

Dear Editor,

Please find enclosed the edited manuscript (file name: 22867-Revised manuscript).

Name of journal: *World Journal of Gastroenterology*

Manuscript NO.: 22867

Column: Topic Highlights

Title: Key players in pancreatic cancer-stroma interaction: cancer-associated fibroblasts, endothelial and inflammatory cells

Authors: Michael Friberg Bruun Nielsen, Michael Bau Mortensen and Sönke Detlefsen

Correspondence to: Sönke Detlefsen, MD, PhD, Clinical Associate Professor, Consultant pathologist, Department of Pathology, Odense University Hospital, University of Southern Denmark, 5000 Odense C, Denmark, sonke.detlefsen@rsyd.dk

Thank you very much for the opportunity to submit a revised manuscript. We thank the reviewers for their constructive comments. The manuscript has been improved according to the suggestions of reviewers:

To reviewers

- 1) **As a minor remark: although the authors state that “published data indicate that PDAC arises from ductal epithelial cells”, the current theory is that PanIN (and pancreatic cancer) develop from acinar cells via ADM (Reviewer’s code: 00001832).**

→ Response: Thank you for asking us to address this topic. We are aware that the origin of PDAC is the topic of an ongoing debate. We have now emphasized that two (not necessarily contradictory) theories exist: one suggesting that PDAC arises from ductal epithelial cells and the other suggesting that the centro-acinar acinar compartment (CAAC) can be the source of PDAC. [Introduction, page 3]

- 2) **I can see two gaps in the manuscript, completion of which will make the review all inclusive. 1. Authors need to include a short paragraph specifically summarising the clinical implication of the cross talk between the components of the stroma. 2. A table presenting the details of drugs/interventions in clinical trial (with results wherever available) that targets the stroma (Reviewer’s code: 00186066).**

→ Response: Thank you for this suggestion. We agree with this recommendation and have now included an additional chapter called 6. *Clinical implications of modulating the pancreatic cancer stroma*. This chapter contains a table presenting a summary of clinical trials that target the pancreatic cancer stroma.

- 3) **Authors need to correct few spelling and linguistic errors (Reviewer’s code: 00186066).**

→ Response: Thank you for addressing this issue. We have made a thorough attempt of correcting spelling and linguistic errors. Further, an external language editing service (NPG Language Editing (Nature Publishing Group)) has revised the manuscript.

To administrator:

- 4) Please put the reference numbers in square brackets in superscript at the end of citation content or after the cited author's name.**

→ Response: All reference numbers has been put in square brackets in superscript.

- 5) Author names should be given first, then the complete name of institution, city, province and postcode.**

→ Response: Author affiliations have been updated according to the guidelines.

- 6) Please provide language a certificate letter from a professional English language editing company (Classification of the manuscript language quality evaluation is B).**

→ Response: We have provided a language editing certificate from NPG Language Editing (Nature Publishing Group).

On behalf of the authors,

Kind regards,

Yours sincerely,



Sönke Detlefsen, MD, PhD

Dept. of Pathology

Odense University Hospital

University of Southern Denmark

Odense, Denmark