

# Study reveals origins of a cancer affecting the blood and bone marrow

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A new study by the NYU Cancer Institute, an NCI-designated cancer center, sheds light on the origins of myeloid leukemia, a type of blood cancer that affects children and adults. The researchers discovered that novel mutations in an intracellular communication pathway called Notch led to the cancer, pointing to a potential new target for treating this disease. Notch has already been implicated in another type of blood cancer called T-cell acute lymphoblastic leukemia, but the new research found an unexpected role for it in myeloid leukemia. The study is published in the May 12, 2011 issue of the journal *Nature*.

"This study shows the power of the Notch signaling pathway in myeloid leukemias," says Iannis Aifantis, PhD, associate professor in the Department of Pathology at NYU Langone Medical Center and a member of the NYU Cancer Institute, who led the new study. "This discovery," he says, "suggests a potential for future targeted therapies." Dr. Aifantis is also a Howard Hughes Medical Institute Early Career Scientist.

Last year, [acute myeloid leukemia](#) was diagnosed in more than 12,000 adults and the disease claimed nearly 9,000 lives in the United States, according to the [National Cancer Institute](#). The [blood cancer](#) is the most common type of [acute leukemia](#) in adults. Normally, the bone marrow makes blood stem cells (immature) that mature over time. Some of these are a form called myeloid and others are lymphoid. The lymphoid stem cell develops into a white blood cell, while the more-versatile myeloid stem cell develops into [red blood cells](#), [white blood cells](#), and platelets,

which prevent clotting. Cancer occurs when too many immature myeloid stem cells are produced in the blood and bone marrow.

The Notch signaling pathway, the complex web of intracellular interactions that occurs after a protein called Notch is activated on the cell's surface, is a well known actor in cancer, but the new study reveals that the varied members of this pathway function in unexpected ways to produce disease. Notch is named for a particular kind of mutation, first identified almost 100 years ago, that gives fruit flies notched wings.

The study evaluated mutations in the Notch pathway in mice models of the disease, and also in blood samples from patients with chronic myeloid leukemia. Researchers identified several mutations that inactivated or silenced the pathway, leading to the accelerated accumulation of abnormal blood cells. Most importantly, the study also revealed that the reactivation of the silenced genes in the pathway blocked the disease, providing additional support for the potentially crucial role that Notch might play in the development of cancer.

In a commentary accompanying the study in *Nature*, Demetrios Kalaitzidis and Scott A. Armstrong of Dana Farber Cancer Institute and Children's Hospital Boston, note that the study defines a new role for Notch signaling as a suppressor of leukemia development. They note that further research is needed to understand the intricacies of Notch signaling in normal and cancerous tissue, which will help determine "the best approaches to manipulating this pathway for optimal therapeutic response."

Provided by New York University School of Medicine

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