

## UF scientists work to develop simple bladder cancer test

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University of Florida researchers have identified a set of proteins that appear to signal the presence of bladder cancer, a discovery they hope will lead to a simple, fast and noninvasive test that can detect the disease early.

Working with colleagues at the University of Michigan, the scientists used advances in technology to isolate nearly 200 proteins from the urine of patients with and without bladder cancer. Several appear promising as potential biomarkers, including one that studies conducted elsewhere have already linked to liver and ovarian cancer. The findings, available online, are scheduled to be published in the July 6 print edition of the American Chemical Society's *Journal of Proteome Research*.

Developing a simple “dipstick” test that would better single out patients whose symptoms are linked to cancer would enable those who simply have an infection to avoid a battery of screenings that typically include cystoscopy, a painful procedure that uses a small camera threaded through the urethra to image the bladder’s interior. Such a test also could be used to detect cancer sooner, possibly before its signs even surface.

“With any cancer, the earlier you find it the better because it’s not as aggressive in its early stages, and of course it’s much easier to remove any cancer anywhere in the body if you catch it while it’s relatively small,” said Steve Goodison, an associate professor of surgery at the UF College of Medicine-Jacksonville.

“What would really help in this disease would be a test you could use to monitor these patients just by monitoring their urine,” he added. “If we could develop this test to try to narrow down those who’ve got infections versus something more serious, that would relieve the patient from pain and worry and (cut health-care costs). The final aim would be to make a test cheap and convenient enough that you can start to think of screening people who don’t have any symptoms.”

Bladder cancer ranks among the five most common malignancies. The American Cancer Society estimates that in 2007 there will be about 67,160 new cases of bladder cancer diagnosed in the United States. Four times more men than women contract the disease, and smoking as well as exposure to industrial toxins increases the risk. Although the five-year survival rate is about 94 percent when it is detected early, bladder cancer is extremely difficult to cure because it tends to recur.

“Imagine the bladder like a balloon, and the tumors grow into the interior of the balloon,” Goodison said. “So the surgeons go in and want to be as least disruptive as possible, so they nip these growths off from the inside, but unfortunately once it’s happened it’s very likely going to happen again -- once you have bladder cancer you are at a high risk of recurrence for the rest of your life, which makes monitoring it a real problem.”

As a result patients need to be closely monitored, with most undergoing cystoscopy every few months in the first year after diagnosis and as frequently as every six months thereafter. Meanwhile, the urine tests currently used to detect recurrent bladder cancer miss 60 percent to 75 percent of all malignancies, especially those that are low-grade or early stage.

“They haven’t proven to be accurate enough to make the urologists confident to use them instead of doing manual inspection to date (using

cystoscopy),” Goodison said. “The trouble is, a lot of tests tend to look at only one biomarker, and one biomarker is never really going to do it, you need to do a panel. You need something like six biomarkers on a dipstick and if four of the six come up then you have an accurate answer. Tests that look at one protein are not going to do it because cancer is so different between individuals.”

In the current study, scientists used a technique to search for glycoproteins -- a subset of proteins naturally secreted into the urine from the bladder lining -- in urine samples from 10 individuals, five of whom had bladder cancer. Each sample was small, on average about 30 milliliters, equivalent to a fluid ounce. In contrast, previous urine protein profiles required large-volume samples.

Of the 186 proteins identified in the study, five were present only in the patients with cancer. The findings also substantially add to the urinary proteome database, which until now only contained 146 proteins. Additional studies are planned to screen samples from a larger number of bladder cancer patients with a variety of disease stages and grades, Goodison said.

“Even though our study involved a small number of patients so far, this was really a proof of principle that we can use these new techniques to detect proteins in the urine,” Goodison said. “Nobody could do that at this (degree of) sensitivity until now.”

The study was funded through a grant from the Florida Department of Health. Goodison’s collaborators included UF urologic surgeon Dr. Charles Rosser, and David Lubman, a protein chemist at the University of Michigan.

“The development of novel non-invasive methods for early detection of bladder cancer is very exciting and represents a major step in (making)

routine screening of patients with urological disease feasible in the future,” said Nicholas C. Popescu, chief of the molecular cytogenetics section at the National Cancer Institute's Laboratory of Experimental Carcinogenesis. “In addition, interactions among specific proteins could lead to the development of effective therapy of bladder cancer, a major cause of cancer death worldwide.”

Source: University of Florida

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