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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 38303

**Title:** Mucosa Repair Mechanisms of Tong-Xie-Yao-Fang Mediated by CRH-R2 in Murine, DSS Induced Colitis

**Reviewer's code:** 02440884

**Reviewer's country:** Germany

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2018-02-13

**Date reviewed:** 2018-02-14

**Review time:** 1 Day

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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input 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 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 type="checkbox"/> No	

### COMMENTS TO AUTHORS

The experimental study was intended to analyze effects of tong-xie-yao-fang (TXYF) on DSS-colitis in mice. The focus was given on corticotropin-releasing hormone receptor 2 (CRH-R2). In the study, the anti-inflammatory function of CRH-R2 was demonstrated with a CRH-R2 inhibitor Ast2B. In addition, TXYF exerts anti-inflammatory effects via CRH-R2. Comments 1. The statement that CRH-R2 regulates intestinal epithelial migration in DSS-colitis is not sufficiently addressed. Cellular migration should be separately investigated. 2. An increase of intestinal epithelial migration by TXYF is not clearly shown and additional experiments are necessary. 3. Figures 4 and 5: the images are not helpful; higher magnification of positive cells are helpful 4. spelling: CRH-R2 or CRHR2.



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**Reviewer’s code:** 00068278

**Reviewer’s country:** Turkey

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2018-02-13

**Date reviewed:** 2018-02-25

**Review time:** 12 Days

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 checked="" 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 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**

The study is a well designed and conducted one. Although the title of the article is “Mucosa repair mechanisms of Tong-xie-yao-fang mediated by CRH-R2 in murine DSS induced colitis”, in the abstract there is insufficient data about the effect of TXYF on mucosal healing and CRH pathway.



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**Manuscript NO:** 38303

**Title:** Mucosa Repair Mechanisms of Tong-Xie-Yao-Fang Mediated by CRH-R2 in Murine, DSS Induced Colitis

**Reviewer's code:** 00058340

**Reviewer's country:** United States

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2018-02-19

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**Review time:** 6 Days

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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input 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 checked="" 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**

Major comments. 1) One of the important mechanisms of experimental ulcerative colitis is endothelial damage and vascular injury which leads to ischemia, hypoxia and necrosis. Blood vessels and microvessels are critical for delivery of oxygen and nutrients and thus essential for tissue viability. Also, during the healing of ulceration, the regeneration of blood vessels through angiogenesis and vasculogenesis is a critical event, without which reepithelialization and regeneration of epithelial structures could not occur. See reference below. Unfortunately in the introduction and the discussion the authors did not even mention the role of blood vessels in injury and healing process. For them the healing consists of migration, proliferation and regeneration of epithelial cells. Wang SY1 et al. Effects of initiating time and dosage of Panax notoginseng on mucosal microvascular injury in experimental colitis. World J Gastroenterol. 2017 Dec



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21;23(47):8308-8320. doi: 10.3748/wjg.v23.i47.8308. Tolstanova G1,2 et al. Role of Dopamine and D2 Dopamine Receptor in the Pathogenesis of Inflammatory Bowel Disease. *Dig Dis Sci*. 2015 Oct;60(10):2963-75. doi: 10.1007/s10620-015-3698-5 Tolstanova G1 et al Early endothelial damage and increased colonic vascular permeability in the development of experimental ulcerative colitis in rats and mice. *Lab Invest*. 2012 Jan;92(1):9-21. doi: 10.1038/labinvest.2011.122 2) In table 2 description is incorrect. Score 1 should be 1/3 of luminal (NOT BASAL), the same for score 2 2/3 of luminal (NOT BASAL). 3) In abstract the abbreviation CRH-R2 should be explained and used uniformly - either CRH-R2 or CRHR2 4) there are numerous linguistic errors