

ANSWERING REVIEWERS



April 24, 2018

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 39040-minireview.doc).

Title: HBV pathogenesis: Fresh insights into HBV RNA

Author: Kazuma Sekiba, Motoyuki Otsuka, Motoko Ohno, Mari Yamagami, Takahiro Kishikawa, Tatsunori Suzuki, Rei Ishibashi, Takahiro Seimiya, Eri Tanaka, Kazuhiko Koike

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 39040

The manuscript has been improved according to the suggestions of editor and reviewer:

1 Revision has been made according to the suggestions of the editor and reviewer

(1) **Editor:**

Response:

We thank the editors for the valuable comments. We revised the manuscript according to the comments as below.

Changes to the text are underlined and highlighted in red.

- 1. A language certificate letter by professional English language editing companies is attached.*
- 2. Manuscript number is provided.*
- 3. ORCID numbers for all authors are provided.*
- 4. Grant support information is provided.*
- 5. Audio core tip is attached.*
- 6. All authors' abbreviation names and manuscript title have been added.*
- 7. No repeated references are confirmed.*
- 8. We uploaded the original ppt files as Image files.*

(2) **Reviewer # 02861124:**

Comments to Authors: The mini-review presents the current knowledge on the role of HBV RNA molecules in its pathogenesis. Overall the gathered information are very informative and important for HBV researchers and clinicians.

Response: *We thank the Reviewer #1 for his/her critical reading of the manuscript and positive comments.*

Comments to Authors: However, the manuscript is not well written and greatly lacks citations. My suggestions/comments are highlighted (track change) in the attached manuscript file.

Major: Introduction- It lacks vital information of the virus and needs to be rewritten properly. It would be great to give some details on how HBV RNA intermediate is formed- its known.

Response: *We thank the Reviewer for raising these issues. In accordance with this suggestion, we added*

sentences and citations in the INTRODUCTION as follows;

(Page 5, line 2-7.) Hepatitis B virus (HBV) is a small enveloped DNA virus which belongs to the Hepadnaviridae virus family. HBV may establish a chronic infection in the liver, which can, in turn, lead to cirrhosis and hepatocellular carcinoma (HCC). Although HBV has infected humans for at least 500 years [1], the virus was not discovered until 1966 [2], and Dane et al. identified the virus particle in 1970 by electron microscopy [3]. After these findings, the antiviral therapy has developed;

(Page 6, line 5-8.) The viral genes are transcribed by the cellular RNA polymerase II from cccDNA. Two enhancers designated enhancer I (EnhI) and enhancer II (EnhII) have been identified in the HBV genome, which drive and regulate the expression of the complete viral transcripts [18].

Comments to Authors: Figure legends- If the figures are not constructed by the authors or modified from the original, the original source or reference must be cited.

Response: *While we do understand the Reviewer's concern, all of the figures were originally constructed by ourselves for this mini-review article, using an Adobe Illustrator CC software.*

We sincerely thank Reviewer #1 for the critical reading of our manuscript and the constructive comments, which have helped us to improve our manuscript substantially.

We thank the editors and the reviewers again for the kind consideration of our manuscript.

Sincerely yours,

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