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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 30135
Title: Association between endotoxinemia and histological features of NAFLD
Reviewer's code: 00058872
Reviewer's country: Italy
Science editor: Ze-Mao Gong
Date sent for review: 2016-09-16 12:18
Date reviewed: 2016-09-16 18:25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] 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
[ ] 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

Authors are firmly requested to lessen of importance the hypothesis that dosage of LPS is inadequate to justify obtained data. They should emphasise on the basis of their results that the previously evidenced association between endotoxemia and onset or worsening of NAFLD has not been confirmed and thus this study casts serious doubts about this mechanism. In order to reinforce their novel findings, they ought to refer to a recent paper dealing with gut flora modifiers, i.e., Future Microbiol. 2015;10(5):889-902. doi: 10.2217/fmb.15.13. Systematic review on intervention with prebiotics/probiotics in patients with obesity-related nonalcoholic fatty liver disease

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 30135
Title: Association between endotoxinemia and histological features of NAFLD
Reviewer's code: 00004157
Reviewer's country: Italy
Science editor: Ze-Mao Gong
Date sent for review: 2016-09-16 12:18
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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

The role of endotexemia in the pathogenesis of liver damage progression in human nonalcoholic fatty liver disease (NAFLD) is still disputed. In this manuscript, Kitabatake and coworkers examined the association of surrogate biomarkers of endotexemia, including LPS binding protein (LBP) and EndoCab IgG with histological severity of liver damage in 126 Japanese patients with histological NAFLD. They found that LBP was significantly correlated with severity of steatosis and hepatocellular ballooning, and consistently with aminotransferases levels and inflammatory markers, such as CRP and fibrinogen. Conversely, EndoCab IgG was not associated with liver damage. It is concluded that data do not conclusively support a role of LPS in NASH, and better biomarkers are needed. This is a well conducted study a relatively large cohort of patients with serum samples available at the time of liver biopsy. The manuscript is well written and results cautiously interpreted and very well discussed. I have a few comments that I think may be useful to improve the manuscript: * Table 1: report results also in patients stratified according to the presence of histological NASH, and correspondent P values. * To identify the determinant of circulating LBP concentration,iIt would be useful to analyse the independent predictors (including both histological and biochemical

variables significant at univariate analysis) at multivariate linear regression analysis. * It would be important to know whether the association between histological steatosis and inflammation with circulating LBP levels is modified by genetic risk factors for these traits, especially the PNPLA3 I148M variant, which is a major determinant of these traits. * Even if I agree with Authors that measurement of circulating LPS levels may be flawed by several methodological limitations, it would be nevertheless useful to add it to this study, or acknowledge the lack of as a limitation. * In the core tip it is reported this is the first study to correlate endotoxemia surrogate markers with histological features of NAFLD, whereas previous literature is cited in the discussion.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] 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
[Y] 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

This report, written by Kitabatake et al, is of an important retrospective study that has been carried out to disclose pathological mechanisms of NAFLD/NASH as well as its diagnosis. Especially, the close relationship between LBP and NASH is very interesting. However, the following two points should be elucidated. 1) Although the study design is similar to that of Wong et al (ref.14), the results are partially and substantially different. The previous study concluded that LBP was related to the degree of steatosis but did not link to NASH. The present study suggested that LBP was significantly higher in NASH than in NAFL. The authors should sufficiently discuss and explain the difference. 2) The authors previously reported the usefulness of CK18 in clinical diagnosis of NASH (ref.15). Because many readers will be interested in the potential association between CK18 and LBP, CK18 should be evaluated and the data should be added to Table 3.