Key pathway in end-stage prostate cancer tumor progression blocked

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Prostate cancer advances when tumors become resistant to hormone therapy, which is the standard treatment for patients, and begin producing their own androgens.

Researchers at UT Southwestern Medical Center have found that blocking one of the enzymatic steps that allow the tumor to produce androgens could be the key in halting a tumor's growth.

The findings, appearing online and in the August issue of *Endocrinology,* suggest that this step might one day provide a new avenue of therapy for patients with end-stage prostate cancer. Health care experts estimate that more than 2 million men in the U.S. have prostate cancer, with more than 27,000 deaths related to the disease in 2009.

"We were able to block the androgen response, which is a central pathway for tumor progression," said Dr. Nima Sharifi, assistant professor of internal medicine and the study's senior author.

End-stage prostate tumors typically are treated with hormones that suppress the levels of the androgens, or male hormones like testosterone, that cause prostate cancer cells to grow. Eventually, however, the tumors become resistant to this therapy and resume their growth.

Using prostate cancer cell lines, Dr. Sharifi and his colleagues found that the hormone dehydroepiandrosterone (DHEA) is converted by the tumors into androgens. By blocking the enzyme 3?-hydroxysteroid dehydrogenase (3?HSD), which is responsible for the first enzymatic step that is required to convert DHEA to androgens, researchers were able to shut down the tumors' lifeline.

"Enzymes in general can make great drug targets, so this process conceivably could be targeted for the development of new treatments for end-stage prostate cancer, which has limited therapeutic options right now," said Dr. Sharifi, an investigator in UT Southwestern's Harold C. Simmons Comprehensive Cancer Center. "The goal would be to develop a drug that targets that enzyme to be used for the advanced, incurable stage."

No standard treatments currently target this enzyme, but there is proven clinical evidence that this pathway is central to driving tumor progression.

Provided by UT Southwestern Medical Center