

Answering Reviewers

Reviewer #1:

The study reviews the role of succinylation in liver pathologies. The review idea is innovative. However, there are several issues to address.

1. Abstract requires a lot of improvements. Authors should avoid using vacuous phrases. Current Abstract is too general and should be improved/re-written. Example: “the liver being an important organ for this kind of modification” . It is necessary to use academic language and be highly specific.

Response: Thank you for your kind suggestion. We have re-written the Abstract to make it more specific.

2. Abstract should indicate the most important enzymes involved into the regulation of succinylation in the liver. The enzymes should be accented regarding their role in the liver-related pathologies, be specific and mention the exact liver pathologies which can be targeted via the regulation of succinylation. Authors should use Core Tips for improvement of their Abstract.

Response: This comment could greatly improve the quality of the manuscript. We indicated the function of histone acetyltransferase 1 (HAT1) and desuccinyltransferase sirtuin 5 (SIRT5) on hepatic metabolism. In addition, we accented that HAT1, lysine acetyltransferase 2A (KAT2A), SIRT5, and sirtuin 7 (SIRT7) are closely related to the development of liver diseases.

We supplemented Core Tips in the revised manuscript.

3. Succinylation is not “newly” discovered process, considering that they cite a paper from 2010. Authors should amend the Introduction (page 3). Authors should use academic language and avoid vacuous generalisations. English language profession editing is recommended.

Response: Thank you for your comments. The words “newly discovered” were deleted. The Introduction has been completely revised and the language has been improved by a native English speaker.

4. Figure 1, 2, 3 etc should be cited in the text. All figures were not mentioned in the text. it is essential they are mentioned at least once in the text.

Response: Thank you for your kind suggestion. Done as requested. Figures 1, 2, and 3 have been cited in the corresponding places in the text. All the changes have been highlighted in the text.

5. Some phrases are hard to understand (it could be wrong grammar/style). For instance, the section 3.1 title “3.1 Succinylation with hepatic glucose and amino acid metabolism” – is unclear. Did you mean “ Succinylation of enzymes involved into regulation of hepatic glucose and amino acid metabolism”???

Response: Your suggestion really means a lot to us. Indeed, the previous description of the section 3.1 and 3.2 were inaccurate, we have changed the headings 3.1 (now 2.1) and 3.2 (now 2.2) to “2.1 The influence of protein succinylation on glucose metabolism and amino acid metabolism.” and “2.2 The influence of protein succinylation on lipid metabolism.” All the changes have been highlighted in the text.

6. The role of succinylation during aging, alcoholic liver disease etc should be described properly.

Response: Thank you for your kind suggestion. The present manuscript mainly focuses on the relationship of succinylation with fatty liver, hepatitis, and HCC, whereas the role of succinylation during aging seem to be deviated from our topic. Additionally, most of the current studies focused on the metabolic fatty liver, and there were few reports of succinylation targeting alcoholic fatty liver.

7. Conclusion section should be improved and provide more specific recommendation for future direction of treatment targeting succinylation in liver cells.

Response: Thank you. The conclusion section has been largely improved as you suggested.

Reviewer #2:

The title reflect the main subject of the manuscript. The abstract summarize and reflect the work described in the manuscript. The key words reflect the focus of the manuscript. The manuscript describe methods in adequate detail.

1. Please improve and extent your introduction.

Response: We appreciate very much for the comment. The Introduction has been re-written and you will find it has been largely improved.

2. Please add more conclusion to your article.

Response: Thank you for your kind suggestion. The conclusion has been extensively improved. All the changes have been highlighted in the text.

ABBREVIATIONS:

Response: Thank you. Done as requested.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific classification: Grade B and Grade D.

2 Language classification: Grade B and Grade C.

3 Specific comments:

(1) Please provide the Figures cited in the original manuscript in the form of

PPT. All text can be edited, including A,B, arrows, etc. With respect to the reference to the Figure, please verify if it is an original image created for the manuscript, if not, please provide the source of the picture and the proof that the Figure has been authorized by the previous publisher or copyright owner to allow it to be redistributed. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: .

Response: Thank you for your kind suggestion. The figure legends have been formatted to a general title and explanation for each figure. Figure 3 has been revised as requested. Figure1 and Figure 2 are separate images without A, B or C sections, so we provide the explanation of Figure1 and Figure 2 for the entire picture.

(2) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published, and correctly indicate the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. *World J Gastroenterol* 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

Response: Thank you for your kind suggestion. Figures are original.

(3) Please provide the PMID numbers and DOI citation numbers to the reference list and list all authors of the references. If there is no PMID or DOI, please provide the website address.

Response: Thank you for your kind suggestion. The PMID numbers and DOI citation numbers have been provided to the reference.

(4) Please add the author's contribution section. The format of this section will be as follows: Author contributions: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; Wang CL, Liang L and Fu JF wrote the paper.

Response: Thank you for your kind suggestion. The author's contribution section has been added in the text.

(5) Please provide the filled conflict-of-interest disclosure form.

Response: Thank you. The filled conflict-of-interest disclosure form has been provided as requested.