Study shines light on cancer survival and a key gene mutation

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Scientists and doctors have known about the p53 gene for a long time, and that it plays a role in halting tumour growth. Credit: Hush Naidoo via Unsplash

University of Toronto researchers have shone light on a well-known but mysterious gene that plays a key role in the growth of cancer.

Genes contain blueprints for making proteins, the molecules that actually carry out tasks in a cell. The p53 gene helps make a protein known as p53, which tells cells to grow or not. This protein helps stop tumours from growing.

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But p53 has remained rather mysterious. Even though doctors have been aware that the p53 gene is the most frequently mutated gene when a person is diagnosed with cancer, and collect information about what mutations are present, they haven't really known how best to use that information in their clinics.

The new study looked at decades of DNA analyses of the p53 gene in cancer patients and compared the survival data with how specific p53 gene mutations affect the way p53 protein works.

Researchers found a big variation in survival rates in men with stomach or brain cancer – depending how much of the activity of the p53 protein was lost due to a specific mutation. The key was the way it mutated.

Now physicians can look more closely at the gene and use the information to help discuss treatment options with patients and keep a closer eye on others who are at higher risk for tumour growth.

"If p53 is mutated but still working at about 5 per cent, that is good news for patients," says Professor Jean Gariépy, of the departments of medical biophysics and pharmaceutical sciences, and a senior scientist at Sunnybrook Research Institute.

"If it's known that p53 will do some of the work to suppress the tumour growth, perhaps other harsh forms of treatment can be avoided and the

tumour can still be controlled."

Think of it like a cellphone battery, Gariépy says. "If you have 5 per cent battery left, you can still call 911. You can still send a text message. It's only when you actually reach 0 per cent battery that you can no longer use the cellphone."

The same seems to be the case with p53. Some mutations result in a p53 form that is still working well, while other mutations cause p53 to not work at all.

The researchers have now put together a chart of all the known p53 mutations observed in the clinic and categorized them based on their "battery power".

"People with mutations that lead to a totally idle p53 have a poorer survival outcome and therefore might be considered for more aggressive treatment," says Nicholas Fischer, a Ph.D. student in Gariépy's lab and lead author of the study.

The study is a great step towards more personalized treatment, he says: "We hope this data will help oncologists and their patients make better informed decisions about their care plan."

More information: Nicholas W. Fischer et al. Survival in males with glioma and gastric adenocarcinoma correlates with mutant p53 residual transcriptional activity, *JCI Insight* (2018). DOI: 10.1172/jci.insight.121364

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