Dear editor

Thank you very much for your kind letter and the constructive comments from the Reviewer about our paper submitted to World Journal of Gastroenterology (Manuscript Number 83909). We have checked the manuscript and revised it according to the comments. We submit here the revised as well as a list of changes (manuscript83909_Auto_Edited.docx). We would like to thank the reviewers again for taking the time to review our manuscript. If you have any question about this paper, please don't hesitate to let me know.

Sincerely yours,

Best Regards.

Yours Sincerely,

Jun-Hua Fan

Department of Gastroenterology, Guangxi Medicine University School of Medicine

Response to Reviewer 1:

Thanks for your comments on our paper, regarding the revision and advice of the above paper in World Journal of Gastroenterology. Overall the comments have been fair, encouraging and constructive. We have learned much from it.

Response to Reviewer 2:

Thanks for your comments on our paper, regarding the revision and advice of the above paper in World Journal of Gastroenterology. Overall the comments have been fair, encouraging and constructive. We have learned much from it. We have revised our paper according to your comments.

1.The authors mentioned that compared with the control group, AnxA1 expression was significantly increased in the CCl4 model group, and was higher at week 8 than week 4, suggesting that AnxA1 was related to the development of liver fibrosis. In contrast, the authors showed that the lesions in the AnxA1-/- group were more severe than in the wild-type mice. If AnxA1 can attenuate the progression of liver injury, the reviewer thinks that AnxA1 expression will be lower at week 8 than week 4. The authors should show the reason why AnxA1 was higher at week 8 than week 4, suggesting that AnxA1 was related to the development of liver fibrosis.

Author response: We thank the reviewer for the very good comment. When the pathogenic factors act on the body, a variety of injurious changes occur, but they also stimulate the body to produce defense, adaptation, compensation and other anti-injury responses. As ccl4 continued to act on mice, it caused an imbalance between attack and protection factors, although the protection factors (such AnxA1) were also elevated simultaneously, which may eventually lead to the development of hepatic fibrosis in mice due to the overexpression of attack factors. the expression of Anxa1 continued to increase with disease progression, AnxA1 protein and mRNA levels in the liver fibrosis model group were higher than those in the normal control group, and were time-dependent. AnxA1 began to increase at 4 wk, peaked at 8 wk, and then began to decline, Anxa1 expression had decreased to normal levels

at 12 weeks. Although the fibrosis was more severe in the mice at 12 weeks and had progressed to cirrhosis, but the expression of Anxa1 at 12 weeks was the same as normal. In order to better study the mechanism of Anxa1 in liver fibrosis, mice in the ccl4-induced model groups received 20% CCl4 and CCl4+Ac2-26 with or without Boc2 for intraperitoneal injection twice weekly, at 4 and 8 wk after injection, animals were anesthetized. In the coming years, we will continue to study the role of Anxa1 in liver fibrosis and cirrhosis even further. Based on the recommendations of the reviewer, we have revised the article and added relevant content. Please see page 14 of the revised manuscript, lines 13-15, and lines 24-27.

2. Furthermore, it is unclear if all data were significantly different between CCL4 4W group and CCL4 8W group, and between wild type and AnxA1 KO mice. Please show more minutely differences between these groups.

Author response: We apologize for our neglected to compare the within-group and between-group. As Reviewer suggested, we compared the differences between the CCL4 4W and CCL4 8W groups, as well as between wild-type and AnxA1 KO mice, and displayed the differences on bar charts. Statistical analyses were performed using Kruskal-Wallis one-way analysis of variance. Please see image file: page 2, figure1C; page 3, figure2B、2C; page 4, figure3B、3C；page 5, figure3D、3E).

3. The authors also mentioned that the collagen deposition in the liver of AnxA1-/-mice was significantly aggravated by CCl4, and the degree of liver fibrosis was even more severe. However the authors did not show the degree of the collagen deposition in the liver by 8week CCl4 was more severe in AnxA1-/-mice than those in wild type mice.

Author response: We agree with the reviewer that it is important to describe the difference in collagen deposition between wild mice and Anxa1-/-mice at 8wk. We have revised the text based on the suggestions of the reviewers. Please see page 11 of the revised manuscript, lines 5-7, and lines 9-14.

4. Minor comment. Although the authors showed that representative histological findings in each groups, it was unclear whether the differences of inflammation and fibrosis between wild type groups and AnxA1-/- mice.

Author response: We are grateful for the suggestion. We have revised the text to address reviewer concerns and hope that it is now clearer. Please see page 10 of the revised manuscript, lines 9-17; page 11, lines 5-14.

Response to Reviewer 3:

Thanks for your comments on our paper. regarding the revision and advice of the above paper in World Journal of Gastroenterology. Overall the comments have been fair, encouraging and constructive. We have learned much from it.