

# Multipotential Hematopoietic Stem Cells in the Bone Marrow

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## **Abstract**

It has been generally held that human hematopoietic stem cells are lineage-negative CD34<sup>+</sup> CD38<sup>-</sup>. However, murine hematopoietic stem cells were reported to be CD34<sup>-</sup>. We have characterized the surface phenotypes of murine hematopoietic stem cells by using a murine transplantation model. Our studies revealed that the majority of the stem cells in normal adult mice are CD34<sup>-</sup> while a minority (15%-20%) being CD34<sup>+</sup>. Our studies also revealed that stem cells that are activated by injection of 5-fluorouracil in vivo, exposure to cytokines in vitro, or mobilization by G-CSF are CD34<sup>+</sup> and that CD34 expression is reversible. It has been reported that fetal murine hematopoietic stem cells are CD34<sup>+</sup>. Our studies revealed that stem cells of juvenile mice are CD34<sup>+</sup> and that the developmental change from CD34<sup>+</sup> to CD34<sup>-</sup> state takes place between 7 and 10 weeks of age. In adult mice, expression of CD38 by steady-state and activated stem cells was completely reciprocal of CD34 expression. Activated stem cells and the minority population of the stem cells in the normal mice are CD34<sup>+</sup> CD38<sup>-</sup>. In contrast, the majority of stem cells in normal adult mice are CD34<sup>-</sup> CD38<sup>+</sup>. Recently, we studied CD38 expression by stem cells of neonatal and juvenile mice. Stem cells of newborn mice are CD38<sup>-</sup>. About half of the stem cells of 5-week-old mice are CD38<sup>+</sup>. Finally, our studies indicated that some of the CD34<sup>+</sup> stem cells in the bone marrow of normal adult mice express lineage markers such as Mac-1 and CD4. These studies in a murine model clearly documented that expression of both CD34 and CD38 by stem cells is under developmental control and may be subject to changes induced by activation of the stem cells. In order to test whether or not these principles apply to human stem cells we tested surface phenotypes of human stem cells using two xenotransplantation techniques. Studies based on human/sheep xenograft model indicated that a significant portion of adult human long-term engrafting cells are CD34<sup>-</sup>. Similar to mouse stem cells expression of CD34 by human stem cells was reversible. Studies based on our newborn NOD/SCID/ $\beta$ -microglobulin<sup>null</sup> mice indicated that human cord blood stem cells are CD34<sup>+</sup> CD38<sup>-</sup>. These results appear to support the validity of studies of murine stem cells to provide insight into human stem cells.

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