

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 25989

Title: A new horizon for radical cure of chronic HBV infection

Reviewer's code: 00068156

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2016-03-28 17:32

Date reviewed: 2016-03-29 10:14

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this editorial, the author provided an overview of the current evidence-based information on the research progression of radical cure of chronic HBV infection targeting cccDNA. The author also discussed various clinical trials regarding agents tested targeting the life cycle of HBV in hepatocytes, including the elimination of cccDNA. This editorial is described in detail, which, as a valuable information, could help the readers that have better understand the first-hand knowledge of this topic to start novel studies. This review is recommended to be published in the journal.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 25989

Title: A new horizon for radical cure of chronic HBV infection

Reviewer's code: 00742524

Reviewer's country: China

Science editor: Ya-Juan Ma

Date sent for review: 2016-03-28 17:32

Date reviewed: 2016-04-02 23:24

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This editorial provided a general overview of the cure of HBV infection, with a special emphasis on the recent finding on the role of IFN- γ and TNF- α on cccDNA. There are many omissions and the editorial is not particularly well written. The topic has also been extensively reviewed by leaders in the field in mainstream journals, so it is unlikely and questionable that this editorial will be highly cited. At least the deficiencies should be remedied before the manuscript can be accepted for publication. 1) Many other recent reviews have already been published. The following are just a small fraction: Virus Res 213:205-213, 2016; Lancet Infect Dis 16:e10-e21, 2016; Nat Rev Gastroenterol Hepatol 13:239-248, 2016. 2) A major controversy in the field concerns the possible curative effect of IFN- α through the action of APOBEC3 (Ref. 17: Science 343:1221-1228, 2014). This should not be omitted in this editorial. The critical issues and the unmet challenge should be discussed. A key recent paper on the role of IFN- γ and TNF- α mediated through APOBEC3 (Ref. 50: Gastroenterology 150:194-205, 2016) should also be discussed together here.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 25989

Title: A new horizon for radical cure of chronic HBV infection

Reviewer's code: 00160243

Reviewer's country: Australia

Science editor: Ya-Juan Ma

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

A true cure for chronic hepatitis B virus (HBV) infection is extraordinarily difficult to achieve. The key intrahepatic replicative form of HBV, the cccDNA, is believed to play a key role in maintenance of chronic HBV infection and is likely to be responsible for relapse of disease after completion of antiviral therapy. As well as being recalcitrant to treatment, HBV cccDNA can persist even after seroconversion and HBsAg loss. This manuscript discusses current and impending strategies to eliminate chronic HBV infection with the major focus on targeting the HBV cccDNA. It is a substantial topic to cover and on the whole the authors have reviewed much of the relevant literature. There are a few factual errors that should be corrected and I have some minor points for the authors to consider. 1. In the description of the HBV replication cycle, it is incorrectly stated that the relaxed circular genomic DNA is released into the cytoplasm where it is converted to cccDNA and then enters the nucleus. The cccDNA is formed after infection when the encapsidated viral genomic DNA is translocated to the cell nucleus (actually transported to the nuclear pore where the HBV DNA is released) where it persists as a stable episome and acts as the transcriptional template for production of viral mRNA. 2. The cytoplasmic pgRNA and polymerase protein are not packaged into envelope

proteins but rather into immature core particles. 3. The functional receptor on the hepatocyte surface for HBV, the sodium taurocholate cotransporting polypeptide, is mentioned by the authors but the role of HBV entry inhibitor, Mycludex B, has not been discussed. 4. With a strong focus on HBV cccDNA, perhaps a small section on the difficulties in quantification of this intermediate could have been included. 5. In the discussion of immune tolerance, a worthwhile reference is that of Lang et al (2011; J Hepatol 55: 762-9) where they describe the role of HBeAg in modulation of the toll-like receptor (TLR) signal transduction pathway. This is relevant as the authors later describe TLR-7 agonists as an immunotherapeutic approach. 6. In the article title, HBV should be spelt in full – hepatitis B virus. 7. The sentence at the end of the section on “Inhibitory receptors” would be better as “Although radical cure (Table 1) is desirable, it is problematic because of the difficulty in eliminating HBV cccDNA from the liver.” 8. In the “Inhibition of HBV replication” section Gilead Sciences is listed as Giliad.