Reviewer’s report

Title: Longitudinal fluctuations in PD1 and PD-L1 expression in association with changes in anti-viral immune response in chronic hepatitis B

Version: 1 Date: 29 March 2012

Reviewer: Frank Tacke

Reviewer’s report:

This is an interesting and concisely written article on fluctuating levels of PD1 and PDL1 in patients chronically infected by hepatitis B virus. My major concern is that many studies have investigated on this topic before, thus limiting the novelty of the article. Moreover, the findings in this paper are mainly observational.

Specific concerns are (all major compulsory revisions):

1. Figures 1 and 2 need quantitative evaluations (data partially presented in Figure 6), and it is important to also back-calculate to the total number of cells. Statistical significant differences need to be indicated in the figure. The legend is misleading - these are not 15 independent experiments, but 15 individual patient samples.

2. It is important to comprehensively analyze PD1 and PDL1 expression from livers in a quantitative manner. Numbers of positive cells and the expression level (minimally extracted from qPCR data) need to be given.

3. The relevance and the specificity of the findings remain obscure. Thus, I believe it is crucial to have two additional control populations, at least for circulating cells: HCV-infected patients and NASH patients, both groups matched for the fibrosis stage as assessed by histology.

4. Findings on PD1 and PDL1 should be correlated to disease stage not only based on serum levels (ALT, HBV-DNA), but also based on histology (staging, grading).

5. The authors need to point out more clearly what the key point of the paper is. This would somewhat overcome the limited novelty of the study.

Minor essential revisions:

6. Presentation of FACS data is not optimal. Labeling of the axes is difficult to read.

Level of interest: An article whose findings are important to those with closely related research interests
**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.