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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12351
Title: Heme oxygenase-1 protects rat liver against warm ischemia/reperfusion injury via a Mechanism involving TLR2/TLSu-Xin Gou-triggered MyD88- and TRIF-dependent signaling pathways
Reviewer code: 02446015
Science editor: Su-Xin Gou
Date sent for review: 2014-07-04 15:03
Date reviewed: 2014-07-11 20:39

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	[ ] Rejection
[Y] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Minor revision
[ ] Grade E: Poor		[ ] Existing	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The ms by Han Fei Huang et al needs some revisions before publication. I suggest to re-write the Discussion Section in order to get more importance to obtained results. I suggest also to use more up-to-date references.

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Title: Heme oxygenase-1 protects rat liver against warm ischemia/reperfusion injury via a Mechanism involving TLR2/TLSu-Xin Gou-triggered MyD88- and TRIF-dependent signaling pathways
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Science editor: Su-Xin Gou
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Minor revision
[ ] Grade E: Poor		[ ] Existing	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

General comments: This manuscript examined the effects of Heme oxygnnease-1 (HO-1) on the ischemia/reperfusion injury model in rat liver. The data shows that the HO-1 inducer CoPP inhibited the liver injury that was induced by ischemia/reperfusion treatment, while HO-1 inhibitor ZnPP deteriorated the ischemia/reperfusion liver damage. The liver protection by the CoPP was coincided with the decrease in the number of neutrophils, T- cells and macrophages that infiltrated in the liver. Furthermore, the protective effect by the CoPP on liver damage was associated with the inhibition of TLR4 triggered TRIF dependent pathway, TLR2/TLR4-triggered MYD88 dependent pathway, kinase phosphorylation, and up-regulation of negative regulators of TLR signaling. Based on these data, the authors conclude that HO-1 protects the ischemia/reperfusion-mediated liver injury by inhibiting the TLR2/TLR4 triggered MyD88 and TRIF dependent signaling pathways and the increased expression of negative regulators of TLR signaling. Overall, the work is well performed; however, the conclusion is not experimentally confirmed. Specific comments: Major 1. The CoPP and ZnPP were used as the inducer or the inhibitor for the HO-1 in this study. However, it is not clear how they affect the HO-1. Do they increase or decrease the expression of HO-1? 2. The authors demonstrates that CoPP inhibits the liver damage induced by the I/R treatment in rats. This was coincided with the inhibition of TLR4 triggered TRIF dependent pathway, TLR2/TLR4-triggered MYD88 dependent

pathway, kinase phosphorylation, and up-regulation of negative regulators of TLR signaling. Although these data suggests that the protective effect by CoPP on liver damage is mediated by these signaling pathways as claimed by the authors, this idea is not experimentally confirmed in the manuscript. The authors need to either prove this or temper the conclusion. 3. In the last line on page 4, it is says CoPP treatment livers showed a significant "increase" in neutrophils…. This is in contrast to what is shown in figure 3. The "increase" should be "decrease". Minor The line 12 in the abstract, of is redundant. Please fix.