



Ain Shams University
Faculty of Science
Department of Biochemistry

Micro RNA Expression Levels as Diagnostic Biomarker for Hepatocellular Carcinoma in Patients with Chronic Hepatitis C

A Thesis

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By
Christina Atef Soliman

Under supervision of
Prof. Dr. Shadia A. Fathy

Professor of Biochemistry Faculty of Science
Ain Shams University

Dr. Manal Asem Emam
Assistant Professor of Biochemistry
Faculty of Science
Ain Shams University

Dr. Sara Hassan Abo Agwa
Assistant Consultant of Clinical
& Chemical Pathology Medical Research
Center Faculty of Medicine
Ain Shams University

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Dedication

This thesis is dedicated to my family who has always stood by me in everything I did. Thanks to my mother who has always been so loving and caring.

*This thesis is also dedicated to my wonderful husband, **Fady**, whom I cannot possibly thank enough for all of his support and encouragement.*

Declaration

*This thesis has not been submit for
adegree at this or any other university*

Christina Attet



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List of Abbreviations

<i>Abbr.</i>	<i>Full-term</i>
AASLD	: American Association for the study of liver Disease
ADAM10	: A disintegrin and metalloprotease 10
AFP	: α -fetoprotein
AFP-L3	: Lens culinaris agglutinin reactive fraction of Alpha- L
AFU	: Fucosidase
AGO	: Argonaute family of proteins
AKT	: Protein kinase B
ALB	: Albumin
ALT	: Alanine amino transferase
AP-1	: Activator protein 1
APC	: Adenomatous polyposis coli
AST	: Aspartate amino transferase
AUC	: Area Under Curve
BCL2	: B cell lymphoma 2
BMF	: Proapoptotic protein B-cell lymphoma
C.elegans	: Caenorhabditis elegans
Cdk	: Cyclin-dependent kinase
CDKI	: Cyclin dependent kinase inhibitor
cDNA	: Complementary deoxyribonucleic acid
CEA	: Carcinoembryonic antigen
CLD	: Chronic liver disease
CRC	: Colorectal cancer
CSDC2	: Cold-shock domain-containing protein C2
Ct	: Comparative cycle threshold
CT	: Computed tomography
CYR61	: Cysteine-rich angiogenic inducer 61
CYR61	: Cysteine- rich protein 61
DCP	: Des-gamma-carboxyprothrombin
DEPC	: Diethylpyrocarbonate
DM	: Diabetes mellitus

DNA	: Deoxyribonucleic acid
EASL	: European Association for the study of liver
EDRN	: Early detection research network
EGF	: Epidermal growth factor
ELISA	: Enzyme linked immunosorbent Assay
ERK	: Extracellular signal related kinase
ERK-5	: Extracellular signal regulated kinase-5
eRNA	: Enhancer RNA
ESCs	: Embryonic stem cells
ESLC	: Egyptian Society of Liver Cancer
Exp 5	: Exportin-5
FAM	: 6-carboxyfluorescein dye
FDA	: Food and drug administration
FNA	: Fine needle aspiration
gDNA	: Genomic DNA
GGT	: Gamma-glutamyl transferase
GGTmRNA	: Gamma-glutamyl transferase mRNA
GP73	: Golgi protein 73
GPC3	: Glypican-3
HBeAg	: hepatitis B e antigen
HBsAg	: Hepatitis B surface antigen
HBV	: Hepatitis B virus
HCC	: Hepatocellular carcinoma
HCCR	: Human cervical cancer oncogene
HCV	: Hepatitis C virus
HGF	: Hepatocyte growth factor
HGF	: Hepatocyte growth factor
HH	: Hereditary hemochromatosis
HIV	: Human Immuno-deficiency Virus
HNF4A	: Hepatocyte nuclear factor 4 alpha
HOXD10	: Homeobox D 10
HRPO/HRP	: Horse raddish peroxidase
hTRETmRNA	: Human telomerase reverse transcriptase mRNA
HULC	: Highly upregulated in Liver Cancer

IGF	: Insulin-like growth factor
IGF1R	: Insulin-like growth factor 1 receptor
IGF-II	: Insulin-like growth factor II mRNA
INR	: International normalized ratio
iPSCs	: Induced pluripotent stem cells
LcRNA	: Long non-coding RNA
MACC1	: Metastasis associated in colon cancer
MALAT-1	: Metastasis associated lung adenocarcinoma transcript 1
MAP2K3	: Mitogen-activated protein kinase-kinase 3
MAPK14	: Mitogen activated protein kinase
MASPIN	: Mammary Serine Protease Inhibitor
MDK	: Midkine
MGB	: Minor groove binder
miRISC	: RISC loading complex
miRNAs	: microRNAs
MMP9	: Matrix metalloproteinase 9
MRI	: Magnetic resonance imaging
MRI	: Magnetic resonance imaging
mRNAs	: Messenger RNAs
mTOR	: Mammalian Target Of Rapamycin
MVB	: Multivesicular body
MVIH	: Microvascular invasion in hepatocellular carcinoma
MVs	: Microvesicles
MYC	: Myelocytomatosis viral oncogene
NAFLD	: Non Alcoholic fatty liver disease
NASH	: Steatohepatitis
NASH	: Non alcoholic steatohepatitis
NCI	: National cancer institute
NFQ	: Non fluorescent quencher
NPM1	: Nucleophosmin 1
OD	: Optical density
OLT	: Orthotopic liver transplant
OPN	: Osteopontin

PAK4	: P-21 activated kinase 4
PAT	: Parenteral antischistosomal therapy
PBS	: Phosphate buffer saline
PCD4	: Programmed cell death 4 protein
PCR	: Polymerase chain reaction
PDGFR	: Platelet-derived growth factor receptor
PHC	: Primary hepatocellular carcinoma
PI3K	: Phosphatidyl inositide 3 kinase
piRNA	: Interacting RNAs
PIVKA II	: Prothrombin induced by vitamin K II
PKm2	: Pyruvate kinase muscle isozyme 2
PP2R2A	: Protein-coding, protein phosphatase 2A subunit
Pre-miRNA	: Precursor miRNA
Pri-miRNA	: Primary miRNA
PSA	: prostate specific antigen
PT	: Prothrombin time
PTEN	: phosphatase and tensin homolog
PTENP1	: Phosphate and tension homolog pseudogene 1
P-value	: Probability value
qRT-PCR	: Quantitative Reverse Transcription Polymerase Chain Reaction
Ras	: Rat sarcoma
Rb	: Retinoblastoma
REC	: Research Ethics Committee
RHOB1	: Ras-Homology gene family, member B
RISC	: RNA-induced silencing complex
RNA	: Ribonucleic acid
RNAa	: RNA activation
RNAi	: RNA-mediated interference
RNF43	: Ring finger 43
RNUX2	: Runt-related transcription factor 2
ROC-curve	: Receiver operating characteristics curve
RT	: Reverse transcription
SCCA	: Squamous cell carcinoma antigen

SD	: Standard deviation
SDS	: Sodium dodecyl sulfate
SE	: Standard error
siRNA	: Small interfering RNA
SIRT 7	: Sirtuin 7
Snail	: Family of Zinc-finger proteins
snoRNAs	: Small nucleolar RNAs
snRNAs	: Small nuclear RNAs
SPRY2	: Sprouty 2
SPSS	: Statistical Package for Social Science
STAT3	: Signal transducer and activator of transcription 3
STAT3	: Signal transducer and activator of transcription 3
suPAR	: Soluble urokinase plasminogen activator R
TAA s	: Tumor-derived autoantibodies
TCF4	: Transcription factor 4
TE buffer	: Tris - EDTA buffer
TF s	: Transcription factors
TGFB1	: Transforming growth factor
TIMP3	: Metalloproteinase inhibitor 3
T_m	: Melting Temperature
TMB	: Tetramethylbenzidine
TNFα	: Tumor necrosis factor α
TNM	: Tumor-Nodes-Metastases
TRAIL-	: TNF-related apoptosis-inducing ligand
TRX s	: Thioredoxins
U/S	: Ultrasonography
US	: Ultrasound
UTRs	: Untranslated regions
VEGFR	: Vascular endothelial growth factor receptor
v-Raf	: Virus induced rapidly accelerated Fibrosarcoma
WHO	: World health organization

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