



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 42113

Title: Mononuclear Phagocyte System in HCV Infection

Reviewer’s code: 02451134

Reviewer’s country: Spain

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-10

Date reviewed: 2018-09-13

Review time: 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript “Mononuclear phagocyte system in HCV infection” by Yu Yang et al. discusses the findings published in several articles on the interaction of HCV and the mononuclear phagocyte system. The review includes the three cell types: monocytes, dendritic cells and macrophages, and their role in HCV infection. Also, it describes the



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function and impairment of these cells after HCV infection. The paper is well written and includes a large number of references. The discussion of the papers is well conducted and argued. The authors have performed appropriate comments. However, for publication, there are some details to improve: - Most of the articles discussed are in vitro studies, which are the most abundant in the literature. But there are also several in vivo published studies, with cells or tissues from infected HCV patients. The results obtained from these last papers are more convincing. Therefore, it would improve the review if more in vivo studies were included. For example, studies such as the following could be included: Journal of Medical Virology 88:843–851 (2016) by Aintzane Zabaleta et al; Molecular Therapy – Methods & Clinical Development (2015) 2, 15006 by Aintzane Zabaleta et al. - There is a wrong underline on page 6 - Typographical error in pag. 10, Type I INF must be replaced by Type I IFN. - The end of paragraph “Regulatory function of monocytes following HCV infection” (pag 13, reference 107) would need a little more description. - The format of the bibliography must be carefully reviewed. There are several errors in the references. For example, in some the DOI is missing, the city of the journal should not appear, etc. - Table 1 should fit the text of the manuscript

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 42113

Title: Mononuclear Phagocyte System in HCV Infection

Reviewer’s code: 00012966

Reviewer’s country: Netherlands

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-30

Date reviewed: 2018-10-16

Review time: 16 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The review by Yu Yang et al summarizes and discusses the literature on the mononuclear phagocyte system in HCV infection. The review discusses the effect of HCV on monocytes, Kupffer cells and dendritic cells in patients in detail and provides a good overview of current knowledge. The review is interesting, well-written and



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concise. However, I do have a number of comments that need to be addressed and most of them relate to the fact that parts of the review lack nuance and that the authors pretend like some information is not controversial, whereas the data available is conflicting. 1. referentie 30 and 31 on page 6 are not correct. These should be references to the original paper and not a review. Please check all references. 2. The part on infectability of the MPS by HCV is the opinion of the authors and does not reflect the general belief by all scientists in the field. The authors should stress that this is their personal opinion, and not pretend like this is commonly accepted. I would suggest to remove this part completely, since it does not add to the message of the review. 3. Page 10 "We hypothesize that HCVc induces hyporesponsiveness, leading to the evasion of immunity in the early period of infection, whereas IFN- γ -induced loss of tolerance may contribute to inflammation and subsequent liver damage in chronic infection". It is unclear to me what this statement is based on, and why the authors hypothesize this. 4. The sentence on page 10 "The expression of TLR2 is significantly correlated with serum TNF- α and alanine transaminase (ALT) levels [76], indicating that the inflammation associated with HCV infection is partially attributed to production of proinflammatory cytokines in a TLR2-dependent manner." is pure speculation, and this should be stressed. Throughout the review there are many more of these kind of statement that over-interpret a finding in a manuscript. All of these statements should be checked and rephrased. For instance "IL-10, an anti-inflammatory cytokine, is primarily produced by monocytes. " and "IL-10 preferentially targets TLR4 signaling". But also words that certain mechanisms are "vital" or "critical role". So, please double check all. 5. Page 13 "IL-18 and IL-36 inhibitory proteins, which can reduce NK cell activation". IL-18 does not reduce NK cell activation 6. Not all studies demonstrate that mDC and pDC frequency and function are impaired by HCV. All these studies should be discussed as well to give a balanced view. 7. The statement "Therefore, persistent viral infection and



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inflammation could be attributed to the decrease in IFN- α -producing” is too simplistic and not supported by data. Similarly, “Altered TLR signaling is the most probable cause for abnormal cytokine production in HCV infection.” Also this statement is not based on facts 8. “monocytes are the major contributors to the regulation of the immune system following HCV infection” Why is this not true for macrophages, and why are macrophages “tightly associated with HCV-induced inflammation and cirrhosis”, but not monocytes?? So overall, the review is good, detailed and with a lot of references, it may need to be a bit less prejudiced and more balanced.

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