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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37880
Title: Gender disparity in viral load, inflammation and liver damage on transgenic mice models carrying hepatitis B virus full genome with preS1 W4P mutation
Reviewer's code: 01805500
Reviewer's country: Italy
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-13
Date reviewed: 2018-01-13
Review time: 4 Hours

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

COMMENTS TO AUTHORS

Authors correctly state that.....In this study, we sought to construct the W4P TG mice model system constructively expressing HBV full genomes, which can help us to study the gender disparity of liver disease progression, including chronic hepatitis, steatohepatitis, cirrhosis and HCC in HBV chronic infection....but do not offer readers a complete view of the role of IL-6, key cytokine also in NAFLD/NASH that is the leading cause of HCC, due to obesity pandemic, see.....Could metabolic syndrome lead to hepatocarcinoma via non-alcoholic fatty liver disease? World J Gastroenterol. 2014 Jul 28;20(28):9217-28.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37880
Title: Gender disparity in viral load, inflammation and liver damage on transgenic mice models carrying hepatitis B virus full genome with preS1 W4P mutation
Reviewer's code: 00068723
Reviewer's country: Japan
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-13
Date reviewed: 2018-01-14
Review time: 1 Day

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

COMMENTS TO AUTHORS

The authors investigated the role of preS1 W4P mutation in liver carcinogenesis male preference. Male showed higher liver weight and increased fat accumulation and liver enzymes as compared with female. More information on preS1 W4P would be necessary. For example, comparison of sequence between wild type and the mutant. Findings of the liver of the transgenic mice were fat accumulation, increased liver weight, and elevated liver enzymes. How did the author speculate about the findings? Fat accumulation indicated fatty liver. In some liver congenital conditions, liver weight increases. Were there any relations between preS1 W4P mutation and fat accumulation? Was increased liver weight related with fat accumulation? It was not clear that preS1 W4P would cause hepatocellular carcinoma via fat accumulation, increased liver weight and liver enzymes.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37880
Title: Gender disparity in viral load, inflammation and liver damage on transgenic mice models carrying hepatitis B virus full genome with preS1 W4P mutation
Reviewer's code: 00722239
Reviewer's country: Japan
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-13
Date reviewed: 2018-01-14
Review time: 1 Day

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

COMMENTS TO AUTHORS

The authors have successfully developed W4P-TG mouse model system and showed gender disparity in hepatomegaly, liver enzyme and steatosis in their model. This is the very interesting study. Although the authors referred to the male predominance in HBV-related HCC in their introduction, the results of this study did not prove the male predominant carcinogenesis of HBV-related HCC. Generally, risky lifestyle such as alcohol intake and smoking differ between male and female and these risky lifestyles may be involved in the reason of male predominant liver carcinogenesis. Even in countries in which hepatitis C is the main cause of liver carcinogenesis like Japan, the incidence of HCC is predominantly higher in male. I consider that this is a conclusive study regarding development of W4P-TG mouse model but further studies are necessary to clarify the mechanism of male predominant liver carcinogenesis. The authors should

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describe these limitations in the text.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37880
Title: Gender disparity in viral load, inflammation and liver damage on transgenic mice models carrying hepatitis B virus full genome with preS1 W4P mutation
Reviewer's code: 02451157
Reviewer's country: Taiwan
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-11
Date reviewed: 2018-01-15
Review time: 3 Days

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

COMMENTS TO AUTHORS

This is an interesting paper that discover the mutation in LHBsAg in liver disease progress. The data fits the content. However, this paper needs minor language polishing.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37880
Title: Gender disparity in viral load, inflammation and liver damage on transgenic mice models carrying hepatitis B virus full genome with preS1 W4P mutation
Reviewer's code: 00053888
Reviewer's country: United Kingdom
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-13
Date reviewed: 2018-01-15
Review time: 2 Days

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

COMMENTS TO AUTHORS

The authors have produced an excellent manuscript and carried out an interesting molecular study. The preS1 W4P mutation in HBV seems to confer an advantage to the development of HCC in those with HBV but only male mice are affected. This has significant potential clinical applications. The study is well designed, well carried out and the manuscript is well written. There are only a small number of grammatical/typographical errors that need correcting but otherwise this manuscript should be published.