

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 85778

Title: Impact of gut microbiome in the development and treatment of pancreatic cancer:
Newer insights

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00004011

Position: Associate Editor

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: United States

Manuscript submission date: 2023-05-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-05-18 15:10

Reviewer performed review: 2023-05-18 15:13

Review time: 1 Hour

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 Grade E: Do not publish
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 type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in 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 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

it is a well written and documented manuscript. It will be helpful if the authors emphasize regarding microbiome and different PC ie adenocarcinoma, IPMN etc

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Title: Impact of gut microbiome in the development and treatment of pancreatic cancer:
Newer insights

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03252941

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2023-05-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-05-16 23:16

Reviewer performed review: 2023-05-23 11:30

Review time: 6 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
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
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Re-review	<input type="checkbox"/> Yes <input checked="" 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

Bangolo et al. performed a comprehensive review on the impact of gut microbiome in the development and treatment of pancreatic cancer (PC). Beginning with a review of the diagnosis and treatment of PC, the impact of gut microbiome on inflammation, carcinogenesis and treatment is adequately described, citing appropriate references. This is a well-written review. Especially, association between periodontitis and PC is a timely and interesting topic. While reading this manuscript, I noticed some minor points. I will list them below. 1. (Line 54) Approximately 15 percent of PCs are related to genetics: The meaning of this sentence is obscure. As described below, familial PC comprises 10% of PC patients. On the other hand, nearly all PC must have genetic aberrations in cancer-related genes including K-ras, CDKN2A, p53, and SMAD4. Please explain what this 15% means. 2. (Line 109) as the aggressive or palliative care approach could be applied based on the "same": Based on the "stage"? 3. (Lines 209-211) PPAD (Porphyromonas Peptidyl Arginine Deaminase) is a protein produced by P. gingivalis that has been associated with cancer development by the way of P53 activity and KRAS (Kirsten-ras) mutation [52]: Please make a brief explanation how PPAD affects P53



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activity and causes K-ras mutation. 4. (Lines 261-262) Furthermore, bile acids can modulate the composition of the microbiome and facilitate bacterial translocation into tissues,: According to the cited reference, I assume that loss of bile acid facilitate bacterial translocation. 5. (lines 316-318) In a mice model, a “special group” represented the mice with a defective Toll-like receptor (TLR) signaling pathway, demonstrating no response to oxaliplatin treatment.: What is a “special group”? And, please cite a reference.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04091933

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor, Senior Researcher

Reviewer's Country/Territory: Russia

Author's Country/Territory: United States

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Reviewer chosen by: AI Technique

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Reviewer performed review: 2023-05-28 21:00

Review time: 12 Days and 23 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 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
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Re-review	<input checked="" type="checkbox"/> Yes <input 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

The topic of the manuscript is generally relevant and concerns the role of the gut microbiome in pancreatic cancer (PC). The manuscript as a whole is well written, but a number of important points need to be clarified. 1. The mechanisms by which the microbiota modulates carcinogenesis in PAC, such as the role of natural killers, are poorly understood (Yu Q et al, 2022). It is desirable to show how the fecal microbiota may influence the course and survival/outcomes in PC. 2. The possible role of fungi (mycobiota) (there is only one reference) and the virome (no references) in the pathogenesis of PC has not been disclosed. 3. It is required to significantly supplement the information on the involvement of bacterial metabolites (SCFA, including butyrate, tryptophan metabolites, etc.) in PC oncogenesis and in response to treatment. 4. The claim that Fusobacteria is associated with a reduced risk of pancreatic adenocarcinoma may be misleading to the reader. It is required to add the specific Leptotrichia genus associated with risk reduction, as other genera and species (eg Fusobacterium nucleatum) may conversely be associated with increased risk. 5. Not enough references 2022 (only 6) and 2023 (none). Please also check all references and eliminate possible duplication (for example, references 10 and 113 are duplicated [Fan X et al., 2018]) 6. The lack of illustrative material in the review is depressing. It is advisable to add a table and/or figure on the topic of the manuscript, for example, mechanisms of microbiota involvement or microbiota changes associated with PC). 7. Many taxa have outdated names (for example, Proteobacteria, Firmicutes, Fusobacteria, Bacteroides vulgatus, Bacteroides dorei, Lactobacillus casei, etc) We strongly recommend using a modern taxonomic classification (primarily for recently reclassified phyla and taxa). Old and



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incorrect names should be corrected to valid ones (eg Bacillota instead of Firmicutes, Fusobacteriota instead of Fusobacteria, Pseudomonadota instead of Proteobacteria).

Please see:

<https://www.microbiologyresearch.org/content/journal/ijsem/10.1099/ijsem.0.005056>.

Please use italics for taxa and correct spelling errors in taxa and abbreviations (for example, *Helicobacter Pylori*, Staph. A, Porphyromonas Gingivalis, etc). Please also correct other grammatical errors/typos, for example, replace pancreatic CA with pancreatic cancer or PC, etc. After a major revision, the manuscript may be recommended for publication.