

Could There Be an Interplay between Periodontal Changes and Pancreatic Malignancies?

Dear Editor,

Thank you and the reviewer very much for the valuable suggestions to improve the scientific quality of our manuscript. We appreciate the journal's reviewing process and have tried to respond to the reviewer's comments as close as possible. Please find below our point-by-point corrections and the required explanations. The English language was revised.

Company Editor-in-Chief

I recommend the manuscript to be published in the World Journal of Clinical Cases. Before final acceptance, the author(s) must add a table/figure (medical imaging) to the manuscript. There are no restrictions on the figures (color, B/W). Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

We thank to the company editor-in-chief for the valuable suggestions which helped us to improve the scientific quality of our paper. Accordingly, a table was added and references were changed.

Reviewer #1

In a review manuscript, the authors describe a possible relationship between periodontal diseases, which affect up to 20% of adults in their

acute forms, and malignant tumors of the pancreas, which have a very high mortality rate. Therefore, this topic is extremely important and is part of a recent research trend to describe the molecular mechanism of the observed correlation between periodontal diseases and other systemic diseases. However, before publication in the World Journal of Gastroenterology, the manuscript requires minor revisions, which are listed below:

- page (p.) 5: "...is the ability of certain species (*Fusobacterium nucleatum* or *Porphyromonas gingivalis*), known as "keystone pathogens,...": the etiology of periodontal diseases is very complicated, and its model has changed in recent years. However, the de facto keystone pathogen is *P. gingivalis* only. In addition, in the bacterial complexes theory, the so-called red complex, in addition to *P. gingivalis*, was formed by *Treponema denticola* and *Tannerella forsythia*. *F. nucleatum* is not considered the main or crucial pathogen in both theories but more as an opportunistic one. Thus, this content needs to be changed; Thank you for your valuable suggestion. The content has been revised.

- p. 10: "... gene may be caused by the peptidyl arginine deaminase enzymes that are common in oral bacteria.": peptidyl arginine deaminase (PAD) is unique to *Porphyromonas* species and is not produced by other plaque bacteria, especially those considered crucial in the etiology of periodontitis. PAD is an important virulence factor and possibly significant in the molecular link between periodontal disease and rheumatoid arthritis; Done, the content has been changed.

- review articles in references related to the article's main topic: e.g. numbers 37 and 38: such reviews in the reference should be avoided, and more citations to original works should be made. References to review articles are possible in the case of topics that are not the main subject of the reviewed article; Done, the references no. 37 and 38 have been modified accordingly.

- p. 3: "microbiota, especially the microbiome of tumors, ...": I would avoid such unequivocal statements, especially since, despite numerous attempts, it is impossible to culture live periodontopathogens. Only their DNA or protein products are found, e.g. in the work of Dominy et al., 2019 (PMID:

30746447), which does not mean that there are live bacteria there; **Done, the content has been removed from the abstract and from the main text.**

- the manuscript under review consists of plain text only. And often, in such works, some diagrams/schemes or tables increase the attractiveness for the reader. I think adding at least a table with a set of articles and methods used (what was detected: DNA or proteins) in which bacteria from the oral cavity were detected in tumors: of the pancreas or other parts of the digestive system (e.g. esophagus). **Done, a table has been introduced.**

Reviewer #2

The authors of this paper have done an excellent job and systematically introduced the relevant situation between periodontal changes and pancreatic malignancies. However, there is a small problem that needs further explanation: is there any difference in the study of periodontal changes in different pathological types of pancreatic cancer? **We thank the reviewer for revising our scientific paper. Regarding periodontal changes that occur in different histological subtypes of pancreatic cancer, at this moment we could not find relevant data in the scientific literature. Considering that pancreatic ductal adenocarcinomas account for over 90% of pancreatic malignancies, being probably the most investigated of the cancerous pathologies of the pancreas, future research is needed for a better understanding of the bacteria's implications in different pathological types of cancer.**