Dear Editor,

Thank you for carefully reviewing our manuscript previously titled "Hepatitis B virus upregulates host expression of α-1,2-mannosidases via the PPARα pathway" for possible publication in the World Journal of Gastroenterology. We are grateful to you and your reviewers for their constructive critique. I have been in accordance with the requirements of the Journal changed my manuscript. We have revised the manuscript, highlighting our revisions in red. and have attached point-by-point responses detailing how we have revised the manuscript in response to the reviewers' comments below.

Thank you for your consideration and further review of our manuscript. Please do not hesitate to contact us with any further questions or recommendations.

Yours Sincerely,

Deying Tian

For Reviewer #1:

1. Comment

1) General comments Background of the study: Hepatitis B virus (HBV) infection is the most common chronic viral infection worldwide. Because of insufficient immune response, some HBV-infected patients will develop chronic hepatitis and possibly liver cirrhosis and hepatocellular carcinoma (HCC). In the present study, the authors aimed to explore one of the mechanisms able to impair dendritic cell (DC) function in patients suffering from chronic hepatitis B: they hypothesized that HBV could promote the demannosylation of HBV glycoprotein coat by increasing the expression of alfa-mannosidase 1 allowing HBV to escape from host immunity. 2) Specific comments The overall structure of the manuscript is good. The Title and the abstract are satisfactory with the main relevant data developed in the manuscript, the introduction is clear and interesting. Major data allowing us to retain the importance of the present work: The aim of the manuscript 29674 was to explore one of the mechanisms of HBV escape showing that HBV infection increases the expression of alfa-mannosidase I via the PPAR-alfa signaling pathway. The main results of the present study showed that (1) alfa-1,2-mannosidase is upregulated in a stably transfected HBV cell line; (2) alfa-1,2-mannosidase is upregulated in human liver tissues, especially in non-tumorous liver tissues in HBV-related HCC patients; (3) after the application of the PPAR-alfa inhibitor MK866, the effects of HBV on alfa-1,2-mannosidase expression was neutralized. Expected complementary data to be produced by the authors: - Complementary details are only expected in the Discussion/Conclusion section: Thus, the discussion should be enriched with an additional paragraph and the help of a synthetic Figure 5 (to be added) explaining the overall mechanisms of HBV escape from host-related immunity with a focus on the role of class I alfa-mannosidases via the PPAR-alfa pathway which has been developed in the present manuscript.

Response:

Thanks for the suggestion. In the revised manuscript, we added a synthetic Figure 5 to explaining the overall mechanisms of HBV escape from host-related immunity with a focus on the role of class I alfa-mannosidases via the PPAR-alfa pathway which has been developed in the present manuscript in the discussion.