

ROUND 1

Dear Editors and Reviewers,

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "TATA-box-binding protein-associated factor 15 is a Novel Biomarker that Promotes Cell Proliferation and Migration in Gastrointestinal Stomal Tumors". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Reviewer:

1. Responds to the reviewer's comments: This study initially implements a proteomic analysis to find new molecular therapeutic targets for GIST and discusses the expression level and underlying biological function of TAF15 in GIST. It point out that TAF15 would be a novel molecular biomarker for therapeutic targets of GIST. This brings new hope for the treatment of GIST. It's an interesting research direction.

Response: We appreciate it very much for your warm work earnestly, and it is my great honor to receive your recognition for this work!

Editor:

1. Response to comment: Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

Response: Thank you for this suggestion. We have uniformed the presentation for figures in the revised text.

2. Response to comment: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: Thank you for pointing this out. We have provided decomposable figures and organized them into a single PowerPoint file.

3. Response to comment: 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: Thank you for pointing this out. We have corrected standard three-line tables in the revised text.

4. Response to comment: 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: Thank you for this suggestion. All of the figures are original, and we have added the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright © Cheng-Ming Guo, Li Tang, Xu Li, Liu-Ye Huang 2022.

5. Response to comment: Before final acceptance, 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.

Response: We would like to thank you for your kind comments, and we supplemented and improved the highlights of the latest cutting-edge research results that are marked in red in the revised text. In addition, the manuscript has been sent out for language polishing.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

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

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

Sincerely

Liuye Huang

Dear Editors and reviewers,

Thank you for your letter and for your comments concerning our manuscript (ID: 81899). Those comments are very helpful for revising and improving our paper! We have studied comments carefully and have made responds which we hope meet with approval. The responds to the editor's and reviewer's comments are as flowing:

1. Response to comment: When selecting GIST cases, does the author have requirements for the number of cases classified as high risk, medium risk, low risk and very low risk?

Response: We appreciate the reviewers for this kind comment. We admit that we have requirements for the number of cases classified as high risk, medium risk, low risk and very low risk when selecting GIST cases. Because we plan to analysis the differentially expressed proteins in subgroup, and at least 3 cases per subgroup were required for statistical analysis. Therefore, in the beginning we only collected 12 matched samples (including 3 high risk paired cases, 3 medium risk paired cases, 3 low risk paired cases and 3 very low risk paired cases), which were sent for proteomic analysis, followed by another 6 matched samples (including 3 high risk paired cases and 3 medium risk paired cases). However, the small sample size used for this study was due to the difficulty of collecting paired GIST tumour specimens, which might affect the accuracy of some data. In further studies, we will validate some data through western blotting assay in larger GIST cohorts.

2. Response to comment: Whether all pathological tissues are surgical gross specimens or biopsy specimens; If there is biopsy tissue, will it affect the results?

Response: Thank you for pointing this out. All pathological tissues are surgical gross specimens from the Department of Gastrointestinal Surgery, Yantai Yu Huang Ding Hospital of Qing Dao University. The GIST patients with high risk and medium risk were more than that with low risk and very low risk in the Department of Gastrointestinal Surgery, therefore we collected 6 high risk paired cases and 6 medium risk paired cases, while, only 3 low risk paired cases and 3 very low risk paired cases, respectively.

We appreciate Editors and Reviewers' warm work earnestly, and hope that the reply will meet with approval.

Sincerely

Liuye Huang

ROUND 2

Dear reviewer,

Thank you for your comments concerning our manuscript entitled “TATA-box-binding protein-associated factor 15 is a Novel Biomarker that Promotes Cell Proliferation and Migration in Gastrointestinal Stomal Tumors”. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to comments are as flowing:

Responds to the reviewer’s comments:

1. Response to comment: Why were other targets showing higher fold-change or statistical significance (Table-2) not considered? Was the selection of TAF15 as a target premeditated even before the execution of the study and start of experiments? If the decision was based on prior reported literature, a stronger justification must be provided, with support from relevant references.

Response: Thank you for pointing this out. In fact, our research team have studied all of the top 10 up-regulated proteins, including COL4A5, LY6H, HMGN2, HMGN4, FLG, HMGA2, B3GNT9, TAF15, AGFG2, UCHL1. Because of time, energy and other factors, each team member studied one protein respectively, and the doctoral tutor assigned TAF15 to Cheng-Ming Guo for further study. So far, the studies of other top 10 up-regulated proteins have yielded a great number of positive results. Now we want to publish the research results of TAF15 first because Cheng-Ming Guo will graduate with his MD in June this year. Further study, we also will conduct research of all of the top 10 down-regulated proteins.

Therefore, the selection of TAF15 as a target was not premeditated before the execution of the study and start of experiments, and it's part of our research.

In addition, we agree with the reviewer's suggestion, and added some relevant references in the introduction section (page 6, lines 13 to 21) to support the reason of the selection of TAF15 for further study.

2. Response to comment: In the methodology, it is stated that the human subjects were enrolled between March 2020 to June 2022. When was the Ethical clearance for use of human subjects/material taken from the relevant authorities/Committee? At present the document No.2022–48 submitted pertains to use of animals and not human subjects and is dated 13th May 2022. It must be provided, clearly showing that the Ethical clearance was obtained BEFORE sample collection.

Response: Thank you for this suggestion. We have been approved for an Ethical clearance for human subjects on 31st November 2019, and the Ethical clearance was uploaded.

3. Response to comment: The Core Tip matches exactly with sentences in the Abstract section, it may be re-worded emphasizing on the gist and key takeaways from the study.

Response: Thank you for pointing this out. We have revised the Core Tip (page 4, lines 19 to 27), and we hope that could highlight the innovative points of the study.

4. Response to comment: Few sentences in the last paragraph of the Introduction section describing the results & data may be removed.

Response: Thank you for this suggestion. We have removed the sentences in the last paragraph of

the Introduction section describing the results & data (page 6, lines 23 to 26).

5. Response to comment: In Discussion, more information about previous studies on GIST including other biomarkers/ targets must be included with references. Also, some more information on FAT15 may be included either in the Introduction or Discussion section.

Response: We would like to thank you for your kind comments, and we added more references about other biomarkers/ targets for GIST that are marked in red in discussion section (page 16, lines 1 to 15), and also added some more information on FAT15 that are marked in red in Introduction section (page 6, lines 13 to 21).

6. Response to comment: Conclusion section needs major changes; the last few sentences of this section need to be broken into two or more separate sentences.

Response: Thank you for your kind suggestion, and the last sentence of conclusion section have been broken into three separate sentences in the revised text (page 18, lines 7 to 11) .

7. Response to comment: While the methodology and data presented in the results section study look interesting, the authors may consider revising or rewriting other sections of the manuscript to enhance its quality. At present, there are several grammatical errors and few sentences look incomplete. For example (specific to the entire text of the manuscript):a). At several points throughout the manuscript, there is a confusion on the plural or singular form of GIST and the subsequent use of "is" or "are". It is recommended that GIST may be referred to the singular form, followed by use of "is" and plural may be abbreviated as GISTs, to be followed by "are". These changes need to be made throughout the text of the manuscript. b). "in vivo" must be italicized at all places in the manuscript. Section-wise minor corrections to be addressed: In the Abstract: a) The word "understand" may be incorporated between the words "and" and "the" in AIM of the Abstract. b) Replace "a unmet" with "an unmet" in Background section c) Replace "inhibit" with "inhibited" and "decrease" with "decreased" in the Results section d) "GIST tumor tissues" may be replaced by "GIST tissues" in Conclusion. In the Introduction:a) In Line No. 10, "Indeed" may be replaced by "In fact"b) In the sentence " Before the clinical application of imatinib of patients was only 27–34%", is the highlighted word correct or is some text missing? Otherwise, it may be changed to "by".c) In the following phrases, a word or some text appears missing "been highly effective life of GIST " and "high rate drug"d) "large unmet need" may be changed to "critical" or "important".Methodology: a) Due reference for "Chinese clinical guidelines" may be provided. b) In the paragraph for Western blotting, "1 h" may be changed to "1 hr" to maintain uniformity.c) In the paragraph for Modeling of GIST xenografts in nude mice "4 wk" may be written as "4 weeks". Discussion: a) "in recent years" in the first sentence may be removed or due references to recent papers may be added. b) In the second sentence, "Our study performed a proteomic analysis in patients" may be changed to "In the present study, proteomic analysis was performed in patients" c) "As a result" may be removed. d) The word "discovered" may be replaced by a more appropriate word as the study was not focussed on discovery of any new proteins.e) "confirmed" may be replaced by "confirm" Research. objectives: a) "GIST progress" may be changed to "GIST progression" These are some of the errors that I could find. Efforts must be made to find and correct any other grammatical and/or language errors. In conclusion, I feel that it is an interesting and relevant study and after making the necessary corrections and addressing the concerns/queries, it should appeal to the readers of WJG.

Response: We would like to thank you for your kind comments, and we have revised grammatical errors of the whole manuscript, especially revised errors as follows:

- a) revised the plural or singular form of GIST and the subsequent use of "are" or "is" throughout the text of the manuscript.
- b) italicized "in vivo" at all places in the whole manuscript.
- c) incorporated the word "understand" between the words "and" and "the" in AIM of the Abstract.
- d) replaced "a unmet" with "an unmet" in Background section.
- e) replaced "inhibit" with "inhibited" and "decrease" with "decreased" in the Results section.
- f) replaced "GIST tumor tissues" with "GIST tissues" in Conclusion.
- g) replaced "Indeed" with "In fact" in Line No. 10 in the Introduction.
- h) some words missed in the sentence "Before the clinical application of imatinib of patients was only 27–34%", and we have added the missed words that marked red in the revised text (page, lines).
- i) In the following sentence, "the life of GIST patients who had developed metastasis and even then, the 5-year overall survival (OS)" was redundant, therefore, we have deleted them (page, lines).
- j) replaced "a large unmet need" with "critical" in the Introduction section (page, lines).
- k) added the reference for "Chinese clinical guidelines" (page, lines)
- l) changed "1 h" to "1 hr" in the paragraph for Western blotting.
- m) changed "4 wk" to "4 weeks" in the paragraph for Modeling of GIST xenografts in nude mice.
- n) removed the first sentence in the discussion section (page, lines).
- o) "Our study performed a proteomic analysis in patients" was changed to "In the present study, proteomic analysis was performed in patients" in the second sentence in the discussion section.
- p) "As a result" was removed in the third sentence in the discussion section.
- q) replaced "discovered" with "revealed" in the third sentence in the discussion section.
- r) replaced "confirmed" with "confirm" in the discussion section (page, lines).
- s) changed "GIST progress" to "GIST progression" in the whole manuscript.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate Reviewer's warm work earnestly, and hope that the correction will meet with approval.

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

Sincerely

Liuye Huang