Author's response to reviews

Title: Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor

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Version: 3 Date: 12 June 2010

Author's response to reviews: see over
June 12, 2010

Melissa Norton, M.D.
Editor-in-Chief, *BMC Gastroenterology*

MS: 507892330076144

Dear Dr. Norton,

Thank you very much for your letter on May 26, 2010 regarding our manuscript entitled “Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor” by Tsutomu Fujii and Bryan C. Fuchs, et al. We have made every effort to improve our paper following the reviewers’ suggestions. The changes made in the revised version are summarized in the accompanying Response to Reviewers.

We continue to believe that this manuscript is suitable for publication in *BMC Gastroenterology* and would be of interest to your readership. Thank you in advance for your further consideration of our revised submission.

Sincerely yours,

Kenneth K. Tanabe, M.D.

Reviewer's report
Title: Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor

Version: 2 Date: 26 April 2010

Reviewer: Biserka Radosevic-Stasic

Reviewer's report:
I found that the authors of the manuscript: «Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor» answered on all my queries and improved their original data, answering on additional questions of the reviewers.

We thank the reviewer for their response.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.

Reviewer's report

Title: Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor

Version: 2 Date: 20 April 2010

Reviewer: Frank Tacke

Reviewer's report:
The manuscript has been greatly improved after revision.

We thank the reviewer for their response.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I declare that I have no competing interests

Reviewer's report

Title: Mouse model of carbon tetrachloride induced liver fibrosis: Histopathological changes and expression of CD133 and epidermal growth factor

Version: 2 Date: 10 May 2010

Reviewer: helene gilgenkrantz

Reviewer's report:
1. The new data showing CD133 and a-SMA immunohistochemistry in the same area on serial sections are not really convincing. Particularly a-SMA staining looks as an artefact in injured cells or area. Therefore it should only be indicated that « CD133 positive cells could probably correspond to HSC ».

We have made this change according to the reviewer’s suggestion in both the Results and Discussion.

2. The new data showing phosphorylated EGFR expression shows a clear up-regulation - in contrast to what has been seen with the non –phosphorylated form of EGFR-. It is in correlation with PCNA expression and therefore probably with cell proliferation. The discussion has be improved on this point.

We have added increased discussion around this point in the Results.

3. Recent evidences suggest that Amhiregulin, that has been found up-regulated in the new version, plays a unique role not only in liver fibrosis but also in liver tumorigenesis and in the maintenance of the neoplastic phenotype of hepatocarcinoma cells, particularly in humans. This point gives some clinical relevance to the model developed here.

We thank the reviewer for pointing this out. We agree and have discussed this point further in the Discussion.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests