Prostate cancer's multiple personalities revealed

November 3 2010

Scientists at Weill Cornell Medical College have taken an important step toward a better understanding of prostate cancer by uncovering evidence that it is not one disease, as previously believed, but rather several factors which can be measured and, in the future, destroyed by targeted therapy.

The research team led by of Dr. Mark A. Rubin, the Homer T. Hirst Professor of Oncology in Pathology and vice chair for experimental pathology at Weill Cornell Medical College, identified secondary mutations that cause some types of prostate cancer cells to be lethal. The team believes that their discovery will lead to better tests for prostate cancer, sparing thousands of men from unnecessary biopsies, and leading to more specific and individualized therapy for prostate cancers that are likely to become deadly. The study results were published in the Oct. 29 online edition of the journal Genome Research.

The current research expands on the team's previous work with Arul M. Chinnaiyan's group at the University of Michigan that reported the first evidence that gene fusions, hybrid genes formed from two previously separate genes, play a widespread role in prostate cancer. At the time, it was known that gene fusions could drive the development of blood cancers but were only rarely detected in common solid cancers. Their finding was hailed as a landmark discovery by colleagues when it was first published in 2005 in the journal *Science*.

In their newly published work, Dr. Rubin and colleagues report evidence

that gene fusion prostate cancers are susceptible to secondary mutations. This novel observation supports the view that aggressive cancers need to accumulate multiple mutations. Using discoveries made in this study, clinicians may be better able to diagnose and target potentially deadly tumors.

"In the future, these fusions, specific to certain types of prostate cancer, may help physicians prescribe tailored therapies for their patients," says Dr. Rubin. "This is an important step toward providing specific therapies that target individual cancer variants, and our hope is these findings will help doctors diagnose a patient's specific disease," explains Dr. Rubin.

Prostate cancer is the most common type of non-skin cancer found in American men and is the second leading cause of cancer death in men. According to the American Cancer Society, one in six men will get prostate cancer during his lifetime, and it will kill one in 36 men. The Society estimates that there will be about 217,730 new cases of prostate cancer and about 32,050 deaths in the United States this year.

Traditionally, screening for prostate cancer has been done by a blood test known as the Prostate Specific Antigen (PSA) test. However, it has not found to be as reliable as once thought. "PSA testing is inadequate. It detects men with cancer but also many men with benign conditions," according to Dr. Rubin. "As we have seen from two major studies on PSA screening, for every 100 men with a positive PSA screening, only 25 will have cancer."

Dr. Rubin's prior research has focused on a better understanding of prostate cancer and finding a test that will distinguish clinically significant prostate cancer from indolent disease that does not require additional treatment. Their research has led Dr. Rubin and his colleagues to co-develop the diagnostics for a new test for prostate cancer with the University of Michigan and two commercial partners, Gen-Probe and

Ventana/Roche.

"The new test being developed will identify cells that are seen only in people with prostate cancer, allowing us to know with great certainty who has prostate cancer," according to Dr. Rubin. "This will result in fewer unnecessary biopsies, which have potential side effects, including infections, bloody semen, and rectal bleeding."

Provided by New York- Presbyterian Hospital