New findings could be life-changing for genetic syndrome sufferers

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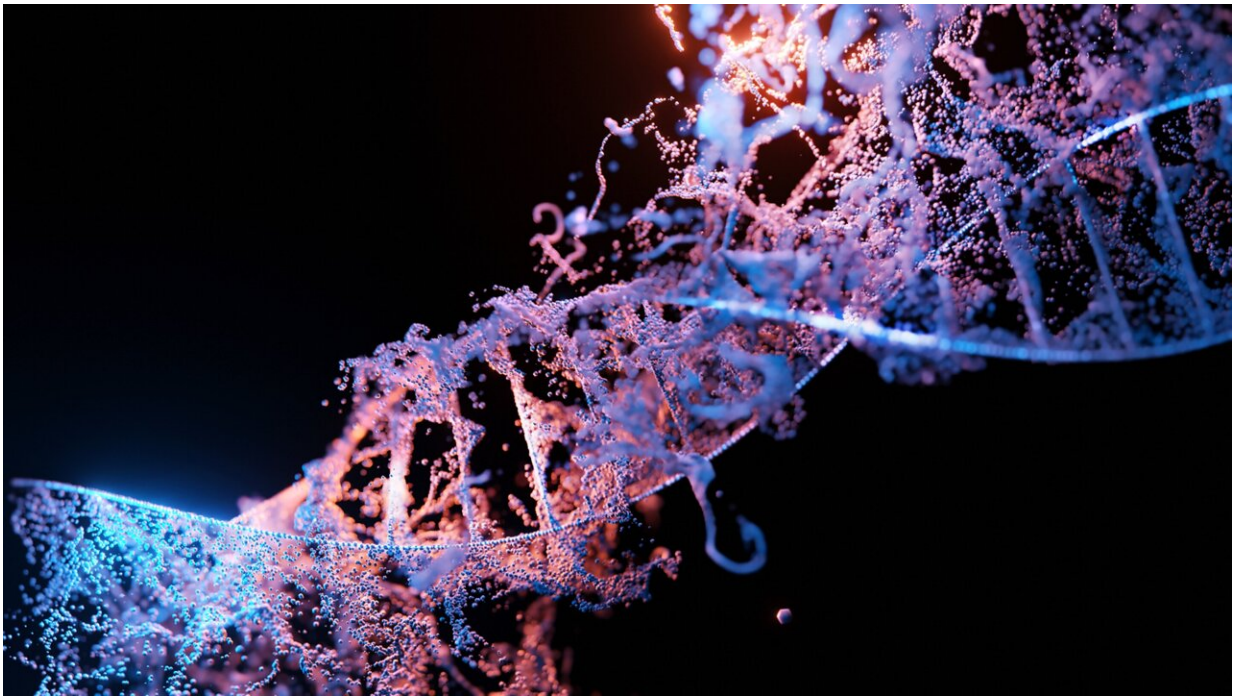

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An international research team led by QIMR Berghofer and Peter MacCallum Cancer Center has discovered that people with the hereditary cancer disorder Li Fraumeni syndrome are at greater risk of a much broader spectrum of cancers than previously thought.

Li Fraumeni syndrome is a rare but devastating condition, which occurs

when people have a fault in a gene called TP53. This fault (a pathogenic variant) puts them at extremely high risk of developing multiple cancers during their lifetime.

The study, published in *JCO Precision Oncology*, assessed data from 146 TP53-positive families in Australia, Spain, and the U.S. (comprising 4,028 individuals).

The new research shows that this risk extends to cancers not traditionally associated with the syndrome, including leukemia, colorectal, lung and gastric cancers, with higher risks in females compared to males.

QIMR Berghofer researcher and lead author Dr. Cristina Fortuno said the findings, which provide accurate estimates of risk by cancer type, age and sex, could help improve early cancer diagnosis and treatment for people with the syndrome.

"The study calculated specific cancer risks by age and sex for each cancer and all cancers combined. Importantly, it identified increased lifetime risks for additional cancers outside the core Li Fraumeni syndrome cancers," said Dr. Fortuno.

"This information is crucial for improving screening and clinical management strategies for carriers of the TP53 gene fault and will help clinicians to detect and manage cancer at an earlier stage."

Co-author Professor Amanda Spurdle, Group Leader of QIMR Berghofer's Molecular Cancer Epidemiology Laboratory, said the research substantiates the use of broad surveillance strategies including dedicated brain and whole-body Magnetic Resonance Imaging, but emphasizes the need to extend screening methods.

"The findings highlight the critical role of dedicated breast screening for

women from a young age. They also raise the question of whether more consideration should be given to offering other targeted risk management approaches such as colonoscopy, prostate cancer screening and risk reducing surgery to prevent ovarian cancer, as standard care for people with Li Fraumeni syndrome," said Professor Spurdle.

Lead collaborator from the Peter MacCallum Cancer Center, clinical geneticist Professor Paul James, highlighted the importance of the findings for families.

"Routine screening and check-ups are essential for people with Li Fraumeni syndrome, but the ability to calculate which cancers may affect people at various ages could be life-changing. We hope this new knowledge will help enhance the existing management guidelines for people with these gene faults and will encourage more research into this syndrome," said Professor James.

It is estimated that one in 10,000 people have Li Fraumeni syndrome. The "core" cancers most commonly linked to the condition include breast cancer, osteosarcoma (bone cancer), and cancer of the soft tissue and brain.

More information: Cristina Fortuno et al, Cancer Risks Associated With TP53 Pathogenic Variants: Maximum Likelihood Analysis of Extended Pedigrees for Diagnosis of First Cancers Beyond the Li-Fraumeni Syndrome Spectrum, *JCO Precision Oncology* (2024). DOI: 10.1200/PO.23.00453

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