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Research identifies cells that may be responsible for prostate cancer recurrence

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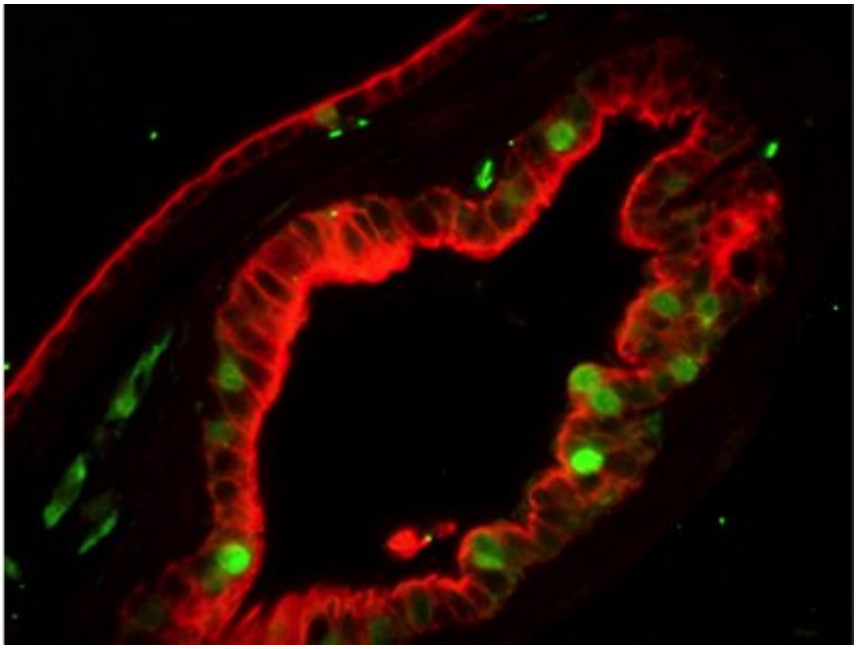

Slide illustrating resistance to androgen-deprivation therapy in a newly identified population of dormant prostate luminal stem cells. Credit: Roswell Park Cancer Institute

Although men with prostate cancer usually respond to standard treatment with hormone therapy or chemotherapy, many will eventually experience progression or recurrence despite treatment—particularly those with high-risk or aggressive forms of the disease. In preclinical laboratory research, a team led by Dean Tang, Ph.D., Chair of Pharmacology and Therapeutics at Roswell Park Cancer Institute has discovered a unique

population of normal stem cells that are intrinsically resistant to conventional treatments and may enable prostate cancer relapse. In a new publication in the journal *Stem Cell Reports*, the team reports its development of a novel preclinical model that allows not only the labeling but also the purification of this rare but persistent population of prostate stem cells, which are dormant and, strikingly, resemble high-risk prostate cancer at the molecular level.

The normal prostate and most prostate tumors contain a small number of cells called luminal progenitors that, unlike the bulk of cancer cells, are generally dormant. They behave like stem cells, lacking expression of the molecules targeted by current cancer treatments. As a result, these cells evade prostate cancer treatments such as chemotherapy and radiation, which generally target and eliminate cells that are rapidly multiplying and dividing. Unlike most prostate cancer cells, these dormant, stem-like cells are also less dependent on androgens, making them relatively unresponsive to chemical castration or hormone therapy, approaches designed to "starve" tumors by depriving them of their androgen fuel.

"The existence of a population of quiescent or slow-cycling cells in the prostate has been suggested, but their identity and characteristics were unknown because they are rare and very difficult to study," explains Dingxiao Zhang, Ph.D., an Assistant Professor with the Department of Pharmacology and Therapeutics at Roswell Park and first author on the new study. "We were able to identify a unique population of cells that might serve as the origin of treatment-resistant prostate cancer. Our genetic model paves the way toward the next step, which is the development of therapies that can target these dormant cancer cells, which are expected to significantly improve the treatment of prostate cancer and delay or even prevent its recurrence."

More information: Dingxiao Zhang et al. Histone 2B-GFP Label-

Retaining Prostate Luminal Cells Possess Progenitor Cell Properties and Are Intrinsically Resistant to Castration, *Stem Cell Reports* (2017). DOI: 10.1016/j.stemcr.2017.11.016