# New method reveals possible prostate cancer therapy

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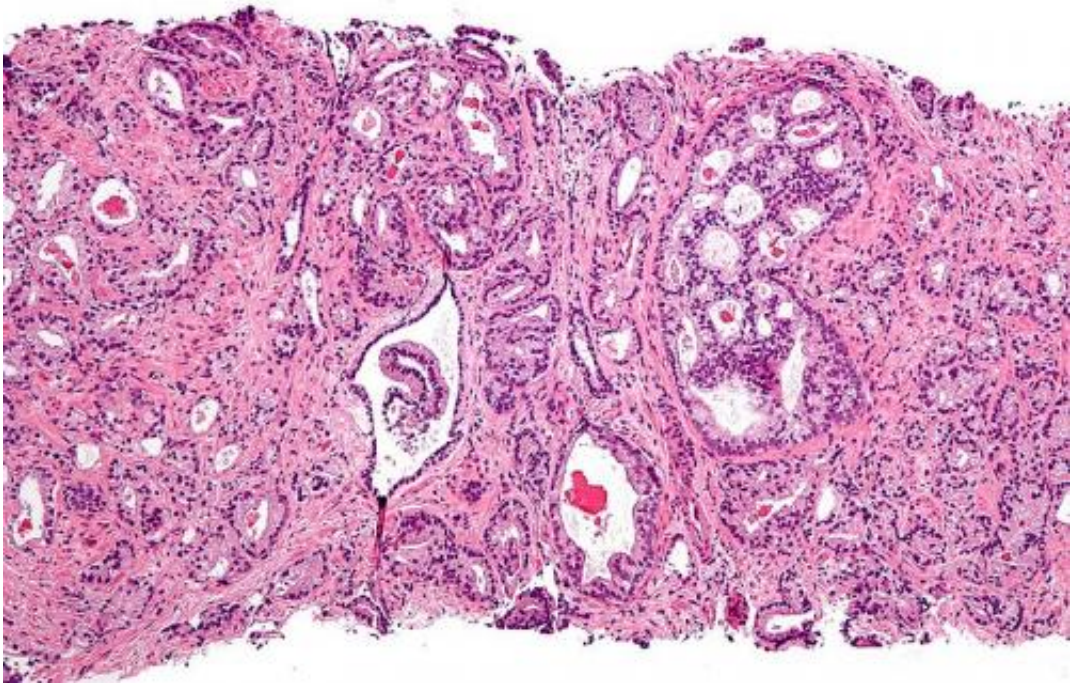

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

The steroid dexamethasone could potentially deter the growth of a prostate cancer subtype that was previously thought to be difficult to treat with medications, Weill Cornell Medicine researchers report. Their findings were published in the June 2 issue of *Cell Reports*.

"Prostate cancer is very often linked to a mutation and over-expression

in a gene called ERG that many people thought was undruggable, meaning there's no way to target the mutation with medications to disrupt the disease," said Dr. Olivier Elemento, one of the study's senior authors.

Elemento is an associate professor in the Department of Physiology and Biophysics and associate director of the HRH Prince Alwaleed Bin Talal Bin Abdulaziz Alsaud Institute for Computational Biomedicine at Weill Cornell Medicine.

Not only do mutations in ERG occur frequently in prostate cancer, but research conducted by Dr. David Rickman, an assistant professor of pathology and laboratory medicine at Weill Cornell Medicine and co-senior author of the paper, found that such mutations make prostate cancer more resistant to taxane, a commonly prescribed therapy.

Seeking to disrupt the function of the ERG mutation, Elemento and his colleagues developed a new computational method to screen for drugs that may offer promising activity against ERG. They investigated the many genes that ERG binds to and regulates. They then evaluated thousands of drugs in available databases to narrow down which ones might interrupt the activity of these genes, potentially helping to arrest cancer by reversing the effect of the ERG mutation.

"It's like match-making between drugs and mutations," said Elemento, a member of the Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine.

Kaitlyn Gayvert, a doctoral candidate in Elemento's lab who Forbes Magazine recognized earlier this year on its "30 Under 30" list, developed the computational method, which found that dexamethasone was a top candidate for interrupting cancer activity spurred by the ERG mutation. While dexamethasone is used interchangeably with prednisone

to treat a variety of conditions, the computational method did not predict that prednisone would produce the same effect on prostate cancer.

Rickman's laboratory experiments in prostate cancer cells supported the modeling, finding that using dexamethasone reversed the mutation's effects, including cell invasion and cell migration.

Using further analysis of electronic medical records from Columbia University Medical Center, the researchers found that patients given dexamethasone for reasons other than prostate cancer were less likely to develop the malignancy than those who had not received the steroid. They say the results suggest that the drug may offer some protection against prostate cancer.

While more research is needed, dexamethasone or similarly acting drugs may one day be routinely prescribed to men with prostate cancer who test positive for ERG mutations, the authors said.

"There's also a significant proportion of other cancer subtypes that are driven by mutations considered undruggable," said Rickman, adding that some colon cancers and lymphomas are among these. "The techniques used in this study may help us find ways to repurpose already existing safe drugs to target other undruggable mutations."

**More information:** Kaitlyn M. Gayvert et al. A Computational Drug Repositioning Approach for Targeting Oncogenic Transcription Factors, *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.05.037

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