WJG Editorial Office

World Journal of Gastroenterology

Dear Editors:

We are very grateful for the reviewer's detailed comments on our manuscript (Manuscript NO. 38315). The comments have been helpful in allowing us to revise and improve our manuscript. Below, we have attempted to answer the comments and questions raised by the reviewers.

Response to Reviewer 01805500

Comments to Authors

Authors state that..... NASH mice were fed an HF diet for 4 weeks, intraperitoneally injected with CCl4 twice a week for the final 2 weeks, and intraperitoneally injected with T0901317 solubilized in DMSO for the final 5 days. The CCl4 dose was 0.1 mL/kg, and the T0901317 dose was 2.5 mg/kg ..... referring to other authors. First of all, not only NASH but also simple fatty liver of donors is a drawback for liver transplantation. This review is a little bit perplexed about this model of NASH, due to previous data of literature, i.e.,The LXR activator T0901317 produces several severe side effects, including hepatic steatosis....(quoted ref. n 28). Other data of literature offer a different approach, i.e. ..... The liver X receptor agonist T0901317 protects mice from high fat diet-induced obesity and insulin resistance. AAPS J. 2013; 15: 258–66.

Answer to Reviewer 01805500

Thank you very much for your constructive comments. The LXR activator T0901317 dose was 2.5 mg/kg in this study. T0901317 dose in protocol induced obesity and insulin resistance was 50 mg/kg (AAPS J : 2013; 15:

258–66). So, we consider that it is difficult to compare the results in two reports because of the different doses. In addition, other reports also showed the effect of fatty liver by T0901317 (AAPS J. 2013; 15(3): 744–752, et al). Moreover, in our previous reports (reference 28), we evaluated the effect of T0901317. We compared four groups, HF, HF + CCl4, HF + T091317, and HF + CCl4 + T091317 groups. HF + T0901317 group was produced a clinical picture similar to fatty liver. Although the detailed mechanism remains unclear, we have discussed that interaction of three factors, HF, CCl4 and T0901317 caused NASH liver and insulin resistance in this mice model.

Response to Reviewer 02536349

Comments to Authors

A successful animal study regarding the capacity of regeneration and function of residual liver in fatty liver compared to normal liver in mice. ps: Some recommendations for grammar. 1- In Conclusion section: Instead of "The function of the residual NASH liver is impaired compared with normal liver. A larger residual volume is required to maintain liver function in NASH" It may be better as: "The function of the residual liver is impaired in fatty liver compared to normal liver. A larger residual volume is required to maintain liver functions in mice with NASH" 2- Instead of "Mice of each group were sacrificed at 6 and 12 h after PH" "Mice of each group were sacrificed at 6h and 12 h after PH" 3- Instead of "steatotic liver" use "fatty liver" since No exact match found for "steatotic" in any English dictionaries. Some recommendations for grammar. 1- In Conclusion section: Instead of "The function of the residual NASH liver is impaired compared with normal liver. A larger residual volume is required to maintain liver function in NASH" It may be better as: "The function of the residual liver is impaired in fatty liver compared to normal liver. A larger residual volume is required

to maintain liver functions in mice with NASH" 2- Instead of "Mice of each group were sacrificed at 6 and 12 h after PH" "Mice of each group were sacrificed at 6h and 12 h after PH" 3- Instead of "steatotic liver" use "fatty liver" since No exact match found for "steatotic" in any English dictionaries.

Answer to Reviewer 02536349

Thank you very much for your constructive comments. We have changed the sentence construction and replaced "steatotic liver" to "fatty liver" in the revised manuscript.

Response to Reviewer 02636166

Comments to Authors

Dear Editor: Dr. Ozawa and colleagues made a novel experiment in NASH mice to demonstrate that the liver resection volume may affect the survival rate in subjects with NASH. In general, the study was well designed and the results were promising. I have only one concern that did the authors measure the histology and pathology NASH severity from the resected liver tissue in the three groups? It might be helpful to make a tight control that the NASH severity might be similar among groups at the surgery.

Answer to Reviewer 02636166

Thank you very much for your constructive comments. We have already examined organization assessment in the model mice using the NAFLD activity scores (NAS), as in reference 28. The normal liver mice as the control have been not added any reagent and the histology and pathology have been not change. In 30% PH and 70% PH of the NASH liver group, liver specimens were evaluated by an experienced pathologist in a blinded fashion, the histology and pathology finding in the NASH severity of each groups

have resulted in no difference in the NAS.
Therefore, we added the sentences in the revised manuscript (page 8, from line 12 to line 17).

Thank you for your consideration.

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