Researchers discover traits of aggressive form of prostate cancer

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Researchers led by a team at the Michigan Center for Translational Pathology at the University of Michigan Health System have identified traits of an aggressive type of prostate cancer that occurs in about 10 percent of men who have the disease. They hope the discovery could lead, possibly within the next few years, to a simple urine test that will help to diagnose this variation of prostate cancer.

Previous studies by this group of researchers have shown that most prostate cancer is caused in part by a gene fusion – the merging of two unrelated genes, which plays a role in at least 50 percent of prostate cancer cases.

To shed light on the prostate cancers that don't involve gene fusion, the researchers in the current study analyzed data on 1,800 prostate cancers to find commonalities in their genetic aberrations. They learned that a gene called SPINK1 (serine peptidase inhibitor, Kazal type 1) was over-expressed, or found in excess amounts, in prostate cancers that do not have gene fusions. The finding suggests that SPINK1 is a biomarker – a molecule in bodily fluids, blood and tissue that can be a signal of a disease – for a subtype of prostate cancer.

The findings, reported in the June issue of the journal *Cancer Cell*, also suggest that men with SPINK1–related prostate cancers tend to have a quicker recurrence of the disease than those with other types of prostate cancer.

"Our study is really the first to look at what is happening molecularly with fusion-negative prostate cancers," says Scott Tomlins, Ph.D., first author of the paper and an M.D./Ph.D. student at the U-M Medical School.

"Because SPINK1 can be found non-invasively in urine, a test could be developed that would complement current urine testing that is used to detect some prostate cancer or future urine tests for gene fusions," adds senior author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and S.P. Hicks Endowed Professor of Pathology at the U-M Medical School.

An estimated 186,320 new cases of prostate cancer will be diagnosed this year, according to the National Cancer Institute, and more than 28,000 men will die from the disease this year. More than 70 percent of men diagnosed with prostate cancer are older than 65.

Current tests for prostate cancer include prostate-specific antigen (PSA) blood tests. Increased levels of PSA can indicate that prostate cancer is present. Another test is a digital rectal examination, which can detect abnormalities in the prostate. Another urine-based test screens for PCA3 as a specific biomarker of prostate cancer.

Background: In 2005, Chinnaiyan and his team made the landmark discovery that in prostate cancer, pieces of two chromosomes trade places with each other. This switch, or translocation, causes two unrelated genes to be placed next to each other and fuse together. The abnormal gene fusion associated with prostate cancer occurs when one of two genes, ERG or ETV1, merges with a prostate-specific gene called TMPRSS2.

Before this discovery, it was thought that gene fusions only occurred in blood cancers, such as leukemias and lymphomas, but not in common

solid tumors such as prostate cancer. Chinnaiyan's discovery demonstrated that these gene fusions could be found in solid tumors and has opened an entire field of research. This discovery may lead to better diagnostic tests and new treatments for prostate cancer.

Earlier this year, Chinnaiyan's team published a study about a urine test that more accurately detects prostate cancer than any other screening method currently in use. They built on the PCA3 test by screening for six additional biomarkers and some molecules. In their research, the team accurately identified 80 percent of patients who were later found to have prostate cancer, and they were 61 percent effective in ruling out disease in other study participants.

Methodology: In the current study, the team used a bioinformatics analysis method called Cancer Outlier Profile Analysis (COPA) developed by Tomlins and Daniel Rhodes, Ph.D., in Chinnaiyan's laboratory. COPA makes it possible for researchers to detect extremely high expression levels of outlier genes, or genes with characteristics outside the norm.

Using data from seven studies, they found SPINK1 was over-expressed in prostate cancer when compared to benign prostate cells, and that it was found exclusively in cancers that did not involve ERG or ETV1 gene fusions.

Source: University of Michigan

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