

## Format for ANSWERING REVIEWERS



September 16, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5223 edited.docx).

**Title:** The core promoter: a critical region where the hepatitis B virus makes decisions

**Author:** Jorge Quarleri

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 5223

The manuscript has been improved according to the suggestions of reviewers (original suggestion from reviewers are bolded):

**1. Reviewer #1 (02446172)** No corrections were suggested.

**2. Reviewer #2 (02445074):**

**1. Abstract and many times elsewhere: be consistent and use 3'-end, 5'-end**

It was amended throughout the whole manuscript following an uniform criteria.

**2. Introduction: up to ~1011 virions per day**

It was corrected

**3. Introduction: But Raney et al. (2001) reported cccDNA in certain transgenic mice.**

This reference was added and commented briefly as suggested (see paragraph at bottom on page 3)

**4. HBV genomic ...: cis-acting**

It was corrected.

**5. secreted soluble HBeAg ...: here and many times elsewhere correct the changes in font, especially the references.**

It was corrected.

**6. many places where a space remains between the text and the bracketed citation**

Such space was deleted.

**7. CP region, mostly at BCP, and varying in length**

It was included

**8. The author declares no competing ...**

The expression was replaced

**9. The references need some changes to agree with requested journal formatting. The first author needs to be in bold face. The journal issue number can be removed. And for example in ref 62, what is this silly [pii]?**

The references were amended. The format of the references was adjusted by updating the EndNote software with the file containing the specific format of WJG which was downloaded from the.

**3. Reviewer #3 (00053542)**

**General comments:** The article is very detailed, written in a professional and scholarly manner. However, there are some redundancies throughout the paper that make it too long and in times also complicated, raising the concern that only very few readers who are experts in the molecular biology of HBV will find an interest in the paper. To simplify things and to make them more accessible I suggest the following:

**1. A table summarizing the mutations found in the core/BCP region among HBV patients and their clinical**

**associations will be very helpful**

The Table suggested by the reviewer is included in the Revised version.

**2. I suggest to focus on the topic of the article, i.e, the core promoter as the decision maker of HBV. This is not a general review on the molecular biology of HBV! Therefore, please shorten too detailed discussions on replication strategy (page 4 bottom) Polymerase structure and function (page 5 middle), detailed transcription regulation of the S and X products (page 7).**

These paragraphs were shortened following strictly the suggestions made by the reviewer.

**Also, the discussion about gender differences in HBV expression (page 7 top) seems irrelevant to this review.**

This expression was removed.

**Specific comments: 1. Page 4 bottom- "Once the viral (-) strand DNA synthesis is completed, a residual short RNA oligomer derived from the 5' end pgRNA remains covalently bond to the 5' end of the (+) strand DNA to serve as a template for (-) strand DNA synthesis"- it seems that the + and - here were switched, i.e, the sentence should be: ..."to the 5' end of the (-) strand DNA to serve as a template for (+) strand DNA synthesis"**

Yes, the reviewer is right and this sentence was properly amended.

**2. Page 6 bottom- EnhII also increases the transcription of the pg/pc mRNAs and not only preS1,preS2 and X as could be mistakenly understood from the text.**

This concept was included in the sentence according the suggestion.

**3. page 9 5 lines from bottom- "...binding HNFA and TR2..." what does HNFA mean?**

It was a mistake made by the author. "HNFA" was replaced by "HNF4" as correspond.

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

Sincerely yours,



Jorge Quarleri/Ph.D

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