Blocking protein kills prostate cancer cells, inhibits tumor growth

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Researchers at Jefferson's Kimmel Cancer Center in Philadelphia have shown that they can effectively kill prostate cancer cells in both the laboratory and in experimental animal models by blocking a signaling protein that is key to the cancer's growth. The work proves that the protein, Stat5, is both vital to prostate cancer cell maintenance and that it is a viable target for drug therapy.

The scientists, led by Marja Nevalainen, M.D., Ph.D., associate professor of Cancer Biology at Jefferson Medical College of Thomas Jefferson University, wanted to prove that Stat5 was indeed necessary for prostate cancer cells to be viable.

They blocked the protein's expression and function in several ways, including siRNA inhibition, antisense inhibition and adenoviral gene delivery of an inhibitory form of Stat5. All of these techniques killed the prostate cancer cells in cell culture. The researchers also showed when they transplanted such cancerous tissue into mice and blocked Stat5 expression, prostate tumors failed to grow.

"This provides the proof of principle that Stat5 is a therapeutic target protein for prostate cancer, and may be specifically useful for advanced prostate cancer, where there are no effective therapies," Dr. Nevalainen says. "These results are very reproducible." She and her team report their findings March 1, 2008 in the journal Clinical Cancer Research.

Hormone resistant prostate cancer is especially dangerous. 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, often leaving few treatment options.

The findings, Dr. Nevalainen notes, are particularly relevant because her team worked with urologists to get human prostate cancer tissue specimens from surgeries, putting them into cell tissue cultures. That way, she says, the hypothesis could be tested in real human prostate cancer tissue specimens.

While she and her team continue to work on establishing Stat5 as a therapeutic target for hormone-resistant prostate cancer, they are also testing whether or not blocking Stat5 can make prostate cancer cells more sensitive to other treatments, such as radiation and chemotherapy. Another next step in the work, Dr. Nevalainen says, is to find pharmacological agents that inhibit the protein.

In work reported recently in Cancer Research, Dr. Nevalainen and her co-workers showed that Stat5 is turned on in nearly all recurrent prostate cancers that are resistant to hormone therapy. In addition, the researchers also showed that the convergence of Stat5 and androgen receptor could be responsible for making such prostate cancers especially dangerous.

Source: Thomas Jefferson University