RE: submission of the revised version of the article (ID92037) entitled “HepG2.2.15-derived exosomes facilitate the activation and fibrosis of hepatic stellate cells” by Li et al.

Dear Editor(s) at World Journal of Gastroenterology:

Thanks very much for your editorial efforts regarding our manuscript and for your recommendation that we submit a revision of this manuscript. We also thank the reviewers for their constructive comments to strengthen this manuscript, which has been accommodated appropriately.

We have carefully revised the manuscript in order to the points and concerns raised by the reviewers. In particular, we have undertaken the following major revisions:

(1) We submitted the required attachments to the editorial department, including the Biostatistics Review Certificate, the conflict-of-interest disclosure form, and the Institutional Review Board’s official approval, etc;
(2) We included “Article Highlights” section in the article as required;
(3) We prepared the figures in PPT format according to the requirements of the article;
(4) We provided PMID numbers and DOI citation numbers to the reference list and list all authors of the references as requested by the journal;
(5) We re-wrote the background part of the abstract and the conclusion section at the end of the paper to make the paper look more reasonable;
(6) We typeset the article according to the requirements of journal.

In the revised manuscript, major revisions are shown in RED. Our detailed responses on a point-by-point basis and the revisions made to the manuscript are described below.

We believe that the manuscript has been greatly strengthened by the critique of the
reviewers and hope that both you and the reviewers will now find the paper suitable for publication.

Thank you and the reviewers again for carefully reviewing our work.

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Reply to Reviewer #1

Scientific Quality: Grade A (Excellent)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (High priority)

Specific Comments to Authors:
The authors provide solid and clear information documenting that exosomes derived from HBV infected HepG2 cell line are taken by the stellate cell line LX2 and elicit activation of multiple processes, related to LX2 differentiation and activation of genes related to fibrosis. The data are clearly presented and the plethora of activated genes will be of interest to investigators of HBV and of liver fibrosis in general. The paper is very interesting and useful. There are no major comments, as the data use standard methodologies related to analysis of genes and pathways. The only minor comment is that the authors should specify the properties of WRL68 cells, in the Materials and Methods. For that, please check and refer to PubMed PMID 7522099.

REPLY: Many thanks to the reviewer for pointing it out. We briefly described the properties of WRL68 cells in the Materials and Methods section "WRL-68 cells, resembling hepatocytes, are pertinent for in vitro liver studies due to their similar morphology, protein secretion, cytokeratin pattern, and key liver enzyme activities."

Reply to Editorial Office’ Comments

Language Quality: Grade B (Minor language polishing)
Scientific Quality: Grade A (Excellent)

1. Language evaluation: The English-language grammatical presentation needs to be improved to a certain extent. There are many errors in grammar and format, throughout the entire manuscript. Before final acceptance, the authors must 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.

REPLY: Many thanks to the reviewer for pointing it out. We have polished the article according to the requirements and uploaded the English Language Certificate as attachment

2. Please provide the primary version (PDF) of the Institutional Review Board’s official approval, prepared in the official language of the authors’ country.

REPLY: Many thanks to the reviewer for pointing it out. We uploaded the ethical consent form of the hospital as a PDF attachment.

3. Please provide the primary version (PDF) of the Informed Consent Form that has been signed by all subjects and investigators of the study, prepared in the official
language of the authors’ country.

**REPLY:** Many thanks to the reviewer for pointing it out. We did not include human in this study, so no informed consent was required.

4. **Please provide the ARRIVE Guidelines.**

**REPLY:** Many thanks to the reviewer for pointing it out. We upload the ARRIVE guidelines Checklist as an attachment.

5. **Please provide the Biostatistics Review Certificate.**

**REPLY:** Many thanks to the reviewer for pointing it out. We uploaded the Biostatistics Review Certificate as an attachment.

6. **Please provide the filled conflict-of-interest disclosure form.**

**REPLY:** Many thanks to the reviewer for pointing it out. We uploaded the conflict-of-interest disclosure form as an attachment.

7. **Please upload the approved grant application form(s) or funding agency copy of any approval document(s).**

**REPLY:** Many thanks to the reviewer for pointing it out. We uploaded the approval certificate of the fund as the attachment.

8. 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:** Many thanks to the reviewer for pointing it out. We add the “Article Highlights” section at the end of the main text.

9. **Please provide the Figures cited in the original manuscript in the form of PPT. All text can be edited, including A, B, arrows, etc. All legends are incorrectly formatted and require a general title and explanation for each figure. Such as Figure 1 title. A: ; B: ; C: .**

**REPLY:** Many thanks to the reviewer for pointing it out. We prepared the figures in PPT format according to the requirements of the journal.

10. **Please provide the PMID numbers (https://pubmed.ncbi.nlm.nih.gov/) and DOI citation numbers (https://doi.crossref.org/simpleTextQuery) to the reference list and list all authors of the references. If a reference has no PMID and DOI, please provide the source website address of this reference.**

**REPLY:** Many thanks to the reviewer for pointing it out. We provided PMID numbers and DOI citation numbers to the reference list and list all authors of the references as requested by the journal.