Reviewer's report

**Title:** Changes of Treg and Th17 balance in the development of acute and chronic HBV infection

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**Reviewer:** Christoph Neumann-Haefelin

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Xue-Song et al. study the impact of Treg and Th17 balance in the course of HBV infection. Their findings are largely confirmative when compared to recent studies (e.g., Zhang et al., Hepatology 2010, 51:81-91; Zhai et al., Viral Immunol 2011, 24:303-10; Niu et al., BMC Immunol 2011, 19;12:47). Most importantly, the correlation of Th17 cells with ALT levels and increased frequency of Th17 cells as well as the decreased Treg:Th17 ratio have been described previously.

In addition, there are several discrepancies and other issues in the study that need to be addressed.

**Major:**

- The abstract needs to be better organized. In particular, the methods section should introduce the different patient groups studied and also introduce the abbreviation used later (CHB, ACHBLF etc.). Unspecific terms such as “acute liver inflammation” and “chronic inflammation” should be avoided, and the specific patient groups should be stated in the results section.

- Introduction section: previous findings regarding Th17 cells and the Treg:Th17 ratio need to be explained in more detail in order to indicate that purpose and significance of the study.

- The authors find increased Th17 cytokine profiles in acute hepatitis B (AHB) and acute-on-chronic hepatitis B liver failure (ACHBLF) patients, but increased Treg cytokine profiles in chronic hepatitis B (CHB) patients. This finding is not consistent, however, with the significantly reduced Treg:Th17 cell ratio in both, ACHBLF as well as CHB patients (Fig. 2d). Therefore, the conclusion that “CHB patients showed too strong Treg cell-mediated immunity and ACHBLF patients showed too strong Th17 cell-mediated immunity” (page 6), or, similarly, “Immunosuppression by Treg cells mainly occurs in CHB and Th17-mediated inflammatory damage mainly occurs in ACHBLF” (page 7) is not strongly supported by the data presented.

- In Figure 3, the authors include all patient groups in their correlation of immunological parameters with clinical parameters. This is not suitable, since the patient cohorts show a clear clustering in these analysis (e.g., the acute hepatitis B cohort clusters due to their high ALT levels in Fig. 3a+c, while the acute-on-chronic hepatitis B liver failure cohort clusters due to high total bilirubin levels in Fig. 3b+d+g.). Thus, separate analysis for the individual patient cohorts are necessary.
The authors find an inverse correlation of Th17 cells and viral load, which is in contrast to the findings of Zhang et al. (Hepatology 2010, 51:81-91). This needs to be discussed.

Original data, most important dot blots of intracellular IL-17 and Foxp3 stainings need to be displayed.

The manuscript needs revision by a native scientist. For example, the authors often used “were correlated” instead of “did not correlate with”.

Minor.

Page numbers are missing.

“Tbil” is not a usual abbreviation and should be replaced by total bilirubin in the abstract and manuscript.

Page 3: “More than 20 billion people have been infected with HBV globally...”: Is this a estimation of people infected in history? I did not find this number in the references given (refs 1 and 2).

Page 3: “In chronic hepatitis B (CHB), Foxp3+ Treg cells are closely related with the development and progress of the disease (refs 10-12).”: Ref 11 does not deal with HBV.

Page 4: IL-2 is not a good Treg marker.

Page 4 and Figure 2d: Treg/Th17 ratio is a pure number, not a percent value.

Page 5: Which “liver inflammation indexes” were used? Were these based on serological markers or histology?

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.