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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 11884
Title: Occult infection related Hepatitis B surface antigen variants showing lowered secretion capacity
Reviewer code: 02567528
Science editor: Su-Xin Gou
Date sent for review: 2014-06-12 11:08
Date reviewed: 2014-06-20 08:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Kim et al studied the secretion capacity and intracellular expression of the hepatitis B virus (HBV) virions and HBsAgs of 10 HBsAg variants derived from patients with occult genotype C HBV infection in a transient co-transfection system. They found that all variants exhibited lower levels of HBsAg secretion compared with the wild type, and that most variants exhibited normal virion secretion capacities comparable with, or even higher than, the wild type. Furthermore, most variants generated higher reactive oxidative species (ROS) production than the wild type. Their findings are interesting and provide a mechanistic explanation for occult HBV infection of genotype C and its potential link to liver disease progression. Two major comments are: 1. Does the extracellular HBV DNA level of the HBsAg variants in the transient transfection system (Table 3 and Figure 2) correlate with the serum HBV DNA level of the individual patient from whom the HBsAg variant was cloned? Please include the serum HBV DNA level of each patient in Table 2. 2. The Group III HBsAg variants (CNR, LL and PAHS) showed negative or weakly positive HBsAg expression or secretion yet increased levels of viral DNA production and secretion as compared to the wild type. If protein stability was the reason for reduced HBsAg expression, how can the HBV virion be formed without HBsAg? Please provide an explanation.

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ESPS PEER REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

A key conclusion of this study is that occult infection may be attributed to defects in HBsAg secretion. The data behind this conclusion rely on the ability of the HBsAg assays used in the study to detect the secreted/intracellular HBsAg in the expression system. In samples classified into groups I, II, or V, the results suggest that the assays were sufficient for detection of the variant HBsAg forms. However, for groups III and IV, particularly samples ALK and KD, there is the question of whether the HBsAg assays could detect the variant HBsAg if it was expressed. Although ALK and KD have mutations outside the 'a' determinant, this is not sufficient to conclude that the variants would be detected by the HBsAg assay used. The detection of recombinant HBsAg samples with commercially available HBsAg assays can be highly dependent on the combination of mutations, expression system, post-translational modification, and other variables associated with generating recombinants. The authors need to demonstrate independently that the HBsAg assays are capable of detecting such variants if they are present. Additional comments: Methods section: Sentence two is unclear and needs revision. Introduction: The references cited linking occult HBV infection to severe forms of liver disease date from over 30 years ago. The authors should include more recent references that support this link. Discussion: It would be helpful if the authors could discuss the ratios of HBsAg to HBV DNA/virions among the ten cloned samples relative to the ratios observed In chronic HBsAg-positive HBV infection.