'Sister' factors promote survival of blood-system stem cells

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Stem cells of any kind are defined by their eternal nature, reproducing themselves and providing a pool of cells from which more differentiated tissues arise.

Now a group of researchers from Baylor College of Medicine in collaboration with researchers in Australia and the United Kingdom, demonstrate that two specific "sister" genes that control transcription play often overlapping roles in maintaining this pool of hematopoietic or blood cell-forming stem cells.

In a report in the current issue of the journal *Cell Stem Cell*, the scientists show that genes for two transcription factors -- the stem cell leukemia gene (Scl) and the lymphoblastic leukemia gene 1 (Lyl1) - play overlapping or redundant roles in maintaining this pool of hematopoietic (blood-forming cells) stem cells. These are so-called "adult" stem cells because they can differentiate only into tissues of the blood system.

"Both genes are involved in T-cell acute lymphoblastic leukemia," said Dr. Margaret Goodell, director of the Stem Cells and Regenerative Medicine (STaR) Center of Baylor College of Medicine and senior author of the report that appears in the current issue of the journal *Cell Stem Cell*. "No one knew what role Lyl1 played in hematopoiesis (the formation of blood and related cells). The two of them have a functional redundancy. If one is missing, the cell might be a little 'sick,' but it survives. If both are missing, the cells die pretty quickly."

"Scl has been well studied and is a paradigm for hematopoiesis," she said. "Lyl1 was a lost sister. Only recently have a few groups studied it."

Previous studies had shown that when animals lacked the gene Scl in the embryonic stage, they did not make progenitor cells intrinsic to the formation of the blood cells and had defects in the blood vessel system. When the gene Scl is turned off in adult animals, blood cells are not repopulated in the short term but they do come back over the long term, the researchers noted.

George Souroullas, a graduate student in Goodell's laboratory at BCM and first author of the paper said, "Up to this point, it was believed that Scl was dispensable for maintaining adult hematopoietic stem cell function after development. Our study however, shows that not only is it not dispensable, but it collaborates with Lyl1, and both necessary for cell survival."

When blood-forming stem cells lack Scl and have only one copy of the Lyl1 gene, they can still be used successfully in a stem cell transplant, enabling animals to continue to make blood cells in the long-term. However, if these stem cells lack Lyl1 and Scl, they die rapidly.

This suggests that Scl and Lyl1 are not only important in the formation of these kinds of stem cell but also for their maintenance in adults, the researchers said.

"If these genes work together in stem cells, they might play a similar role in leukemia cells," said Goodell.

While she describes the two as sister genes, Goodell believes they have distinct roles as well.

Souroullas said, "While these genes are very similar and functionally

redundant in adult stem cells, some molecular differences in protein structure, supported by other data in our lab, suggest that they may in fact have distinct functions in differentiated blood cell types"

Goodell added that "one may be more important in the embryo while the other in the adult."

Source: Baylor College of Medicine