Genomic differences may be key to overcoming prostate cancer disparities

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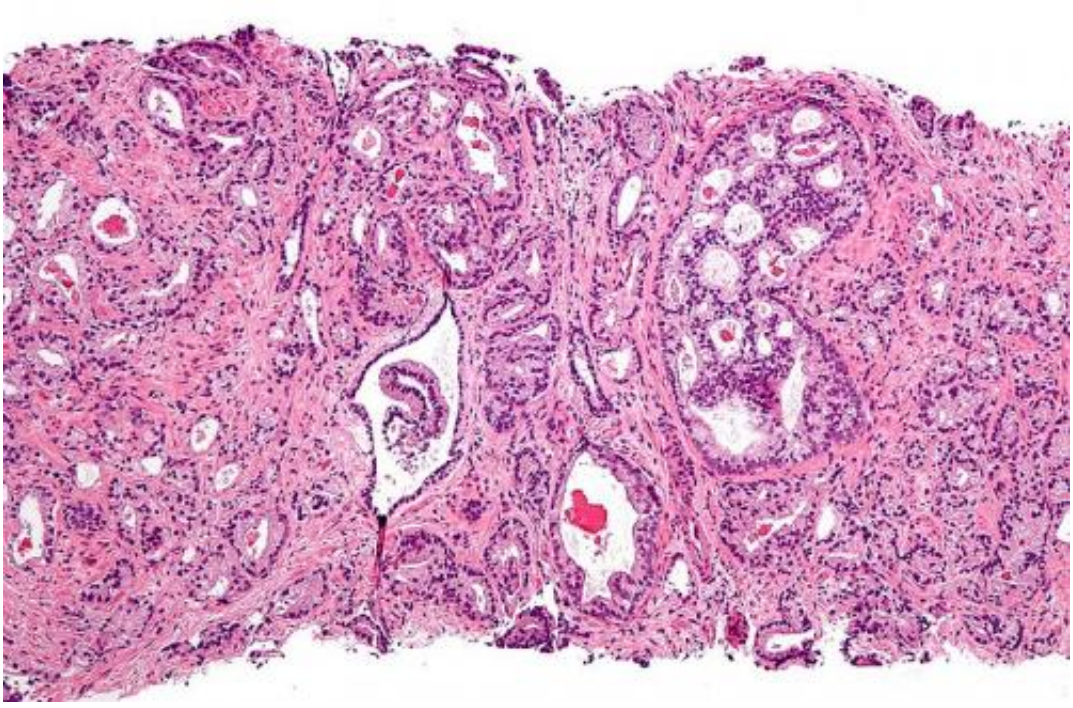

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Prostate cancer is the most common type of cancer among American men after skin cancer, but the disease does not affect all races equally. African American men are nearly two times more likely to develop prostate cancer, and more often have an aggressive form of the disease that grows and spreads quickly. They are also two times more likely to die from prostate cancer compared to white men. While the health care

community is aware of this disparity, little is known about why prostate cancer affects African American men differently. It has become increasingly evident that both socio-economic and biological factors may contribute to the disparity.

Moffitt Cancer Center researchers are taking a closer look at the genomic features of prostate cancer tumors among men of different races in hopes of better understanding why African Americans are more susceptible to the disease. In a new article published in *Clinical Cancer Research*, the research team describes the immune-oncologic differences in prostate cancer tumors of African American men and how those variations may be exploited to develop more personalized treatment approaches for this population.

"Previous studies have looked at the immune landscape of prostate cancer in white or European American men but have lacked validation among their African American counterparts," said Kosj Yamoah, M.D., Ph.D., lead study author and assistant member of the Radiation Oncology and Cancer Epidemiology Programs at Moffitt. "Our genomic analysis, the largest of its kind, revealed there are major immune pathways that are significantly elevated in African American men, which can correlate with risk of cancer recurrence and poor outcomes."

The Moffitt researchers analyzed whole transcriptome data from nearly 1,200 proctectomy samples in the Decipher Genomic Resource Information Database registry. Transcriptomic data provides a complete look at all the RNA sequences within a cell, which in turn can show when and where each gene is turned on or off. The team focused on 1,260 immune specific genes to determine differences between prostate cancer tumor cells in African American and European American men.

They discovered striking differences between the two races. Major immune pathways, including cytokine, interferon and interleukin

signaling, are elevated in African American prostate tumors. These pathways can contribute to and escalate the growth and spread of cancer cells. The immune biologic signatures suggest prostate cancer tumors in African American men may be more sensitive to radiotherapy and could have a better response to immunotherapy.

"Currently there are only two immunotherapy options for prostate cancer patients: the sipuleucel-T cell vaccine and pembrolizumab. However, not everyone responds to those therapies," said Yamoah. "Our study shows that African American men have higher overall immune content within their tumor microenvironment and higher expression of T lymphocytes. We can use that information to select a therapy that better targets their tumor and therefore improve their outcome."

The team also discovered six genes that expression levels were consistently different between African American and European American men. One gene, IFITM3, is often an indicator that a patient has a significantly higher risk of biochemical recurrence, meaning their prostate antigen score continues to rise despite surgery or radiation. In addition to cancer progression, this gene also plays an important role in metastasis.

The researchers say further study will be needed to determine if their findings can have positive implications on the treatment and management of prostate cancer in African American men.

More information: Shivanshu Awasthi et al, Comparative genomics reveals distinct immune-oncologic pathways in African American men with prostate cancer, *Clinical Cancer Research* (2020). DOI: 10.1158/1078-0432.CCR-20-2925

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