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New, noninvasive prostate cancer test beats PSA in detecting prostate cancer

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An experimental biomarker test developed by researchers at the University of Michigan more accurately detects prostate cancer than any other screening method currently in use, according to a study published in the February 1 issue of Cancer Research, a journal of the American Association for Cancer Research.

The researchers say a simple urine test that screens for the presence of four different RNA molecules accurately identified 80 percent of patients in a study who were later found to have prostate cancer, and was 61 percent effective in ruling out disease in other study participants.

This is far more accurate than the PSA blood test currently in use worldwide, which can accurately detect prostate cancer in men with the disease but which also identifies many men with enlarged prostate glands who do not develop cancer, researchers say. Even the newer PCA3 test, which screens for a molecule specific to prostate cancer and which is now in use both in the U.S. and Europe is less precise, they say.

“Relative to what is out there, this is the best test so far,” said the study’s lead author, Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology at the University of Michigan.

He also says that this “first generation multiplex” biomarker test will likely be improved upon as researchers continue to uncover the molecular underpinnings of prostate cancer.

“We want to develop a test to allow physicians to predict whether their patients have prostate cancer that is so accurate a biopsy won’t be needed to rule cancer out,” Chinnaiyan said. “No test can do that now.”

Chinnaiyan and the Michigan researchers developed the test based on their recent finding that gene fusions – pieces of chromosomes that trade places with each other, causing two genes to stick together - are common in prostate cancer, and that by overriding molecular switches that turn off excess growth, they may be the causative factor in some forms of the disease. In 2005 they identified a prostate-specific gene called TMPRSS2 which fuses with either ERG or ETV1, two genes known to be involved in several types of cancer. In 2007, they identified another five genes that fuse on to ERG or ETV1 to cause prostate cancer.

In the current study, researchers built upon the PCA3 test by screening for six additional biomarkers, including TMPRSS2:ERG as well as some molecules generally over-expressed in prostate cancer, and some which are over-expressed in specific cancer subtypes.

Researchers collected urine samples from 234 men with rising PSA levels before they underwent prostate biopsy at a University of Michigan urology clinic. Among this group, biopsy results confirmed a diagnosis of prostate cancer in 138 patients; 96 patients were cancer-free.

Correlating the urine biomarker test results with the biopsy data, researchers found that, in combination, four of the seven biomarkers were significant predictors of prostate cancer: GOLPH2, which is generally over-expressed in prostate cancer; SPINK1, over-expressed in a subset of these cancers; the PCA3 transcript expression; and TMPRSS2:ERG fusion status. Of the seven markers, only PCA3 had been previously reported as a diagnostic biomarker.

When tested as individual biomarkers, GOLPH2, PCA3, and SPINK1

each outperformed PSA, which had identified all of the men in the study as potentially positive for prostate cancer. “PSA was not predictive at all,” Chinnaiyan said. “You might as well have flipped a coin.”

The combination of the four biomarkers achieved a specificity and positive predictive value of greater than 75 percent, which they found to be five percent better than use of a PCA3 test alone, he says. Specificity is the probability that a test indicates a negative result if a person does not have a disease, and the positive predictive value is the proportion of patients with positive test results who are correctly diagnosed.

Chinnaiyan believes that any tests that are developed and widely tested would first be used to supplement a PSA blood screen.

Source: American Association for Cancer Research