Source of tumor growth in aggressive prostate cancer found

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Researchers have discovered a molecular switch that explains, at least in part, how some fast-growing prostate cancers become resistant to hormone treatment, a new study conducted in human cell cultures and mice finds. The results were presented Saturday at The Endocrine Society's 95th Annual Meeting in San Francisco.

A factor not normally found in the prostate, called Steroidogenic Factor 1, stimulates production of new steroid hormones and increases cell multiplication to fuel growth of the tumor, researchers from the University of Wisconsin-Madison, found.

"This breakthrough exposes a potential biological marker and critical therapeutic target for the prevention or treatment of deadly prostate cancer," said the study's principal investigator, Joan Jorgensen, DVM, PhD.

Men with prostate cancer that has recurred or has spread outside the prostate routinely receive androgen deprivation therapy, which blocks the action of the male hormones and shrinks the tumor. This castration occurs with medications or, less often, through surgical removal of both testes, which make the steroid hormones. Although initially effective, this hormone-blocking treatment eventually stops working in most patients, and the cancer becomes deadly, Jorgensen said. This type of cancer is called castration-resistant prostate cancer.

Research evidence suggests that prostate cancer cells acquire the ability

to produce their own steroids that promote the aggressive growth of the tumor, but the mechanism that causes this steroid synthesis was unclear, according to Jorgensen.

Steroidogenic Factor 1 is a transcription factor, or protein that binds to the genes. It is required for cell survival and cell proliferation during development and is necessary to stimulate steroid synthesis during development and in adulthood, Jorgensen said. Her group found that this factor is expressed in prostate cells only in samples of castration-resistant prostate cancer.

The group conducted several studies, which received funding from the University of Wisconsin-Madison Graduate School and a training grant from the National Institutes of Health. In one study, the researchers used a human cell line of an aggressive prostate cancer model. Cells with "knockdown," or repression, of Steroidogenic Factor 1 expression exhibited decreased steroid production and had problems with cell growth, compared with cancerous prostate cells with normal levels of the factor, the authors reported. When the investigators forced the expression of Steroidogenic Factor 1 in benign prostate cells, the result was increased steroid production and cell growth, she said.

Finally, 12 castrated male mice, which replicate the environment of a patient with treatment-resistant cancer, received transplants of the cultured human prostate cancer cells that were either normal (controls) or deficient in Steroidogenic Factor 1. The results showed that repressing Steroidogenic Factor 1 led to much smaller tumors than the controls had, Jorgensen said.

Steroidogenic Factor 1 likely is one of many molecular switches in the growth of castration-resistant prostate cancer, but Jorgensen said it appears to be an important one.

"This new knowledge eventually will enable us to design more personalized therapy regimens to attack aggressive castration-resistant prostate cancer using established treatments along with agents that block Steroidogenic Factor 1," she said.

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