
October 16, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5392-review.doc).

Title: Targeting of circulating hepatocellular carcinoma cells to prevent postoperative recurrence and metastasis

Author: Yu Zhang, Zhilong Shi, Xia Yang, Zhengfeng Yin

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5392

Thank you very much for your letter and the comments from the referees about our paper.

We have made corresponding revision according to the suggestions. Our response to the comments is enclosed at the end of this letter, and the revised manuscript is also submitted. Words in red are the changes we have made in the text.

Furthermore, Xia Yang has been added as the third author in the revised version due to her contribution to the new section "THE METHODS FOR ENRICHMENT AND DETECTION OF HCC CTCs".

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer.

Question 1 (Reviewer No. 00225318)

The only limitation is the lack of references to molecular methods for early detection of circulating tumor cells. An additional short section focused on this issue must be added at the end of the manuscript emphasizing the possible future development of this kind of methodology.

Response:

A number of reviews focused on the methods for detection of CTCs have been published before. According to the suggestion, we have added a short section at the beginning of the manuscript, which outlined the different approaches available for detection of HCC CTCs, and emphasized the possible future development of this kind of methodology.

Question 2 (Reviewer No. 00503546)

[page 5, line 13] prognosis → prognos.

Response:

Thank you for your meticulous review. We apologize for our carelessness in the work of edit. In addition to correcting this spelling mistake, we also corrected several other

grammatical/spelling errors.

Question 3 (Reviewer No. 00012156)

Zhang et al. described circulating hepatocellular carcinoma cell and recurrence of HCC. There were only a few referenced papers with relationship between circulating hepatocellular carcinoma cell and recurrence of HCC. Therefore, the contents of this paper had no evidence of their opinion. Story for read is interesting but not scientific. There is nothing new nor helpful for reader. Comments: There is no referenced paper that indicate the relationship between circulating hepatocellular carcinoma cell and recurrence of HCC. The recognition of circulating hepatocellular carcinoma cell and recurrence of HCC is different story, isn't it? Between p4-p11 there is no paper described on circulating hepatocellular carcinoma cell. affecting HCC cells?

Response:

Thank you for your question. However, to our knowledge, we can't agree with you.

With the development of new and robust technologies for the capture and characterization of CTCs, there are more and more evidence indicating that circulating HCC cells, including those stem cell-like HCC CTCs, play an important role in the recurrence of HCC. Our paper have cited the literature (REFERENCE 4, 17, 18, 19, 20). Based on experimental and clinical observations, these references have consistently demonstrated an important relationship between circulating HCC cells and recurrence of HCC. Therefore, we think that the contents of this paper have provided the evidence of our opinion.

As HCC CTCs are increasingly recognized as the main source of recurrence and metastasis after radical hepatectomy, here we have proposed some HCC CTC-based strategies for the treatment of HCC, which will guide future research on HCC CTCs in preclinical and clinical settings and may lead to effective therapeutic approaches to prevent metastatic relapse of HCC. So we think that our article has provided something new or helpful for the readers.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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