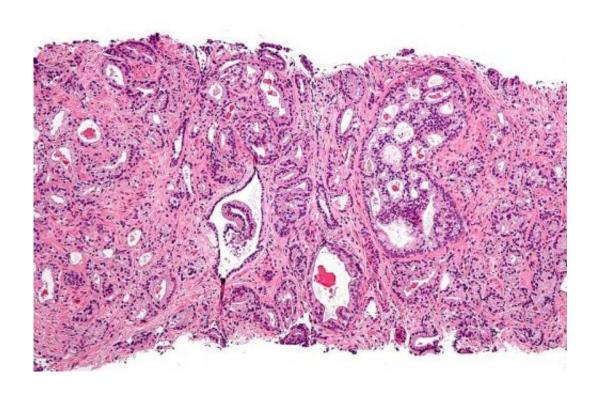


Compound shows promise as next-generation prostate cancer therapy

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Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, <u>CC BY-SA 3.0</u>

In the search for new ways to attack recurrent prostate cancer, researchers at Duke Health report that a novel compound appears to have a unique way of blocking testosterone from fueling the tumors in mice.

The potential foundation for a next-generation therapy, called tetraaryl



cyclobutane, or CB, is being studied as an option for prostate tumors that have grown resistant to current anti-androgen drugs, notably enzalutamide.

"Prostate <u>cancer</u> is the most prevalent form of cancer in men, and the principal driver of <u>tumor</u> growth is the androgen receptor," said John D. Norris, Ph.D., associate research professor in the Department of Pharmacology & Cancer Biology at Duke and senior author of a study published online Aug. 8 in the journal *Nature Chemical Biology*.

"Suppression of androgen receptor function by anti-endocrine therapies is initially effective, but most tumors develop resistance, resulting in a more aggressive cancer," Norris said. "Our research has been focused on finding a new approach to suppressing androgen receptor activity, because even in situations where tumors are resistant to current therapies, the androgen receptor remains a viable target."

Norris and colleagues focused on a group of CB compounds developed in collaboration with scientists at the University of Illinois at Urbana-Champaign. The compounds act as competitive inhibitors of androgen receptors, but are structurally different from current anti-androgens such as enzalutamide.

One of the CB compounds, in particular, inhibits mutant forms of the androgen receptors that promote resistance to enzalutamide. It functions by preventing the <u>androgen receptor</u> from entering the nucleus of the cell where it can promote <u>tumor growth</u>.

"It's encouraging that this compound has a different mechanism of action when compared to current therapies, which gives it a good chance of having efficacy in resistant disease," Norris said. "We have shown in animal models that the compound has activity against <u>prostate tumors</u> where enzalutamide fails."



Norris said additional studies are underway in additional animal models and in tests with other forms of cancer, including breast cancer.

More information: Inhibiting androgen receptor nuclear entry in castration-resistant prostate cancer, *Nature Chemical Biology*, <u>DOI:</u> 10.1038/nchembio.2131

Provided by Duke University Medical Center

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