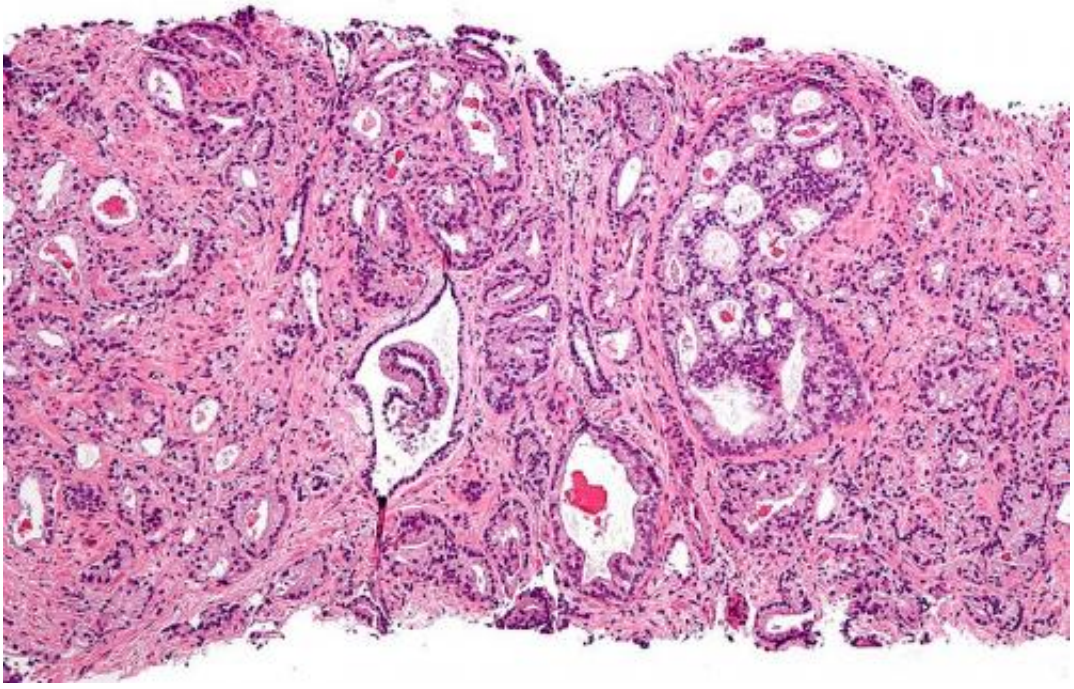
New target for prostate cancer treatment discovered

February 20 2015



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

Keck Medicine of the University of Southern California (USC) scientists have found a promising new therapeutic target for prostate cancer. The findings offer evidence that a newly discovered member of a family of cell surface proteins called G-protein coupled receptors (GPCRs) promotes prostate cancer cell growth. The protein, GPR158, was found while the researchers were looking for new drug targets for glaucoma.

Prostate cancer is the second most common cancer in American men, after skin cancer, according to the American Cancer Society (ACS). The ACS projects more than 27,000 deaths from prostate cancer in 2015 and is the second leading cause of cancer death in American men, behind lung cancer. One man in seven will be diagnosed with prostate cancer during his lifetime.

"When a prostate cancer tumor is in its early stages, it depends on hormones called androgens to grow," said Nitin Patel, Ph.D., research scientist at the Institute for Genetic Medicine at the Keck School of Medicine of USC, and corresponding author on the research. "Eventually it progresses to a more lethal form, called castration-resistant prostate cancer (CRPC), and is resistant to drugs that block androgen receptors. We found that GPR158, unlike other members of the GPCR family, is stimulated by androgens, which in turn stimulates androgen receptor expression, leading to tumor growth."

The team also discovered that GPR158 is associated with neuroendocrine transdifferentiation (NED) of epithelial prostate tumor cells, which plays a critical role in development of resistance to contemporary androgen receptor-target therapies. The scientists found that prostate cancer patients with elevated GPR158 expression experienced recurrence of prostate cancer. The GPR158 protein is a likely target for new prostate cancer drugs.

The researchers used a conditional Pten knockout mouse model of prostate cancer in collaboration with Keck School of Medicine of USC researchers Mitchell Gross, Chun-Peng Liao and Pradip Roy-Burman.

The team is now exploring the molecular pathways involved in the functional role of GPR158 in NED in the development of CRPC and exploring GPR158-targeted antibody therapeutics.

More information: The study, titled "Expression and Functional Role of Orphan Receptor GPR158 in Prostate Cancer Growth and Progression," will be published Feb. 18, 2015 in the peer-reviewed journal *PLOS ONE*.

Provided by University of Southern California