

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 16368

Title: IS THERE A ROLE FOR ADAPTIVE IMMUNE IN NONALCOHOLIC STEATOHEPATITIS (NASH)?

Reviewer's code: 00503062

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2015-01-16 19:52

Date reviewed: 2015-02-11 12:45

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript by Sutti et al. briefly reviewed the evidence showing the involvement of adaptive immune responses in NASH pathogenicity including authors' works. They pointed out that Th1-type cellular immune responses against oxidative stress-derived antigens contribute to the progression of NASH. The paper is informative and basically well written. The size of the paper is reasonable for readers. But, the manuscript has some room to be improved. Page 4, line 1 to page 5, line 11. The paragraph seems too long. It is better to divide this part to several paragraphs. There are many careless and grammatical mistakes through manuscript. Correct them. Title: "adaptive immune" should be "adaptive immunity" or "adaptive immune responses". Abstract. Page 2, lines 7, 8. The last part of the last sentence should be "their possible mechanisms involved in sustaining hepatic inflammation in NASH". Page 3, line 7 from bottom. "In spite" reads "In spite of". Page 4, line 18. "Interesting" reads "Interestingly". Page 4, line 24. "that originate" reads "originated". Page 4, line 1 from bottom. Remove a comma (,) after "noteworthy". Page 5, line 11. "ricks" reads "risk". Page 5, line 14. "malonildialdehyde- (MDA)" reads "malonildialdehyde (MDA)-". Page 5, line 20. The



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description of "Th-1 activated CD4+ T-cells" is strange. "activated Th-1 CD4+ T cells" is better. Page 5, line 3 from bottom. The description of "Th-1-mediated CD4+ T lymphocyte" is strange. "Th-1 CD4+ T cells" is better. Page 6, line 5. "Th-17 activated CD4+ T-lymphocytes" should be "Th-17 CD4+ T cells". Page 6, line 11. "DC4+ Th-17 T-cells" reads "Th-17 CD4+ T cells". Page 7, line 1. "depletion present" reads "decrease". Page 7, line 7. "IL-15 mRNA" reads "IL-15 mRNA level". Page 7, line 5 from bottom. "the Th-1 activation of CD4+ T-lymphocytes" should be "activation of Th-1 CD4+ T cells".

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Name of journal: World Journal of Hepatology

ESPS manuscript NO: 16368

Title: IS THERE A ROLE FOR ADAPTIVE IMMUNE IN NONALCOHOLIC STEATOHEPATITIS (NASH)?

Reviewer's code: 00291808

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Sutti et al. present an editorial on the possible involvement of adaptive immunity in sustaining liver inflammation during nonalcoholic steatohepatitis (NASH). NASH is a severe liver disease associated with excessive inflammation often evolving to fibrosis and cirrhosis. The role of innate immune cells in NASH onset and progression is well established, while the contribution of adaptive immune cells remains poorly characterized. Authors reported several evidences (although preliminary) pointing to a possible role of CD4+ T cells (Th1 and Th17 subsets), anti-MDA antibodies and NKT cells in mice in which NASH has been induced by methionine/choline deficient (MCD) diet. These findings in mice have been supported by observations made in adult and pediatric NASH cohorts. The manuscript is overall well written, informative and within the journal scope. It describes established concepts and also open questions that still need to be addressed. Sutti et al. report results obtained from murine studies using the MCD diet experimental model, which is known to be very aggressive causing robust weight loss and oxidative stress. It should be noted that NASH is strictly associated to insulin resistance and obesity and not with leanness. Thus, if available, data in genetic models of obesity (e.g.



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ob/ob and db/db mice, or Zucker rats) could also be reported. Authors should also discuss new potential therapeutic options in the treatment of NASH in relation to these recent findings on the role of adaptive immunity in NASH pathology. Minor points: 1. "immune" in the title should be changed in immunity or immune response. 2. Reference 16 and 17 in the text seem flipped. 3. All Greek symbols are missing from the manuscript. 4. Pag.6, line 10: DC4+ should be corrected in CD4+.