

Dear Editors and Reviewers:

Thanks for your letter and for the reviewers' comments concerning our manuscript entitled "Analysis of invasiveness and tumor-associated macrophage infiltration in solid pseudopapillary tumors of pancreas" (Manuscript NO.: 77625). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied the comments carefully and have made the revision. The responses to the Reviewer's and Editor's comments are as follows:

**Reviewer 1#**

**Comments 1:** Do you see the same results between malignant and non-malignant SPNs?

**Response:**

We appreciate the reviewer's insightful suggestion and agree that it would be helpful to analyze between malignant and non-malignant SPNs. However, considering the smaller sample size (only 6 patients were diagnosed as malignant SPNs according to the WHO-defined criteria), such an analysis is beyond the scope of our paper, which aims only to show the malignant behavior and tumor-associated macrophage (TAM) infiltration between different histopathologic features (capsule or invasion) of SPT patients. It is interesting to note that, the invasion detected under

the microscope was associated with malignant behavior and TAM infiltration. We will explore this question raised by the reviewer in the following research.

### **Reviewer 2#**

**Comment 1:** There are many grammar problems in the manuscript, which should be addressed by a native English speaker.

**Response:** We apologize for the grammar problems in our manuscript. We have now worked on language and readability and involved native English speakers in language corrections. We hope that the flow and language level have been substantially improved.

**Comment 2:** In ABSTRACT, the conclusion section should be stated more comprehensively.

**Response:** According to the reviewer's suggestion, we have rewritten the conclusion section in ABSTRACT as follows: "This finding can help in future investigations of the underlying mechanism of TAM-mediated SPT malignant behavior."

**Comment 3:** In the Method in IHC analysis, the following references could be added: (<https://doi.org/10.1038/s41598-021-00886-3>), (<https://doi.org/10.1038/s41598-021-89106-6>)

**Response:** Immunohistochemistry (IHC) and image analysis are common experimental techniques. The method of the two references provided by the Reviewer is reasonable and similar to our experimental method. We have added the references In the Method of IHC analysis as the reviewer suggested.

**Comment 4:** In statistical analysis, it is better to provide some information about the evaluation of the normality and homogeneity of data.

**Response:** As the reviewer suggested, we have added the information about the evaluation of the normality and homogeneity of data in the statistical analysis as follows:

“Normality and homogeneity of the data were assessed by Shapiro–Wilk’s and Levene’s tests, respectively.”

### **Company editor-in-chief**

**Comment 1:** Before final acceptance, uniform presentation should be used for figures showing the same or similar content. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright

information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

**Response:** As the editor-in-chief suggested, we have provided the figures according to the guideline and organized them into a single PowerPoint file. The copyright information for the original figure has also been added.

**Comment 2:** Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

**Response:** We have provided the standard three-line tables as the editor-in-chief suggested.

**Comment 3:** 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).

**Response:** By using the Reference Citation Analysis (RCA), we have found a recent review that tumor-associated macrophages could

promote the invasiveness of tumors. We have added it to our manuscript in the discussion section as follows: “Of interest, a recent study found that lipid-loaded TAMs could also sustain invasiveness in prostate cancer [24]. “

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

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

Best wishes,

Yong-Hua Chen