

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 64718

Title: Intestinal Wnt in the transition from physiology to oncology

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05927046

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-20 13:53

Reviewer performed review: 2021-06-24 06:34

Review time: 3 Days and 16 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1. In this manuscript, the authors reviewed intestinal WNT pathway in the transition from physiology to oncology. In the canonical Wnt/ β -catenin signaling, it consists of the transmembrane complex (Lrp5/6 and Frizzled), a destruction complex (Axin, APC, GSK3, CK1, PP2A) and β -catenin. In introducing of WNT signaling in intestinal mucosal physiology, whether the transmembrane complex, destruction complex or β -catenin are relative to stomach, small intestine and colon, please describe the detailed mechanism or the current research progress. 2. In the part "HYPERACTIVATION OF WNT SIGNALING DRIVES PATHOPHYSIOLOGY AND ONCOLOGY" Oncology should be a type of pathophysiology? Choose one of them maybe better. 3. In the Figure 4, the experiment was conducted by the author? Or are they from other references? Please illustrate in the legend.

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Peer-review model: Single blind

Reviewer's code: 02523682

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-06-19 03:40

Reviewer performed review: 2021-06-27 10:26

Review time: 8 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This manuscript reviewed the Wnt/ β -catenin signaling pathway, the regulatory mechanism of this pathway and its role in intestinal homeostasis, the molecular mechanisms and the histomorphological features of Wnt hyperactivation, and the central role of Wnt signaling pathway in intestinal carcinogenesis as well as its clinical relevance in colorectal carcinoma. Although the manuscript is well organized and described, the novelty of this manuscript still need to be considered because there are published papers including review about Wnt signaling pathway and intestine. 1. The title is "Intestinal WNT in the transition from physiology to oncology". However, this manuscript seems to focus on the physiology of Wnt while describing oncology role of Wnt signaling in a slightly simpler way. The author should reinforce the the transition from physiology to oncology and the clinical cancer relevance of Wnt activation. 2. In the Section "THE NECESSITY OF WNT SIGNALING IN INTESTINAL MUCOSAL PHYSIOLOGY", the authors mentioned three organs: Stomach, Small intestine, and Colon. However, in the Section "Clinical relevance of Wnt activation in colorectal cancer", the authors only described the prognostic value of Wnt activation and as a potential target in in colorectal cancer. How about the roles and status of Wnt activation in stomach? 3. In the Section "CLINICAL RELEVANCE OF WNT ACTIVATION IN COLORECTAL CANCER", the authors only focus on the role of APC in CRC prognosis, 5-ASA and WNT-induced chemoresistance. In fact, there are many protein factors in the Wnt pathway that are associated with tumors, including colon cancer, and many therapeutic targets and drugs are available for the treatment of colon cancer such as PROTAC peptide (Cell Discov. 2020 Jun 9;6:35. doi: 10.1038/s41421-020-0171-1), Oncolytic adenovirus (Biomedicines. 2020 Dec 11;8(12):593. doi:

10.3390/biomedicines8120593; Biochem Biophys Res Commun. 2017 Sep 16;491(2):469-477. doi: 10.1016/j.bbrc.2017.07.041) and An aggregon (Nat Commun. 2019 Sep 18;10(1):4251. doi: 10.1038/s41467-019-12203-8) et al. This Section is the important section in this manuscript. The authors also draw the figure or or list a table about the potential target in Wnt/ β -catenin signaling for the prevention and treatment of colorectal cancer.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Oncology*

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Peer-review model: Single blind

Reviewer's code: 02523682

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Germany

Manuscript submission date: 2021-02-23

Reviewer chosen by: Jing-Jie Wang (Online Science Editor)

Reviewer accepted review: 2021-11-12 06:18

Reviewer performed review: 2021-11-29 01:55

Review time: 16 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I reviewed the revised manuscript, the authors have well done the issues that the reviewers questioned. The language is great. I think it is fit to accept it.