

*Assessment of conserved peptides within the
envelope (E2) glycoprotein of hepatitis C virus as
candidates for development of neutralizing
antibodies*

A Thesis

Submitted in Partial Fulfillment of the
Requirements for the Degree of

PHD

In

Pharmaceutical Sciences

(Microbiology and Immunology)

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2010

بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

صدق الله العظيم

Dedication

I dedicate this work

To my family:

My Kind Mum

My Great Dad

My Beloved Sister

My Dearest Husband

My sweethearts Hamdy & Farida

I thank God for choosing you to be my family

Thank you for supporting me

*With kindness, patience, patience, patience and
love*

Yours,

Yasmine Sayed El Abd

To My Dear Husband

***I am very grateful & pleased with
Everything you do for me***

***Thanks a lot for your
Encouragement
Thoughtfulness
Assistance
Patience
Care
And
Love***

To My little angles

Hamdy & Farida

**I hope one day,
You read this thesis
& be proud that
I'm your mother**

**Thanks God
For the Gorgeous
& Precious Gift
My sweethearts**

Hamdy & Farida

**Who fill my life with
Happiness
Smiles &
Blesses**

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ACKNOWLEDGMENT

I thank **ALLAH** for giving me the ability and enthusiasm to complete this work and for granting me with the most respectable and great supervisors.

I would like to express my deepest appreciation, gratefulness & sincere thanks to the kind soul of my great **late Professor Dr. Hussein A. Sheob**, Professor of microbiology and immunology, Faculty of Pharmacy, Cairo University for his kind supervision, help, encouragement, guidance and advice. It was really a gift from GOD to deal with such a person who is always giving. Peace upon his soul.

I would like to express my thanks and gratitude to **Professor Dr. Alaa El Dien M.S. Hosny**, Professor of microbiology and immunology, Faculty of Pharmacy, Cairo University for his kind supervision, help, encouragement, guidance and advice.

My deepest heartfelt gratefulness and appreciation is to **Professor Dr. Mostafa K. El Awady**, Professor of Molecular Genetics, Biomedical Technology Department, National Research Center, for suggesting the point of this thesis and for his kind supervision, continuous support and valuable guidance. I am very lucky to have this great opportunity to be one of his students.

My sincere thanks and gratitude to **Dr. Ashraf abdou tabll**, assistant professor and head of Biomedical Technology Department, National Research Center for his kind supervision, continuous support, valuable guidance and generous help in all the theoretical and practical aspects

also for his encouragement to submit articles write projects and join conferences everywhere. I am honored having him as an eminent member of the supervision part.

I am deeply indebted to **Dr. Noha Gammal El-Din**, Researcher, Biomedical Technology Department, National Research Center and internal supervisor for this work in the NRC, for her sincere guidance, generous help in all the theoretical and practical aspects and for building up the hypothesis related to the results, encouragement, patience and love. No words are sufficient to express heartfelt thanks to her.

I would like also to thank my colleagues **Reem El Shenawy, Rehab Mostafa and Khaled Atef**, Assistant Researchers, Biomedical Technology Department, National Research Center, for their help, support continuous encouragement, advice, care & kindness.

I would like to express my thanks to **Dr Mahmoud Hefnawy**, Researcher, National Research Center for his kind help with bioinformatic techniques for peptides design and my colleague **Ahmad Noshay**, Assistant Researcher, Biomedical Technology Department, National Research Center for his kind assistance with computer skills.

The present work is supported in part by National Research Center project number: 8041177 to Dr. Ashraf Tabll

Finally, I would like to express my deep thanks to my friends, colleagues and to everybody in Biomedical Technology Department, who helped me to accomplish this work.

Abstract

The reason(s) why human antibodies raised against hepatitis C virus do not offer protection against multiple viral infections may be related to either genetic variations among viral strains, low titers of anti E2 antibodies or interference of none or low neutralizing antibodies with the function of neutralizing antibodies. This study was designed to assess the immunogenic properties of genetically conserved peptides derived from envelope E2 region and test their neutralizing activities to determine the possibility of their development to potential therapeutic and/or prophylactic vaccines against HCV. Goats immunized with E2 conserved synthetic peptides termed Pep.36 (a.a 430-447), Pep.37 (a.a 516-531) and Pep.38 (a.a 412-420) generated high titers of antibody responses higher than comparable titers of antibodies to the same epitopes in chronic HCV patients. Also Pep.38 elicited approximately 2 fold increase in cell proliferation of specific antibody-secreting peripheral blood mononuclear cells from immunized goats. When using *invitro* culture model of Huh7 cell lines for infection and neutralization experiments antiPep.37 and anti Pep.38 were proven to be neutralizing to HCV particles in sera from patients infected predominantly with genotype 4a (75% & 87.5% respectively). On the other hand antiPep.36 exhibited weak viral neutralization capacity on the same samples (31.25%). Taking together the results of humoral immunity and cellular responses suggest that E2 conserved peptides Pep.37 and Pep.38 represent essential components of a candidate peptide vaccine against HCV infection

Key words

Hepatitis C virus (HCV), anti E2 antibodies, neutralizing antibodies, invitro culture model for HCV, candidate peptide vaccine for HCV.

List of Abbreviations

a.a	Amino acid
Abs	Antibodies
BCIP/NBT	5-Bromo-4-Chloro-3'-Indolyphosphate p-Toluidine Salt / Nitro-Blue Tetrazolium Chloride
bDNA	Branched DNA
bp	Base pair
BSA	Bovine Serum Albumin
C	Cytidine
CD	Cluster of differentiation
Co ₂	Carbon dioxide
DAB	Diaminobenzidine
ddH ₂ O	Double distilled water
DMEM	Dulbecco's Modified Eagle's Medium
DMSO	Dimethylsulfoxide
DNA	DeoxyriboNucleic Acid
dNTP	Deoxynucleoside Triphosphate
Dot-EIA	Dot Enzyme Immunoassay
E	Envelop
E1	Envelope protein 1
E2	Envelope protein 2
ECMV	Encephalomyocarditis virus
ELISA	Enzyme Linked Immunosorbent Assay
EMCV	Encephalomyocarditis
ER	Endoplasmic Reticulum
FACS	Fluorescence Activated Cell Sorting
FBS	Fetal Bovine Serum
FCS	Fetal Calf Serum
FITC	Fluorescein isothiocyanate
GAGs	Glycosaminoglycans
gps	glycoproteins
GTP	guanosine triphosphate
HAV	Hepatitis A Virus
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HCVcc	Cellular clone of HCV
HCVpp	Hepatitis C Virus pseudoparticles
HDL	High Density Lipoprotein