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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36386
Title: Cell culture-adaptive mutations in HCV promote viral production by enhancing viral replication and release
Reviewer's code: 02453015
Reviewer's country: United States
Science editor: Ze-Mao Gong
Date sent for review: 2017-12-01
Date reviewed: 2017-12-09
Review time: 8 Days

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

Major concerns: 1. English needs to be improved by native speakers. 2. Novelty should be emphasized. 3. The abstract is not in the correct format. 4. How did the authors determine Low and High viral titers? What is the threshold level? 5. Figure 1B. How to show single site mutations with similar length by electrophoresis? It can only be shown by sequencing. 6. The rationale for the combinations of mutations should be described. Why not try other combinations?

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36386
Title: Cell culture-adaptive mutations in HCV promote viral production by enhancing viral replication and release
Reviewer's code: 00503405
Reviewer's country: Hungary
Science editor: Ze-Mao Gong
Date sent for review: 2017-12-01
Date reviewed: 2017-12-09
Review time: 8 Days

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

In this original study the authors assayed the mechanism of in vitro cell culture adaptive viral mutations responsible for enhanced viral production in cell lines. They provided evidence that the adaptive C-virus mutations led to a robust infectious titer via promotion of viral replication and release. The study is well designed and well presented, all the used techniques are adequate for answering the original aims. Some minor language polishing are needed. Also, the format of the manuscript must be changed to the requirement of WJG. After minor revision I suggest to accept the manuscript for publication.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36386
Title: Cell culture-adaptive mutations in HCV promote viral production by enhancing viral replication and release
Reviewer's code: 01564209
Reviewer's country: Germany
Science editor: Ze-Mao Gong
Date sent for review: 2017-12-01
Date reviewed: 2017-12-12
Review time: 11 Days

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

Dr. Wang and colleagues presented an experimental study in which they aimed to explore the role of recently identified cell culture-adaptive HCV mutants in terms of viral replication and secretion. To show this the colleagues established a HCV-replicon HuH-7.5 cell culture system and analysed the identified 6 mutations in the HCV JFH genome responsible for enhanced virus titres in cell culture. As a result the authors showed that the combinations of the 6 mutations in different regions of the HCV genome and especially of NS5A and p7 mutations are potential candidates for an improved HCV cell culture system. However, LD localisation and phosphorylation of NS5A was not affected by these mutations. Overall, this is a well-designed study and the manuscript is concise in its content showing mainly convincing data. However, there are some comments which should be addressed. Comments 1. English typing and grammar

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needs attention at places and should be checked carefully best by a native English speaker. Also there are frequently missing space between two words. 2. Fig. 1B is not convincing. The size of the "HCV RNA" seemed to be much larger than the expected 9.6 kb. In my opinion the denoted HCV RNA bands are artefacts. 3. Fig. 2 How many experiments were performed in order to determine ffu/ml? A statistical calculation should be performed and significance should be annotated best from in minimum three independent experiments. 4. Fig. 3B. I assume that Fig 3B shows two parallel experiments; however, a stistical diagram summarizing the two to (more convincing) three Western blot experiments should be shown including statistical analysis evaluating the differences between the 6 mutants. 5. Chapter 3.3. 3rd and 12th line. What are exactly the "ten" HCV RNAs? Please specify. 6.Fig. 4C. How can you show beta-actin in supernatant? 7. Chapter 3.3. The virion release should be discussed in more detail. From the Western Blot analysis (Fig. 4C) one can infer dramatic differences in terms of the 6 HCV mutants. 8. Discussion and Conclusion section. A summary and conclusion of the key results of the experiments are missing leaving the reader alone with the findings of this well performed experimental study.