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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 108747

Title: Innovative insights into gut microbiota modulation in colorectal cancer: From microbial dysbiosis to therapeutic strategies

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07181981

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Türkiye

Manuscript submission date: 2025-04-21

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-04-29 01:48

Reviewer performed review: 2025-05-08 03:22

Review time: 9 Days and 1 Hour

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

Not Applicable

Is the description of the experiments clear and complete? **Not Applicable**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable**

Are the experimental data of the Results true and reliable? **Not Applicable**

Are the quality and resolution of the images up to standard? **Not Applicable**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Not Applicable**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **Yes**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?



	Yes Are additional experiments needed for the study? No Does the research scope comply with ethics? Yes
Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

Overall Summary: This article explores the key role and potential treatment methods of gut microbiota dysbiosis in colorectal cancer (CRC). The article cites research emphasizing that the gut microbiota patterns of CRC patients are significantly different from those of healthy individuals. Harmful bacteria such as *Clostridium nucleatum* and *Bacteroidetes fragilis* are excessive, while beneficial bacteria such as *Faecalibacterium prausnitzii* are reduced. Microbial metabolites such as butyric acid are beneficial to colon



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cells, while secondary bile acids produced by high-fat and high protein diets are harmful. Intestinal microbiota also affects the immune system, with *Fusobacterium nucleatum* and others affecting immune responses through TLR4 signaling. New methods such as fecal microbiota transplantation (FMT), engineered probiotics, and multi omics data modeling have shown therapeutic potential, but there are safety issues. In the future, microbiota based technology may become a routine approach for precision treatment of CRC. Specific Comments: - Abstract: The abstract effectively summarizes the research objectives and conclusions, but should not include references. We should be clear that references will not appear in the abstract of academic papers that meet the standards. It should explain what contents were discussed in the paper, with a focus on highlighting the key points. some contents are too colloquial and should be more academic and professional, even though there are no grammatical errors. Please revise the abstract. - Keywords: A paper usually contains 5 keywords. You can leave "Colorectal cancer; Fecal microbiota transplantation; Gut OncoMicrobiome Signatures; Gut microbiota; Artificial intelligence". - You mentioned "artificial intelligence; machine learning" in the abstract and keywords, but there is no relevant discussion in the main text. - In fact, fecal microbiota transplantation (FMT) is no longer a new treatment method, and there has been extensive research in this area. The new treatment methods also include Targeting microbiota, design bacterial vectors such as Bacteriophages, engineered bacteria etc. - The role of gut microbiota in the progression of CRC has been confirmed, but current research has found that the role of intratumoral microbiota cannot be ignored. Please refer to these references (DOI: 10.1038/s41392-022-01304-4).



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Peer-review model: Single blind

Reviewer's code: 06318098

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Türkiye

Manuscript submission date: 2025-04-21

Reviewer chosen by: Jia-Lin Zhang

Reviewer accepted review: 2025-04-29 06:24

Reviewer performed review: 2025-05-08 03:37

Review time: 8 Days and 21 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? Yes Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Yes

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

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Do authors omit important references? **Yes**

Are all references related to the topic of the manuscript? **Yes**

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Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **Yes**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	No
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

The intestinal flora imbalance in patients with colon cancer is manifested as a decrease in beneficial bacteria and an increase in pathogenic bacteria. Intestinal flora imbalance promotes the occurrence and development of colorectal cancer through pathways such as promoting inflammation, disrupting the intestinal microenvironment, and exacerbating metabolic disorders. However, its mechanism of action remains unclear. Some studies, through the integrated analysis of single-cell transcriptome, microbiome, metabolome and clinical cohort data of colorectal adenoma and colorectal cancer, have confirmed that during the progression of colorectal adenoma-adenocarcinoma, the host



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urea cycle metabolic pathway is significantly activated, accompanied by the absence of intestinal symbiotic bacteria with urea degradation function represented by Bifidobacterium. High urea load can disrupt intestinal immune homeostasis by inhibiting the binding efficiency of the p-STAT1 and SAT1 promoter regions in macrophages and promoting the differentiation of macrophages into immunosuppressive subtypes. (1) What is the mechanism of intestinal flora imbalance in patients with colon cancer? How does intestinal flora imbalance affect the development of colorectal cancer? (2) What is the role of Bifidobacterium in colon cancer? What is the role of the urea cycle metabolic pathway in colorectal cancer? How does the urea cycle metabolic pathway affect intestinal immune homeostasis? (3) What are the effects of high urea loading on macrophages?



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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 108747

Title: Innovative insights into gut microbiota modulation in colorectal cancer: From microbial dysbiosis to therapeutic strategies

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07181981

Position: Peer Reviewer

Academic degree and professional title: PhD

Reviewer's Country/Territory: China

Author's Country/Territory: Türkiye

Manuscript submission date: 2025-04-21

Reviewer chosen by: Meng-Liu Luo

Reviewer accepted review: 2025-06-16 12:17

Reviewer performed review: 2025-06-17 08:44

Review time: 20 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? Yes Is there any Key Word that is not included in the manuscript title? No Do authors' affiliations correspond to the content of the manuscript? Yes Does the Abstract contain the contents of each part of the manuscript (IMRaD)? Yes Are the Key Words complete? Yes
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Is the description of the experiments clear and complete? **Yes**

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Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

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Do authors omit important references? **Yes**

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Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?
Yes

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

SPECIFIC COMMENTS TO AUTHORS

This study can be accept now.