Medical Xpress

Study finds gene linked to aggressive prostate cancer

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Results from two genome-wide association studies have identified a genetic variant of the DAB2IP gene that is associated with the risk of aggressive prostate cancer. Research teams from the Translational Genomics Research Institute (TGen), Wake Forest University School of Medicine, the Karolinska Institute in Stockholm, Sweden, and Johns Hopkins Medical Institutions made the discovery jointly.

Researchers suspect that the DAB2IP gene is involved in tumor suppression, suggesting that this protective mechanism goes awry in men with the variant form. The finding, reported today in the Journal of the National Cancer Institute, might one day help doctors tailor treatment based on a patient's genetic makeup.

Both genetic and environmental factors are important in the development of prostate cancer, and it is only recently that some of the consistent genetic factors have been identified. It is not clear at present whether men who are genetically prone to the disease tend to have more aggressive disease than men who are not.

"Because there is no way to tell whether a person has or will have the aggressive version versus the mild version of prostate cancer, both forms are treated the same—with radiotherapy or surgery to remove the prostate gland. The identification of this genetic variant could lead to better risk assessment for aggressive disease, providing doctors with more information on how to best treat men who may be diagnosed with prostate cancer," said John Carpten, Ph.D., director of TGen's Division

of Integrated Cancer Genomics and senior author of the paper.

Analysis of 3,159 samples led the researchers to conclude that men possessing the DAB2IP variant appear to carry a nearly 36 percent increased risk of advanced prostate cancer.

“In most cases, prostate cancer is not a death sentence, but it would be ideal to identify men with an aggressive form of disease,” said Jianfeng Xu, M.D., Dr.PH, a senior author and a professor of epidemiology and cancer biology at Wake Forest University School of Medicine. “Our finding suggests the possibility of developing a blood test to gauge disease type so doctors could decide if more aggressive treatment is needed.”

The researchers screened DNA samples from 500 men with advanced prostate cancer and 500 healthy men of the same age in Sweden. This DNA screening examined the entire genome for more than 550,000 single nucleotide polymorphisms (SNPs), which are locations on chromosomes where a single unit of DNA, or genetic material, may vary from one person to the next. The team then focused on 60,000 SNPs that have also been evaluated by a similar study conducted by the National Cancer Institute (NCI) called Cancer Genetic Markers of Susceptibility (CGEMS). Evaluation of these 60,000 SNPs identified seven SNPs that appeared to be linked to disease aggressiveness.

Additionally, researchers screened another 1,242 men with advanced disease and 917 healthy men who were part of a research project at Johns Hopkins Medical Institutions. This group included both African and European Americans. Through these multiple screenings, the researchers found that the variant form of DAB2IP is associated with an increased risk of having aggressive disease.

Senior authors Henrik Gronberg, M.D., Ph.D., a professor of

epidemiology from Karolinska Institute, and William Isaacs, Ph.D., a professor of urology at Johns Hopkins Medical Institutions, both agree that the findings were possible because advances in technology allow researchers to take a more systematic approach to looking at the entire genome. Instead of solely studying genes that they suspect may be related to disease susceptibility, they can study the entire genome and look for associations.

“By using state-of-the-art technologies, we can find genes that were not previously known or thought to be involved with disease risk,” said David Duggan, Ph.D., head of TGen’s Advanced Genomics Technology Lab. “If we can then learn more about the proteins they produce, it could lead to new understanding about disease mechanisms and new treatments.”

Source: The Translational Genomics Research Institute