Scientists find protein spurs spread of prostate cancer

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(PHILADELPHIA) Researchers from the Kimmel Cancer Center at Jefferson have found that Stat5, a signaling protein previously found to be key to survival of prostate cancer, is also involved in metastasis.

Their study, published in the online edition of *Endocrine-Related Cancer*, demonstrates in both laboratory and animal models that nuclear Stat5 over-expression leads to a deadly spread of the cancer. They add that their work with mice was unique in that it was the first time Stat5 was associated with prostate cancer metastasis processes in an animal model.

"Until now, we thought that Stat5 was involved in primarily promoting tumor growth, but this study indicates it could be one of the key players in pushing prostate cancer to spread," said Marja Nevalainen, M.D., Ph.D., associate professor of Cancer Biology, Urology and Medical Oncology at Jefferson Medical College of Thomas Jefferson University. "This seminal paper is sure to open up a new avenue of research, including investigation of therapies that could target Stat5 expression. Fresh approaches are needed since there are no effective therapies for prostate cancer that has metastasized."

This study is just the latest from Dr. Nevalainen's laboratory to show the increasing importance of the Stat5 transcription factor - a protein that can regulate expression of other genes. In 2004, she found that nuclear Stat5 is often over-expressed in high-grade human prostate cancer, and in 2005, she demonstrated that Stat5 activity was associated with recurrence of prostate cancer in patients who had already been treated.

She then showed in 2008 that nuclear Stat5 was especially prevalent in recurrent prostate cancers that are resistant to hormone therapy. Her research has also demonstrated that blocking Stat5 in laboratory and in animal models effectively destroyed prostate cancer.

"We know that Stat5 is absolutely critical to the survival of prostate cancer cells," she said.

In this study, the researchers found that Stat5 is activated in 61 percent of distant metastases of clinical human prostate cancers. Gene expression profiling indicated that 21 percent of Stat5-regulated genes were related to metastases, 7.9 percent were related to proliferation, and 3.9 percent were linked to cell death.

Digging deeper, they found that active Stat5 expression induced rearrangement of parts of the cytoskeleton of prostate cancer cells and suppressed expression of proteins that bind cells to each other - activities that help ready a cell to migrate from a tumor.

Then they made a key finding. When they injected human prostate cancer cells that over-expressed Stat5 into mice, they found that the cancer readily spread to the lungs.

"This result is important because laboratory observations on invasiveness or migration of cells in culture do not necessarily translate into cells having the ability to metastasize in animals," Dr. Nevalainen said. "This work provides the first evidence of the involvement of Stat5 in metastatic progression of human prostate cancer cells in a living system."

The findings need to be replicated in other studies, which are now ongoing. She said they want to use other model systems of metastatic prostate cancer to evaluate whether Stat5 is involved in prostate cancer that spreads to the lymph nodes or to bones.

The normal function of Stat5 is also not yet known, Dr. Nevalainen said.

Provided by Thomas Jefferson University