Genetic testing can identify men at six-fold increased risk of prostate cancer

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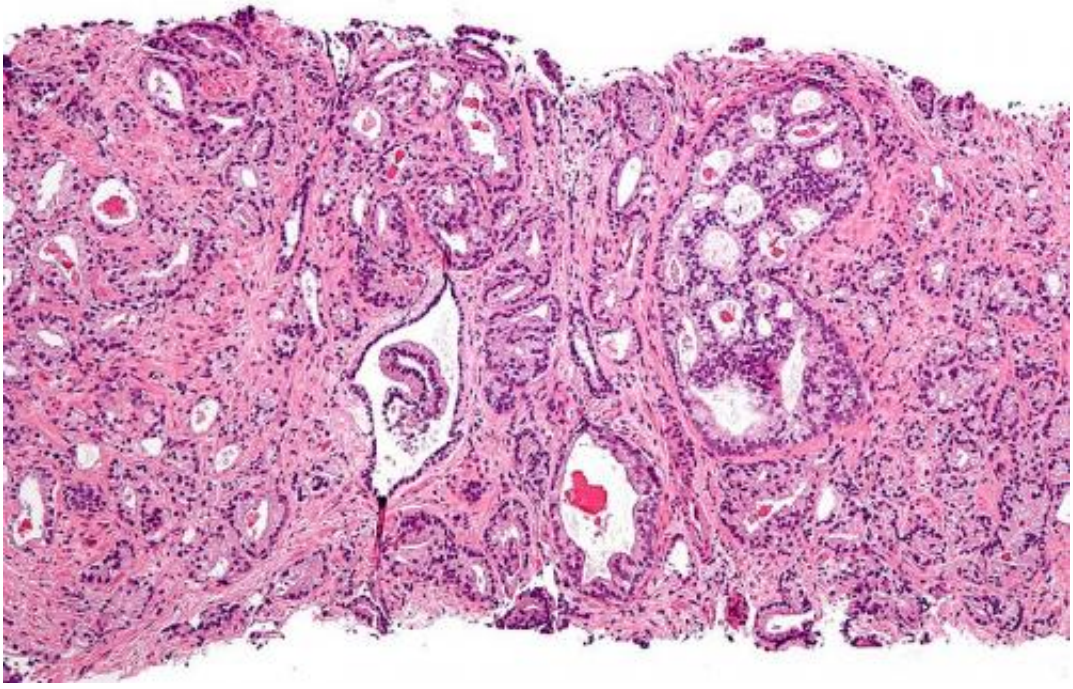

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Scientists can now explain a third of the inherited risk of prostate cancer, after a major international study identified 23 new genetic variants associated with increased risk of the disease.

The study brings the total number of common genetic variants linked to prostate cancer to 100, and testing for them can identify 1% of men with

a risk of the disease almost six times as high as the population average.

Scientists at The Institute of Cancer Research, London, and in Cambridge, UK, and California led a huge search for new genetic variants including almost 90,000 men and for the first time combining populations with European, African, Japanese and Latino ancestry.

The research, published today (Sunday) in *Nature Genetics*, was funded in equal amounts by Cancer Research UK, Prostate Cancer UK, the EU and the National Institutes for Health in the US.

Researchers found that assessing the top 100 variants identified 10% of men with a risk almost three times as high as the population average, and said that this was high enough to investigate whether targeted genetic screening was merited. They plan to lead a new clinical trial to test whether genetic screening can be effective.

In European men, scientists had previously found 77 genetic variants which were known to increase the risk of prostate cancer.

In the new research, scientists from The Institute of Cancer Research (ICR), University of Cambridge and the University of Southern California in the US examined the genetic information of 87,040 men from all over the world.

They combined genetic population studies of 43,303 men with prostate cancer and 43,737 controls from European, African, Japanese or Latino heritage to improve statistical power and increase their chances of identifying new variants.

From this combined population, they identified 16 new genetic markers linked to prostate cancer risk in European men - one of them associated with increased risk of early-onset disease - and seven in men of mixed

heritage.

The study means that scientists can now explain 33% of the inherited origins of prostate cancer in European men. A new clinical trial called BARCODE, which aims to genetically screen 5,000 men for prostate cancer, will investigate if these genetic markers can improve on other tests for the disease.

They are investigating whether genetic testing could help diagnose more men at risk of developing dangerous forms of prostate cancer that need urgent treatment – something that the current PSA test is unable to tell us.

The new study shows that for European men assessed for the 100 common variants, the 10% at highest risk are 2.9 times more likely than the average person to develop prostate cancer, while the top 1% are 5.7 times more likely to develop the disease.

Professor Ros Eeles, Professor of Oncogenetics at The Institute of Cancer Research, London, and Honorary Consultant in Clinical Oncology at The Royal Marsden NHS Foundation Trust, said: "Our study tells us more about the effect of the genetic hand that men are dealt on their risk of prostate cancer. We know that there are a few major genes that are rare and significantly affect prostate cancer risk, but what we are now learning is that there are many other common genetic variants that individually have only a small effect on risk, but collectively can be very important. To use the playing cards analogy again, sometimes multiple low cards can combine to form a high risk score.

"We can now explain a third of the inherited risk of prostate cancer, and will shortly be conducting a clinical trial to find out whether testing for genetic variants in men can successfully pick up the disease early, and

help direct targeted interventions for patients."

Professor Malcolm Mason, prostate cancer expert for Cancer Research UK, said: "This important research continues a quest to unravel the complex picture of the genetic factors that increase a man's risk of prostate cancer.

"Building on previous research this study gives a more complete list of these factors, bringing us closer to knowing who may need screening for prostate cancer and which men may benefit from early treatment. More work needs to be done, but identifying these genetic factors will allow us to better understand the disease and maybe even develop new treatments."

Dr Matthew Hobbs, Deputy Director of Research at Prostate Cancer UK said: "There's no doubt that genetic testing for prostate cancer is an exciting area of research. The results of this study could take us a step closer to targeted screening by allowing us to identify those most at risk of the disease based on the genes that they possess. However, this is not the end of the story and the challenge now lies in translating this knowledge into a reliable test that can be used on a large scale through the NHS to find those men at highest risk.

"It is also absolutely vital that researchers build on this work to discover which of these genetic variants can tell us whether a man's cancer is aggressive and likely to go on to kill him, or one that may never cause any harm. This would save those men with non-aggressive disease from undergoing unnecessary treatment."

More information: A meta-analysis of 87,040 individuals identifies 23 new susceptibility loci for prostate cancer, *Nature Genetics*, DOI: 10.1038/ng.3094

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