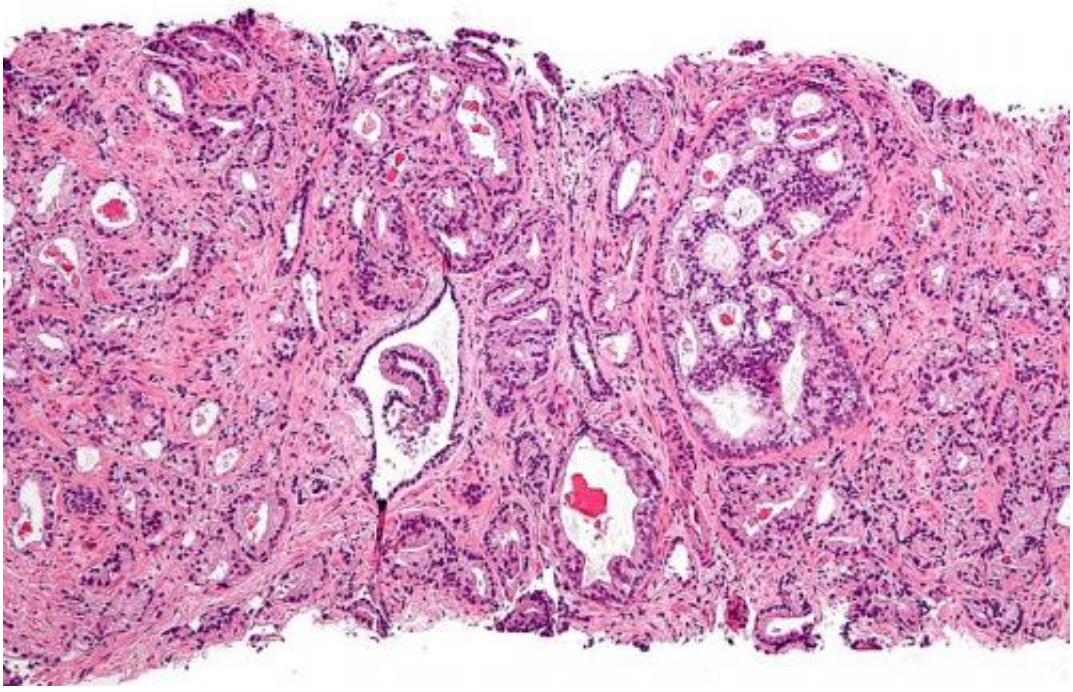
Compound shows promise as next-generation prostate cancer therapy

August 8 2016



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

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 cancer is the most prevalent form of cancer in men, and the principal driver of tumor 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 androgen receptor from entering the nucleus of the cell where it can promote tumor growth.

"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 prostate tumors 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*, DOI: 10.1038/nchembio.2131

Provided by Duke University Medical Center