

Format for ANSWERING REVIEWERS



October 25, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5972-review.doc).

Title: Predictive and prognostic biomarkers with therapeutic targets in advanced colorectal cancer: Current evidence and future perspectives

Author: Huiyan Luo, Ruihua Xu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5972

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

The first reviewer

- (1) I could not find a complete list of contributing authors and affiliations.
Already finished in the authors information.
- (2) Abbreviations should be consistently clarified.
Already made revisions.
- (3) Major English revision is warranted,
Already made revisions by professional translation service.
- (4) I think that they should revise some sections and include rather some general meta-analyses, as for examples listed below.
Already made revisions, add those references mentioned by this reviewer.

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The second reviewer

(1) they did not discuss the potential applications of these biomarkers for this disease in the clinic. For example: (i) They did not conclude the possibility and reliability of using these biomarkers as molecular targets for CRC. (ii) Whether these biomarkers can be used for monitoring response to therapy or treatment effectiveness in CRC? (iii) Whether these biomarkers can be used for monitoring disease progression and prognosis in patients with CRC?

We have already added the relevant discussion and made conclusion of the potential applications of these biomarkers for this disease in the clinic.

(2) Although the authors have reviewed several important growth factor receptors, they should also discuss FGFR2, FGFR3, and PDGFR in this article.

Already made revisions.

(3) Although the authors have reviewed several important oncogenes and tumor suppressor genes, they did not mention MACC1, MYC, MDM2, COX2, ERCC1, and HSP70/HSP90 in the paper. This reviewer believes that these genes are critical to CRC

Since our manuscript mainly focus on the target therapy in mCRC. Those gene such like MACC1, MYC, MDM2, COX2, ERCC1, and HSP70/HSP90, were more applied to predict the efficacy and toxicity of cytotoxic chemotherapy, so we didn't discuss in this manuscript due to the content limitation.

(4) Epigenetic mechanisms are involved in gene regulation and the pathogenesis of tumors including CRC; therefore, the authors should also discuss the epigenetic markers as the potential therapeutic targets in CRC.

Already made revisions..

(5) The minor comment mentioned by the reviewer 2, such like "Pay more attention to the punctuation mark, the conclusion section needs to be revised".

I have already checked up carefully and made relevant revisions.

The third reviewer

Why has the discussion been completely restricted to genetic parameters while ignoring issues such as patient factors (age, smoking, diabetes) and inflammatory parameters (GPS, CRP etc)?

Our manuscript mainly focus on the genetic parameters due to the content limitation, other factors may be discussion in our next review.

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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