Peer Review File

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Reviewer comments

The paper titled "The emerging role for CAR T cells in solid tumor oncology" is interesting. These technological developments will hopefully lead to enhanced clinical activity and improved patient outcomes in the near future. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) CAR T-cell therapy is an emerging option for cancer treatment, but its efficacy is limited, especially in solid tumors. This is partly because the CAR T cells become dysfunctional and exhausted in the tumor microenvironment. What are the key pathways responsible for impaired function of exhausted cells? It is suggested to add relevant contents.

   Reply: We thank the reviewer for this important note. We already discuss certain aspects of the tumor microenvironment in the original manuscript (see line 320-366). Since we wanted to focus in our review on relevant aspects for more direct clinical translation, we only addressed the most important mechanisms.

2) What role does the CAR T cell amplification program play in overcoming the immune metabolic barrier in tumor microenvironment? It is suggested to add relevant contents.

   Reply: We discuss aspects of the expansion and persistence of CAR T cells from line 270 to 318.

3) What are the functions of the chemokine/chemokine receptor axis in cancer immunity? What are the challenges and prospects for improving the effect of chimeric antigen receptor T cells by reversing the mismatch between chemokines and chemokine receptors? It is suggested to add relevant contents.

   Reply: We agree with the reviewer on the importance of chemokines and chemokine receptors, which is why we already included a part on this topic in the original manuscript (see line 325-330). As mentioned above, we put a focus on approaches which are already closer to clinical translation.

4) What are the effects of high glucose consumption and the competition for key amino acids by tumor cells on T cell energy? It is suggested to add relevant contents.

   Reply: We already included a part on glucose metabolism in the original manuscript (see line 355-366). As mentioned above, we put a focus on approaches which are already closer to clinical translation.

5) How does nanotechnology promote CAR-T treatment? It is suggested to add relevant contents.

Reply: We thank for the interesting suggestions, however, to keep the review more focused we decided not to include this topic into the manuscript.

6) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “A narrative review of chimeric antigen receptor-T (CAR-T) cell therapy for lung cancer, PMID: 34268421”. It is recommended to quote the article.

Reply: The suggested reference was added to the manuscript.
Changes in the text: See line 54, reference 8.

7) How to enhance the specificity and safety of CAR T cell therapy? What is the important information about the application of CAR T cells in solid tumors today and in the future? It is suggested to add relevant contents.

Reply: We discuss the specificity and safety, as well as how to improve it in the future in the manuscript from line 250 to 267.