

Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Tumor budding in gastric cancer" (Manuscript NO.: 82515). These comments are all valuable and very helpful. I have studied the comments carefully. After reading these comments carefully, we revised our manuscript. The main responses to the reviewer's comments are as follows:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: No comments.

Response:

Thank you for your acceptance of our review.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: Dear Editor, It is a pleasure to be invited to review this manuscript. Although the authors write with the expectation of improving the prognosis of GC patients through TB prediction, both in terms of preoperative pathology, preoperative, postoperative treatment, etc., although it has been successful in colorectal cancer. However, I found the manuscript to be of average writing quality, with limited significance of the findings cited in the text, less guidance on the current realization of clinical significance, and the English language could be improved. I therefore consider that the manuscript cannot be published. Thank you for your invitation! Best regards Yours sincerely.

Response:

Despite the rejection, we still thank you for your comments. As you have stated, TB has limited application potential in clinical situation, however, it is also the reason

we reviewed this topic, for its challenges, also for its opportunities.

Reviewer #3:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: This is an excellent summary of our current understanding on the mechanisms of tumor budding and its role in the prognostic and predictive diagnostics of gastric cancer.

Response:

Thank you for your acceptance of our review and the valuable suggestions.

Just some minor comments: 1. Page 7: It is not indicated what CSC stands for. Please make sure that the first time an abbreviation appears in the text, the full term is also displayed.

Response:

We have supplemented the full term in the text the first time the CSC appears.

2. Page 12: "In addition, in those low TB activity and high inflammation regions, cancer cells exhibited high microsatellite instability (MSI) [13]." In reference 13, the MSI status of the tumor cells of the invasion front was not assessed separately, only the MSI status of the whole tumor. The MSI status of the invasion front cells is otherwise typically not different from the MSI status of the rest of the tumor. Please, change this sentence accordingly. For example: "MSI high (MSI-H) tumors are often characterized by a pushing border type invasion front, no or low TB and a strong peritumoral inflammatory infiltrate [13]."

Response:

Thank you for pointing out our misinterpretation, and the description has been revised as your suggestion.

3. Page 19: "In early GC, modified TB was more predictive of lymph node involvement than conventional TB, while SRC-matched TB showed a greater tendency toward groups without lymph node metastasis [32]." The second part of the sentence is difficult to understand.

Response:

The sentence was revised as “In contrast, SRC-matched TB had no significant association with lymph node metastasis; rather, it showed a greater tendency toward patients without lymph node metastasis”.

LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Response:

The revised manuscript has been edited by AJE AI, and we hope that the language quality of our manuscript will meet the publication requirement.

In addition, as the figure was created with BioRender.com, when it was transformed into ppt, only the text portions are editable, we hope such format will meet the requirement. In addition, the publication and licensing rights of the figure was obtained and has been submitted with the figure.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Yours sincerely,

Shuomeng Xiao, Jian Li