PROGNOSTIC SIGNIFICANCE OF CD123 AND CD96 IN ADULT ACUTE MYELOID LEUKEMIA

THESIS

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Abstract

Acute myeloid leukemia (AML) is considered to be a stem cell disease. The poor response to therapy in AML raises the expectations of the presence of leukemic stem cells (LSCs). **Aim of work:**To investigate the expression of CD96 and CD123 in adult patients with acute myeloid leukemia and their use as markers for prognosis. **Methodology:**Using muli-color flow-cytometry, we analyzed the expression of CD96 and CD123 among **[CD34+/CD38-]** cell population in AML patients. The study was conducted on 40 AML patients collected among cases referred to Adult Haematology and Oncology Department,Ain Shams University Hospitalsover the period from March 2017 to February 2018. Forty samples were studied at time of initial diagnosis and D28 of AML patients, compared to 16 bone marrow samples of patients with non-hematological malignancies as a control group. **Results:**It was found that the **percentage** of **CD123** was significantly higher among **[CD34+/CD38-]** cells in AML cases at diagnosis and D28(means19.4%and 19.9% respectively)than the control group (mean:3.6%) and this difference shows a high statistical significance***(P value < 0.001 in both)***. Also, the **percentage** of **CD96+** cells was significantly higher among **[CD34+/CD38-]** cells in AML cases at diagnosis and D28 (means22.5% and 26.6% respectively) than the control group(mean:2.5%) and this difference shows a high statistical significance***(P value < 0.001 in both)***. CD96 exhibited negative correlation to both peripheral blood as well as bone marrow blast percentages either at diagnosis or on day 28 post-induction.AML with differentiation (M2,3,4,5) was predominant FAB type in CD96 and CD123 positive cases. CD96 expression on day 28 was positively

correlated to its expression on day 0 as well as to CD123 expression at diagnosis with P-values of <0.001 and 0.034 respectively.CD96 positive expressors at diagnosis exhibited shorter PFS as compared to negative expressors, and shorter median overall survival but neither differences culminated into statistical significance. **Conclusion:**CD96 and 123 may be used as markers for detection of leukemic stem cells and may be used as markers of prognosis in adult AML ,so targeting therapy for these two marker may carry hope for adult patient with AML.

Key words: Acute myeloid leukemia,leukemic stem cell,CD123, CD96.

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List of Abbreviations

Af1q	All 1 fused gene from chromosome 1q
AKT	Protein kinase B
ALDH	Aldehyde dehydrogenase activity
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
AMMOL	Acute myelomonocytic leukemia
AMOL	Acute monoblastic leukemia
ANA	α naphthyl acetate
ANB	α naphthyl butyrate
ANC	Absolute neutrophilic count
APL	Acute promyelocytic leukemia
APL-V	Acute promyelocytic leukemia variant
ATO	arsenic trioxide
ATP	Adenosine-5'-triphosphate
ATRA	all-trans retinoic acid
BAALC	Brain and acute leukemia cytoplasmic
BCL-2	B-cell lymphoma 2
BCL-XL	B-cell lymphoma-extra- large
BCR-ABL	Breakpoint cluster region- Abelson
BM	**Bone marrow**
CAE	Chloroacetate esterase
CBF	Core binding factor complex
CD	Cluster of differentiation
CEBPα	CCAAT/enhancer binding-protein alpha
C fos	FBJ Murine osteosarcoma
CFU	colony-forming units

CLL1	C-type lectin-like molecule-1
CLPED	cleft lip/palate ectodermal dysplasia syndrome
CML	chronic myelogenous leukemia
CNAML	cytogenetically normal AML
CNS	Central nervous system
CR	Complete remission
CRi	Complete remission with incomplete hematologic recovery
CRTAM	Class-I MHC-restricted T-cell-associated molecule
DIC	Disseminated intravascular coagulopathy
DNAM-1	CD226 DNAX accessory molecule-1
EDTA	Ethylenediaminetetraacetic acid
EMD	extramedullary disease
EPO	Erythropoietin
ERG1	Early growth response 1
ERK1	extracellular signal-regulated kinase 1
ERK2	extracellular signal-regulated kinase 2
EVI1	Ecotropic viral integration site 1
FAB	French-American-British
FDCP1	murine factor dependent hematopoietic cell line
FISH	Fluorescence in situ hybridization
FITC	Fluorescein isothiocyanate
FLT3	Fms-like tyrosine kinase-3
FLT3-ITD	Fms-like tyrosine kinase 3- Internal tandem duplications
GATA2	GATA binding protein 2
G-CSF	Granulocyte colony-stimulating factor
GM-CSF	Granulocyte macrophage colony-stimulating factor
GM-CSFR	Granulocyte-macrophage colony-stimulating factor receptor
GEP	gene expression profiling

Grb2	growth factor receptor-bound protein-2
GST	glutathione S-transferases
Hb	Hemoglobin
HiDAC	High dose cytarabine
HIF	hypoxia-inducible factors
HLA	Human leucocyte antigen
HSC	Hematopoietic stem cells
HSCT	Haematopoietic stem cell transfusion
HUVEC	human umbilical vein endothelial cells
IDH1	Isocitrate dehydrogenase 1
IKB	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor
IL3	Inerleukin-3
IL5	Inerleukin-5
IL3R	Inerleukin-3 receptor
IL5R	Inerleukin-5 receptor
ITIM	immune-receptor tyrosine-based inhibitory motif
JNK	c-Jun amino-terminal kinases
KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog gene
KMT2A	Lysine methyltransferase 2A
K-Ras	Kirsten rat sarcoma viral oncogene
LDH	Lactate dehydrogenase
LP	lumbar puncture
LSCs	leukemic stem cells
LTC-IC	long-term culture-initiating cells
M4 Eos	M4 with eosinophil
MAC 1	Membrane attack complex 1