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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 17785
Title: The cross talk between the immune system, the adipose tissue and the liver in Non-Alcoholic Steatohepatitis: pathology and beyond.
Reviewer's code: 02860874
Reviewer's country: Mexico
Science editor: Yue-Li Tian
Date sent for review: 2015-03-26 18:56
Date reviewed: 2015-04-03 04:58

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 editorial explains clear and easily main inflammatory and inmuologic factors related to NASH, in my opinion it was well conducted and must be published

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology
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Title: The cross talk between the immune system, the adipose tissue and the liver in Non-Alcoholic Steatohepatitis: pathology and beyond.
Reviewer's code: 02861012
Reviewer's country: United Kingdom
Science editor: Yue-Li Tian
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] 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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The study is clear and well-written, however, there are several spelling errors that should be addressed. Moreover, there are several points that should be further clarified and explained. 1. In page 3, the authors state "Considering the T lymphocytes, although the CD3+ cells are stable in the liver, a relative increase of the CD8+ cells in comparison with the CD4+ cells (an increased CD8+/CD4+ cell ratio) has been described". The authors need to explain further what this increased CD8/CD4 ration means means? What is the effect? 2. In page 4, the authors state "although immunohistochemical evaluation of liver biopsies from NAFLD/NASH patients showed an increase of cells expressing the forkhead/winged helix transcription factor (FOXP3), which is crucial for the Tregs function, in NASH patients with a more advanced disease. " This is unclear, please re-write. What about patients at an early stage? In the same paragraph "A Treg decrease can be favoured also by a dendritic cell (DC)-induced down-regulation" please explain further, how does this happen? 3. In page 5, "…to mediate an allogenic T cell and antigen-restricted CD4+ T cell stimulation and a Treg down-regulation" is this correct? 4. In page 5, the authors state "Opposite to these findings, other

studies showed a reduction of the Th17 in the visceral adipose tissue of mice fed a HFD [12] and demonstated the role of IL17 as a negative regulator of adipogenesis and glucose metabolism in mice, delaying the development of obesity", please explain further, where is this difference attributed?\ 5. In page 6, the authors state "Considering the B lymphocytes, they rapidly increase in serum and adipose tissue of mice fed a HFD and seem to be implicated in insulin resistance", how B cells "seem" to be implicated in insulin resistance? Explain further. 6. Recent study in JCI have demonstrated the link between amine oxidase activity of VAP-1 and hepatic inflammation and fibrosis, and suggested that targeting VAP-1 may have a therapeutic potential for NAFLD. This should be also reported in this manuscript.

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ESPS PEER-REVIEW REPORT

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Reviewer's country: Greece
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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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

I read with great interest the review from Vonghia and Francque. It is a well written paper, describing in a satisfactory way the role of the immune system in NASH. The authors have focused on the role of immune cells. However, there is mounting evidence that cytokines secreted from adipose tissue, namely adipokines (such as leptin, adiponectin, resistin, TNF-α, IL-6, visfatin, etc), are implicated in the pathogenesis and progression of NAFLD. Besides, novel treatment strategies are based on these findings, thus there is a need for the extension of this review in order to include and discuss this knowledge. Moreover, the addition of tables and figures will improve the quality of this paper and will help the readers. Statement in page 3 (1st paragraph) that "there is no approved pharmacological treatment for NAFLD" should be corrected as pioglitazone and vitamin E could be used in specific cases of NASH according to AASLD guidelines.