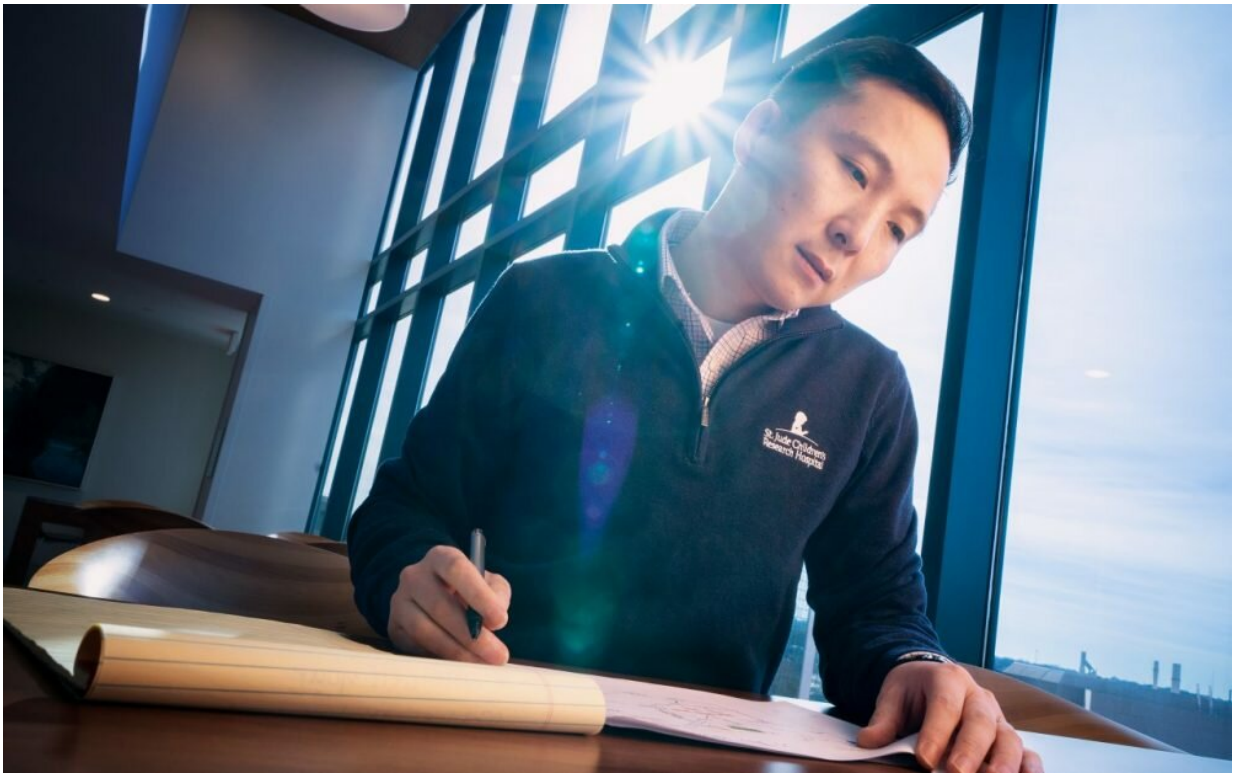
Inherited genetic variation linked to risk of T cell leukemia in children

April 2 2019



Corresponding author Jun J. Yang, Ph.D., of the St. Jude Departments of Pharmaceutical Sciences and Oncology. Credit: St. Jude Children's Research Hospital

A study led by St. Jude Children's Research Hospital has identified a novel risk variant associated with T cell acute lymphoblastic leukemia (T-

ALL). The findings appear as an advance online publication in the *Journal of the National Cancer Institute*.

"The inherited genetics underlying this rare type of leukemia were mostly unknown prior to our study," said senior investigator and corresponding author Jun J. Yang, Ph.D., of the St. Jude Departments of Pharmaceutical Sciences and Oncology. "Now, we have definitively identified a gene associated with increased odds of developing T-ALL."

The researchers conducted a genome-wide association study to analyze the inherited (germline) DNA of more than 1,000 children with T-ALL as well as more than 12,000 control samples. These ALL cases were individuals treated at St. Jude and through clinical trials run by Children's Oncology Group, the world's largest cooperative pediatric cancer research organization.

The study identified a novel variant of the USP7 gene as playing a role in increasing the risk of developing T-ALL. This USP7 risk variant is found more often among individuals of African ancestry and may help explain why T-ALL is more common in this group.

Understanding the function of USP7

There is a genetic subtype of T-ALL characterized by overexpression of TAL1. Building upon previous research at St. Jude, Yang and his team have now shown that genetic changes in USP7, either inherited or in the DNA of the cancer cells, occur in 56 percent of TAL1 overexpressed T-ALL, more than any other T-ALL subtype.

"These findings really confirm that T-ALL is very different from other types of leukemia, with its unique set of genetic risk factors ," Yang said. "This work adds evidence to support the notion that USP7 plays an important role in the development of T-ALL."

The researchers conducted additional analyses to shed light on the function of USP7 to help understand its role in the development of T-ALL. Their work shows that the inherited genetic variant is linked to lower expression of USP7 and therefore some degree of reduced USP7 function.

More information: Genome-wide association study of susceptibility loci for T-cell acute lymphoblastic leukemia in children. *Journal of the National Cancer Institute*. doi.org/djz043

Provided by St. Jude Children's Research Hospital