



August 25, 2013

Dear Editor,

file name: 4471-review.doc.

Title: Amelioration of carbon tetrachloride-induced cirrhosis and portal hypertension in rat using adenoviral gene transfer of Akt

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Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Major concerns.

①. There is evidence of expression of the control vector mainly in the liver with less in the kidney. Images of Ad-EGFP tissue expression are not clear (Sup Fig 1) and higher magnification is required.

Thank you very much. However, we feel so sorry that we could not supply images with a higher magnification, due to the limitation of our photographic equipment. However, we could supply a clearer image.

②. Surprisingly liver Akt protein expression was not increased only pAkt levels (Fig 3+4). Why is that?

Thanks a lot. We also feel confused about this result. Thus, at this time, we thawed the original tissues, and performed WB for three times. Our data showed that the liver Akt protein expression was increased. We have revised our paper with new data.

③. VG staining is low quality and it is difficult to detect collagen deposition. The VG stained Akt-cirrhosis section is poor and there is evidence of many vacuoles, which are not seen in the corresponding HE section (Fig 2).

Thank you very much. We have changed the images according to your request.

④. No detail of the hepatocyte isolation procedure for the flow cytometry experiments was provided. How was it assessed whether hepatocytes or mixed population of liver cells were used (Fig 3). Furthermore, protein expression in whole tissue was presented in Fig 4 so it is not known which types of cells are undergoing apoptosis.

Sorry for our carelessness. We did not isolate hepatocytes. Actually, we determined the apoptosis of the mixed population of liver cells.

⑤. It is not clear whether total caspase 3/9 or cleaved caspase3/9 protein expression was measured (Fig 3). Changes in cleaved not total caspase levels are associated with apoptosis.

Sorry for our carelessness. Actually, we measured the protein expression of the cleaved caspase3/9.

Minor concerns.

①. page 4 para 1. Provide references for (i) Frank L Graham's method (9) and (ii) Akt "primer pair as we previously reported."

Thanks. We have provided these details in the new version according to your request.

②. page 5, para 3. Provide details of automatic biochemical analyser used to measure ALT, AST, ALB levels.

Thanks. We have provided these details in the new version according to your request.

3 References and typesetting have been corrected

Thank you again for evaluate our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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