

Dear Dr. Ma,

Thank you very much for giving us an opportunity to revise the manuscript "Aberrant expression of peroxiredoxin 1 and its clinical implications in liver cancer". We revised the manuscript in accordance with the reviewer's comments, and carefully re-formatted the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic Study.

We would like to express our sincere thanks to the reviewers for the constructive and positive comments. Here below is our description on revision according to the reviewer's comments.

Reviewer: 1

This manuscript titled, "Aberrant expression of peroxiredoxin 1 and its clinical implications in liver cancer" has been well written to suggest that Prdx 1 overexpressed in the tumor tissue of liver cancer can be served as a poor prognostic factor for overall survival and might be modified by SUMO to play specific roles in hepatocarcinogenesis. However, as mentioned in discussion, authors have not confirmed sumoylation of Prdx1 and its function in hepatocarcinogenesis. Further study will prove it. Anyway I think this manuscript can suggest a role of Prdx1 in hepatocarcinogenesis. Minor comment -Full names for abbreviations (AJCC, PTEN, OS, RFS) are needed in manuscript.

The authors' Answer: Thanks for the reviewer's kindly mention. We had added the full names of PTEN and AJCC, and replaced OS and RFS with the full names of "overall survival" and "recurrence-free survival".

In addition, as mentioned in our discussion part and the reviewer's comments, some further studies on the confirmation of sumoylated PRDX1 and its roles in hepatocarcinogenesis need to elucidate. In fact, our lab had started to explore it. However, it will take a long time. We hope to present our further results in the future.

In addition, for the revision checklist, due to the Language Grade of our manuscript is A, it is not necessary to provide a language editing certificate based on the policies of World Journal of Gastroenterology. We had prepared the other

1 18480-Revised manuscript

We had revised your manuscript according to the reviewers' comments and re-formatted the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic Study.

2 18480-Answering reviewers

We had prepared the response letter.

3 18480-Copyright assignment

We had prepared the scanned signed copyright assignment.

4 18480-Audio core tip

We made an audio file describing the final core tip of the manuscript.

5 18480-Institutional review board statement

This study was approval by the Institutional Review Board of the Cancer Institute and Hospital of Chinese Academy of Medical Sciences.

6 18480-Institutional animal care and use committee statement

This study was not involved in animal experiments.

7 18480-Animal care and use statement

This study was not involved in animal experiments.

8 18480-Biostatistics statement

9 18480-Conflict-of-interest statement

We have no conflict of interest to declare.

10 18480-Data sharing statement

This study was not involved in data sharing.

11 18480-Google Scholar

We searched our final title in Google Scholar, and we did not find any similar work.

12 18480-CrossCheck

We did not use the CrossCheck program this time. We can declare that there is no plagiarism and fake data in our manuscript. If the editor thought that it is necessary, we can do it.

13 18480-Language certificate

Due to the Language Grade of our manuscript is A, it is not necessary to provide a language editing certificate based on the policies of World Journal of Gastroenterology.

Thank you and all the reviewers for the kind advice.

Sincerely yours,

Xiaohang Zhao

Professor of Cancer Institute of CAMS

Dear Dr. Lee and Dr. Ma,

Thank you very much for giving us some constructive advice to improve the manuscript "Aberrant expression of peroxiredoxin 1 and its clinical implications in liver cancer". We had revised the manuscript in accordance with your comments. Here below is our description on revision.

Remarks:

This is a well-written paper, but I have some recommendations. The reason for these recommendations is that there is an obscure point in the role of PRDX1 expression on the aggressive tumor behavior. Recurrence was the same, but overall survival was worse in high PRDX1 expression. This suggests two possibilities. The tumor was more aggressive once it had recurred, or the patient died of other reason, for example, hepatic failure. In your univariate and multivariate analyses, there was no variable associated with liver function (CTP score), which has been known a potent prognostic factor for survival or recurrence. Therefore, please provide the information about the liver function. Another point is that I think that you'd better to analyze the data in patients who did not have residual tumor, which means the data should be analyzed in patients who had received a curative resection.

The authors' Answer: Thanks for the kindly and helpful suggestions. We had added the Child-Pugh classification (CTP score) in our univariate and multivariate Cox regression analyses (Table 1) and clinicopathologic characteristics analysis (Figure 1C). The relevant description was also modified in the full text. We found that Child-Pugh classification was an independent poor prognostic factor for overall survival in liver cancer. Moreover, when Child-Pugh classification was included, *PRDX1* mRNA expression got a significant *P* value in multivariate analyses. In comparison, it showed only marginal significance in our previous results.

In addition, according to the second comment, we re-performed the Kaplan-Meier survival curves and log-rank tests in patients with R0 resection (n=310). It showed similar tendency for overall survival and recurrence-free survival compared with those in total cases. The results were depicted in Supplementary Figure S1.

Thank you for the kindly advice.

Sincerely yours,

Xiaohang Zhao

Professor of Cancer Hospital of CAMS