

Research identifies genes vital to preventing childhood leukemia

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Researchers at The University of Western Ontario have identified genes that may be important for preventing childhood leukemia. Acute lymphoblastic leukemia (ALL) is a cancer of the blood that occurs primarily in young children. It's frequently associated with mutations or chromosomal abnormalities that arise during embryonic or fetal development. Working with mice, researchers led by Rodney DeKoter identified two key genes that appear essential in the prevention of B cell ALL, the most common form of ALL in children. The study is published online in *Blood*, the Journal of the American Society of Hematology.

In the study, mice were generated with mutations in two genes called PU.1 and Spi-B. Mutation of either PU.1 or Spi-B individually had little effect. Unexpectedly, mutation of both genes resulted in 100% of the mice developing <u>B cell</u> ALL. Eighty percent of ALL cases in children are of the B cell type. The study found PU.1 and Spi-B have unanticipated functional redundancy as "tumor suppressor" genes that prevent leukemia.

"You can think of PU.1 and Spi-B proteins as brakes on a car. If the main brake (PU.1) fails, you still have the emergency brake (Spi-B). However, if both sets of brakes fail, the car speeds out of control," explains DeKoter, an associate professor in the Department of Microbiology & Immunology at Western's Schulich School of Medicine & Dentistry. "And uncontrolled cell division is an important cause of leukemia."



PU.1 is an essential regulator in the development of the immune system, and mutations in this gene have been previously associated with human ALL. DeKoter hopes these studies will ultimately lead to improved, less toxic, therapies for childhood leukemia. Currently, about 80% of ALL patients go into complete remission when treated with aggressive chemotherapy.

More information:

http://bloodjournal.hematologylibrary.org/content/early/2011/07/15/bloo d-2011-02-335539.abstract

Provided by University of Western Ontario

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