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14. ABSTRACT

In 2019, an estimated 174,650 men will be newly diagnosed with prostate cancer and 31,620 men will die from this disease in the United States. The burden of the disease is particularly heavy on African Americans, who are 1.5 times more likely to develop prostate cancer and 2.5 times more likely to die of this disease, compared to Caucasian Americans. Studies have shown that there are significant differences in clinical presentation between African American and Caucasian Americans at time of initial cancer detection. However, data on early markers of detection for PCa specific to African American men are very limited, potentially leading to sub-optimal care. Our study goal is to provide data and tools that can be used to predict cancer events based on a patient's self-reported race, his tumor characteristics, and his health status, so that patients can make *treatment* decisions based on sound scientific data and physicians can tailor prostate cancer therapy to African American patients to achieve optimal outcomes. ***This proposal will biological factors that may contribute to racial disparities in PCa incidence and outcomes.***

1) To provide comprehensive data for the entire prostate cancer course among African American men. The Center for Prostate Disease Research has collected detailed clinical data for over 25 years on more than 29,500 men, of who roughly one-third (10,000) remain cancer free and two thirds are biopsy-confirmed for PCa (20,000). Within this cohort, 20% of men self identifies as an African American (6,000). This cohort is uniquely suited to provide the most comprehensive race-specific data about prostate cancer status and aggressiveness. There is no expert consensus on how to predict which men will be detected with cancer that has already spread to other parts of the body. But this study is anticipated to help answer that question, with an ability to determine whether the same factors can be used across race to address this important question. Moreover, this study cohort is made up of a military health care beneficiary population and results from this study could provide unique information to the patients with early-stage prostate cancer or patients whose cancer returns after initial treatment.

One important clinical benefit and implication of this work will be the potential impact on improving patient quality of life. Most patients

15. SUBJECT TERMS

Prostate cancer, racial disparity, metastasis, African American, proteomics

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Introduction

In 2019, an estimated 174,650 men will be newly diagnosed with prostate cancer and 31,620 men will die from this disease in the United States. The burden of disease is particularly heavy among African Americans (AA), who have 1.5-fold incidence and 2.5-fold mortality rates, as compared to Caucasian Americans (CA). Reasons for such racial disparities have been extensively researched and may be a function of both biological and social determinants of cancer development and aggressiveness. Early detection, when cancer is still confined to the prostate gland, greatly improves the disease-specific survival probability. However, very little is known about the molecular determinants of prostate cancer (PCa) that contribute to metastatic potential at time of initial cancer detection. Generating race-specific information about the molecular changes that occur during the PCa disease course is key to understanding the addressing the racial disparities in PCa outcomes. Predictive models that incorporate both clinical and biological expression data are urgently needed to identify men at earlier times points in life, who are fated for aggressive disease early in the cancer care continuum, especially for AA men. ***This proposal specifically addresses <u>biological</u> factors that may contribute to racial disparities in PCa incidence and outcomes.***

There is also an unmet clinical need to identify predictors of aggressive PCa, to avoid overtreatment of clinically indolent disease but ensure proper treatment intensity for men whose disease may be fated to metastasize. Use of mass spectrometry-based **quantitative proteomics** to analyze biopsy tissue is a critical and growing area in cancer research. These advanced analytic approaches will be used to generate and verify protein biomarker candidates and develop models to predict prostate cancer aggressiveness in a racially diverse cohort of military health care beneficiaries.

The overarching study objective is to elucidate biopsy tissue-derived proteomics biomarkers of prostate cancer development and lethality at time of initial prostate cancer detection, with an emphasis on examining racial variation in such markers of aggressiveness.

Keywords: Prostate cancer, racial disparity, metastasis, African American, proteomics

Accomplishments: Due to delays in negotiating the contract between the two organizations, CWRU and PNNL, the accomplishments for Year 1 were limited to the following:

September 1, 2020: Start date is assigned to the grant; protocol is written and submitted for IRB review

October 2020: Monthly standing calls are initiated between PI of CWRU (Jennifer Cullen) and PNNL (Tao Liu)

January 2021: IRB approval, HIPAA Waiver, and Consent Waivers are granted for the study at CWRU

March 2021: Contract and Material Transfer Agreement (MTA) are drafted and submitted for review at CWRU and PNNL

June 2021: REDCap database is built at CWRU to identify eligible study subjects, in anticipation of contract and MTA execution, including a tracking system for location/quantity of biospecimen materials

September 2021: All final agreements (inter-institutional contract, MTA) have all been executed

September 29, 2021: HRPO approval is granted

Impact:

One in six American men will be diagnosed with prostate cancer (PCa) during his life-time. The burden of this disease disproportionately impacts African Americans (AA) who demonstrate 1.5-times the incidence rate and 2.5 times the mortality rate compared to Caucasian American men. If PCa is detected early, patient outcomes are greatly improved. But there is an unmet clinical need to identify early predictors of CaP aggressiveness. Such markers could help avoid overtreatment of clinically indolent disease, which is costly in terms of dollars but also in terms of reductions in patient quality of life, and to ensure proper treatment intensity for men whose disease may be fated to metastasize.

This proposed study will utilize a prostate *disease* database with detailed longitudinal clinical and outcomes data, compiled over the last 25+ years. A unique aspect of this cohort (that will be leveraged in this proposal) is a large subset of men who were under *suspicion for prostate cancer* but who have undergone multiple, negative transrectal ultrasound (TRUS)-guided biopsies and persistently show no evidence of cancer. Such biopsy negative patients serve as an ideal comparison group to men detected with prostate cancer since both groups have been subjected to the same rigor of cancer ascertainment.

Short term study impact:
By addressing biological underpinnings in the form of protein expression of indolent versus aggressive PCa at diagnosis, as well as comparing protein expression in men who remain under suspicion for PCa but do not develop cancer, this study could have immediate relevance for informing timing, type, and intensity of treatment for men undergoing biopsy due to suspicion for PCa. While findings will need to be confirmed in other health care settings, a key advantage to studying the proposed aims in this study cohort will be the potential impact on improving treatment decision making in African American men.

Long-term study impact:
The findings of this project will also provide comprehensive race-specific data for the prostate disease course—for those under suspicion for PCa, to those with indolent versus aggressive disease. This patient cohort is racially diverse which makes this study setting optimal for examining cancer health disparities. The markers examined could elucidate who can be spared repeat biopsy in the future, as well as how to optimize the cancer care of African American men.

Changes/Problems: *None to report*

Products: *None to report*

Participants & Other Collaborating Organizations: *NA*

Special Reporting Requirements: *NA*

Appendices: *None*