**Name of journal: World Journal of Gastrointestinal Pathophysiology**

**ESPS Manuscript NO: 6067**

**Columns: Letter to the Editor**

**Controversial issues regarding roles played by IL-10 and IFN-γ in active /inactive chronic hepatitis B**

Khorramdelazad H *et al*. Hepatitis B and IL-10

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**Author contributions:** Khorramdelazad H wrote and editing of paper; Hassanshahi G edited of paper; Arababadi MK contributed to design of question and letter idea.

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**Received:** September 30, 2013  **Revised:** December 3, 2013

**Accepted:** April 17, 2014

**Published online:**

**Abstract**

According to the important role played by cytokines in induction of appropriate immune responses against hepatitis B virus (HBV), Dimitropoulou *et al* have examined the important cytokines in the patients. They have reported that the serum levels of IL-10 and IFN-γ were decreased in patients with HBeAg negative chronic active hepatitis B compared to inactive hepatitis B virus carriers (Dimitropoulou *et al* 2013). The controversy can be considered for the authors discussion regarding decreased serum levels of IFN-γ in the HBeAg negative chronic active hepatitis B patients. Authors have concluded that subsequent to decreased expression of IFN-γ, processes of HBV proliferation lead to liver disease. Previous studies stated that HBV is not cytopathic for the infected hepathocytes directly 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, it looks like that author discussion deserves more attention as well as revision. Additionally, downregulation of IL-10 in chronic active hepatitis B infected patients also confirm our claim. IL-10 is an anti-inflammatory cytokine which its expression is increased in inactive forms in order to downregulate immune responses (Arababadi *et al*, 2012). Thus, based on the Dimitropoulou *et al*, results it can be concluded that increased immune responses in chronic active hepatitis B infected patients is related to declined expression of IL-10 and interestingly IFN-γ is not involved in induction of immune responses in these patients.

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**Key words****:** Hepatitis B virus; IFN-γ; IL-10

**Core tip:** Cytokines play central roles in the induction of appropriate immune responses against hepatitis B, as well as the clinical manifestations of the disease. Dimitropoulou *et al*, reported that serum levels of IL-10 and IFN-γ decreased in patients with HBeAg negative chronic active hepatitis B compared to inactive hepatitis B virus 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, not the actual replication of the HBV particles.

Khorramdelazad H. Hassanshahi G. Arababadi MK. Controversial issues regarding roles played by IL-10 and IFN-γ in active /inactive chronic hepatitis B.

**Available from:**

**DOI:**

**TO THE EDITOR**

We have carefully reviewed the article by Dimitropoulou *et al*[1] (Dimitropoulou *et al*[1],2013) which examined the serum levels of some 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 carriers. It is well established that the serum levels of cytokines change during various clinical presentations of hepatitis B (Arababadi *et al*[2], 2011; Arababadi *et al*[3], 2010). Based on the important roles played by cytokines in the induction of appropriate immune responses against hepatitis B virus (HBV), Dimitropoulou *et al*[1] examined the most relevant cytokines in hepatitis B infected patients. They reported that the serum levels of IL-10 and IFN-γ were decreased in patients with HBeAg negative chronic active hepatitis B compared to inactive hepatitis B virus carriers (Dimitropoulou *et al*[1], 2013).

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 lead to liver disease. Previous studies have demonstrated that HBV is not directly cytopathic to the infected hepathocytes and that the main destruction of hepatocytes is caused by host immune responses (Chisari *et al*[4], 2010). Researchers believe that immune responses against HBV are stronger in active forms of chronic HBV infected patients as opposed to the inactive forms (Zhang *et al*[5], 2012). Therefore, the author may wish to review the discussion addressing these observations and potentially considering a revision. Additionally, downregulation of IL-10 in chronic 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 (Arababadi *et al*[2], 2012). Thus, based on the results presented by Dimitropoulou *et al*[1] it can be concluded that increased immune responses in chronic 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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**P-Reviewers:** Herath CB, Takagi H **S-Editor:** Qi Y

**L-Editor: E-Editor:**