Genetic and functional comparison of primitive CD34⁺ leukemic cells that reside in the marrow compartment and in circulation

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Acute myeloid leukemia (AML) is characterized by an abnormal increase in leukemic blast. These blast cells accumulate in the bone marrow (BM), often results in severe cytopenia. Extravasations of these leukemic blast cells out of the BM into the circulation, and sometimes infiltration of other organs have also been noted in some patients. Previous *in vitro* assays showed that BM leukemic blast cells have a higher surface CXCR-4 expression and displayed a higher response to SDF-1 induced migration as compared to circulating blasts. However, the intrinsic properties of peripheral blood (PB) and BM blast cells and any possible differences between the two populations in terms of homing efficiency and leukemia initiating potential has never been clearly investigated. In the present study, primitive CD34⁺ cells of paired BM and PB samples from AML patients were collected and the expression of a panel of phenotypic markers, as well as the homing efficiency of each paired samples were assessed by xenotransplantation into NOD/SCID mice. While there was no significant difference in the expression of surface markers such as CD133, CD123, CD117, CD38 and CD44 between paired BM and PB CD34⁺ leukemic samples, *in vivo* homing assay showed that PB CD34⁺ cells home to the marrow compartment more efficiently than BM CD34⁺ cells ($P < 0.05$). In addition, we compared the gene expression profiles of CD34⁺ cells of 5 paired BM and PB leukemic samples using cDNA microarray. Despite of having a highly similar expression profile, a number of genes involving in G-protein signaling, cell cycle, regulation of apoptosis and also the mitogen activated protein kinase (MAPK) signaling pathway have been found to have a decreased expression in PB CD34⁺ population. Base on these data, we hypothesized that primitive CD34⁺ leukemic cells that reside within the BM compartment are vigorously subjected to the influence of the microenvironment. Egress of these cells out of the BM is probably an active event and may reflect a change in cellular properties. Also, the loss of the BM microenvironmental effect on circulating CD34⁺ leukemic cells may lead to further cellular changes.

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