PLASMA CIRCULATING HUMAN TELOMERASE REVERSE TRANSCRIPTASE GENE AS A USEFUL MARKER FOR EARLY DETECTION OF LUNG CANCER

Thesis

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BY

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Abstract

Telomeres are specialized DNA–protein structures that cap the ends of linear chromosomes. Telomerase is a large ribonucleoprotein (RNP) complex that maintains telomeric DNA. Over 80% of human cancers show an activation of telomerase. The present study aimed to report the development of a quantitative assay for the measurement of hTERT expression in plasma of cancer lung patients based on real-time quantitative RT-PCR (qRT-PCR). The results of the study showed that the level of the enzyme in plasma increases in 73% of the study group. The sensitivity and the specificity were 73.7 &90.0 respectively.

(Key Words):

(Telomerase enzyme – cancer lung- free RNA in plasma)

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List of Abbreviation

53BP1	p53 Binding Protein 1
ADC	adenocarcinoma
ALT	alternative lengthening of telomere
ATM	ataxia telangiectasia mutated homolog
ATR	ataxia telangiectasia and Rad3 related
BLM,	Bloom syndrome
BRCA1	Breast Cancer Gene 1
BRCT motif proteins	Base Repair Cycle Time
CD	Cluster of differentiation
CD4+ cells	helper T-lymphocytes
CD8 cells	cytotoxic T-lymphocytes
cDNA	Complementary DNA
CEA	carcinoembryonic antigen
CHART	Continuous hyperfractionated accelerated radiotherapy
CHK1	CHeckpoint Kinase
CHK2	CHK2 checkpoint homolog
c-Myc	myelocytomatosis viral oncogene
CR4	CR4–CR5 domain of mammalian telomerase RNA
CR5	CR4–CR5 domain of mammalian telomerase RNA
cRNA	Complementary Ribonucleic Acid
CTL	cytotoxic T lymphocyte
Cy3	Cyanine 3
Cyfra 21-1	Cytokeratin 19 fragments
DCs	dendritic cells

DKC	Dyskeratosis congenita
DNA	Deoxyribose Nucleic Acid
DNA PK	DNA-dependent Protein Kinase
dNTP	Deoxynucleotid triphosphate
DSBs	double stranded breaks
dsDNA	double-stranded DNA
dTTP	deoxy thymidine triphosphate
dUTP	Deoxyuridine Triphosphate
ECOG PS	Eastern Cooperative Oncology Group Performance Status
EGFR	epidermal growth factor receptor
ELISA	The Enzyme-Linked ImmunoSorbent Assay
erb-b2	erythroblastic leukemia viral oncogene homolog 2
ERα	Estrogen receptor-α
FDG	Fluorodeoxyglucose
FDG-PET	Positron Emission Tomography
FISH	fluorescence in situ hybridization
FITC	fluorescein isothiocyanate
FNA	fine needle aspiration
FNAC	fine needle aspiration cytology
Gar1	gibberellin responsive1
GLUT4	insulin-responsive glucose transporter 4
Grb14	Growth factor receptor-bound protein 14
H/ACA	A ribonucleoprotein complex containing small nucleolar RNA of the box H/ACA type.
H2AX	H2A histone family, member X
H3-K9	histone H3-K9
HEK 293	Human Embryonic Kidney cells

HLA	human leukocyte antigen
HR	homologous recombinational repair
HRP-1	Hepatoma-Derived Growth Factor-Related Protein 1
hTERC	Human Telomerase RNA component
hTR	Human Telomerase RNA component
hTRT	Human Telomerase Reverse Transcriptase
HuVec	(human umbilical vein endothelial
IRAP	Interleukin-1 Receptor Antagonist Protein
IS	Internal standard
ISH	in situ hybridization
ISSLC	The International System for Staging Lung Cancer
ITAS	internal telomerase assay standard
Ki-67	A cell cycle and tumor growth marker which can be readily detected by immunocytochemistry methods. It is a nuclear antigen present only in the nuclei of cycling cells.
KPS	The Karnofsky Performance Status
Ku	is one component of a protein complex, Ku70 and Ku80, that functions as a heterodimer to bind DNA double-strand breaks and activates DNA-dependent protein kinase
Ku70	Ku70 is part of the non-homologous end joining (NHEJ) machinery involved in DNA double-stranded break (DSB) repair
Ku86	Ku86 is part of the non-homologous end joining (NHEJ) machinery involved in DNA double-stranded break (DSB) repair
MAPK	Mitogen-activated protein kinase
MDC1	Mediator of DNA damage checkpoint 1
MHC	major histocompatibility complex
MRE11	Meiotic recombination 11
Mre11	meiotic recombination 11

MRI	Magnetic Resonance Imaging
MRN	DNA damage repair complexMre11-Rad50-Nbs1
mRNA	Messenger RNA
Nbs1	Nibrin
NBS1	Nijmegen breakage syndrome 1(Mre11 complex subunit Nbs1)
NFBD1	nuclear factor with BRCT domains protein1
NHEJ	non-homologous DNA end-joining
Nhp2	non-histone chromosome protein 2
Nop10	nucleolar protein 10
NSCLC	Non-small-cell lung cancer
NSE	nucleotide sugar epimerase Neuron-specific enolase
p185(c-neu)	A cell surface protein-tyrosine kinase receptor that is found to be overexpressed in a significant number of adenocarcinomas.
P53	tumor suppressor protein p53
PAGE	Polyacrilamide gel electrophoresis
PARP	poly-ADP ribosylases
PCa	Prostate cancer
PCR	Polymerase chain reaction
PINX1	telomere length-control protein
PNA	peptide nucleic acid
POT1	protection of telomeres 1 homolog
PRINS	primed in situ labeling
RAP1	Repressor/Activator Protein: transcription factor
RecQ	ATP-dependent DNA helicase RecQ
RLT Buffer	RNeasy Lysis Buffer
RMN	RAD50-MRE11-NBS1

RNA	Ribose Nucleic Acid
RNP	ribonucleoprotein
RT-PCR	Reverse transcriptase-PCR
SCCA	Squamous Cell Carcinoma Antigen
SCLC	small cell lung carcinoma
snoRNPs,	small nucleolar ribonucleoproteins Small nucleolar RNAs
TANK1	Tankyrase 1(TRF1-interacting ankyrin-related ADP-ribose polymerase)
TANK2	Tankyrase 2 (TRF1-interacting ankyrin-related ADP-ribose polymerase)
Taz1	Tafazzin(transcriptional coactivator protein zinc-containing)
TBE	template boundary element
TBNA	Transbronchial needle aspiration
TER	Telomerase RNA component
TERC	Telomerase RNA component
TERT	Telomerase Reverse Transcriptase
TIN2	TRF 1-interacting nuclear factor 2
TNM staging	Tumor-no
TPA	tissue polypeptide antigen
TRAP	telomeric repeat amplification protocol
TRF	Telomeric repeat binding factor
TRF1	Telomere repeat binding factor-1
TRF2	Telomere repeat binding factor-2
TTNA	transthoracic needle aspiration biopsy
UNG	uracil-N-glycosylase
VEGF	vascular endothelial growth factor
WRN	WERNER SYNDROME ,Werner Syndrome helicase; Werner syndrome protein

WS	Werner Syndrome