Combined chemotherapy and immunotherapy shows promise for advanced prostate cancers

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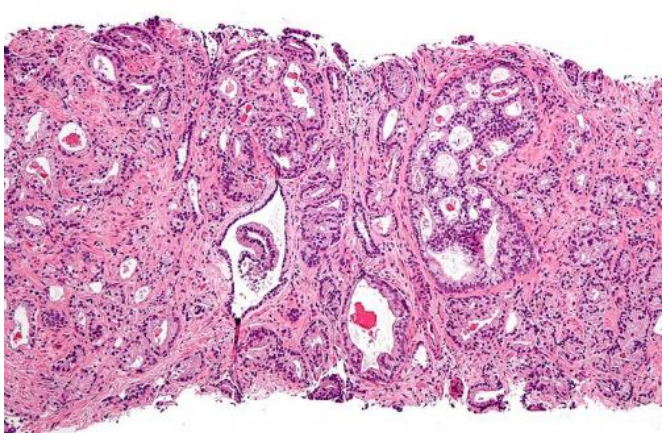

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia

Chemotherapy can be very effective against small prostate tumors. Larger prostate tumors, however, accumulate cells that suppress the body's immune response, allowing the cancer to grow despite treatment. Researchers at the University of California, San Diego School of Medicine now find that blocking or removing these immune-suppressing cells allows a special type of chemotherapy—and the immune cells it activates—to destroy prostate tumors. This novel combination therapy, termed chemoimmunotherapy, achieved near complete remission in mouse models of advanced prostate cancer.

The study is published April 29 in *Nature*.

Advanced or metastatic prostate cancer does not typically respond to chemotherapy. Prostate cancers also fail to respond to a promising new type of immunotherapy drugs, called checkpoint inhibitors, which disable cancer cells' cloaking mechanism so that a person's own immune system can better fight the tumor. This specific resistance is likely due in part to immunosuppressive B cells, which are more common in larger prostate tumors in mice, as well as in advanced and metastatic prostate cancer in humans. As the name suggests, these cells keep the immune system at bay, rendering most therapies ineffective and allowing malignant tumors to grow unchecked.

In this study, researchers worked with three different mouse models of advanced prostate cancer. All three models were resistant to low doses of the chemotherapy drug oxaliplatin, which has the unique ability to activate cancer-killing immune cells. But when the researchers blocked the development or function of immunosuppressive B cells or removed them entirely before treating the mice with low-dose oxaliplatin, the prostate tumors were almost completely destroyed by the mice's own immune cells. The team got similar results when low-dose oxaliplatin was combined with a checkpoint inhibitor.

"The presence of such B cells in human prostate cancer calls for clinical testing of this novel therapeutic approach," said Shabnam Shalapour, PhD, postdoctoral researcher and first author of the study.

Prostate cancer is the second leading cause of cancer-related death in American men. About one in seven men will be diagnosed with prostate cancer during their lifetimes.

"In addition to prostate cancer, similar immunosuppressive B cells can be detected in other human cancers," said senior author Michael Karin, PhD, Distinguished Professor of Pharmacology and Pathology at UC San Diego. "This indicates that B cell-mediated

immunosuppression might be the reason several other cancers are also unresponsive to checkpoint inhibitors, raising the hope that chemoimmunotherapy will have broader applications for many cancer types."

More information: Immunosuppressive plasma cells impede T-cell-dependent immunogenic chemotherapy, *Nature*, DOI: 10.1038/nature14395

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