To World Journal of Hepatology

Dear Editor,

Please find attached the revised manuscript of our review entitled “Aberrant expression of the isoforms of transcription factors in hepatocellular carcinoma” (#39458).

We thank you for your consideration of our manuscript for publication in World Journal of Hepatology and for the opportunity to resubmit our article for publication after minor revision. We have thoroughly addressed all comments and suggestions made by reviewers, the details are described in the accompanying “Response to reviewers”.

Yours sincerely,

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Response to Reviewers

We would like to thank the reviewers for their helpful comments and suggestions on our manuscript. We have corrected text of the manuscript and figures according to Reviewers’ suggestions to address the Reviewers’ concerns. Please find the list of changes and specific responses below.

Reviewer # 03259512

1) The abstract should state that this is a review; the transcription factors should be listed there and included as the keywords

We have added this information to the abstract and listed the most investigated TFs. The latter have also been included as the keywords.

2) The subheadings should be descriptive

We extended (where applicable) subheadings to clarify the main functions of the TFs or their isoforms relevant for hepatocarcinogenesis and/or to indicate the common pattern of their aberrant expression in HCC.

3) Table 1 should be mentioned earlier in the text

We have mentioned it at the end of the introduction so that the readers could consult it whenever they find it necessary.

4) A diagram should be drawn to represent the network of TFs involved in regulation of HCC

We agree that such diagram would be useful. Since the data on interaction between the isoforms are scarce, and the complete network of all TFs involved in HCC regulation would include multiple intermediate nodes, the figure would be overloaded with details and thus hard to comprehend. Thus we have prepared a less complex diagram (Figure 2) that is included in the Conclusion and Perspectives part of the article and demonstrates which processes involved in hepatocarcinogenesis are presumably regulated by the isoforms of the TFs we reviewed.

As of the interactions between the isoforms of the TFs, available data on some of them are given in the text (e.g., about HNF4α and TCF7L2, PGC1α and nuclear receptors, C/EBPs).

5) Limitations of the *in vitro* studies should be presented at the end of some chapters as conclusive remarks

We agree with the reviewer that cell culture based studies of gene expression might not precisely reflect expression signatures observed in tissues and that solely in vitro studies are not sufficient to clearly predict the effects of the isoforms that may be observed in vivo. In order to meet the reviewer's suggestion and stay concise, we have added a brief paragraph concerning the limitations of the *in vitro* studies to the conclusive part of the article and cited several articles on the issue.

6) Available *in vivo* clinical studies should be included at least shortly

We have updated the manuscript with the latest data on *in vivo* and/or clinical studies of the isoforms of the reviewed TFs. We added information on association of HNF4A-P2 variants and TAp63 with clinical parameters and survival of patients with HCC, the link between C/EBPb LAP1 isoform expression, Ki67 proliferation marker and stemness of cancer cells confirmed in xenograft experiments and cited the study demonstrating that in spite of the conflicting data on expression and the role of C/EBPa in hepatocarcinogenesis, its reactivation with saRNA leads to disease reversal in rodent models of liver disease including reduction of tumor burden in HCC.

Reviewer # 02444752

We thank the reviewer for consideration of our manuscript.

Reviewer # 02529007

1) Manuscript needs to be edited by an English scientific editor for required English corrections.

According to the WJH polices and along with the reviewer's suggestions on language polishing, the revised manuscript has been edited by a native English-speaking editor.

2) There are several new 2018 reviews and articles related to TFs in HCC and some of which might be pointed and quoted at least in the introductory part even if they are not directly related to isoforms.

As the reviewer pointed out, there were several new articles related to transcription factors in HCC. We have updated the manuscript with the data related to the isoforms of the TFs in HCC. In particular, we improved the sections about HNF4a, p53 family members and C/EBPs. As for the articles published in 2017-2018 that do not directly consider the isoforms, we believe that this information might be excessive, since almost none of the TFs reviewed there will be mentioned further in the text.