COUP-TFII sparks prostate cancer progression

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Prostate cancer presents a dilemma for patients and the physicians who treat them. Which cancers are essentially indolent and present no risk and which are life threatening? Which can be watched and which need aggressive treatment?

Drs. Ming-Jer and Sophia Tsai, both professors in the department of molecular and cellular biology at Baylor College of Medicine, think a receptor called COUP-TFII that they have long studied may point the way to an answer. In a study that appears online in the journal *Nature*, they show that high levels (overexpression) of COUP-TFII can overcome a natural barrier to progression of prostate cancer, allowing tumor cells to grow and spread throughout the body – a process called metastasis.

"Levels of COUP-TFII provide a good prognostic marker for prostate cancer when added to other known markers of the disease," said Dr. Ming-Jer Tsai.

"COUP-TFII is an important 'second hit' for the progression of prostate cancer and metastasis," said Dr. Sophia Tsai. In other words, one "hit" or mutation might start the process of cells becoming cancerous. The second "hit" would make them more aggressive.

In studies of patient samples, loss of a protein called PTEN or mutations in another signaling pathway called PI3K show up in prostate tumors. However, tumors in which PTEN is lost can remain indolent. One theory is that loss of PTEN increases TGF-beta signaling, which creates a barrier to prostate cancer progression.

The Tsais' studies in mice that lack PTEN show that loss of COUP-TFII inhibits the development of prostate tumors in the animals. When mice have a gene that produces insufficient levels of PTEN, COUP-TFII overexpression enhances prostate tumor progression. Further studies in mice that lost PTEN showed that high levels of COUP-TFII promoted the metastatic spread of the prostate cancer.

Studies in cell cultures and in human tissues confirmed the activity of COUP-TFII in promoting a more aggressive form of prostate cancer that could spread and metastasize.

The next step is find out how to inhibit COUP-TFII and prevent so-called indolent prostate cancers from becoming more aggressive, said Ming-Jer Tsai.

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