

Detecting the Undetectable in Prostate Cancer Testing

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(PhysOrg.com) -- A team of Northwestern University researchers, using an extremely sensitive nanotechnology-based tool known as the biobarcode system, has detected previously undetectable levels of prostate-specific antigen (PSA) in patients who have undergone radical prostatectomy. This new assay, just one of many being developed by investigators at the Nanomaterials for Cancer Diagnostics and Therapeutics Center for Cancer Nanotechnology Excellence (Northwestern CCNE), is 300 times more sensitive than commercially available PSA tests.

The ability to easily and quickly detect very low levels of PSA may enable doctors to diagnose men with [prostate cancer](#) recurrence years earlier than is currently possible. Prostate cancer is the second leading cause of cancer death for men in the United States. (Only lung cancer is more deadly.) "We have defined a new zero for PSA," said Chad Mirkin, Ph.D., principal investigator of the Northwestern CCNE. "This level of sensitivity in detecting low concentrations of PSA will take the blinders off the medical community, especially when it comes to tracking residual disease." This study, which was led by Mirkin and C. Shad Thaxton, M.D., appears in the [Proceedings of the National Academy of Sciences](#) (*PNAS*).

"This new PSA assay may alter the management of patients who have been treated with surgery for prostate cancer," said William J. Catalona, M.D., director of the Clinical Prostate Cancer Program at Northwestern's Lurie Cancer Center. He was the first to demonstrate that

the [PSA test](#), a simple blood test, could be used as a screening tool for prostate cancer. "Studies have shown that postoperative [radiation therapy](#) given early to patients with adverse pathology, called adjuvant radiation, reduces the recurrence rate and improves survival," Catalona said. After the removal of the prostate gland, patients typically have PSA levels that are undetectable when measured using conventional diagnostic tools. "Because the 'nano-PSA assay' is more sensitive than the current commercially available PSA tests, it may allow physicians to target adjuvant radiation for patients destined to have a life-threatening tumor recurrence."

The study is an early indicator of how nanotechnology can be used to improve medical diagnostics and early cancer detection. In the case of prostate [cancer recurrence](#) following primary surgical treatment, patients with detectable but non-rising PSA levels could be reassured that their cancer will not recur. This reassurance potentially could be delivered much earlier than with conventional diagnostic tools. For patients with increasing levels of PSA, detected before conventional tools are able, doctors could diagnose a recurrence and intervene accordingly.

Furthermore, the effectiveness of post-operative treatment could be assessed by monitoring a patient's PSA levels. Tracking PSA levels early, before conventional tools are able, may allow doctors to validate treatments for recurrent cancer, such as radiation, hormone therapies and chemotherapies. The most effective will be able to keep down PSA levels.

"The first route to a new therapeutic is a good diagnostic tool, and that's what we have here," said Mirkin. "This bio-barcode assay, or a variant of it, could be a commercial tool in as little as 18 months. The technology is there. Now it's a business decision."

PSA is a protein produced by the cells of the prostate gland and found in

the bloodstream. This pilot study looked at serum samples from 18 post-prostatectomy patients collected over the course of a number of years.

The researchers were able to reliably and accurately quantify PSA values at less than 0.1 nanograms per milliliter, the clinical limit of detection for commercial assays. The lower limit of detection for PSA using the bio-barcode assay is approximately 300 times lower than the lower limit of detection for commercial tests. The PSA measurements were used to classify the patients as either having no evidence of disease or having a relapse of disease. The Northwestern team is now conducting a similar retrospective study of 260 patients and eventually plans to do a large prospective study.

The ultra-sensitive technology is based on gold nanoparticle probes decorated with DNA and antibodies that can recognize and bind to PSA when present at extremely low levels in a blood sample. A magnetic microparticle, outfitted with a second antibody for PSA, also is used in the assay. When in solution, the antibody-functionalized particles "recognize" and bind to PSA, sandwiching the protein between the two particles.

The key is that attached to each tiny gold nanoparticle are hundreds of identical strands of DNA. Mirkin calls this "bar-code DNA" because they have designed it as a label specific to the PSA target. After the "particle-protein-particle" sandwich is removed magnetically from solution, the DNA is removed from the sandwich and read using a Verigene® ID system, a nanotechnology platform designed to detect and quantify DNA. The amount of PSA present is calculated based on the amount of bar-code DNA. For each molecule of captured PSA, hundreds of DNA strands are released, which is one of the ways the PSA signal is amplified.

This work, which is detailed in a paper titled, "Nanoparticle-based bio-

barcode assay redefines 'undetectable' PSA and biochemical recurrence after radical prostatectomy," was supported by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. Investigators from the Innsbruck Medical University in Austria also participated in this study. An abstract of this paper is available at the [journal's Web site](#).

Provided by National Cancer Institute ([news](#) : [web](#))

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