

Exposing the prostate cancer genome through mapping

The entire genome of a prostate cancer tumour has been mapped for the first time, in a study by researchers from the Garvan Institute of Medical Research, the University of Sydney in Australia and by the University of Pretoria (UP).



Professor Vanessa Hayes, head of the Human Comparative and Prostate Cancer Genomics Laboratory at the Garvan Institute

The study has provided an entirely new lens through which to view the disease and the results could potentially be used to help characterise an individual's prostate tumour and direct clinical treatment.

In the Western world, prostate cancer has the highest incidence rate of all male-associated cancers and the second highest mortality rate. In African countries, including South Africa, the incidence of this type of cancer among non-migrant Africans is uncertain, but a trend towards earlier age at diagnosis has been observed. It is estimated that among South African men, at least one in every 23 will develop prostate cancer within their lifetime.

Clinical potential

The team's efforts in this study represent the world's first comprehensive next-generation mapping of an entire prostate cancer genome and has uncovered 10 times more chromosome genomic rearrangements than previous technology has ever been able to detect.

clinical potential for prognosis, diagnosis, or therapeutics. In addition, it could eventually also help to define African-specific risk areas and the genomic signature of prostate cancer observed in South African men.

Very little is understood about what drives these tumours despite the fact that prostate cancer has been researched for a number of years, says Professor Vanessa Hayes, head of the Human Comparative and Prostate Cancer Genomics Laboratory at the Garvan Institute.

She says that one of the biggest clinical challenges is distinguishing which patients' cancers are going to spread and become life-threatening, and which patients could be spared harsh treatment that may actually be unnecessary. To do this, it is vital to first understand the genetic drivers of each individual tumour.

Next-generation mapping

"From previous genome sequencing studies we know that, while most cancers are driven by small DNA mutations in a number of key genes, prostate cancer has very few small genetic changes, but rather, is more likely driven by large complex genomic rearrangements. Until now, we had no way of observing these rearrangements or structural variants," she says.

The researchers used next-generation mapping technology in combination with whole genome sequencing to uncover the most complete picture of the prostate cancer genomic landscape to date. They studied a prostate tumour from a South African man with a Gleason score of seven, the most commonly diagnosed form of prostate cancer, which is clinically highly unpredictable, and eventually identified 85 large structural rearrangements, with over a third of these directly impacting genes with known cancer promoting potential.

The team says that it is unlikely that they would have achieved these results with sequencing technology alone. They explain that while whole genome sequencing is invaluable in identifying small DNA mutations, it may not detect when a gene has been completely deleted, transferred to another chromosome, or multiplied many times - which is what they found over the course of this study. Using next-generation mapping, the team saw large amounts of large-scale rearrangements, and genome sequencing which in turn enabled them to identify the genes affected by these rearrangements.

"Whole genome sequencing opened a huge number of doors for our understanding of prostate cancer – next-generation mapping just doubled the number of doors," says Hayes. "I believe this technology will compliment next generation sequencing as a key to personalised medicine for prostate cancer."

The team published their findings in the journal Oncotarget in March this year.

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