

# **EXPRESSION OF THE ANTIAPOPTOTIC GENE SURVIVIN IN ACUTE LEUKEMIAS**

*Thesis*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ رَبِّ زِدْنِي عِلْمًا

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## DEDICATION

*I dedicate this work to my supportive  
and loyal family and friends  
for all their sacrifices*

## *ABSTRACT*

Acute leukemias are clonal expansions of uncommitted or partially committed haematopoietic precursor cells.

Abnormalities in the control of programmed cell death (apoptosis) play an important role in leukemogenesis. Survivin is a member of Inhibitor of Apoptosis Proteins (IAP) family. Survivin prevents apoptosis by blocking caspase activity. Dramatic overexpression of Survivin was demonstrated in solid tumours of pancreas, oesophagus, lung as well as in leukemias and lymphomas. The present study assessed Survivin gene expression using Real-Time PCR.

**Key words:**

Acute leukemias - Apoptosis- Survivin- Real-Time PCR.

## *LIST OF ABBREVIATIONS*

A:	Adenine
aa:	amino acid
ABL:	Abelson gene
Ala:	Alanine
ALL :	Acute Lymphoblastic Leukemia
ALP :	Alkaline Phosphatase
AML:	Acute Myeloid Leukemia
AML1:	Acute Myeloid Leukemia1 gene
ANA:	Alpha-naphthyl acetate esterase
ANB:	Alpha-naphthyl butyrate esterase
Anti MPO :	Anti Myeloperoxidase
Anti TCR $\alpha\beta$ :	Anti T-Cell Receptor $\alpha\beta$
Anti TCR $\gamma\delta$ :	Anti T-Cell Receptor $\gamma\delta$
AP:	Acid Phosphatase
Apaf-1:	Apoptosis activating factor-1
APL:	Acute Promyelocytic Leukemia (M3)
Ara-C:	Cytosine arabinoside
Asp :	Aspartic acid
ASP 71:	Aspartic acid 71
ATL :	Adult T-cell Leukemia
ATRA :	All-trans-retinoic acid
B:	Basophils
Bax:	Bcl-2 associated x protein

Bcl-2:	B-cell leukemia lymphoma -2
BCR:	Breakpoint Cluster Region
BIR:	Baculoviral Inhibitor of apoptosis protein Repeat
BIRS:	Baculoviral Inhibitor of apoptosis protein Repeats
Bl :	Blast
BM:	Bone Marrow
B-ME:	B-MercaptoEthanol
BMT :	Bone Marrow Transplantation
bp:	base pair
c/cell :	copy number per cell
c:	cytoplasmic
C:	Cytosine
Ca:	Calcium
CACCC motifs :	Cytosine Adenine Cytosine Cytosine Cytosine motifs
cal :	calibrator
CALLA:	Common Acute Lymphoblastic Leukemia Antigen.
caspases :	cysteine aspartate specific proteases
CBC:	Complete Blood Count
CBF $\alpha$ :	Core Binding Factor $\alpha$ gene
CBF $\beta$ :	Core Binding Factor $\beta$ gene
CD 4:	T-Helper lymphocyte
CD 8 :	T-Cytotoxic lymphocyte
CD:	Cluster Differentiation
CD34:	Stem cell marker
CDKIs:	Cyclin Dependent kinase Inhibitors

CDks:	Cyclin Dependent kinases
cDNA:	copy DNA
CF:	Calibrator Fluorescence
cIg:	cytoplasmic Immunoglobulin
CLL :	Chronic Lymphocytic Leukemia
CML:	Chronic Myeloid Leukemia
CNS:	Central Nervous System
Conc:	Concentration
CP :	Crossing Point
CR :	Complete Remission
CSF:	Cerebrospinal Fluid
C <sub>t</sub> :	Comparative threshold
CTLs:	Cytotoxic T-lymphocytes
Cys/His:	Cysteine/ Histidine
cyt CD22:	cytoplasmic CD22
cyt IgM :	cytoplasmic IgM
dATP :	deoxy Adenosine triphosphate
dCTP :	deoxy Cytidine triphosphate
DD:	Death Domain
DED:	Death Effector Domain
del:	deletion
DFS:	Disease Free Survival
dGTP :	deoxy Guanosine triphosphate
DIC:	Disseminated Intravascular Coagulation
Diff Leucocytic Count:	Differential Leucocytic Count



DNA:	Deoxyribonucleic acid
dNTP:	deoxy Nucleotides triphosphates
ds DNA:	double stranded DNA
dTTP :	deoxy Thymidine triphosphate
e.g :	For example
E:	Effector Protease Receptor-1 gene
E:	Efficiency
EC:	Endothelial Cells
EDTA :	Ethylenedimine tetraacetic acid
EGIL:	European Group for the Immunological Characterization of Leukemia
Eqs:	Equations
ETO :	Eight-Twenty one gene
F:	Female
FAB:	French American British
FADD:	Fas Associated Death Domain Protein
Fas L:	Fas Ligand
FISH:	Fluorescence Insitu Hybridization
FLT3:	Fetal Liver Tyrosine kinase 3
FRET :	Fluorescence Resonance Energy Transfer
G:	Guanine
G0:	Gap 0
G1:	Gap 1
G2:	Gap 2
GAPDH :	Glyceraldehyde-3 Phosphate Dehydrogenase

GF:	Glyceraldehyde-3 Phosphate Dehydrogenase Forward Primer
GR:	Glyceraldehyde-3 Phosphate Dehydrogenase Reverse Primer
GT rich sequences:	Guanine Thymine rich sequences
GvHD:	Graft versus Host Disease
GvL:	Graft versus Leukemia
HB:	Haemoglobin
HCT:	Haematocrit
HLA-DR:	Human Leucocyte antigen class II
HPV DNA:	Human Papilloma Virus Deoxyribonucleic acid
HPV:	Human Papilloma Virus
hr:	hour
HSILS:	High-grade Squamous Intraepithelial Lesions
i	isochromosome
I.P.T:	Immunophenotyping
IAP:	Inhibitor of Apoptosis Proteins
Ig:	Immunoglobulin
inv:	inversion
Je:	Juvenile
Kb	Kilobase
KDa:	KiloDalton atom
KLF-5:	Krupple Like Factor-5
L:	Lymphocyte
LC:	Light Cycler

LDH:	Lactate Dehydrogenase
LSILS:	Low-grade Squamous Intraepithelial Lesions
M phase:	Mitosis phase
m:	membranous
M3v:	M3 variant
M4Eso:	M4 associated with Eosinophilia
MAC:	Membrane Attack Complex
MCH:	Mean Corpuscular Haemoglobin
MCHC:	Mean Corpuscular Haemoglobin Concentration
MCV:	Mean Corpuscular Volume
Mdm2:	Murine double minute2 gene
MDR-1:	Multi Drug Resistance-1
MDS:	Myelodysplastic Syndrome
MF :	Mean Fluorescence
min:	minute
MLL:	Mixed Lineage Leukemia gene
MPD :	Myeloproliferative Disorders
MPO:	Myeloperoxidase
mRNA	messenger RNA
Myelo:	Myelocyte
MYH11:	Smooth Muscle Myosine Heavy Chain 11 gene
n:	nuclear
NaF:	Sodium Fluoride
NCI :	National Cancer Institute
NK:	Natural Killer cells

Normo :	Normoblast
NRC:	National Research Centre
NSE:	Nonspecific esterase
Oligos :	Oligonucleotides
ORF:	Open Reading Frame
ORO :	Oil Red O
OS:	Overall Survival
P.B blasts :	Peripheral Blood blasts
p:	Short arm of chromosome
PAS:	Periodic Acid Schiff
PCR :	Polymerase Chain Reaction
Ph:	Philadelphia Chromosome
Pl:	Plasma cell
Plt :	Platelets
PML :	Promyelocytic Leukemia gene
PR:	Partial Remission
Pro:	Promyelocyte
Proerythro :	Proerythroblast
PS:	Phosphatidylserine
q:	Long arm of chromosome
R:	Ratio
RAR $\alpha$ :	Retinoic Acid Receptor $\alpha$ gene
Rb:	Retinoblastoma
RBCs:	Red Blood Corpuscles
Real-Time PCR :	Real Time Polymerase Chain Reaction

rec DNA:	recombinant DNA
rec RNA :	recombinant RNA
ref :	reference
RFS:	Relapse Free Survival
RNA:	Ribonucleic acid
ROS:	Reactive Oxygen Species
RQ:	Relative Quantitation
RT Buffer :	Reverse Transcriptase Buffer
RT enzyme	Reverse Transcriptase enzyme
RT:	Reverse Transcription
RT-PCR:	Reverse Transcription- Polymerase Chain Reaction
S phase :	Synthesis phase
S:	Survivin gene
SBB:	Sudan Black B
SD :	Standard Deviation
SE:	Specificesterase
sec:	second
Seg:	Segment
SF:	Survivin Forward Primer
sIg :	surface Immunoglobulin
Smac :	Second mitochondria-derived activator of caspase
Sp/KLF:	Specific proteins/ Kruppel Like Factors
SR:	Survivin Reverse Primer
St:	Staff
STAT3:	Signal Transducer And Activator of Transcription 3

T/2:	Half-life
t:	translocation
T:	Thymine
t-AML:	therapy related-AML
TCC:	Transitional Cell Carcinoma.
TCR:	T-Cell Receptor
TdT:	Terminal deoxynucleotide transferase
TGA:	Thymine Guanine Adenine
TGF $\beta$ :	Transforming Growth Factor $\beta$
Thr 34:	Threonine at position 34
TLC:	Total Leucocytic Count
t-MDS:	therapy related-MDS
TNF $\alpha$ :	Tumour Necrosis Factor $\alpha$
TNF-R:	Tumour Necrosis Factor- Receptor
TRADD :	TNF- Receptor Associated Death Domain Protein
TRAIL :	TNF-Related Apoptosis Inducing Ligand
tRNA	transfer Ribonucleic acid
V:	Variables
VEGF:	Vascular Endothelial Growth factor
WBC :	White Blood Cells
WHO:	World Health Organization.
$\Delta$ :	Delta
-5:	Monosomy 5
-7:	Monosomy 7

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