PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 69861

Title: Review on hepatitis B virus precore/core promoter mutations and their correlation with genotypes and liver disease severity

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 04770380

Position: Editorial Board

Academic degree: DSc, PhD

Professional title: Professor

Reviewer’s Country/Territory: Russia

Author’s Country/Territory: India

Manuscript submission date: 2021-07-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-15 11:58

Reviewer performed review: 2021-07-20 15:05

Review time: 5 Days and 3 Hours

<table>
<thead>
<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[ ] Grade C: Good</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Grade D: Fair</td>
<td>[ ] Grade E: Do not publish</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Language quality</th>
<th>[ ] Grade A: Priority publishing</th>
<th>[ ] Grade B: Minor language polishing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Grade C: A great deal of language polishing</td>
<td>[ ] Grade D: Rejection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>[ ] Accept (High priority)</th>
<th>[ ] Accept (General priority)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Minor revision</td>
<td>[ ] Major revision</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Re-review</th>
<th>[ ] Yes</th>
<th>[ ] No</th>
</tr>
</thead>
</table>
SPECIFIC COMMENTS TO AUTHORS
The submitted manuscript entitled “Xihuang pills induce apoptosis and growth inhibition in hepatocellular carcinoma cells by suppressing the PI3K/Akt/mTOR signalling pathway” by Teng YJ et al aimed to study proapoptotic role of Xihuang pills (XHP) in HCC cell line. However, there is a great concern regarding experimental design of this study. First of all, the authors used SMMC-7721 human cell line, which was identified as belonged to false and cross-contaminated cell lines (see Ye F, Chen C, Qin J, Liu J, Zheng C. Genetic profiling reveals an alarming rate of cross-contamination among human cell lines used in China. FASEB J. 2015 Oct;29(10):4268-72. doi: 10.1096/fj.14-266718). Second, SMMC-7721 cell viability and apoptosis as well as PI3K/Akt/mTOR signalling were investigated using a XHP extract that is composed of a mixture of different compounds, and it is difficult to judge which compound cause these effects. Instead, the authors are recommended to use any purified XHP component identified by mass- spectrometry. The above-mentioned circumstances make the results obtained in this study invalid and can lead to harmful therapeutic strategies.
PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 69861

Title: Review on hepatitis B virus precore/core promoter mutations and their correlation with genotypes and liver disease severity

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 01221925

Position: Editorial Board

Academic degree: AGAF, FACS, FICS, MD, PhD

Professional title: Professor

Reviewer’s Country/Territory: Greece

Author’s Country/Territory: India

Manuscript submission date: 2021-07-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-14 18:34

Reviewer performed review: 2021-07-24 09:40

Review time: 9 Days and 15 Hours

<table>
<thead>
<tr>
<th>Scientific quality</th>
<th>Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language quality</td>
<td>Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection</td>
</tr>
<tr>
<td>Conclusion</td>
<td>Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection</td>
</tr>
<tr>
<td>Re-review</td>
<td>Yes [ ] No [ ]</td>
</tr>
</tbody>
</table>
SPECIFIC COMMENTS TO AUTHORS
This is an interesting paper reviewing HBV promoter mutations and their correlation with genotypes and liver disease severity. Could the authors please respond to the following questions/comments? 1) The author uses a “first person – narrator “ approach, ie “Now I will discuss..”. May wish to reconsider this for a paper. 2) The author may wish to consider adding a discussion section where the potential clinical utility and any efforts to-date in that direction are discussed 3) Could the author elaborate on how these mutations interact with other mutations at other parts of the virus?
RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 69861

Title: Review on hepatitis B virus precore/core promoter mutations and their correlation with genotypes and liver disease severity

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 04770380

Position: Editorial Board

Academic degree: DSc, PhD

Professional title: Professor

Reviewer’s Country/Territory: Russia

Author’s Country/Territory: India

Manuscript submission date: 2021-07-14

Reviewer chosen by: Jing-Jie Wang (Online Science Editor)

Reviewer accepted review: 2021-12-18 15:42

Reviewer performed review: 2021-12-24 04:28

Review time: 5 Days and 12 Hours

<table>
<thead>
<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[Y] Grade B: Very good</th>
<th>[ ] Grade C: Good</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Grade D: Fair</td>
<td></td>
<td>Grade E: Do not publish</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Language quality</th>
<th>[ ] Grade A: Priority publishing</th>
<th>[Y] Grade B: Minor language polishing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Grade C: A great deal of language polishing</td>
<td>[ ] Grade D: Rejection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>[ ] Accept (High priority)</th>
<th>[Y] Accept (General priority)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Minor revision</td>
<td>[ ] Major revision</td>
</tr>
</tbody>
</table>

| Peer-reviewer      | Peer-Review: [Y] Anonymous | [ ] Onymous |


| statements | Conflicts-of-Interest: [ ] Yes [ ] No |

**SPECIFIC COMMENTS TO AUTHORS**

Accept
RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Hepatology
Manuscript NO: 69861
Title: Review on hepatitis B virus precore/core promoter mutations and their correlation with genotypes and liver disease severity
Provenance and peer review: Invited manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 05224602
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Doctor, Professor
Reviewer’s Country/Territory: China
Author’s Country/Territory: India
Manuscript submission date: 2021-07-14
Reviewer chosen by: Jing-Jie Wang (Online Science Editor)
Reviewer accepted review: 2021-12-24 06:02
Reviewer performed review: 2021-12-26 04:50
Review time: 1 Day and 22 Hours

Scientific quality

| [ ] Grade A: Excellent | [ ] Grade B: Very good | [ ] Grade C: Good |
| [ ] Grade D: Fair | [ ] Grade E: Do not publish |

Language quality

| [ ] Grade A: Priority publishing | [ ] Grade B: Minor language polishing |
| [ ] Grade C: A great deal of language polishing | [ ] Grade D: Rejection |

Conclusion

| [ ] Accept (High priority) | [ ] Accept (General priority) |
| [ ] Minor revision | [ ] Major revision | [ ] Rejection |

Peer-reviewer

Peer-Review: [ ] Anonymous | [ ] Onymous
SPECIFIC COMMENTS TO AUTHORS
Accept.