

Dear Editor,

Thank you very much for your letter and the comments from the reviewers about our paper submitted to *World Journal of Gastrointestinal Surgery* (Manuscript ID: 88060).

We have examined the manuscript carefully and revised it according to the comments. Here we have submitted the revised manuscript and the reply to the opinions of reviewers.

Unfortunately, in the previously submitted manuscript, we forgot to include another project (No. 2020GY39) that supports this study in the manuscript. We have included this project in the revised manuscript.

Thank you again for the help provided by you and the reviewers. If you have any question about this paper, please let me know without hesitation.

Yours sincerely,

Heng Zhou

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Comment1: In the "INTRODUCTION" section, the review suggests changing the description of "there have traditionally been no drugs generally recognized as safe and effective for clinicians to use to promote liver regeneration" to "there are no drugs generally recognized as safe and effective for clinicians to promote liver regeneration".

Response1: Thank you very much for your detailed guidance on our manuscript. We have adopted your suggestions and made corresponding modifications in the revised manuscript.

Comment 2: In the "INTRODUCTION" section, the reviewer suggested deleting or adding citations to sentence "Several research teams have also noticed a possible role of the vagus nerve in liver regeneration; unfortunately, this process involves a variety of cytokines, chemokines, and signaling pathways, which we know little about"

Response2: Thank you for your guidance. We have added a citation to this sentence in the revised manuscript.

Comment3: The review experts suggest placing the content of the third paragraph of the "INTRODUCTION" section in the "DISCUSSION" section.

Response3: Thank you very much for your meticulous guidance on our manuscript.

The third paragraph of the "INTRODUCTION" section aims to introduce readers the scientific hypotheses proposed in this article to address the current shortcomings, to provide a simple and concise description of the research we have conducted and the results and conclusions we have obtained.

The "DISCUSSION" section includes the above content, and here we have conducted a more detailed and in-depth discussion on these contents.

Comment4: In section "MATERIALS AND METHODS—*Animals and Treatment*", the review's suggestion is "the specific surgical procedures are described 122 in detail below"

Response4: We have added the sentence "The specific surgical (PHx and Hv) procedures are described in detail below" in the revised manuscript and provided a detailed description of the surgical procedures for PHx and Hv in the "MATERIALS AND METHODS" section.

Comment5: In section "MATERIALS AND METHODS—*Analysis of Liver Injury*", the review requires "Describe how H&E was used as marker of liver injury".

Response5: We have added a description of "In previous studies, we found that mice undergoing 70% PHx showed varying degrees of residual liver damage after surgery, manifested as liver parenchymal hemorrhage and necrosis^[18]" in the revised manuscript.

Comment6: In section "MATERIALS AND METHODS—*Measurement of IL-22 Levels*", the review requires "Briefly describe the procedure".

Response6: We have added a description of "In short, add standards and samples to the microplate strips, then sequentially add antibodies, IL-22 conjugate, substrate solution, and stop solution. Finally, measure the optical density values of each well at a wavelength of 450nm within 30 minutes" in the revised manuscript.

Comment 7: In section "MATERIALS AND METHODS—*Western Blot Analysis*", the review requires "Briefly describe".

Response 7:We have added a description of "The protein was extracted from hepatic tissue, separated by SDS-PAGE, and transferred to PVDF membrane. After incubated with primary and secondary antibodies, the protein bands were visualized using a luminescent reagent kit" in the revised manuscript.

Comment 8: In section "MATERIALS AND METHODS—*Statistical Analysis*", the review suggests swapping the positions of the two sentences "All data in this paper are expressed as mean \pm standard deviation values" and "Comparisons between two groups were performed with Student's *t*-test; for more than two groups, one-way analysis of variance followed by Tukey's post hoc test was used".

Response 8: We have made corresponding modifications according to the review's requirements.

Comment 9: The review suggests deleting the first sentence "IL-22 release increases after liver injury " from the third paragraph of the "DISCUSSION" section.

Response 9: In the revised manuscript, we have deleted this sentence.

Comment 10: In Figure 1, the review's comment is "Which are the white and

black groups? I think that the color legend is referred only to graphs C,E,F"

Response 10: According to the requirements of the review, we have added the color legend to Figure 1B, which will make reading easier.

Comment 11: In Figure 2, the review's comment is "GRAPH A add color legend"

Response 11: According to the requirements of the review, we have added the color legend to Figure 1A.

Comment 12: The review provides guidance on individual words in multiple parts of the manuscript, including adding, deleting, or replacing them.

Response 12: Thank you very much for the detailed and professional guidance provided by the reviewer on our manuscript, which moved and inspired us greatly. We accept all the guidance provided by the review regarding individual words and make corresponding modifications according to the instructions. We have made revisions to every comment raised in the review, the revised parts have been color marked in the manuscript.