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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 33280
Title: Involvement of CRF2 signaling in enterocytic differentiation of colorectal cancer cells
Reviewer's code: 03437591
Reviewer's country: China
Science editor: Ze-Mao Gong
Date sent for review: 2017-03-17
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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

This manuscript demonstrated that Ucn3-induced CRF2 signaling could modulate intestinal epithelial cell differentiation and epithelial cell permeability. The authors found CRF2 was associated with a poor differentiated status of IEC. Then, they proved CRF2 signaling altered the trans- and para-cellular permeability, and delayed colonic cell differentiation. In general, the work would be potentially useful to reveal the roles of CRF2 signaling in tumor progression. However, the manuscript requires some modifications before publication. More specially, the authors should adequately address my following points: MAJOR COMMENTS 1. The authors mainly used HT-29 and Caco-2 cells to investigate CRF2 signaling in colorectal cancer cells. However, some results were only obtained from one cell line. For example, the result that CRF2 signaling increased trans-epithelial permeability was only showed in HT-29, while the result that Ucn3 decreased the mRNA and protein expression of KLF4 was only shown in Caco-2. Generally, consistent phenomena in multiple cell lines will increase reliability. 2. Some

conclusions should be supported by proper statistical tests. For example, the result that CRF2 expression is also inversely correlated to E-cadherin expression in these cell lines should be tested in Wilcoxon signed rank test. 3. Did the reduced expression of KLF4 was indirectly induced by CRF2 activation, e.g., direct interaction, or an indirect effect? More evidences are required. MINER COMMENTS 1. Did Ucn3 reduce both the mRNA and protein levels of DPPIV and AP, or only protein levels? 2. Figure 3A compared trans-epithelial electrical resistance with or without A2b overnight before addition or not of Ucn3. However, the results of Ucn3 untreated cells were not shown. The same problems existed in Figure 4A. 3. There were many mistakes in format. For example, " Cdx2, Hox, HNF, GATA4, KLF4..." should be "Cdx2, Hox, HNF, GATA4, KLF4, etc." Also, "differentiation processes that occur during organogenesis and migration along the cryptvillus axis [29]–[31]" should be "differentiation processes that occur during organogenesis and migration along the cryptvillus axis [29-31]".