Variation in prostate stem cell antigen gene raises bladder cancer risk

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Researchers have pinpointed a specific gene variation that causes increased risk of urinary bladder cancer, according to a scientific team led by The University of Texas M. D. Anderson Cancer Center.

These findings were reported today in the advance online publication of Nature Genetics, and determined that people with the variant had a 30 percent to 40 percent higher risk for bladder cancer. Scientists hope the results of this large, multi-site international study may help determine who is at high risk to contract this deadly cancer, which may lead to better survival rates and the development of chemopreventive interventions.

"With this research, we were able to find a novel specific gene and a functional variation that are independent of the previous suspects. We found a 'why' to many of the questions about genetic causes of bladder cancer," said Xifeng Wu, M.D., Ph.D., professor in M. D. Anderson's Department of Epidemiology, Division of Cancer Prevention and Population Sciences, the lead and corresponding author of this publication. "The neighboring genomic region has been identified previously as a possible problem for breast, prostate, colorectal and bladder cancer, but we didn't know why."

Genetic risk factors have been elusive

Bladder cancer is the fourth most common cancer in men in the United

States. In this country, it is projected that more than 68,800 new cases will be diagnosed and approximately 14,400 people will die because of the disease this year.

Cigarette smoking and occupational exposure to certain chemicals are known risk factors, but almost one-third of people who get the disease have an inherited genetic susceptibility. People with first-degree relatives with bladder cancer have a 50 percent to 100 percent higher risk of getting the disease.

However, the exact genetic explanation for bladder cancer has remained elusive, and this study may have helped to solve some of the puzzles, Wu said.

Prostate stem cell antigen (PSCA) is over-expressed in prostate cancer, and the level of PSCA increases with tumor grade and stage. However, the cellular function of PSCA in prostate cancer is not clear.

While PSCA's involvement in bladder cancer had been suggested previously, this is the first time it has been linked definitively.

6,667 cases, 39,590 controls

The first step of this study was a genomewide evaluation of 969 people with bladder cancer and 954 healthy people. To validate their findings, researchers evaluated patients from three additional U.S. and nine European groups, for a total of 6,667 people with bladder cancer and 39,590 healthy people.

A variant in the PSCA gene (rs2294008) was associated consistently with bladder cancer. Researchers then re-examined the PSCA gene region and found rs2294008 was the only common missense genetic variation in the PSCA region. A missense mutation occurs at a single

point in the genome and swaps one amino acid for another in a protein.

Low levels of PSCA were found in the bladders of healthy people, but it was over-produced in the majority of patients with bladder cancer. Previous reports suggest that measurement of PSCA in urine may be a simple and accurate marker to help diagnose bladder cancer.

Potential for chemoprevention, treatment

Next, the group plans to fully analyze data jointly with other participating centers, possibly uncovering additional genes for bladder cancer.

Wu said she hopes the group's findings will help targeted bladder cancer prevention efforts.

"When we've identified all the genes that are linked to bladder cancer, we plan to develop a web-based tool so physicians can calculate accurately and easily a patient's risk of getting the disease," she said. "Early identification of risk may help save lives with chemoprevention or early treatment."

In addition, Wu's team is working with a hospital in Spain to compare findings of the study to clinical outcomes. "How do these genes affect survival, recurrence and progression of bladder cancer?" she said. "As we get more information, we hope to be able to predict clinical outcomes and optimize therapy."

Source: University of Texas M. D. Anderson Cancer Center (news : web)