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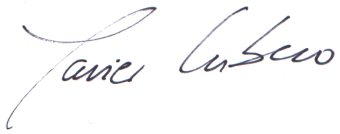
Madrid, November 8th, 2018

Dear Editorial Office, World Journal of Gastroenterology:

Please find attached the revised form of our Review titled ¨ **Alcoholic liver disease (ALD): Utility of animal models**¨ that we would like to resubmit to WJG.

We thank the Reviewers and the Editors for their comments and hope that now our article is now acceptable for publication in **World Journal of Gastroenterology** and look forward to your reply.

Sincerely yours,



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REPLY TO REVIEWERS

Reviewer 1 (03538879):

Alcoholic liver disease (ALD) is a major cause of acute and chronic liver injury. The author summarized the current incidence, physiopathology and modeling of ALD, and hope to provide an overview of the pros and cons of experimental models of ALD to study ALD, and the advances and implementation of new animal models that show great potential. The review is comprehensive, while there are still some aspects which need to be improved. 1. In the "Introduction" part, it seems like a little long that the authors described most of the prevalence of ALD. Or the author may increase a part of "the prevalence of ALD" to describe it in detail. Nevertheless, in this "Introduction" part, the author should precisely illustrate the purpose of the review in order to let readers understand the aim of the whole review. 2. Actually, the author major focused on the models of ALD, thus I think the whole manuscript should be revised carefully and delete some descriptions especially about the incidence, physiopathology of ALD. 3. In page 8, "PATHOPHYSIOLOGY OF ALCOHOLIC LIVER DISEASE (ALD)" should be changed into "PATHOPHYSIOLOGY OF ALD". 4. In "Table II: Comparison of experimental models of alcoholic liver disease", since the authors summarized the characteristics of different experimental models of ALD, the information such as the mouse or rat, related references, advantages and disadvantages should be included better. 5. In the references (DOI 10.1002/hep.27036, 10.1038/nprot.2013.032), the authors described a method of ALD with chronic-binge ethanol consumption model, and further to induce liver fibrosis, mice were either fed a liquid diet containing 4% ethanol or pair-fed a control diet, and mice were injected (intraperitoneally, two times per week) with 0.1 mL/kg body weight of CCl4 for 8 weeks. If it is possible, the present review can summarize the characteristics of related ALD models carefully in the field of ALD.

REPLY: Thank you for your comments. We have considered your points and changed the Abstract and refocused the Introduction, deleted the incidence paragraph and summarized the pathophysiology of ALD. Accordingly, we have changed the title to ¨ **Alcoholic liver disease: Utility of animal models**¨. Moreover, as suggested by Reviewer#1, we have changed Table II and specified animals and related ALD models carefully.

Reviewer 2 (00034151):

The manuscript entitled "Alcoholic liver disease: Incidence, pathophysiology and modeling" was an informative one regarding animal models of ALD. However, separate and in-depth review for chronic and binge ethanol feeding model (NIAAA model) is required.

REPLY: Thank you for your comments. As suggested by the Reviewer, we have added a paragraph summarizing the NIAAA model, which was extensively discussed in our recent review by Guo *et al.* The Lieber-DeCarli Diet-A Flagship Model for Experimental Alcoholic Liver Disease published in Alcohol Clin Exp Res. 2018 Oct;42(10):1828-1840.