دراسة بعض النواحي البيولوجية لسرطان الكبد في مرضي الالتهاب الكبدي الفيروسي (سي)

رسالة مقدمة تمصيدا للحصول عليى درجة الدكتوراء في الكيمياء الحيوية

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قسم الكيمياء الحيوية كلية العلوم—جامعة عين شمس 2005

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Molecular Aspects of Hepatocellular Carcinoma (HCC) in Patients with HCV Infection

Thesis Submitted for Fulfillment of Ph.D. Degree in Science (Biochemistry)

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2005

Abstract

Carcinogenesis involves a multistep process whereby a normal healthy cell undergoes both immortalization and oncogenesis. It has been suggested that cell immortalization and level of telomerase activity are directly related. In order to investigate the diagnostic value of NO, TNF- α , and telomerase enzyme activity versus the classical clinicopathological factors and classical tumor marker like AFP, we analyzed 41 patients with HCC, 25 patients with chronic HCV infection, and 22 healthy persons served as a control group for the expression of theses markers (AFP, NO and TNF- α), in addition to 30 selected tissue samples for the detection of telomerase enzyme activity using TRAP technique and i-NOS expression using western blotting technique. Significant increased of NO, TNFα, and AFP were observed in both HCC and HCV infected patients groups when compared with the normal control group. NO had the best sensitivity (98.5%) at cutoff value 23.4 umol/L, while AFP had the best specificity (95.5%) at cutoff value 2.5 ng/ml, which indicates that the expression of these markers was increased according to the severity of liver injury and may play an important role in early detection of HCV diseased patients with or without HCC, while NO could used as a useful prognostic marker for HCC patients.

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The level of relative telomerase enzyme activity increased significantly in HCC patient group when compared with HCV infected group. This indicates that telomerase is a very sensitive marker more than standard tumor marker AFP for the early detection of HCC patients and might be a discriminative marker that shows significant signals in the transition phase of carcinogenesis.

i-NOS was expressed in HCC patients and in some cases of chronic HCV patients. This indicates that the increased level of NO may expressed by i-NOS.

Correlation tests revealed that there was no significant difference between telomerase activities and each of NO, TNF α , and AFP levels (P> 0.05). These indicate that there was a difference in the respective expression of these markers during different phases of the HCV diseased patients.

Key words: HCC, HCV,NO, TNF-α, Telomerase enzyme.