

Dear editor and reviewer,

Thank you so much for the valuable comments. We have made the point-by-point correction as follows:

Editor:

We have made all the corresponding correction as you marked in the manuscript, we added all the sections as you required.

Reviewer:

- 1) What was the point of setting up Ad-PTEN group (wild-type PTEN transfection) and Ad-G129E group (mutant PTEN transfection) simultaneously with there were no significant differences in both groups?

Answer: In the pre-experiment, MTT assay showed that HSCs viability decreased to 83.74% in Ad-G129E group compared to 74.74% in Ad-PTEN group. So we kept both of them to further investigate the effects on collagen deposition.

- 2) Except ALT and AST, other relevant serum markers of liver fibrosis such as the procollagen III N-terminal peptide (PIIINP), collagen type IV, hyaluronic acid (HA), and laminin (LN) should also be detected in all groups at the same time to confirm the PTEN's protective effect, indicating that it can alleviate liver fibrosis of CCl₄-induced rats. In addition, hydroxyproline is a major component of the protein collagen and plays a key role in collagen stability, thus hydroxyproline content could estimate the collagen amount in fibrotic livers and should be detected.

Answer: We actually tested the HA, LN, PIIINP in this study and got no significant differences between them. We didn't check the hydroxyproline in this study. We will do this in the next experiment.

- 3) Due to the great toxicity of CCl₄, liver fibrosis in rats can lead to irreversible cirrhosis and thereby results in death with continuous administration. Were there animals died during the experimental period? If yes, how many?

Answer: We tried 50% CCl₄ Olive oil solution through intraperitoneal injection in the pre-experiment, 90% of the rats died in 4 weeks, the rest of them all got liver cirrhosis. Then we optimized the protocol, the rats got liver fibrosis in 3 weeks post-hypodermic injection of 40% CCl₄ Olive oil solution. The latter was what we used in this study.

- 4) In view of the importance of mechanism, further information about

signaling pathways and the relationship between them are needed in Introduction and Discussion section.

Answer: We have put more information into Introduction and Discussion section.

- 5) The manuscript was not composed at a level that can be published. It needs to be edited to the native English level before it can be published.

Answer: We send our manuscript to a Language Editing Institution and got well edition as well as English Editing Certificate.

Any more questions, please just let me know.

Thank you.

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