Immunotherapy may be effective for some prostate cancers

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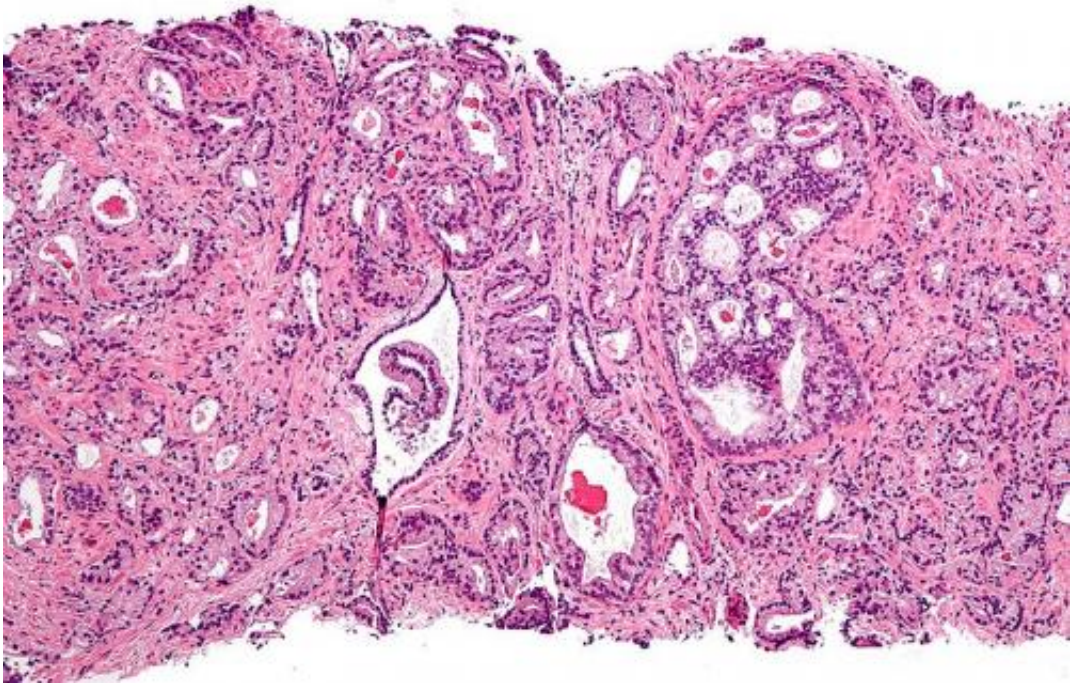

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

In recent years, cancer immunotherapy has been effective in treating patients with immunogenic, or so-called "hot" tumors with increased levels of inflammation and the presence of immune cells in and around the tumors. Prostate cancer, however, is considered a "cold" tumor, with few immune cells recognizing and infiltrating prostate malignancies. Accordingly, prostate cancer has been found to respond poorly to the

class of immunotherapies known as immune checkpoint inhibitors.

In previous work, a team led by medical oncologists at Beth Israel Deaconess Medical Center (BIDMC) identified a subset of prostate cancers that exhibited characteristics more typical of hot cancers. Now, in a paper appearing in the journal *Clinical Cancer Research*, researchers report that about a quarter of localized prostate cancers may demonstrate these immunologic traits, suggesting that a substantial number of patients with prostate cancer may, in fact, benefit from immunotherapies.

"We were surprised to find all the features of more traditionally immunogenic cancers in these prostate cancers, and that this is not a rare subtype, observed in about a quarter of high risk tumors," said co-corresponding author David J. Einstein, MD, a medical oncologist at BIDMC and an assistant professor of medicine at Harvard Medical School (HMS). "We're interested in whether there is a subset of patients with localized prostate cancer, especially more aggressive ones, whose cancers might be more recognized by the immune system and therefore more treatable with immunotherapies. These would also be some of the patients at greatest risk for relapse and metastatic spread."

Einstein and colleagues, including co-corresponding author Steven Balk, MD, Ph.D., a physician at BIDMC, focused on two characteristics that make traditionally immunogenic cancers susceptible to immunotherapy: PD-L1 expression and T cell infiltration. PD-L1 is a protein involved in tumor evasion of the immune system. T cells are the sentinels of the immune system, patrolling the body for potential pathogens or disease.

The researchers identified prostate cancers that had been removed from patients, looking for those that had areas of high PD-L1 expression and then looked for the presence of infiltrating T cells. Next, the team compared the T cell landscape in the more immunogenic prostate cancers to that of more typical prostate cancers, as well as to kidney

cancer, one of the most immunogenic tumor types. Finally, the team used DNA sequencing to compare the genetic profiles from these immunologically hot areas to that of the so-called cold areas in the same tumors, as well as to the genomic landscape of immunogenic cancers in general.

The scientists were surprised to learn how many more T cells infiltrated the immunogenic prostate cancers compared with more typical prostate cancers, and to observe all the features of more traditionally immunogenic cancers like kidney cancer in these more immunogenic prostate cancers. They also noted significantly more loss of some key tumor suppressor genes in these immunogenic prostate cancers compared with typical prostate cancer, a difference that could potentially serve as markers to find cancers more treatable with immunotherapies.

"We're hoping to be able to identify patients with immunogenic tumors in advance of treatment, so that we can develop clinical trials for this subset of patients and offer a more personalized strategy than treating all-comers the same way," said Balk, who also a professor of medicine at HMS.

The team is currently conducting a clinical trial to test the effect of a PD-1 inhibitor in prostate cancer patients that will allow them to gather evidence as to whether any of these findings in immunogenic prostate cancer translate into clinical responses in response to PD-1 inhibition.

More information: Carla Calagua et al, A Subset of Localized Prostate Cancer Displays an Immunogenic Phenotype Associated with Losses of Key Tumor Suppressor Genes, *Clinical Cancer Research* (2021). DOI: 10.1158/1078-0432.CCR-21-0121

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