Leukemia stem cells have more in common with embryonic stem cells than adult stem cells

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Research using a mouse model of human leukemia has provided critical insight into the genetic factors related to the generation and maintenance of myeloid leukemia stem cells. The study, published by Cell Press in the February 6th issue of the journal *Cell Stem Cell*, is likely to have a profound impact on the future design of therapeutic approaches targeted against cancer stem cells.

Leukemia stem cells (LSCs) were initially described as rare cells that share characteristics with normal hematopoietic stem cells (HSCs). HSCs are a type of partially committed adult stem cells that can give rise to multiple types of blood cells. However, recent research has demonstrated that LSCs can represent a significant fraction of leukemic cells and exhibit characteristics associated with more mature, differentiated myeloid cells rather than the more versatile HSCs.

"Since LSCs may be more numerous and mature than originally proposed, the nature and generality of the hierarchical organization of malignancies has recently been questioned," says senior study author Dr. Michael L. Cleary, from the Department of Pathology at Stanford University. Dr. Cleary and colleagues used a mouse model of human AML to investigate the genes that maintain LSC frequencies and leukemia cell hierarchies.

The researchers found that LSCs are maintained in a self-renewing state

by subversion of a transcriptional program that shares features with pluripotent embryonic stem cells (ESCs). This transcriptional program is transiently expressed in normal myeloid precursor cells rather than HSCs or fully mature white blood cells. The authors go on to reveal a link between activation of genes associated with ESCs at an inappropriate stage of white blood cell development, the number of LSCs, and a poor prognosis in leukemia.

"Importantly, the shared transcriptional features of LSCs, ESCs, normal mid-myeloid lineage cells, and a diverse set of poor-prognosis human malignancies support the broader conclusion that cancer stem cells may be aberrantly self-renewing downstream progenitor cells," explains lead study author Dr. Tim Somervaille.

The study also highlights the potential of therapeutic strategies aimed at genes and pathways that are of greater importance to the function of LSCs than HSCs. "These findings may have a substantial clinical impact, as normal HSCs are necessary for regeneration of hematopoiesis following chemotherapy," offers Dr. Cleary.

Source: Cell Press