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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 19522
Title: Analysis of peripheral blood dendritic cells as a non-invasive tool in the follow-up of patients with chronic hepatitis C
Reviewer's code: 02450445
Reviewer's country: United States
Science editor: Jing Yu
Date sent for review: 2015-05-12 11:50
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] 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

This is a timely review by Crosignani et al., on the contribution of peripheral blood dendritic cells to HCV pathogenesis, and the potential use of this cell population as a non-invasive tool in the follow-up of patients with chronic HCV. The review is well written and adds on a gap on HCV-related literature analysis. The manuscript would benefit of the addition of at least one figure model that recapitulates the current view on peripheral blood DCs on HCV pathogenesis.

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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	[ ] 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	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The review manuscript written by Crosignani et al. describes the role of DCs in the natural course and treatment of HCV infection. The review is interesting and well summarized the reports on the issue. However, there are some concerns that need to be addressed. Major pints, 1. The review should focus on the role of DCs in HCV infection. Therefore epidemiology, natural course, and clinical management of HCV infection should be more concise. 2. In page 13, the statement "multiple viral and non-viral mechanisms may directly and indirectly contribute to the decrease of mDCs and pDCs in the circulation" needs reconsideration, because reduction of the numbers of DCs might be due to the enhanced recruitment of DCs to the inflamed liver. Is there a negative correlation between HCV viral load and the numbers of DCs in HCV-infected patients? 3. Regarding the alterations in the function of DCs, most studies examined the cytokine production by DCs after in vitro stimulation with high concentrations of cytokines, which is an extremely abnormal condition in vivo. Therefore, the interpretation of those data may be questionable. Minor points, 1. In page 6, "Both pegIFN and RBV are indirect antiviral agents because they do not target a specific HCV protein or nucleic acid,

while they have different immunomodulating actions" needs to be revised. Antiviral action of pegIFN is not specific for HCV, but has direct antiviral activity through induction of various antiviral proteins. 2. TIM3, LAG3, and CTLA4 in page 10, and DPP4 in page 11 should be full-spelled. 3. In page 12, the statement "strongly support a role for DCs in the activation of HCV-specific immune responses in the liver environment." should be reconsidered, because DC activation occurs in the liver but antigen-specific T cell activation by the DCs could mainly occur in the drainage lymph nodes (there is no evidence for antigen-specific T cell activation in the liver).