Nanoparticle PSA test predicts if prostate cancer will return

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Men who have just had their cancerous prostate gland removed have one pressing question for their doctors: Am I cured? But conventional tests haven't been sensitive enough to provide a concrete answer. Current tests that measure the level of protein called PSA (prostate-specific antigen), which signals the presence of cancer, often detect no PSA, only to have cancer return in up to 40 percent of the cases.

New research from Northwestern University Feinberg School of Medicine and the University International Institute for Nanotechnology shows that an ultrasensitive PSA test using nanoparticle-based technology (VeriSens PSA, Nanosphere, Inc., research-use-only) may be able to definitively predict after surgery if the cancer is cured long term or if it will recur.

The new test, which is based upon assays invented at Northwestern in the laboratories of co-principal investigator Chad A. Mirkin, is 300 times more sensitive than currently available commercial tests and can detect a very low level of PSA that indicates the cancer has spread beyond the prostate. The test also may pick up cancer recurrence at a much earlier stage, when secondary treatment is most effective for a patient's survival.

"This test may provide early and more accurate answers," said co-principal investigator C. Shad Thaxton, M.D., an assistant professor of urology at Feinberg and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. "It detects PSA at levels in the blood that cannot be detected by conventional tests.

It may allow physicians to act at the earliest and most sensitive time, which we know will provide the patient with the best chance of long-term survival."

This ability to 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.

Not only may the new test more accurately predict the course of the disease, it also gives an early indication of whether secondary treatments, such as radiation and hormone therapy, are working. If not, then doctors can quickly begin alternative treatment and refer patients to clinical trials.

The study results will be presented June 2 at the American Urological Association 2010 Annual Meeting. These and the results of other Northwestern PSA studies will be presented at the meeting by Lee Zhao, Dae Kim and Hannah Alphs, urology residents at Feinberg.

"These studies suggest that the nanotechnology PSA test might become the preferred postoperative PSA test for men who have been treated with radical prostatectomy," said William Catalona, M.D., professor of urology at Feinberg, a physician at Northwestern Memorial Hospital and director of the clinical prostate cancer program at the Lurie Cancer Center. "It should be especially useful in the early identification of men who would benefit from adjuvant postoperative radiation therapy and those who need postoperative salvage radiation therapy for recurrence." Catalona, a senior investigator on the study, was the first to demonstrate that the PSA test could be used as a screening test for prostate cancer.

The study confirms and builds on the previous findings of a 2009 pilot study Thaxton conducted with Mirkin, the George B. Rathmann

Professor of Chemistry in the Weinberg College of Arts and Sciences, and other colleagues.

PSA is a protein normally secreted out of the prostate cells into the semen in high concentrations. Usually, very little diffuses into the blood stream, and the normal PSA value for men without prostate disease is less than 2 nanograms per milliliter. When the prostate gland has a disease process, such as inflammation, benign enlargement or cancer, the barriers to PSA diffusion into the blood stream are breached, and PSA levels rise. In a man who has his cancerous prostate removed, there should be no PSA in the blood except for a minute amount produced by the periurethral glands. However, any PSA produced by cancer recurrence ends up in the blood stream and can be detected earlier with the more sensitive nanotechnology PSA assay.

For the new study, researchers obtained blood serum retrospectively from men whose PSA serum samples had been frozen after surgery and whose assays (blood analysis) showed an undetectable PSA level based on the conventional test. Northwestern researchers then tested those serum samples using the more sensitive nanotechnology-based test. They wanted to see if they could detect PSA at levels below the limit of the conventional test, and if those results could predict the cancer outcome for those patients, who were followed for up to 10 years.

Using the new test, Thaxton and colleagues found that the low and non-rising PSA levels (presumably produced by the normal periurethral glands) of patients meant that the prostate cancer was effectively cured and did not return over a period of at least 10 years. Scientists also found a PSA level higher than that expected from the periurethral glands based on the new test meant the patients would have their disease recur.

As result of the study, researchers were able to assign a PSA level number to a cure for the first time as well as a number that indicated the

disease would recur and if it would recur aggressively. These newly identified levels were below what could have been detected with the conventional PSA test. The researchers were able to quantify PSA values at less than 0.1 nanograms per milliliter, the clinical limit of detection for commercial assays.

Thaxton said the next step for scientists is a prospective clinical trial to compare the nanoparticle-enhanced PSA assay to traditional PSA assays and determine if earlier detection and treatment can save lives.

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