

## 21291-Answering reviewers

### Reviewer 1

#### Comments To Authors

This paper presents a novel therapy method for ALF. The main problem with the paper is that it is very poorly written; most sentences contain grammatical and/or spelling mistakes or are not complete sentences. The authors must have their work reviewed by a proper translation/reviewing service before submission

Response: Thank you for your insightful suggestions, we have already had our manuscript revised by professional service of English writing.

### Reviewer 2

#### Comments To Authors

This study provided a new way to restore or treat ALF. The result of the study showed the combination therapies of MSC with IL-1Ra can increase the liver regeneration post hepatectomy in the Chinese swine model. The study appears promising and provides the preclinical application of MSC. However, the manuscript is not written smoothly. Many errors need to be corrected.

Response: Thank you for your insightful suggestions, we have already had our manuscript revised by professional service of English writing.

### Reviewer 3

#### Comments To Authors

This paper provides additional information about possible therapies to treat acute liver failure. Using a swine model, authors demonstrated that blocking of IL-1 improve parameters such as liver function, inflammation, proliferation and apoptosis, that previously were described by others that used only MST therapy. I suggest minor revisions that may improve the manuscript.

1. Spell checking is recommended.

Response: Thank you for your insightful suggestions, we have already had our manuscript revised by professional service of English writing and all the spelling and

grammar mistakes have been already corrected.

2. Review the cite 13, that does not correspond to the cited information.

Response: Thank you for your insightful suggestions, the reference of 13 has been already changed to be a proper one.

3. Correct the word “stimulation” in page 4. Correct “flowcitometry” , “indicatng” in section Results. Serum levels of ALT and AST were significantly elevated within 1-7 days after hepatectomy, although progressively only of ALT. Correct in section Results.

Response: Thank you for your insightful suggestions, it has been already corrected.

4. Serum levels of hepatic enzymes were measured 1, 3, 5 days and 1-2 weeks after surgery, not 1-3 weeks.

Response: Thank you for your insightful suggestions, it has been already corrected.

5. Panels in some figures are missing: figure 1, figure2, panel F is missing in figure 8 Scale bars in histological analysis are not clear in figure 6.

Response: Thank you for your insightful suggestions, it has been already corrected

6. In figure 6, sinus silation means sinus dilation?

Response: Thank you for your insightful suggestions, it has been already corrected

7. Take in consideration the sequence of the events that happen in inflammatory processes. At the beginning, it is so important the first immune response in order to repair mechanisms following trauma and to content the disorganized proliferation. As well, cytokines are involved in wound healing and post-traumatic pain. Then, the time window is crucial in different steps of the recovery process. Speculate about the time of administration of IL-1Ra regarding to the injection of mesenchymal cells and to block complete or partially the effect of IL-1. It is suggested further information regarding ILRa secreted by mesenchymal stem cells. Recommended bibliography: Meier, et al. 2015. Journal of hepatology. Microencapsulated human mesenchymal stem cells decrease liver fibrosis in mice.

Response: Thank you for your insightful suggestions, you advice is very important and developmental; we will consider your suggestion in our further studies!