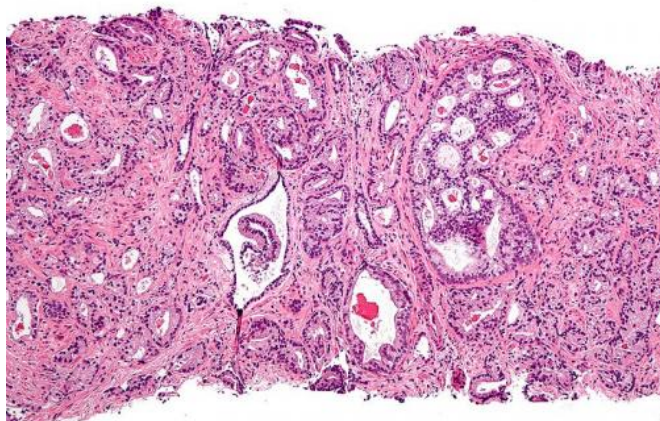


# Researcher discovers metabolite of prostate cancer drug more effective at treating aggressive tumors

1 June 2015



Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Cleveland: Cleveland Clinic researchers have discovered for the first time that a metabolite of an FDA-approved drug for metastatic prostate cancer, abiraterone (Abi), has more anti-cancer properties than its precursor. The research will be published online June 1st in *Nature*.

Cleveland Clinic researcher Nima Sharifi, M.D., found that abiraterone, a steroid inhibitor, is converted into the more physiologically active D4A (?4-abiraterone) in both [patients](#) and animal models with [prostate cancer](#) who take the drug. Furthermore, they found that D4A is more effective than abiraterone at killing aggressive prostate [cancer cells](#), suggesting that some patients may benefit from direct treatment with D4A.

Prostate cancer cells are fueled by androgens (male hormones). When prostate cancer spreads, androgen deprivation therapy ("medical castration") is used to cut off the tumor's energy

supply. However, aggressive, metastatic tumors can become resistant to this type of therapy. In a landmark 2013 publication in *Cell*, Dr. Sharifi described a genetic mutation that enables [prostate cancer cells](#) to produce their own hormones for fuel, making them resistant to traditional hormone deprivation therapies.

Abiraterone works by blocking CYP17A1, an enzyme that is crucial for the production of androgens. Dr. Sharifi's team found that the more active D4A inhibits two additional enzymes responsible for producing androgens, as well as blocks the androgen receptor, which renders existing androgens inactive. They found that 12 patients on active abiraterone therapy had detectable serum levels of D4A. D4A levels varied among patients, however, suggesting that individuals may differ in their metabolism of abiraterone to D4A.

"More studies are needed to uncover the exact mechanisms involved, but we predict that direct treatment with D4A could prolong survival in some patients with [metastatic prostate cancer](#)," said Dr. Sharifi, "Further studies will also help us develop a potential biomarker profile to predict which patients will respond to D4 - abiraterone."

Dr. Sharifi holds positions in Cleveland Clinic's Lerner Research Institute, Glickman Urological & Kidney Institute, and Taussig Cancer Institute, and is the Kendrick Family Endowed Chair for Prostate Cancer Research.

Prostate cancer is the most common cancer in men, with nearly 240,000 new cases diagnosed each year in the United State. According to the American Cancer Society, there will be an estimated 30,000 deaths due to prostate cancer in 2013. Almost every man who dies of prostate

cancer dies with castration-resistant prostate cancer.

**More information:** Conversion of abiraterone to D4A drives anti-tumor activity in prostate cancer, [DOI: 10.1038/nature14406](https://doi.org/10.1038/nature14406)

Provided by Cleveland Clinic

APA citation: Researcher discovers metabolite of prostate cancer drug more effective at treating aggressive tumors (2015, June 1) retrieved 22 November 2022 from <https://medicalxpress.com/news/2015-06-metabolite-prostate-cancer-drug-effective.html>

*This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.*