Association of neighborhood gentrification with prostate cancer and immune markers in African American and European American men" and published in *Cancer Medicine* (PMID: 38151903). However, this is not what we observed. From our analysis, gentrification is rather weakly linked to prostate cancer and systemic immune function and inflammation (abstract below):

Background: Prior studies showed that neighborhood deprivation increases the risk of lethal prostate cancer. However, the role of neighborhood gentrification in prostate cancer development and outcome remains poorly understood. We examined the relationships of gentrification with prostate cancer and serum proteome-defined inflammation and immune function in a diverse cohort.
Methods: The case-control study included 769 cases [405 African American (AA), 364 European American (EA) men] and 1023 controls (479 AA, 544 EA), with 219 all-cause and 59 prostate cancer-specific deaths among cases. Geocodes were linked to a neighborhood gentrification index (NGI) derived from US Census data. Cox and logistic regression, and MANOVA, were used to determine associations between NGI, as continuous or quintiles (Q), and outcomes.
Results: Adjusting for individual socioeconomic status (SES), continuous NGI was positively associated with prostate cancer among all men (odds ratio (OR) 1.07, 95% confidence interval (CI) 1.01-1.14). AA and low-income men experienced the highest odds of prostate cancer when residing in tracts with moderate gentrification, whereas EA men experienced reduced odds of regional/metastatic cancer with increased gentrification in SES-adjusted analyses. Continuous NGI also associated with mortality among men presenting with localized disease and low-income men in SES-adjusted Cox regression analyses. NGI was not associated with serum proteome-defined chemotaxis, inflammation, and tumor immunity suppression.
Conclusions: Findings show that neighborhood gentrification associates with prostate cancer and mortality in this diverse population albeit associations were heterogenous within subgroups. The observations suggest that changing neighborhood socioeconomic environments may affect prostate cancer risk and outcome, likely through multifactorial mechanisms.

These 3 research publications completed all work related to **Specific Aim 1.** We published a total of 6 peer-reviewed research publications using datasets generated by Aim 1-related tasks – see also products and appendix. Thus, the research has been very productive.

Progress with Specific Aim 2

Specific Aim 2: Assess whether germline genetic variants are associated with immune-inflammation markers and PCa using a genome-wide association approach (GWAS).		NCI
Major Task 1: Perform GWAS genotyping with Infinium HumanOmni5-Quad BeadChip	Months	
Subtask 1: Prepare DNA samples for shipment • Obtain IRB approval covering the NCI-Maryland Prostate study • Aliquot DNA samples from 900 cases and 900 controls, perform quality control, and ship to Cancer Genomics Research Laboratory, DCEG/NCI	1-8	Ambs, Dorsey, Minas
Subtask 2: Genotyping with Infinium HumanOmni5-Quad BeadChip, covering more than 4 million SNPs • Perform genotyping and preliminary data analysis at Cancer Genomics Research Laboratory. Receive data and add to database.	8-14	Ambs, Minas, Tang
Major Task 2: Statistical analysis		
Assess whether germline genetic variants are associated with immune-inflammation markers and PCa. Perform a combined analysis of the NCI-Maryland and NCI-Ghana Prostate studies. Genotyping data for the NCI-Ghana Prostate study exist already.	14-24	Ambs, Cook, Minas, Tang, Butler
Major Task 3: Preparation of manuscript and revisions		
Preparation and submission of manuscripts including revisions that occur in the review process	20-36	Ambs, Cook, Minas, Tang, Butler

Under **Specific Aim 2**, Major Task 1, we generated high-quality genotyping data covering millions of germline single nucleotide polymorphisms (SNPs) for 1450 men (694 African American, 756 European American), as described in our 2022 annual report for the award. The genotyping data for these 1450 men have been deposited in the public database, dbGaP, under submission number phs002939.v1.p1. We submitted the data together with descriptors of the study population. The release date of the data was February 2023. This task completed the laboratory-based tasks for **Specific Aim 2**.

After completion of Major Task 1, we continued with Major Task 2 and worked with the raw genotyping data from the NCI-Maryland study (694 African American with 350 controls and 344 cases; 756 European American with 394 controls and 362 cases) and 1113 men from the NCI-Ghana study, with 4,426,323 SNPs passing study specific quality control for the NCI-Maryland study and 2,786,417 SNPs for NCI-Ghana study. Genotyping data for the NCI-Ghana study have previously been generated using another funding source. SNP coverage from the Infinium HumanOmni5-Quad BeadChip SNP genotyping array was increased through imputation using the TOPMED Imputation Reference Panel using the Michigan Imputation Server (https://topmed.nhlbi.nih.gov/), resulting in 46,919,584 assigned variants for NCI-Maryland and 307,510,644 variants for NCI-Ghana studies. 38,317,621 variants in the NCI-Maryland study and 298,483,657 variants in the NCI-Ghana study were removed due to falling below the minor allele threshold of 0.05, resulting in a total of 8,601,963 variants contained within the NCI-Maryland dataset and 9,026,987 variants contained within the NCI-Ghana dataset.

Using this resource, a quantitative trait analysis was performed by Hunter Schaumloffel, currently a Special Volunteer with our laboratory and guided in his research by PI Ambs. In this analysis, Hunter linked the variant genotypes (SNPs) to 36 circulating immune markers. Data for these markers have previously been generated under tasks described for Aim 1. The markers represent a subset of the 82 circulating immune-oncology markers that we described in our 2022 *Nature Communications* publication (PMID: 35365620). Hunter performed his analysis with adjustments for age and global ancestry, under the guidance by our data scientist, Huaitian Liu, and with the help of Sonja Berndt, a new collaborator and principal investigator with NCI's Division of Cancer Epidemiology & Genetics (DCEG). Dr. Berndt is an expert in genetic epidemiology. With their mentorship, Hunter generated Manhattan plots depicting association signals arising within genetic loci across all chromosomes that associate with the levels of these 36 markers (**Figures 1-4**). We applied a $P < 1.2 \times 10^{-9}$ significance threshold to all observed associations that accounts for multiple comparisons on the genotype and marker levels, applying the commonly used significance threshold of $P < 5 \times 10^{-8}$ to the genome-wide SNP data and then accounting for the 36 markers that were

simultaneously analyzed

Key findings: 1) The circulating levels of MCP1/CCL2, MCP4/CCL13, CXCL1 and CXCL5 showed associations with variants in the *DARC/ACKR1* locus in chromosome 1, consistent with previous reports, among African American and European American men but not Ghanaian men (**Figure 1**). In Ghanaian men, variant allele frequencies at this locus are too infrequent to show significant associations. In addition we found a common association of the expression of these markers with the *IFI16* locus among African American men, also consistent with previous reports. We judge these findings as validation of our study design and methodology, suggesting that findings from our study are likely representative. 2) Found associations of multiple SNPs in chromosome locus, 19p13.3-11, with circulating levels of IL12RB1 and CD70 across all three population groups (**Figure 2**). The associated SNPs are located either within the gene loci or nearby, indicating a cis-protein quantitative trait loci (cis-pQTL) relationship. Soluble CD70 contributes to T cell activation by binding to the receptor, CD27. However, tumor cell-secreted soluble CD70 may also increase lymphocyte apoptosis and decrease anti-tumor immunity. 3) Found cis-pQTL associations of multiple SNPs in chromosome locus, 12p13.31, with circulating levels of CD4 and CD27 (**Figure 3**). Associations with CD4 were observed in all three population groups whereas the association with CD27 was restricted to Ghanaian men. Soluble levels of CD27 are positively

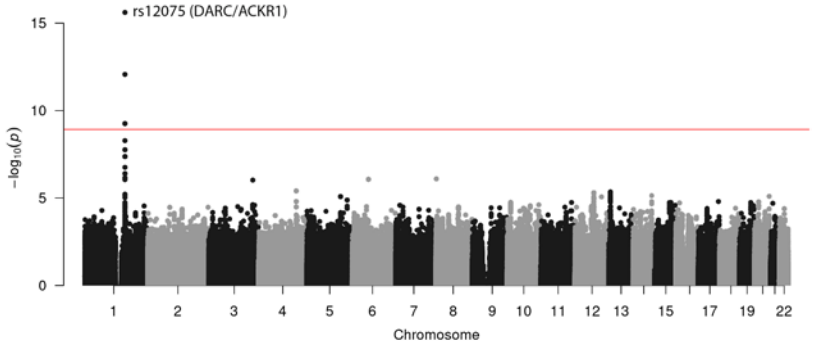

Figure 1: Manhattan plot for the association of the *DARC/ACKR1* SNP, rs12075, with circulating MCP4/CCL8 levels in European American men.

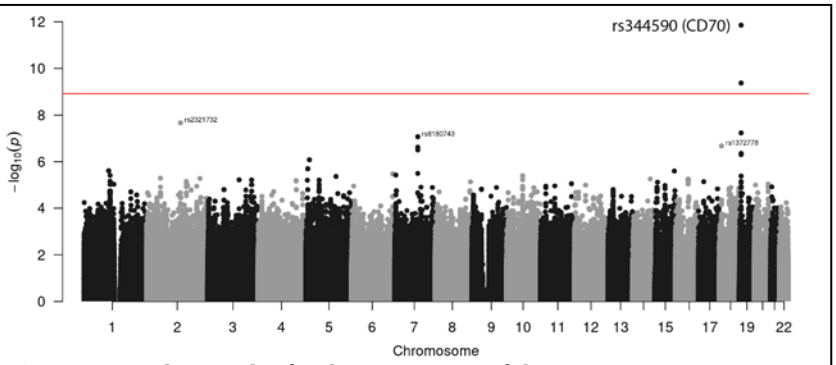

Figure 2: Manhattan plot for the association of the *CD70* SNP, rs344590, with circulating CD70 levels in African American men.

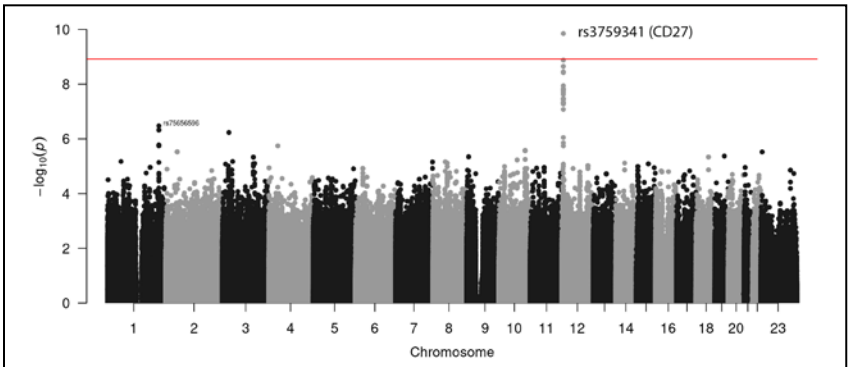

Figure 3: Manhattan plot for the association of the *CD27* SNP, rs3759341, with circulating CD27 levels in Ghanaian men.

associated with the risk for non-Hodgkin lymphoma and correlate with immune exhaustion and immunotherapy failure in patients with solid tumors. 4) Found cis-pQTL associations of multiple SNPs in chromosome locus, 17q12, with circulating levels of CCL3, MCP2/CCL8, MCP4/CCL13, and CCL23. Associations with CCL3 and MCP4/CCL13 were restricted to African American and Ghanaian men, but not for MCP2/CCL8 and CCL23. 17q12 is a locus encoding multiple CC chemokines with cancer-related functions. Circulating CCL23 have recently been described to be down-regulated in men with prostate cancer, when compared to controls, and to be lower in African American than European American men. 5) Found associations of SNPs in chromosomes 2 & 6 with circulating levels of CD8A in African American and European American but not Ghanaian men. Chromosome 2: cis-pQTL association. Chromosome 6: trans-pQTL association. Reports indicate that soluble CD8A may interfere with T cell activation and proliferation, thus may have immune suppressive function. 6) Found cis-pQTL association of SNPs in chromosomes 20q13.12 with circulating levels of CD40 across all three population groups. The soluble form of CD40 is increased in cancer patients and its presence tends to be associated with a poor prognosis. A likely mechanism is interference with antitumor immunity. 7) Found associations of SNPs in chromosomes 11q13.4 with circulating levels of IL18 in Ghanaian men (**Figure 4**).
IL18 is located at 11q23.1. The key SNP, rs2096784 is also a trans-pQTL for the gene, *AHSP*. Association among African American men did not reach statistical significance. A heritability analysis conducted by us among men without prostate cancer suggests that 57.3% and 40.7% of the variance in circulating IL18 is explained by germline genetics among Ghanaian and African American men, albeit the estimate reached statistical significance only among the Ghanaian (P = 0.007) but not the African American men (P = 0.19). There was no heritability signal among European American men. 8) Found cis-pQTL association of SNPs in chromosomes 4p21.1 with circulating levels of CXCL11 in African American and Ghanaian but not European American men. In summary, one can see our study revealed multiple previously known and unknown relationships between germline genetic factors and circulating immune markers that may relate to cancer susceptibility and response to immune therapies.

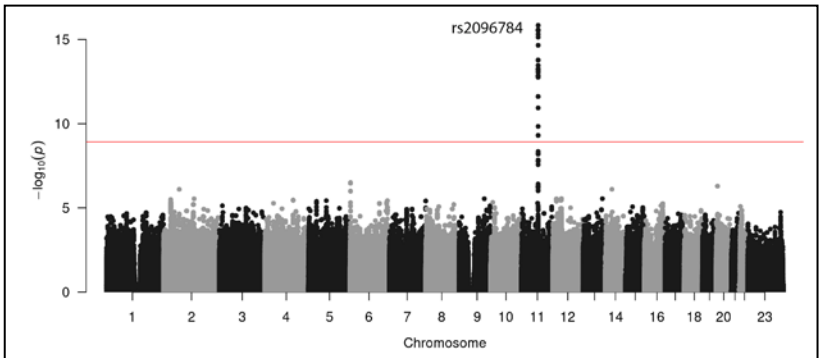

Figure 4: Manhattan plot for the association of the *IL18* SNP, rs2096784, with circulating IL18 levels in Ghanaian men.

As next steps towards a manuscript, we generated circus plots for better graphical display of our findings in the manuscript and are working on combined Manhattan plots, showing the most significant associations across all chromosomes for the 36 immune markers in one plot. In addition, we completed a heritability analysis for 12 of the 36 markers (IL12RB1, CD70, CD4, CD27, CCL3, MCP2/CCL8, MCP4/CCL13, and CCL23, CD8A, IL18, TNFRS9, PTN), with the support of Bill Wheeler at IMS, who is a contractor to Dr. Berndt. This analysis was aimed to show how much of the variability in the circulating levels of a marker can be explained by germline genetics. The analysis found a large impact of genetics on circulating levels IL18 among men of African ancestry

that reached statistical significance for Ghanaian men. Other ongoing tasks include an examination that compares the abundance levels of the 36 markers between cases and controls in the three population groups to describe those immune markers in the manuscript that associate with a prostate cancer status. As a last task, we will generate boxplots graph that show levels of circulating markers by genotype to capture how much certain genotypes may influence the levels of these markers in the population. We are aiming for completion and submission of this manuscript by late spring.

Besides this main project, we will be using the generated genotyping data for other analyses. Data from a study that investigated the genetic control of circulating fatty acids, a project started by Amy Zhang, a former NCI PostBac, showed robust differences in their genetic control between African ancestry and European ancestry men that have not been reported by others. Key findings were included in our *Nature Communications* publication entitled "Circulating trans fatty acids are associated with prostate cancer in Ghanaian and American men" (PMID: 37468456). There are also plans to incorporate the genotyping data into a study of the viral infection history of men and how this history may relate to prostate cancer risks and germline genetics. This study includes the application of VirScan, which was developed by Stephen Elledge of Harvard Medical (PMID: 26045439). It is a powerful technology to determine the viral exposure history of an individual. It uses a human virome peptide library displayed by bacteriophages to screen for antivirome antibodies in blood samples. Theoretically, the method should allow for detection of any viral infection in a subject that triggered an immune response in the past. The VirScan technology has been established in our laboratory. We are currently applying this technology to the NCI-Maryland and NCI-Ghana studies and will investigate how germline genetics may associate with the infection history of men with and without prostate cancer.

Progress with Specific Aim 3

For Specific Aim 3, management of Major Tasks 1 & 2 falls primarily under the responsibility of Dr. Clayton Yates. Yet, his group and the NCI research teams have been working on these tasks together, in close collaboration, involving Tiffany Dorsey, Wei Tang, and now Huaitian Liu from the Ambs group.

As previously reported, we could not perform RNA and DNA sequencing using the sequencing facility at Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research, as specified under Major Task 1. Instead we used the service provider, HudsonAlpha. The company delivered good quality RNA-seq data for 167

Specific Aim 3: Determine the prevalence of an immune-inflammation signature in prostate tumors of men of European and African ancestry, and evaluate how this signature relates to other gene expression patterns, genomic alterations, and chromatin structure in these tumors, and to patient characteristics.		NCI	TU
Major Task 1: Perform RNA sequencing (RNA-seq), whole exome sequencing (exome-seq), and Assay for Transposase-Accessible Chromatin with high throughput sequencing (ATAQ-seq) for 250 tumors	Months		
Subtask 1: Prepare RNA and DNA for sequencing • Obtain IRB approval and MTAs covering the two study sites, NCI and University of Tuskegee. • Receive tumors from NCI (50 African-American and 50 European-American patients). Isolate RNA and DNA from NCI tumors and tumors from 150 Nigerian patients. Process all tumor tissues, including macro- and microdissection of tumor epithelium as needed. • Perform quality control of RNA and DNA	1-8(10)	Ambs	Grizzle, Wang, Yates
• Ship RNA and DNA samples to the sequencing facility at Leidos Biomedical Research, Inc., Frederick National Laboratory for Cancer Research. Facility will perform RNA-seq, exome-seq, and ATAQ-seq. Obtain raw output data together with quality control assessment data. Perform initial quality control analysis of datasets.	8(10)-14	Ambs, Tang	White, Yates
Major Task 2: Statistical analysis of transcriptomics and genomics data			
Analyze the RNA-seq, exome-seq, and ATAQ-seq data for gene expression pattern, mutational signatures, and open chromatin structure in tumors from Nigerian, African-American, and European-American and examine relationships between gene expression patterns, genomic alterations, and chromatin structure in these tumors.	14-24	Ambs, Tang	White, Yates
Major Task 3: Perform immunohistochemistry (IHC) for immune markers such as PD-1, PD-L1/2, CD45, CD68, CD80, CD86, CD163, and CD206.	Months		
Subtask 1: Perform immunostaining • Establish optimized protocol and perform IHC	8-24		Karanam, Yates
Subtask 2: Analyze immunohistochemistry • Determine intensity and distribution of stains and develop an IHC sum score	12-24		Karanam, Yates

human prostate tumors but failed to deliver good quality DNA-seq data. We could not resolve this problem of poor quality DNA-sequencing data with this company. Thanks to a second approach using NCI-Leidos for WES, previously initiated with NCI financial support, the Yates group and collaborators obtained good quality WES data for a cohort of 45 advanced stage, treatment-naïve Nigerian primary prostate cancer tumors. The WES data were then analyzed by Jason White. Findings from this study were recently published in the peer-reviewed AACR journal, *Cancer Research Communications* entitled "Whole-exome Sequencing of Nigerian Prostate Tumors from the Prostate Cancer Transatlantic Consortium (CaPTC) Reveals DNA Repair Genes Associated with African Ancestry" (PMID: 36922933).

Abstract: *In this study, we used whole-exome sequencing of a cohort of 45 advanced stage, treatment-naïve Nigerian (NG) primary prostate cancer tumors and 11 unmatched nontumor tissues to compare genomic mutations with African American (AA) and European American (EA) in The Cancer Genome Atlas (TCGA) prostate cancer database. NG samples were collected from six sites in central and southwest Nigeria. After whole-exome sequencing, samples were processed using GATK best practices. BRCA1(100%), BARD1 (45%), BRCA2 (27%), and PMS2 (18%) had germline alterations in at least two NG nontumor samples. Across 111 germline variants, the AA cohort reflected a pattern [BRCA1 (68%), BARD1 (34%), BRCA2 (28%), and PMS2 (16%)] similar to NG samples. Of the most frequently mutated genes, BRCA1 showed a statistically ($P \leq 0.05$) higher germline mutation frequency in men of African ancestry and increasing variant frequency with increased African ancestry. Disaggregating gene level mutation frequencies by variants revealed both ancestry-linked and NG-specific germline variant patterns. Driven by rs799917 (T>C), BRCA1 showed an increasing mutation frequency as African ancestry increased. BRCA2_rs11571831 was present only in MAA, and BRCA2_rs766173 was elevated in NG men. A total of 133 somatic variants were present in 26 prostate cancer–associated genes within the NG tumor cohort. BRCA2 (27%), APC (20%), ATM (20%), BRCA1 (13%), DNAJC6 (13%), EGFR (13%), MAD1L1 (13%), MLH1 (11%), and PMS2 (11%) showed mutation frequencies > 10%. Compared with TCGA cohorts, NG tumors showed statistically significant elevated frequencies of BRCA2, APC, and BRCA1. The NG cohort variant pattern shared similarities (cosign similarities ≥ 0.734) with Catalogue of Somatic Mutations in Cancer signatures 5 and 6, and mutated genes showed significant ($q < 0.001$) gene ontology (GO) and functional enrichment in mismatch repair and non-homologous repair deficiency pathways. Here, we showed that mutations in DNA damage response genes were higher in NG prostate cancer samples and that a portion of those mutations correlate with African ancestry. Moreover, we identified variants of unknown significance that may contribute to population-specific routes of tumorigenesis and treatment. These results present the most comprehensive characterization of the NG prostate cancer exome to date and highlight the need to increase diversity of study populations.*
Significance: *Men of African ancestry have higher rates of prostate cancer incidence and mortality, however, are severely underrepresented in genomic studies. This is the first study utilizing whole-exome sequencing in NG men to identify West African ancestry-linked variant patterns that impact DNA damage repair pathways.*

We are currently working on finalizing the data analysis for a second manuscript using the RNA-sequencing data for 167 human prostate tumors from Nigerian, African American and European American patients, generated under Major Task 1. The lead person for this analysis is Isra Elhussin, a postdoctoral fellow with Dr. Yates. Huaitian Liu in the Ambs group is helping her with this task.

This manuscript will report on differences in tumor biology between the 3 patient groups. It is one key findings that a prevalent immune-inflammation signature in prostate tumors of African American men in the US is not present in tumors of Nigerian men. This manuscript will also contain findings describing the occurrence of fusion gene transcripts in these tumors. New software tools are now available that allow the detection of these structural rearrangements in RNA-sequencing data and have been applied by Drs. Elhussin and Liu to describe their occurrence in this dataset.

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.

The award provided training opportunities to the following fellows: Jason White and Isra Elhussin (both Tuskegee University and mentored by Clayton Yates); Tsion Minas, Maeve Bailey-Whyte, Brittany Jenkins-Lord, Amy Zhang, Margaret Pichardo, Catherine Pichardo, and Hunter Schaumloffel (all NCI-associated and mentored by Stefan Ambs).

Jason White and Isra Elhussin were both PhD students at Tuskegee University and successfully defended their thesis work at the end of 2022, thereby earning their Ph.D. degree. Jason White is now a postdoctoral fellow with Melissa Davis at Morehouse School of Medicine whereas Isra Elhussin followed Dr. Yates to Johns Hopkins University to become a postdoctoral fellow in his new laboratory. The DoD grant provided the basis for their graduate work and thesis projects. Both obtained extensive training in data science and have gained the experience to independently perform advanced data analysis using various software tools including R programming. For them, the award was critically important in advancing their analysis skills and career development towards earning a PhD degree. Their research was further enabled because they had access to the NIH Biowulf Cluster for high-performance computing, as part of the collaboration between the Ambs and Yates laboratories. Both were co-mentored by two staff scientists and data science experts in the Ambs group, namely Drs. Wei Tang and Huaitian Liu. Here, one can certainly say that the award has made a significant impact in advancing the career of two junior scientists at Tuskegee University. I had the opportunity of discussing with them their career options and provided career advice, in addition to Dr. Yates' mentorship. Dr. Elhussin is a physician scientist with a minority background who wants to stay in biomedical research focusing on cancer. Her acquired skill set, being a physician with data science skills, should set her apart from others and should provide her with many opportunities for an academic research career.

Tsion Minas, Maeve Bailey-Whyte, Brittany Jenkins-Lord, Amy Zhang and Margaret Pichardo completed their training in the Ambs laboratory and have moved into new career opportunities. Dr. Tsion Minas, a former postdoctoral fellow, departed the Ambs lab at the beginning of 2022 and remains a Fulbright U.S. Scholar in Ethiopia, studying why human papillomavirus infection is spontaneously cleared in most women but persists in others, increasing their risk for cervical cancer. Her success was highlighted by the NCI (https://ccr.cancer.gov/news/article/ccr-postdoctoral-researcher-awarded-fulbright-to-study-hpv-and-cervical-cancer-in-africa). Tsion was the second recipient of a Fulbright grant among the trainees supported by this DoD award after Anuoluwapo Ajao, a postbaccalaureate fellow mentored by Tsion, received a Fulbright Research Fellowship in 2021, to study risk factors for breast cancer in Nigeria. It is Tsion's plan to become an independent researcher with a focus on cancer in Africa. It is my understanding that she has been offered opportunities to return to the United States as a tenure-track investigator. Yet, she is considering of staying in Ethiopia for additional years. She has been very productive as a postdoctoral fellow with her research studying prostate cancer in men of African descent. Her 2022 publication in *Nature Communications* (PMID: 35365620) was covered in the NCI's Center for Cancer Research 2023 Milestones publication (https://ccr.cancer.gov/news/milestones-2023/bridging-the-health-disparities-gap), which highlights some of the most outstanding research conducted in the NCI intramural program in 2022. This research was largely funded through the award. Here again, the DoD award was instrumental to a trainee's success.

Dr. Maeve Bailey-Whyte, a former NCI Cancer Prevention Fellow, returned to Ireland in 2021. She is now a Clinical Trials Coordinator at Serosep Ltd in Limerick, Ireland. Her research work showing that thromboxane A2 formation is a risk factor for lethal prostate cancer among African American men, a research project that was entirely funded by the DoD award and published in *JNCI* (PMID: 34264335) and was covered as a 2021-22 research highlight as part of the NCI's Center for Cancer Research 2022 Milestones publication (https://ccr.cancer.gov/news/milestones-2022/a-new-application-for-an-old-medicine), a great achievement. Maeve's involvement with this project provided her with first-of-its-kind experience in epidemiology and working with a patient cohort, collecting data for this cohort and analyzing them.

Dr. Brittany Jenkins-Lord, a NCI Cancer Prevention fellow prior to her departure, partnered with Tsion Minas and Amy Zhang in the investigation of circulating fatty acids and their relationship with germline genetics and prostate cancer in Ghanaian, African-American, European-American men. Findings from this collaborative work have now been published in *Nature Communications* in 2023 (PMID: 37930698), with her being co-first author. Brittany remains involved with the study that assesses the genetic and ancestral basis of prostate cancer-associated inflammation using a genome-wide association approach. Here, she works with Hunter Schaumloffel in conducting analyses to finalize the manuscript. Brittany's research with these projects, all epidemiology and data science-based, allowed her to learn several new methods for data analysis and display. Brittany presented a virtual poster of their findings at the 2021 AACR conference on the Science of Cancer Health Disparities entitled "Determining the association between circulating fatty acids, immune oncological markers, and prostate cancer risk in a diverse cohort" and received an AACR Scholar-in-Training-Award for this submission. She was also selected as a NextGen Star speaker at the 2023 AACR Annual Meeting. In addition, she received the Eddie Méndez Scholar Award from the Fred Hutchinson Cancer Research Center. The award recognizes outstanding postdoctoral fellows who are conducting cancer research and are from backgrounds that are underrepresented in science.

Fitting to her success, she has been offered and then accepted a tenure-track Assistant Professor position at the Johns Hopkins University School of Public Health. She started in this position in August of 2023. Her DoD-sponsored research contributed to this success.

Amy Zhang was a postbaccalaureate fellow who performed data analysis with the genome-wide genotyping dataset that was generated with funding from this award, linking germline variants to circulating levels of fatty acids and immune-oncology markers to study their control by germline genetics. Although Amy could not finish all parts of the analysis, she generated a finalized dataset with imputed genome-wide genotypes for the NCI-Maryland study that was submitted to dbGaP for curation in a public database. Amy's work familiarized her with the principles of a genome-wide association study and quantitative trait analysis and provided her with new skills in using the R software. Like Anuoluwapo Ajao, Amy successfully competed for acceptance into a MD/PhD program and has joined the University of North Carolina Medical School. I would argue that the experience that Amy gained by being involved with research sponsored by the award contributed to this success.

Dr. Margaret Pichardo began to be involved with research related to this award starting in 2020. She, together with her sister, Catherine Pichardo, has been instrumental in establishing a research project that collected geospatial neighborhood data for the NCI-Maryland Prostate Cancer Study. They obtained census tract data for 1990, 2000, and 2010 and developed a neighborhood deprivation index. The linkage of census tract data to study participants in the NCI-Maryland Prostate Cancer study became a multi-year effort. Margaret's research explored the relationship of the neighborhood deprivation index with prostate cancer risk and outcomes among African American men, and how this index may influence immune-oncology marker expression and the immune response related to prostate cancer. Her research, which relied on data that we generated with the award funds, has been very productive. Her findings have been published in *JAMA Network Open* in 2023 (PMID: 36662526). Margaret is a rising star. She completed her PhD in epidemiology at Yale in 2021 and is now a resident at the University of Pennsylvania after finishing medical school at Howard University. It is Margaret's career plan to become a physician scientist. Her research, partly made possible by the award, is aimed at helping her in achieving this goal. Margaret has received several awards including the AACR Minority Scholar in Cancer Research award.

Dr. Catherine Pichardo has begun working with us in 2022. She is a postdoctoral fellow with the NCI's Division of Cancer Control and Population Sciences and completed an analysis studying the relationship of neighborhood gentrification with prostate cancer and circulating immune-oncology marker, similar to the approach of her sister, Margaret, but focusing on neighborhood gentrification instead of neighborhood deprivation. Like Margaret, she used data that we generated with the award funds and recently published her findings in *Cancer Medicine* (PMID: 38151903). Catherine is now involved in a study asking the question how genetic ancestry may influence prostate cancer risk and mortality in the context of neighborhood deprivation.

Hunter Schaumloffel remains a Special Volunteer with the Ambs laboratory. He started as a summer intern and has been the key data analyst assessing the genetic and ancestral basis of prostate cancer-associated inflammation using a genome-wide association approach. Hunter came to us as a highly recommended college student but has since graduated with a bachelor's in science

degree from Colgate University. He has now been accepted into a veterinary medicine program. Although previously untrained in data science, Hunter has made great progress in completing an analysis linking germline genetic variants to circulating levels of 36 immune markers in Ghanaian, African American, and European American in the NCI-Ghana and NCI-Maryland studies. His success is based on his ability to quickly learn new codes and analysis approaches, and his perseverance in troubleshooting the problems arising from working with huge datasets. Most of his work is conducted using the NIH Biowulf Cluster for high-performance computing. Hunter is one of the most outstanding college students we have ever trained and remains highly motivated in getting his work published.

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.

We disseminated our research findings mainly through presentations at scientific meetings, publications, and postings with social media.

Tsion Minas gave the first data presentation at the 2019 AORTIC Cancer in Africa conference in Maputo, Mozambique, based on findings from this grant. She was selected for a Lightning Talk entitled: "Distinct circulating immune-oncological markers in men of African descent". She was also selected to be on the African Cancer Leadership Institute associated with this international cancer conference and received a grant to participate at this conference. Tsion presented more of her findings as a speaker at an NCI Interlaboratory Seminar in 2020. In 2021, Tsion gave 10 minutes invited presentations at the 3rd NCI Symposium on Cancer Health Disparities and in the Hot Topic session at the 2021 AACR virtual conference on the Science of Cancer Health Disparities entitled "Blood levels of TNFRSF9 and PTN predict lethal prostate cancer among African-American men". She also gave a short presentation on this subject at the 2021 AORTIC Cancer in Africa virtual conference in November. Maeve Bailey-Whyte presented a poster at the AACR conference on the Science of Cancer Health Disparities, October 2-4, 2020. She presented findings from the urinary eicosanoid metabolites study. Her abstract was entitled "High urinary thromboxane B2 associates with aggressive prostate cancer and inversely correlates with aspirin use". She had an additional poster presentation at the 2021 AACR virtual conference on the Science of Cancer Health Disparities entitled "Association of urinary PGE-M with all-cause mortality in men with prostate cancer is influenced by aspirin use", for which she received an AACR Student and Early Career Investigator Scholarship. Maeve had two additional presentations: an oral abstract at the 2021 AORTIC Cancer in Africa virtual conference and an invited speaker presentation at the 7th Biennial Science of Global Prostate Cancer Disparities in Black men Conference, November 2021. Brittany Jenkins-Lord presented a poster at the 2021 AACR virtual conference on the Science of Cancer Health Disparities and gave a short presentation on the same subject ("Exploring the relationship of circulating fatty acids and immune-oncological markers with prostate cancer in a diverse cohort of men") at the AORTIC Cancer in Africa 2021 virtual conference. She presented her findings in other talks, including her invited talk as a NextGen Star speaker at the 2023 AACR Annual Meeting.

Stefan Ambs was an invited speaker at the 6th Biennial Science of Global Prostate Cancer Disparities in Black men Conference in 2020 and at the 3rd NCI Symposium on Cancer Health Disparities in 2021, both virtual meetings. The presentations focused on results from this grant ("An investigation of how inflammation may underlie the excessive burden of prostate cancer in men of African ancestry"). In addition, Dr. Ambs presented work related to this grant in invited talks at the NCI Laboratory of Genitourinary Cancer Pathogenesis seminar series, the NIH Academy, and the NCI TRACO lecture series, to support health disparity research. He was also invited to Grand Rounds at the University of Maryland (Frontiers in Oncology) where he presented the prostate cancer research related to this grant. More recently, he presented the newest findings at the 2022 CCR-DCEG Cancer Health Disparities workshop and at the Schoodic Scientific Workshop (2022 Redox and Metabolism in Inflammation and Disease Workshop) in Maine and gave a presentation at the Association of Health Care Journalists Fellowship meeting, again focusing on prostate cancer health disparities and work sponsored by the award. Moreover, he has given multiple invited lectures, mainly virtual, promoting cancer health disparity research and presenting research sponsored by this DoD award as an example of health disparity research that integrates basic, translational, population, and social science research to investigate the causes of cancer health disparities. These lectures have always been very well received, creating interest in fellow researchers to follow this example.

Lastly, our research was highlighted by the NCI at https://ccr.cancer.gov/news/article/protein-signature-in-the-blood-linked-to-prostate-cancer-lethality-in-men-of-african-ancestry, https://ccr.cancer.gov/news/milestones-2022/a-new-application-for-an-old-medicine, https://ccr.cancer.gov/news/milestones-2023/bridging-the-health-disparities-gap, NIH at https://irp.nih.gov/blog/post/2022/07/african-ancestry-may-influence-immune-response-to-prostate-cancer, and by The Geneva Foundation on their website at https://genevausa.org/news/story/reducing-lethal-prostate-cancer-in-men-with-african-descent/ As one can see from the list of presentations, the fellows have been highly successful in disseminating the research findings from this grant at various national and international meetings, giving many invited talks and receiving awards for their contribution.

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).

The award pursued the hypothesis that both systemic and tumor-associated inflammation and immune suppression in the circulating blood promote prostate cancer progression, with a larger impact in men of African ancestry.

Previously we showed that many prostate tumors found in African American men harbor a distinct immune-inflammation signature that coincides with greater disease severity. Additional research funded by this award revealed that this signature also occurs systemically. Inflammation is known to activate the oncogenic cyclooxygenase (COX) signaling pathway. We studied this pathway by measuring stable urinary COX-related metabolites and found that a subgroup of African American men with prostate cancer had elevated levels of the pro-metastatic metabolite, thromboxane A2 (TXA2), which is primarily produced by the cyclooxygenase enzyme located in blood platelets (PMID: 34264335). We linked high TXA2 to more prostate cancer metastasis and prostate cancer-specific deaths. Additionally we showed that TXA2 levels inversely correlate with aspirin use. Taken together, these findings increase our understanding of how regular aspirin use, or use of other anti-inflammatory drugs, may benefit African American men by potentially reducing their risk of developing aggressive prostate cancer and dying from the disease. The findings are especially important given that, compared to European-American men, African American men are more likely to develop prostate cancer and are twice as likely to die from it. We think our work discovered a mechanism that appears to have a significant effect and could potentially contribute to metastatic and lethal disease in this high-risk population for prostate cancer. The findings indicate that systemic inflammation enhances prostate cancer metastasis and are consistent with a previous report from our group that regular aspirin use among African American men with prostate cancer decreases the risk of disease progression and recurrence (PMID: 28292923). Thus, regular aspirin use before and after a prostate cancer diagnosis may prevent the development of lethal prostate cancer in these men through effects that reduce systemic and tumor-associated inflammation. See also https://ccr.cancer.gov/news/milestones-2022/a-new-application-for-an-old-medicine

In addition to this observation, our research discovered that circulating proteins known to suppress the ability of the immune system to control tumor growth, known as tumor immunity, were more prevalent in African American and Ghanaian men, and the presence of these proteins was associated with worse outcomes for men with prostate cancer (PMID: 35365620). This makes sense because cancer more easily evades immune system surveillance and spreads when tumor immunity is suppressed. The findings suggest the existence of a systemic “Suppression of Tumor Immunity” protein signature that is 1. more prevalent in men of African descent and 2. increases the odds of cancer metastasis. We argue that this signature may partly arise because of chronic inflammation and could be targeted by therapy to prevent metastasis and lethal prostate cancer. The research further revealed that men with African ancestry in this study population were most likely to have lethal prostate cancer when they had high blood levels of two specific proteins: Pleiotrophin, a protein normally found during embryonic development, and a soluble form of TNFRSF9, a receptor protein usually expressed on immune system cells, that has been linked to immune suppression in its soluble form. These proteins are known to influence tumor health and immunity. Thus, we hypothesize that when these proteins are at high levels, the immune system fails to recognize the cancer cell and destroy it, putting a person at risk of metastatic and lethal disease. Together, we think our observations enhance our knowledge about factors that contribute to excessive burden of lethal prostate cancer among African American men. It is the novelty of our observations that systemic immunity, not tumor-associated immunity, might be an important factor in driving the prostate cancer healthy disparity. Moreover, the work may have discovered mechanisms and markers that can be targeted by therapy to improve survival among African American men. Why would this signature develop in African American men? Our follow-up study showed that social determinants of health and neighborhood factors could be one cause (PMID: 36662526). See also

https://ccr.cancer.gov/news/article/protein-signature-in-the-blood-linked-to-prostate-cancer-lethality-in-men-of-african-ancestry.

Our research of how inflammation may underlie the excessive burden of prostate cancer in men of African ancestry is a concept that has impacted the prostate cancer health disparity field. The research interest in the distinct immune-inflammation signature that is prevalent in prostate tumors of African American men, first reported by us (Wallace et al. 2008; PMID: 18245496), has surged with the recent finding by Sartor and colleagues that the cancer vaccine, Sipuleucel T, may specially improve survival of African American men with metastatic castration-resistant prostate cancer (PMID: 32111923). The presence of an embedded interferon signature in these tumors that our group described (PMID: 18245496,30012562) would suggest that African American prostate cancer patients may respond better to cancer vaccines than European American men because of this signature. Thus, we believe that the research questions that we pursued under this award could have important implications for immune therapy in African American men with otherwise lethal prostate cancer. Furthermore, tumors with an interferon-stimulated gene signature are susceptible to inhibition of adenosine deaminase acting on RNA (ADAR1), as was recently discovered (PMID: 30575730). These inhibitors are being developed for clinical use by pharmaceutical industry and may have therapeutic activity particularly in African American men with prostate cancer as their tumors frequently harbor an interferon signature.

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.

We are not specifically aware of the impacts that our research may have had on other disciplines. Our description of an inflammation signature in African American men with prostate cancer has reinforced the hypothesis that an environmentally-induced systemic inflammation may affect the African American community more so than other communities. Inducers of this inflammation may include neighborhood factors and persistent exposure to racism – as we have discussed (PMID: 36662526). This inflammation signature may well be a cause of other acute and age-related diseases that are more prevalent in the African American community than other US communities. We wrote a review in *Trends in Cancer* on comorbidities and cancer, with a health disparity focus, in which we discuss the adverse impact of co-occurring chronic diseases in cancer patients (PMID: 33446449). With our publication by *Minas et al.* in *Nature Communications* (PMID: 35365620), we made our immune-oncology marker data publicly available. As was recognized by the reviewers, this could be an important resource for others, in disciplines beyond prostate cancer, as it covers 82 circulating proteins measured in almost 3000 Ghanaian, African American, and European American men. Lastly, we deposited the genome-wide genotyping data for the NCI-Maryland prostate cancer study in dbGaP (phs002939.v1.p1). This large-scale germline genetic dataset, covering 4 million SNPs in 1450 men, together with the measurements of immune-oncology markers and circulating fatty acids can be a rich resource for many researchers, beyond prostate cancer.

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.*

Our research is not expected to have an immediate impact in reducing the excessive burden of prostate cancer among African American men. The main impact on society is making it aware of the existence of persistent cancer health disparities in the United States, what causes them, and how we can reduce them and their detrimental impact in minoritized and underserved communities. It is my experience that the research funded by this award achieved this goal – increased awareness. I have given a lecture at the Association of Health Care Journalists Fellowship meeting. The lecture focused on findings related to the grant and emphasized to these young journalists the excessive burden of cancer that is experienced by African Americans and other underserved communities. Furthermore, I have been invited to a data science and health disparities panel discussion on the Federal Insights Exchange (https://web.cvent.com/event/d97e56a7-c5f9-4f3e-8dc0-988cdf1ba618/summary), discussing how data science can help overcome health disparities and how partners from industry can support these efforts. This discussion was sponsored by the American Council for Technology and Industry Advisory Council (ACT-IAC).

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:***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 for the past 12 months. For the Ambs group, the last remaining task is to complete and submit the final manuscript entitled "Quantitative trait analysis reveals relationships between germline genetics and 36 circulating immune markers in American and Ghanaian men". The

completion of the manuscript experienced delays because of staff departures. However, we are currently working on finalizing this manuscript.

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.

None.

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

None.

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

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).*

13 publications in PubMed (10 research papers and 3 reviews), all with acknowledgement of DoD award support (W81XWH1810588):

Minas, T.Z., Lord, B.D., Zhang, A.L., Candia, J., Dorsey, T.H., Baker, F.S., Tang, W., Bailey-Whyte, M., Smith, C.J., Obadi, O.M., Ajao, A., Jordan, S.V., Tettey, Y., Biritwum, R.B., Adjei, A.A., Mensah, J.E., Hoover, R.N., Hsing, A.W., Liu, J., Loffredo, C.A., Yates, C., Cook, M.B., and Ambs, S. Circulating trans fatty acids are associated with prostate cancer in Ghanaian and American men. Nat Commun., 14: 4322, 2023. PMID: 37468456

Bailey-Whyte, M., Minas, T.Z., Dorsey, T.H., Smith, C.J., Loffredo, C.A., and Ambs, S. Systemic Inflammation Indices and Association with Prostate Cancer Survival in a Diverse Patient Cohort. Cancers (Basel), 15: 1869, 2023. PMID: 36980755

Pichardo, M.S., Minas, T.S., Pichardo, C.M., Bailey-Whyte, M., Tang, W., Dorsey, T.H., Wooten, W., Ryan, B.M., Loffredo, C.A., and Ambs, S. Association of Neighborhood Deprivation With Prostate Cancer and Immune Markers in African American and European American Men. JAMA Netw Open, 6: e2251745, 2023. PMID: 36662526

White, J.A., Kaninjing, E.T., Adeniji, K.A., Jibrin, P., Obafunwa, J.O., Ogo, C.N., Mohammed, F., Popoola, A., Fatiregun, O.A., Oluwole, O.P., Karanam, B., Elhussin, I., Ambs, S., Tang, W., Davis, M., Polak, P., Campbell, M.J., Brignole, K.R., Rotimi, S.O., Dean-Colomb, W., Odedina, F.T., Martin. D.N., and 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., 2: 1005-1016, 2022. PMID: 36922933

Minas, T.Z., Candia, J., Dorsey, T.H., Baker, F., Tang, W., Kiely, M., Smith, C.J., Zhang, A.L., Jordan, S.V., Obadi, O.M., Ajao, A, Tettey, Y., Biritwum, R.B., Adjei, A.A., Mensah, J.E., Hoover, R.N., Jenkins, F.J., Kittles, R., Hsing, A.W., Wang, X.W., Loffredo, C.A., Yates, C., Cook, M.B., and Ambs, S. Serum proteomics links suppression of tumor immunity to ancestry and lethal prostate cancer. Nat Commun., 13: 1759, 2022. PMID: 35365620

Jenkins, F.J., Minas, T.Z., Tang, W., Dorsey, T.H., and Ambs S. Human herpesvirus 8 infection is associated with prostate cancer among IFNL4-ΔG carriers. Prostate Cancer Prostatic Dis. 2022 Apr 25. doi: 10.1038/s41391-022-00546-1. Online ahead of print. PMID: 35468990

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Kiely, M., and Ambs, S. Immune inflammation pathways as therapeutic targets to reduce lethal prostate cancer in African American men. Cancers, 13: 2874, 2021. PMID: 34207505- review

Minas, T.Z., Kiely, M., Ajao, A., and Ambs, S. 40th Anniversary Review Article: An overview of cancer health disparities: new approaches and insights and why they matter. Carcinogenesis, 42:2-13, 2021. PMID: 33185680 - review

Tang W, Fowke JH, Hurwitz LM, Steinwandel M, Blot WJ, Ambs S. Aspirin Use and Prostate Cancer among African-American Men in the Southern Community Cohort Study. Cancer Epidemiol Biomarkers Prev., 30: 539-544, 2021. PMID: 33293340

Online first

Pichardo CM, Ezeani A, Pichardo MS, Agurs-Collins T, Powell-Wiley TM, Ryan B, Minas TZ, Bailey-Whyte M, Tang W, Dorsey TH, Wooten W, Loffredo CA, Ambs S. Association of neighborhood gentrification with prostate cancer and immune markers in African American and European American men. Cancer Med. 2023 Dec 27. doi: 10.1002/cam4.6828. Online ahead of print. PMID: 38151903

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.

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*
  - *othe*

We made publicly available 1. the large-scale serum marker proteomics, 2. circulating fatty acids, and 3. genome-wide genotyping datasets that were generated under the award.

Databases: dbGaP submission phs002939.v1.p1; preview at https://www.ncbi.nlm.nih.gov/projects/gapprev/gap/cgi-bin/preview1.cgi?GAP_phs_code=E78nwI8ib0BMjFZB

Description in dbGaP: The study seeks to examine the genetic and ancestral basis of prostate cancer-associated inflammation using a genome-wide association approach. The study population are the participants of the NCI Maryland Prostate Cancer Case-Control study. This study recruited both African American and European American men, and investigated the causes for the excessive burden of prostate cancer among African American men in more general terms. We measured 82 blood-based immune-oncology markers, and genotyped the participants using the HumanOmni5-Quad BeadChip, which provides a significant genome coverage for genetically-admixed and diverse populations (about 4 Million SNPs) , to evaluate the genetic basis and evidence for causality of any immune-inflammation marker that is associated with prostate cancer risk. We want to assess how germline genetics influence the abundance levels of these 82 markers in African American and European American men, which may contribute to differences between them.

- Study Design:
    - Case-Control
- Study Type:
    - Case-Control
- dbGaP estimated ancestry using GRAF-pop
- Total number of consented subjects: 1450

Data: *Minas et al., Serum proteomics links suppression of tumor immunity to ancestry and lethal prostate cancer, Nature Communications 13: 1759, 2022. PMID: 35365620*

Data availability description as part of the publication:

Data availability of measured 82 serum immune-oncology marker measurements in almost 3000 men with annotations: Clinical, demographic and molecular data used for this study (i.e., self-reported race, degree of West African ancestry, age, BMI, education, income, aspirin use, diabetes use, smoking status, NCCN risk score, PSA, treatment type, proteomics data, and survival data) are deposited at the Open Science Framework at https://osf.io/327ha (https://doi.org/10.17605/OSF.IO/327HA)75 and as a public GitHub repository at https://github.com/juliancandia/ProstateCancerProteomics (https://doi.org/10.5281/zenodo.5815262)76.

Data: *Minas et al. Circulating trans fatty acids are associated with prostate cancer in Ghanaian and American men. Nature Communications, 14: 4322, 2023. PMID: 37468456*

Data availability description as part of the publication:

Clinical, demographic and molecular data used for this study (i.e., self-reported race, age, BMI, education, aspirin use, diabetes, smoking status, NCCN risk score, proteomics data, GWAS data,

and fatty acid data) are deposited in the Open Science Framework database (https://osf.io/tscgh/) under the accession code TSCGH70 and as a public GitHub repository at https://github.com/tsionzminas/Prostate-Cancer-and-Circulating-Fatty-acids or at Zenodo under the accession code 802318671. The full proteomics data was deposited in the Open Science Framework database under the accession code 327HA72. The remaining data are available within the paper, Supplementary Information, and Supplementary Data. Source data are provided with this paper.

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".

The assembly of databases, data analysis, and preparation of manuscripts and their revisions have been the major tasks in the Ambs laboratory in the reporting period. All tasks related to **Specific Aim 1** have been completed. Preparation and submission of a final manuscript will be the only task moving forward to complete the tasks specified under **Specific Aim 2**. The Yates lab at Tuskegee University now Johns Hopkins University has the lead on research and tasks specified under **Specific Aim 3**. However, all tasks under this aim are collaborative, involving efforts by both the Yates and Ambs laboratories.

The following individuals have worked on the described tasks in the past 12 months. They are either members of the Ambs laboratory or with the co-PI (Yates). There are additional time commitments by the Yates laboratory and their collaborators in Nigeria, as it relates to tasks under **Specific Aim 3**, that are not captured here. Other time commitments included learning of new methods for data analysis, preparation of abstracts, posters, and talks, and mentoring using Zoom calls. The Ambs and Yates labs continued their collaborative interactions related to project management, data analysis, and mentorship.

Staff and contribution

Name	Tsion Minas
Project Role	Volunteer – previously postdoctoral fellow
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Project manager for the immune-oncology marker and GWAS studies; data analysis for research in the immune-oncology marker and fatty acid studies and preparation of manuscript(s); preparation of abstracts, posters, and talks
Funding support	Fulbright Scholar in Addis Ababa, Ethiopia, and a volunteer with NCI

Name	Tiffany Dorsey
Project Role	Laboratory Manager/Microbiologist
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Key person for all biospecimen-related tasks; also data manager: prepares data summaries and databases for all projects; communication with service providers; shipment of samples from repository to laboratory and from laboratory to service providers
Funding support	NCI intramural program

Name	Maeve Bailey-Whyte
Project Role	Volunteer – previously postdoctoral fellow
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Project manager for the urine metabolite study; data analysis for research in the urinary eicosanoid marker study and preparation of manuscript(s) including two reviews; preparation of abstracts, posters, and talks
Funding support	NCI Cancer Prevention Fellowship and University of Limerick, Ireland, now a volunteer with NCI

Name	Brittany Lord
Project Role	Volunteer – previously postdoctoral fellow
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Analysis of the existing fatty acid data in partnership with Tsion Minas; preparation of manuscript(s), abstracts, posters, and talks
Funding support	NCI Cancer Prevention Fellowship and Johns Hopkins University, now a volunteer with NCI

Name	Catherine Pichardo
Project Role	Volunteer; postdoctoral fellow with another research group
Researcher Identifier	
Nearest person month worked	4
Contribution to Project	She has the lead for the study with geospatial neighborhood data; obtained census tract data for 1990, 2000, and 2010 and developed neighborhood gentrification and deprivation indices. Linkage of census tract data to study participants in the NCI-Maryland study; establishment of database with gentrification index data for all study participants. Analyzed data and prepared and submitted a research manuscript.
Funding support	NCI intramural program

Name	Hunter Schaumloffel
Project Role	Volunteer
Researcher Identifier	
Nearest person month worked	4
Contribution to Project	Data analyst for Specific Aim 2, investigating the germline genetic control of the 82 immune-oncology markers
Funding support	Volunteer status with NCI; former student at Colgate University, NY; was a sponsored summer student in 2023

Name	Jason White
Project Role	PhD student/postdoctoral fellow
Researcher Identifier	
Nearest person month worked	4
Contribution to Project	Key person for all biospecimen-related tasks at Tuskegee University; project manager for the RNAseq and WES study with Hudson alpha; analyst of RNAseq and WES data; preparation of manuscript(s), abstracts, posters, and talks
Funding support	Tuskegee University, now Morehouse School of Medicine

Name	Isra Elhussin
Project Role	PhD student/postdoctoral fellow
Researcher Identifier	
Nearest person month worked	2
Contribution to Project	Analysis of RNAseq data; preparation of manuscript(s), abstracts, posters, and talks
Funding support	Tuskegee University, now Johns Hopkins University

Name	Huaitian Liu
Project Role	Staff Scientist
Researcher Identifier	
Nearest person month worked	2
Contribution to Project	Co-mentor of Isra Elhussin and Hunter Schaumloffel; data analysis
Funding support	NCI intramural program

Name	Balasubramanyam Karanam
Project Role	Adjunct Associate Professor
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Key personnel for the Akoya CODEX system and lead researcher of immune marker spatial expression analysis in prostate tumors; established Akoya CODEX system at Tuskegee University; biospecimen management
Funding support	Tuskegee University

Name	Stefan Ambs
Project Role	Principal Investigator
Researcher Identifier	ORCID ID: https://orcid.org/0000-0001-7651-9309
Nearest person month worked	1
Contribution to Project	Project management including staff, service providers, and Geneva Foundation; guidance with data analysis and manuscript preparation
Funding support	NCI intramural program

Name	Clayton Yates
Project Role	Principal Investigator
Researcher Identifier	
Nearest person month worked	1
Contribution to Project	Project management including staff and service providers; guidance with project design (**Specific Aim 3**): RNA-seq, DNA-Seq and image analysis with Akoya CODEX system; guidance with data analysis and manuscript preparation
Funding support	Tuskegee University, now 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.

Not in the past 12 months. As previously reported, PI Michael Cook left the team in 2022 and has not been replaced.

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.*

We have established a collaboration with the Southern Community Cohort (SCCS) to investigate whether aspirin use among African American men is a viable strategy to prevent the development of lethal prostate cancer in these men. This collaboration also seeks to validate findings from the NCI-Maryland and NCI-Ghana study related to this award in the SCCS cohort – the immune and inflammation markers and their relationship to lethal prostate cancer among African American men. We also shared part of the generated genotyping data with a consortium led by Dr. Christopher Haiman, University of Southern California, and Wei Zheng, Vanderbilt University. This consortium will perform the yet largest genome-wide association study to identify novel risk loci for prostate cancer among men of African ancestry by combining all existing datasets from many research institutions including the NCI. An NCI data transfer agreement has been signed. If this analysis leads to a publication, funding support by the DoD award W81XWH-18-1-0588 will be acknowledged. The research proposed by this consortium does not overlap with research aims in our award. Most recently, we have established a collaboration with Sonja Berndt at the NCI Division of Cancer Epidemiology & Genetics. Dr. Berndt is an expert in genetic epidemiology and will support us with her expertise in drafting the manuscript "Quantitative trait analysis reveals relationships between germline genetics and 36 circulating immune markers in American and Ghanaian men". None of these partner organizations provided financial/in-kind support.

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.*

Not applicable

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

Not applicable

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.*

PDF of 13 peer-reviewed publications (10 research reports, 3 reviews), all published in 2021-2023, with acknowledgement of the funding support by DoD award W81XWH-18-1-0588.

Pichardo CM, Ezeani A, Pichardo MS, Agurs-Collins T, Powell-Wiley TM, Ryan B, Minas TZ, Bailey-Whyte M, Tang W, Dorsey TH, Wooten W, Loffredo CA, Ambs S. Association of neighborhood gentrification with prostate cancer and immune markers in African American and European American men. Cancer Med. 2023 Dec 27. doi: 10.1002/cam4.6828. Online ahead of print. PMID: 38151903

Minas, T.Z., Lord, B.D., Zhang, A.L., Candia, J., Dorsey, T.H., Baker, F.S., Tang, W., Bailey-Whyte, M., Smith, C.J., Obadi, O.M., Ajao, A., Jordan, S.V., Tettey, Y., Biritwum, R.B., Adjei, A.A., Mensah, J.E., Hoover, R.N., Hsing, A.W., Liu, J., Loffredo, C.A., Yates, C., Cook, M.B., and Ambs, S. Circulating trans fatty acids are associated with prostate cancer in Ghanaian and American men. Nat Commun., 14: 4322, 2023. PMID: 37468456

Bailey-Whyte, M., Minas, T.Z., Dorsey, T.H., Smith, C.J., Loffredo, C.A., and Ambs, S. Systemic Inflammation Indices and Association with Prostate Cancer Survival in a Diverse Patient Cohort. Cancers (Basel), 15: 1869, 2023. PMID: 36980755

Pichardo, M.S., Minas, T.S., Pichardo, C.M., Bailey-Whyte, M., Tang, W., Dorsey, T.H., Wooten, W., Ryan, B.M., Loffredo, C.A., and Ambs, S. Association of Neighborhood Deprivation With Prostate Cancer and Immune Markers in African American and European American Men. JAMA Netw Open, 6: e2251745, 2023. PMID: 36662526

White, J.A., Kaninjing, E.T., Adeniji, K.A., Jibrin, P., Obafunwa, J.O., Ogo, C.N., Mohammed, F., Popoola, A., Fatiregun, O.A., Oluwole, O.P., Karanam, B., Elhussin, I., Ambs, S., Tang, W., Davis, M., Polak, P., Campbell, M.J., Brignole, K.R., Rotimi, S.O., Dean-Colomb, W., Odedina, F.T., Martin. D.N., and 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., 2: 1005-1016, 2022. PMID: 36922933

Minas, T.Z., Candia, J., Dorsey, T.H., Baker, F., Tang, W., Kiely, M., Smith, C.J., Zhang, A.L., Jordan, S.V., Obadi, O.M., Ajao, A, Tettey, Y., Biritwum, R.B., Adjei, A.A., Mensah, J.E., Hoover, R.N., Jenkins, F.J., Kittles, R., Hsing, A.W., Wang, X.W., Loffredo, C.A., Yates, C., Cook, M.B., and Ambs, S. Serum proteomics links suppression of tumor immunity to ancestry and lethal prostate cancer. Nat Commun., 13: 1759, 2022. PMID: 35365620

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Kiely, M., Milne, G.L., Minas, T.Z., Dorsey, T.H., Tang, W., Smith, C.J., Baker, F., Loffredo, C.A., Yates, C., Cook, M.B., and Ambs, S. Urinary Thromboxane B2 and lethal prostate cancer in African American Men. J Natl Cancer Inst., 114: 123-129, 2022. PMID: 34264335

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Kiely, M., and Ambs, S. Immune inflammation pathways as therapeutic targets to reduce lethal prostate cancer in African American men. Cancers, 13: 2874, 2021. PMID: 34207505- review

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Tang W, Fowke JH, Hurwitz LM, Steinwandel M, Blot WJ, Ambs S. Aspirin Use and Prostate Cancer among African-American Men in the Southern Community Cohort Study. Cancer Epidemiol Biomarkers Prev., 30: 539-544, 2021. PMID: 33293340