Scientists find protein potential drug target for treatment-resistant prostate cancer

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Scientists at Jefferson's Kimmel Cancer Center in Philadelphia have found that a signaling protein that is key to prostate cancer cell growth is turned on in nearly all recurrent prostate cancers that are resistant to hormone therapy. If the findings hold up, the protein, called Stat5, may be a specific drug target against an extremely difficult-to-treat cancer.

In addition, the researchers, led by Marja Nevalainen, M.D., Ph.D., associate professor of Cancer Biology at Jefferson Medical College of Thomas Jefferson University, also showed that the convergence of two biological pathways could be responsible for making such hormone-resistant prostate cancers especially dangerous.

They have found that a synergy between Stat5 and hormone receptors in recurrent prostate cancer cells helps each maintain its activity. Dr. Nevalainen and her co-workers report their findings January 1, 2008 in the journal *Cancer Research*.

"These findings validate Stat5 as a potential drug target in prostate cancer, and in particular, in a form of prostate cancer for which there are no effective therapies," Dr. Nevalainen says.

Men with primary prostate cancer usually have either surgery or radiation, whereas subsequent disease is frequently treated by hormone therapy. But if the cancer recurs again, years later, it can be more aggressive and typically fails to respond to hormone treatment. In previous work, the researchers showed that when Stat5 is turned on in

primary prostate cancer, men are more likely to have recurrent disease.

In the current study, the team examined human prostate cancer cells of 198 patients with prostate cancer recurrence. They found that Stat5 was active in 74 percent of all recurrent prostate cancers. Of these patients, 127 had been treated with androgen deprivation therapy. The researchers found Stat5 was active in 95 percent of these hormone resistant tumors, meaning it was more likely to be active if the patient had been treated with hormone deprivation therapy.

Dr. Nevalainen shows that Stat5 interacts with the androgen receptors and keeps them “transcriptionally active.” Next, the scientists would like to conduct tests in animal models to see if this synergy promotes androgen-independent prostate tumor growth, and whether or not Stat5 synergizes with androgen receptors activated by adrenal androgens, which are present in the absence of testicular androgens during the hormone therapy of prostate cancer in patients.

Source: Thomas Jefferson University