Greater prostate cancer incidence; mortality among Black men linked to genetic alterations

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Prostate cancer tumors from African American men had higher frequencies of certain genetic alterations that may be associated with aggressive disease, compared with prostate cancer tumors from white men, according to results from a study published in *Molecular Cancer Research*, a journal of the American Association for Cancer Research.

"Prostate cancer incidence and mortality are highest in African American men, but the exact reasons for the disparity are not fully understood," said Jianfeng Xu, DrPH, Vice President of Translational Research at NorthShore University HealthSystem and senior author of the study. "The disparity is likely due to multiple factors, including socioeconomic differences and biology. We suspect that differences in the genetic changes that occur within tumors may play a critical role."

In this study, Xu, together with first author Wennuan Liu, Ph.D., and colleagues, sequenced 39 genes of interest in tumors and matched normal tissue from 77 African American patients with prostate cancer. They found that over 35 percent of these patients' tumors harbored potentially damaging mutations in several genes, including the DNA repair genes ATM, BRCA2, and ZMYM3, among other genes. ZMYM3, which regulates chromatin and DNA repair, was found to be among the most frequently mutated genes in these patients. Nine of the 77 African American patients (11.7 percent) had tumors harboring mutations in ZMYM3, compared to 2.7 percent of tumors from 410 white patients

whose data were included in the Genomic Data Commons database.

In addition, Xu and colleagues examined whether there were differences in the copy number alterations —when genetic material is gained or lost—between the prostate tumors of African American and white patients. The researchers pooled data representing 171 African American patients and 860 white patients from several public databases. They found distinct copy number alterations between African American and white patients in the more aggressive, high-grade prostate tumors (Gleason score 7 or higher), but not in low-grade tumors. High-grade tumors from African American patients were more likely to have additional copies of the MYC oncogene and deletions of the LRP1B, MAP3K7, BNIP3L, and RB1 genes than tumors from white patients. Gain of MYC and loss of MAP3K7 or RB1 were also associated with more advanced tumor stage.

"Our findings suggest that distinct genetic alterations in the prostate cancers of African American men, in comparison to white men, may contribute to more aggressive prostate cancer and could lead to a higher mortality rate," said Xu. "If confirmed in other studies, these results will not only help to understand the racial disparity of prostate cancer but could also help guide personalized clinical management, such as predicting prognosis and guiding targeted therapy."

Future work from Xu and colleagues will aim to understand how genetic alterations in African American men affect recurrence, metastasis, treatment, and prostate cancer-specific death. In addition, they are interested in developing tests to detect such genetic changes.

Limitations of the study include the small sample size, the use of different platforms to generate genetic data, and technical differences in how sequencing was performed between samples from African American men in this study and those from white men in the Genomic

Data Commons database.

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