Peer Review File

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Reviewer A

The association between immunological features and the survival of cancer patients have been reported numerously in the literature. The authors are mostly relying on external tools to calculate the scores of immunological features/TILs. I don't see any novelty about the analysis between the immunity and survival of TNBC patients.
The authors proposed a TMErisk score, but they didn't show the superiority to previously reported TME scores (such as the ESTIMATE scores used in this study) in terms of predicting the prognosis, and therefore the TMErisk score is not providing much significance to this study.
The methods, conclusion, and even some of the figures are very similar to "ATP2C2 Has Potential to Define Tumor Microenvironment in Breast Cancer" published in 2021.
https://www.frontiersin.org/articles/10.3389/fimmu.2021.657950/full
Although the above study discusses the association between ATP2C2 and breast cancer in general, they did not discuss the influence of ATP2C2 specifically in TNBC. Therefore, this study is novel and valuable in terms of their analysis on TNBC datasets and IHC study of samples from TNBC patients.
This manuscript should be proofread by the authors before being published. There are many typos especially in the terms around the scores.

Specific comments:

Comment 1: The explanation about the TMErisk score is insufficient. There should be an explanation about how the expression data was normalized and converted into a coefficient.
Reply 1: Thanks for your comment, we have added an explanation about TMErisk.
Changes in the text: See Page 6-7, line 122-127; page 10-11, Line 207-210 and Supplementary table 1.

Comment 2: I didn't understand how to read Fig3C. Is the x-axis corresponding with Fig3A? Is the color corresponding with Fig3A? It seems that there are more green dots than the red dots. What does these color mean?
Reply 2: Thanks for your comment. First of all, I am very sorry that legend of Fig.3A and Fig.3C are not clearly marked. The x-axis in Fig. 3C is corresponding with the Fig. 3A, but the red and green dots in the figures represent different meanings. In Fig. 3A, the red dots represent high-risk groups, and the green dots represent low-risk groups. However, the red dots represent dead patients, and the green dots represent alive patients in Fig. 3C. We have redrawn the figures and added the legends in Fig.3A-3D.
Changes in the text: See Fig 3A-3D.

Comment 3: The red line is missing in Fig3H.

Reply 3: Thanks for your comment, about the ROC curve in Fig. 3H, data analysis showed that the 3-year and 5-year AUC values of patients were exactly the same in GSE25055 database. The ROC figure showed that the two curves were coincident, so only blue line was displayed.

Comment 4: Fig4A: the label for the y-axis is missing
Reply 4: Thanks for your comment, we added the label of y-axis in Fig.4A.
Changes in the text: See the Fig.4A

Comment 5: Fig4B: The graph is stretched. The label about BRCA is not located properly. It seems that all the figures on Fig 4 is stretched.
Reply 5: Thank you very much for your comments. We carefully reviewed the Fig.4B, found that the label about BRCA was redundant, and removed it. The ratios of all the figures on Fig. 4 were adjusted.
Changes in the text: See the Fig.4

Comment 6: Fig 5A and Fig 5L is showing a MicroenvironmentScore which is not mentioned in the manuscript. Is this the TMErisk score? Please provide necessary information.
Reply 6: Thanks for your comment. MicroenvironmentScore is not TMErisk score in Fig. 5A and Fig. 5L. This score is calculated by using "xCell" R package for immune infiltration analysis. We added the information about MicroenvironmentScore in the manuscript.
Changes in the text: See Page 12-13, line 249-253.

Comment 7: Figures in Fig6 is also stretched. Please check the entire manuscript and check the quality of the figures.
Reply 7: Thanks for your comment, we have checked and revised all figures in the manuscript.
Changes in the text: See all the figures.

Comment 8: In the discussion, the authors are claiming that "the greater the score of the three genes, the worse the prognosis". This is probably not correct since P3H2 is correlated with favorable prognosis.
Reply 8: Thanks for your comment, I'm sorry that we made an error about this sentence. In our manuscript, P3H2 was showed to be correlated with favorable prognosis. However, TMErisk model of SCN3B, ATP2C2 and P3H2 genes was constructed, and the greater the score of the TMErisk model, the worse the prognosis. We have modified "the greater the score of the three genes, the worse the prognosis" to "According to K-M plot analysis, the greater the score of the TMErisk model, the worse the prognosis".
Changes in the text: See Page 14-15, line 292-293.

Comment 9: K-M plots: The label for the y-axis is saying it is in % but the graph is not showing the probability as percentage. This is seen in all K-M plots in the manuscript.
Reply 9: The y-axis of the K-M plots represents the survival probability, while the x-axis represents the survival time of patients in the high and low groups. Each point on the K-M curve represents the patient's survival probability at that point in time. When the x-axis was 0, follow-up had just begun and no patients had died, so the survival rate was 100% in both groups. For

example, in Fig. 5I, at the 60th month of the x-axis, the corresponding y-axis point was about 0.8 in the low-risk group (blue curve), which showed that the survival probability of patients in the low-risk group was 80% at the 60-month follow-up (Figure 3I). We also described the survival probability of patients in the results section of the manuscript (Page 11, line 215-218)

Comment 10: The term ESTIMATEScore is sometimes used as ESTIMATE score or Estimate score. I also saw a typo as ESTAMEScore. Please check the whole manuscript and use the same format. ImmuneScore is sometimes shown as Immunescore.

Reply 10: Thanks a lot for your comment, we have reviewed the full manuscript and revised "ESTAMEScore" to "ESTIMATEScore", and modified "Immunescore" to "ImmuneScore".

Changes in the text: See Page 10, line 192,195-196; Page 14, line 283.

Reviewer B

This manuscript describes the potential of ATP2C2 as a novel immune-associated marker in the microtumor environment of triple negative breast cancer. This is thought to be an important data as a new biomarker for the diagnosis of TNBC, and is very interesting. Therefore, this paper is suitable for publication in the TCR journal.

Reply: Thank you for your comment and suggestion concerning our manuscript.