

## REVIEWERS' COMMENTS

### Reviewer #1:

Specific Comments to Authors: An Excellent review that covers well a complex role and relationship of exosomes and NLRP3 in the pathogenesis of IBD with a view to identifying novel therapeutic avenues. Li et al. importantly highlight the role of further assessing the potential cross talk to identify novel therapeutic targets for UC. This article neatly sets up future potential scientific avenues that must be pursued to improve understanding of disease pathogenesis and improve the current spectrum of IBD therapeutics.

Reply: Thanks for your guideline. Thank you for your comments and your understanding of our review is thorough and correct.

### Reviewer #2:

Specific Comments to Authors: The role of exosomes on NLRP3 inflammasome, the directions of exosome-NLRP3 inflammasome in the UC are so complex and this article brings more complexity but no resolution, Therefore, it is concluded that further research on this topic is needed.

Reply: Thanks for your nice comments. As stated by the reviewer, the role of exosomes on NLRP3 inflammasome, and the directions of exosome-NLRP3 inflammasome in the UC are so complex. Therefore, to systematically sort out the current evidence in this area, we conducted the present review. Notably, although we did not address the current issues of UC in this review, we identified the current complexity of this field and suggested future research directions, which may be informative for researchers working in this field. (Pages 17-18, lines 334-335)

## 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:

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: .

Reply: Thanks for your guideline. The Figures covered in this review were generated by the authors using AI software. Since the Figures were not formed using PPT, we are not able to provide PPT versions of the Figures, but we do provide the original editable image files in AI format. All text of the AI format Figures can be edited, including A,B, arrows, etc. In addition, the images are not originated from a third party and therefore do not need to obtain copyright granted by other publishers or authors.

Furthermore, all legends had been updated in accordance with the formatting requirements of the journal. (Page 49, lines 960-964; page 50, line 967; page 51, lines 970-971)

(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.

Reply: Thanks for your guideline. The pictures covered in this review were generated by the authors through Adobe illustrator software and did not originate from a third party, and therefore did not require a copyright granted by another publisher or author.

(3) Please don't include any \*, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP <0.05, bP <0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP <0.05 and dP <0.01 are used, and a third series of P values is expressed as eP <0.05 and fP <0.01.

Reply: Thanks for your guideline. The type of this paper is a review, so it does not involve the presentation of statistical significance.

(4) Please add the Core tip section. The number of words should be controlled between 50-100 words.

Reply: Thanks for your guideline. the Core tip section had been added in this revision. The number of words was controlled to be 87 words. (Page 2, lines 31-38)

(5) Please provide the PubMed 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.

Reply: Thanks for your guideline. The PubMed numbers and DOI citation numbers to the reference list and list of all authors of the references had been provided in this revision. (Pages 19-48)

(6) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text (and directly before the References).

Reply: Thanks for your guideline. The “Article Highlights” section had been added at the end of the main text (and directly before the References) in this revision. (Pages 18-19, lines 358-363)

(7) Please provide all fund documents.

Reply: Thanks for your comments. All fund documents had been provided in this revision.

**(2) Company editor-in-chief:**

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. However, the quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, it is recommended that the author(s) provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>. When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a new tool, the RCA, of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>, or visit PubMed at: <https://pubmed.ncbi.nlm.nih.gov/>.

Reply. Thank you very much for your guidance.

(1) For reviewers' comments: We have revised the manuscript point-by-point based on the reviewers' comments, and the response to reviewers' comments are as above, with the revised content also highlighted in yellow color in the revised manuscript.

(2) For English Language: we have checked all English expressions in the full text and sent the manuscript to Bullet Edits Limited again for the linguistic editing and proofreading of the manuscript. We have attached the English polishing certificate as supplementary material in the Manuscript Tracking System.

(3) For the application of PubMed or RCA: All of the literature on the corresponding topics referenced in our manuscript was derived from PubMed and the "Impact Index Per Article" was used to prioritize reference citations. In this revised manuscript, we have also updated the formatting of all literature to provide the PubMed numbers and DOI citation numbers to the reference list.