Published online 3 August 2011 | Nature | doi:10.1038/news.2011.455

Urine predicts prostate cancer risk

Test could reduce unnecessary needle biopsies.

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Wanted: a better screen for prostate cancer.Blend Images / Alamy

A new screening test makes use of urine, rather than blood, to identify the men most at risk of prostate cancer, and may even provide information about how aggressive a tumour is likely to be.

The standard screening test for prostate cancer is a blood test for a protein called prostate specific antigen (PSA). But PSA is also produced by non-cancerous conditions such as enlarged prostates or infection, so is not very specific. "Most men with elevated PSA levels don't have prostate cancer," says Arul Chinnaiyan, director of the Michigan Center for Translational Pathology in Ann Arbor.

Chinnaiyan and his colleagues have developed a new test that detects two markers specific to prostate cancer. One, called TMPRSS2:ERG, is the fusion of two genes, TMPRSS2 and ERG, and is found in around half of prostate tumours found through PSA screening. The other, a non-coding RNA called PCA3, is a very sensitive marker, found in unusually high levels in more than 95% of prostate cancers.

The researchers studied 1,065 men from three academic medical centres and seven community-based hospitals, who had been shown in screening to have elevated PSA. They used their test to stratify the men into low-, intermediate- and high-score groups. Biopsies confirmed cancer in 21% of the low-score group, 43% of the intermediate group and 69% of the high group. The results are published today in Science Translational Medicine[1].

Futher studies will allow refinement of the test, but the researchers say patients in the high risk group should definitely get a biopsy. High-scoring men with a negative biopsy might also choose to be closely monitored given their high risk.

Higher urine test scores also correlated with the aggressiveness of the cancer, as determined by the size of the tumour and a standard metric of cell abnormality called the Gleason score. This

is something that biopsies cannot do reliably.

The results pave the way for Gen-Probe, the molecular diagnostic company based in San Diego, California, that has licensed the test, to seek approval from the US Food and Drug Administration (FDA).

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"This is one big step towards better risk assessment for individual patients," says Jack Schalken, director of research in the urology department at Nijmegen Centre for Molecular Life Sciences in the Netherlands. It is also a significant move towards the goal of personalized medicine, he says, as different subtypes of cancer are likely to require different treatments. "Clinicians are sitting in front of only one person; we need a way to assess how aggressive that patient's cancer is."

Other researchers are cautiously optimistic. Shiv Srivastava, scientific director at the Center for Prostate Disease Research in Rockville, Maryland, says that the study is "a major advance" but that independent studies are needed across races and in more general populations to confirm whether or not the findings extend to all men. The patients in Chinnaiyan's study were mostly white, and Srivastava's recent work suggests that ERG expression is lower in prostate tumours of African American men than in those of caucasian men[2].

Biomarker to bedside

Srivastava and Schalken agree, however, that the big advantage of the test over PSA is that it uses markers that are specific to prostate cancer.

Chinnaiyan's team first detected TMPRSS2:ERG in 2005[3]. The finding was surprising because at the time, gene fusions were thought to occur mainly in blood cancers or in rare soft-tissue tumours.

But it makes sense, says Chinnaiyan, because the fusion combines an androgen-regulated gene (TMPRSS2) with a transcription factor (ERG). "Androgen signalling is an important driver of prostate cancer, so it's not surprising that hooking these two genes together can disrupt hormone signalling to the point of causing cancer," he says.

Chinnaiyan's team has discovered more than 25 other gene fusions that are found in smaller percentages of prostate-cancer cases, and hopes that these biomarkers will one day be added to the urine-based test to improve detection rates.

But urine-based tests are not likely to replace the PSA test any time soon. "We are initiating long-term, prospective trials to begin gathering enough data to determine whether this test could, one day, serve as a replacement," says Chinnaiyan. "But the bar will be pretty high when attempting to replace a test physicians have used for so long."

- # References

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