Learning to Care for Those in Harm's Way

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Release No. 22-03-15
March 15, 2022
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Newly-identified inherited mutations linked to prostate cancer in African American men

Bethesda, Md. – Federal researchers have identified specific inherited, or "germline," gene mutations associated with prostate cancer development specifically among African American men. This discovery could impact cancer screening and prevention and also lead to more effective, targeted treatments and better outcomes for individuals who have these mutations. These findings were published in Nature Communications on March 15, 2022.

The study, "Germline mutation landscape of DNA damage repair genes in African Americans with prostate cancer highlights potentially targetable RAD genes" led by scientists at the Department of Defense's Uniformed Services University of the Health Sciences (USU), analyzed the inherited DNA Damage Repair Gene mutations, or DDRG mutations, which have not yet been fully defined among African American patients. Previous studies have looked primarily at DDRGs in Caucasian men. Past studies have also shown that African American men are diagnosed with prostate cancer more commonly than Caucasian men and, upon diagnosis, are usually at a more advanced stage. They are also more likely to succumb to prostate cancer than Caucasian men, but scientists have not fully understood why.

In this study, the researchers examined DNA specimens from 259 African American men and 272 Caucasian men who were being treated for prostate cancer within the equal-access Military Health System. USU's Center for Prostate Disease Research (CPDR) has a long history of treating an ethnically diverse military population with equal access to screening, treatment, and follow-up care. Therefore, CPDR researchers have been able to study differences in cancers between people of different ancestry and, ultimately, identify risk factors among this patient population.

In looking at 276 DDRGs within this cohort, they found a clear racial disparity of germline mutations in the DDRGs across African American and Caucasian men. Twenty-three percent of DDRGs were mutated in African American men, approximately three times greater than what has been reported in previous studies. In particular, they noticed a higher percentage of African American men compared to Caucasian men who harbored a potentially targetable subset of DDRGs, belonging to the RAD genes. Germline mutations in the DDRGs were associated with poor disease outcome and progression in African American men.

"Commercially available genetic tests are designed based on mutations seen largely in Caucasian cohorts," said Navy Cmdr. (Dr.) Gregory Chestnut, director of CPDR and a co-author on the study. "However, we can now propose they include these new germline mutations to study and better understand the specific characteristics of all our patients, and potentially treat them in the future by precision medicine therapy. Our findings identify mutations uniquely affecting African American

prostate cancer patients and begins to better characterize potential genetic drivers of prostate cancer among African American men.

“Through these findings, we may be able to address some of the disparities African American prostate cancer patients endured for such a long time by potentially targeting these newly recognized inherited mutations,” said Dr. Gyorgy Petrovics, a Henry M. Jackson Foundation for the Advancement of Military Medicine employee working in support of CPDR. Petrovics is also the assistant director of CPDR’s Basic Science Research Program and senior author on the study. “As these are inherited mutations, they are often present in family members, and testing them may help identify others in the family for earlier, even preventive, interventions, as DDRGs are also important for other cancers as well,” Petrovics said.

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About the Uniformed Services University of the Health Sciences: The Uniformed Services University of the Health Sciences, founded by an act of Congress in 1972, is the nation’s federal health sciences university and the academic heart of the Military Health System. USU students are primarily active-duty uniformed officers in the Army, Navy, Air Force and Public Health Service who receive specialized education in tropical and infectious diseases, TBI and PTSD, disaster response and humanitarian assistance, global health, and acute trauma care. USU also has graduate programs in oral biology, biomedical sciences and public health committed to excellence in research. The University's research program covers a wide range of areas important to both the military and public health. For more information about USU and its programs, visit www.usuhs.edu.

About the Center for Prostate Disease Research (CPDR): The Uniformed Services University’s Center for Prostate Disease Research, established by Congress in 1992, integrates a multidisciplinary approach to prostate cancer and continues to make great strides in clinical and basic sciences research for improving the entire spectrum of care to include diagnosis, treatment, management, and follow-up for patients with prostate cancer. CPDR's strategy is to focus investigators on potential breakthrough basic science and clinical research within its three major research programs - Clinical Program, Basic Science Program, and Multicenter National Database - and maintain the core support requirements for all programs. For more information about CPDR, visit https://cpdr.org.