شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

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شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

بعض الوثائق الاصلية تالفة

بالرسالة صفحات
لم ترد بالاصل

Genetic mutation study among hepatocellular carcinoma patients (Case – control) Study

Thesis

Submitted in Partial Fulfillment of M.D. Degree
In Public Health

By

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2006

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توطئة للحصول على درجة الماجستير / الدكتوراه
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تحت عنوان : باللغة الانجليزية : ....
Genetic Mutation Study Among hepatocellular Carcinoma Patients (case-control study)

: باللغة العربية : ....
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بناء على موافقة الجامعة بتاريخ / / ٢٠٠ تم تشكيل لجنة الفحص والمناقشة للرسالة المذكورة أعلاه على النحو التالى :-

١. أ.د. [illegible] .... عن المشرفين
٢. أ.د. [illegible] .... ممتحن داخلى
٣. أ.د. [illegible] .... ممتحن خارجى

بعد فحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم انعقدت اللجنة مجتمعة فى يوم الاثنين بتاريخ ٢ / ٧ / ٢٠٠٦ بقسم [illegible] بكلية الطب – جامعة القاهرة وذلك لمناقشة الطالب فى جلسة علنية فى موضوع الرسالة والنتائج التى توصل اليها وكذلك الأسس العلمية التى قام عليها البحث .

قرار اللجنة : ....
قبول الرسالة

توقيعات أعضاء اللجنة :-

المشرف الممتحن	الممتحن الداخلى	الممتحن الخارجى
[signature]	[signature]	[signature]

عصام

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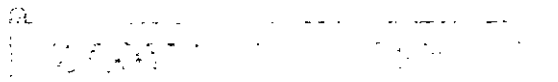
ABSTRACT

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide. The aim of the present study was to assess the association of mutation of specific genes: cytochrome P450 1A1 (CYP1A1), cytochrome P450 2D6 (CYP2D6), microsomal epoxide hydrolase (EPHX) and paraoxonase (PON1) and environmental exposures on the risk of HCC in Egypt. A case-control study was conducted on 459 subjects with confirmed HCC recruited from the National Cancer Institute, Cairo University, Egypt, and 634 controls recruited from orthopedic department, Cairo University Hospital, Egypt and from two villages in Menoufiya governorate. Patients who agreed to participate signed a consent form, answered a questionnaire and gave a blood sample for hepatitis virus and genetic testing. PON1 polymorphism was inversely related to HCC, OR was 0.7 (95% CI: 0.5-1.1). EPHX1 Slow activity was significantly associated with HCC (OR= 1.5, 95% CI: 1.1-2.2) compared to high metabolizers after adjustment with age, sex, current HCV and current HBV infection. CYP1A1 mutation was not associated with HCC in the present study (OR= 2.0, 95% CI: 0.4-10.2). CYP2D6 extensive metabolizers was associated with HCC (OR= 1.8, 95% CI: 1.1-3.0) compared to poor metabolizers. No significant interaction between smoking or pesticides exposure and the studied genes. As expected, the strongest risk factors for HCC in this study were HCV RNA (OR = 11-13) and current HBV infection (OR = 6-9). This study therefore suggests that mutation in the studies genes are additive risk factors to current HCV and HBV infection.

Key words:
Hepatocellular carcinoma, Gene-Environment interaction, PON1, EPHX1, CYP1A1, CYP2D6, HCV, HBV



LIST of ABBREVIATIONS

AFB1	Aflatoxin B1
AFP	Alpha-fetoprotein
BP	Benzo[a]pyrene
CI	Confidence Interval
COMT	Catechol-*O*-methyltransferase
CT	Computed Tomography
CYP	Cytochrome-P450
CYP1A1	cytochrome P-450 1A1
CYP2D6	Cytochrome P450 2D6
DMEs	Drug metabolizing enzymes
DNA	Deoxyribonucleic Acid
EH	Epoxide hydrolases
EIA	Enzyme Immunoassay
ELIZA	Enzyme-linked Immunosorbant Assay
EM	Extensive metabolizer
EPA	Environmental Protection Agency
EPHX1	Microsomal epoxide hydrolase
ER	Endoplasmic Reticular
GSH	Glutathione
GSTM1	Glutathione-S-transferase mu1
GSTP	Glutathione-S-transferase pi
GSTs	Glutathione-S-transferases
GSTT1	Glutathione-S-transferase theta1
HBcAb	Antibody to Hepatitis B Virus Core Antigen
HBsAg	Hepatitis B Virus Surface Antigen
HBV	Hepatitis B Virus

HCC	Hepatocellular Carinoma
HCV	Hepatitis C Virus
HCV-Ab	Antibody to Hepatitis C Virus
HDV	Hepatitis D Virus
ID	Identification number
Ile-Val	Isoleucine-valine
IMs	Intermediate metabolizer
LDL	Low-density lipoprotein
MCCH	Malignant Complication of Chronic Hepatitis C infection
mRNA	messenger RNA
NAT2	N-acetyltransferase 2
NATP1	N-acetyltransferase pseudogene 1
NCI	National Cancer Institiute
NHL	Non-Hodgkin lymphomas
NIEHS	National Institute of Environmental Health Science
OD	optical density
OR	Odds Ratio
PAHs	Polycyclic Aromatic Hydrocarbons
PCR	Polymerase Chain Reaction
PhIP	2-amino-1-methyl-6-phenylimidazo [4, 5-b] pyridine
PM	Poor metabolizer
PON1	Paraoxonase
RFLP	Restriction Fragment Length Polymorphism
RNA	Ribonucleic acid
RT	Reverse Transcriptase
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
SEER	Surveillance, Epidemiology, and End-Results

SNPs	Single Nucleotide Polymorphisms
UM	Ultrarapid metabolizer
VHRL	Viral Hepatitis Research Lab