Genetic variant associated with aggressive form of prostate cancer

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Researchers at Wake Forest University Baptist Medical Center and colleagues have identified the first genetic variant associated with aggressive prostate cancer, proving the concept that genetic information may one day be used in combination with other factors to guide treatment decisions.

The research will be reported online next week (Jan. 11-15) in the Proceedings of the National Academy of Sciences.

"This finding addresses one of the most important clinical questions of prostate cancer - the ability at an early stage to distinguish between aggressive and slow-growing disease," said Jianfeng Xu, M.D., Dr. P.H., professor of epidemiology and cancer biology. "Although the genetic marker currently has limited clinical utility, we believe it has the potential to one day be used in combination with other clinical variables and genetic markers to predict which men have aggressive prostate cancer at a stage when the disease is still curable."

According to the authors, prostate cancer accounts for one-fourth of all cancer diagnoses in the United States. Autopsy studies suggest that most aging men will develop prostate lesions that, if detected clinically, would be diagnosed as cancer.

Although most men have a slow-growing form of the disease, aggressive prostate cancers are currently the second-leading cause of cancer death in the U.S., accounting for 27,000 deaths annually.

"The current inability to accurately distinguish risk for life-threatening, aggressive prostate cancer from the overwhelming majority of slow-growing cases creates a treatment dilemma," said Xu.

While researchers, including Xu's team, have identified multiple genetic variants associated with the risk of developing prostate cancer in the first place, until now there have been no genetic factors associated with disease aggressiveness.

Based on existing evidence that some men are genetically predisposed to developing aggressive prostate cancer, the researchers hypothesized that inherited genetic variants exist that could be used as markers to identify these men at an early, curable stage of disease.

"Identifying factors that are associated with a risk of having or developing aggressive disease is urgently needed to reduce over-diagnosis and over-treatment of this common cancer," said Karim Kader, M.D., Ph.D., a Wake Forest Baptist urologist specializing in prostate cancer and a co-author on the paper.

The study involved the analysis of genetic information from 4,849 men with aggressive disease and 12,205 with slow-growing disease to determine if the men with aggressive disease had genetic variants in common. The analysis included participants in the Genetic Markers of Susceptibility study performed by the National Cancer Institute (NCI) as well as additional study populations in the U.S. and Sweden.

The researchers identified a genetic variant (rs4054823) that was associated with a 25 percent higher risk of developing aggressive disease.

"A single variant with a moderate effect such as this is unlikely to be sufficient on its own at predicting risk," said Xu. "But its identification

is significant because it indicates that variants predisposing men to aggressive disease exist in the genome."

He said that as more variants associated with aggressive disease are identified, it is possible that doctors could test men to determine their risk of aggressive disease not only at the time of diagnosis, but early enough in their lives to target them for increased screening.

"We speculate that a panel of variants could be an important part of developing a screening strategy that could reduce the number of men requiring screening, thereby reducing over-diagnosis, while also identifying men at risk for developing aggressive disease at a stage when the disease is potentially curable."

Provided by Wake Forest University