

Point by point response

Reviewer-1

The authors should consider whether structuring the manuscript in different order would make it easier for the reader to go through the review. The definition of fibrosis provided in page 10 for example could be the first section of the introduction followed by the types of EMT which appear in the page 14. The role of the TGF- β (described in page 12) followed by the mesenchymal markers could be the next following these sections. Studies providing evidence for or against EMT occurrence during liver fibrogenesis performed in cells, animal models and finally cirrhotic patients could be the next sections. Minor typographical and spelling errors should be corrected: am ample (page 2) et al (page 6)

Answer: Thanks! We really appreciate the constructive suggestions. We have re-organized the structure of the manuscript and checked the text for spelling errors.

Reviewer-2

In the present review authors want to discuss whether epithelial-mesenchymal transition (EMT) occurs during liver fibrogenesis and whether the parenchymal cells like hepatocytes have any role during this process. For this purpose, authors provide some supporting and opposing observations in in-vitro, in-vivo and patients samples. Authors propose that EMT might occur during chronic liver disease and parenchymal cells might show mesenchymal properties in response to high levels of surrounding pro-EMT factors, e.g. TGF- β .

Comments:

1. Several recent articles are available that addressed the issues regarding hepatic EMT and fibrosis. Hence authors should clear the novelty and the aim of this article.

Answer: Thanks for the question. Unfortunately, we cannot agree with the reviewer at this point. This is a review. As we stated in the paper, the aim of this review is “provides a personal notion about whether a complete EMT occurs in human fibrotic livers” (page 4). Thus, this manuscript does not provide any “novelty”.

2. The article should be concise and should discuss according to their objectives.

Answer: We cannot agree the comment. This is not a long manuscript. All discussion are organized according to the aim of the manuscript. It will be greatly helpful and appreciated if the reviewer can point out which parts of the text are not concise, or not organized in term of the objectives.

3. Type 1 EMT is not relevant in this regard, if so authors should provide explanation.

Answer: We do not understand why type 1 EMT is not relevant in this review. Concept of EMT is originated from embryogenesis. When an EMT review discusses other types of EMT, introducing three types of EMT is quite necessary.

4. Authors should provide pictorial representation to explain their hypothesis.

Answer: The hypothesis is difficult to be explained by picture. WE HAVE clarified the hypothesis on page 13-14.

5. Apart from TGF- β pathway, other molecular pathways like Self renewal pathways and their down-stream target genes might regulate EMT in hepatocytes. Thus, Authors should discuss mechanisms of EMT during liver fibrosis.

Answer: We agree, in addition to TGF- β , there are other signaling pathways, i.e. Wnt, microRNA, et al, as well contribute to EMT. However, summarizing molecular mechanisms of EMT is not the main aim of the review. Many elegant reviews, for examples, those from Massague J, Moustaks A, et al., have provided detailed State of Art in this regard. Thus, this review will not focus on this issue.

6. Authors should provide prospective therapeutic importance in this article.

Answer: Again, we cannot agree with the reviewer. Type 2 EMT is still a highly controversial issue to date, which is why we discuss our view of the issue here. We consider it premature to confer a “prospective therapeutic importance” to such a debated issue at this point in time.