

January 22, 2015

Dear Editor,

Title: Integrative analysis of the aberrant wnt signaling pathway in HBV-related HCC

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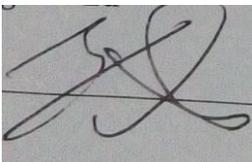
Thank you for your consideration of our manuscript for possible publication. We have revised the manuscript according to the reviewers' comments, and our point-by-point responses to these comments are listed below. What's more, other corrections have been made following the Resubmission Instruction in the revised manuscript. Please find enclosed the edited manuscript in Word format (file name: 16018-review.doc).

First. Format has been updated. Words and grammar were modified. Data and pictures have been updated according to the updated data in COSMIC database.

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

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

Sincerely yours,

A square image containing a handwritten signature in black ink on a light background. The signature is stylized and appears to be 'Fengmin Lu'.

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Here are our corrections and point-by-point responses:

(1) Reviewer No. 742224:

The authors present a comprehensive study. The methodology is correct. The conclusions are consistent with the results obtained. Represents a significant contribution in the advancement of study of the process of hepatocarcinogenesis. The only shortcoming is that the report of patient consent is not present.

Response: The reviewer's comment is reasonable. In the last paragraph of chapter **HCC tissue samples** in part **Resources**, we claimed that the informed consents were obtained from all patients and donors before the start of the study. If additional information was needed, please let us know.

(2) Reviewer No. 3011315:

Introduction: The aim of the study is not clear.

Response: Thanks for the review's comment. Now the aim of the study has been added at the last part of **Introduction**.

Material and methods: It is not clear if the study is retrospective or prospective. The authors declared: "The study was approved by the Ethics Committee in the university, and the informed consents were obtained from all patients and donors before the start of the study." But that sentence is in contrast with the declaration in the "Academic rules and norms" sent to the Editor.

Response: Thanks for the comments. We have claimed that the study is retrospective in chapter **HCC tissue samples** in part **Resources** in the edited manuscript. We have corrected the declaration about patient consent re-submitting.

No statistical analysis chapter is described.

Response: We have added the statistical analysis chapter in the revised manuscript, and the analysis data is now available in supplementary table 4.

Results: The authors wrote: "As shown in Figure 1B, the CTNNB1 mutation rate in chronic HBV-related HCC was 10.79%, which was similar to that in HBV/HCV co-infection related HCC, but significantly lower than those with HCV-related HCC or non-viral HCC. Even though, the CTNNB1 mutation rate in chronic HBV-related HCC was still higher than that in several other human tumors like ESCC, lung cancer and gastric cancer." And again: "...the CTNNB1 mutation rate in HCC is 19.24%, which was significantly higher than the mutation rates in other tumors..." and again: "the CTNNB1 mutation rate in chronic HBV-related HCC was 10.79%, which was similar to that in HBV/HCV co-infection related HCC,

but significantly lower than those with HCV-related HCC or non-viral HCC" If the authors wrote "significantly higher" or "significantly lower" a statistical analysis is important to do.

Responses: We agree with the reviewer. We have updated the data and now statistical analysis data including *P-values* were added in Supplementary Table 4.

Tables: Please substitute "?" with NA (Not Available)

Responses: Thanks for the comments. Now the substitutions have been made in supplementary tables 1~3.

- (3) References and typesetting were corrected
- (4) A file signed by all of the authors has been provided