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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6916
Title: Transcriptional regulation of SERT by EGF affects development of visceral hypersensitivity
Reviewer code: 00502953
Science editor: Ya-Juan Ma
Date sent for review: 2013-10-31 13:27
Date reviewed: 2014-01-02 12:27

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

1, please do not have abbreviations in the title. 2, please add the study rationale to the introduction; how do you put the low levels of EGF and visceral hypersensitivity together and design this project. 3, the paper lacks a study hypothesis; you need to add it to the introduction section. 4, in the introduction, you need to briefly describe the findings of the study. 5, current study models of visceral hypersensitivity are required to be described in the introduction. 6, some spots of English errors need to be edited; such as "a blinded pathologist"; n=10 each. 7, the cell culture condition is not correct. 8, the Western blotting procedures can be simplified. 9, how did you calculate the qRT-PCR results? 10, the "T test" should be "t test". 11, the findings need to be verified by human data; this reviewer suggests collect blood samples from IBS patients to see if the levels of EGF are lower than healthy subjects. 12, what does the sentence mean, "Each point represents the mean of 10 rats from 3 independent experiments" in figure 1 legend. 13, figure 1-3 legends need to be re-organized. 14, the description of the statistical results of figure 4 is quite confused; please re-word the whole legend. 15, as if you used vehicles in control group in figure 4 and figure 5; it is not a proper control agent. Please carry out the experiments again using an irrelevant protein as controls.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 6916
Title: Transcriptional regulation of SERT by EGF affects development of visceral hypersensitivity
Reviewer code: 02447122
Science editor: Ya-Juan Ma
Date sent for review: 2013-10-31 13:27
Date reviewed: 2014-01-07 21:32

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

In this manuscript, Cui et al aimed to investigate the changes in epidermal growth factor (EGF) levels in a visceral hypersensitivity rat model, and if EGF regulates serotonin transporter (SERT) expression and function. The authors show that EGF levels (determined by ELISA) are decreased in colon tissues and plasma of rats with visceral hypersensitivity. Also, serotonin transporter (SERT) expression is decreased both at protein and mRNA levels (Western blot and real time PCR, respectively) in these animals with respect to controls. They also show that EGF-treatment induces SERT expression through EGF receptor (EGFR) in rat intestinal crypt cells. It is already known that EGF up-regulates SERT gene expression in intestinal cells and that SERT expression and function are down-regulated in colon and rectal tissues of patients with irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). However, this research could be important because it is still uncertain whether the decreased levels of EGF can lead to SERT down-regulation and ultimately to visceral hypersensitivity, which is a characteristic of IBS. Major comment: 1. Authors entitled their manuscript as follows: “Transcriptional regulation of SERT by EGF affects development of visceral hypersensitivity”. However, their results don’t demonstrate that EGF (through EGFR) levels modulate visceral sensitivity regulating SERT expression and function. They only used the Pearson's correlation analysis and say that there is a correlation between EGF and SERT levels in colon tissues. Thus, authors should better confirm their hypothesis. If they inhibit EGFR function (with a blocking antibody or a pharmacologic inhibitor) in vivo, do SERT levels in colon decrease? Do these treated-rats develop visceral hypersensitivity? Also, authors could use dominant-negative EGFR point mutation mice (used in reference No. 20) to test the hypothesis that the EGFR signaling

pathway is involved in SERT expression and visceral hypersensitivity. Minor comments: 2. References No. 24 and 26 are the same. 3. Almost half of the references were published 15 or more years ago. Authors should update the references list.