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Researchers develop method for early detection of common post-transplant cancer

Cancer-personalized profiling by deep sequencing identifies type of lymphoma that affects organ recipients 10 to 15 times more often than general population

ORLANDO, Fla April 3, 2019 -- With suppressed immune systems, people who receive organ transplants have a higher risk for getting cancer. But new research has identified a way to detect a common post-transplant cancer earlier than standard methods, offering hope for organ transplant recipients, including children. The research was presented by Kiran Khush, MD, Stanford University, at the International Society for Heart and Lung Transplantation's 39th annual meeting in Orlando, Fla. today.

Organ transplant recipients have a 10- to 15-fold higher incidence of cancer compared to the general population. What's more, they tend to get aggressive cancers, such as Post-Transplant Lymphoproliferative Disease (PTLD), which impacts between 2 to 10 percent of heart transplant recipients by five years post-transplant. PTLD is a type of lymphoma that may be related to Epstein Barr virus infection. Because its symptoms can be vague – fatigue, night sweats, weight loss – it's usually not diagnosed until the cancer is advanced, at which point patients have a 50 percent survival rate.

"It's heartbreaking when a patient almost dies of end-stage heart disease, only to get cancer," said Khush. "We hope this work can go a long way in impacting survival rates for organ transplant recipients."

Detecting DNA

Khush and several Stanford colleagues have developed methods that can detect fragments of DNA from PTLD in the patient's blood, similar to the way testing during pregnancy can identify genetic mutations in a fetus. Using Cancer Personalized Profiling by deep Sequencing (CAPP-Seq), the researchers designed a lymphoma mutation panel, by taking tissue from the tumors of PTLD patients and other lymphomas, sequencing the DNA, identifying genetic mutations and

tailoring their targeted panel. The panel is comprised of nearly 300 genes recurrently mutated in these lymphomas, along with other frequently mutated regions from human genome and the genome of Epstein Barr Virus. Since the panels include mutations common to PTLDs, this enables researchers to look for PTLD-specific mutations in DNA that is circulating in the blood.

Khush and team looked at stored blood samples from an exploratory cohort of patients at Stanford who had contracted PTLD and the researchers were able to identify biomarkers indicating the presence of the cancer from several weeks to more than a year before patients were clinically diagnosed. Researchers are extending this same technique to develop non-invasive screening tests for early detection of lung and colorectal cancers in transplant recipients as other common tumors in this population, with the framework potentially also being feasible for other tumor types.

"This is logistically challenging work since we study serial blood samples – which are stored – going back to see the earliest presence of cancer," said Khush.

Researchers hope to see this test used clinically in three to five years. In the meantime, the Stanford team hopes to partner with other transplant centers around the world that have biobanks in order to broaden their pool of stored blood samples from patients who have developed cancer after transplantation.

Also on the Stanford team:

Joanne Soo, MD
Joseph Shroers-Martin, MD
Andrea Garofalo, BSc
David Kurtz, MD
Nathan D'Emilio, BSc
Helen Luikart, RN
Max Diehn, MD
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About ISHLT

The International Society for Heart and Lung Transplantation is a not-for-profit, multidisciplinary professional organization dedicated to improving the care of patients with advanced heart or lung disease through transplantation, mechanical support and innovative therapies. With more than 3,800 members in more than 45 countries, ISHLT is the world's largest organization dedicated to the research, education and advocacy of end-stage heart and lung disease. ISHLT members represent more than 15 different professional disciplines. For more information, visit www.ishlt.org.