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315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7119

Title: Control of hepatitis B virus replication by interferons and Toll-like receptor signaling pathways

Reviewer code: 02539216

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-05 17:17

Date reviewed: 2013-11-14 18:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

I would ask you to add the list of abbreviations and the description of Fig.1. Fig. 2 should be added showing TLR and its ligands involvement in hepatitis B. Besides, several grammar errors should be corrected. 220 - the sentence is unclear.



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ESPS Manuscript NO: 7119

Title: Control of hepatitis B virus replication by interferons and Toll-like receptor signaling pathways

Reviewer code: 00052848

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-05 17:17

Date reviewed: 2013-11-15 15:07

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Major comments: Overall this is a well written review of current advances in the area of control of HBV infection by interferon and TLRs. On broad lines, I would suggest to add a sentence or two addressing the potential complexity of effects on HBV replication mediated by miRNA for TLR. The section on TLRs is relatively short compared to the more extensive review of molecular events involving IFNs, which is understandable because interferon research has been progressing for far longer. For the same paragraph, current data indicate that HBV does not activate innate immune response. However, it should be considered that this interpretation applies only to known factors that have been tested so far. I would suggest to soften the implications of line 289, and say 'Though HBV itself does not appear to trigger innate immune responses,etc'. On the paragraph discussing APOBECs, lines 200-203 correctly indicate that info on APOBEC levels in several studies were done in culture supernatants or serum. This should be tested in a cell-associated form, since this is the form most likely efficient in interfering with viral processes, and the authors could expand a little bit on this sense. Finally, some caution is advised on section 6, paragraph 'HBV inhibits PRR and IFN signal transduction'. Reduced expression of TLRs in peripheral blood may or may not reflect events in the liver (lines 312-313), and even if we extrapolate findings in circulation to liver tissue, changes on TLRs expression may be temporal, or may reflect exhaustion of these receptors due to overactivation. Minor comments: Line 67, mediate should say 'mediating'. Lines 73 to 91, references should be added here. These are likely the same listed in the following 2 paragraphs. Line 82, please correct to 'polymerase'. Line 94, please define ISGs. Line 97, change was for 'has not'. Line 98, change humane for 'human'. Line 112, please define DHBV. Line 127, please define ISRE. Line 139, delete 'in'. Line 160, delete 'the' (should say: Similar conclusion, etc). Line 198, should say: The



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control of HBV by members of the APOBEC family, etc.... Line 214, please define epsilon. Line 226, should say 'the APOBEC family'. Line 229, please define GTPase. Line 235 should say 'female'. Line 241, please delete 'the'; should say: Using co-immunoprecipitation and fluorescence...etc. Line 284, please spell out ppp-RNA. Line 285, reads better 'block HBV replication' instead of 'have anti-HBV activity'. Line 297, should say 'In a hepatoma cell line' or 'In hepatoma cells' ...etc. Line 297: should say 'the adaptor protein...etc'. Line 301, delete 'the'; add 'a' so it reads 'replication in a murine'...etc. Line 302, should be 'conditioned media' instead of 'conditional media'. Line 319, please define SOCS-1. Line 320, please define BDCA-2. Line 325, hepatocyte should be plural. Line 336, please define CHB. Line 344, please define PC/BCP mutants. The references should be edited to fit the format of the journal



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ESPS Manuscript NO: 7119

Title: Control of hepatitis B virus replication by interferons and Toll-like receptor signaling pathways

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<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Pei et al., review the field of HBV regulation by type I IFN. They nicely described the details of HBV life cycle and IFN-inducible genes that regulate viral replication. In addition to these items, the authors gave an explanation about how type I IFN inhibits HBV propagation. However, they only minimally mention the participation of PRRs including TLRs in inhibition of HBV replication. The review is superficial and conventional, but just summarizes current literatures which might be helpful to the readers. The title is inappropriate: "Control of hepatitis B virus replications by interferons and innate immunity" would be better than the current one, since this review does not focus on TLRs in HBV infection. Comments 1. The manuscript is very stereotyped with no authors's interpretations. I would recommend the authors to add their idea and critical comments on the current concepts or findings reported in the references. Then, the manuscript will be improved. 2. Please add one Table, where the authors mention what kinds of PRRs or innate factors participate in which steps of the HBV life cycle. 3. There are many type errors; for example, line 83, polymerase; line 87, transcribed; line 94, though.