Peer Review File

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Review Comments

The paper titled “Pan-cancer prognostic model and immune microenvironment analysis of natural killer cell-related genes” is interesting. In this study, 63 prognostic solid tumor markers were investigated using NK cell-related genes, and for the first time, a pan-cancer prognostic model was constructed to analyze their role in the immune microenvironment, which may contribute new insights into tumor research. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) The background did not indicate the clinical needs for this research focus, and needs further revisions.

2) What valuable insights can this study provide for personalized medication? Suggest adding relevant content.

3) What is the relationship between NK cell-related genes and tumor-infiltrating immune cells? What role does NK cell-related genes play in prognosis in tumor? It is recommended to add relevant content.

4) Some fonts need to be enlarged, as shown in Figures 2,5,7,8.

5) What is the greatest advantage of the prognostic model in this study? What is the biggest problem we are facing? It is suggested to add relevant content to the discussion.

6) This study is based on bioinformatics analysis. It is recommended to increase in vivo and in vitro experimental studies, which may be more meaningful.

Reponses:

1) We have revised the Introduction section to provide a more detailed overview of the current research status of NK cell-based tumor immunotherapy and to clarify the clinical need addressed by this paper (see Page 3-4, line 87-113).

2) We have modified our text as advised (see Page 3-4, line 113-117).

3) Disappointedly, we did not conduct an analysis related to NK cell-related genes and tumor-infiltrating immune cells. Our primary focus was on analyzing the relationship between NK cell-related genes and tumor prognosis, which we provided further interpretation in the "Analysis of the immune microenvironment and prognosis of core genes" section (see Page 8, line 282-291).

4) We have revised the figures as advised (see [Figure 2] Page 17, line 580; [Figure 5] Page 20, line 623; [Figure 7] Page 22, line 648; [Figure 8] Page 22, line 658; [Figure S1] Page 31, line 713-721).

5) We have emphasized this point in the conclusion section. Following your suggestion, we have further refined the advantages and issues addressed in this paper (See Page 12,

line 414-426).

6) We greatly appreciate your suggestions. Regrettably, due to a lack of external support, we were unable to conduct in vivo and in vitro experiments. Nevertheless, two genes identified in this study, ASPM and DEPDC1, exhibit promising potential for further experimentation, as elaborated upon in the Discussion section (See Page 10-12, line 344-410).