LAPTM4B: A Novel Biomarker for Hepatocellular Carcinoma

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By

Marwa Ahmed Ali Mohammed Ali Elgebili
Assistant lecturer of Biochemistry and Molecular Biology
Fayoum University
Under supervision of

Dr. Olfat Gamil Shaker
Professor of Medical Biochemistry and Molecular Biology
Faculty of Medicine, Cairo University

Dr.Yasser Hessein Nassar
Professor and head of Medical Biochemistry and Molecular Biology Department
Faculty of Medicine, Cairo University

Dr. Amr Aly Zahra
Assistant Professor and head of Medical Biochemistry and Molecular Biology Department
Faculty of Medicine, Fayoum University

Dr. Aymen Yousry
Professor and head of Tropical Medicine Department
Faculty of Medicine, Cairo University

Faculty of Medicine
Cairo University

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SUMMARY

HCC is the fifth most common cancer in men and the eighth most common in women. Five-year survival rates are quite low. With approximately 600,000 deaths annually.

Lysosome associated protein transmembrane 4 beta (LAPTM4B), a novel gene upregulated in hepatocellular carcinoma (HCC) and their cell lines, cells transfected with LAPTM4B cDNA displayed profound changes, including increased cell growth and proliferation rates, increased colony-formation efficiency in soft agar, reduced serum dependence and morphological alterations such as the increase of microvilli on cell surfaces.

Previous studies showed that the LAPTM4B polymorphism was significantly associated with the susceptibility of lung cancer, gastric cancer, colorectal cancers, lymphoma, and cervical cancer, but not in esophageal carcinoma, rectum carcinoma or nasopharyngeal carcinoma.

Aim of our study is to explore the association of LAPTM4B gene polymorphism with HCC in Egyptian patients and whether this genetic polymorphism is associated with the clinicopathological characteristics of the disease.

This study was conducted on 120 subjects classified into 2 groups: Group I which included 70 with hepatocellular carcinoma; Group II (controls) which included 50 healthy subjects. A detailed history taking, Physical and clinical examinations were done to all subjects. 10 ml of blood were collected from each subject. The following was done; Liver function tests, CBC, DNA extraction from whole blood, genotyping of LAPTM4B gene by PCR, agarose gel electrophoresis and quantitation of protein level of LAPTM4B by ELISA.

Statistical analysis was performed to demonstrate any relation between LAPTM4B gene polymorphism with HCC in Egyptian patients and whether this genetic polymorphism is associated with the clinicopathological characteristics of the disease.

Concerning LAPTM4B polymorphism, the result of the current study revealed that higher proportions of genotype *2/2 in HCC patients (28.6%) compared with healthy population (10%). Comparing the genotypes (2*/2* and 1*/2*) in the 2 different groups, taking 1*/1* as reference the p =0.006 and 0.251 respectively.

Also, there was a clear difference between baseline of LAPTM4B protein level in blood of hepatocellular carcinoma patients and controls. Higher LAPTM4B protein (1391± 673.51) were found in blood sample of HCC patients than samples from controls (388.18 ± 141.48) with p= <0.001

By analyzing Association between LAPTM4B genotypes and LAPTM4B protein in HCC patients, there was higher level of LAPTM4B protein among HCC patients genotype 2*/2* (1680.82±654.89) than those have genotype 1*/2*(1216.25±650.89) and those have genotype 1*/1* (1144.80 ± 659.98).

In the present study, both genotypes of LAPTM4B and its protein level in plasma have negative correlation with [Age, sex, AFP, Child score, BCLC, Liver size(CT), Liver PV(CT), Spleen size(CT), ascites, Hg, TLC, PLT, ALT, AST, ALP and ALB]. But, there was significant association of LAPTM4B genotypes and protein level in HCC patients and TNM staging.