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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15278
Title: Hepatitis C virus-specific cytotoxic T cell response restoration after treatment-induced hepatitis c virus control
Reviewer's code: 00504141
Reviewer's country: Ireland
Science editor: Ya-Juan Ma
Date sent for review: 2014-11-19 09:11
Date reviewed: 2014-11-25 00:06

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	PubMed Search:	[Y] 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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Larrubia et al have written a concise review on the role of HCV specific cytotoxic T cell responses after clearance of HCV. The review is well written although there are a few places which need sentences to be rewritten. The review brings together recently published data and places the reported findings in the context of what we have known about chronic HCV infection. Specifically, the infection of chimpanzees with HCV from sera which has been harvested from patients treated with an interferon based regimen and achieved an SVR. The sectional structure is unusual, i.e., the authors need to introduce paragraphs into the review. The authors on page 9 suggest that HCV specific CTL responses at 12/52 of treatment has a 100% PPV. The authors should comment on the practicalities of performing CTL responses and perhaps how this could be manoeuvred into the clinical management of HCV. The authors mention and reference in Figure 2 that occasionally they can detect HCV 5'UTR in sera from some SVR patients several months after the EOT. The COBAS AMPLICOR HCV assay has been superseded by a TAQMAN based assay with a notable improvement in the LOD to ~10-15 IU per mL with a 95% CI. I wonder if these sera were tested with

these more sensitive diagnostic assays would the previously mentioned non-detectable "SRV" patients, still remain SVR! The authors should support their UTR findings by amplification of another region of the genome and publishing the resultant genome sequences. Ultralow copy PCR is more prone to difficulties of interpretation than high titre samples. By supporting the UTR findings with additional genomic information, the authors would provide enhanced evidence that their findings are robust. Figure 4 needs a more expansive legend. This review is likely to be cited.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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Reviewer's country: Spain
Science editor: Ya-Juan Ma
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	PubMed Search:	[Y] Accept
[Y] Grade B: Very good	[ ] 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 review "The role of HCV-specific cytotoxic T cell response after restoration anti-HCV treatment." Larrubia presented by J. R Larrubia et al. discusses in great depth a topic of great interest especially in these times when treatments against chronic HCV infection are showing excellent effectiveness. The analysis from the point of view of the restoration of the immune system as a very important factor to maintain the response to these treatments, is focused excellently and prove of great use to the scientific community. So it is very interesting discussion on the usefulness of this type of analysis as a predictor of treatment response. However, in this sense, the authors should add that this type of analysis would be useful for tracking those patients with situations of immunosuppression that having achieved sustained virologic response who will be in risk of recurrence until his immune system is unable to activate appropriately, as has been observed in liver transplant patients or in cancer treatment. Minor Comment: The paragraph on page 4: "In our group, we have also been reliable to amplify HCV 5'-untranslated region (UTR) RNA by an in-house nested RT-PCR in SVR will be from some patients several months after end of treatment , even though classified as they had

been SVR based on undetectable plasma HCV RNA by Cobas Amplicor HCV test (Not published data, Fig.-2). "must be removed because it is a not contrasted or reviewed result and is not necessary for the right argument of the bearer data from the literature

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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[ ] 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
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[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This review article summarized the immune response in hepatitis C virus infection. The contents are interesting, however, there are some issues to add as followings. Comments; 1. In 'IS IT NECESSARY TO RESTORE THE HCV-SPECIFIC CTL RESPONSE TO OBTAIN A SUSTAINED VIRAL RESPONSE? ', the authors mentioned many evidences of HCV detection even in sustained viral responders to interferon based treatment. However, in clinical, most of the patients show sustained free of serum viremia with usual PCR assay and sustained clinical remission that are different from HBV. This part should have overestimated the HCV positive results in experimental assays. The authors are recommended to mention that usual sustained viral responders show clinical remission and the meaning is different from HBV reactivation. 2. The function of HCV proteins such as NS3/4A protease to interfere the innate immune system such as RIG-I pathway should be added to explain the anti-viral immune system defect in chronic hepatitis C (such as Meylan E, et al. Nature 437).