

DETECTION OF GLUTATHIONE-S-TRANSFERASE NULL GENOTYPES IN ACUTE AND CHRONIC MYELOID LEUKAEMIAS

Thesis

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بسم الله الرحمن الرحيم

"قالوا سبحانك لا علم لنا إلا ما علمتنا
إنك أنت العظيم الحكيم"

صدق الله العظيم

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List Of Abbreviation

A CML	Atypical CML.
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid leukaemia.
ANLL	Acute non lymphoblastic leukaemia
AP	Accelerated phase.
APL	Acute promyelocytic leukaemia.
ASCT	Autologus stem cell transplantation.
ATRA	All trans retinoic acid
AUL	Acute undifferentiated leukaemia.
BC	Blastic crisis.
BM	Bone marrow
BC	Blastic crisis.
BCR	Breakpoint cluster region.
Ca	Calcuim.
CAE	Chloroacetate esterase.
CALLA	Common acute lymphoblastic leukaemic antigen
CBC	Complete blood count.
CD	Cluster of differentiation
CDNB	1chloro 2, 4 dinitrobenzene.
CEL	Chronic eosinophilic leukaemia.
CFU	Colony forming unit.
CFU GEMM	Colony forming unit, granulocyte, erythroid &myeloid
CFU GM	Colony forming unit, granulocyte & monocyte
CHR	Complete haematological remission.
CI	Confidence interval.
CIMF	Chronic idiopathic myelofibrosis
CMML	Chronic myelomonocytic leukaemia
CMPD -U	Unclassified chronic myeloproliferative disorders
CNL	Chronic neutrophilic leukaemia.
CR	Complete remission.
Cyt	Cytoplasmic.
DAV	Doxorubicin vincristine .
DIC	Dissiminated intra vascular coagulopathy
DLCL	Diffuse large B cell lymphoma .
DNA	Deoxy ribonucleic acid.
ECM	Extracellular matrix

ELISA	Enzyme linked immunosorbant assay.
EM	Electron microscope.
ET	Essential thrombocythaemia.
FAB	French American British
FISH	Fluorescence In Situ Hybridization
FLT3	Fms like tyrosine kinase 3 receptor.
G CSF	Granulocyte colony stimulating factor.
GM CSF	Granulocyte
GST	Glutathione S Transferase
GSTM1	Glutathione s Transferase-Mu
GSTT1	Glutathione s Transferase-Theta
Hct	Haematocrit value.
HES	Hyper eosinophilic syndrome
HGFs	Haematopoietic growth factors.
HLA	Human leukocyte antigen.
HPLC	High performance liquid chromatography.
Ig	Immunoglobulin.
IL1	Interleukin one
IL4	Interleukin four
IL5	Interleukin five
IL6	Interleukin six
IL7	Interleukin seven
INF-α	Interferon-α.
IR	Incomplete remission.
JCML	Juvenile CML.
LDH	Lactate dehydrogenase.
LM	Light microscope.
MCD	Mast cell disease.
MCS	Monocyte colony stimulating factor
MDS	Myelodysplastic syndrome.
Mg Cl	Magnesium chloride.
MMM	Myelosclerosis with myeloid metaplasia
MPD	Myeloproliferative disorders.
MPO	Myeloperoxidase
MRD	Minimal residual disease.
NAP	Neutrophil alkaline phosphatase
NEC	Non erythroid cell.

NK	Natural killer.
NSE	Non specific esterase.
OR	Odd's ratio.
PAH	Polycyclic aromatic hydrocarbons.
PAS	Periodic acid Schiff.
PB	Peripheral blood
PCR	Polymerase chain reaction.
Ph. Chromosome	Philadelphia chromosome
PV	Polycythaemia Vera.
RB	Retinoblastoma.
RBC	Red blood cells.
ROS	Reactive oxygen species.
SBB	Sudan black B.
SCF	Stem cell factor.
SD	Standard deviation.
SDS PGAGE	Soduim Diacyl Sulphate Polyacrylamide Gel Electrophoresis.
Sm	Surface membrane.
SPSS	Statistical Package for the Social Science.
SWOG	South west oncology group
t AML	Therapy related AML.
Taq	Thermus aquaticus
TdT	Terminal deoxy nucleotydyl transferase.
UAL	Undifferentiated acute leukaemia.
WBC	White blood cells
WT1	Wilm's tumour gene.

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Abstract

Glutathione-S-transferases (GSTs) are xenobiotic metabolizing enzymes contributing to the detoxification of activating carcinogens as environmental pollutants, benzopyrenes and other polycyclic aromatic hydrocarbons. Inherited differences in the capacity of these enzymes might be an important genetic factor leading to susceptibility to cancer .

Glutathione-S-transferases (GSTs) have been implicated as susceptibility genes in this context for a number of cancers including hematological malignancies like AML – CML . Individuals carrying less efficient alleles of detoxifying genes, vary in their ability to metabolize carcinogens and hence to detoxify chemicals, leading to different risk in getting cancer ..

Myeloid leukaemias are heterogeneous diseases which are subdivided into acute and chronic myeloid leukaemias. Acute myeloid leukaemia is neoplastic proliferation in haematopoietic precursor cells, resulting in overgrowth of myeloblast and other immature myeloid cells. The malignant cells replace the bone marrow, circulate in the blood and may accumulate in other tissues.

Acute myeloid leukaemia (AML) in adults has a 20% 5-years disease-free survival, despite treatment with aggressive cytotoxic chemotherapy. For several decades AML has been characterized on the basis of morphology, special stain, cytogenetics, and cell surface markers. However, recent studies on molecular characterization of