

Lian-Sheng Ma, Science Editor, Company Editor-in-Chief, Editorial Office
World Journal of Gastrointestinal Oncology

July, 3 2021

Re: **Manuscript NO: 66189**

Dear Editor-in-Chief Ma,

We have attached a copy of our revised manuscript entitled "**Exosomes as Potential Diagnosis and Treatment for Liver Cancer**". We want to thank you and the reviewers for carefully reading the manuscript and the helpful comments.

Since the manuscript type changed from Frontier Article to SYSTEMATIC REVIEWS, the whole text was widely revised. Because Xiao-Cui Wei focused on revising another manuscript (NO:67569), this manuscript (NO: 66189) was mainly revised by Li-Juan Liu. As a result, we hope to note that Dr. Li-Juan Liu and Xiao-Cui Wei equally contributed to this manuscript.

We have carefully addressed the reviewer's questions and the editorial office's comments point-by-point (please refer to the following pages for the details of change).

As suggested, we have deeply revised the abstract section to explain the content of this study simply and directly. We have also renewed the information on liver cancer epidemiology in both the Abstract and Introduction sections. Moreover, we have added the cited literature sources to carry out the research and the applied techniques.

Since the manuscript type was changed, we renewed the methods of research and updated the data to June 2021, which are presented in the MATERIALS AND METHODS section and Figure 1. We sorted out the cited documents, deleted some documents without clinical samples and animal experiments, refined the results, and

divided Table 1 into two new tables (Table 1 and 2) according to the expression levels of exosome contents. The formats of the Abstract and text have also been revised following the author's guideline of SYSTEMATIC REVIEWS.

We believe that the revised manuscript has been substantially improved and hope it meets the standard for publication in the World Journal of Gastrointestinal Oncology. We look forward to hearing from you.

Sincerely yours,

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RESPONSES TO THE REFEREE'S COMMENTS (blue texts are the original comments)

Many thanks for the valuable comments on the manuscript. We have made a substantial revision to the manuscript. Please see below for details of our responses to your comments.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The present article presented by the authors, introduces citing liver cancer and as the greatest adversities faced in the late diagnosis and as consequences for the patients' lives, since most of the conclusive diagnoses for cancer it presents in the middle or late stage.

(1) In the text, more precisely in the abstract, the authors exhaustively cite the terms “exosomes”, removing the necessary cohesion that is necessary to compose the summary of the article, and it is advisable to explain about the content of the study in a simple and direct way in order to attract attention of the reader.

Response: Thank you for reminding us of that. As suggested, we have deeply revised the abstract section to explain the content of this study simply and directly (pages 2-3). We think it will attract the attention of the reader.

(2) In the passage “Liver cancer is the third most significant cause of cancer death in the world” present in the summary, it is again important to seek concrete information and / or reference the data reported and related to the World Health Organization. American Health (PAHO) in conjunction with the World Health Organization (WHO) published in September 2018 and updated in October 2020, liver cancer is the fourth most significant cause of cancer-related death.

Response: Many thanks for your reminder. We have sought concrete information and revised the information on liver cancer epidemiology in both the Abstract section (page 2, paragraphs 1) and the Introduction section (page 4, paragraphs 1). We have also updated the reference (Ref. 1).

(3) In the methodology, it was less cited from the literature sources used to carry out the research as well as from the applied techniques, it was widely cited about the therapeutic effect and mechanism of exosomes in liver cancer. The methodology relies on the precise description of the methods used in a very complete way, even though there are few clinical studies and publications.

Response: Many thanks for reminding us of that. As your suggestion, we have added the literature sources used to carry out the research and the applied techniques as references (Ref. 12, a paper on conducting a systematic review; Ref. 13, an article for data processing method of systematic review).

(4) The authors conclude the work by explaining the advantages of working with suitable biomarkers in the fight to treat diseases, making it an interesting work to read. Finally, the work presents structure, font size, the font used and its appropriate formatting.

Response: Thank you for your help.

EDITORIAL OFFICE'S COMMENTS

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

Science editor:

1 Scientific quality: The manuscript describes a systematic review of the role of exosomes in liver cancer. The topic is within the scope of the WJG. (1) Classification: Grade C; (2) Summary of the Peer-Review Report: The present article presented by the authors, introduces citing liver cancer and as the greatest adversities faced in the late diagnosis and as consequences for the patients' lives, since most of the conclusive diagnoses for cancer it presents in the middle or late stage. The methodology relies on the precise description of the methods used in a very complete way, even though there are few clinical studies and publications. The authors conclude the work by explaining the advantages of working with suitable biomarkers in the fight to treat diseases, making it an interesting work to read. Finally, the work presents structure, font size, the font used and its appropriate formatting. The questions raised by the reviewers should be answered;

Response: Thank you for your kind reminder. We have revised the manuscript according to the reviewer and given a point-by-point answer to all questions. We hope that the revised paper meets the standard for publication.

(3) Format: There are 4 tables and 1 figure. (4) References: A total of 89 references are cited, including 41 references published in the last 3 years; (5) Self-cited references: There are no self-cited references; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

Response: Thank you very much for your help.

2 Language evaluation: Classification: Grade B. 3 Academic norms and rules: The authors need to provide the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the PRISMA checklist. No academic misconduct was found in the Bing search.

Response: Many thanks for your reminder. We have provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the PRISMA checklist attached to the revised manuscript.

4 Supplementary comments: This is an invited manuscript. The study was supported by National Natural Science Foundation of China; and the Medical Science Advancement Program (Clinical Medicine) of Wuhan University. The topic has not previously been published in the WJG. The corresponding author has not published articles in the BPG. 5 Issues raised: (1) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: Many thanks for reminding us of that. We have uploaded the approved grant application forms attached to the revised manuscript.

(2) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: Thank you for reminding us of that. We have provided original pictures using PowerPoint to ensure all graphs or arrows or text portions can be reprocessed by the editor.

(3) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Response: Thank you for your kind reminder. We have revised the reference format and added PMID and DOI numbers.

(4) I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text;

Response: Many thanks for your reminder. We have added the “Article Highlights” section at the end of the main text.

(5) I have changed the manuscript type “frontier” to “systematic review”. The authors need to provide the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the PRISMA checklist. 6 Re-Review: Required. 7 Recommendation: Conditionally accepted.

Response: Thank you very much for your help. We have revised the manuscript according to the format of the systematic review. We also have provided the Biostatistics Review Certificate, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement, and the PRISMA checklist attached to the revised manuscript.

Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, 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.

Response: Thank you very much for your help.