Peer Review File

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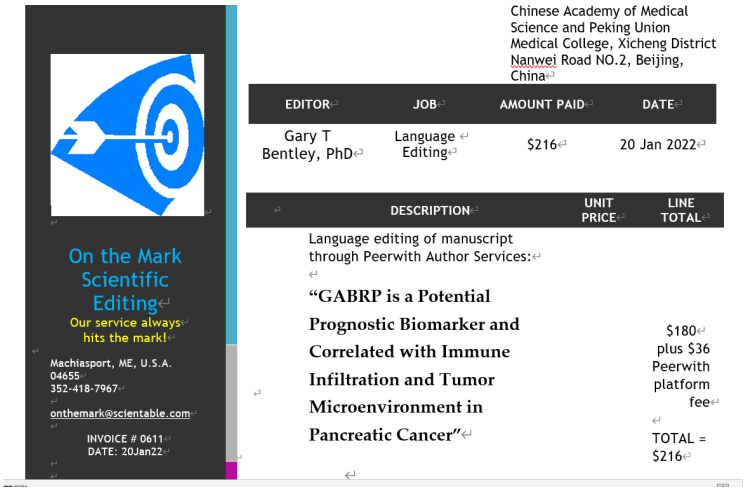
Reviewer A

First, please have the paper edited by native English-speaking professionals before the submission of the revised version. Second, in the background of the abstract part, please indicate the potential clinical significance of the current research topic. In the part of methods, please briefly describe the research methodology of this study. In this part, please describe how the research samples were obtained, how the prognosis outcomes were assessed, and which outcomes were collected. In the part of results, please use detailed figures such as the expression levels and their corresponding P values to describe the findings. The conclusion should have some suggestions on the possible clinical implications of the findings. Third, in the introduction part of the main text, the authors need to briefly review known biomarkers associated with prognosis of pancreatic cancers, have comments on their limitations and knowledge gaps, and explain why GABRP is potentially useful and deserved to be studied. Please also have comments on the clinical need for this biomarker. The second issue is that the authors should explain why bioinformatics analysis is appropriate for answering the research question. Fourth, the methodology part is a little long and I suggest the authors to use a flowchart figure to indicate the study procedures. Finally, in the statistics part, please consider to exclude the confounding effects of other clinical factors when analyzing the prognostic role of GABRP. For the nomogram, please specify the training and validation samples, and clearly indicate the criteria for assessing a good nomogram.

Thank the reviewer for constructive comments and suggestions! The enclosed revised version of our manuscript includes changes as reviewer suggested, as summarized below. All changes in the manuscript were underlined. We tried our best to answer all questions pointed by the reviewer.

Comment 1: Please have the paper edited by native English-speaking professionals before the submission of the revised version.

Reply 1: *Thank the reviewer for the constructive suggestions. Language of the manuscript was corrected by professor Gary Bentley in the Peerwith Company. Peerwith company provides a secure peer-to-peer environment where academics connect with researcher service experts from across the world. (* ***We had paid the service.****)*



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Comment 2: In the background of the abstract part, please indicate the potential clinical significance of the current research topic. In the part of methods, please briefly describe the research methodology of this study. In this part, please describe how the research samples were obtained, how the prognosis outcomes were assessed, and which outcomes were collected. In the part of results, please use detailed figures such as the expression levels and their corresponding P values to describe the findings. The conclusion should have some suggestions on the possible clinical implications of the findings.

Reply 2: *Thank the reviewer for the constructive suggestions. In the background of the abstract part, we have indicated the potential clinical significance of the current research topic* (see ***Page 2, line 35-36***). *In the part of methods, we have briefly described the research methodology of this study* (see ***Page 2-3, line 37-45***). *In the part of results, we have used detailed figures such as the expression levels and their*

corresponding P values to describe the findings (see ***Page 3, line 46-49, 55-57***). *In the part of conclusion, we put forward some suggestions on the possible clinical implications of the findings* (see ***Page 3, line 59-62***).

Comment 3: In the introduction part of the main text, the authors need to briefly review known biomarkers associated with prognosis of pancreatic cancers, have comments on their limitations and knowledge gaps, and explain why GABRP is potentially useful and deserved to be studied. Please also have comments on the clinical need for this biomarker. The second issue is that the authors should explain why bioinformatics analysis is appropriate for answering the research question.

Reply 3: *Thank the reviewer for the constructive suggestions. We have briefly reviewed known biomarkers associated with prognosis of pancreatic cancers, have comments on their limitations and knowledge gaps and explain why GABRP is potentially useful and deserved to be studied* (see ***Page 4-5, line 77-84***). *We also have had comments on the clinical need for this biomarker and explain why bioinformatics analysis is appropriate for answering the research question* (see ***Page 6, line 105-108***).

Comment 4: Fourth, the methodology part is a little long and I suggest the authors to use a flowchart figure to indicate the study procedures.

Reply 4: *Thank the reviewer for the constructive suggestions. We have designed a flowchart to indicate the study procedures (see* ***Figure 1A***).

Comment 5: Finally, in the statistics part, please consider to exclude the confounding effects of other clinical factors when analyzing the prognostic role of GABRP. For the nomogram, please specify the training and validation samples, and clearly indicate the criteria for assessing a good nomogram.

Reply 5: Thank the reviewer for the constructive suggestions. We have further

elucidated the details of the construction of nomogram and the criteria for assessing a good nomogram (see ***Page 8-9, line 157, 169-177***).

Reviewer B

Manuscript "GABRP is a potential prognostic biomarker and correlated with immune infiltration and tumor microenvironment in pancreatic cancer" by Yang et al.

This study is mostly composed of analyses and correlation of different available datasets and databases. No novel data was generated or is presented. No verification analyses or real proof of some statements are included.

Dysregulation of GABRP in PDA has been described before.

The statement that GABRP is a prognostic biomarker is not supported by the data. To be a prognostic biomarker the marker should be only upregulated in PDA. Therefore, the expression in pancreatitis should also be investigated and included.

Thank the reviewer for constructive comments and suggestions! The enclosed revised version of our manuscript includes changes as reviewer suggested, as summarized below. All changes in the manuscript were underlined. We tried our best to answer all questions pointed by the reviewer.

Comment 1: This study is mostly composed of analyses and correlation of different available datasets and databases. No novel data was generated or is presented. No verification analyses or real proof of some statements are included.

Reply 1: *Thank the reviewer for the constructive suggestions. In the present study, we comprehensively and systematically integrated multiple omics data about pancreatic cancer from multiple authoritative databases and utilized bioinformatics analysis to analyze the expression profile, clinicopathological characteristics and potential molecular mechanism of GABRP in pancreatic cancer. For the first time, we elucidated the potential mechanism of GABRP dysregulation and GABRP might participate in regulating pancreatic tumor infiltrating cells and tumor microenvironment, which*

further confirm the important role of GABRP as a prognostic biomarker and therapeutic target in pancreatic cancer as well as a possible regulator of tumor microenvironment affecting the efficacy of immunotherapy. Furthermore, the result of IHC had proved the upregulation of GABRP in PAAD, which was a verification for our bioinformatic analysis. In the future, we will further verify the epigenetics regulation of GABRP expression level and deepen the underlying mechanism of the specific interaction between GABRP and immune infiltration and tumor environment.

Comment 2: The statement that GABRP is a prognostic biomarker is not supported by the data. To be a prognostic biomarker the marker should be only upregulated in PDA. Therefore, the expression in pancreatitis should also be investigated and included.

Reply 2: *Thank the reviewer for the constructive suggestions. We have investigated the expression of GABRP in pancreatitis using the data in GEO database and the result showed that no significant change in the expression of GABRP in pancreatitis. The corresponding data was presented in Supplementary table 1.* (See ***Supplementary table 1, Page 7, line 129-135 and Page 13, line 268-270***).