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Scientists find second site for prostate cancer gene

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Scientists at Wake Forest University School of Medicine and colleagues who are studying a prostate cancer gene called HNF1B have found a second independent site within the HNF1B gene on chromosome 17 (17q12) – increasing the number of genetic variants that may contribute to risk of developing the disease.

After comparing the newly-discovered site with a previously discovered site in the same gene among two large groups of patients in Sweden and at Johns Hopkins Hospital in Baltimore, "these data strongly suggest that the two sites are genetically independent," said Jianfeng Xu, M.D., Dr. Ph.H., senior researcher on the study.

"We found another genetic variant associated with prostate cancer risk," Xu said. "The more genetic variants we discover, the better off we are. As we find more of these, it improves our ability to predict prostate cancer risk."

Xu, a professor of epidemiology and cancer biology and Director of the Center for Cancer Genomics, reported the results with 30 colleagues in the current on-line version of *Nature Genetics.*

The researchers conducted what they termed a "fine-mapping study" in the two groups, one called CAPS, from Sweden, that had 2,899 prostate cancer cases and 1,722 control participants, and the Johns Hopkins study that had 1,527 prostate cancer patients and 482 control participants.

They found two separate clusters of prostate-cancer-associated SNPs (single nucleotide polymorphisms), one in a region previously identified and one in a new region. The researchers then worked to see whether the genetic variants were associated with risk of developing the disease. They looked at the same locations in five other large studies of prostate cancer patients and found that prostate cancer risk was higher among men who had the genetic variants. Earlier this year, the same research group reported in the *New England Journal of Medicine* that genetic variants have a strong cumulative effective. A man with four of the five previously discovered variants has a 400 percent increased risk of developing prostate cancer compared to men with none of the variants.

Xu said that as the number of genetic variants associated with prostate cancer risk continues to mount, it improves the precision of risk prediction. But he predicted that prostate cancer will be found to be polygenic, "not dependent on one gene, but a group of genes."

Prostate cancer risk might be plotted on a bell-shaped curve, with men with a family history of the disease and multiple variants being at the upper end of the curve.

The researchers are exploring another finding, that the HNF1B gene is also associated with diabetes. But if a patient with the HNF1B gene has diabetes, the prostate cancer risk decreases, "We still don't know how," Xu said.

Source: Wake Forest University Baptist Medical Center