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OPEN PEER REVIEW

In Silico and Experimental Analyses of Long Non-coding RNA *TMPO-AS1* Expression in Iranian Patients with Gastric Cancer

Elaheh Mohammadali, Reza Safaralizadeh, Arash Poursheikhani, Tooraj Asvadi, Shahram Teimourian, Behzad Baradaran

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1 Original submission

0 comments

No public comments in this round.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editor

Thank you very much for reviewing our manuscript (**130586**) entitled **"In Silico and Experimental Analyses of Long non-coding RNA TMPO-AS1 Expression in Iranian Gastric Cancer Patients"**. The authors would like to also thank the distinguished referees who diligently reviewed our paper. We all appreciate their valuable comments, and have implemented their suggestions to the best of our ability. Please find below our responses to the reviewer's comments with changes within the attached revised version of the manuscript in highlighted format. Hope this is to you and reviewers satisfaction.

Sincere thanks,

Reviewer 1:

The article (In Silico and Experimental Analyses of Long non-coding RNA TMPO-AS1 Expression in Iranian Gastric Cancer Patients. ID: 130586) has very poorly written with repetitive sentences. The introduction and discussion need essential revision.

Abstract:

Introduction:

1. Explain the relationship of TMPO-AS1 with gastric cancer.

Relevant explanations were written in the introduction section.

Material and Methods:

2. The characteristics of the examined samples should be explained

It was written both in the text in the methods section and in table 1.

Results:

3. In the results should be written the result of the analysis between gene expression and demographic information.

In the results section, it was written both in the text and in Table 3.

Conclusion:

4. The role of the TMPO-AS1 biomarker is determined by examining the ROC curve. The author should be rewritten this part.

The content related to the ROC curve was included in the abstract, materials and methods, results, discussion, and conclusion. The ROC curve is displayed in Figure 2.

Introduction:

5. Remove the repetitive words and sentences that are used in the introduction.

The sentences repeated in the abstract and introduction were corrected.

6. Referencing in the entire article should be corrected.

References have been corrected.

The author must explain the function of TMPO-AS1 and its role in carcinogenesis.

It was explained in the introduction and discussion.

7. Explain why was hypothesized that TMPO-AS1 is associated with gastric cancer.

It was written in the introduction.

Material and methods:

8. The inclusion and exclusion criteria should be stated in the article.

Descriptions related to this section have been added.

9. Which formula was the sample volume obtained from this project?

The sample volume was selected according to similar studies that examined gene expression on gastric cancer samples with the same number. Also, according to the inclusion and exclusion criteria of the study, we could only sample a limited number of patients who underwent surgery in the hospital during the research period. In addition, our work is a preliminary study, and more research (with more samples and different laboratory tests such as cell culture and animal studies) is needed to reach more reliable results.

10. The volume of the qRT-PCR reaction should be expressed by the concentration of the substances.

This information was placed in the text.

11. The conditions for the replica of both genes should be explained separately.

It was written separately for each gene in the text.

12. To state the purpose of bioinformatics analysis and how was related to qRT-PCR.

In this study, *TMPO-AS1* overexpression was observed in gastric cancer by analyzing the results of the qRT-PCR method. To confirm the correctness of this study, we also analyzed the prepared databases in The Cancer Genome Atlas, a landmark cancer genomics program, molecularly characterized over 20,000 primary cancer and matched normal samples spanning 33 cancer types.

Results:

13. How was TCGA information obtained? Be explained.

We used ready databases in The Cancer Genome Atlas and analyzed the data using GEPIA and TANRIC online tools.

14. In line 118, TMPO-AS1 expression was not related to stage and differentiation, but it was significant with Lauren's classification. Why?

It can be due to the limited number of samples and differences in the number of different groups.

15. Table 2 does not show TMPO-AS1 expression and demographic information. What was your mean the values of Low and High and on what basis were they divided?

Table 3 shows the results of analyzing the correlation between *TMPO-AS1* expression ($2^{-(\Delta\Delta CT)}$) and demographic and clinicopathological data. The patients were divided into two groups (high expression and low expression) according to the Median expression of *TMPO-AS1*.

16. The statistical analysis of the results needs to be revised.

The statistical analysis of the results was revised.

17. In Figure 1, use the terms control and case are not appropriate. Change according to the description of the abstract.

In Figure 1, the words tumor and tumor’s adjacent were written instead of control and case.

18. An explanation of figures 3 and 4 is added and p-values are marked with symbols on the graphs. Check the error bars.

P-values were added to Figure 4. In figure 5, P-values are written as P(HR) or hazard ratio p-value. (Since a figure related to the ROC curve

has been added to the article, the number of figures 3 and 4 has been changed to 4 and 5.)

Discussion:

19. The discussion begins by interpreting the research results.

The interpretation of research results was included in the discussion.

20. The discussion of repeating the contents is an introduction and the contents are not within the scope of the research.

The content in the discussion section was reviewed, and changes were made.

21. The results of the study should be compared with other similar and different studies.

In the discussion text, these explanations were added, and comparisons were made.

References:

22. References are very old. At least 5 new references should be added to the text and other items should be replaced with newer references.

References were revised, and six new references were added.

Reviewer 2:

In the present study, the authors aimed to assess the expression of lncRNA TMPO-AS1 in Iranian gastric cancer (GC) patients. A total of 40 gastric tumor samples and 40 marginal noncancerous counterparts were recruited and evaluated by qRT-PCR analysis. They also retrieved TCGA data for TMPO-AS1 and analyzed via Gepia and TANRIC online tools. According to the oncogenic role of TMPO-AS1 in different kinds of human cancers, the approach is relevant. However, the authors are invited to revise the manuscript according the following comment:

In the present study, the authors concluded that lncRNA TMPO-AS1 could be considered as a biomarker in GC

To consider TMPO-AS1 as a biomarker, it is necessary that an ROC analysis is performed and assessed both the sensitivity and specificity performance of a biomarker test signal. In this regard, AUC represents the degree or measure of separability.

The part related to the ROC curve and its results were added in the text of the article and Figure 2.

Reviewer 3:

Dear Editor

The manuscript is written scientifically and is interesting. It meets all criteria of the journal.

I think it is worth publication.

2 Revision 1

1 comment · 23 Nov 2022

Associate Editor

MINOR REVISION 23 Nov 2022

Dear authors,
Thank you for revising your manuscript. It seems that some parts of Table 1 have been omitted. Please correct this table and submit your manuscript again.

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editorial Board of ***International Journal of Cancer Management***,

Thank you for sending the reviewer's comment and inviting revision and resubmission of our manuscript entitled "In ***Silico and Experimental Analyses of Long non-coding RNA TMPO-AS1 Expression in Iranian Gastric Cancer Patients***". The manuscript was revised in accordance with the suggestion of the associate editor and the question was addressed. All the parts related to the revision request are highlighted in yellow in the main manuscript. We hope the manuscript is now acceptable.

Yours Sincerely,

Dr. Reza Safaralizadeh

Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.

Associate Editor 1:

Dear authors, Thank you for revising your manuscript. It seems that some parts of the table 1 have been omitted. Please correct this table and submit your manuscript again.

Comment: It seems that some parts of the table 1 have been omitted. Please correct this table and submit your manuscript again.

Response: We would like to thank the associate editor for the careful and thorough reading of this manuscript. In line with the first revision, Table 1 was changed. In this way, the clinicopathological characteristics of patients were displayed in Table 1 in the methods section. Additionally, the results of analyzing the correlation between *TMPO-AS1* expression and demographic and clinicopathological data are shown in Table 3 in the results section.

3 Revision 2

0 comments

No public comments in this round.