Scientists Identify Molecular Signature for Leukemia Stem Cells

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Scientists studying chronic myeloid leukemia, more commonly known as CML, are one step closer to decoding the "genetic signature" of stem cells in this disease. They've identified a marker in a tiny but powerful subset of leukemia cells that could enable scientists to halt cancer cell growth in CML, and perhaps in other forms of cancer.

Their work is published in this week's Proceedings of the National Academy of Sciences. Among the authors is Francis J. Giles, M.B., M.D., professor and chief of hematology and medical oncology at The University of Texas Health Science Center at San Antonio. Dr. Giles also is deputy director of the Cancer Therapy and Research Center at the UT Health Science Center, and director of the CTRC's Institute for Drug Development.

About 4,500 new cases of chronic myeloid leukemia were diagnosed in 2006, mostly in adults. The disease, marked by massive growth of white blood cells in the body, results from a change in the DNA of a stem cell in the bone marrow. The stem cell's changed DNA gives the malignant (cancerous) cell an advantage over normal stem cells in terms of growth and survival. Scientists do not yet understand what produces this change in the DNA, which is not present at birth.

"Well over 90 percent of patients with CML improve with the front-line and second-line treatments, imatinib and nilotinib," says Dr. Giles, a leading developer of nilotinib, approved in 2007 by the Food and Drug Administration. "But if you're among those who don't respond or you

lose your prior response, this research finding is very important.

“We believe stem cells are the obstacle to a cure for leukemia. If we’ve killed nearly all of a patient’s cancer cells, but we haven’t killed the stem cells, we haven’t cured the patient. A marker helps us find the elusive stem cells, quantify them, and follow their behavior in patients. Then we can see how the stem cell behavior differs from that of other more mature cancer cells, and develop stem cell-directed new therapies.”

Dr. Giles says this marker, an abnormality in the Wnt/ß catenin self-renewal pathway, may enable scientists to develop a test that could be given to leukemia patients following treatment to make sure the stem cells have been eliminated. Another potential application is to test drugs under development in San Antonio and elsewhere to change the stem cells’ instructions.

“Perhaps we can tell the stem cells to ignore their previous instructions and get them to change into another type of cancer cell that we know how to kill,” Dr. Giles theorizes.

Much of the laboratory work that identified the abnormality was conducted at Moores Cancer Center at the University of California San Diego. Aside from Dr Giles’ role in the design and conduct of the research, CTRC patients with CML contributed samples of blood and bone marrow, and the CTRC’s Institute for Drug Development is testing drugs that may alter cancer stem cell function in the leukemias or in solid tumors.

Provided by University of Texas Health Science Center at San Antonio