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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 29492
Title: Three-dimensional perfused human in vitro model of non-alcoholic fatty liver disease
Reviewer's code: 02485834
Reviewer's country: Japan
Science editor: Jing Yu
Date sent for review: 2016-08-17 15:26
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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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Authors showed develop a human in vitro model of non-alcoholic fatty liver disease by using primary hepatocytes cultured in a three-dimensional perfused platform. In this model, hepatocytes cultured in fat medium were found to accumulate fat more than lean cells although ALT and AST did not change. Furthermore, inflammatory and fibrotic genes associated with NAFLD were upregulated in hepatocyte cultured in fat medium. Finally, authors concluded that the 3D in vitro NAFLD model recapitulates many features of clinical NAFLD and is an ideal tool for analyzing the efficacy of anti-steatotic compounds. This original paper is interesting, and manuscript is well written. However, there are several revision points in your manuscript as follow. Major point 1. Authors demonstrated that fat accumulation and the levels of free fatty acids increased in hepatocyte cultured in fat medium. However, the cytotoxic effect did not change in this system. Authors should discuss about these points. Why do free fatty acids increase in these conditions? From where do free fatty acids increase? 2. Several inflammatory genes associated with NAFLD were increased in this system. However, authors should discuss regarding the other inflammatory genes including IL-1β, IL-6 did

not change in this system. Why does only IL-8 and MIF increase in this system? 3. What does the increment of MIF mean? 4. Metformin or PGZ showed anti-steatotic effect in this system. Does this effect correlate with the suppression of inflammatory and fibrosis marker? Authors can check the effect of metformin and PGZ on inflammation and fibrosis in this system. 5. Please show the reason why authors select the concentration of metformin (100 ?M) or PGZ (1-10 ?M). What is the action site in PGZ? Minor point Authors should show the composition of lean media.