

Study identifies first molecular steps to childhood leukemia

July 15 2009

A Massachusetts General Hospital (MGH)-based research team has identified how a chromosomal abnormality known to be associated with acute lymphoblastic leukemia (ALL) - the most common cancer in children - initiates the disease process. In the July issue of *Cell Stem Cell*, they describe how expression of this mutation in hematopoietic stem cells (HSCs), which usually occurs before birth, leads to the development of leukemia many years later.

"Based on their longevity, it had been assumed but never shown that HSCs were the cells in which the first steps of leukemia occur. We now unequivocally demonstrate that HSCs can be involved in the early evolution of leukemia and that cells expressing an [oncogene](#) can continue contributing to blood formation while serving as a hard-to-detect reservoir of malignancy-prone cells," says Hanno Hock, MD, PhD, of the MGH Cancer Center and Center for Regenerative Medicine, corresponding author of the *Cell Stem Cell* article. "We hope that better understanding the latency period of childhood leukemia will help us interfere with the disease earlier and in a more targeted, less toxic manner."

[Acute lymphoblastic leukemia](#) (ALL) represents 23 percent of all cancer diagnoses in children under 15. Although treatment of childhood ALL has been a major success story, with 85 percent of patients surviving five years or more, it involves two to three years of complex chemotherapy. Studies have identified leukemia-associated genetic and molecular abnormalities that can precede development of symptoms by several

years and also pointed to a chromosomal translocation called TEL-AML1 as the first step toward ALL. But how and in which cells this process begins was not clear.

Previous examinations of the role of the TEL-AML1 allele in initiating ALL, conducted using less refined systems, had inconsistent results. In the current study, the research team developed a [mouse model](#) in which they could induce the expression of TEL-AML1 at various stages of blood cell development using the same chromosomal regulatory elements active in leukemic cells. They found that, when the mutation is expressed in more differentiated progenitor cells, those cells do not survive long enough to acquire subsequent mutations required for malignant transformation. But expression of TEL-AML1 in HSCs, the only blood-forming cells that continually renew themselves, leads to a persistent overpopulation of altered HSCs that are particularly sensitive to secondary, transformational mutations.

"Basically, TEL-AML1 expands HSCs and puts them into a dormant but malignancy-prone state, setting the stage for the catastrophe to come," says Hock. "We are now looking at what happens when TEL-AML1 combines with other mutations occurring later in the development of this type of leukemia, to put together the complete biology of the disease. If we can generate a disease model that incorporates all the steps leading to full-blown [leukemia](#), that should help us further study the biology of the disease and test new, targeted therapies." An assistant professor of Medicine at Harvard Medical School, Hock is also a member of the Harvard Stem Cell Institute.

Source: Massachusetts General Hospital ([news](#) : [web](#))

Citation: Study identifies first molecular steps to childhood leukemia (2009, July 15) retrieved 25

April 2024 from <https://medicalxpress.com/news/2009-07-molecular-childhood-leukemia.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.