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Evaluation of Serum Voltage Gated Calcium Channel α2δ1 as a Novel Marker for Diagnosis of Hepatocellular Carcinoma in Cirrhotic Egyptian Patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Internal Medicine

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List of Abbreviations

Abb.	Full term
A2	
<i>AA</i>	
ACS	
<i>AFB1</i>	
<i>AFP</i>	-
	Adrenal aldosterone-producing adenomas
<i>AUC</i>	
<i>CaM</i>	
<i>CaMK</i>	
	Contrast-enhanced ultrasound
CP110	Centrosomal protein
<i>CREB</i>	c-AMP-responsive element binding
<i>CSPH</i>	Clinically significant portal hypertension
<i>CT</i>	Computed tomography
<i>DCP</i>	$Des\gamma$ -carboxyprothrombin
EGFR	Epidermal growth factor receptor
EPO	Erythropoietin
	Endoplasmic reticulum
FDG-PET	Positron emission tomography with
	fluorodeoxyglucose
FOXM1	Forkhead box M1
<i>GP73</i>	Golgi protein-73
<i>GPC3</i>	
	Glycosyl-phosphatidylinositol
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
<i>HEK</i>	Human embryonic kidney
HR	Hazard ratio
<i>MAPK</i>	Mitogen-activated protein kinase
<i>MDK</i>	Midkine
miRNAs	MicroRNAs
MRI	Magnetic resonance imaging
mTOR	Mammalian target of rapamycin

List of Abbreviations cont...

Abb.	Full term
MARID	
	Nonalcoholic fatty liver disease
	Nonalcoholic steatohepatitis
<i>NFAT</i>	Nuclear factor of activated T-cell
<i>OPN</i>	. Osteopontin
<i>OS</i>	Overall survival
<i>PDGF</i>	Platelet-derived growth factor
<i>PIVKA</i>	.Prothrombin induced by vitamin K absence
	II
<i>RAF</i>	Rapidly accelerated fibrosarcoma
<i>RFA</i>	.Radiofrequency ablation
SCCA	Squamous cell carcinoma antigen
<i>SIRT</i>	.Selective internal radiation therapy
STAT3	Signal transducer and activator of
	transcription 3
<i>suPAR</i>	.Soluble urokinase plasminogen activator
	receptor
<i>TACE</i>	Trans arterial chemoemboliation
TRXs	Thioredoxins
<i>US</i>	Ultrasound
<i>VEGF</i>	Vascular endothelial growth factor
VGCC	Voltage Gated Calcium Channel

ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the most common primary liver tumor and represents the third-leading cause of cancerrelated death in the world. The incidence of HCC continues to increase worldwide, with a unique geographic, age, and sex distribution. The most important risk factor associated with HCC is liver cirrhosis, with the majority of cases caused by chronic infection with hepatitis B (HBV) and C (HCV) viruses and alcohol abuse, although nonalcoholic fatty liver disease is emerging as an increasingly important cause. Primary prevention in the form of HBV vaccination has led to a significant decrease in HBV-related HCC, and initiation of antiviral therapy appears to reduce the incidence of HCC in patients with chronic HBV or HCV infection. Additionally, the use of ultrasonography enables the early detection of small liver tumors and forms the backbone of recommended surveillance programs for patients at high risk for the development of HCC. Cross-sectional imaging studies, including computed tomography and magnetic resonance imaging, represent further noninvasive techniques that are increasingly employed to diagnose HCC in patients with cirrhosis.

Objectives: Evaluation of Serum voltage gated calcium channel $\alpha 2\delta 1$ as a novel Marker for diagnosis of Hepatocellular Carcinoma in Cirrhotic Egyptian Patients. Patients and Methods: This study had been carried out on 90 subjects, age range 21-73 year selected from Internal medicine and Hepatology outpatient clinics and inpatient wards at Ain shams university hospitals. Subjects were divided as follow: Group A(Case): 40 patients with liver cirrhosis without Hepatocellular carcinoma and group B (Control): 40 patients with liver cirrhosis and Hepatocellular carcinoma and group C: 10 normal population for detecting normal value of the marker with exclusion criteria including age < 18 years old and Patients diagnosed with malignancy other than HCC. Results: The study subjects are classified into three groups: Group A cirrhotic patients without HCC, Group B cirrhotic patients with HCC and Group C normal individual subjects. Conclusion: Serum voltage gated calcium channel levels were significantly higher in patients with HCC and mildly elevated in patients with liver cirrhosis compared to the control group. Thus it can be used as a tumor marker for HCC.

Keywords: Hepatocellular Carcinoma, Voltage Gated Calcium Channel A2δ1, Alpha Fetoprotein.