بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأفلام قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار المناد الم

بعض الوثائـــق الأصليــة تالفـه

بالرسالة صفحات لم ترد بالاصل

Telomerase Enzyme Activity in Hepatocelluar Carcinoma Patients With and Without Viral Infection

A Thesis Submitted in Partial Fulfillment of the Master Degree in Biochemistry

Submitted By
Amany Yousef El-Kazaz

M.B.B.Ch, 1993

Supervisors

Prof. Dr. Taher Ibrahim El-Serafi

Prof. of Biochemistry
Faculty of Medicine – Suez Canal University

Dr. Mohamed Tarek M. Ali Mansour

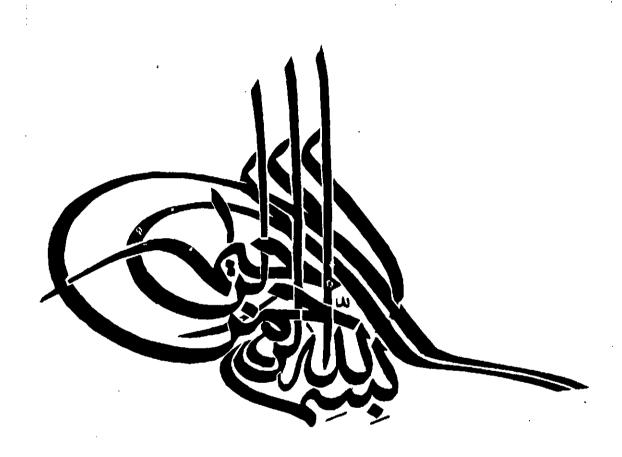
Assist. Prof. of Virology and Immunology
Cancer Institute – Cairo University

Dr. Samir Mohamed Abdel-Moneim

Assist. Prof. of Biochemistry
Faculty of Medicine – Suez Canal University

2 ×

Faculty of Medicine Suez Canal University 2000



ACKNOWLEDGMENT

Control Watch Life Company

First and foremost, I thank God, the beneficent and the merciful.

1

U

Many people helped me during the preparation of the thesis I would like to thank the following in particular:

- Prof. Dr. Taher El-Serafi, Professor and head of Biochemistry Department, Faculty of Medicine, Suez Canal University, for his generous help, kind supervision, expert guidance and for reading and re-reading this work aiming for perfection.
- Dr. M. Tarek M. Ali Mansour, Assistant Prof. of Virology and Immunology, National Cancer Institute, Cairo University, for his clarity of thoughts, valuable suggestions and for being a source of continual stimulation during actual work.
- Dr. Samir M. Abd El-Moneim, Assistant Prof. of Biochemistry, Faculty of Medicine, Suez Canal University for his continuous encouragement and unfailing support.
- Dr. Emad Abd El-Fatah, Assistant Prof. of Biochemistry, Faculty of Medicine, Suez Canal University, for his judicious guidance and support and his expert guidance.

CONTENTS

	Page
Introduction	1
Aim of the Work	7
Review of Literature	8
Telomere structure and function	8
• Telomerase	10
- Telomerase biochemistry	12
- In vivo effects of telomerase alteration	18
- Replication of Telomeric DNA	25
- The telomerase reaction	29
- The mechnism of telomeric DNA synthesis by telomerase	30
- Telomeres, Telomerase, Cellular aging and immortality	33
- Telomeres, telomerase and cancer	37
Hepatocellular carcinoma	44
Viral hepatitis	51
Materials and Methods	60
Results	70
Discussion	94
Summary and Conclusion	102
Recommendation	104
References	105
Appendix	
Arabic Summary	

LIST OF ABBREVIATION

A Adenine
C Cytosine

C Cytosine
Cdc Cell division cycle

DIG Digoxigenin

DNA Deoxyribonucleic acid

dNTp Deoxy nucleotide triphosphate

ELISA Enzyme linked immunosorbant assay

Est Ever shortening telomere

Fig. Figure Guanine

HBV Hepatitis B virus

HCC Hepatocellular Carcinoma

HCV Hepatitis C virus

hTRT Human Telomerase reverse transcriptase

Kbp Kilo base pair
Kd Kilodalton
M Mitosis

MTP Microtitre plate

PCR Polymerase chain reaction

POD Peroxidase

Rap Repressor activator protein

RNA Ribonucleic acid

rpm Revolution perminute

rTp Replication telomere protein

SD Standard deviation
SE Standard error

T Thymine

Taq Thermus aquaticus

TBp Telomere binding protein

TEL Telomerase

TLC Telomerase component

TLP Telonerase protein
TMB Tetramethyl benzid

TMB Tetramethyl benzidine
TRAP Telomeric repeat amplification protocol

TRF Telomere repeat binding factor

LIST OF TABLES

		Page		
Table (1)	List of telomere-binding proteins from			
	Various Organisms	21		
Table (2)	Sex distribution among all tissue samples of			
	HCC	72		
Table (3)	Age distribution among all tissue samples	73		
Table (4)	Table (4) Sex distribution among HCC only, HCC with			
	HBV and HCC with HCV	74		
Table (5)	Age distribution among HCC only, HCC with			
	HBV and HCC with HCV	75		
Table (6)	Table (6) Distribution of pathological grades of HC			
	among HCC only, HCC with HBV and HCC			
	with HCV	76		
Table (7)	Telomerase activity among all tissue samples			
	of HCC	77		
Table (8)	Telomerase activity among HCC only, HCC			
	with HBV and HCC with HCV			
Table (9)	Relationship between telomerase activity and			
	sex among HCC samples	80		
Table (10)	Relationship between telomerase activity and			
	age ámong HCC samples	81		
Table (11)	Relationship between telomerase activity and			
	pathological grades of HCC	82		
Table (12)	Sex distribution among telomerase positive			
	samples including HCC only, HCC with			
	HBV and HCC with HCV	84		
Table (13)	Age distribution among telomerase positive			
	samples including HCC only, HCC with			
	HBV and HCC with HCV	85		

		Page
Table (14)	Distribution of pathological grades among	
	telomerase positive samples including HCC	
	only, HCC with HBV and HCC with HCV	86
Table (15)	Mean value of (ALT) (u/L) in telomerase	
	positive and telomerase negative in HCC	
	tissue samples	88
Table (16)	Mean value of AST (u/L) in telomerase	
	positive and telomerase negative in HCC	
	tissue samples	89
Table (17)	Mean value of total Bilirubin (mg/dL) in	
	telomerase positive and telomerase negative	
	in HCC tissue samples	91
Table (18)	Mean value of Albumin (g/dL) in telomerase	-
	positive and telomerase negative in HCC	
	tissue samples	92
Table (19)	Mean value of Prothrombin Concentration in	
	telomerase positive and telomerase negative	
	in HCC tissue samples	93

.

.

-

LIST OF FIGURES

		Page
Figure (1)	Sequences of the template domain (boxed)	
	and surrounding region of telomerase RNAs	
	from Tetrahymena spp. And Glaucoma and	
	Euplotes.	16
Figure (2)	Synthesis of telomeric DNA by the	
	ribonucleoprotein enzyme telomerase from	
	Tetrahymena.	31
Figure (3)	Hypothetical model of cellular	
	immortalization.	36
Figure (4)	Genomic structure of HBV codes for	
	multiple proteins.	51
Figure (5)	Scheme of typical clinical and laboratory	
	features of acute viral hepatitis B.	54
Figure (6)	Scheme of typical laboratory features of	
	chronic viral hepatitis type B.	56
Figure (7)	Sex distribution among all tissue samples of	
	hepatocellular carcinoma	72
Figure (8)	Age distribution among all tissue samples	73
Figure (9)	Sex distribution among HCC only, HCC	
	with HBV and HCC with HCV	74
Figure (10)	Age distribution among HCC only, HCC	
	with HBV and HCC with HCV	75
Figure (11)	Distribution of pathological grades of HCC	
	among HCC only, HCC with HBV and	
	HCC with HCV	76
Figure (12)	Distribution of telomerase activity among	
	all tissue samples of HCC	77
Figure (13)	Telomerase activity among HCC only, HCC	
	with HBV and HCC with HCV	79
Figure (14)	Sex distribution among telomerase positive	
	and telomerase negative samples of HCC	80

	Pa	ıge
and	totomorano megani, e amin'h an an an a	81
amo	ribution of pathological grades of HCC ong telomerase positive and telomerase ative samples of HCC	82
sam	distribution among telomerase positive ples including HCC only, HCC with V and HCC with HCV	84
sam	e distribution among telomerase positive uples including HCC only, HCC with V and HCC with HCV	85
Figure (19) Dis	tribution of pathological grades among merase positive samples including HCC	86
Figure (20) Me	an value of ALT (u/L) in telomerase itive and telomerase negative in HCC ue samples	88
Figure (21) Me pos	an value of AST (u/L) in telomerase itive and telomerase negative in HCC	89
Figure (22) Me	ue samples an value of total Bilirubin (mg/dL) in omerase positive and telomerase negative	91
Figure (23) Me	HCC tissue samples an value of Albumin (g/dL) in omerase positive and telomerase negative	91
Figure (24) Me Co	HCC tissue samples an of readings of Prothrombin ncentration in telomerase positive and	
telo	omerase negative in HCC tissue samples	93

•

.

.

INTRODUCTION