

Answering Reviewers

Journal: World Journal of Hepatology

Manuscript number: 80470, Review.

Title: " Therapeutic interventions of acute and chronic liver disorders: A comprehensive review "

Authors: Fares E.M. Ali, Mostafa K. Abd El-Aziz, Elham I. Sharab, Adel G. Bakr

We would like to thank the editors and the reviewers for their precious time and thoughtful review of the manuscript. They raise important issues, and their inputs are very helpful for improving the manuscript. We agree with almost all their comments, and we have carefully modified the manuscript accordingly, and the detailed corrections are listed below point by point. (The reviewer comments were made in *Italic*)

Reviewer 1# 05868418:

1." *They cause hepatocyte injury when they produce ROS and proteases once they are within the parenchyma "*. How they facilitated by proinflammatory cytokines?

Response: It was explained in the revised manuscript.

2. *"TNF- α , on the other hand, has also been demonstrated to have an anti-fibrogenic impact in rat HSCs by lowering glutathione and decreasing pro-collagen 1 expression". TNF- α has an anti-fibrogenic impact in HSCs, maybe involve any signal pathway?*

Response: It was explained in the revised manuscript.

3. *"Almost all liver illnesses, regardless of their underlying causes, have been found to exhibit oxidative stress". Whether it indicates that ROS is most important for the liver?*

Response: It was amended in the revised manuscript.

4. *Should uppercase and lowercase be uniform? Or do they have different meanings? MiRs, mir, miR?*

Response: It was carefully revised and unified as the reviewer recommended.

5. *In treatment, what parts were used for or involved in autophagy?*

Response: We added a new part regarded to the treatments depending on autophagic regulation.

6. *Full text is too long, cell part is not considered to simplify*

Response: The manuscript was simplified as the reviewer recommended.

Reviewer 2 # 03850800:

1. *In page 4, "damaged cells and can trigger the innate immune response. [9]." please to revise.*

Response: It was revised and corrected as the reviewer recommended.

2. *In page 5, "proinflammatory mediators like tumor necrosis factor," which type tumor necrosis factor?*

Response: Tumor necrosis factor-alpha (TNF- α) is the intended type. We revised and corrected all TNF to TNF- α .

3. *In page 6-7, "Reactive oxygen species, cytokines, and/or growth factors, such as TNF and TGF", please to clarify which type TNF and TGF?*

Response: TNF- α and TGF- β . We revised and corrected all TNF to TNF- α and TGF to TGF- β

4. *In manuscript, in some part, TGF-1, and another TGF- β , please to check and revise.*

Response: We apologize for this unintended mistake. TGF-1 was corrected to TGF- β through the manuscript