

PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 73679

Title: The role of hepatitis B virus in the development of hepatocellular carcinoma: Focus on cccDNA

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00011431

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-11-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-02 06:25

Reviewer performed review: 2021-12-09 03:25

Review time: 6 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: ☒ Anonymous ☐ Onymous

Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

While the title is “role of Hepatitis B virus in the development of hepatocellular carcinoma: Focus on cccDNA”, this review actually summarizes the general information of HBV, with a focus on the function of cccDNA on viral replication and our current efforts to the detection and targeted inhibition of cccDNA. The authors have discussed three major mechanisms underlying HBV-related carcinogenesis (1 chronic inflammation; 2. HBV DNA integration; 3. expression of oncogenic viral proteins), but cccDNA was not even mentioned in that part. Thus, how cccDNA promotes the initiation and progression of HCC is still unclear after reading the whole text. And there was also no evidence showing that using the approach targeting cccDNA can prevent the development of HCC.

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Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02842879

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor, Chief Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2021-11-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-01 12:34

Reviewer performed review: 2021-12-10 03:06

Review time: 8 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<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
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**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

This review is a comprehensive summary of the role of cccDNA in the pathogenesis of CHB, especially in HBV replication. And the review also well summarizes the current choice of cccDNA detection and which as a current target for treatment. But unfortunately, the above aspects have been related reported. This article is not deep enough for the mechanism of cccDNA and HCC. However, this should be a key point and mostly interest. On the other hand, it is still possible in the pathogenesis of HCC although HBV has been inhibited even HBsAg has been cleared.