

## Response letter

**Reviewer's code:** 03478635

### SPECIFIC COMMENTS TO AUTHORS

This is an interesting study about the role of ORM2 as prognosis factor associated with cancer-promoting pathways in liver cancer. Figure 5 may be revised to indicate what panel G indicates more in detail.

**Reply:** We thank the reviewer's insightful suggestion. And in the revised manuscript , more detail information was included in the panel G of Figure 5.

**Reviewer's code:** 02536349

### SPECIFIC COMMENTS TO AUTHORS

Thank you for conducting this highly scientific and complex subject. I have some issues - mainly typographic- suggestions. I read the well-organised article titled "Downregulation of ORM2 acts as prognosis factor associated with cancer-promoting pathways in liver cancer"

1- The title itself should be corrected as "Downregulation of ORM2 acts as a prognostic factor associated with cancer-promoting pathways in liver cancer" The correction should include "running title, keywords and whole manuscript.

**Reply:** We thank the reviewer's suggestion, and we corrected this point in the whole manuscript. And the corrected content was highlighted in red.

2- "Liver cancer has a higher mortality and morbidity in the world" should be "high mortality" , since it is not the highest.

**Reply:** We thank the reviewer's suggestion, we revised it in the revised manuscript.

3- "the prognosis of liver cancer patients was poor, and the complex reasons contributed ..." should be "the prognosis of liver cancer patients is poor, and the complex reasons contribute..."

**Reply:** We thank the reviewer's suggestion, we revised it in the revised manuscript.

4- "Previous study showed its upregulation upon inflammation" should be "Previous studies showed their upregulation upon inflammation"

**Reply:** We thank the reviewer's suggestion, we revised it in the revised manuscript.

5- "ORM1 and ORM2 were specific highly expressed in the liver" should be "ORM1 and ORM2 were specifically and highly expressed in the liver" or omit "specific"

**Reply:** We thank the reviewer's suggestion, we deleted the "specific" in the revised manuscript.

6- "liver tissues. And ORM1 and ORM2" Instead of beginning with "And" use a comma after tissues.

**Reply:** We thank the reviewer's question, and we corrected the error.

7- "acute-phage protein" should be "acute-phase protein" Besides these, there are numerous grammar mistakes and typographical errors. They should be corrected before publishing.

**Reply:** We thank the reviewer's careful review, and we revised these errors in the revised manuscript.

8- The following highly relevant article should also be cited "Zhang X, Xiao Z, Liu X, Du L, Wang L, Wang S, Zheng N, Zheng G, Li W, Zhang X, Dong Z, Zhuang X, Wang C. The potential role of ORM2 in the development of colorectal cancer. PLoS One. 2012;7(2):e31868."

**Reply:** We thank the reviewer's careful review, and we cited this paper in the discussion section.