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Researchers find protein signatures for accurate noninvasive diagnosis of prostate cancer

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Researchers at the Ontario Institute for Cancer Research (OICR) and University Health Network (UHN) in Toronto, along with researchers at the Eastern Virginia Medical School, have created protein signatures that accurately diagnose prostate cancer and can distinguish between patients with aggressive versus non-aggressive disease using a simple urine sample. The findings could be developed into a non-invasive "liquid biopsy" that could provide a faster, cheaper and easier method to detect prostate cancer with fewer complications for patients. The findings were published today in the journal *Nature Communications*.

Researchers performed an initial discovery screen on urine samples from men who were diagnosed with prostate cancer and those who were not to look for all proteins that might be different between them. They also screened for all proteins in the urine that might be different between patients with aggressive and non-aggressive disease. From these initial discoveries, they identified a subset of proteins unique to each grouping and developed two signatures: one that could be used to accurately indicate whether a patient has prostate cancer or not and a separate signature to indicate outcome.

"The amazing thing about these signatures is that their rate of accuracy is as good or better than the invasive tests that are used today, with far fewer drawbacks," said Dr. Paul Boutros, a Principal Investigator at OICR and a lead author on the paper. "They can replace invasive,

expensive, uncomfortable tests with something much easier and simpler. This type of cheap, non-invasive testing could allow patients to be screened much more frequently, allowing for more accurate monitoring of patients' non-aggressive cancer over time, sparing patients biopsies, imaging tests and even unnecessary surgeries."

Current methods to diagnose prostate cancer usually include a combination of digital rectal exams, prostate specific antigen (PSA) tests and biopsy, all of which have drawbacks, including their invasiveness for patients, potential complications and false-positive results (tests finding evidence of cancer when none is there). Finding new ways to accurately diagnose prostate cancer is considered a priority for many research institutions, including OICR, because the result of these tests' shortcomings is in many cases over-diagnosis and over-treatment.

There were three sites involved in the discovery and each brought their own unique expertise to the project. The Eastern Virginia Medical School developed clinical resources, while UHN researchers were generating large amounts of proteomic data and were developing new techniques to test proteins in blood. All of the proteomic and clinical data flowed to OICR where it was pieced together using computational biology, and where the proteins in the discovery screen were identified.

"Computational biology can help to identify the most probable protein biomarkers that show significant change of expression between two clinical or pathological conditions and could be involved in cancer development and progression," said Dr. Clare Jeon, a bioinformatician at OICR who led the computational biology portion of the study. "Initial proteomics work in this study generated expression information from 624 proteins. Computational analyses performed here at OICR reduced the number of proteins by identifying significantly differentially expressed proteins and finally characterized a set of six protein biomarkers for diagnosis and a set of seven protein biomarkers for

prognosis of prostate cancer."

"Congratulations to all researchers who worked hard to make this important discovery," said Reza Moridi, Ontario's Minister of Research, Innovation and Science. "Your collaboration demonstrates the kind of world-class research taking place in Ontario that will soon pave the way for future advancements in the fight against prostate cancer."

The study has to date gone through development and initial validation and it is now ready for a large retrospective validation study, which the collaborators are now designing. After validation is successfully completed it would then move into clinical trials.

Prostate cancer is the most common cancer among Canadian men. Over 24,000 Canadian men were diagnosed with prostate cancer in 2015, representing almost a quarter of all new male cancer cases. Prostate cancer is the third leading cause of cancer death among men in Canada.

More information: Yunee Kim et al, Targeted proteomics identifies liquid-biopsy signatures for extracapsular prostate cancer, *Nature Communications* (2016). DOI: 10.1038/ncomms11906

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