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TITLE: **Genomic and Biological Risk Prediction of Aggressive and Lethal Prostate Cancer in African American Men**

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14. ABSTRACT

Despite robust and consistent evidence showing African-American men have poorer prostate cancer-specific outcomes, risk stratification tools (based on prostate-specific antigen, Gleason score, and tumor stage) are not currently able to incorporate racial disparities in a clinically meaningful way and identifying which men are at an increased risk of lethal prostate cancer remains a major challenge to the field. To this end, the purpose of this project is to develop a novel genomic/biological risk prediction approach to prostate cancer in men of African descent by identifying and developing a genomic signature/risk-classifier that is predictive of aggressive and potentially lethal prostate cancer. The resulting genomic/biological signature could identify African-descent men most likely to be at risk of lethal prostate cancer. We proposed to do this by: Aim 1: Identify and validate scenarios where current prostate cancer risk assessment tools are least prognostic in African-American men. Aim 2: Identify and characterize the prostate cancer genomic risk profile in African-descent men compared with European-descent men, particularly in clinical scenarios identified in Aim 1. Aim 3: Incorporate the findings from AIMs 1 and 2 into the development of a genomic-risk classifier/biomarker signature that is targeted toward the prediction of aggressive and potentially lethal prostate cancer in men of African descent and to determine whether the signature adds prognostic value to current clinical nomograms. Preliminary work from this grant has demonstrated that there could be genomic differences observed by race, particularly in metastatic disease: in a study of over 2k patients, Black men were most likely to have AR alterations, DDR alterations, and alterations in targetable genes (Mahal, NEJM 2020). My more work continued in 2021 in partnership with Foundation Medicine has shown in a study of nearly 12k patients with advanced PCa that there are ancestry-specific mutational landscapes were observed, however alteration prevalence in AR, DNA damage response pathway, and other actionable genes were similar across ancestry (this has been expanded to include fractional ancestry & been published in June, 2023 by Lancet Digital).

15. SUBJECT TERMS
Prostate cancer, Disparities, Cancer Disparities, Genomics, Translational Epidemiology

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1. Introduction

Despite robust evidence suggesting African-descent men have a higher risk of dying from prostate cancer compared to other men, clinical tools used to predict prognosis are not currently able to incorporate race to predict which men may be at the highest risk of lethal forms of prostate cancer. This is mostly due to genomic efforts being highly Eurocentric, which as a form of structural bias, has the potential to widen prostate cancer disparities. As such, clinical tools used to determine prognosis and guide treatment recommendations that have been developed based on studies that have historically underrepresented the African-descent population are still applied to men of African descent. These prognostic tools do poorly in predicting which men of African descent may be most at risk of lethal disease and therefore may contribute to disparities in prostate cancer outcomes. Furthermore, current prognostic tools/nomograms have proven to be suboptimal in predicting the patients with potentially inherently aggressive biology which may be at risk of lethal prostate cancer. To date, there are no specific risk prediction tools that have been developed for men of African descent, and the biology and genomics of prostate cancer in African-descent men is not well characterized. To this end, the purpose of this project is to develop a novel genomic/biological risk prediction approach to prostate cancer in men of African descent by identifying and developing a genomic signature that can predict for aggressive and potentially lethal prostate cancer. This project will utilize rich data from several large data sources and registries to evaluate the impact of genetic biomarkers and other clinical factors on the risk of lethal prostate cancer in men of African descent. The resulting genomic findings could help improve currently used clinical tools to identify African-descent men most likely to be at risk of lethal prostate cancer.

2. Keywords

Prostate cancer, Disparities, Cancer Disparities, Genomics, Translational Epidemiology, Community Outreach

3. Accomplishments

Please note that the project timeline has been altered for a few reasons that are described in greater detail under "Changes/Problems": 1) I was recruited to The University of Miami Miller School of Medicine (UM), Sylvester Comprehensive Cancer Center (SCCC) as Assistant Director of Community Outreach and Engagement in the middle of the pandemic (July 2020) and therefore I put hiring on hold anticipating a transfer. 2) I had a 2 month leave for multiple surgeries due to a sinus surgery complication. 3) The week I returned from my two month leave, research operations were halted at DFCI due to the COVID pandemic. 4) I ultimately transferred to UM-SCCC in July, 2020—and in doing so, I requested an extension on my award period given I did not use any of my funds through these major barriers that occurred during the initial award period. **This was all noted in a prior technical report, and copied here as a reminder.**

Regardless, through these hurdles, I was able to make significant progress through the transfer process and in my early time at UM-SCCC. **Full details of accomplishments by tasks are listed below in this technical report. Components D and E represent updates from the date of last technical report (January 2023) until present.**

A. Regarding research specific tasks, the following provides updates on completed tasks related to the project.

	Specific Aim 1: To identify and validate scenarios where current prostate cancer risk assessment tools are least prognostic in African-American men.	
Major Task 1: Identify clinical scenarios where disparities are greatest and where current clinical nomograms are least prognostic in African-American men.	**Months**	**Status**
	Subtask 1 (**for Aims 1-3**): Prepare Regulatory Documents.	
Coordinate with site for IRB protocol submission.	1-3	This was initially completed at DFCI and has now been completed at UM-SCCC after transfer
Coordinate with site for local IRB review.	1-3	This was initially completed at DFCI and is currently under review at UM-SCCC.
Coordinate with site for Military 2nd level IRB review (USAMRMC/ORP/HRPO)	1-6	Completed at UM.
	Subtask 2: Coordinate data collection in preparation for data analysis.	
Milestone Achieved: Data collected, curated, and primed for analyses to address Aim 1.	6-9	Milestone achieved. We have collected data from AACR project GENIE and I have recently signed an agreement with Foundation Medicine to access over 12k prostate cancer samples, including over 1k men with African ancestry. This was used for analyses related to this study.
	Subtask 3: Data Analysis	
Develop a comprehensive multivariable Fine-Gray competing risks regression model to evaluate the combined effects of clinical risk predictors on PCSM by race in various cohorts (described in Biostatistical plan) including SCORE (N>1000) and CPDR (N>4,000) cohorts.	9-12	Completed during transfer period.
Fit a model that uses the predictive score in existing models (that is, the summation of log relative hazards multiplied by the predictors) as the risk predictors. These analyses can help us understand the performance of existing clinical nomograms in African-descent populations.	9-12	Completed during transfer period.
Milestones Achieved: clinical scenarios where disparities are greatest are identified and results are reported in abstract and manuscript form. The findings inform areas of focus for Aims 2 and 3.	12	Completed during transfer period.
	Specific Aim 2: To identify and characterize the prostate cancer genomic risk profile in African-descent men compared with European-descent men, particularly in clinical scenarios identified in Aim 1.	
Major Task 2: Characterize genomic risk profile in African-descent men.	**Months**	**Status**
	Subtask 1: Prepare Regulatory Documents.	
Complete all tasks related to regulatory documents as listed above under Subtask 1, specific aim 1.	1-6	Ongoing, as per above
	Subtask 2: Coordinate data collection in preparation for data analysis.	
Collect and curate data.	6-12	Completed, as per above
Milestone Achieved: Data collected, curated, and primed for analyses to address Aim 2.	12	Completed, as per above
	Subtask 3: Data Analysis	
Develop relative African ancestry scores to address potential heterogeneity within the gene-pool of the African-descent population.	12-15	These analyses are now completed through collaboration with Foundation Medicine.
Use prostate cancer biosamples from the SCORE (N=775 banked tumor blocks for African-descent men) and CPDR (N=545 banked tumor blocks for African-descent men) cohorts to perform comparative genomic analysis of Gleason score-matched cases in tumors from African compared to European-descent patients and establish racial differences in genomic risk profiles, particularly in clinical scenarios identified	12-18	We ultimately increased the sample size to over 12k patients from Foundation Medicine's genomic database. These analyses are now

in aim 1.		completed through collaboration with Foundation Medicine.
Milestone Achieved: Similarities and/or differences in biomarker expression patterns will allow us to identify genetic factors that may contribute to disparities in aggressive prostate cancer. Any observed racial differences in biomarker expression patterns may lead to the discovery of a novel biomarker profile unique to men of African descent.	18	These analyses are now completed through collaboration with Foundation Medicine.
Milestone Achieved: The findings are reported in abstract and manuscript form.	18	Presented as a scientific abstract at ASCO 2021 as an oral abstract: "Ancestral characterization of the genomic landscape, comprehensive genomic profiling utilization, and treatment patterns may inform disparities in advanced prostate cancer: A large-scale analysis." This study expaned to include fractional ancestry has been accepted at Lancet Digital (In press, 2023)
	Specific Aim 3: To incorporate the findings from Aims 1 and 2 into the development of a genomic-risk classifier/biomarker signature that is targeted toward the prediction of aggressive and potentially lethal prostate cancer in men of African descent and to determine whether the signature adds prognostic value to current clinical nomograms.	
Major Task 3: Identify a genomic-risk classifier/biomarker signature for men of African descent.	**Months**	**Status**
Subtask 1: Prepare Regulatory Documents.		
Complete all tasks related to regulatory documents as listed above under Subtask 1, specific aim 1.	1-6	Completed as per above
Collect and curate data.	6-12	Completed, as per above
Milestone Achieved: Data collected, curated, and primed for analyses to address Aim 2.	12	Completed, as per above
Subtask 3: Data Analysis		
Utilize the transcript/gene expression and alternative splicing abundance measures to identify biomarkers that differ by race using logistic regression.	18-24	**Completed: Notably there were no differences in genomics across ancestry in genes targetable by therapy or prognostic for prostate cancer. Therefore the conclusion is that differences in genomics are ultimately unlikely to drive disparities across ancestry in advanced prostate cancer.**
Combine the significant biomarkers, utilizing biological information and published literature to partially winnow the space of potential biomarkers, to create a gene signature.	18-24	**Completed: Notably there were no differences in genomics across ancestry in genes targetable by therapy or prognostic for prostate cancer. Therefore the conclusion is that differences in genomics are ultimately unlikely to drive disparities across ancestry in advanced prostate cancer.**
Examine the incremental value of a biomarker for PCSM by evaluating the relationship of each biomarker one at a time with PCSM using Fine-Gray competing risks regression analysis adjusted for standard risk predictors.	18-24	**Completed: In addition to there being no differences in genomics that may drive advanced prostate cancer across ancestry, there were no differences in survival when adjusting for stage and genomics in this large cohort.**
Milestone Achieved: Discovery of novel tumor biomarker signature(s) for men of African descent that will be immediately translatable in the clinical setting as predictive tools.	24	**Completed: As described above, there are no novel signatures and the novel finding is that genomics are unlikely to drive differences in ancestry related disparities.**
Milestone Achieved: Publication of findings in abstract and manuscript form.	24	**Completed: Findings published in final form as follows:** **Sivakumar S, Lee JK, Moore JA, Hopkins J, Newberg JY, Madison R, Graf R, Schrock AB, Kobetz E, Vince R, Franco I, Seldon C, Frampton GM, Mills J, Venstrom J, Mahal BA. Comprehensive genomic profiling and treatment patterns across ancestries in advanced prostate cancer: a large-scale retrospective analysis. Lancet Digit Health. 2023 Jun;5(6):e380-e389. doi: 10.1016/S2589-7500(23)00053-5. PMID: 37236698.**

B. Furthermore, for training specific tasks, I have:

- Attended scientific research workshops to help develop a better understanding of biomarker development and cancer genetic epidemiology.
- Participated in a private and tailored educational curriculum to continue training in biomarker development and cancer genetic epidemiology.
- Received weekly formal didactic/teaching sessions (from my mentors) in applying methods from epidemiology, statistics, molecular biology, and classical genetics toward translational research.
- Collaborate with and acquire skills from Dr. Rebbeck's (mentor) close network of epidemiologists, biostatisticians, translational research scientists and clinicians, and basic scientists. I've also expanded my network to include mentors at my current institution including Dr. Erin Kobetz as primary mentor.
- Attended and presented research at weekly/monthly research group meetings. I now Host my own lab meetings with presentations at UM-SCCC.
- Prepared manuscripts relevant to biomarker development and cancer genetic epidemiology in prostate cancer disparities.
- More recently I have become Vice Chair of Research of the Department of Radiation Oncology (November 2022, and I continue in this role) and I have created the Prostate Cancer Research Group (PCRG) at UM-SCCC.

C. From the above described progress on goals, in 2020 I was able to publish a major manuscript in NEJM:
   1. Racial Differences in Genomic Profiling of Prostate Cancer. **Mahal BA**, Alshalalfa M, Kensler KH, Chowdhury-Paulino I, Kantoff P, Mucci LA, Schaeffer EM, Spratt D, Yamoah K, Nguyen PL, Rebbeck TR. **N Engl J Med.** 2020 Sep 10;383(11):1083-1085. doi: 10.1056/NEJMc2000069. PMID: 32905685

The study examined tumor genomic profiles across race in a novel diverse cohort. Specifically, next generation sequencing tumor genomic data obtained from patients treated for prostate cancer at either MSKCC or DFCI were extracted from the AACR Project GENIE-v7.0 registry (released January, 2020). Mutational profiles of 474 genes were examined by race (White, Black, Asian) and stage (primary versus metastatic)[4]. The Benjamini-Hochberg method was used to control for false discovery rate (FDR). Notable findings were that in In metastatic cases, 6.8% of Black men had >20 mutations. AR mutations occurred more often in Black (18.3%) compared with White men (8.1%, PropDiff 0.10[0.01-0.19], P=0.004). TP53 mutations occurred more often in Asian (62.0%) compared with Black (22.5%, PropDiff 0.40[0.21-0.58], P=0.008) and White men (36.4%, PropDiff 0.26[0.10-0.41], P=0.004). DNA repair and actionable gene mutations occurred more often in Black (22.5% and 26.7%, respectively) compared with White men (15.6%, PropDiff 0.07[-0.01 - 0.18], and 18.0%, PropDiff 0.09[0.00-0.20], respectively) (P=0.05 for both). BRAF mutations also occurred more often in Black compared with White men (7.0% versus 1.5%, PropDiff 0.05[0.00-0.10], P=0.002).

This work was also presented at the 2020 Prostate Cancer Foundation annual retreat and at the 2020 SUO (Society for Urological Oncology) meeting.

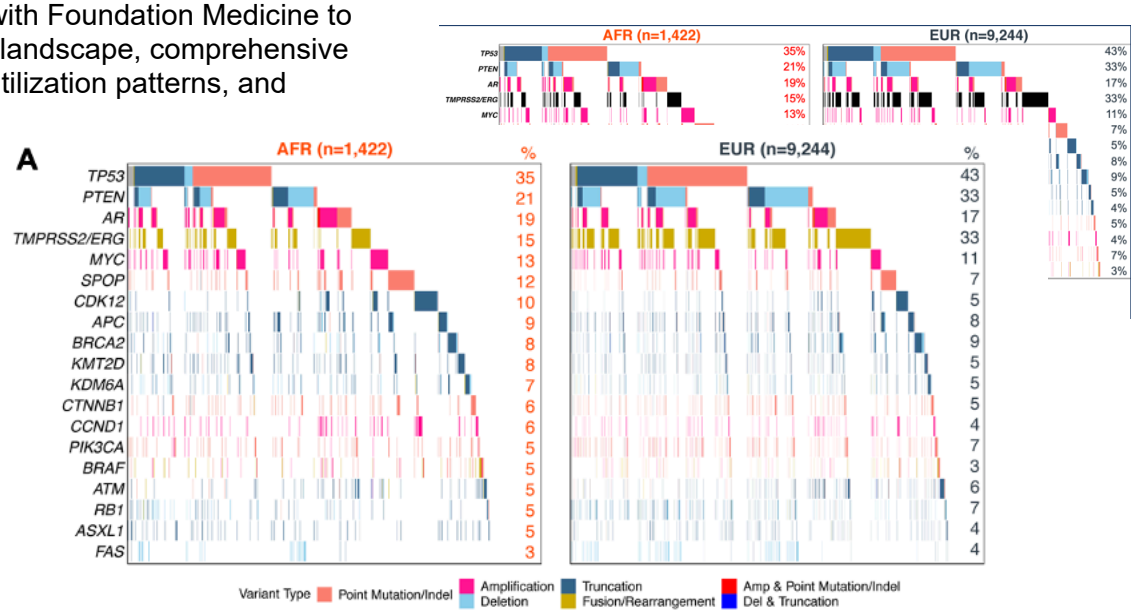
I have gained recognition for this work, and other accomplishments as a direct result of this work include me being invited to serve on several expert committees and panels, including The Lancet Commission on Prostate Cancer, American Cancer Society (ACS) National Advisory Team on Prostate Cancer Disparities, AdMeTech Blue Ribbon Expert Panel, and Prostate Cancer Foundation Disparities Working Group.

In 2021 I was able to publish an oral abstract at ASCO:

D. **Ancestral characterization of the genomic landscape, comprehensive genomic profiling utilization, and treatment patterns may inform disparities in advanced prostate cancer: A large-scale analysis.** Smruthy Sivakumar, Jessica Kim Lee, Jay A. Moore, Julia Hopkins, Justin Newberg, Alexa Betzig Schrock,

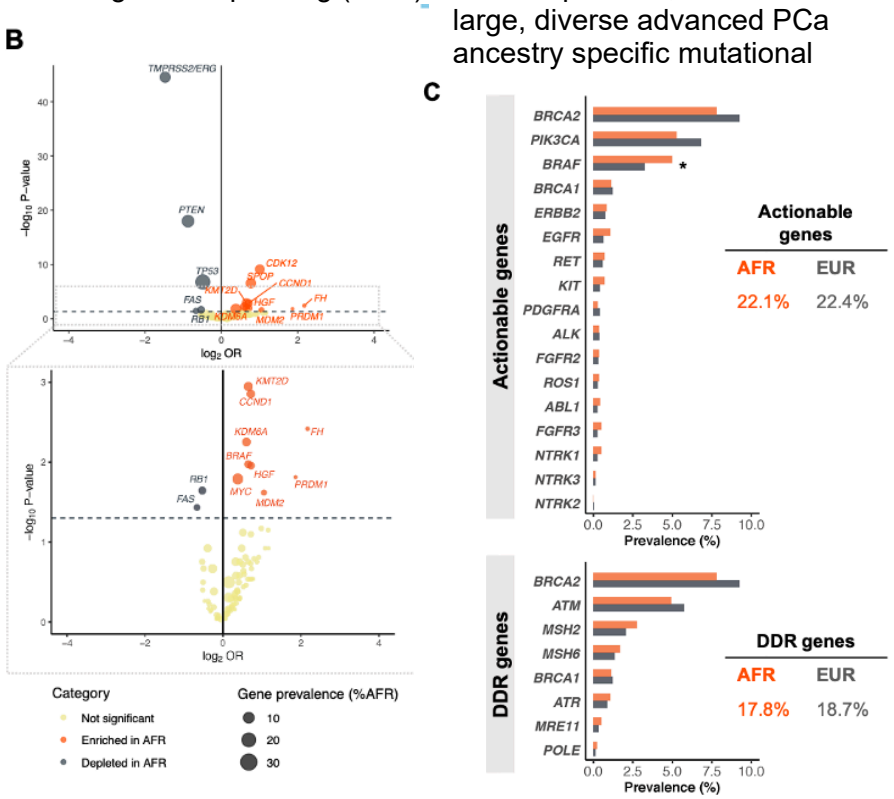
Randy Vince, Idalid Ivy Franco, Crystal Selesteen Seldon, JENNIFER MILLS, Jeffrey Michael Venstrom, Brandon Arvin Virgil Mahal. ASCO 2021 (Genitourinary Cancer- Prostate, Testicular, and Penile).

In this study, I partnered with Foundation Medicine to characterize the genomic landscape, comprehensive genomic profiling (CGP) utilization patterns, and treatment patterns across ancestry in a large, diverse advanced PCa cohort. Specifically, examining nearly 12k patients with advanced PCa from FMI's genomic database, ancestry-specific mutational landscapes were observed, however alteration prevalence in AR, DNA damage response pathway, and other actionable genes were similar across ancestry (**Figures to the right).** Ancestry-specific mutational landscapes were observed, however alteration prevalence in AR, DNA damage response pathway, and other actionable genes were similar across ancestry. AFR men received CGP later in their treatment course and were less likely to go on trial after CGP. Ultimately, these findings suggested differences in biology may not be a significant driver of disparities in advanced PCa. Later CGP utilization and lower rate of clinical trial enrollment observed in AFR men could further impact genomics, outcomes, and ultimately disparities (this study was presented as a scientific oral at ASCO 2021**).**



In 2021-2023 I expanded on the aforementioned work and a manuscript was submitted to Lancet Digital

There were several additional analyses that were performed in 2022-2023 that I will highlight here (based on feedback of reviewers). Again, this study was done in partnership with Foundation medicine and sought to characterize the genomic landscape, comprehensive genomic profiling (CGP) utilization patterns, and treatment patterns across ancestry in a large, diverse advanced PCa cohort. As mentioned above, there were ancestry specific mutational landscapes observed as demonstrated in the **Figure A (to the right)** Patterns of gene alterations from comprehensive genomic profiling based on their predicted genomic ancestry (n=1,422 AFR and n=9,244 EUR). Genes most frequently altered in the cohort are shown, along with annotations describing the specific type of alterations detected within each gene.



Furthermore, updated analyses in the final manuscript showed the following: **(FIGURE B, to the right)** Patterns of enrichment and depletion of gene alterations based on ancestry, using a Fisher's exact test, corrected for multiple

hypothesis testing using false discovery rate. Genes exhibiting statistically significant ($p < 0.05$) enrichment in AFR are shown in orange, while genes identified to be significantly depleted in AFR are shown in black. Nevertheless ultimately alternations in actionable genes and DDR genes was similar across Ancestry (**See Figure C, to the right**): Ancestry-based prevalence of actionable gene alterations as well as alterations in the DNA damage response (DDR) pathway (* denotes $p < 0.05$ using a Fisher's exact test). DDR genes include MRE11, POLE, MSH2, MSH6, ATR, ATM, BRCA1/2. Actionable gene alterations include ABL1, EGFR, ERBB2, BRAF, BRCA1/2, FGFR2/3, KIT, NTRK1/2/3, PDGFRA, RET, ROS1, ALK, and PIK3CA.

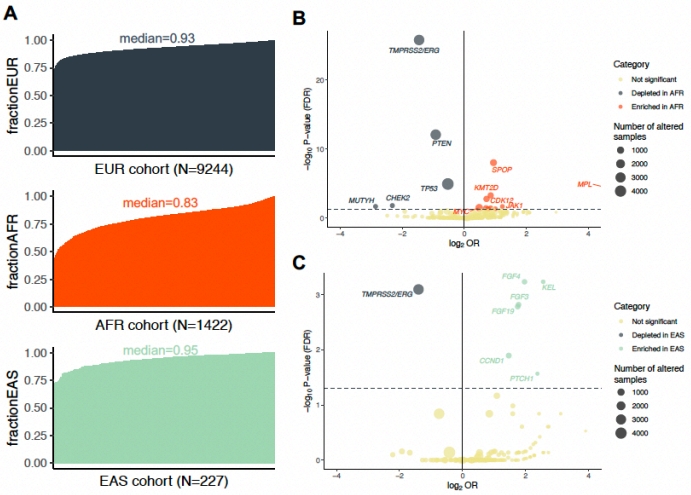


Figure S7. Admixture-derived fraction ancestry and associated gene alterations. (A) Distribution of fraction ancestry derived from admixture analysis, for each predicted ancestry subgroup (n=227 East Asian, EAS and n=9,244 European, EUR, n=1,422 African, AFR). Patients within each ancestry group are ordered based on their fraction and the median fraction is presented for each ancestry subgroup. Assessment of AFR-associated (B) and EAS-associated (C) patterns of gene enrichment/depletion using logistic regression with multiple hypothesis testing using false discovery rate (See Methods). Gene alterations exhibiting statistically significant patterns ($p \leq 0.05$) are labelled. For the analysis in (B) and (C), only AFR, EUR and EAS samples with at least 50% fraction of predicted ancestry from admixture analysis, were included (See Methods). Detailed data accompanying this analysis is provided in Table S4 and Table S5.

Reviewers noted the weakness of not including fractional ancestry, and therefore over the course of 2022-23 we aquired data on fractional ancestry and performed additional analyses. Specifically, Admixture-derived ancestry fractions for each patient was also interrogated. Ultimately, similar genomic landscapes were observed in analyses that accounted for admixture-derived ancestry fractions. A vast majority of cases had at least 50% of the predicted ancestry, based on the admixture analysis: EUR (99·9%), AFR (98·2%), EAS (100%). When limiting to these cases, largely similar trends of gene alterations were observed in the EAS and AFR subgroups (**See Figure S7, to the right**).

E. Ultimately based on the feedback from the reviewers above, we were able to publish the final product of this work in Lancet Digital Health in **June 2023** as follows (with me listed as senior author):

Sivakumar S, Lee JK, Moore JA, Hopkins J, Newberg JY, Madison R, Graf R, Schrock AB, Kobetz E, Vince R, Franco I, Seldon C, Frampton GM, Mills J, Venstrom J, Mahal BA. **Comprehensive genomic profiling and treatment patterns across ancestries in advanced prostate cancer: a large-scale retrospective analysis.** Lancet Digit Health. 2023 Jun;5(6):e380-e389. doi: 10.1016/S2589-7500(23)00053-5. PMID: 37236698.

Ultimately we found that there were no differences in genomics across ancestry in genes targetable by therapy or prognostic for prostate cancer. Furthermore, in addition to there being no differences in genomics that may drive advanced prostate cancer across ancestry, there were no differences in survival when adjusting for stage and genomics in this large cohort.

Therefore the conclusion is that differences in genomics are ultimately unlikely to drive disparities across ancestry in advanced prostate cancer. Additional analyses are described on the next page of this report.

Additional analyses that we performed that support these conclusions included the following:

-No differences in tumor mutational burden by ancestry (S3, below)
-No differences in microsatellite instability by ancestry (S4, below)
-No differences in genomic loss of heterzygosity by ancestry (S5, below)
-No differences in survival by ancestry after adjusting for clincogenomics (S9, below)

Figure S3

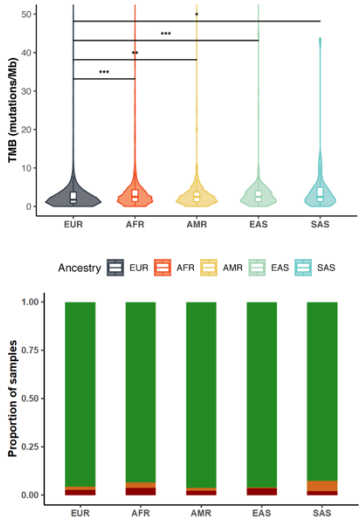


Figure S4

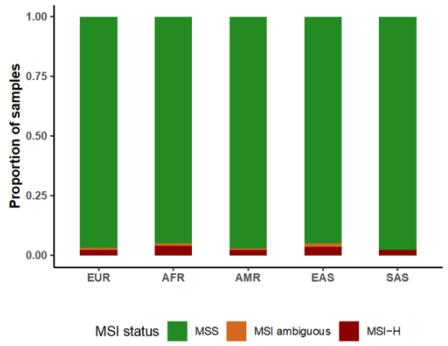


Figure S4. Distribution of microsatellite instability by ancestry. A stacked bar plot displaying the proportion of patients, based on their microsatellite instability status, across the different ancestry groups: microsatellite stable (MSS), high microsatellite instability (MSI-H), and the remaining classified as MSI-ambiguous. The ancestry groups included European (EUR), African (AFR), Admixed American (AMR), East Asian (EAS) and South Asian (SAS). In the overall cohort, 2.6% of samples showed MSI-H, with additional ancestry-associated trends. The AFR cohort had a higher rate of MSI-H samples (3.9% AFR vs. 2.4% EUR, p=0.002); the EAS cohort also exhibited a higher MSI-H rate than EUR, although it was not statistically significant, perhaps limited by the smaller EAS cohort size (3.6% EAS vs. 2.4% EUR, p=0.3).

Figure S5

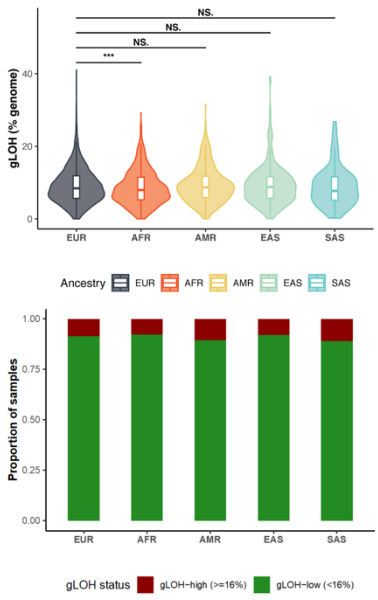


Figure S5. Distribution of genomic loss of heterozygosity by ancestry. Violin plot displaying the distribution of genomic loss of heterozygosity (gLOH; top) and a stacked bar plot displaying the proportion of patients based on their gLOH status (≥16% defined as gLOH-high; bottom) across the different ancestry groups: European (EUR), African (AFR), Admixed American (AMR), East Asian (EAS) and South Asian (SAS). The distribution in each ancestry group was compared to the EUR ancestry using a Wilcoxon rank sum test (p-value thresholds: *: 0.05, **: 0.01, ***: 0.001, NS: Not significant). Patterns of gLOH were similar across ancestry groups, with a median gLOH of 8.4% in the overall cohort. Although we observed subtle differences in the overall gLOH distribution between AFR and EUR, samples displaying a gLOH of at least 16% were observed at similar rates (7.7% AFR vs. 8.5% EUR, p = 0.6).

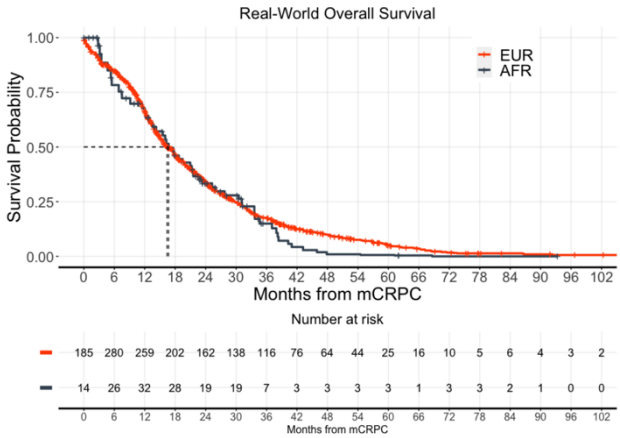


Figure S9. Trends of overall survival between patients of African and European ancestry. Kaplan-Meier curve displaying patterns of overall survival, defined as the time from mPCa (top) and mCRPC (bottom) diagnosis to date of death, between the European (EUR) and African (AFR) subgroups performed in an unmatched setting.

4. Impact

The above described work suggests that though there may be race/ancestry specific genomic landscapes, clinically significant alterations likely to not account for prostate cancer disparities Later CGP utilization and lower rate of clinical trial enrollment observed in AFR men could further impact genomics, outcomes, and ultimately disparities. This could have implications for prognosis, therapy response, and enrollment of minority populations in clinical trials and precision oncology studies. Furthermore, fracionional ancestry analyses suggests that analyses remain robust when analyzing by ancestry fraction. **Ultimately survival analyses and additional analyses (including TMB, MSI, gLOH) support these conclusions. With regards to disparities in advanced prostate cancer, the drivers are unlikely to be related to genomics and therefore we ultimately discovered that there are no signatures that would predict for survival differences.**

5. Changes/Problems (Copied and modified from prior report)

As described above, the original project timeline has been altered for several reasons: 1) I was recruited to The University of Miami Miller School of Medicine (UM), Sylvester Comprehensive Cancer Center (SCCC) as Assistant Director of Community Outreach and Engagement and therefore I put hiring on hold anticipating a transfer. 2) I had a 2 month leave for multiple surgeries due to a sinus surgery complication. 3) The week I returned from my two month leave, research operations were halted at DFCI due to the COVID pandemic. 4) I ultimately transferred to UM-SCCC in July, 2020—and in doing so, I requested an extension on my award period given I did not use any of my funds through these major barriers that occurred during the initial award period.

Despite these challenges, I was able to work independently self-teach many critical aspects of bioinformatics, and through my transfer I was able to complete a major project as described above. Furthermore, given my transfer, it may be difficult for me to obtain specimens allocated to DFCI. Therefore, I formed a relationship with Foundation Medicine who I collaborated with to complete many aspects of this proposal (including analyses for over 12k prostate cancer samples).

Given these challenges, I did not spend funds during my first year, and requested a one-year extension.

Since then there have been no changes/problems encountered.

Regarding ancestry specific genomic signatures, the drivers are unlikely to be related to genomics and therefore we ultimately discovered that there are no signatures that would predict for survival differences.

6. Products

Publications:

1. Racial Differences in Genomic Profiling of Prostate Cancer. **Mahal BA**, Alshalalfa M, Kensler KH, Chowdhury-Paulino I, Kantoff P, Mucci LA, Schaeffer EM, Spratt D, Yamoah K, Nguyen PL, Rebbeck TR. **N Engl J Med.** 2020 Sep 10;383(11):1083-1085. doi: 10.1056/NEJMc2000069. PMID: 32905685
2. **Ancestral characterization of the genomic landscape, comprehensive genomic profiling utilization, and treatment patterns may inform disparities in advanced prostate cancer: A large-scale analysis.** Smruthy Sivakumar, Jessica Kim Lee, Jay A. Moore, Julia Hopkins, Justin Newberg, Alexa Betzig Schrock, Randy Vince, Idalid Ivy Franco, Crystal Selesteen Seldon, JENNIFER MILLS, Jeffrey Michael Venstrom, Brandon Arvin Virgil Mahal. ASCO 2021 (Genitourinary Cancer- Prostate, Testicular, and Penile).
3. Sivakumar S, Lee JK, Moore JA, Hopkins J, Newberg JY, Madison R, Graf R, Schrock AB, Kobetz E, Vince R, Franco I, Seldon C, Frampton GM, Mills J, Venstrom J, Mahal BA.

Comprehensive genomic profiling and treatment patterns across ancestries in advanced prostate cancer: a large-scale retrospective analysis. Lancet Digit Health. 2023 Jun;5(6):e380-e389. doi: 10.1016/S2589-7500(23)00053-5. PMID: 37236698.

7. Participants & Other Collaborating Organization

Name:	*Mohammed Alshalalfa, PhD*
Project Role:	*Computation Biologist/Bioinformatician/Collaborating Scientist*
Researcher Identifier (e.g. ORCID ID):	0000-0001-8405-3035
Nearest person month worked:	*5*
Contribution to Project:	*Mohammed has assisted with critical aspects of bioinformatics on this project.*
Funding Support:	*Mohammed was partially funded by this project.*

Name:	*Foundation Medicine*
Project Role:	*Collaborating Organization*
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	0 (new relationship as of 12/2022)
Contribution to Project:	*Provided over 12k samples for analyses*
Funding Support:	*N/A*

8. Special Reporting Requirements

N/A

9. Appendices

The PDF documents for the publication described in “Products” is submitted along with this report.