

Dear editor,

RE: Manuscript 66604

We would like to thank the World Journal of Gastroenterology for giving us the opportunity to revise our manuscript.

We thank the reviewers for their careful read and thoughtful comments on previous draft. We have carefully taken their comments into consideration in preparing our revision, which has resulted in a paper that is clearer, more compelling, and broader.

We appreciate for all your valuable advice and the manuscript have been edited by a professional English team at MedE Medical Editing Group recommended by the science editor. The edited paper has reached grade A in language evaluation, and the proof of editing has also been submitted on the system. The revised manuscript based on the comments of reviewers and editors has been submitted.

Below is our point-by-point response to the referee's comments.

1st Revision – authors' response

To reviewer #1:

We want to begin by thanking Referee #1 for writing that “This is a promising idea based and methodologically well-organized research”. We also appreciated the constructive criticism and suggestion. We addressed all the points raised by the reviewer, as summarized below.

- 1. Comments:** The introduction is unproportionably extended. An excessive information addressing Materials and Methods should not be placed here; as well as some basics of immunology...

Response: Thanks for reviewer's consideration for the structure. Based on the

suggestion, **1)** We completely agree with this valuable suggestion about the “ Materials and Methods should not be placed here; as well as some basics of immunology” by the reviewer. And since that’s not necessary here, we delete it. **2)** We have made appropriate adjustments to paragraphs 4 and 5 of the introduction based on the suggestion 'Authors' considerations on the role of investigated variables in pathogenesis of AP should be reserved for Discussion section, not for the Introduction. ”

- 2. Comments:** In the Discussion section the authors have to concentrate discussing results of the study avoiding basic details on specific roles of Th1 and Th2 cells. Repetitions... some statements duplicate ones from the Introduction section The Discussion section appears as a repetition of the Results and speculations, not based on data from other research papers. A further collection of statements from other research publications is presented. A clear “story” of the presentation in the Discussion section is lacking.

Response: **1)** We have concentrated the discussion based on the results and removed basic details on specific roles of Th1 and Th2 cells. **2)** We have added the paragraph 2 of discussion based on data from other research papers. **3)** And we have made a lot of changes to the discussion to present a clear “story” in the discussion section .

- 3. Comments:** Thirdly, in the cases of pancreatitis combined with cholecystitis, cholecystitis might affect the results of the study. - an interesting point. No data has been provided on the rate of acute cholecystitis in the investigated cohort. There is usually no association between acute pancreatitis and acute cholecystitis; biliary stones should be addressed instead.

Response: Many thanks to the reviewer for pointing out this in the article, it is really an interesting point. Cholecystitis and pancreatitis, although being the two

commonest gallstone-related conditions, these cholecystitis and pancreatitis rarely occur concurrently. Thus there are only limited reports in the literature. Nevertheless, recent pathological and radiological studies have demonstrated their concomitant occurrence may be much higher than thought to be, the majority of the concomitant cases may be subclinical. In our research, we have added the incidence of acute cholecystitis with AP in the results and table1 and addressed biliary stones instead. The incidence of acute pancreatitis with acute cholecystitis in our study is 4.8% and there was no significant difference between the groups for cholecystitis.

- 4. Comments:** The Conclusions are too straightforward considering the study limitations as proposed by the authors.

Response: Thanks reviewer for this kindly suggestion and many thanks to the reviewer for the careful consideration of our conclusion. After careful consideration, we modify the conclusion of this study to " In conclusion, the present findings demonstrated that the serum concentration of sST2 may be related to severity of AP, which revealed that elevated sST2 may be used as a novel inflammatory marker in predicting the severity of AP. On the other hand, we found an immune imbalance of Th1 and Th2-related cytokines in AP patients, suggesting sST2 might regulate the function of IL-33/ST2L-mediated Th1 and Th2 lymphocytes in the homeostasis of AP."

- 5. Comments:** The function of Th1 and Th2 cells has been investigated but not the cell numbers...

Response: Thanks to reviewer for putting forward such a serious question. This is one of the limitation of this study, we have pointed this in the discussion, and in our future work, we will pay more attention to the cell numbers.

- 6. Comments:** English language needs editing throughout the manuscript, especially in the Discussion section.

Response: We have had the manuscript edited by the professional English editorial team and submitted proof of editing on the system.

To reviewer #2:

We appreciate for the Referee #2's constructive and valuable suggestion. We addressed all the points raised by the reviewer as summarized below.

1. **Comments:** Please avoid abbreviations in the Tables and figures because they need to be self-explaining.

Response: We have modified the abbreviation accordingly.

2. **Comments:** The literature should be updated and revised according to the policy of the journal

Response: We have updated and revised the literature according to the policy of the journal.

To Editorial Office's comments

To Science editor:

We want to thank Science editor for constructive and insightful criticism and advice. We addressed all the points raised by the editor as summarized below.

1. **Issues raised:** The language classification is Grade C. Please visit the following website for the professional English language editing companies we recommend:
<https://www.wjgnet.com/bpg/gerinfo/24>

Response: We appreciate for all your valuable advice and the manuscript have

been edited by MedE Medical Editing Group recommended by the editor. The edited paper has reached grade A in language evaluation, and the proof of editing has also been submitted on the system.

2. **Issues raised:** The title is too long, and it should be no more than 18 words.

Response: Many thanks to the reviewer for this constructive comment. We have amended the title to "Serum soluble suppression of tumorigenicity 2 as a novel inflammatory marker predict the severity of acute pancreatitis". It is 17 words in total.

3. **Issues raised:** The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

Response: We have submitted proof of the approved grant application form on the system.

4. **Issues raised:** The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor

Response: We have submitted the original figures using PowerPoint.

5. **Issues raised:** PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Response: We have added the PubMed numbers and DOI citation numbers to the reference list and listed all authors of the references.

6. Issues raised: The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text

Response: We have added the “Article Highlights” section at the end of the main text.

To Company editor-in-chief:

We thanks the editor for giving us the opportunity to revise our manuscript.

Issues raised: Before its final acceptance, please upload the primary version (PDF) of the Institutional Review Board’s official approval in official language of the authors’ country to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Response: We have uploaded the primary version (PDF) of the Institutional Review Board’s official approval in official language of our country to the system.

Thanks for all the help.

Best wishes,

Yours sincerely,

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Dear editor,

RE: Manuscript 66604 for RevisionReviewReport

We thank the World Journal of Gastroenterology for considering our revision of our manuscript.

Below is our point-by-point response to the reviewer's comments.

- 7. Comments:** However, the length of the “Introduction” remains excessive. I would suggest shortening it and highlighting the idea of your project. Similarly Methods should not be mixed with the aim of study at the end of the Introduction: ... “In this study, we investigated whether the IL-33/ST2L pathway was involved in AP in patients with different clinical severity of AP. sST2 and IL-33 were measured in patients enrolled between January 2018 and August 2020. Expression levels of Th1- and Th2-related cytokines were detected for better understanding the mechanism of the IL-33/ST2L pathway.”

Response: Thanks for reviewer's valuable advice, considering the length of the “Introduction” remains excessive and similarly methods should not be mixed with the aim of study at the end of the Introduction , we delete the methods mixed in the “Introduction” based on the comments.

- 8. Comments:** In The conclusions in the abstract and body text have the same meaning; however wording is different and at the end of the manuscript imprecise and too complicated. I would suggest to use the “Abstract version” of the Conclusions. CONCLUSION (abstract) sST2 may be used as a novel inflammatory marker in predicting AP severity and may regulate the function and differentiation of IL-33/ST2-mediated Th1 and Th2 Lymphocytes in AP homeostasis. CONCLUSION (body text) In conclusion, the present findings demonstrated that the serum concentration of sST2 may be related to severity of AP, which revealed that elevated sST2 may be used as a novel inflammatory

marker in predicting the severity of AP. On the other hand, we found an immune imbalance of Th1- and Th2-related cytokines in AP patients, suggesting sST2 might regulate the function of IL-33/ST2L-mediated Th1 and Th2 Lymphocytes in the homeostasis of AP.

Response: Thanks for reviewer's suggestion for the conclusions in the abstract and body text. Based on the reviewer's comments, we use the "Abstract version" of the Conclusions in the body text section.

Thanks for all the help.

Best wishes,

Yours sincerely,

Changju Zhu, MD, Ph.D.

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Zhengzhou University**

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