Medical Xpress

Blood test detects tumors early in families with Li-Fraumeni syndrome

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Researchers from The Hospital for Sick Children (SickKids), the Ontario Institute for Cancer Research (OICR) and University Health Network (UHN) have demonstrated that by analyzing patients' blood

samples, they are able to detect cancer earlier in individuals with Li-Fraumeni syndrome, an inherited condition with an almost 100% lifetime risk of developing cancer.

The research, led by Drs. Trevor Pugh and Raymond Kim at Princess Margaret Cancer Center, UHN and OICR and Dr. David Malkin at SickKids, has been published in *Cancer Discovery*. The study would not have been possible without the generosity of the patients who participated.

Li-Fraumeni syndrome is an inherited condition associated with a very high risk of developing cancer—often tumors affecting the breast, soft tissue, brain and other organs. It is caused by changes in the TP53 gene, which encodes a protein that helps to prevent tumor formation and is commonly termed the "guardian of the genome."

Cancerous cells and healthy cells release pieces of DNA into the blood. By analyzing these DNA fragments, researchers are developing methods to detect whether a tumor has developed in the body. Testing blood samples for signs of cancer—often called liquid biopsies—is an attractive screening approach compared to imaging methods, which require specialized machines, and biopsies, which are more invasive.

The research team analyzed 170 blood samples from 82 individuals with Li-Fraumeni syndrome collected over several years, as well as 30 blood samples from individuals without Li-Fraumeni syndrome, providing a proof-of-principle framework that may support the detection of specific cancers earlier for individuals with Li-Fraumeni syndrome.

For Luana Locke and her family, early detection is invaluable and has prolonged her life many times already. Luana was diagnosed with breast cancer at age 25 and later discovered that her mother, children and many members of her extended family carried the same TP53 genetic change.

Luana, who has since had sarcoma, lung cancer, thyroid cancer and skin cancer, and her children have regular screenings, blood tests, MRIs of the entire body, and ultrasounds at Princess Margaret Cancer Center and SickKids, to detect cancers early. After years of these scans Luana's daughter, Juliet, was diagnosed with leukemia at age 14, a condition they have since learned may have been detected months earlier with this new blood sample analysis.

"Even though I have LFS, I never really felt cancer anxiety until after I was diagnosed," says Juliet. "While my check-ups are reassuring, getting more precise diagnoses earlier is the next level in care."

Dr. Malkin been monitoring Luana's children for almost 20 years, including her son who was one of the first people to follow a cancer surveillance protocol known as the "Toronto Protocol," while Dr. Kim has been monitoring Luana for almost 10 years.

"This is a full circle moment for us. From being part of the first Toronto Protocol to what may now be the next step in early detection and diagnosis for families with LFS, our family has relied on the advancements made at SickKids and The Princess Margaret," says Luana. "Regular scans and check-ups are routine when you have LFS, but the ability to predict when and where cancers develop rather than react when one has already developed would be life changing."

The team will conduct a clinical trial to further test this approach and screen patients in the hope of finding their cancer earlier. These patients will include those with different types of high-risk cancer predisposition syndromes, including Li-Fraumeni syndrome, Lynch Syndrome, and Hereditary Breast and Ovarian Cancer; all of which are brought under a nation-wide research consortium that Drs. Pugh and Kim founded in 2017.

More information: Early Cancer Detection in Li-Fraumeni Syndrome with Cell-Free DNA, *Cancer Discovery* (2023). DOI: 10.1158/2159-8290.CD-23-0456

Provided by The Hospital for Sick Children