
LIST OF TABLES

Tables	Pages
Table (1): Genotypes/subtypes that are presently defined in the database -----	13
Table (2): Treatment outcome classification according to generally accepted terminology-----	16
Table (3): Side effects of HCV therapy (modified from-----	20
Table (4): QRT-PCR Procedure-----	49
Table (5): The allele calls and the IL28B rs1297980 genotyping according to the fluorescence signals of the sample -----	52
Table (6): Statistical Analysis of Baseline Demographic, and Biochemical Characteristics of Apparently Healthy Subjects and HCV Patients-----	56
Table (7): Statistical Analysis of of Baseline Demographic and Biochemical Characteristics of Non Responders and Responders HCV Patients-----	59
Table (8): Baseline Clinico-pathological characteristics of HCV Patients as well as Non-responders and Responders HCV patients -----	60
Table (9): Logistic Regression of Some Factors Associated with Response in Patients with HCV-----	61
Table (10): Distribution of IL-28 rs12799860 genotypes (CC, CT and TT) in apparently healthy subjects and in HCV patients -----	74
Table (11): Exploring the Consistence of IL-28 rs12799860 SNP genotypes distribution with Hardy-Weinberg Equilibrium in Apparently Healthy subjects and HCV Patients Groups -----	76
Table (12): Allele frequencies of rs12799860 Polymorphism Among Apparently Healthy Subjects and HCV Patients Groups and it Relation to HCV-----	77
Table (13): IL-28B Polymorphism in Relation to Response of HCV in Patients -----	77
Table (14): Statistical Analysis of Baseline of Some Biochemical Characteristics in All HCV Patients According to IL-28B rs12979860 Genotypes -----	78
Table (15): Distribution of Degree of in Non- Responders and Responders HCV Patients According to IL-28B rs12979860 Genotypes -----	78

LIST OF FIGURES

Figures	Pages
Table (16): Hepatitis C virus particle structure -----	3
Table (17): A schematic representation of HCV genome, structural and nonstructural proteins -----	4
Table (18): The predicted secondary structure of HCV 3'-NTR -----	5
Table (19): Schematic representation of the lifecycle of hepatitis C virus -----	10
Table (20): Hypothetical HCV replication cycle -----	12
Table (21): HCV genotypes prevalence -----	14
Table (22): The development of HCV -----	16
Table (23): Interferon signaling pathway -----	19
Table (24): Obesity is associated with insulin resistance and decreased antiviral efficacy. -----	23
Table (25): Interaction between hepatitis C virus core, insulin- and interferon- α signaling pathways continuous lines represent activation -----	24
Table (26): Factors associated to non-response to pegylated interferon plus ribavirin treatment -----	27
Table (27): Step One Applied Biosystem -----	40
Table (28): Thermal profile setup of HCV RT-PCR -----	40
Table (29): Digital photo shot of the gel showing the bands of the genomic DNA -----	44
Table (30): 5'-nuclease assay process (TaqMan® SNP Genotyping Assay -----	47
Table (31): Results from matches and mismatches between target and probe sequences in TaqMan SNP Genotyping -----	48
Table (32): IL-28B genotyping Thermal cycling -----	49
Table (33): A multicomponent plot showing the growth of the three fluorescent signals FAM, VIC and ROX vs Cycles -----	50
Table (34): The graph of Rn versus cycle number -----	51
Table (35): TaqMan® Genotyper Software automatically determines sample genotypes and displays data. -----	52
Table (36): Heterozygote -----	53

Table (37):	Homozygote-----	53
Table (38):	Liver fibrosis and histological activity according to METAVIR-----	54
Table (39):	The Percentage Distribution of HCV Patients According to the Response to Standard Treatment -----	57
Table (40):	Average Age (year) of the different Studied Groups-----	62
Table (41):	Mean Body mass index (kg/m ²) in the Different Studied Groups -----	62
Table (42):	Mean Serum Activity Level of ALT (IU/L) in the Different Studied Groups-----	63
Table (43):	Mean Serum Activity Level of AST (IU/L) in the Different Studied Groups-----	63
Table (44):	Mean Serum Activity Level of ALP (IU/L) in the Different Studied Groups-----	64
Table (45):	Mean Serum Activity Level of GGT (IU/L) in the Different Studied Groups-----	64
Table (46):	Mean Serum Concentration Level of Albumin (g/dl) in the Different Studied Groups-----	65
Table (47):	Mean Serum Concentration Level of Total bilirubin (mg/dl) in the Different Studied Groups-----	65
Table (48):	Mean Serum Concentration Level of Direct bilirubin (mg/dl) in the Different Studied Groups-----	66
Table (49):	Mean Serum Concentration Level of Creatinine (mg/dl) in the Different Studied Groups-----	66
Table (50):	Mean Serum Concentration Level of Fasting blood sugar (mmol) in the Different Studied Groups -----	67
Table (51):	Mean Serum Concentration Level of Postprandial Blood Sugar (mg/dl) in the Different Studied Groups -----	67
Table (52):	Mean Serum Concentration Level of Fasting insulin (μ IU/ml) in the Different Studied Groups-----	68
Table (53):	Mean Serum Concentration Level of TSH (μ IU/ml) in the Different Studied Groups-----	68
Table (54):	Mean Level of HOMA-IR in the Different Studied Groups -----	69
Table (55):	Mean Serum Concentration Level of Triglycerides (mg/dl) in the Different Studied Groups-----	69

Table (56):	Mean Serum Concentration Level of Total Cholesterol (mg/dl) in the Different Studied Groups-----	70
Table (57):	Mean Serum Concentration Level of HDL Cholesterol in the Different Studied Groups (mg/dl)-----	70
Table (58):	Mean Serum Concentration Level of LDL cholesterol (mg/dl) in the Different Studied Groups-----	71
Table (59):	Mean Count of WBC($\times 10^3/\mu\text{L}$) in the Different Studied Groups -----	71
Table (60):	Mean Concentration Level of Hemoglobin (mg/dL) in the Different Studied Groups -----	72
Table (61):	Mean Count of Platelets ($\times 10^3/\mu\text{L}$) in the Different Studied Groups -----	72
Table (62):	Mean Level of INR in the Different Studied Groups -----	73
Table (63):	Mean Level of AFP (mg/ml) in the Different Studied Groups -----	73
Table (64):	Distribution of IL-28 rs12799860 genotypes (CC, CT and TT) in apparently healthy subjects and in HCV patients-----	75
Table (65):	Distribution of IL-28 rs12799860 genotypes (CC, CT and TT) in HCV patients. -----	75

LIST OF ABBREVIATIONS

(+)	: Positive.
(-)	: Negative.
$\Delta A/min$: Absorbance rate per minute.
aa	: amino acid.
A	: Absorbance.
A600/800nm	: Absorbance 600/800 Nano-miter.
A (1→4)	: Grad of activity evaluates intensity of necro inflammatory.
ABI	: Applied biosystem.
ADP	: Adenosine diphosphate.
AE	: Elution buffer of cell nucleic acid.
AFP	: Alpha fetoprotein.
AGE	: A garose gel electrophoresis.
Ag-Ab	: Antigen-Antibody complex.
AL	: Cell lysis buffer.
ALB	: Albumin.
ALP	: Alkaline phosphatase.
ALT	: Alanine aminotransferase.
ANA	: Anti-Nuclear Antibody.
Apo-B	: Apoprotein-B.
AST	: Aspartate transferase.
ATP	: Adenosine triphosphate.
AUC	: Area under the curve.
AVE	: Eluted viral nucleic acid.
AVL	: QiaAmp Viral Lysis.
AW	: Washing nucleic acid.
bp	: Base Pair.
BCIP	: 5-Bromo-4-chloro-3-indolyl-phosphate.
BCP	: Bromocresol purple.
BMI	: Body mass index.
BT	: Breakthrough.
C	: Core.
°C	: Degree centigrade.

CD81	: Cluster of Differentiation 81.
cDNA	: Complementary DNA.
CI	: Confidence interval.
CHC	: Chronic hepatitis C.
CKII	: Casein kinase II.
CLDN	: Claudin-1 receptor mediate HCV entry
CLIA	: Chemiluminescent enzyme immunometric assay.
Cr	: Creatinine.
CREs	: The cis-acting replication elements.
CTLA4	: Cytotoxic T-lymphocyte-associated protein 4.
Cs	: Known standard Concentration.
D	: Domain.
dATP	: 2'-deoxyadenosine triphosphate.
D.Bil	: Direct bilirubin.
dCTP	: 2'-deoxycytidine 5'-triphosphate.
DCs	: Dendritic cells.
DExH/D-box	: proteins are the largest group of enzymes in eukaryotic RNA metabolism
dGTP:	: 2'-deoxyguanosine 5'-triphosphate.
DNA	: Deoxyribonucleic acids.
dNTPs	: Deoxynucleoside, 5' triphosphates.
dTTP	: 2'-deoxythymidine 5'-triphosphate.
E	: Envelope glycoproteins.
EDTA	: Ethylene Diamine Tetra Acetic Acid.
eIF3	: Eukaryotic initiation factor 3.
ELISA	: Enzyme Linked Immuno Sorbent Assay.
EMCV	: Encephalo myocarditis virus.
EoTR	: End-of treatment response.
ER	: Endoplasmic reticulum.
et al	: et alter.
EtOH	: Ethanol.
EVR	: Early Virological Response.
F(1-4)	: Stage of liver fibrosis from 1 to 4
FAM	: 6-carboxy fluorescein
FBS	: Fasting blood glucose.

FFAS	: Free fatty acids.
Fig	: figure.
FRET	: Fluorescence (or Forster) Resonance Energy Transfer
g	: Relative centrifugal force.
G/U	: Guanine/ uracil nucleotides.
GAS	: Gamma activated sequence.
GBV	: The GB viruses (hepatitis G virus (HGV) also known as HPgV.
GBV-B	: Hepatitis GB virus B.
GGT	: Gamma Glutamyl Transferase.
GLUT-4	: Glucose transferase-4.
GWAS	: Genome-wide association studies.
g/L	: Gram per liter.
g/dL	: Gram per deciliter.
g/ml	: gram per millimeter.
µg/kg/week	: microgram per every kilogram every week.
H₂O	: Water.
H₂O₂	: Hydrogen peroxide.
HBs-Ag	: Hepatitis B virus surface antigen.
HBV Ag	: Hepatitis B virus antigen.
HBV	: Hepatitis B virus.
HCC	: Hepatocellular Carcinoma.
HCV	: Hepatitis C virus.
HCV Ab	: HCV antibodies.
HCV-Ag	: HCV antigen.
HCV-GT 1	: Hepatitis C Virus genotype-1.
HCV 4	: Hepatitis C Virus genotype 4.
HCVcc	: HCV in cell culture.
HCVpp	: HCV pseudo particle.
HDL	: High-Density lipoprotein
HDL-C	: High density lipoprotein cholesterol.
HIV	: Human Immunodeficiency Virus.
HOMA-IR	: Homeostasis Model for Assessment of insulin resistance.
HPLC	: High performed liquid gas chromatography.
Huh-7	: Human hepatocyte cell-7.

IFCC	: International Federation of Clinical Chemistry.
IFN	: Type I interferon.
IFNAR	: The interferon alpha/beta receptor.
IFNAR2c	: Interferon alpha receptor chain 2.
IFNGR	: The interferon gamma receptor.
IFN-λ	: Interferon- lambda.
IFN-α	: Interferon-alpha.
IFN-β	: Interferon-beta.
IFN-γ	: Interferon-gamma.
IL	: Interleukin.
IL-10R	: Interleukin-10 receptor.
IL-28B	: Interleukin-28B.
INR	: International Normalized Ratio.
Ins	: Insulin.
IR	: Insulin resistance.
IRES	: Internal ribosome entry site.
IRF9	: Interferon regulatory factor 9.
IRS	: Insulin receptor substrates.
ISDR	: Interferon sensitivity determining region.
ISGF3	: Interferon stimulated gene factor 3.
ISGs	: Interferon stimulated genes.
IU/L	: International unit per liters.
IU/mL	: International unit per milliliters.
JAK1	: Janus kinase 1.
Kb	: kilo base.
Kbp	: kilo base pair.
KDa	: Kilo Dalton
Kg	: Kilogram.
Kg/m²	: Kilogram/meter square.
LDL	: Low-density lipoprotein.
LDL-C	: Low density lipoprotein cholesterol.
LDs	: Lipid droplets.
LMP7	: Low molecular mass polypeptide 7.
M	: Male.

MBL	: Monoclonal B-Cell Lymphocytosis.
mg	: Milligram.
µg/kg/week	: Microgram per kilogram every week.
µmol/L	: Micromole per liter.
µL	: Microliter.
µIU/ml	: Micro international unit per millimeter.
MGB	: Minor groove binder.
mg/dL	: Milligram per deciliter.
mg/kg/day	: Milligram per kilogram per day.
min	: Minute.
miR	: MicroRNAs.
miRNAs	: Micro ribonucleic acid.
mIU/L	: Micro international unit per liter.
mmol/ L	: Millimole per liter.
mRNA	: Messenger ribonucleic acid.
MxA	: Myxovirus Resistance Gene A.
MX1	: Myxovirus-resistant 1.
N	: Negative.
NAD	: Nicotinamide adenine dinucleotide.
NADH	: Nicotinamide adenine dinucleotide hydrogenates.
NANBH	: Non-A, non-B hepatitis
ng/µl	: Nanogram per microliter.
nm	: Nano-meter.
NMR	: Nuclear magnetic resonance.
NFQ	: Non-fluorescent quencher.
NR	: Non-Response.
NS	: Nonstructural proteins
NS4A	: Nonstructural proteins 4A.
nt	: Nucleotides.
NTC	: Non Template Control.
NTPase	: Nucleoside triphosphatases.
NTRs	: Non translated RNA segments.
OAS1	: genes encoding active 2'-5'oligoadenylate synthetase (OAS) enzymes.
OAS	: 2'-5'oligoadenylate synthetase.

OCN	: Occludin receptor.
OR	: Odds Ratio.
ORF	: Open reading frame
p	: Probability.
p7	: Protein (ion channel or viroporin).
p53	: Protein 53(tumor suppressor).
PBS	: peripheral blood sample.
PCR	: Polymerase chain reaction.
PEG	: Polyethylene glycol.
PEG-INF	: Pegylated interferon.
PI3K	: Phosphatidyl-inositol-3-kinase.
PKR	: Protein kinase R.
PMT	: Photomultiplier tube.
PNR	: Primary Non-Response.
PO₄	: Phosphate.
PP2h	: Postprandial glucose level after 2 hour.
PPBI	: Postprandial blood glucose.
PRKR	: Protein kinase RNA-regulated.
PT	: Prothrombin time.
PC	: Prothrombin concentration.
R	: Responder.
RBV	: Ribavirin.
RDRP	: RNA dependent RNA polymerase.
RIG-I	: Retinoic acid inducible gene.
RNA	: Ribonucleic acid.
Rn	: Reporter normalized.
RF	: Replicative form.
ROC	: Receiver-operator characteristic
Rpm/rpm	: Round per minute/ Revolutions per minute.
RT	: Reverse transcriptase enzyme.
Rs60	: rs12979860.
RVR	: Rapid Virological Response.
S	: Standard.
SCH.Ab	: Schistosomal antibodies.

SD	: Standard deviation.
SDS	: Sequence Detection System.
S.E	: Standard Error.
S.Ins	: Serum insulin.
SL	: Stem-loop.
SNP	: Single Nucleotide polymorphisms.
SOC	: Standard of care.
SOCS3	: Suppressor of cytokine signaling 3.
SPSS	: Statistical Package for the Social Science.
SR-BI	: Scavenger receptor class B member I.
SREBP-1c	: Sterol regulatory element-binding protein 1c.
STAT	: Signal transducer and activator of transcription.
SVR	: Sustained Virological Response.
T	: Test.
Taq	: <i>Thermus aquaticus</i> .
T.Bil	: Total bilirubin.
TBE	: Tris Borate EDTA.
TC	: Total Cholesterol.
T2DM	: Type 2 diabetes.
TG	: Triglycerides.
TGF-β	: Transforming growth factor-beta.
Th	: T helper cell.
TLRs	: Toll-like receptors.
TM	: Trans membrane.
Tm	: melting temperature.
TMA	: Transcription-mediated amplification.
TMB	: Tetra methyl benzidine.
TNF- α	: Tumor necrosis factor α .
TRAIL	: Tumor necrosis factor (TNF)-related apoptosis inducing ligand.
TSH	: Thyrotropin (Thyroid-Stimulating hormone).
TYK2	: Tyrosine kinase 2.
U/L	: Units/L.
3'UTR	: 3 prime untranslated region.
5'UTR	: 5 prime untranslated region.

UTR	: Untranslated region.
U/UC	: Uracil/Uracil C.
UV	: Ultraviolet.
VLDL	: Very- Low-density lipoprotein.
VSL	: Variable Stem-loop.
λ	: Wave length (lambda).
χ^2	: Chi square.
X	: Mean.