

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 43106

Title: Claudin-7 gene knockout causes the destruction of intestinal and death of mice

Reviewer's code: 00038747

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-11-09

Date reviewed: 2018-11-13

Review time: 11 Hours, 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Xu et al used three different knockout mouse models to study the role of Claudin-7 in intestinal structure and function. This is an interesting study. I have few comments/suggestions to improve the quality of the manuscript. 1. How did they determine the mental status of the mice as authors stated in the abstract and elsewhere



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7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https:// www.wjgnet.com

in the manuscript. 2. Discussion is confusing should be shortened with clarity.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 43106

Title: Claudin-7 gene knockout causes the destruction of intestinal and death of mice

Reviewer's code: 03567380

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-10-25

Date reviewed: 2018-11-15

Review time: 15 Hours, 21 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
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			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The study by Xu et al. characterizes the role of claudin-7 in intestinal structure and survival. To accomplish this, the authors use a total knockout, intestinal knockout and inducible intestinal knockout of claudin-7 in mice. This approach is a great strength of this study as the use of all three of these models definitively demonstrates the role of



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claudin-7 in intestinal structure and overall survival of mice. Overall, the findings are interesting and the use of the conditional knockout identifies the role of claudin-7 as a suppressor of dysplasia and adenoma of the intestine. That being said, there are areas the authors should address to improve their submission: Major: 1) My major concern with this study is that while the findings are interesting, there is a lack of depth of investigation, particularly involving the inducible claudin 7 KO mice. The authors should expand their studies to better classify cell proliferation with determinations of which cells are proliferating and a more detailed analysis of the stem cell niche. In addition, cytokines and/or determination of the types of immune cells infiltrating into the intestine should be determined. Finally, gut function should be assessed to determine if uptake of nutrients is dysregulated, if endotoxins are entering portal tract, or other measures of gut function. This could help identify why the mice with claudin-7 KO are dying and better classify these mice would be very useful to the field. 2) In the CKO mice the authors state that the mice had slow growth and died on the third day. Similar findings were reported in the cKO mice. Are these observations with growth due to changes in food intake, lack of absorption of macronutrients or some other effect? 3) The appropriate controls for the villin-CreERT2 mice would be to do tamoxifen injections in one group and sunflower oil injections into a second group of mice. Minor: 1) The authors use the words "poor spirited" or similar wording when the mice are sick. It would be better to describe this as lethargy or lack of activity or something along those lines to better describe the mice. 2) On figure 2 the methodology used for marking the blots is inconsistent and fonts are different sizes. Please make figure larger and use larger fonts for 2C and 2D. 3) For H&E images and IHC the authors should label in a manner that is consistent and easy to read. In particular, figure 4 it is difficult to see control listed in the bottom right panel. 4) The nomenclature used to identify conventional vs conditional knockouts (CKO vs. cKO) could be improved.



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