

Dear Dr./Prof. Ma,

Thank you very much for your decision letter and advice on our manuscript (Manuscript 31348) entitled "**Non-ALT biomarkers for markedly abnormal liver histology among Chinese PNALT-CHB patients**". We also thank the two reviewers for the valuable comments and suggestions. Accordingly, we have revised the manuscript. All amendments are highlighted in red in the revised manuscript. In addition, point-by-point responses to the comments are listed below this letter.

This revised manuscript has been edited and proofread by Medjaden Bioscience Limited.

We hope that the revision is acceptable for the publication in your journal.

Look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Jin-Lin Cheng

First, we would like to express our sincere gratitude to the reviewers for their valuable comments.

Replies to Reviewer 1

Specific Comments

The data presented in the report are very suggestive of a new 'reformulation' of liver injury in CHB patients. In my opinion, the inclusion of new markers of necroinflammation may even reinforce the current data, since the present frame of statistical analysis is too limited to ensure the generalization of the proposal. I suggest DNA markers or inflammatory markers associated to other cell types as 'suggestive' of prognosis of CHB. Regarding the present data, please increase the size of the lettering in the figures and include the bars of statistical analysis on Fig 4.

Response: Thank you for your insightful suggestions. We agree that additional markers of viral DNA or/and necroinflammation may further improve the prognostic value. However, such inclusion will be best performed in a future study, which will be expanded from the current study. We plan screening out possible prognosis markers from the serum and tissues of the PNALT-CHB patients with molecular and proteomic tools, and combine them with clinical parameters to make better prediction of prognosis. Several sentences have been added in Discussion of the revised manuscript (Page 15, Lines 14-17) to address this issue.

We have reformatted the font size and bars in the figures in Fig 4 per the WJG format guidelines.

Replies to Reviewer 2

Specific Comments

The paper deal with an interesting approach to CHB patients and liver damage and this approach, even if interesting, is not enough supported by a statistical analysis of a huge number of data. Notwithstanding, data are interesting and deserve publication.

Response: Thank you for your comment.