

August 17, 2021

Lian-Sheng Ma, Science Editor, Company Editor-in-Chief
Editorial Office
Baishideng Publishing Group Inc

Re: Revision of Manuscript (Manuscript NO: 62517)

Dear Editor:

We would like to thank you very much for your decision letter and advice on our manuscript entitled “**Novel roles of LPS and TLR4 / NF- κ B signaling pathway in the inflammatory response to liver injury in Budd-Chiari syndrome**”. The valuable comments and suggestions have helped us to improve the manuscript.

We have carefully read your letter and considered the comments/suggestions. Accordingly, we have revised the manuscript accordingly, and all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the comments are listed below this letter. We believe that the manuscript has been much improved.

This revised manuscript has been edited and proofread by Medjaden Inc.

As always, we are grateful to you for interest in our study. If you and the reviewers have any remaining concerns, we shall make an improvement under your guidance. We look forward to hearing from you soon.

Yours sincerely,

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Point-by-point responses to Reviewers' comments

Replies to Reviewer 1

General Comments:

1. Typing errors. English language corrections

Response: Thank you for bringing this issue to our attention. We have checked the manuscript and corrected the typographic errors. In addition, the revised manuscript has been edited and proofread by Medjaden Bioscience Limited.

2. The article contains 6 Tables and 10 Figures. Figures in the text should be no more than 3 and no more than 2-3 Tables. All other material should appear as a Supplement

Response: Your suggestions have been well taken. We have deleted non-essential tables and re-grouped figures. After having done so, three figures and one table are presented in the main text, while Supplementary figures have been put in Supplementary Material.

Major Comments:

1. (Page 7, Line 9): Please omit the phrase.

Response: After reading your comments, we tried to address the issue but were unclear about which phrase you were referring to. This could be because we have different numbers of Pages and Lines.

2. (Page 7, Line 10): ... and usually caused by myeloproliferative liver diseases.

Response: We are sorry to say that we don't know what you would suggest us to do with "and usually caused by myeloproliferative liver diseases.".

3. (Page 8, Lines 6-9): The question is whether LPS increase is a cause or result of BCS. The odds are that LPS is an effect of liver outflow obstruction. Many other causes of LPS increases in the blood, as gram-negative infections, are not associated

with BCS in patients with a normal or cirrhotic liver.

Response: Thank you for your question, and LPS increase is a result of BCS.

4. (Page 9, Lines 13-15): Authors should clarify the exact placing of the suture closing of the IVC, in relation to hepatic venous outflow.

Response: As you suggested, we have made the following clarification about the exact placing of the suture closing of the IVC in the revised manuscript: “A silk thread was used to ligate the IVC at a position 5-10 mm above the opening of the hepatic vein.

5. (Page 11, Lines 3): In a sentence following the title, please write: “By an RT-qPCR, β -actin, TLR4, NF- κ Bp65, IL-2, TNF- α and IFN- γ was measured”.

Response: Your good suggestion has been well taken, and the title has been followed by the suggested sentence “By an RT-qPCR, β -actin, TLR4, NF- κ Bp65, IL-2, TNF- α and IFN- γ was measured” in the revised manuscript.

6. (Page 11, Lines 16): Please write: “Western blot (WB) analysis was performed to detect the protein levels of β -actin, TLR4, NF- κ Bp65, IL-2, TNF- α , IFN- γ ”.

Response: We have followed your good suggestion and included the sentence ““Western blot (WB) analysis was performed to detect the protein levels of β -actin, TLR4, NF- κ Bp65, IL-2, TNF- α , IFN- γ ” in the revised manuscript.

7. (Page 13, Lines 15): Biochemical measurements usually are not distributed normally. Authors should verify that their data is normally distributed, before expressing them as mean \pm 1SD values. Otherwise, their expression should be as medians (IQR) and be compared by non-parametric statistics.

Response: Thanks for your comment on statistical analysis and we have looked back at our original data analysis. It has been confirmed that the data were normally distributed and thereby were expressed as mean \pm SD.

8. (Page 15, Line 8): Please omit the “F” value at this point and everywhere else in the text.

Response: As you suggested, the “F” vale has been omitted in the revised manuscript.

9. (Page 19, Line 8): Please explain abbreviations when first mentioned in the text.

Response: We have followed your good suggestions to spell out the abbreviations for first appearance in the revised manuscript.

Minor Comments:

1. (Page 1, Line 7): Please replace “in” with “associated with”.

Response: Thank you for your good suggestion and we have replaced “in” with “associated with” in the revised manuscript.

2. (Page 10, Line 21): “attempted” has an ambiguous meaning. It may mean that the azo reagents were or were not finally mixed. Please explain what was finally done.

Response: Thank you for bringing this issue to our attention. “we attempted to add” has been changed to were added” in the revised manuscript.

3. (Page 15, Line 2): Please write: “Hepatic and plasma levels of LPS in rats with BSC”.

Response: “Hepatic and plasma levels of LPS in rats with BSC” is better and we have addressed this issue in the revised manuscript.

4. (Page 18, Line 4): BCS-induced liver damage.

Response: As suggested, we have made correction in the revised manuscript.

5. (Page 18, Line 7 & 9): HV outflow.

Response: We have checked and made correction in the revised manuscript.

6. (Page 19, Line 2): ...but could not completely resolve....

Response: We have followed your good suggestion and made correction in the revised manuscript.

7. (Page 19, Line 8): Relatively small.

Response: We have checked and made correction in the revised manuscript.

8. (Page 19, Line 14): Becomes markedly elevated in BCS

Response: Thank you for your good suggestion, accordingly we have made correction in the revised manuscript.

As always, we sincerely appreciated your thoughtful comments and suggestions. If you have any remaining concerns, we shall make further amendments under your guidance.

Replies to Reviewer 2

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: Thank you very much for your constructive comments and suggestions, which have helped us in our efforts to improve the manuscript. Accordingly, we have uploaded the approved grant application form.

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: As you suggested, we have provided original images of Western blot. In addition, the figures were prepared and arranged using PowerPoint, allowing the editor to reprocess the graphs, arrows, or text portions.

(3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text;

Response: We have followed your suggestion and added “Article Highlights” at the

end of the main text.

(4) For PMID and DOI numbers of references from English-language journals, please ensure PMID and DOI numbers in the square brackets.

Response: As suggested, PMID and DOI numbers of references have been included in the list of References in the revised manuscript.

Again, thank you so much for your help. If you have any remaining concerns, we shall make an improvement under your guidance.