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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 23377
Title: Recombinant Adenovirus Containing Hyper-interleukin-6 and Hepatocyte Growth Factor Enhances Therapeutic Efficacy on Acute-on-Chronic Liver Failure in Rats
Reviewer's code: 02543990
Reviewer's country: United States
Science editor: Ya-Juan Ma
Date sent for review: 2015-11-26 16:53
Date reviewed: 2015-12-17 00:45

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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In present study, Gao D et al examined the biological effect of adenoviruses containing hyper-interleukin-6 and Hepatocyte Growth Factor on pathogenesis of acute-on-chronic liver failure (ACLF) in rat induced by the heat-stable antigen (HSA) D-galactosamine (D-Gal) and lipopolysaccharide (LPS). They observed that administration of Ad-HGF-HIL-6 can significantly reduce serum levels of alanine aminotransferase (ALT), endotoxin, tumour necrosis factor-α (TNF-α), interferon-α (IFN-γ) and high-mobility-group box-1 (HMGB1), attenuate hepatic damage, which was associated with increased Ki67 expression and reduced apoptotic index or related gene expression when compared to that in rats received Ad-HGF, Ad-HIL-6 or control treatment, suggesting that Ad-HGF-HIL-6 might be a potential reagent for the treatment of ACLF. Overall, this is an interesting study, I have additional concerns: 1. For therapeutic effect, the rats should be observed longer time, while in present study all of the rats were sacrificed for blood and tissue sample collection only at 24 hr later after adenoviral administration, during which adenoviral mediated gene expression may not reach the peak stage, and no information is available on the recovery of damaged liver in this study.

Thus, the results do not support the notion of therapeutic efficacy as claimed in the title, or the title should be reworded. 2. In Figure 1, serum levels of IL-6, HGF should be also tested to show whether the reduced serum levels of ALT, PT, endotoxin, and HMGB1 are correlated with increased serum levels of IL6, HGF. 3. Fig 2 and 3 should be combined together to show representative photos and quantitative analysis of the imaging data. The similar is true for Fig 5 and Figure 6. 4. IL-6 is a strong pro-inflammatory cytokine, while ACLF is primarily caused by inflammatory damage; it is not known why IL-6 has a protective effect in this model, which should be discussed in the text. Additional minor issues: 1. IL-6 is not a "transcription factor" (on page 5). 2. It is not clearly described how adenoviral vectors were administrated; via iv injection? 3. The control adenoviral vector is not empty, it still contains GFP. It is confusing to use Ad0. It is proposed to use Ad-GFP for the control adenoviruses.

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Title: Recombinant Adenovirus Containing Hyper-interleukin-6 and Hepatocyte Growth Factor Enhances Therapeutic Efficacy on Acute-on-Chronic Liver Failure in Rats
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

I read with great interest the manuscript entitled "Recombinant Adenovirus Containing Hyper-interleukin-6 and Hepatocyte Growth Factor Enhances Therapeutic Efficacy in Acute-on-Chronic Liver Failure in Rats" by Gao Dandan et al. Although a high number of orthographical and grammatical errors have been found throughout the manuscript limits its readability and scientific value, the field is of interest and the Authors well performed the study. Another criticism is the time point adopted by the Authors: 24 hours is a too short fraction of time and the Authors should evaluate also the efficacy and the dynamics 48 and 72 hours after the treatment. In addition, the Authors should emphasize the importance to translate their findings in the human being and in the clinical practice. See the manuscript: Bernal W et al. Acute-on-chronic liver failure. Lancet. 2015 Oct 17; 386 (10003):1576-87.