

## The Central Role of Hematopoietic Stem Cells in Leukemia such as Acute Lymphoblastic Leukemia or Chronic Myeloid Leukemia

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Leukemia is the most common type encountered in pediatric and adult patients. In acute leukemia, hematopoietic stem cells (HSCs) reside in specialized niche in the bone marrow (BM). These stem cells are thought to provide signals that support key HSC properties. Normality, cytokines regulate a variety of hematopoietic cell functions through the activation of multiple signal transduction pathways. In this regard, regulation of proliferation and differentiation of HSCs is related by the gene expression pattern in the cell and the composition of external signals from the BM niche. Transcription factors regulate expression of gene; meanwhile external signals can be mediated by cell-cell interactions, cell-extracellular matrix interactions and growth factors as well which may promote proliferation, differentiation, migration and apoptosis. Moreover, HSCs are multipotent stem cells defined by their ability to self renewal, differentiation and maintenance of all blood cell types in hematological system. These properties make HSCs like other tissue stem cells, prime targets for malignant transformation. Also we know molecular advances of acute leukemia have led to discovery of numerous additional changes including mutation involving key cellular pathways in myeloid and lymphoid development, tumor suppression, and cell cycle regulation as well. Hence, I want to explain concerning genetic basis of acute leukemia particularly in acute lymphoblastic leukemia (ALL), HSCs source as well, also malignant and nonmalignant hematopoietic progenitor cells. BCR-ABL was the first chromosomal abnormality shown with a specific malignancy in humans. In this regard, murine models have demonstrated that disruption of the hematopoietic microenvironment can initiate myeloproliferative disease and even leukemia. Also in murine models, activation of the normal from HSC niche improves recovery from radiation and chemotherapeutic injury and suppresses chronic myeloid leukemia (CML) progression, impairing leukemic stem cell maintenance in the syngeneic model. In hematologic malignancies, clonal neoplastic cells alter the hematopoietic microenvironment so that it becomes supportive of LSCs and becomes less supportive of normal HSCs, ultimately leading to decreased normal hematopoietic. In CML,

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it is sustained by a range of biological characteristics that enable their long-term survival, and accumulation of myeloid cells that differentiate in normal and abnormal clones, which can change to acute lymphoblastic leukemia (ALL) in accelerated phase possibly. Furthermore, leukemia induced decrease in CXCL12 expression results in reduced retention of LSCs in CML bone marrow. Moreover, leukemia induced abnormalities in cytokine in CML bone marrow result in selective suppression of normal stem cell growth and enhanced growth of LSC. Told all, I accept that there is a complexity of BM hematopoietic stem cell niche; in spite of all that if we see to central role of malignant stem cell with self-renewing toward capable initiating and maintaining of leukemia, so we'll go to understand the role of single HSC which HSC acquires the clonal advantage that can drive toward the aberrant HSC and also a better understanding that how can restore the balance in hematopoietic cells for restore the infrastructural of hematopoietic system including hematopoietic microenvironment, HSCs, progenitor and precursor cells and the other cells of niche. Notability of single cell analysis will permit us to know how can highly, precisely demonstrate to the role of hematopoietic cells in therapy in different hematopoietic malignancy.