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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75596

Title: Expression of the methylcytosine dioxygenase Ten-Eleven Translocation-2 and Cx43 in inflammatory bowel disease and colorectal cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05775860
Position: Editorial Board
Academic degree: PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Lebanon

Manuscript submission date: 2022-02-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-07 00:55

Reviewer performed review: 2022-02-08 07:20

Review time: 1 Day and 6 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled "Expression of the methylcytosine dioxygenase TET-2 and Cx43 in inflammatory bowel disease and colorectal cancer" reports the expression levels of Cx43 and TET-2 in IBD and CRC by examining cell lines, DSS-induced colitis mouse model and patient samples. The authors used media collected from PMA- and LPS-activated THP-1 cells for colon cell culturing, to create an inflammatory milieu. Moreover, the authors generated HT-29 Cx43D (highly expressing Cx43) and HT-29 Cx43- (down-regulation of Cx43 mRNA) cells to investigate cell phenotype and gene expressions. Various independent methods were applied to support the conclusions. In addition, the data are well presented. The below lists my suggestions that the authors may consider. 1. All the H&E and immunofluorescence images should have scale bars.

2. What factors may cause the expression differences of Cx43 and TET-2 between human samples and cell/mouse models? 3. The authors may consider to present a schematic figure for readers to understand the roles of Cx43 and TET-2 expressions in IBD and CRC. How may TET-2 regulate expression of Cx43? 4. The additional File 1 cannot be found in the submitted files. 5. The information of antibodies, including companies and catalogs, should be presented in the materials and methods section.

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Peer-review model: Single blind

Reviewer's code: 05262508
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Lebanon

Manuscript submission date: 2022-02-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-13 10:48

Reviewer performed review: 2022-02-22 04:17

Review time: 8 Days and 17 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This study shows the expression of CX43 and TET2 in intestinal inflammation and discusses the expression of CX43 and TET2 in intestinal inflammation. The authors attempted to verify the relationship between CX43 and TET2 in intestinal inflammation in vivo and in vitro, and provide new targets for clinical treatment. In this paper, part of the mechanism is studied through experiments，but the mechanism research is not deep enough. Actually, the mode of action and pathway between CX43 and TET2 is not involved. This article can further explore the relationship between TET2 and intestinal inflammation.

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Peer-review model: Single blind

Reviewer's code: 05618903
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Deputy Director, Doctor, Professor
Reviewer's Country/Territory: China
Author's Country/Territory: Lebanon

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Reviewer chosen by: AI Technique
Reviewer accepted review: 2022-02-14 00:16
Reviewer performed review: 2022-02-25 06:36
Review time: 11 Days and 6 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [Y] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [Y] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

It is known that colonic inflammation caused by excessive inflammatory bowel disease can initiate the colitis-associated cancer, but the mechanisms remain elusive. The authors set to bridge chronic inflammation and cancer onset in the colon using expression profile of the methylcytosine dioxygenase TET-2 and gap junction protein Cx43 in inflammatory bowel disease and colorectal cancer. They found that levels of TET-2 expression and activity increased under inflammatory conditions, in cells downregulating gap junctional protein Cx43 and in colon tissues from mice exposed to carbenoxolone, a pan-gap junction blocker, and then concluded that dysregulated expression of TET 2 may contribute to inflammation--associated colorectal cancer. Major concerns: 1. Although the expression profile of the two targets from in vitro, in vivo and patient samples is impressive, mechanism explorations should not ever be waived. 2. Without colitis-associated cancer model, the conclusion was over-stated. 3. The logic behind a special gap junction protein to be the mechanism target of intestinal inflammation is not persuasive.