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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 31752
Title: Urinary Metabolomics Analysis Identifies Key Biomarkers of Different Stages of Nonalcoholic Fatty Liver Disease
Reviewer's code: 00003472
Reviewer's country: Japan
Science editor: Ya-Juan Ma
Date sent for review: 2016-12-06 21:09
Date reviewed: 2016-12-11 10:46

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] 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	[Y] 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

Dong S et al. challenged to find out new markers to distinguish NASH from NAFLD using urine samples. This report is a valuable paper because there are few investigations that examine urine sample to distinguish NASH from NAFLD. To strength the data, I have several recommendations. 1. The authors found that 31 metabolites were different between NAFLD and NASH in urine samples. The authors should demonstrate that these potential markers are correlated with the histological severity of NASH. 2. In addition, the author should demonstrate levels of some nucleic acids and amino acids in blood samples. The readers of WJG want to know these potential markers are correlated with hepatic inflammation (ALT levels) and/or fibrogenetic markers (M2BPGi, type 4 collagen S etc). 3. Same data are presented in Table 2 and Figure 2. In addition, no units are shown in Table 2. 4. Some uncommon methods are used in the present study. For instance, ESI in Figure 3, PLS and OPLS in Figure 4. The authors should explain these methods (not technical explanations but the purpose of these methods) 5. The authors mentioned that S-plot showed obvious metabolic difference in figure 3. However, it is difficult to understand the authors' description.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 31752
Title: Urinary Metabolomics Analysis Identifies Key Biomarkers of Different Stages of Nonalcoholic Fatty Liver Disease
Reviewer's code: 00007116
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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[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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Title: Urinary Metabolomics Analysis Identifies Key Biomarkers of Different Stages of Nonalcoholic Fatty Liver Disease The paper submitted by Dong et al. anazyled urinary metabolics to identify key biomarkers that distinguish NASH from NAFLD. The authors compared the urine and blood samples from the patients with NAFLD, those with NASH, and healthy controls. The authors found that NAFLD and NASH have 31 different urinary metabolites, mainly nucleic acids and amino acids. The authors demonstrated that the pathways of energy, amino acid metabolism, and pentose phosphate pathway were closely associated with pathological processes in NAFLD and NASH. I have the following comments. This article was stimulating enough in trying to find biomarkers that distinguish NASH from NAFLD via non-invasive tests. Nevertheless, this study has some limitations. First, I have found that their definition of NASH can be rather controversial. The authors defined NASH as hepatic steatosis by image or histology, and significant increase in ALT activity while the current guidelines specifically require a liver biopsy for its diagnosis. Second, no validation group was presented to support their findings. Minors thing to comment are that the excessive use of table

and figures distract readers a bit and the table 2 doesn't have any unit information for its figures.