

## Possible Role of Lymphotoxin $\alpha$ , $\beta$ and their Receptor (TL $\beta$ Rs) in Promoting Liver Carcinogenesis during Infection with Hepatitis C Virus

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### Abstract

**Background** Lymphotoxin  $\alpha$ ,  $\beta$  and their receptor play an important role in the control of lymphoid organ development and support of immune responses against pathogens.

**Objective** To investigate expression of the lymphotoxin  $\alpha$ ,  $\beta$  and their receptor TL $\beta$ Rs using immunohistochemistry technique in patients with chronic active hepatitis and hepatocellular carcinoma.

**Methods** Thirty five formalin fixed, paraffin embedded liver tissues, obtained from Liver and Digestive System Technical Hospital and private laboratories in Baghdad, were studied. In addition, thirteen apparently normal liver autopsies were collected from the Forensic Medicine Institute Archives after permission and used as control group.

Liver tissue sections were cut at 4  $\mu$ m and placed on positively-charged slides, used for the detection of lymphotoxin  $\alpha$ ,  $\beta$  and receptor TL $\beta$ Rs by immunohistochemistry technique.

**Results** The expressions of lymphotoxin  $\alpha$ ,  $\beta$  and receptor TL $\beta$ Rs were detected in most patients infected with HCV, 88%, 84%, 76% respectively in patient with chronic active hepatitis and 80%, 70%, 90% respectively in patients with hepatocellular carcinoma while low level of expression of these markers was observed in healthy control group.

**Conclusion** Lymphotoxin  $\alpha$ ,  $\beta$  and their receptor TL $\beta$ Rs may play an important role in the development and progression of HCV associated liver pathology.

**Key words** lymphotoxin, TLR, carcinogenesis hepatocellular carcinoma.

### Introduction

Inflammation is a defensive process initiated by innate and specific cellular and humoral immune component in response to an insulting agent, which in most instances an infectious agent <sup>(1,2)</sup>. Initiation of the inflammatory process is triggered by activation of the immune component through the release of vasoactive and chemotactic substances elicited due to trauma or infection <sup>(3)</sup>.

Tumor necrosis factor (TNF) superfamily comprises several cytokines including, but not limited to, lymphotoxin (LT)  $\alpha$ ,  $\beta$  and their tumor necrosis factor receptor (TLRs). These factors are known to play a role in the induction of necrotizing activity of neoplastic cells <sup>(4)</sup>.

Lymphotoxins  $\alpha$  and  $\beta$  are known to be responsible for organogenesis and lymphoid tissue maintenance <sup>(5)</sup>. They are generally produced, under normal physiological circumstances, by activated T, B and NK