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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 28046
Title: AAV-Thymosin β4 ameliorates dextran sulfate sodium- and 2,4,6-trinitrobenzene sulfonic acid-induced murine colitis
Reviewer's code: 02637557
Reviewer's country: United States
Science editor: Jing Yu
Date sent for review: 2016-06-28 20:32
Date reviewed: 2016-09-02 23:55

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

The article submitted by Zheng X et al seeks to evaluate the efficacy of AAV-Thymosin β4 in dextran sulfate sodium- and 2,4,6-trinitrobenzene sulfonic acid-induced murine colitis While the study is interesting and has merit in the setting of experimentally-induced (DSS and TNBS) murine colitis, but, the current form of manuscript raised few significant issues in regards of their experimental findings and the conclusion they made. The role of Thymosin β4 in colitis is novel and may shed new insight for future therapeutic use. However, it is not unexpected that Thymosin β4 may have the ability to reduce inflammation and limit the apoptosis in the development of colitis. But, this would a first report to claim this fact. My major concerns are listed below: 1. The rationale of the study should be clarified. It is not that nobody has studied before, so, you took the initiative to study. Authors should provide logic to study the role of Thymosin β4 in the setting of colitis/IBD. You may corroborate with the reason how Thymosin β4 reduce the inflammatory response or apoptosis, etc. 2. Authors should provide a reason for using AAV2 serotype where AAV9 is more acceptable type for murine model. 3. There was a discrepancy noted in regards to deliver the viral particle in DSS and TNBS

models. Check the method section of animal experiment (second paragraph) and DSS-induced colitis model. Please clarify it. 4. The Figure 1D showed DSS treatment increased Thymosin β4 level significantly compared to TNBS-induced model. Please discuss this in your discussion. Would that mean the amount of Thymosin β4 in these models are not sufficient enough to provide the protection? How does the viral mediated Thymosin β4 supplementation work? 5. Did author check the antibody is not raised in the murine system after delivery of AAV Thymosin β4? 6. The figure 5 stated but the authors that Thymosin β4 treatment reduced apoptosis in the colonic mucosal cell. TUNEL staining did not provide any evidence that apoptosis occurred in the mucosal cells. Authors should provide evidence by double staining with mucosal cells that those cells were TUNEL positive. 7. Authors should also provide data for marker for apoptosis like caspase 3 or Bcl2 or BAK, etc. to support their observation. The staining is not sufficient to make a conclusion that apoptosis has occurred. 8. Discussion is descriptive in nature. Authors should discuss the Thymosin β4 action and how it reduces all the parameters that authors tested in their manuscript. 9. What is your conclusion? Has any future plan to expand this study? Authors should discuss these in the discussion. 10. Authors should discuss their novelty in their study which is lacking.