

Significance of the Expression of CD 90, 96, 117 and 123 in Egyptian Patients with Acute Myeloid Leukemia, Relation to Prognosis and Response to Treatment

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ABSTRACT

Investigating the expression pattern of CD 90, 96, 117 and 123 in bone marrow or peripheral blood from adult patients with acute myeloid leukemia and their use as markers for diagnosis and prognosis. Patients and methods: Using Multi-color flowcytometry, we analyzed the expression of CD90, 96, 117 and 123 among [CD34+/CD38-] cell population in AML patients at initial diagnosis. Results: It was found that percentage of CD90+ cells was lower among [CD34+/CD38-] cells in of AML cases than control group, however this difference didn't reach any statistical significance (p value=0.06), the percentage of CD96+ cells among CD34+CD38- cells was higher in AML cases than for control group (that show a highly statistically significant difference (p value<0.001), the percentage of CD117 cells was higher among CD34+CD38- cells in AML cases than for control group, however this difference didn't show statistical significance (p value=0.079), While percentage of CD123 was significantly higher among [CD34+/CD38-] cells in AML cases than the control group and this difference shows a high statistical significance (P value<0.001).

Acute Myeloid Leukemia (AML) is a life-threatening haematopoietic disease that is characterized by clonal growth and accumulation of myelopoietic progenitor cells. Many data have shown that each AML clone consists of Leukemic Stem Cells (LSC) and their progeny and that AML stem cells differ from more mature cells in several aspects, including survival and target antigen profiles.

Stem cells possess two defining characteristics: the ability to self-renew and the capacity to differentiate. A number of major cancers including acute myeloid leukemia have been shown to follow a cancer stem cell model in which cancer cells are hierarchically organized.

CD34 is a cell surface transmembrane protein that is expressed primarily on the surface of immature hematopoietic normal progenitor cells. It has been widely used as a marker to assist in the identification and isolation of Hematopoietic Stem Cells (HSCs) and progenitors. Cell surface expression of CD34 is developmentally regulated in hematopoiesis and is inversely related to the stage of differentiation, as CD34 expression is lost beyond the committed progenitor stage. The functional significance of CD34 expression on hematopoietic progenitor cells and developing blood vessel is unknown, except that CD34 on vascular endothelial cells binds to L-selectin. It is not lineage restricted and thus not useful for distinguishing AML from acute lymphoblastic leukemia (ALL). In addition, CD34 is involved in cellular adhesion and mediates resistance to apoptosis.

CD90 or Thymocyte differentiation antigen 1 (THY-1) is a cell surface glycoprotein expressed on some early T and B lymphocytes, fibroblasts and neural cells. It is also expressed on primitive hematopoietic cells. In this latter cell population, in normal BM, about 5-25% of CD34+ cells co-express CD90. It seems to be involved in proliferation and expansion processes. A higher

expression level of CD90 in HSCs than in LSCs was further emphasized in another study.

In non-hematopoietic tissue, CD96 is expressed in the convoluted tubular epithelium of the kidney, the mucosal epithelium of the small and large intestines and the vascular endothelium.

A possible function of this receptor in natural killer (NK) cell mediated killing activities were suggested recently. Moreover, CD96 was described as a tumor marker for T-cell acute lymphoblastic leukemia and acute myeloid leukemia. It has been shown to be expressed at high levels on hematopoietic cells from adult AML patients, whereas its expression in cells from hematologically normal subjects is significantly reduced.

The c-kit proto-oncogen (CD 117) has been shown to be present in several cell types including normal and neoplastic hemopoietic cells. Among normal Bone Marrow (BM) cells, CD117 expression has been found in about half of the CD34+ precursors including progenitors committed to the erythroid, granulomonocytic and megakaryocytic cell lineages. In addition, strong CD117 expression is detected in bone

marrow mast cells as well as in a small subset of NK cells displaying strong reactivity for CD56, and in a relatively important proportion of CD3/CD4/CD8 prothymocytes. These results suggest that CD117 expression can be detected in both myeloid and lymphoid lineages although for the lymphoid lineage it would be restricted to a small NK-cell subset and early T-cell precursors.

In acute leukemias, CD117 expression was initially associated with AML. Nevertheless, at present it is well established that CD 117 expression may also be found in a relatively important proportion of T-ALL while it is usually absent in B-lineage ALL.

CD123, the α -subunit of the interleukin-3 (IL-3) receptor, has generated considerable interest as a cell-surface antigen with potential clinical application because it is highly expressed on stem/progenitor cells from adult AML, whereas it is practically absent on their normal hematopoietic counterparts.

The aim of this study was to investigate the expression pattern of CD, 90, 96, 117 and 123 in bone marrow or peripheral blood from adult patients with acute myeloid leukemia and their value as markers for diagnosis.

Keywords: Acute myeloid leukemia; Leukemic stem cell; CD 90, 96, 117, 123.