

Editor in Chief, *World Journal of Gastroenterology*  
Lian-Sheng Ma, President and Company Editor-in-Chief  
Xue-Jiao Wang, Science Editor, Editorial Office

March 31, 2018

Dear Editors and Reviewers,

Thank you and the reviewers for a thorough review of our manuscript entitled “**Mini-review: Autonomic Nervous System Network and Liver Regeneration**” (No 38740) by myself for publication as a mini review in *World Journal of Gastroenterology*. **The provided ID for this invited review is (00188507).**

The positive comments and suggestions from the reviewers are greatly appreciated. In preparing for revision, we have carefully studied reviewers’ comments and incorporated many of their suggestions into the revised manuscript. For your convenience, we have highlighted the changes made in blue. We hope this revised manuscript is now acceptable for publication in *World Journal of Gastroenterology*.

We declare that this work is original, the manuscript is not under consideration by other journals, and the material has not been previously published. All authors approved the contents submitted. We look forward to hearing from you at your earliest convenience.

Thank you for your consideration.

Sincerely yours,

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Dear Editors and Reviewers:

Thank you very much for your thoughtful comments and suggestions. In preparing the revision, we have carefully studied your comments and incorporated many of your suggestions into the revised manuscript. The following are our point-by-point responses to your comments/concerns. For your convenience, we have highlighted the changes made in blue.

### **Reviewer #1**

*This is a review article based on the authors' recent work published in Ref. 49, on the role of the sympathetic nervous system in liver regeneration involving serotonin released from intestinal chromaffin cells following hepatic injury. While the topic of this article is certainly of interest, and Table 1 recapitulating various cytokines and growth factors is informative, Fig. 1-3 are reproduction of the data presented in ref. 49 (and possibly in Ref 50) in a different format. As these data are represented in Fig. 4, it is better to remove Fig. 1-3 from this review, which would not diminish the message this review intends to convey. The acknowledgement and contribution sections should also be modified accordingly as this is not a regular research paper. The article is informative, however the authors could make it coherent through language editing to improve readability.*

**Response:** We appreciate for a thorough review of our manuscript and are grateful for the positive comment. We have removed Figure 1, 2, and 3 as recommended. According to this modification, original Figure 4 has been changed to be the new Figure 1, and manuscript and legends have been modified. We have also significantly modified the acknowledgement and contribution section to meet the mini-review (page 12, line 2 from the top; page 12, line 3 from the bottom), and modified the manuscript to make it coherent (page 10, line 11 from the top) and the certificate of language editing has been attached.

### **Reviewer #2**

**The authors have considered most of the criticism, issued in the report. The minireview is interesting**

**Response:** We appreciate for the positive comment and thank the reviewer for her/his time and effort on reviewing our paper.

### **Reviewer #3**

*1. It was difficult to interpret whether the figures author provided bring direct correlation to liver regeneration. The figures should be an essential, because the detailed description is not made in the manuscript. A short description and insufficient figures do not make any sense. I request to prepare the chronological results in figure 1 and 2. Only 1 point of 24hr in Figure 1 and 48hr in Figure 2 are insufficient. Several points would be needed. In addition, more information about the figures should have been made available. What is lacking in this manuscript is the lack of adequate information on the Figures. What is Cap+PH? There is no detailed information of the word. Even "PH". For figures 1 and 2, the authors would be better to prepare even photos, separately. We know the PCNA staining for mouse is tricky. The authors stated "While it is difficult to apply these results directly in humans, we believe that this study may represent a step toward the development of essential therapeutics to promote liver regeneration." What is this meaning? How do the authors propose to promote liver regeneration, and what is the authors perspection and expectation?*

**Response:** We thank the reviewer for the thorough review on our manuscript. According to the suggestions from the Reviewer #1, (While the topic of this article is certainly of interest, and Table 1 recapitulating various cytokines and growth factors is informative, Fig. 1-3 are reproduction of the data presented in ref. 49 (and possibly in Ref 50) in a different format. As these data are represented in Fig. 4, it is better to remove Fig. 1-3 from this review, which would not diminish the message this review intends to convey.) we have removed the Figure 1, 2, and 3 to clarify the focus of this review. Therefore, we believe that this modification could convince you and your concerns could be solved.

*2. The authors stated "While it is difficult to apply these results directly in humans, we believe that this study may represent a step toward the development of essential therapeutics to promote liver regeneration." What is this meaning? How do the authors propose to promote liver regeneration, and what is the authors perspection and expectation?*

**Response:** We thank the reviewer for the thorough review on our manuscript. We have significantly modified the Abstract (page 4, line 5 from the bottom) and Conclusions (page 11 line 2 from the bottom).