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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36223
Title: β-arrestin 2 attenuates lipopolysaccharide-induced liver injury via inhibition of TLR4/NF-κB signaling pathway mediated inflammation in mice
Reviewer's code: 02791367
Reviewer's country: USA
Science editor: Ke Chen
Date sent for review: 2017-09-12
Date reviewed: 2017-09-18
Review time: 6 Days

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	
		[ ] No	

COMMENTS TO AUTHORS

This paper shows that β-arrestin 2 protects against LPS-induced hepatocyte injury and hepatic inflammation via inactivation of TLR4 and NF-κB pathways. Major comments: 1. Authors have used very high dose of LPS (5mg/kg). Can they justify the use of that high dose of LPS. 2. Does β-arrestin 2 directly protects hepatocytes from LPS-induced cell death, like inhibiting hepatocyte apoptosis or favoring hepatocyte proliferation? It is possible that absence of β-arrestin 2 impairs hepatocyte proliferation and therefore facilitates injury. 3. Fig 1: Authors have shown hepatocyte apoptosis by histological scoring. Staining for TUNEL or cleaved caspase 3 will be preferred to demonstrate hepatocyte apoptosis. 4. It was not clear how β-arrestin 2 protected against TLR4 signaling. Minor comment: 1. Correct the spelling for the word Expression in the legend of Figure 4. 2. In the methods authors shows that they used 3 strains of mice, β-arrestin

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2-WT, β-arrestin 2-KO and the C57BL6/J. Did they really use the C57BL/6J mice in any of these studies? Otherwise please correct it.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36223
Title: β-arrestin 2 attenuates lipopolysaccharide-induced liver injury via inhibition of TLR4/NF-κB signaling pathway mediated inflammation in mice
Reviewer's code: 00038362
Reviewer's country: United States
Science editor: Ke Chen
Date sent for review: 2017-09-12
Date reviewed: 2017-09-24
Review time: 12 Days

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
[ ] 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	
		[ ] No	

COMMENTS TO AUTHORS

In this article the investigators determine the influence of beta-arrestin on LPS-induced liver injury using knockout mice and in vitro using RAW264.7 cells. Both in vivo and in vitro results show that absence of beta-arrestin aggravates LPS toxicity and release of cytokines. The role of beta-arrentin in inflammation and inflammatory responses are well know. The absence of beta-arrestin is known to reduce the infiltration of immune cells into site of injury. Also, beta-arrestin null mice developed more severe arthritis. Therefore, this findings are not surprising. Analysis at a single time-point (4 hrs) was not justified and seems insufficient, strong mechanistic data documenting the role of TRL-4 is lacking and furthermore, the practically of inhibiting beta-arrestin as a therapeutic target must be handle with caution due to the role of this molecule in controlling the function and activity of many other signaling pathways.