

Format for ANSWERING REVIEWERS

Jan 14th, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format, it is an invited review.

Title: Prospects for inhibiting the post-transcriptional regulation of gene expression in hepatitis B virus

Author: Augustine Chen, Nattanan Panjaworayan T-Thienprasert and Chris M Brown

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6626

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

1 Format has been updated

Done.

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1

The manuscript appropriately reviews post-transcriptional regulation of gene expression in the HBV lifecycle, which are aspects that are uncommonly investigated, nevertheless puts into a clinical context these informations.

However, to my opinion the only modification that is worthy to provide regards the last section.

Indeed a speculation about drugs derived from natural products is beyond the aim of the paper and decreases the scientific value of the manuscript. This section should be integrated in the conclusions, underling that there is not enough evidence to support the clinical usefulness of those substances.

In this section we introduced the idea that there are known compounds that act *in vitro* as antivirals without known molecular targets. We had also included this section, as it is an area of research expertise for one of the authors. This section was covered briefly and we believe conservatively at the end of the review. However, we have modified this section to reiterate that there is not yet enough evidence for the clinical usefulness of these substances, as suggested.

Revised sections-

"The current natural products are not immediately useful as drugs in most cases^[85]. However, they may be further developed as potent drugs through chemical modification or serve as novel pharmacophores for a drug design, or identify novel viral targets for treatment.

Conclusions

In this review we have outlined the current knowledge of post-transcriptional regulation of gene

expression in the HBV lifecycle. We have also speculated on the idea that compounds from natural products with unknown molecular targets might target these types of steps. However, there is currently not enough evidence as to how they act, or to support the clinical use of these substances [85].

The review has emphasized where HBV post-transcriptional processes differ from the host machinery as these are potential sites of new antivirals. However, the potential of antivirals to target these steps has received little attention. New compounds might target these steps directly either through the conserved sites in the viral RNAs or via the host and viral proteins that interact with them."

Reviewer 2

The authors are advised to put in consideration the suggested remarks provided in the area of comments to author. Minor Comment: ? The editing of the manuscript needs minor revision. ? Language level: A

1. *TITLE Reflect the major content of the article.*
2. *ABSTRACT fulfill the journal requirements.*
3. *Text: The section is almost well organized; an overall theoretical analysis concerning the provided data is well covered.*

Figures are descriptive and informative, however and in order to satisfy the reader, the authors are better to describe the structure of HBV genome as four overlapping open reading frames (S, C, and X & P) as well as their translated viral proteins.

Added a sentence to 'The HBV RNA pregenome and mRNAs' to describe the proteins.

Added a sentence to 'HBV lifecycle: sites of regulation and potential intervention'

Added a section to the legend to Figure 1, explaining it more clearly.

Also, the following point is better to be considered: ? Nuclear export of HBV RNA: Third paragraph: Huang et al. (1996) HAS TO BE CORRECTED: Huang and Yen (1996)38.

Corrected as requested, article is now cited at the end of the sentence.

4. References: Relevant and sufficient updated references, especially the most current literatures were cited (60/91 references were cited from publications \geq 2008, 18 of them are within the current year [2013]). The journal style for writing this section is well maintained, however, PMID was missing for references No: 5 and 67.

Thankyou. A PMID is not available for reference 5, we have added the DOI. Reference 67 has no DOI or PMID available.

For Reference 67, on reflection, this article would be difficult to obtain and interpret for some readers. Therefore we have substituted a similar more accessible article.

3 References and typesetting were corrected
Done.

Sincerely yours,

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