

Round-1:

Dear editor,

Thank you very much for your letter and advice.

We have revised the manuscript, which we would like to submit for your consideration for publication. We have addressed the comments raised by the reviewers, and the changes are highlighted in red in the revised manuscript. Point-by-point responses to the reviewers' comments are provided below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

We look forward to hearing from you soon.

Yours sincerely,

Jiexin Zhang

Department of Laboratory Medicine

The First Affiliated Hospital of Nanjing Medical University

300 Guangzhou Road

Nanjing, 210029, China

E-mail: jiexinzhang@njmu.edu.cn

Response to Reviewers

Reviewer 1

The authors present a straight forward case report related to SCCA expression in gastric cancer. Minor comments:

1. The description of the IHC for SCCA is missing. Was the staining performed in one run together for SCCA with gastric tissues?

Response: Thank you for your helpful suggestion. The relevant content was added in the figure legend below Figure 5. All the changes have been marked in red in the revised manuscript.

2. Figure 3 is kind of the poor quality (if possible provide high quality image).

Response: Thank you for the valuable comments. Figure 3 was replaced by the original figure document and was presented in PowerPoint file.

3. Magnification of IHC figure on SCCA staining would be beneficial in addition.

Response: Thank you for your careful comment. The relevant content was added in the figure legends below Figure 3, 4 and 5. All the changes have been marked in red in the revised manuscript.

4. Some language editing is necessary. Some sentences are not correctly made.

Response: Thank you for the valuable suggestion. The relevant content was revised and highlighted in red in the revised manuscript.

Reviewer 2

This case report however, is the first report of raised SCCA in a patient with adenocarcinoma of the stomach, but surprisingly no histopathological changes of squamous cell carcinoma were noted in the surgical specimen and p63 was also negative. Some comment in this regard will be desirable in "Discussion" section.

Response: The relevant content was added to the fifth paragraph of the discussion. All the changes have been marked in red in the revised manuscript.

Reviewer 3

Wang L et al. reported that high SCCA expression in the gastric carcinoma specimen. Although IHC with SCCA is clear, other clinical and pathological information is mostly missing. It would be valuable if their data could compare the expressions, such as CEA, CAM5.2, CK7, CK20, Ki-67, and E-cadherin.

Response: Thank you for the valuable suggestion. The IHC staining results of CEA, CAM5.2, CK7, CK20, Ki-67, and E-cadherin were added to "FINAL DIAGNOSIS"

and Figure 4. The relevant descriptions have been marked in red in the revised manuscript.

Round-2:

Dear editor, Thank you very much for your letter and advice. We have revised the manuscript, which we would like to submit for your consideration for publication. We have addressed the comments raised by the reviewers, and the changes are highlighted in red in the revised manuscript. Point-by-point responses to the reviewers' comments are provided below this letter. We hope that the revised version of the manuscript is now acceptable for publication in your journal. We look forward to hearing from you soon. Response to Reviewers Reviewer 1 In the revised version of the paper, the authors have successfully addressed my comments related to IHC. Unfortunately, there are still few issues to mention.

1. The authors state that they performed Roux-Y gastric bypass, I am not sure it is correct description. They state to perform distal subtotal gastrectomy, right? Roux-Y gastric bypass is a common surgery in bariatric surgery. May be authors refer to Roux-en Y anastomosis?

Response: Thank you for your valuable comments. The patient had radical distal gastrectomy as well as residual stomach and jejunum Roux-en Y anastomosis. It has been marked in red in the revised manuscript.

2. The authors report to perform SCCA testing on several gastric cancers. However, not data are presented at least no information regarding the number is included. Although, it is ok from my side to have it in this form, my concern is the main conclusion the authors make in the abstract and the main paper: "exhibited in some poorly differentiated gastric adenocarcinoma ... rather than in well-differentiated cases".

Response: Thank you for the thoughtful suggestions. In another follow-up study, we investigated the relation between SCCA expression and gastric adenocarcinoma differentiation degrees by IHC in 40 cases of gastric adenocarcinoma including 20 poorly differentiated cases and 20 highly differentiated cases. The results showed that SCCA overexpression was shown in 20% (4/20) of poorly differentiated cases. And SCCA was negative in all well differentiated tumor cells. Therefore, we showed typical IHC staining figures of SCCA in gastritis and gastric cancer tissues in Figure 5 to enrich the Discussion. If you think it is necessary, I will add this part in the revised manuscript.

3. The authors state that this is the first report regarding the expression of SSCA gastric cancer. This is not fully true, as there is a patent where the authors describe SCCA expression in 1/6 patients with gastric cancer (<https://patents.google.com/patent/EP1930427A1/en>). Furthermore, the group from M. Rugge has published reported that SCCA can be expressed in Barrett adenocarcinoma, which makes it likely that also gastric adenocarcinoma may potentially express SCCA more frequently as currently reported (DOI:10.18632/oncotarget.14108). This information may be important for discussion purpose.

Response: Thank you for the helpful comment. The related content has been added to the "Discussion" and "Conclusion" of the revised manuscript.

4. Some language polishing might be needed. Here are several examples: -Conclusion

abstract:" ...it only exhibited in some poorly differentiated" - Typos and rewording in Core tip is needed (second and third sentence) - Conclusion part in main paper: "... this advanced patients" needs rewording.

Response: Thank you for the valuable suggestion. We have marked the changes in red in the revised manuscript.