CD٦٤ Expression As Marker Of Monocytic Differentiation In Acute Myeloid Leukemia

Thesis

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ظهور سي دي ٦٤ كمميز لخلايا الوحيدات والوحيدات الاولية في ابيضاض الدم النقوي الحاد

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توطئة للحصول علي درجة الماجستير فى

الباثولوجيا الإكلينيكية والكيميائية

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بسم الله الرحمن الرحيم

"قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا

إلاَّ مَا عَلَّمْتَنَا

إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ"

صدق الله العظيم

سورة البقرةالآية (٣٢)

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And To The Soul of My Father.

Soha Abd Elkareem Hamed

List Of Abbreviations

ADH	: Anti diuretic hormone
Ag	: Antigen
AML	: Acute myeloid leukemia
ANLL	: Acute non lymphocytic leukemia
APL	: Acute promyelocytic leukemia
ATRA	: All trnasretinoic acid
BAALC	: Brain and acute leukemia cytoplsmic gene
Bcl-٢	: B-cell lymphoma ٢
BM	: Bone marrow
Ca	: Calcium
CAE	: Chloroacetate esterase
CBC	: Complete blood count
CBFβ	: Core binding factor β
CD	: Cluster of differentiation
CEBPA	: CCAAT/enhancer binding protein alpha
CGH	: Comparative genomic hybridization
C-KIT	: Steal factor
CML	: Chronic myeloid leukemia
CMV	: Cytomegalovirus
CNS	: Central nervous system
CR	: Complete remission
CRD ١	: First complete remission
DIC	: Disseminated intravascular coagulopathy
DNA	: Deoxy ribonucleic acid
EM	: Electron microscope
EPO	: Erythropoietin
FAB	: French –American –British classification
FAB-M٠	: Minimally differentiated acute myeloblastic leukemia
FAB-M١	: Acute myeloblastic leukemia, without maturation
FAB-M٢	: Acute myeloblastic leukemia, with granulocytic maturation
FAB-M٣	: Acute promyelocytic leukemia
FAB-M٤	: Acute myelomonocytic leukemia
FAB-M٥	: Acute monoblastic leukemia
FAB-M٦	: Erythroblastic leukemia
FAB-M٧	: Acute megakaryoblastic leukemia
FcγR	: Fc-gamma-receptor
FISH	: Fluorescence in-situ hybridization

List Of Abbreviations (Cont.)

FLT٣	: Fms-like tyrosine kinase٣
FMF	: Familial meiterranean fever
G-CSF	: Granulocyte –colony stimulating factors
GM-CSF	: Granulocyte-monocyte-colony stimulating factor
GVHD	: Graft versus host disease
HB	: Hemoglobin
HCT	: Hematopoietic stem cell transplantation
HGFs	: Hematopoietic growth factors
HLA	: Human leucocytic antigen
IFN-γ	: Interferon-gamma
Ig	: Immunoglobulines
IL	: Interleukin
IPT	: Immunophenotyping
ITDs	: Internal tandem duplications
K	: Potassium
LDH	: Serum lactate dehydrogenase
LM	: Light microscope
LN	: Lymph node
M-CSF	: Monocyte–colony stimulating factor
MDR	: Mutlidrug resistance
MDS	: Myelodysplastic syndrome
M-FISH	: Multicolor FISH
MLL	: Myeloid/lymphoid gene
MM	: Multiple myeloma
MoAb	: Monoclonal antibodies
MPD	: Myelo-proliferative disease
MPO	: Myeloperoxidase
MRD	: Minimal residual disease
Na	: Sodium
NEC	: Non erythroid cells
NPM	: Nucleophosmin
NSE	: Non specific esterase
PAS	: Periodic acid Schiff
PB	: Peripheral blood
PBSC	: Peripheral blood stem cells
PCR	: Polymerase chain reaction
PDGF-R	: Platelet derived growth factor receptor
Pgp	: P-glycoprotein

List Of Abbreviations (Cont.)

PMNs	: Polymorph nuclear leucocytes
PRINS	: Primed in situ hybridization
PT	: Prothrombin time
PTT	: Partial thromboblastin time
RARA	: Retinoic acid receptor alpha
RB	: Retinoblastoma protein
RBC	: Red blood cell
RNA	: Ribonucleic acid
RT-PCR	: Reverse transcriptase PCR
SB	: Sudan black stain
SCL	: Stem cell leukemia
SCT	: Stem cell transplantation
SD	: Standard deviation
SKY	: Spectral karyotyping
SLE	: Systemic lupus erythrematosus
SN	: Significance
TdT	: Terminal deoxynucleotidyl transferase
TLC	: Total leucocytic count
TNF-α	: Tumor necrosis factor-α
Topo II	: Topoisomerase II
TSG	: Tumor suppressor genes
VEGF	: Vascular endothelial growth factor
vWF	: Von Willebrand factor
WBC	: White blood cell
WHO	: World health organization
WT-١	: Wilms tumor-١ gene

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INTRODUCTION

Acute myeloid leukemia (AML) is a marrow-based clonal malignant disease of hematopoietic tissue, in which there is a replacement of normal bone marrow (BM) with abnormal primitive hematopoietic cells ***(Chee, ٢٠١١).*** It arises because of somatic mutation in pluripotent stem cells or slightly more differentiated progenitor cells, resulting in overgrowth of myeloblasts and other immature cells of myeloid lineage at the expense of other hematopoietic cells ***(Byrd, ٢٠١١).***

According to morphology, French-American-British (FAB) group divided AML into eight subtypes designated M٠ through M٧, based on the type of cells from which leukemia developed ***(Miller and Pihan, ٢٠٠٩).***

The World Health Organization (WHO) classification (٢٠٠٨) for hematopoietic neoplasm utilizes not only morphological findings but also all available information including genetic, immunophenotypic, biological and clinical features to define specific disease entities ***(Advani, ٢٠١١).***

AML is recognized as a heterogeneous molecular disease displaying characteristic patterns of surface antigens ***(Rowe, ٢٠٠٩)***. Flowcytometric immunopheno-

typing is widely used in diagnosis and subclassification of AML, and hence it plays an important role in instituting proper treatment plans ***(Dunphy, ٢٠١٠)***.

CD١٤ is a monocyte-associated antigen most widely used to identify AML with monocytic differentiation, however, it is observed that it is frequently diminished or absent in such cases ***(Krasinskas et al., ٢٠٠٧).***

CD٦٤ is a type of integral membrane glycoprotein known as Fc gamma receptor ١ (FCγR١), and constitutively found only on macrophages and mono-cytes ***(Nimmerjahn and Ravetch, ٢٠٠٦)***. Several recent studies concluded that CD٦٤ is highly sensitive and specific in distinguishing AML with monocytic component from other AML classes ***(Dunphy et al., ٢٠١٠ and Bruze, ٢٠١٠).***

AIM OF THE WORK

The aim of this study was to investigate the value of CD٦٤ expression in AML patients, to detect whether it can distinguish AML cases with monocytic differentiation, and to correlate its expression with different prognostic factors.