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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 34417

**Title:** Functional interaction of endoplasmic reticulum stress and HBV in the pathogenesis of liver diseases

**Reviewer's code:** 02936403

**Reviewer's country:** Taiwan

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-04-25

**Date reviewed:** 2017-05-14

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 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

The manuscript mostly made a good description between ER stress and HBV in the pathogenesis of liver disease. However, it is reported that one of mechanism of standard therapy of HCC, sorafenib is induction of ER stress. It seems conflicting to this model. What is possible interoperation for this?



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 34417

**Title:** Functional interaction of endoplasmic reticulum stress and HBV in the pathogenesis of liver diseases

**Reviewer's code:** 00187828

**Reviewer's country:** Turkey

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-05-27

**Date reviewed:** 2017-06-08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [ Y ] Accept
<input type="checkbox"/> [ Y ] Grade B: Very good	<input type="checkbox"/> [ Y ] 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"/> [ Y ] 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"/> [ Y ] No	

**COMMENTS TO AUTHORS**

The manuscript entitled "Functional interaction of endoplasmic reticulum stress and HBV in the pathogenesis of liver diseases" has been reviewed as follows; The authors did a great job by reviewing HBV infection and ER stress and mitochondrial stress. Under normal physiological conditions, our body has adaptive system to maintain homeostasis from various stresses. Even though faced with pathological conditions, our body can be protected from the conditions by removing and restoring the damaged cells and tissues through innate and adaptive immune system. However, HBV has the abilities to escape from the host's immune response and even to utilize autophagy for viral replication and envelopment. The abilities facilitate chronic infection of HBV, leading to chronic ER and mitochondrial stress, resulting in the pathogenesis of various liver diseases including NAFLD, cholestatic liver disease, viral hepatitis, and liver cancer. Here we indicated the mechanisms by which HBV proteins induce the dysfunction of cellular organelles and



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the hepatic diseases developed by the expression of UPR target genes or by disturbance of cellular signaling pathway. From a therapeutic perspective, it will be important to understand how HBV induce ER or 16 mitochondrial dysfunctions and understanding the mechanisms will provide new treatment options to chronic HBV patients. In conclusion, it is a well-written and a critical review, comprehensively reviewed. It clearly shows the role of HBV infection related pathology through ER stress and mitochondrial stress.