Medical Xpress

Growth factor receptor affects prostate cancer progression

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Breeding mice with a gene for a cellular receptor that can be turned on and off-at will-not only enabled researchers at Baylor College of Medicine in Houston to show how prostate cancer progresses, but also provides a model for studying when a drug targeting a gene will have an effect on the cancer.

A report on the work by BCM researchers with fibroblast growth factor receptor 1 appears today in the journal *Cancer Cell*.

“Since we are manipulating the target gene itself, we can ask, what will happen" If we turn it off, what happens" That recapitulates the effect of a specific drug,” said Dr. David Spencer, professor of immunology at BCM. “By turning the gene on and off at various time points, we can define a ‘susceptibility window’ for that drug, a time in the progression of the disease when the gene would be an appropriate target.”

That therapeutic “window” defines the time when shutting off the gene would also shut down progression of the cancer. Previous studies show that fibroblast growth factor receptor 1 may have a role in initiating prostate cancer, he said. As a result, some companies have developed drugs designed to block the receptor. Spencer’s work looks at what would happen if the receptor is blocked.

In his mouse, he used a synthetic drug that turned the re-engineered fibroblast growth factor receptor on. As the gene product was activated, the prostate gland began dramatic, synchronized changes characteristic

of cancer. However, when he withdrew the drug that turned the receptor on, the changes reversed over several weeks until the prostate gland appeared normal.

However, at a certain point, changes in the tissue reach a point of no-return and transform in to a kind of cancer called adenocarcinoma that does not appear to be reversible, although withdrawing the drug can slow the cancer, too.

During this study, Spencer, his graduate student, Victor Acevedo and their colleagues also studied the changes prostate cells undergo while they spread outside the gland and into surrounding tissue. Understanding the events that take place in cells during the transition from normal to cancer can provide important clues about cancer and potential treatments.

From this study, he has identified some of the genes involved in the transition from normal prostate cells within a secretory gland to more migratory, malignant cells outside the gland. Using special gene chips called tumor microarrays, they have also discovered the up regulation or increase in cellular levels of Fzd4, a gene that might prove to be a new marker for human prostate cancer.

“Victor started out looking for a role of fibroblast growth factor receptor 1 in prostate cancer progression and ended up with a new cancer marker and a model for epithelial cell plasticity, rounding out his productive thesis,” Spencer added.

Source: Baylor College of Medicine

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