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Controversial issues regarding the roles of IL-10 and IFN-γ in active/inactive chronic hepatitis B

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Abstract

According to the important roles played by cytokines in induction of appropriate immune responses against hepatitis B virus (HBV), Dimitropoulou *et al* have examined the important cytokines in their patients. They showed that the serum levels of interleukin 10 (IL-10) and interferon-γ (IFN-γ) were decreased in patients with HBeAg-negative chronic active hepatitis B compared with the inactive hepatitis B virus carriers (Dimitropoulou *et al* 2013). The controversy can be considered regarding the decreased serum levels of IFN-γ in the HBeAg-negative chronic active hepatitis B patients. They concluded that subsequent to decreased expression of IFN-γ, the process of HBV proliferation led to liver diseases. Previous studies stated that HBV is not directly cytopathic for the infected hepatocytes and immune responses are the main reason for destruction of hepatocytes (Chisari *et al*, 2010). Scientists believe that immune responses against HBV are stronger in active forms of chronic HBV infected patients than inactive forms (Zhang *et al*, 2012). Therefore, the findings from Dimitropoulou *et al* may deserve further attention and discussion. Additionally, downregulation of IL-10 in chronically active hepatitis B infected patients has also confirmed our claim. IL-10 is an anti-inflammatory cytokine and its expression is increased in inactive forms in order to downregulate immune responses (Arababadi *et al*, 2012). Thus, based on the results from Dimitropoulou *et al*, it can be concluded that increased immune responses in chronically active hepatitis B infected patients are related to declined expression of IL-10 and interestingly IFN-γ is not involved in induction of immune responses in these patients.

Key words: Hepatitis B virus; Interferon-γ; Interleukin-10

Core tip: Cytokines play a central role in the induction of appropriate immune responses against hepatitis B, as well as the clinical manifestations of the disease. Dimitropoulou *et al* showed that serum levels of interleukin 10 and interferon-γ decreased in patients with HBeAg-negative chronic active hepatitis B compared with inactive hepatitis B virus (HBV) carriers (Dimitropoulou *et al*, 2013) and concluded that this can lead to liver disease. However, we challenge their conclusion because we believe that inappropriate host immune responses are the main causes responsible for the clinical manifestations of the disease, but not the actual replication of the HBV particles.

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TO THE EDITOR

We have carefully reviewed the article by Dimitropoulou

et al[1] who examined the serum levels of both pro-and anti-inflammatory cytokines in patients with hepatitis B e antigen (HBeAg)-negative chronic active hepatitis B and inactive hepatitis B virus (HBV) carriers. It is well established that the serum levels of cytokines change during various clinical presentations of hepatitis B[2,3]. Based on the important roles played by cytokines in the induction of appropriate immune responses against HBV, Dimitropoulou *et al*[1] examined the most relevant cytokines in hepatitis B infected patients. They reported that the serum levels of interleukin-10 (IL-10) and interferon-γ (IFN-γ) were decreased in patients with HBeAg-negative chronic active hepatitis B compared with inactive hepatitis B virus carriers.

The apparent controversy arises from the author's discussion regarding decreased serum levels of IFN-γ in the HBeAg-negative chronic active hepatitis B patients. The authors have concluded that subsequent to decreased expression of IFN-γ, the processes of HBV proliferation can lead to liver diseases. Previous studies have demonstrated that HBV is not directly cytopathic to the infected hepatocytes and that the main destruction of hepatocytes is caused by host immune responses[4]. Researchers believe that immune responses against HBV are stronger in active forms of chronically HBV infected patients as opposed to the inactive forms[5]. Therefore, the discussion addressing these observations should be carefully reviewed, even for a revision. Additionally, downregulation of IL-10 in chronically active hepatitis B infected patients also confirms our claim. IL-10 is an anti-inflammatory cytokine and its expression is increased in inactive forms in order to attenuate immune responses[2]. Thus, based on the results presented by Dimitropoulou *et al*[1] it can be concluded that increased immune responses in chronically active hepatitis B infected patients is related to reduced expression of IL-10 and interestingly IFN-γ is not involved in the induction of immune responses in these patients.

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