# Gene markers located for hereditary prostate cancer

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Researchers at the Johns Hopkins Brady Urological Institute, Wake Forest University and the Karolinska Institute in Sweden have identified an array of gene markers for hereditary prostate cancer that, along with family history for the disease, appear to raise risk to more than nine times that of men without such markers.

The panel, gleaned from a study of more than 4,000 Swedes, found that these markers are common and could account for nearly half of the prostate cancer cases in this study. Results are published online in the Jan. 16 edition of the *New England Journal of Medicine*.

The international research team plans to sample DNA from U.S. populations of men to determine if these genetic changes prevail outside of Sweden. And they caution that the panel of markers cannot tell how aggressive a potential cancer may be.

“This information is not yet available as a genetic test for risk of prostate cancer, but efforts are under way to rapidly develop one,” says William B. Isaacs, Ph.D., of the Johns Hopkins Brady Urological Institute, who participated in the study.

“While these findings need to be validated and refined, it’s a step in the right direction to revealing the genetic-based reasons for this cancer that we have been looking for over the past 15 years,” he added.

In the study, the scientists drew blood from 2,893 prostate cancer

patients and 1,781 men without the disease. White blood cells are a good source of DNA that an individual is born with as opposed to DNA in cancer cells that gets altered by the environment or other means, according to the scientists.

Using DNA from blood cells, they sifted through variations in chemicals called nucleotides that pair up to form the rungs of a DNA ladder which carries genetic instructions. These so-called “single nucleotide polymorphisms” or SNPs, occur when one chemical base pair is swapped for another, altering the information in the DNA alphabet or sequence.

Investigators found 16 SNPs in five different regions of human chromosomes 8 and 17 that were more common to men with prostate cancer than those without the disease. The individual changes were ones previously linked to prostate cancer and other diseases, a good indication, the scientists say, that they were on the right track.

To create their panel, the scientists chose the best SNPs from each of the five regions and tested their cumulative effect on prostate cancer risk. As the number of associated SNPs increased, so did risk. Men with four or more of these SNPs were nearly 4.5 times more likely to have prostate cancer.

“This work strongly suggests that because of the combination of polymorphisms we inherit, one man may be more on the path to developing prostate cancer than another,” says Isaacs, who is the William Thomas Gerrard, Mario Anthony Duhon and Jennifer and John Chalsty Professor of Urology at the Brady Urological Institute and professor of oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Add to that a family history of prostate cancer and the risk doubles. Men with all five SNPs plus a family history of prostate cancer were nearly

9.5 times more likely to have the disease. Further analysis revealed that 46 percent of prostate cancer cases in this population were due to these risk factors. But the scientists estimate that almost 90 percent of the Swedish population carries one or more of the five SNPs, elevating their risk for prostate cancer relative to men who carry none of these factors.

Swedish populations are relatively homogenous, tending to marry other Swedes and well suited for such genetic studies because genetic variation is somewhat more limited than in larger, heterogeneous groups. Socialized medicine in Sweden also enables access to robust registries of patient data.

In addition, Swedes suffer from higher-grade prostate and other cancers, and deaths among their Caucasian populations are 10 to 20 percent higher than among American Caucasians, according to Henrik Gronberg, M.D., Ph.D., professor of epidemiology at the Karolinska Institute and a co-investigator on the study.

Isaacs and his team note that the SNPs may not in themselves lead to increased cancer risk, but could be markers linked to other changes that do so.

Wake Forest and Johns Hopkins' Schools of Medicine have filed patent applications for the technology and results described in this study.

Source: Johns Hopkins Medical Institutions