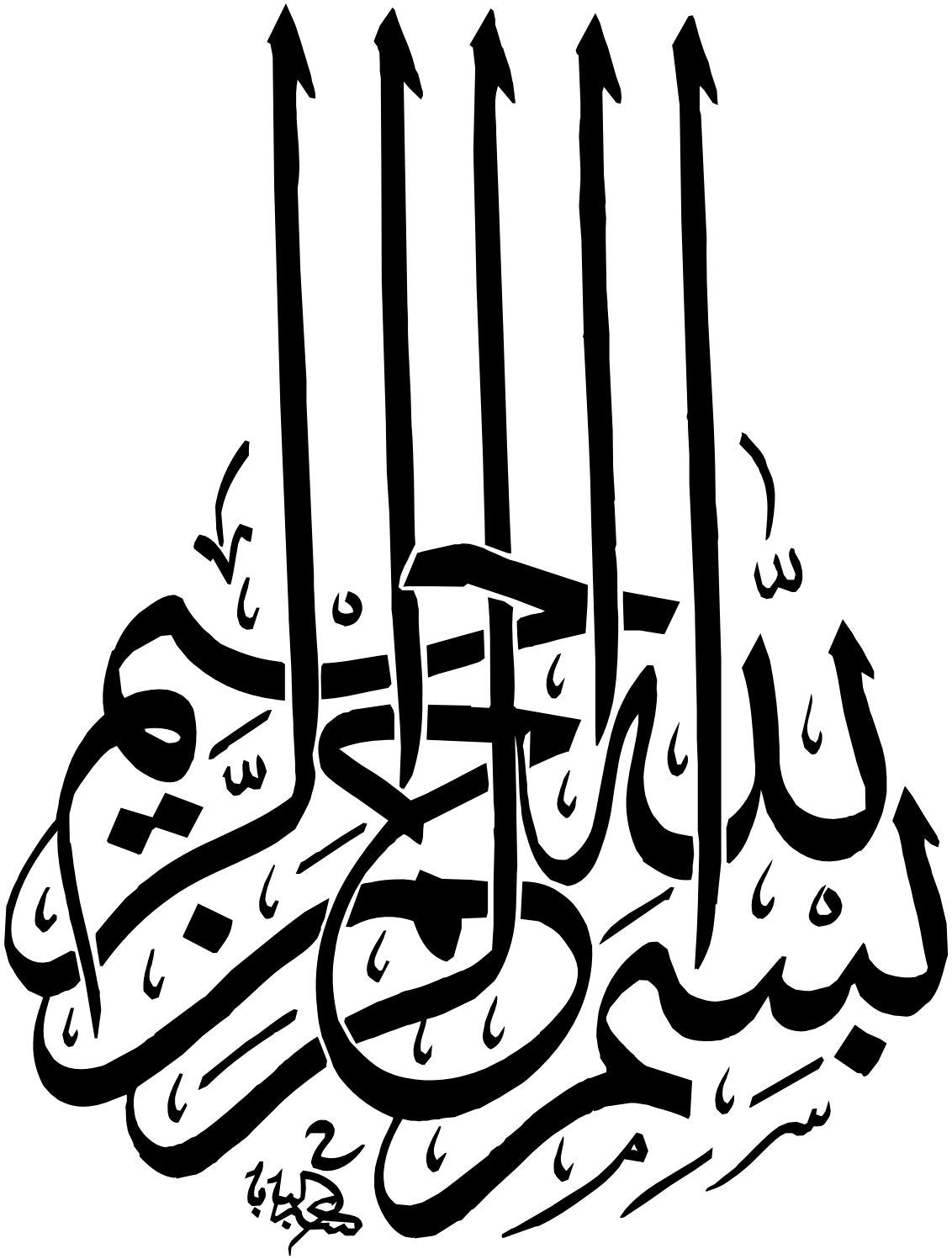
بسم الله الرحمن الرحيم

Detection of CXCL12 Gene polymorphism and CXCR4 Receptor Expression in Egyptian Acute Myeloid Leukemia Patiets

Thesis
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Abstract

CXCL12, a chemokine abundantly produced by the bone marrow microenvironment, and its receptor CXCR4 have crucial roles in malignant cell trafficking.In the present study CXCR4 expression was investigated by flowcytometry and CXCL12 G801A gene polymorphism was detected by PCR-RFLP assay in 42 patients with de novo AML as well as 35 normal subjects as a control group. The CXCR4 positive expression was found exclusively in AML patients and not in the control subjects. The incidence of positive CXCR4 receptor expression was in 54.8% of AML patients. The frequency of the CXCL12 genotypes among AML patient were: 54.8 % had a (GG) alleles genotype while 45.2 % had an (A) allele genotype (38.1 % were A/G & 7.1 % were A/A) while among the control group 82.9% had a (GG) alleles genotype and 17.1% had an (A) allele genotype (All were A/G). The CXCL12 A allele (A/G & A/A) genotype was significantly associated with extramedullary tissue infiltration which was found in 66.7% of CXCL12 A allele (A/G & A/A) genotype AML patients. There was a statistically significant relationship between the CXCL12 genotypes and CXCR4 expression and outcome of treatment. In CXCL12 A allele carrier (A/G & A/A) genotypes AML patients; 13.3% had favorable prognosis and 63% had unfavorable prognosis.In CXCR4 positive group 26.7% of patients had favorable prognosis and 70.4% had unfavorable prognosis .In conclusion CXCR4 expression predicts poor prognosis in AML and *CXCL12* G801A polymorphism is a genetic determinant involved in the clinical presentation of leukemia.

Key words: Acute myeloid leukemia (AML),CXC chemokine receptor 4(CXCR4),CXC chemokine 12(CXCL12)and restriction fragment length polymorphism(RFLP)

List of Abbreviations

Abbreviation	**The Full Term**
aa	Amino acid
ABL	Abelson strain of murine leukemia virus
ALL	Acute lymphoblastic leukemia
AMbL	Acute myeloblastic leukemia
AMgL	Acute megakaryocytic leukemia
AML	Acute myeloid leukemia
AMoL	Acute myelomonocytic leukemia
ANLL	Acute non lymphoblastic leukemia
AP	Acid phosphatase
ARA-C	cytarabine
ATRA	All trans retinoic acid
BAX	Bcl_2- associated protein
Bcl_2	B-cell lymphoma/leukemia-2 oncogene.
BCR	Break point cluster region
BM	Bone marrow
bp	Base pair
CBF	Core binding factor
CBFα	Core binding factor alpha subunit.

CBFβ	Core binding factor beta subunit.
CD	Cluster of differentiation
CEPBA	CCAAT/enhancer binding protein-α
CLL	Chronic lymphocytic leukemia
CML	Chronic myeloid leukemia
CNS	Central nervous system
CR	Complete remission
DFS	Disease free survival
DIC	Disseminated intravascular coagulopathy
DNA	Deoxyribonucleic acid
dNTPs	Deoxynucleoside triphosphate
DW	Distilled water
ECM	Extracellular matrix
EDTA	Ethylene diamine tetra-acetic acid
EM	Electron microscopy
ETO	Eight twenty one
EVI1	Ectopic virus integration 1
FAB	French American British
FLT3	Fetal liver tyrosine kinase 3
FLT3/ITD	Internal Tandem duplication
FLT3/LM	FLT3/length mutation.
FLT3-L	Fetal liver tyrosine kinase 3 ligand

G-CSF	Granulocyte colony stimulating factor
GI	Gastrointestinal
GM-CSF	Granulocyte macrophage colony stimulating factor
GPI	Glucose phosphate isomerase
Hb	Hemoglobin
HIF	Hypoxia inducible factor
HIV	Human immunodeficiency virus
HGFs	Hematopoietic growth factors
HLA	Human leucocyte antigen
HPCs	Hematopoetic progenitor cells
HSCs	Hematopoetic stem cells
IL	Interleukin
inv	Inversion
IPT	Immunophenotyping
LDH	Lactate dehydrogenase
LN	Lymph node
MAP	Mitogen activated protein
MAPK	Mitogen activated protein kinase
M-CSF	Macrophage colony stimulating factor
MDS	Myelodysplastic syndrome
MKL1	Megakaryocyte leukemia-1
ml	Milliliter

MLL	Mixed lineage leukemia
MLL T3	Mixed lineage leukemia translocated to,3
MMP	Matrix metalloroteinase
MPO	Myeloperoxidase
MRD	Minimal residual disease
MYH 11	Smooth muscle myosin heavy chain
NEC	Non- erythroid cells
NF-kB	Nuclear factor kappa beta
NHL	Non Hodgkin lymphoma
no	number
NOS	Not otherwise specified
NSE	Non specific esterase
OS	Overall survival
p	Short arm of the chromosome
P13	Phosphatidyl inositol.
P53	Protein 53 kilodalton
PB	Peripheral blood
PCR	Polymerase chain reaction
Plts	Platelets
PML	Promyelocytic leukemia
P-value	Probability value
PSC	Pluripotent stem cell

q	Long arm of the chromosome
RARα	Retinoic acid receptor alpha
RFLP	Restriction fragment length polymorphism
RNA	Ribonucleic acid
Rpm	Round per minute
SBB	Sudan black BCVA
SCF	Stem cell factor
SCT	Stem cell transplantation
SD	Standard deviation
SDF-1	Stromal cell-derived factor-1
SNP	Single nucleotide polymorphism
STAT	Signal transducer and activator of transcription
STK-1	Human stem cell kinase -1
t	Translocation
t-AML	Therapy related acute myeloid leukemia
TAMs	Tumor associated macrophages
Taq	Thermophilus aquaticus
TCR	T- Cell receptor.
TDT	Terminal deoxynucleotidyl transferase
TGF	Transforming growth factor
TLC	Total leucocytic count
TNF	Tumor necrosis factor

Tris-HCL	Tris-Hydrochloric Acid
UAL	Undifferentiated acute leukemia
UTR	Untranslated region
UV	Ultraviolet
VEGF	Vascular endothelial growth factor
VHL	Von Hipple-Lindau
VLA	Very late antigen
WBCs	White blood cells
WHO	World health organization
WT-1	Wilms` tumor gene-1

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