

15-5-2020

Prof. Na Ma

Editor-in-Chief

*World Journal of Stem Cells*

Dear Na Ma,

I am submitting our revised manuscript titled “*Creating rat hepatocyte organoid as an in vitro model for drug testing*” (Manuscript ID 55067) to be reconsidered for publication in your journal *World Journal of Stem Cells*. We thank the members of your Editorial Board and the reviewer for investing their time in reading our manuscript, and we are grateful for the valuable comments from the reviewer. In this revised manuscript, we checked the accuracy of all ethical documents and verified the completeness of the documents according to the type of manuscript. We resolved all language issues in the manuscript based on the peer review report, and polished our expression in the manuscript. We uploaded funding agency copies of the approval documents, and original pictures and documents were arranged using PowerPoint. Moreover, we added the “Article Highlights” section at the end of the main text. The entire revised manuscript has been edited by a professional English language editing service (Editage) to eliminate non-native language errors.

We feel that the changes made to the manuscript, in light of the comments, have led to significant improvements. Our specific responses to the issues raised by the reviewer are given point-by-point below.

Yours sincerely,

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#### Reviewers' Comments to Author

**Reviewer's code:** 00569670

#### Comments to the Author

The manuscript quality is good overall. The problems that require correction prior to publication are: 1. English spelling and grammatical errors in all parts of the manuscript. 2. It is better to "create" than form the organoids. 3. Remove colloquial language, such as "disaster in a dish" this is not scientifically acceptable. 4. The title is not attractive to readers. I suggest it be changed to: "Creating Rat hepatocyte organoids as an in vitro model to investigate liver disease and test for drug screening." 5. I suggest removing the first sentence of the introduction, since it is confusing and meaningless. 6. In the methods please include the IACUC approval number, and describe how many animals were used, and describe the sex and species of animals, and the methods of euthanasia. 7. In the methods, please describe how many samples/replicates of each experiment were performed. 8. In the discussion, remove the words "in summary." 9. In the figures, please lighten the dark figures to show DAPI staining more clearly.

#### Response to reviewer

Thank for your effort in reading and reviewing our manuscript; we are grateful for your valuable comments. 1. We revised our manuscript, and examined and changed English spelling and grammatical errors in the manuscript. The entire revised manuscript has been edited by a professional English language editing company to eliminate non-native language errors. 2. In the revised manuscript, we use "create organoids" and "generate

organoids" to replace "form organoids"; When the noun form is needed, we use the word "generation". 3. We removed colloquial language; for example, instead of "disaster in a dish", we used "limitation of rapid functional loss of in vitro..." to express our meaning. 4. Indeed, the title we used before was too plain. According to your suggestion, we changed the title to: "Creating rat hepatocyte organoid as an in vitro model for drug testing". We believe that the new title would be more attractive to the readers. 5. We have removed the obscure sentence in the introduction. 6. We added IACUC approval number [2020007A] and animal feeding conditions in the "Animals" part of the methods and described how many animals were used, the sex and species of animals, and the methods of euthanasia in the method of specific experimental steps in "Isolation and preparation of PLECM" and "Isolation of primary hepatocytes". 7. In the statistical analysis part of our methods, we described how many replicates of each experiment were performed. 8. We removed the words "in summary" in the discussion. 9. For the figures, we lightened the dark figures to show DAPI staining more clearly.

Thank you again for your valuable comments and advice.