

November 25, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format.

**Title:** Host cellular MicroRNA involvement in the control of HBV gene expression and replication

**Author:** Yoshiaki Mizuguchi, Toshihiro Takizawa, Eiji Uchida

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 14086

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) Reviewer 01407353

The Introduction and the second paragraph (MicroRNA biogenesis and function) should be merged in a single section with a brief introduction (the first paragraph of the current Introduction), and then the discussion concerning microRNA biogenesis and function (the whole current second paragraph). This new paragraph (which could keep the same title of the current second paragraph), should end with presentation of the topic which will be covered by the review, i.e., that of microRNA involvement in the control of HBV gene expression and replication. Indeed, exactly this one, and not a more generic overview on the role of miRNAs in [liver diseases](#), is the topic of this work.

**We have modified the paragraph according to reviewer's suggestion.**

Consistently, the last paragraph should be more centered on the topic addressed, without extending to the issue of hepatocellular carcinoma, which is another issue.

**We rewrote the paragraph according to reviewer's comment.**

## (2) Reviewer 02444883

The introduction paragraph should be modified and should be more focused on the HBV topic. Mainly, the last sentence should be completely modified: the authors wrote " we review recent advances in the understanding of the mechanism underppinning miRNA regulation, during hepatatis B viral infection as an example...." HBV viral infection is not "an axample" is the main topic of the review!

According to the reviewer's suggestion, we have rewritten the last sentence.

In the paragraph entitled "HBV infection" at page 5 the authors provide a list of "biology and lifecycle of the HBV", in five points. The paragraph is confusing and not completely understandable. This part should be re-written.

We checked the paragraphAfter checking the paragraph, we found and find that the abbreviations were used inappropriately, resulting in confusion. We corrected the abbreviations to improve clarity.

## (3) Reviewer 00503561

If you can add a few sentences on the possible contribution of miRNAs to other (if ever) pathway to hepatic cancer (some of them are discriminate from HBV related and the other would be shared), there readers would have more comprehensive image on this complex situation of liver.

Thank you very much for the positive comments regarding our manuscript.

In this review, we focused on the association between hepatitis and miRNA, but not cancer including HCC. We believe that including topics such as HCC in this manuscript is beyond the scope of the review. Therefore, we did not include the topic of HCC in this paper. In the future, we will submit another manuscript regarding the association between miRNA and HCC to the World Journal of Hepatology.

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3 References and typesetting were corrected.

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4 The original crosscheck said that approximately 5% of our manuscript had overlap with [Hu, Wei et al. "Correction: MicroRNA-141 Represses HBV Replication by Targeting PPARA", PLoS ONE, 2012.]. We confirmed that all of the overlapping sentences are properly cited. Also, we confirmed that all of the references are properly cited.

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All of the authors involved agree with the submission of this manuscript to *World Journal of Hepatology*. There are no relevant papers being submitted concurrently, or in press, by any of the authors, and there are no conflicts of interest related to this paper.

Sincerely,

Yoshiaki Mizuguchi, MD, PhD

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