Study reveals an inherited origin of prostate cancer in families

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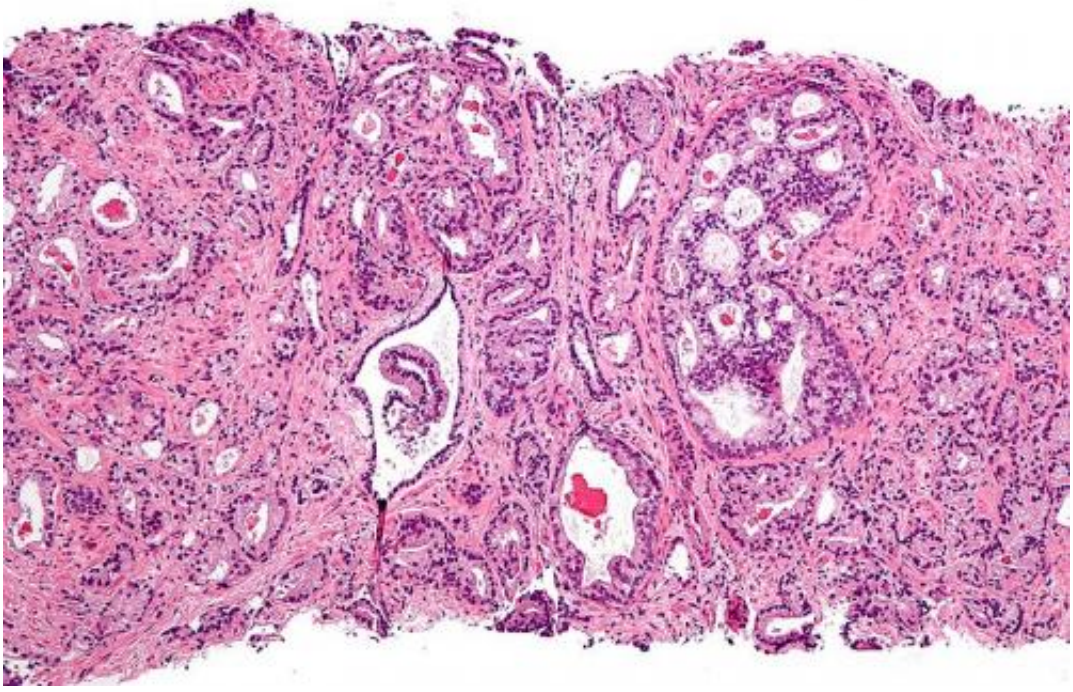

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Vanderbilt researchers have identified haplotypes, ancestral fragments of DNA, that are associated with hereditary prostate cancer (HPC) in a first-of-its-kind genomic study made possible by the study of prostate cancer patients with family histories of the disease.

The researchers analyzed the Nashville Familial Prostate Cancer Study

(NFPCS), in an investigation comparing men with prostate cancer, each from a separate family with a strong history of the disease, to screened men without a personal or family history of prostate cancer. They analyzed haplotypes at a location of chromosome 8 which has been tied to the origin of prostate and numerous additional cancers.

The study, published March 23 in *Nature Communications*, explains roughly 9% of prostate cancer heritability. One mutation increased risk as much as 22-fold. Another mutation increased risk 4-fold, and was observed even among men without a strong family history. It was also associated with an early age of diagnosis. The researchers identified 183 variants associated with HPC at genome-wide significance, including these and others that had not been previously reported.

"We've taken a comprehensive shotgun approach to investigate data at this (chromosome) location and have been able to deconstruct how it contributes to risk, including which of the haplotypes impact age of onset and also aggressiveness," said the study's senior author, Jeffrey R. Smith, MD, Ph.D., associate professor of Medicine.

"Almost 2,300 men of the NFPCS, each with a desire to help others, contributed," Smith said. Data from a separate, even larger study of HPC by the International Consortium for Prostate Cancer Genetics confirmed observations.

The study is believed to be the first to identify haplotypes comprehensively from all associated genetic variants at a locus. The study introduces new methods for finding genetic variants most contributing to risk.

More information: 8q24 genetic variation and comprehensive haplotypes altering familial risk of prostate cancer, *Nature Communications* (2020). DOI: 10.1038/s41467-020-15122-1

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