

Dear Editor:

We are pleased to answer the questions of the reviewers' and the manuscript entitled "Cytokines Predict the Virological Response in Chronic Hepatitis B Patients Receiving Peginterferon Alfa-2a Therapy." (Manuscript ID53601) has also been extensively revised according to the comments.

Reviewer's code: 02208246

Host and viral factors play key roles in the natural history of chronic hepatitis B, the disease activity, and the effectiveness of antiviral therapy. At present, the antiviral strategy for chronic hepatitis B mainly lies in the effective suppression of the virus and the recovery of HBV-specific immune responses. Antiviral treatment with PEG-IFN effectively inhibits HBV replication and may lead to seroconversion of HBeAg, clearance of HBsAg, normalization of ALT levels, and histologic improvement. Screening multiple biomarkers can clarify the immune mechanism of HBV infection and predict the response to antiviral therapy. the relationship between multiple cytokines and chemokines and the responses to peginterferon α -2a therapy in patients with CHB has not previously been clarified. In this study, Fu et al analyzed the serum levels of cytokines in CHB patients treated with peginterferon α -2a in their treatment phases and responses to the therapy. This study is very interesting, and the manuscript is very well written. Minor comments: 1. There are some minor language polishing which should be corrected. 2. I suggest the authors add a reference, and discuss it with this study, "Serum M2BPGi Level Is a Novel Predictive Biomarker for the Responses to Pegylated Interferon- α Treatment in HBeAg-positive Chronic Hepatitis B Patients" by Ming-Yu Zhu et al, J Med Virol, 90 (4), 721-729 PMID: 29247529 DOI: 10.1002/jmv.25010. 3. Tables and figures are very good. Tables may be require an editing.

Answer: Thanks a lot for having reviewed our manuscript. Now we have revised the manuscript according to your comments.

Firstly, we corrected some language errors in the article, including the spelling of words, the use of some advanced vocabulary, and the

adjustment of sentence formats, all these changes are highlighted in the manuscript. As you mentioned, Ming-Yu Zhu et al demonstrated that baseline serum Mac-2-binding protein glycosylation isomer (M2BPGi) level was a novel predictor of VR and SR for PEG-IFN- α treatment in HBeAg-positive CHB patients, more importantly, The AUC was 0.682 (95%CI = 0.568-0.792) of M2BPGi, which was higher than HBsAg (AUC = 0.566) and HBV DNA (AUC = 0.56) in predicting VR. Previous studies have also found that M2BPGi also called WFA+-M2BP, which is a serum biomarker for assessing liver fibrosis in patients with viral hepatitis, and its levels significantly correlated with serum IP-10 levels, our results suggested the AUROC values of the serum IP10 levels were measured before peginterferon therapy were 0.787, Therefore, it may be possible M2BPGi combined with IP-10 as biomarkers before interferon treatment because of higher sensitivity and specificity. Finally, we corrected the Table and removed Table 3, because it is only a summary of Figure 2, these results can be seen in the description of the results section in our manuscript, we have rearranged the format of the Table to make it more beautiful and conform to the rules of scientific tables.

Reviewer's code: 02854801

This study of cytokine/chemokine in PEG-IFN treatment CHB patients is very interesting. The manuscript is very well written. I recommend to accept it for publication as it is. Thank you very much.

Thanks a lot for having reviewed our manuscript, best wishes.