



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 82825

Title: Microbiota regulation in constipation and colorectal cancer

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06392060

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Uganda

Author's Country/Territory: China

Manuscript submission date: 2022-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-28 08:46

Reviewer performed review: 2022-12-28 10:07

Review time: 1 Hour

| | |
|---------------------------|---|
| 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 Grade E: Do not publish |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 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

To further understand the relationship between the gut microbiota, constipation and CRC, ongoing preclinical and clinical research is required. Which future clinical studies would the authors wish to suggest? Any study designs? The authors give an interesting review on the effects of constipation and susceptibility to intestinal diseases such as CRC. In the introduction they state that constipation is a common problem for 16% of individuals overall and 33.5% of seniors (60-101 years). How is old age classified? Why is the cut off age 60 years? The authors correctly mention that gut microbes produce two well-defined genotoxins: cyclotoxic expansion toxins (CDT) and colistin. Please explain the mechanism of how the double-strand DNA breaks through deoxyribonuclease activity and leads to mutations which lead to CRC. Which mutations are caused by *B. fragilis* toxins? Please also explain the mechanism of how *Clostridium perfringens* increases reactive oxygen species, DNA damage and which mutations are caused leading to CRC? Would you consider all patients that are constipated irrespective of age to have a colonoscopy to prevent CRC?



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Reviewer's code: 06412958

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-12-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-28 08:56

Reviewer performed review: 2023-01-06 02:11

Review time: 8 Days and 17 Hours

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|--|--|
| 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 |
| Novelty of this manuscript | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty |
| Creativity or innovation of this manuscript | <input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation |



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|---|--|
| Scientific significance of the conclusion in this manuscript | <input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance |
| 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 type="checkbox"/> Yes <input checked="" type="checkbox"/> No |
| 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

1.From the perspective of the overall structure, the regulation of microorganisms in colon cancer and constipation as well as the possible involvement of constipation in colon cancer are elaborated with clear thinking and reasonable logic. The accompanying pictures are properly colored, the size and format of the notes are comfortable, and the picture sense is excellent. 2.From the perspective of specific content, this paper theoretically elaborates the connection between constipation and colorectal cancer through the regulation of microflora, and draws the conclusion that constipation may cause intestinal motor dysfunction and/or abnormal immune microenvironment due to changes in microflora composition and abnormal metabolites caused by intestinal flora disorders, which is innovative.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Uganda

Author's Country/Territory: China

Manuscript submission date: 2022-12-28

Reviewer chosen by: Han Zhang

Reviewer accepted review: 2023-03-21 15:12

Reviewer performed review: 2023-03-21 15:31

Review time: 1 Hour

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|---------------------------------|---|
| 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 checked="" 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 |



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SPECIFIC COMMENTS TO AUTHORS

I have two further comments to the authors: 1. It would be helpful to explain the mechanism of how clostridium perfringens causes DNA damage and hence which mutations leading to CRC in a flow diagram. 2. Is there any reason why the guidelines propose age 50, both in men and women to have a full colonoscopy if there are no factors that increase their risk of developing cancer.



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Reviewer chosen by: Han Zhang

Reviewer accepted review: 2023-03-22 00:40

Reviewer performed review: 2023-03-22 03:21

Review time: 2 Hours

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|---------------------------------|---|
| 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 |
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SPECIFIC COMMENTS TO AUTHORS

The crosstalk between the gut microbiota, constipation, and CRC, and their specific mechanisms of action were discussed by authors. It provides a theoretical basis for reducing the risk of colorectal polyps and CRC and preventing disease progression. The authors suggest that gut flora may soon become a powerful tool in the fight against colorectal cancer, making meaningful assumptions for future research.