Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 76134

Title: Gut microbiome and pancreatic cancer cachexia: An evolving relationship

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05824934
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: Singapore
Author's Country/Territory: United States

Manuscript submission date: 2022-03-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-03 05:15

Reviewer performed review: 2022-03-11 18:18

Review time: 8 Days and 13 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [ ] Anonymous [Y] Onymous

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

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

SPECIFIC COMMENTS TO AUTHORS

This paper focuses on cachexia in pancreatic ductal adenocarcinoma (PDAC) patients, and investigates the possible role of nutritional support and human gut microbiota in reversing PDAC cachexia. The study reported in this manuscript is very interesting and importance. The authors may further discuss the special role of systemic inflammation in the development of cachexia. Systemic inflammation as one of the main features of cachexia is mentioned by the authors several times in the manuscript. Localized transient Inflammation is the central machinery of our immune system in response to acute tissue damage [1], and such localized transient inflammation is generally protective. It helps to remove the injurious stimuli like infections, trauma and tumor cells, and initiate tissue regeneration. When there are tissue-damaging stimuli like physical injury, infectious pathogens, toxin exposure, chemical irritation, the human immune system will actively induce cell self-destruction (programmed cell deaths [2] like apoptosis, necroptosis and pyroptosis) and reuse the nutrition from the degradation of the dead cell as nutrition source (immuno-nutrition) to repair/regenerate the tissue cells. If the damaging stimuli and the destructed cell debris can be effectively and swiftly removed by inflammation and fully used for tissue regeneration, then inflammation will not be chronic or systemic, and cachexia will not be developed. Yet, when the nutrition from the destructed cells exceeds the tissue regeneration needs, the extra nutrition will be transferred into lipid intermediates and deposits on healthy non-adipose tissues like muscles, and causing lipotoxicity. Lipotoxicity will create new cell death, and leading to the destruction of these cells. Thus, more lipid intermediates are produced by inflammation, with the expenses of lean mass. A vicious positive feedback between cell death and lipid intermediates are established, leading to cachexia, and local transient

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

inflammation becomes systemic inflammation. So when there is cachexia, restrictive eating should be adopted by the patient [3] to avoid over-nutrition and systemic inflammation. The impact of gut microbiota on cachexia is indirect. They are playing the role of full spectrum of immuno-nutrients like essential amino acids to the human body [4]. And, as a nutrition source, if they are overgrown, they will contribute to systemic inflammation and cachexia. So although gut microbiota provide a full spectrum of essential nutrition, their abundance in the gut should also be strictly checked.

Reference: 1. Greten FR, Grivennikov SI (2019) Inflammation and Cancer: Triggers, Mechanisms, and Consequences. Immunity 51(1):27-41. DOI: 10.1016/j.immuni.2019.06.025 2. Yang Y, Jiang G, Zhang P, Fan J. (2015) Programmed cell death and its role in inflammation. Mil Med Res. 2015;2:12. DOI: 10.1186/s40779-015-0039-0 3. Arabi YM, Reintam BA, Preiser JC (2019) Less is more in nutrition: critically ill patients are starving but not hungry. Intensive Care Med 45:1629–1631. DOI: 10.1007/s00134-019-05765-0 4. Hackmann TJ, Firkins JL (2015) Maximizing efficiency of rumen microbial protein production. Front Microbiol 6:465. DOI: 10.3389/fmicb.2015.00465

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 76134

Title: Gut microbiome and pancreatic cancer cachexia: An evolving relationship

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03805255
Position: Peer Reviewer
Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Serbia

Author's Country/Territory: United States

Manuscript submission date: 2022-03-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-03 19:05

Reviewer performed review: 2022-03-12 22:14

Review time: 9 Days and 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

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

SPECIFIC COMMENTS TO AUTHORS

Dear Authors, Your manuscript is very interesting, with an appropriate title, abstract, key words, and well-organised structure. Cachexia is an important problem because it is the first anti-cancer drug, particularly pancreatic cancer. You analyzed a new method for the treatment of cachexia and the role of the gut microbiome in the development and treatment of cachexia. The new method of enteral feeding with peptite-based formula is feasible and warrants further investigation, while change of the gut microbiome has potential for the treatment of cachexia and demands further investigation also.