Replies to the reviewers

0506058 Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Reviewer report Manuscript title: “Downregulation of Hes1 Expression in Experimental Biliary Atresia and its Effects on Bile Duct Structure” In this study, the authors investigated the expression and function of notch signaling target gene Hes1 in a mouse biliary atresia model induced by rhesus rotavirus. The study suggests that Hes1 might contribute the maturation and cellular structure organization of biliary epithelial cells. The study is well designed, methods are accurate and data clearly presented. Comments In the abstract the methods section needs to be re-written and human data added

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Reply: We thank for the suggestions of the reviewer and the modification in the abstract was rewritten in the revised version

03011144 Conclusion: Major revision

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

1. Title explicitly implies that the study is based on animal model, although human sample analysis is also included in the study. 2. Figures and tables are included in the body of the manuscript, whereas the legends are placed at the end of the manuscript. 3. Discussion is too short, with elaborate description of the conduct of the study . 4. Data on the animal and human samples not clearly depicted on a table. How many animals were used in the study? 5. References are not in the same format. (J Pathol vs The Journal of Clinical Investigation) 6. Limitations of the study are not listed. 7. Future directions of the study can be identified and included. 8. Use of high dose Pentobarbitone [affects liver enzymes, Br.J. Anaesth. (1989), 62, 311-315] can be a confounding factor. 9. Why were human BA samples compared with Choledochal cyst samples instead of normal liver samples?

Reply: we thank for the reviewer’s comments which is great help for the manuscript.

1. Yes, the title is mainly based on the animal study, we have done some initial study on Hes1 expression human, but the small sample size (n=10, 5 in BA and 5 in CC) is not enough for us to obtain a firmed conclusion about the function of Hes1 in human BA patients. We are working to increase the sample size and try to combine to the clinical syndromes and hope we can show the data in the next research paper.
2. The figures are moved to the end of the manuscript (after the references) followed the editor’s suggestion.

3. Discussion part was modified in the revised version together with other additional questions from the reviewers.

4. The number of human samples and animal samples were indicated in the figure legends, such as for the body weight, n=15 in the control group and n=23 in the BA group.

5. The format of the reference was corrected in the revised version**.**

6. Limitation of the study was added in discussion as suggested by the reviewer in the revised version.

7. Future direction was added in the discussion part in the revised version.

8. The use of high dose Pentobarbitone might affect the liver function, however, our data have a control group, the difference can be compared and discussed. But a paragraph has been added to the discussion group.

9. The use of Choledochal cyst samples instead of normal liver samples in human sample study is partly by the difficulty to obtain the age matched normal control liver sample, more specifically is that the Choledochal cyst has a similar cholestasis syndrome as BA, but pathologically, the affected area such as portal area is different, therefore the difference between the two diseases might be more interesting in term of disease ethology discovery.

00058405 Conclusion: Minor revision

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Zhang and co-workers investigated the expression and function of notch signaling target gene Hes1 in a rhesus rotavirus-induced mouse biliary atresia model. Authors found that Hes1 might contribute to the maturation and cellular structure organization of biliary epithelial cells. Comments and suggestions: The article is of interest for research field. Experiments are very well reported. Results are clear and support the main conclusions. However, I suggest the authors to improve the Discussion. The Discussion is very short and somewhat incomplete. The authors should discuss the potential clinical implications of their findings, the limitations of their study and also should improve the discussion regarding the pathways of bile structure changes elicited by down regulation of Hes1 expression.

Reply: We thank the reviewer's positive comments. We have added more discussion concerned the clinical implications, the limitations of the study suggested by the reviewer in revised version.