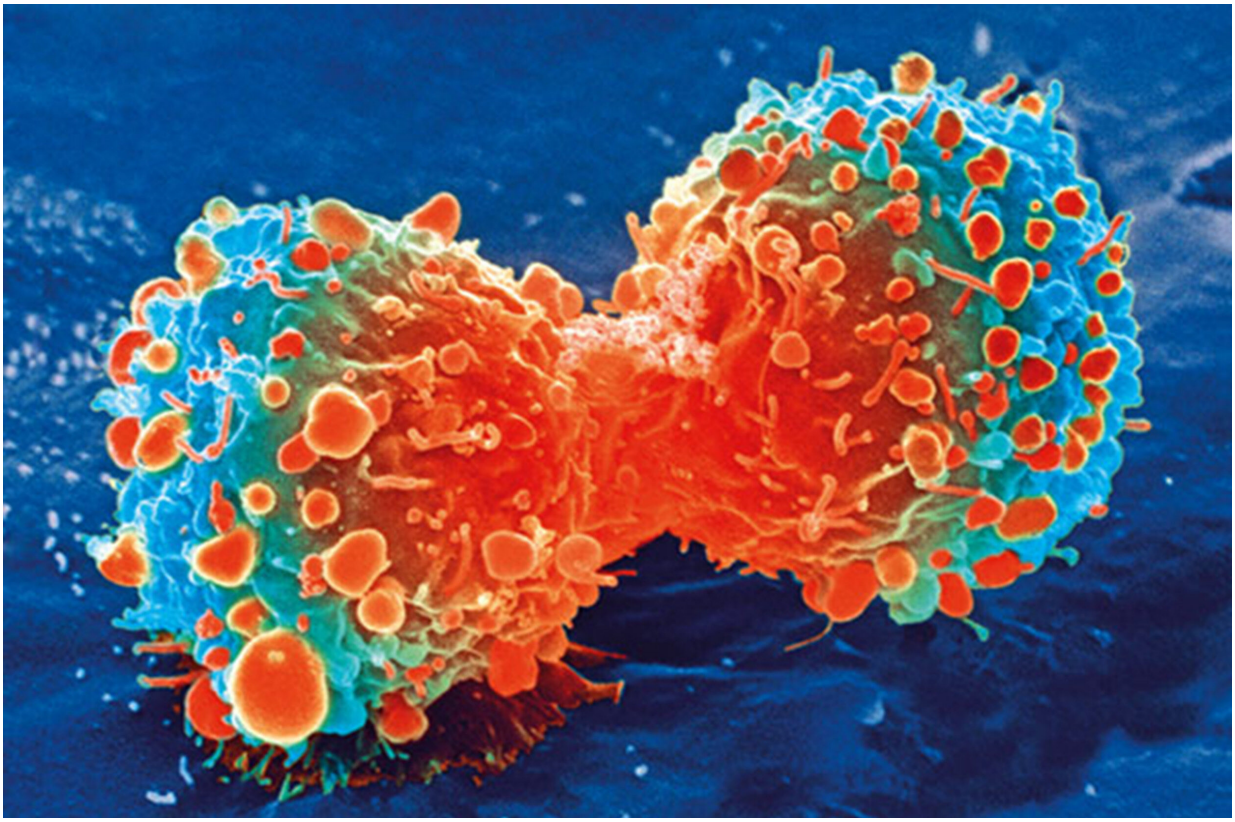
MedicalXpress

Mutation in prostate tumors shown to change epigenetic identity, the make-up of DNA

August 7 2017



Cancer cell during cell division. Credit: National Institutes of Health

Prostate cancer researchers have mapped the impact of an acquired mutation that alters epigenetic identity, the make-up of DNA, in about 50% of patient tumour samples. The discovery also identifies a new

opportunity for targeted therapy.

The findings are published online today in *Nature Genetics*. The research shows how an acquired mutation involving the fusion of two genes (TMPRSS2 and ERG) can change the epigenetic identity of tumours leading to some genes being turned on while others are turned off, says Dr. Mathieu Lupien, corresponding author and Senior Scientist at Princess Margaret Cancer Centre, University Health Network, and a member of its Cancer Epigenetics Program, a team focused on breaking the code of cancer.

The discoveries highlight the power of mutations to influence epigenetics in prostate tumours to change the identity of cancer cells. Dr. Lupien's team exploited this fact to identify mechanisms that drive development of fusion-positive prostate cancer.

"Our findings specifically show that fusion-positive prostate cancer is dependent on the NOTCH signalling pathway, which can be blocked chemically in pre-clinical models," says Dr. Lupien. "This identifies a promising druggable target against fusion-positive prostate cancer and takes us a step closer to providing personalized cancer medicine for up to 50% of prostate cancer patients," he says.

"We're hopeful this research can be translated into clinical care in the near future to offer patients an additional, tailored treatment to complement the current standard of care, based on their fusion profile."

The study team consisted of scientists, pathologists and clinician-scientists involved in the Canadian Prostate Cancer Genome Network (CPC-GENE), the world-leading prostate cancer sequencing program co-led by Dr. Robert Bristow at the Princess Margaret Cancer Centre and Dr. Paul Boutros at the Ontario Institute for Cancer Research.

Dr. Lupien is also an Associate Professor in the Department of Biomedical Physics, University of Toronto.

More information: TMPRSS2–ERG fusion co-opts master transcription factors and activates NOTCH signaling in primary prostate cancer, *Nature Genetics* (2017). DOI: 10.1038/ng.3930

Provided by University Health Network