

Peer Review File

Article information: <http://dx.doi.org/10.21037/tcr-21-2803>

Reviewer #1

Thank you very much for your time involved in reviewing the manuscript and your very encouraging comments on the merits.

Comments:

The reviewed article is very important and well written. Today we know more and more about carcinogenic bacteria and the mechanisms of cancer development. The authors present a meta-analysis about Helicobacter pylori and pancreatic cancer correlation. The study is performed according to PRISMA. They confirmed that H. pylori infection can increase the incidence of pancreatic cancer.

We also appreciate your clear and detailed feedback and hope that the explanation has fully addressed all of your concerns. In the remainder of this letter, we discuss each of your comments individually along with our corresponding responses.

To facilitate this discussion, we first retype your comments in italic font and then present our responses to the comments.

Comment 1: *In the title the name "Helicobacter" should be upper-case.*

Reply1: Thank you for the detailed review. We have capitalized the name as advised.

(see Page 1, line 1. The modification is marked in green.)

Comment 2: *In the Introduction please cite a new paper about microbial associations with pancreatic cancer <https://pubmed.ncbi.nlm.nih.gov/34359685/>, in which are data concerning *H. pylori*.*

Reply2: Thanks for your great suggestion on improving the accessibility of our manuscript. We read this paper carefully and found it rigorous and novel, which fits the idea of our article. We have cited some point of view of this excellent article in the introduction. (see Page 4, line 71-76. The modification is marked in blue.)

Comment 3: *Authors studied CagA-positivity and pancreatic cancer. It would be worthwhile to describe if there is also a relationship between VacA and pancreatic cancer.*

Reply 3: Thank you for your comments to make us realize the shortcomings of the article and make it more scientific. We fully consider your suggestions and make the following modifications:

Firstly, we have made a new analysis about the relationship between VacA and pancreatic cancer and added a new figure according to the result of the analysis. (see Page 12, line 227-233; Page 13, 244-246; Page 14, line 278-280; Figure 8).

Secondly, we add a description about the biological functions of CagA/VacA in the ‘Discussion’ and explained the full name of VacA in the ‘Abstract’. (see Page 13, line 251-255; Page 2, line 36-38; Page 3, line 46-47, line 53-56).

In the end, we have modified some of the subtitles and legends due to the new analysis (see Page 29, line 530-532). (The modification is marked in red.)

Reviewer #2

Thank you for your reminding. Your comment is of great importance to our article. We do believe that this comment has contributed a lot to improve the quality of our article.

Comment: *Authors present very good publication with meta-analysis. They confirmed that H. pylori infection is associated with pancreatic cancer, and this correlation is especially significant in economically underdeveloped countries. The methodology is proper and carried out in accordance with PRISMA. As results are presented 9 figures, 3 tables and 1 scheme.*

I suggest only one correction: in the Introduction, the authors should add a new article <https://pubmed.ncbi.nlm.nih.gov/34359685/>, in which is also shown the correlation between H. pylori and pancreatic cancer.

Reply: We truly appreciate the question suggested. It provides us with an excellent article to prove our point of view, which can make our article more credible. We have cited this paper in the introduction and made a brief description of its excellent point of view. We believe that the quote of this excellent article will make our article more perfect. (see Page 4, line 71-76. The modification is marked in blue.)