*h*TERC Gene Amplification Detection by FISH in Acute Myeloid Leukemia Patients

Thesis

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الكشف عن تضاعف جين ال *h*TERC باستخدام تقنية التهجين الموضعي الفلوريسينتي في مرضى الابيضاض النقيي الحاد

رسالة
توطئة للحصول علي درجة الماجستير
في الباثولوجيا الإكلينية و الكيميائية

مقدمة من
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SUMMARY AND CONCLUSION

Acute myeloid leukemia describes a heterogenous group of hematological disorders characterized by a block in the terminal differentiation of a particular hematopoietic cell lineage. Cytogenetic and molecular assays have allowed patients' follow up aiming for detection of minimal residual disease, prediction of patients' outcome, in addition to providing the rationale for designing novel molecular-targeted therapeutic strategies.

Human telomerase RNA componant (hTERC), encoded by the hTERC gene is frequently amplified in human tumors, which indicates that the hTERC gene may be a target for amplification during the transformation of human malignancies including hematological malignancies. This genetic event has implications in diagnosis, prognosis and therapeutics of cancer.

In this regard, this study aimed to detect hTERC gene amplification in AML patients by FISH analysis and its relation to the standard prognostic factors.

In the current work, BM or PB samples were obtained from 21 adult AML patients, presented at the Hematology/Onclology Unit, Ain Shams University Hospitals. The patients were further divided into two groups; group I (12 patients) containing newly diagnosed AML patients and a relapsed case and group II (8 patients) containing patients taken at 28^{th} day of chemotherapy.

All patients were subjected to complete history, thorough clinical examination and laboratory investigations including: complete hemogram, bone marrow aspiration with examination of Leishman-stained peripheral blood and bone marrow smears, immunophenotyping, karyotyping and detection of hTERC gene amplification using FISH technique.

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Islam Fadel

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List of Abbreviations

A	Alpha
B	Beta
χ^2	Chi-square
-	Monosomy
+	Trisomy
°C	Degrees centigrade
µ	Micro
ALL	Acute lymphoblastic leukemia
ALT	Alternative Lengthening of Telomeres
AML	Acute myeloid leukemia
AMML	Acute myelomonocytic leukemia
AP	Acid Phosphatase
AP1	Activator protein 1
APL	Acute promyelocytic leukemia
ATRA	All-trans retinoic acid
BAALC	Brain and acute leukemia, cytoplasmic
BM	Bone Marrow
bp	Base Pair
c	Cytoplasmic
CBFβ	Core binding factor β
CCA	Conventional Cytogenetic Analysis
CD	Cluster of differentiation
cDNA	Complementary DNA
CEBPA	CCAAT/enhancer-binding protein alpha
CGH	Comparative Genomic Hybridization
CIR	crude incidence rate of cancer
c-KIT	Proto-oncogene tyrosine-protein kinase
CML	Chronic myeloid leukemia
c-myc	Cellular myelocytomatosis
CN	Cytogenetically normal
CNS	Central nervous system
CpG	Cytosine followed by Guanine on the same strand
CR	Clinical remission
CRD	Complete remission duration
C-terminal	Carboxyl terminal
DAPI II	4',6-diamidino-2-phenylindole

Del	Deletion
D-FISH	Double fusion Fluorescence In Situ Hybridization
DFS	Disease free survival
DIC	Disseminated intravascular coagulopathy
DKC	dyskeratosis congenita
DKC1	dyskeratosis congenita gene 1
DNA	Deoxyribonucleic acid
DSB	Double strand breaks
DW	Distilled water
EM	Electron microscopy
EFS	Event free survival
ETS	E-twenty six family of transcription factors
ERG	ETS-related gene
FAB	French-American-British
FdU	Fluorodeoxyuridine
FISH	Fluorescence In Situ Hybridization
FLT3	FMS-like tyrosine kinase 3
FLT3-TKD	Tyrosine kinase domain of FLT3
G	Guanine
gm	Gram
G1	G1 Phase in cell cycle the Pre-synthetic phase
G-banding	Giemsa banding
GEP	Gene expression profiling
G-quadruplex	Guanine-quadruplex
G-rich	Guanine -rich
H	Histone
H/ACA	RNA-protein complex component
H2AX	a phosphorylated variant of histone 2A
H3	Histone 3
H4	Histone 4
HB	Hemoglobin
HCL	Hydrochloric acid
HEST1A	Human ever shorter telomeres-1
HiDAC	High-dose cytarabine
HIF-1	hypoxia-inducible factor 1
HLA	Human leucocyte antigene
hMSC	Human mesenchymal stem cells
hnRNP A1	Heterogenous nuclear ribonucleoprotein A1

hnRNP C	Heterogenous nuclear ribonucleoprotein C
hnRNP D	Heterogenous nuclear ribonucleoprotein D
Hox	Homeobox proteins
HR	Homologous recombination
HRE	Hypoxia response element
HSCT	Hematopoietic stem-cell transplantation
hsp 90	Heat-shock protein 90
HSP70-1	Heat-shock-70 kDa protein
HSP90A	Heat-shock-90 kDa protein 1, alfa
hSTAU	Human staufen homolog; double-stranded RNA-binding protein
hTERC	Human telomerase RNA component
hTERT	Telomerase reverse transcriptase
hTP1	Human telomerase-associated protein 1
Inv	Invesion
ITD	Internal tandem duplication
kb	Kilo-base
kDa	Kilo Dalton
K-EDTA	K-ethylene diamine tetraacetic acid
LDH	Lactate dehydrogenase
LN	lymph node
LSP	Locus specific probe
M1,2	Mortality phase 1, 2
MAPK	mitogen-activated protein kinase
Mb	Mega base
MDM2	Murine double minute
MDR	Multidrug resistance
MDS	Myelodysplastic syndrome
MEKK1	Mitogen-activated protein kinase kinase kinase 1
MFC	Multiparameter Flow Cytometry
MLL	Mixed lineage leukemia lymphoma gene
mm^3	Cubic millimeter
MPO	Myeloperoxidase
MRD	Minimal residual disease
mRNA	Massenger ribonucleic acid
MW	Molecular weight
MYH11	Myosin heavy chain 11
n	Repeats

NaF	Sodium floride
NF-Y	Nuclear Factor Y
NHEJ	Non homologous end joining
NOLA1	Nucleolar protein family A, member 1
NOLA2	Nucleolar protein family A, member 2
NOLA3	Nucleolar protein family A, member 3
NP40	Tergitol-type NP-40, (nonyl phenoxypolyethoxylethanol)
NPM	Nucleuphosmin
NPMc+	Nucleuphosmin (cytoplasmic form)
nt	nucleotide
N-terminal	Amino terminal
OS	Overall survival
P23	Unactive progesterone receptor 23 kD
P53	Tumor protein 53
PAS	Periodic Acid Schiff's
PB	Peripheral blood
PCR	Polymerase chain reaction
PI 3-kinase	phosphatidylinositol 3-kinase
Pin2	NIMA-interacting protein 2. A splicing isoform from TRF1 gene
PinX1	TRF1/Pin2-interacting protein 1
PLT	Platelet
PML-RARA	Promyelocytic leukemia/ Retinoic acid receptor alpha
PMT	Photo-multiplicator
POT1	Protection of telomeres 1
pRb	Retinoblastoma protein
PTD	Partial tandem duplication
PTH	Parathyroid hormone
Rap1	Repressor activator protein 1
RAR	retinoic acid receptor
RNA	Ribonucleic acid
rpm	Revolution per minute
RQ-PCR	Real time quantitative PCR
RT-PCR	Reverse transcription-polymerase chain reaction
SBB	Sudan Black B
scaRNA	Small Cajal body-specific RNAs
SD	Standard deviation

SnoRNA	Small nucleolar RNA
Sp1	Specificity Protein 1
Sp3	Specificity Protein 3
SSC	Standard saline citrate
t	Translocation
T” loop	Telomere loop
TCR	T cell Receptor
TdT	Terminal deoxynucleotidyl transferase.
TIN2	TRF1-interacting protein 2
TLC	Total leucocytic count
TPP1	Tripeptidyl peptidase 1
TRAP	Telomere repeat amplification protocol
TRF1	Telomere repeat binding factor 1
TRF2	Telomere repeat binding factor2
WBCs	White blood cells
WHO	World Health Organization
yr	Year

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