Stem cells central to pathogenesis of mature lymphoid tumors

August 15 2011

New research suggests that blood stem cells can be involved in the generation of leukemia, even when the leukemia is caused by the abnormal proliferation of mature cells. The study, published by Cell Press in the August 16th issue of the journal *Cancer Cell*, may guide future strategies aimed at identifying therapeutic targets for chronic lymphocytic leukemia (CLL).

CLL is a cancer of a type of mature white blood cell called a B lymphocyte. "Most human CLL cases have a precursor phase, called monoclonal B lymphocytosis (MBL), that is an asymptomatic proliferation of B cells," explains senior study author Dr. Dr. Koichi Akashi from Kyushu University Graduate School of Medical Sciences in Japan. "Our question was, if progression from MBL to CLL reflects stepwise proliferation of aberrant cells, at what stage does the first cancer-causing event occur?"

To look for the cell population with cancer-initiating activity in human CLL, Dr. Akashi and colleagues tried to find the specific developmental stage where abnormal clonal B cells first appear. They began at the beginning, with hematopoietic stem cells (HSCs). HSCs are blood stem cells that can give rise to any type of blood cell. The researchers purified HSCs from healthy individuals or HSCs from CLL patients and transplanted them into mice with a deficient immune system. In contrast to the normal HSCs, the CLL HSCs gave rise to B cells similar to those seen in MBL. Interestingly, the CLL HSCs did not have chromosomal abnormalities common to CLL, suggesting that acquisition of

chromosomal abnormalities that transform MBL into CLL are secondary events.

Taken together, the findings suggest that HSCs are involved in the pathogenesis of CLL, even though CLL is a malignancy of a mature cell type. "Our data suggest that the propensity to progress to CLL is already acquired at the HSC stage," concludes Dr. Akashi. "Identification of the intrinsic abnormality of HSCs in patients with CLL should be the key to finding the ultimate therapeutic target in human CLL."

Provided by Cell Press