

November 1, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5884-review.doc).

Title: Implications of biomarkers in human HCC pathogenesis and therapy

Author: Li-Li Han, Yi Lv , Hui Guo, Zhi-Ping Ruan, Ke-Jun Nan

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5884

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

- (1) "Authors should stress in specific biomarkers for pathogenesis and therapy of HCC."
My revised manuscript has been improved to focus on the specific biomarkers for pathogenesis and therapy of HCC.
- (2) "new references in last 3 years."
I have conducted and reviewed more new literatures in last 3 years, and the new references in last 3 years has been increased a lot from 69/136 to 118/137 now in the new manuscript.
- (3) "new markers such as MiRNAs, mRNA"
Both MiRNAs and mRNA as new markers contributes to pathogenesis and therapy of HCC have been expound in my revised manuscript , the MiRNAs especially have been demonstrate point to point in the new manuscript because of its greater significance according to my theme.

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

(1) "The author should provide the sensitivity, specificity, PPV and NPV for all traditional biomarkers including references."

I have already finished it according to the reviewer's advice.

(2) "The original article about miR-122 that recently published in 'New England Journal of Medicine must be cited (NEJM 2013;368:1685-1694). Minor concerns The topic of Sorafenib is missing."

Thanks to the reviewer's valuable advice for me, I read the paper according to his advice, I think it is worthy to be referenced , too. And it has been referenced in my new manuscript.

(3) "The authors may want to provide more details about clinical characteristics of sorafenib, including safety of the drug and main side effects."

I have already finished it according to the reviewer's advice.

(4) "This section should be expanded. - typo error in the bevacizumab section in lines 1-2 - in Table please add a column with main side effects of the drugs and their prevalence." 1,

I have already finished it according to the reviewer's advice.

(5) "They show only the survival rate and benefit of these drugs without clinical background data."

I have already added the clinical background data according to the reviewer's advice.

(6) "It is also true that AFP is widely available and a relatively cheap biomarker for screening. The authors should comment on this. The new biomarkers/ molecules may not be easily available in a clinical settings (especially primary and secondary clinical settings) and accessibility may not be straightforward everywhere."

I agree with the reviewer, and have commented my view in the new manuscript.

(7) "One aspect which is missing is the SNPs as Biomarkers."

I have searched the related article, but the results of search in PUBMEND showed only one paper about SNPs as biomarkers in HCC. So I don't think SNPs as Biomarkers should be added in my manuscript.

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