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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 11186

Title: Mutations of Pre-core and BCP Before and After HBe Antigen Seroconversion

Reviewer code: 00742524

Science editor: Ya-Juan Ma

Date sent for review: 2014-05-08 13:17

Date reviewed: 2014-05-24 11:59

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 checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This work followed a small cohort of HBV patients for 9 years. A predominance of pre-C mutants after HBeAg seroconversion was found. Although this is not surprising, the findings will still be of interest to other investigators in the field. The paper should be further edited to improve the presentation. Since the sample size is small, the full-length HBV sequence should be determined to find out whether there might be additional mutations.



ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 11186

Title: Mutations of Pre-core and BCP Before and After HBe Antigen Seroconversion

Reviewer code: 00030389

Science editor: Ya-Juan Ma

Date sent for review: 2014-05-08 13:17

Date reviewed: 2014-05-24 19:46

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	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The authors investigated the pre-core and/or basal core promoter mutations before and after hepatitis B e antigen (HBeAg) seroconversion. They found that the association of the pre-C mutation on viral load is opposite in patients before and after HBeAg seroconversion. It is an interesting report. However there are several concerns. Major comments. #1. There is significant difference, while the authors described them as tendency. Please described the findings correctly. Please discriminate significant differences from differences in tendency. Please show p values in the manuscript. #2. Introduction, line 25. Do the authors think that HBeAg seroconversion was not associated with either mutation? In the present study, they showed that HBeAg seroconversion was associated with pre-C mutation. In the previous study, did they actually observe the opposite results. #3. They selected the patients without antiviral therapy during the study period of several years. Thus they selected those who did not need antiviral therapy and had normal ALT levels. I worry that the bias of selection may cause the wrong results. Please discuss this problem in discussion. #4. Page 9, lines 15-17. Kawabe N, et al. reported that the loss of HBeAg without precore mutation results in lower HBV DNA levels and ALT levels in chronic hepatitis B virus infection (Journal of gastroenterology. 2009;44: 751-6). Please refer this report and discuss on it. Minor comments. #1. M&M. Determination of pre-C and BCP mutations "since the rate steadily increased to 100% once it surpassed that value". What does this sentence mean? #2. P6, line 2. "Of the 143 samples with determined BCP mutationtypes, 34 (24%) were wild, 11 (8%) were mixed, and 98 (69%) were mutant types". This sentence should be in the results. #3. "anti-HBe status subjects". "positive"should be inserted.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 11186

Title: Mutations of Pre-core and BCP Before and After HBe Antigen Seroconversion

Reviewer code: 00465536

Science editor: Ya-Juan Ma

Date sent for review: 2014-05-08 13:17

Date reviewed: 2014-05-26 13:57

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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	BPG Search:	<input checked="" 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

Kamijo et al. assessed the proportions of pre-C (G1896A) and BCP (A1762T and/or G1764A) mutations as well as HBV DNA VL, HBsAg and HBcrAg in Japanese patients, infected with HBV-C, untreated with NAs, and who showed during their follow-up (i) HBeAg seroconversion (n=25); (ii) a persistent positivity for HBeAg (n=18), (iii) or a persistent positivity for HBeAb (n=43). The median follow-up was long (9 years). It's an interesting and well written paper indicating clearly that the appearance of the pre-C mutation, but not the BCP mutation, is directly associated with seroconversion. The main limitation of this work, as indicated by authors, is the lack of entire genomic sequences to better investigate the mechanisms of "e" system seroconversion. I have only minor comments:

- Abstract, methods section: The sentence "...were analyzed before and after seroconversion in chronic hepatitis B patients who were persistently HBeAg positive (n=18), experienced HBeAg seroconversion (n=25), or were persistently anti-HBe positive (n=43)." is not clear since only 25 patients experienced seroconversion.
- Introduction: short and well presented.
- Material and methods 1/ Patients, second paragraph: it's better to put (for a better clarity) Table 1 (and corresponding text) in a 1st paragraph in the results section. 2/ Determination of pre-C and BCP mutations, second and third paragraphs: the same, it's better to transfer in the results section the frequencies of mutations that the authors obtained (with 154 and 143 samples for pre-C and BCP determination, respectively).
- Results 1/ Changes in pre-C and BCP mutations: The figures (1 and 2) are readable but the authors should try histogram bars (showing modifications in frequencies between start and end of follow-up) to present their data in a more attractive way. Figure 3 is nice.
- Discussion: The 1st paragraph of the discussion should be deleted.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 11186

Title: Mutations of Pre-core and BCP Before and After HBe Antigen Seroconversion

Reviewer code: 01804246

Science editor: Ya-Juan Ma

Date sent for review: 2014-05-08 13:17

Date reviewed: 2014-05-27 15:54

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<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
<input checked="" 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
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<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is an interesting paper well presented. There is need only for minor language corrections.