

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16030

Title: TLJing Yu-HMGB1-, MyD88- and TRIF-dependent signalling in mouse intestinal ischemia/reperfusion injury

Reviewer's code: 03069152

Reviewer's country: China

Science editor: Jing Yu

Date sent for review: 2014-12-23 12:34

Date reviewed: 2015-01-08 22:09

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

1. As a scientific paper, it's really unprofessional for there was no page number. However, the study is overall well done, but the authors should clarify the reasons for choosing antibodies of HMGB1, MyD88 and TRIF but not inhibitors, for there are lots of efficient inhibitors of these proteins used in research. Is there any drug used in clinical to down-regulate HMGB1/TLR4/NF κB pathway? 2. A difference has been shown histologically and via measurements of inflammation. Do these differences manifest clinically. i.e. is there a survival difference? 3. The exact site of lung and liver tissue collected for paraffin embedding was not mentioned in the Materials and Method. 4. The source, location, purity of anti-HMGB1, -TRIF, - MyD88 should be provided. 5. The source, location of SPSS 19.0 software should be provided. 6. Lung injury and intestinal injury should be graded according to the pathological results. 7. A description of the method of animal sacrifice is required. Minor concerns: 1. Consider a diagram detailing the effect of the pathway and the effect of antibodies on such changes to enhance the reading of the manuscript. 2. Please correct " Results were analysed using on-way analysis of variance." "one-way or on-way?" in the last sentence of



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Abstract-Methods. 3. Please correct " The administration of anti-HMGB1, anti-MyD88, and anti-HMGB1 antibody could each significantly reduce the damage caused by I/R, and the role of anti-HMGB1 antibody was the most obvious" in the last sentence of Discussion.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16030

Title: TLJing Yu-HMGB1-, MyD88- and TRIF-dependent signalling in mouse intestinal ischemia/reperfusion injury

Reviewer's code: 02991586

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Date sent for review: 2014-12-23 12:34

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear Authors, your manuscript titled as "TLR4-HMGB1-, MyD88- and TRIF-dependent signalling in mouse intestinal ischemia/reperfusion injury", well organized research. But you can give more place to explain oxidative damage of I/R by using other paper which were done on several organs like muscle, urinary bladder, heart, kidney. You can find my few correction on manuscript as attachment. I wish you and your team further achievements. Best Regards

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16030

Title: TLJing Yu-HMGB1-, MyD88- and TRIF-dependent signalling in mouse intestinal ischemia/reperfusion injury

Reviewer's code: 03011471

Reviewer's country: China

Science editor: Jing Yu

Date sent for review: 2014-12-23 12:34

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> The same title	
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

PEER REVIEW Major points: I have read this paper with great interest. The paper is well organized and readability. The author's team identified an interesting targeted therapy. Such a therapy might be effective when administered before reduction of the strangulated ileus or before the removal of thrombus in the SMA. This paper provides solid data into the role of TLR4/HMGB1 pathway in regulating intestinal I/R injury. My main concern is about its originality or novelty. It was known that anti-HMGB1 antibody has an effective role in alleviating intestinal I/R injury in rat (Kojima et al., J Surg Res, 2012). Thus, the main contribution of this work is confirmation of this pathway in mice. Minor Points: 1. The abstract part should presents the innovative and significant points related to the current study. 2. Sufficiently detailed descriptions (manufacturer's details) is needed for each antibody. 3. The activity of GAPDH in the intestine will seriously changed after ischemia reperfusion (Sola et al., GUT, 1999). Is it appropriate to use GAPDH as internal control of qPCR in this study? 4. Pathology score should be provide along with pathological changes. 5. Discussion should be more concise and logical.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 16030

Title: TLJing Yu-HMGB1-, MyD88- and TRIF-dependent signalling in mouse intestinal ischemia/reperfusion injury

Reviewer's code: 00593657

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Science editor: Jing Yu

Date sent for review: 2014-12-23 12:34

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
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COMMENTS TO AUTHORS

The authors investigated whether intravenously injecting anti-HMGB1, anti-MyD88, anti-TRIF may ameliorate mesenteric ischemia/reperfusion injury using mouse models. They described a lower degree of inflammation and decreased histopathological injury in the liver, lung, and gut after injection of antibodies. However, a number of concerns regarding experimental controls and analysis methods are listed below. Major points: 1. Antibody isotype control group(s) are lacking in the experimental design, which is necessary to compare in conducting functional antibody blockade experiments. 2. Figures 2 and 3 are representative histological images by H&E staining. A more quantification method by a blinded observer is needed for the statement of 'obvious attenuation'. 3. Table 2 and 3 showed the changes in mRNA of HMGB1, NFκB, MyD88, TRIF in lung and ileum. Why would a neutralizing antibody targeting proteins affect its own mRNA levels? Moreover, it is unreasonable that blocking TLR4-downstream pathways (MyD88 or TRIF) would even decrease the endogenous ligand HMGB1 mRNA levels. 4. The authors should check the circulating LPS levels following I/R injury, as well as