

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62850

**Title:** Towards a new era of HBV therapeutics: the pursuit of functional cure

**Reviewer's code:** 03486791

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Greece

**Manuscript submission date:** 2021-01-20

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-01-21 00:26

**Reviewer performed review:** 2021-01-21 00:40

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Thank you for inviting me to review this paper. HBV therapeutics is an important topic. However, to some degree, this paper is not special.

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62850

**Title:** Towards a new era of HBV therapeutics: the pursuit of functional cure

**Reviewer's code:** 05095017

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Greece

**Manuscript submission date:** 2021-01-20

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-01-20 10:18

**Reviewer performed review:** 2021-01-27 02:14

**Review time:** 6 Days and 15 Hours

<b>Scientific quality</b>	[ <input checked="" type="checkbox"/> ] Grade A: Excellent [ <input type="checkbox"/> ] Grade B: Very good [ <input type="checkbox"/> ] Grade C: Good [ <input type="checkbox"/> ] Grade D: Fair [ <input type="checkbox"/> ] Grade E: Do not publish
<b>Language quality</b>	[ <input checked="" type="checkbox"/> ] Grade A: Priority publishing [ <input type="checkbox"/> ] Grade B: Minor language polishing [ <input type="checkbox"/> ] Grade C: A great deal of language polishing [ <input type="checkbox"/> ] Grade D: Rejection
<b>Conclusion</b>	[ <input type="checkbox"/> ] Accept (High priority) [ <input type="checkbox"/> ] Accept (General priority) [ <input checked="" type="checkbox"/> ] Minor revision [ <input type="checkbox"/> ] Major revision [ <input type="checkbox"/> ] Rejection
<b>Re-review</b>	[ <input checked="" type="checkbox"/> ] Yes [ <input type="checkbox"/> ] No
<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

#### **SPECIFIC COMMENTS TO AUTHORS**

This is a comprehensive review focused on novel anti-HBV drugs towards functional cure of HBV. This manuscript covered most of the important therapeutic approaches including direct-acting antivirals and immunotherapy in the pipeline or preclinical. I would like to recommend this manuscript for publication after minor revision: 1) Page 9 Line 26: Bulevirtide is an HBV entry inhibitor, and it has been already reported that it is effective on HBV/HDV co-infected patients (ref 41). How is the effect for HBV infected patients without HDV infection? Is it already tested or on the clinical trial? 2) Page 11 Line 23: Please cite the articles which reported that smc5/6 are the substrates of HBx-DDB1 ubiquitin ligase complex. 3) The headlines for the therapeutics in the text, tables and figures are not always similar (for example, "Silencing viral transcripts", "RNA targeting therapeutics" and "RNA interference"). It would be readable for the readers if they could be unified or expressed similarly. 4) There are some typos to be corrected. For example, Page 10 line 25 and 28 "CRISPR".

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62850

**Title:** Towards a new era of HBV therapeutics: the pursuit of functional cure

**Reviewer's code:** 00032020

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Greece

**Manuscript submission date:** 2021-01-20

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-01-21 00:56

**Reviewer performed review:** 2021-01-27 03:54

**Review time:** 6 Days and 2 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

Manuscript NO: 62850 Title: Towards a new era of HBV therapeutics: the pursuit of functional cure Correspondence to: Christos Triantos, MD This is an informative and educational review. Authors had better add the comment about necessity or possibility of interferon/pegylated interferon for HBV therapy in the future. Is the possibility of combination therapy with interferon/pegylated interferon left in the future? Minor; The bottom line, page 20; Was 'GS-6988' incorrect? The line 16, page 26; 'INF-medicated' should be replace to 'IFN-mediated', if INF means interferon.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

**Manuscript NO:** 62850

**Title:** Towards a new era of HBV therapeutics: the pursuit of functional cure

**Reviewer's code:** 05095017

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Greece

**Manuscript submission date:** 2021-01-20

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-02-24 00:52

**Reviewer performed review:** 2021-02-24 11:18

**Review time:** 10 Hours

<b>Scientific quality</b>	[ <input checked="" type="checkbox"/> ] Grade A: Excellent [ <input type="checkbox"/> ] Grade B: Very good [ <input type="checkbox"/> ] Grade C: Good [ <input type="checkbox"/> ] Grade D: Fair [ <input type="checkbox"/> ] Grade E: Do not publish
<b>Language quality</b>	[ <input checked="" type="checkbox"/> ] Grade A: Priority publishing [ <input type="checkbox"/> ] Grade B: Minor language polishing [ <input type="checkbox"/> ] Grade C: A great deal of language polishing [ <input type="checkbox"/> ] Grade D: Rejection
<b>Conclusion</b>	[ <input type="checkbox"/> ] Accept (High priority) [ <input type="checkbox"/> ] Accept (General priority) [ <input checked="" type="checkbox"/> ] Minor revision [ <input type="checkbox"/> ] Major revision [ <input type="checkbox"/> ] Rejection
<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

The revised manuscript is much improved, and the authors have addressed my issues.

I recommend its acceptance with one very minor correction. As citation ref 57, the first report (Decorsière A et.al, Nature. 2016 Mar 17;531(7594):386-9. doi: 10.1038/nature17170.) would be better. Please replace it.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

**Manuscript NO:** 62850

**Title:** Towards a new era of HBV therapeutics: the pursuit of functional cure

**Reviewer's code:** 00032020

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Greece

**Manuscript submission date:** 2021-01-20

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-02-24 02:54

**Reviewer performed review:** 2021-02-28 03:43

**Review time:** 4 Days

<b>Scientific quality</b>	[ <input checked="" type="radio"/> ] Grade A: Excellent [ <input type="radio"/> ] Grade B: Very good [ <input type="radio"/> ] Grade C: Good [ <input type="radio"/> ] Grade D: Fair [ <input type="radio"/> ] Grade E: Do not publish
<b>Language quality</b>	[ <input checked="" type="radio"/> ] Grade A: Priority publishing [ <input type="radio"/> ] Grade B: Minor language polishing [ <input type="radio"/> ] Grade C: A great deal of language polishing [ <input type="radio"/> ] Grade D: Rejection
<b>Conclusion</b>	[ <input checked="" type="radio"/> ] Accept (High priority) [ <input type="radio"/> ] Accept (General priority) [ <input type="radio"/> ] Minor revision [ <input type="radio"/> ] Major revision [ <input type="radio"/> ] Rejection
<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

Thank you for reply. I am satisfied with the revision.