شبكة المعلومات الجامعية

بسم اللّه الرحمن الرحيم

شبكة المعلومات الجامعية

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

شبكة المعلومات الجامعية

بعض الوثائق الأصلية تالفة

شبكة المعلومات الجامعية

بالرسالة صفحات
لم ترد بالأصل

Epidermal growth factor (EGF) gene polymorphism as a risk factor for development of hepatocellular carcinoma (HCC) in chronic liver disease patients

By

Huda Ramadan Reyad Abass

M.B.B.Ch. in medicine and surgery

Thesis

Submitted for partial fulfillment of MSC degree in Medical Biochemistry

Supervised by

Prof. Dr. Emad Zaki Abass

Professor of Medical Biochemistry

Faculty of Medicine

Cairo University

Prof. Dr .Gamal El-Dein Esmat Mohamed

Professor of Tropical Medicine

Faculty of Medicine

Cairo University

Dr. Ghada Mahmoud Abdel-Aziz

Lecturer of Medical Biochemistry

Faculty of Medicine

Beni-Sweif University

Beni-Sweif University

Faculty of Medicine

2011

Acknowledgment

First and foremost thanks to "Allah" the most beneficial and the most merciful

It is a great pleasure to express my profound gratitude and deep thanks to ***Prof. Dr. Emad Zaki Abass,*** *professor of Medical Biochemistry, faculty of Medicine, Cairo University for his supervision, generous cooperation and great help to end this work.*

I wish to express my sincere thanks to ***Prof. Dr. Gamal Esmat,*** *Professor of Tropical Medicine, faculty of Medicine, Cairo University for his careful supervision on this work, his valuable cooperation and encouragement.*

My deep thanks and grateful acknowledgement to ***Prof. Dr. Olfat Shaker,*** *professor of Medical Biochemistry, faculty of Medicine, Cairo University for her careful supervision on this work and her help in the practical part of thesis and analysis of results.*

I am thankful to ***Dr. Ghada Mahmoud Abd El-Aziz,*** *lecturer of Medical Biochemistry, faculty of Medicine, Beni-Sweif University, for her support and help during this work.*

I would like to express my deep thanks to all staff members in Medical Biochemistry department for their help and support.

I want to thank the patients and healthy volunteers for their cooperation.

Finally, my deepest thanks to my family for all their help and support.

Abstract

Background: Overexpression of epidermal growth factor (EGF) in the liver induces transformation to hepatocellular carcinoma(HCC) in animal models. Polymorphisms in the EGF gene modulate EGF levels.

Objective: to evalute the effect of EGF gene single nucleotide polymorphism and assess its correlation with risk of hepatocellular carcinoma in patient with chronic liver diseases.

Patients and Methods: The present study included ٧٧ subject, divided into 4 groups; Group 1: included 17 asymptomatic healthy control volunteers who matched with age and sex, Group 2: included 20 patients with chronic hepatitis C infection, Group 3: included 20 patients with liver cirrhosis and Group 4: included 20 patients with hepatocellular carcinoma. For all subjects the following investigations were performed; complete blood count, Liver functions tests. Sero markers of hepatitis viruses HBsAg, total anti-HBC, and HCV-RNA by quantitative PCR and Alfa fetoprotein, in addition to full history taking including risk factors of HCV infection, thorough clinical examination and abdominal ultrasongraphic examinations were done. One ml blood was taken on EDTA for DNA extraction and detection of single nucleotide polymorphism of the EGF by polymerase chain reaction (PCR) and restriction enzymes followed by agarose gel electrophoresis stained with ethidium bromide.

Results: The control subjects with GG and GA genotypes had 7.875 and 3.375 folds odds ratio for developing HCC and the control group with GG and GA genotypes had 2.571 and 1.929 folds for developing cirrhosis than AA genotype respectively. The cirrhotic patients with GG and GA genotypes had 3 and 1.75 folds for developing HCC respectively and the chronic hepatitis C patients with GG genotype had 2.333 folds of developing HCC than AA genotype.

Conclusion: The EGF 61 A/G polymorphism might be associated with a high risk for the development of HCC in both chronic liver disease patients and normal healthy subjects and a risk factor for cirrhosis development in normal healthy subjects.

Keywords**:** Epidermal growth factor, Chronic liver disease, Polymorphism and Hepatocellular carcinoma

List of Contents

List of Tables

List of figures

List of abbreviations

A	Adenine
A:T	Adenine:Thymine
AAF	Acetylaminofluorene
ADAM	A disintegrin and metalloprotease
AFB1	Aflatoxin B1
AFP	Alpha Fetoprotein
AKT	Ak, name for a mouse strain developing spontaneous thymic lymphomas t" stands for 'transforming' (anti-apoptotic serine-threonine kinase)
ANGII	Angiotensin 2
ALT	Alanine aminotransferase
ALP	Alkaline phosphatase
AR	Amphiregulin
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
BCL2	B-cell lymphoma 2
BCLC	Barcelona-clinic liver cancer
BMI	Body mass index
BP	Base pair
BTC	Beta-cellulin
C	Cytosine
CCL4	Carbon tetrachloride
CDK	Cyclin dependent kinase
cDNA	Complementary deoxyribonucleic acid
C-FOS	Cellular Finkel–Biskis–Jinkins murine osteogenic sarcoma virus
Chemokine MIP-3	Chemokine macrophage-inflammatory protein-3
CLIP	Cancer of the Liver Italian Program
C-MYC	Cellular myelocytomatosis oncogene

COS 7	cercopithecus aethiops (African green Monkey) fibroblast- like kidney cells 7
COX-2	Cyclooxygenase 2
C-P A	Child-pugh a
CREB	CAMP response element-binding
c-SRC (sarc)	Cellular- Short for sarcoma
CTGF	Connective tissue growth factor
CUPI	Chinese university prognostic index
DNA	Deoxyribonucleic acid
ECM	Extra cellular matrix
EDTA	Ethelene diamine tetra acetic acid
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EIF 2B	Eukaryotic initiation factor 2 B
EPG	Epigen
ER	Estrogen receptor
ERBB	Erythroblastosis binding
EREG	Epiregulin
ERK	Extracellular signal regulated kinase
FAS	Factor of apotosis
FASL	Fas ligand
FDA	Federal drug agency
G	Guanine
G : C	Guanine: cytosine
GRB2	Growth factor receptor bound protein
GAP	Gtpase activation protein
GDP	Guanosine diphosphate
GPCR	G protein coupled receptor
GTP	Guanosine triphsophate
H- RAS	Harvey ras
HB-EGF	Heparin-binding EGF
HBsAG	Hepatitis B surface antigen

HBV	Hepatitis B virus
HBX	Hepatitis B virus X protein
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HCV ab	HCV antibodies
HER	Human epidermal growth factor receptor
HSCS	Hematopoietic stem cells
IAPS	Inhibitor of apoptosis proteins
IG EGF	Immunoglobulin epidermal growth factor
IGF	Insulin-like growth factor
IGF-1R	IGF-1 receptor
IGG	Immunoglobulin G
IGM	Immunoglobulin M
IL-8	Intrleukin 8
IL-1ß	Interleukin-1beta
IL-6	Interleukin-6
IL-1	Interleukin-1
INFγ	Interferon-gamma
JAK	Janus kinase
JIS	Japan integrated staging
JNK	C-Jun N-terminal protein kinase
KBP	Kilo base pair
KCS	Kupffer cells
KDA	Kg dalton
K-RAS	Kirsten RAS
LOH	Loss of heterozygosity
LPS	Lipopolysaccharide
M.B.B.CH	Medicinae Baccalaureus, Baccalaureus Chirurgiae
M TOR	Mammalian Target of Rapamycin
MAPK	Mitogen activated protein kinase
MEK	MAP/Erk kinases
MET Codon	Methionine codon
MKKS	MAP kinase kinases
MNK	Mapk (mitogen-activated protein kinase)-interacting kinase