Peer Review File

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Reviewer A

There are two novel findings. The first is that YB-1 directly inhibits TGFbeta 3 transcription. The second is that YB-1 and TGFbeta 3 are correlated during liver fibrogenesis, suggesting that YB-1 promotes liver fibrosis potentially via down-regulating TGFbeta3. There are several concerns regarding the studies described in this manuscript.

1. English writing needs significant and substantial revision.
   Reply 1: English writing was polished again.
2. All western blotting figures need to label protein sizes.
   Reply 2: We have modified our text as advised (see Figure 1, 2, 3, 5, and 6).
3. More information should be provided regarding the lentivirus overexpressing YB-1, including the promoter.
   Reply 3: We have modified our text as advised (see Page 6, line 157-162).
4. Which cell types can be infected by the lentivirus in the liver? Hepatocytes? Other liver cells? Where was YB-1 overexpressed in the liver? The authors largely used LX-2 cells for their studies. If YB-1 is mainly overexpressed in hepatocytes, then how to interpret most of the data?
   Reply 4: In this experiment, cell localization of YB-1 expression was not performed, because what was mainly discussed was the relationship between YB-1 and TGF-β 3 in the occurrence and development of liver fibrosis. TGF-β1 to activate HSC was introduced in some published papers (see Reference 25) to verify the relationship between YB-1 and TGF-β3. Of course, our previous (unpublished) experimental analysis of YB-1 expression in healthy people and patients with chronic B viral liver fibrosis found that the liver of healthy people expressed little YB-1. Compared with the healthy control group, YB-1 was highly expressed in patients with chronic hepatitis B liver fibrosis, and was positively correlated with the degree of liver fibrosis. YB-1 was significantly increased in the animal model group with liver fibrosis compared with the control group ($p < 0.01$). Our results were consistent with the expression of YB-1 in human liver tissue, suggesting that the model was successfully established. Whether the change of YB-1 expression level in other cells has an impact on the occurrence and development of liver fibrosis will be further studied in the future. Thank you very much for pointing out the shortcomings of our research.

5. The authors keep saying that LX-2 cells are an in vitro model of liver fibrosis. The statement is not appropriate.
   Reply 5: we have modified our text to “TGF-β1-induced HSC activation model in LX-2 cells”.

   Changes in the text : Page2 , line40 ; Page5, line131 ,and line 316,318,339.

6. In the in vivo study described Fig. 2, there is no control virus group. This is a significant defect in the study.
   Reply 6: Thank you for your comments. In fact, Fig.2 in the previous edition CCL_4 is the CCL_4+control virus group. We have modified it in the manuscript (see Page6, line166; Figure 2).
7. The authors conclude that "activation of hepatic stellate cells by YB-1 further activated surrounding cells via TGFbeta 3". The conclusion does not stand because the authors did not enrich or deplete TGFbeta 3 from the culture supernatant, which contained many other factors.
   Reply 7: Yes. That's not a very precise conclusion. Of course, we will further pay attention to the influence of TGF-β3 on the surrounding cells in the process of liver fibrosis by deplete other possible influencing factors in the following studies, so as to obtain more rigorous conclusions.
   Changes in the text: line 50, line455-463.

Reviewer B

This a very interesting experimental study on the Y-box binding protein-1 and its relationship with liver fibrosis. I have some comments:

Lines 57-98 Introduction section. I suggest including a little more information about Y-box binding protein-1.

Reply: Thank you. More information about YB-1 has been added according to your suggestion. Changes in the text: Page4, line100-114.

Lines 57-98 and 322-385 Introduction and discussion sections. It is important to mention that the pathogenesis of liver fibrosis is very complex. There are several pathways involved in this process. In this study you are exploring only one.

Reply: This paper is mainly to explore the relationship between YB-1 and TGF-β 3 in hepatic fibrosis, so we focused on the introduction and discussion of the TGF-β pathway. Thank you for your guidance.We will investigate other pathways in our subsequent research.

Lines 322-385. Discussion section. I suggest including the strengths and weaknesses of these studies.

Reply: we have modified our text as advised about the strengths and weaknesses of these studies (see line455-463)。

Lines 387-397. Conclusion section. I suggest keeping only the first paragraph.

Reply: we have modified our text as advised to delete the second paragraph (see line 476).