MedicalXpress

Study suggests improved treatment alternative for lymphoid leukemia

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Discovering what they call the "Achilles' heel" for lymphoid leukemia, an international research team has tested a possible alternative treatment that eradicated the disease in mouse models.

Reporting their results Feb. 11 in the journal *Cancer Cell*, the scientists said the targeted molecular therapy described in their study could have direct implications for current treatment of Acute Lymphoid Leukemia (ALL) in people.

Led by researchers at Cincinnati Children's Hospital Medical Center and the Institut de recherches cliniques de Montreal (ICRM), the study found that leukemic cells depend on a protein called Gfi1 for survival. Removing the protein in mouse models of the disease weakened and killed the leukemia cells. Researchers said this should make the leukemia more susceptible to chemo and radiation therapies – the current frontline treatments for ALL.

"Chemo and radiation therapies are very non-specific and can be toxic to patients. Our findings suggest that combining the inhibition of Gfi1 with these treatments may allow the use of lower cytotoxic doses and directly benefit patients," said H. Leighton Grimes, PhD, co-senior investigator on the study and researcher in the divisions of Cellular and Molecular Immunology and Experimental Hematology at Cincinnati Children's.

Also collaborating was co-senior investigator, Tarik Möröy, PhD, president and scientific director of the ICRM in Montreal.

The researchers said the need for better treatment options is evident. Beside the potential toxicity of current therapeutic options, many ALL patients relapse after initial remission of their disease.

A cancer that affects blood cells and the immune system, ALL is the most common type of leukemia in children from infancy up to age 19, according to the Leukemia and Lymphoma Society of America. ALL occurs most often in the first decade of life but increases in frequency again in older individuals. According to the National Cancer Institute, the overall survival rate for all ages of people with ALL is 66.4 percent and 90.8 percent for children under the age of 5 years.

During the onset of a disease like ALL, cancer signals among cells activate a protein called p53, which is often referred to as the "guardian of the genome." A repressor of tumor growth, p53 normally initiates a DNA repair program that is supposed to induce programmed cell death to stop or slow down tumor progression.

In the case of ALL, the researchers said the disease relies on the Gfi1 protein to get around p53's tumor repressing capabilities by essentially overriding p53. Gfi1 has an important role in the normal development of lymphoid cells. But analyses of ALL mouse models and primary human tumors showed that Gfi1 is overexpressed in the disease state.

When the researchers removed Gfi1 in established mouse lymphoid tumors, the leukemia regressed through p53-induced cell death. Next, to see if removal of Gfi1 would be effective in modeled human ALL, the research team inserted T-cell leukemia cells from human patients into mice. Inhibiting Gfi1 in this instance stopped the progression of human leukemia in the animals without any harmful effects.

The scientists are continuing their research to see if results of the current study will be translatable to human patients.

Provided by Cincinnati Children's Hospital Medical Center