Dear reviewers and editors,

Firstly, thank you for your valuable suggestions for our manuscript. We have completed the revison of the manuscript according to these suggestions carefully according to these suggestions. And below is the answer list for questions you mentioned before.

1. **Why use human UC-MSC ?**

   UC-MSCs possess an excellent proliferative potential. What's more imortant, they have low immunogenicity and are ease to prepare.

2. **The M1 type can be induced by Interferon γ. If it is true, then why IFN is used to treat HEP.C?**

   (1) TGF-β1 is a potent fibrogenic cytokine, playing an important role in the activation of fibrogenic myofibroblasts.

   (2) Though the M1 type can be induced by Interferon γ (IFNγ) and promote myofibroblast proliferation and apoptosis, the dysequilibrium between M1 and M2 appears to be the major pathogenesis that induces liver fibrosis. Strategies for restraining M1 macrophage mobilization or favoring the M2 macrophage phenotype might prevent liver injury and thus alleviate liver fibrosis.

   (3) Interferon can reduce the secretion of TGF β1 and then prevent the activation and proliferation of hepatic fat storing cells, and finally inhibit mRNA, reduce the expression of collagen, so as to exert anti hepatic fibrosis effect.

3. **In the results part of Liver fibrosis is alleviated by UC-MSCs transplantation,** we mentioned that Densitometry measurements showed that collagen amounts were increased by more than 80-fold in DMN rats compared with normal rats ($P<0.001$); after UC-MSC transfusion, this increase was reduced by about 45% compared with control rats in the DMN model ($P = 0.021$). **You asked 55% not ameliorated?**

   Reduced by about 45%, in this article, we meant through analysising the pathological images, we found that the area of fibrosis deposition decreased by 45%, indicating that after stem cells transfusion the liver fibrosis significantly relieved and there were still 55% fibrosis not ameliorated.

4. **What roles are played by IL-4 and IL-10?**

   We have mentioned in our manuscript

The cytokines produced by different types of macrophages are very important for the development and function of both innate and adaptive immune responses. IL-10 is secreted by M2 macrophages, and its anti-inflammatory effect has been reported in various models of acute and chronic liver injury. Furthermore, Suh et al demonstrated that bone marrow cells can alleviate inflammation and fibrosis through the expression of IL-10. In addition, previous data identified IL-10 as the mediator of M1 KCs

apoptosis induced by M2 counterparts, showing that anti-IL-10 antibodies blunt the pro-apoptotic effects of IL-4 in conditioned media. The increased M1 macrophage mobilization and improvement of liver fibrosis following UC-MSCs transfusion were demonstrated in the present study; elevated IL10 production in plasma and liver were also found. Therefore, it is plausible that UC-MSCs transfusion improves liver fibrosis by the following mechanism: UC-MSCs promote M1 macrophage conversion into M2 macrophages, which secrete IL-10 and subsequently increase M1 macrophage apoptosis.

IL-4 is one of the markers of M2 macrophages. Milner et al found that IL-4 production leads to substantial M2 macrophage accumulation in the liver. Recent evidence has suggested an association between M2 macrophage activity and restriction of fibrosis. So it is likely that IL-4 receptor-deficient mice cannot exhibit an intact alternative activation in Kupffer cells and will increase liver inflammation, fibrosis, and death during acute schistosomiasis by Schistosoma mansoni. Contrarily, IL-4-activated M2 macrophages improve both steatohepatitis and fibrosis during experimental and human nonalcoholic fatty liver disease.

5. About the Figure 4 D, you asked, what value in figure showed increses of CD206 in time-dependent manner and explain that why all numbers in figure 4D were showed as percentages?

After DMN induced animal modle of liver fibrosis was made, UC-MSCs were transfused into the rats at day 7, and the number of CD206 positive M2 cells was measured at day 7、14 and 21. As the cell number was measured by flow cytometry, we had to recored the cell numbers in the form of percentages.