Medical Xpress

# Major study links gene to drug resistance in testicular cancer

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A major research study has uncovered several new genetic mutations that could drive testicular cancer - and also identified a gene which may contribute to tumours becoming resistant to current treatments.

The study is the first to use state-of-the-art sequencing technology to explore in detail testicular germ cell tumours - which make up the vast majority of testicular cancers and are the most common cancers in young men.

It was led by scientists at The Institute of Cancer Research, London, and funded by the Movember Foundation.

The researchers, whose study was published in *Nature Communications* today, used a genetic technique called whole-exome sequencing to examine tumour samples from 42 patients with testicular cancer treated at the Royal Marsden NHS Foundation Trust.

They uncovered a number of new chromosome duplications and other abnormalities that could contribute to the development of this cancer, as well as confirming a previous association with the gene KIT.

Their study also found defective copies of a DNA repair gene called XRCC2 in a patient who had become resistant to platinum-based chemotherapy. They were able to verify the link between XRCC2 and platinum resistance by sequencing an additional sample from another platinum-resistant tumour.

Although generally testicular cancer responds well to treatment, resistance to platinum-based chemotherapy is associated with a poor long-term survival rate. The research provides a clue to why around 3 per cent of patients develop resistance to platinum chemotherapy, as well as new insights into testicular germ cell tumours generally.

Dr Clare Turnbull, Team Leader in Predisposition and Translational Genetics at The Institute of Cancer Research, London, and Honorary Consultant in Clinical Genetics at The Royal Marsden NHS Foundation Trust, said:

"Our study is the largest comprehensive sequencing study of testicular tumours published to date, describing their mutational profile in greater detail than has been possible using previous technologies. We have identified new potential driver mutations for this type of cancer, and provided new evidence of a link between mutations in the gene XRCC2 and platinum treatment-resistant tumours.

"We now need additional studies with a larger number of patients, focusing in particular on platinum-resistant tumours, to help our discoveries lead to new options for those unlucky men whose cancer progresses in spite of the best available treatments."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said:

"This study has used the latest DNA sequencing technologies to provide a window into the development of testicular cancer, and reveals some potentially important clues as to how the disease could be treated more effectively.

"Survival rates for testicular cancer are generally very good, but a subset of men don't respond to standard platinum chemotherapy, and the new

research has identified a possible genetic cause for that drug resistance. Knowing which are the key genes driving a cancer's development or helping it dodge the effects of chemotherapy is crucial to help us use existing drugs more effectively and to design the next generation of drugs for personalized medicine."

Paul Villanti, Executive Director of Programs, Movember Foundation, said:

"As a strategic funder of over 580 men's health programs around the world, we recognise the significance of this development and are proud to have been able to provide funding. Understanding the risk factors for developing a testicular cancer and also what is different in the tumours of men who don't respond to chemotherapy is a critical piece of the puzzle and moves us one step closer to the Movember Foundation's goal of having an everlasting impact on the face of men's health.

Dr Turnbull and her colleagues should be incredibly proud of the progress they are making and, while there is still a great deal of work to be done, they're making the Movember community confident in the knowledge that funds they've raised are genuinely and positively impacting the lives of men."

Provided by Institute of Cancer Research

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