

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 75245

Title: Impact of microbiota-immunity axis in pancreatic cancer management

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04423126

Position: Editorial Board

Academic degree: FACS

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-09 05:42

Reviewer performed review: 2022-02-09 07:26

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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (General priority) <input 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

The topic of the microbiota-immunity axis in pancreatic cancer management is a very interesting starting point. Its importance has already been proven for many diseases. Unfortunately, we do not yet have a lot of data on the treatment of pancreatic carcinoma. This is precisely why the paper is interesting for our readers.

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Manuscript NO: 75245

Title: Impact of microbiota-immunity axis in pancreatic cancer management

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05198253

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Academic Research, Chief Doctor, Doctor, Research Scientist

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Xin Liu

Reviewer accepted review: 2022-04-12 01:24

Reviewer performed review: 2022-04-13 14:14

Review time: 1 Day and 12 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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous

statements

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

SPECIFIC COMMENTS TO AUTHORS

The authors of the article explore a very interesting topic - the association between pancreatic cancer and microbiota. There is a growing body of research suggesting that microbes play an important role in cancer. Although there are not enough studies to provide clinical predictive microbial indicators for pancreatic cancer, the direction is important and worth exploring, and the authors have shed light on the microbiota-immunity axis in pancreatic cancer from a different perspective, making this study worthy of publication. I just have one small comment to point out. I would like to suggest the authors to add a section on comparison with other cancers to show which microbial changes are specific to pancreatic cancer and which are common in pan-cancer.

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Manuscript NO: 75245

Title: Impact of microbiota-immunity axis in pancreatic cancer management

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05189300

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Chief Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Xin Liu

Reviewer accepted review: 2022-04-11 23:20

Reviewer performed review: 2022-04-16 12:03

Review time: 4 Days and 12 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 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 checked="" type="checkbox"/> Accept (General priority) <input 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

statementsConflicts-of-Interest: [] Yes [**Y**] No**SPECIFIC COMMENTS TO AUTHORS**

The complex interplay between microbiota and the immune system at different anatomical districts (mostly gut and pancreas/intratumor) might have a role in both onset and progression of pancreatic cancer. Due to the poor prognosis of this tumor despite global advances in surgery and perioperative management, every effort to find new potential targets is welcome. This review is well organized, which have provided a comprehensive summarize of the existed evidence on the impact of microbiota-immunity axis in pancreatic cancer management, I recommend the publication of the paper.

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Manuscript NO: 75245

Title: Impact of microbiota-immunity axis in pancreatic cancer management

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04015916

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Xin Liu

Reviewer accepted review: 2022-04-12 02:04

Reviewer performed review: 2022-04-17 12:41

Review time: 5 Days and 10 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
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Re-review	<input type="checkbox"/> Yes <input checked="" 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

There is no definite conclusion on the occurrence and development factors of pancreatic cancer, and it is also a research hotspot. This paper reviews the current research in this field from the perspective that the complex interaction between the microbiota and the immune system may play a role in the pathogenesis and progression of pancreatic cancer. However, the current research in this field is relatively superficial, and the clinical significance is not large, and further in-depth research is needed.

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Manuscript NO: 75245

Title: Impact of microbiota-immunity axis in pancreatic cancer management

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04611317

Position: Peer Reviewer

Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Chief Physician

Reviewer's Country/Territory: Thailand

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Xin Liu

Reviewer accepted review: 2022-04-12 05:53

Reviewer performed review: 2022-04-21 07:02

Review time: 9 Days and 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 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

The overall scientific information in this review is fairly good, however the only microbiota factor could not be explained for the causative, preventive, or therapeutic impact of pancreatic cancer. The gut microbiota appear to be an alternative way to be included to the main standard treatment of pancreatic cancer, hence the authors should revise the manuscript to reflect this. This manuscript has an excessive number of paragraphs in the abstract, core tip, and main text, which should be summarized as normal. Figure 1 is too tiny to be recognized especially when published and references are required. Table 1 must be changed to clarify "Higher risk of developing PanCan [michaud13,akshi19,fan18,wei10,farrel12]". The references should be revised as the correct format.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04737076

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Consultant Physician-Scientist, Doctor, Lecturer, Pediatric Gastroenterology Fellow, Professor, Senior Postdoctoral Fellow, Senior Researcher, Senior Scientist

Reviewer's Country/Territory: Russia

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Xin Liu

Reviewer accepted review: 2022-04-14 20:35

Reviewer performed review: 2022-04-26 10:04

Review time: 11 Days and 13 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 statements	Peer-Review: [<input type="checkbox"/>] Anonymous [<input checked="" type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? The present review does not fully reflect the issues of "Impact of the microbiota-immunity axis on the treatment of pancreatic cancer".

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? The annotation includes the main content of the paper.

3 Key words. Do the key words reflect the focus of the manuscript? Keywords reflect the content of the manuscript.

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Introduction It modestly describes the current state of the issue. The name of the work sounds "the effect of the axis of the microbiota-immunity on the treatment of pancreatic cancer", however, it is precisely this issue in the introduction of very little space.

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? The manuscript is dedicated to the review of existing research. However, there are no indications on which the principle was selected by the published works that were taken for the review.

6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? The objectives of the study research is not fully achieved. After reading "the effect of the axis of the microbiota-immunity on the treatment of pancreatic cancer" remained a "mystery". There are many phrases such as "...seem to contribute to PanCa initiation and development...", "... mitis appeared to be reduced...", "... H. pylori could also have a role in development of this cancer.", "...It could elicit chronic mucosal inflammation...", "... while Candida, Aspergillus, or



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Saccharomyces species did not seem to cause cancer development...", "...while high levels of anti-commensal microbes' antibodies seem related to a reduced risk of PanCa", "...Several factors can unbalance the microbiota biodiversity..." etc. But many of these statements have long been proven. Why such uncertainty in the text? Thus, it seems that the author did not introduce anything new. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? There is no discussion in the manuscript, but there are "CONCLUSIONS" from which it follows that there is very little knowledge on this issue. 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? The drawing is good, it does not require any modifications. The table does not require any modification either. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? There is no biostatistics in the manuscript (not provided). 10 Units. Does the manuscript meet the requirements of use of SI units? There are no SI units in the manuscript (not provided). 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? The citations are correct. There are no self-citations. 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? The text of the manuscript requires more precise structuring. The figure shows very well the relationship between microbiota and carcinogenesis (pancreatic cancer). However, in the text, these data are scattered and it is difficult to

understand what is interconnected with what. 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? The manuscript is a review. However, it is not clear, is it a systematic review, meta -analysis? It is advisable to allocate the section "Methods", which reflects the principle for which articles were selected for review. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? The manuscript complies with ethical requirements.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 04611317

Position: Peer Reviewer

Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Chief Physician

Reviewer's Country/Territory: Thailand

Author's Country/Territory: Italy

Manuscript submission date: 2022-01-19

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2022-06-29 07:25

Reviewer performed review: 2022-06-29 07:36

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 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

Thank you for your revision.