

Dear Editors and Reviewers:

Thank you very much for your decision letter and advice on our manuscript entitled "**Metadherin Promotes Stem Cell Phenotypes and Correlated with Immune Infiltration in Hepatocellular Carcinoma**". We also thank the reviewers for the constructive and positive comments and suggestions. Accordingly, we have revised the manuscript. All amendments are highlighted in yellow color in the revised manuscript. In addition, point-by-point responses to the comments are listed below this letter.

We hope that the revision is acceptable for the publication in your journal.

Look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Jian Gao

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

1. "MTDH could promote stemness enhancement in HCC cells, and high expression of MTDH may resist cancer immunotherapy" -actually the demonstrates that it does promote stemness so please remove the word "could".

Response: Thank you for your insightful suggestion, we have changed that sentence to "MTDH promotes stemness in HCC cells and high MTDH expression impede the effectiveness of cancer immunotherapy."The details

can be found in Line 448-449, Page16-17.

2. The study results of Yoo BK et al. showed that MTDH expression gradually increased with phase I-IV and from high differentiation to low differentiation.
- there is no reference number.

Response: I am very sorry that this error was generated. We have added the reference number. The details can be found in Line 459-461, Page 17

3. Figure legends: Figure legends Also the figure just under this title is too small and there is no indication of just what it represents

Response: Thanks for the reviewer's kind suggestions. The main point of this diagram is to make a simple flowchart of the experimental methods used in our research. We have reformatted the images to make them easier to read.

4. Figure 1 MTDH overexpression has been is linked to a worse prognosis in HCC. This figure shows that it is linked.

Response: I am very sorry that this error was generated. We fixed the error, specifically on page 30 of the article

Your help and assistance is highly appreciated and I am looking forward to hearing from you.

Best regards

Yours sincerely,

Jian Gao