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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26959

Title: Elucidation of the early infection machinery of hepatitis B virus by using bio-nanocapsule

Reviewer's code: 00506601

Reviewer's country: United States

Science editor: Jing Yu

Date sent for review: 2016-05-02 15:04

Date reviewed: 2016-05-11 03:29

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a well written review of the research that has been done to establish the sequence of events that takes place as the HBV virus infects a hepatocyte. The authors synthesized a hollow bio-nanocapsule (BNC) in a fungi to deliver HBV -derived infection, machinery. In this way they could study the mechanism of HBV infection in a more controlled atmosphere. Their experiments are both elegant and simple at the same time. I am not a molecular biologist but I found the paper easy to understand and did not find anything to criticize.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26959

Title: Elucidation of the early infection machinery of hepatitis B virus by using bio-nanocapsule

Reviewer's code: 03479014

Reviewer's country: United States

Science editor: Jing Yu

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Date reviewed: 2016-06-03 20:51

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 checked="" 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		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This minireview summarizes recent data using bio-nanocapsule (BNC) as a mimic of HBV virion to investigate functional segments of HBV Large Envelope protein in HBV entry. The authors identified a fusogenic sequence located in the N terminal of pre-S1 protein, which might mediate step of late endosomal escape of HBV (uncoating). Overall, the topic is interesting and it provides new information regarding HBV entry process. However, there are several concerns: 1. A lack of convincing rationale to use BNC as a mimic of HBV virion. The authors argue that HBV particles for infection experiment are difficult to acquire and there is a need to use BNC. This statement is not entirely true because several stably HBV DNA transfected cell lines can produce high level of HBV DNA in medium. A probably more convincing rationale is that BNC is easier for manipulations (loaded with color molecules) than HBV virion. This advantage can simplify the experimental procedure, possibly generate reproducible data. 2. There is no valid comparison between HBV virion and BNC. This comparison should be clearly stated in the text in addition to Fig.1. Main differences include size, density and ratio of three envelope proteins. BNC is composed of exclusive L protein



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while the L protein in HBV virion only accounts to very small portion. Any conclusions resulting from BNC should be verified with HBV virion. 3. It is not clear whether the authors performed similar experiment with HBV virion. Otherwise Fig.3. can be misleading. Where did HBV results come from or just an assumption? Minor issues: 1. there are no line numbers in the manuscript 2. P4. "...HBV as a molecule" incorrect statement 3. P6. there is a lack of clarity in introducing HBV receptors that were mixed with ligand identification contained in HBV. 4. P7. Percentage of HBV vaccination. Exact numbers should be given 5. P8. " BNC infects cells", an inaccurate description 6. P9. More detailed information should be presented in describing no enhancement of interaction and internalization when NTCP was overexpressed. Credible evidence is needed to challenge NTCP as a major receptor or suggest a different one 7. P9. the authors appeared to suggest HBsAg can enter into cells via a same or different receptor? Is this understanding correct? evidence is required if so. 8. English is understandable, but not idiomatic or professional terms were not used.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Elucidation of the early infection machinery of hepatitis B virus by using bio-nanocapsule

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<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 checked="" 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"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Comments to the Author The authors reviewed bio-nanocapsule (BNC) could be used as a model of HBV for elucidating the HBV early infection machinery. They described the model in which each domain of L protein respectively contributes to the attachment onto human hepatic cells through HSPG, the initiation of endocytosis, the interaction with NTCP in endosomes, and consequently the provocation of membrane fusion followed by the endosomal escape. Major points: 1. The paragraph "BNC AS NANOCARRIER" just illustrate BNC infects human hepatic cells by using HBV-derived infection machinery. This paragraph should be re-written. 2. The format of references is not consistent. The format of reference 40 if different from others. There are two reference 28. 3. The format of paragraphs is not consistent. There is space in line header sometimes.