

Dear Editor Anonymous,

I am the author of this manuscript named “**Therapeutic challenge for immunotherapy targeting cold colorectal cancer: A narrative review** (Manuscript ID: 80224)”. It is a great honor to receive an email from your journal that my manuscript has been evaluated and needs to be revised. Thank you!

In accordance with the reviewers' comments, we have made huge revisions. The revised manuscript has been resubmitted in the submission system. We also answer the questions raised by the reviewer as follows:

1. The title does not indicate the manuscript is a review article.

Answer: We have added this item.

2. The review does not mention the methodology of the articles selected and the mode of selection.

Answer: We have added this item.

3. Any conflict of interest declared ?

Answer: We have added this item.

4. What does the review add to the existing knowledge?

Answer: We have added this item.

5. There is no concluding remarks noted in the manuscript

Answer: We have added this item.

6. It must indicate how the bibliographic review has been carried out and what type of review is being carried out. The sources where the references have been obtained, the search criteria...

Answer: We have added this item.

7. A discussion section should be included where the references found are systematized and the review is discussed: what are the lines of work, what advances are made on the above and where the next advances could go,...

Answer: We have added this item.

8. The main contributions of the research and the lines of future work must be included in the conclusions.

Answer: We have added this item.

9. In the middle of a "RELATED STUDIES BASED ON IMMUNE TARGET" section, the type of MSI must be defined. Is MSI low or high?

Answer: The type of MSI is low.

10. The review defined MSI-L type as a cold tumor. However, in the contents, only the research targeting the MSI-H type is described. The MSI-H type CRC is highly responsive to immunotherapy, therefore it could not be defined as a cold tumor. It is considered to be contrary to the purpose of this review.

Answer: We have added this item.

11. A summary of clinical studies to overcome immune resistance in patients with MSI-L colorectal cancer is needed.

Answer: We have added this item.

We are very cherish the opportunity to be published in your journal and look forward to hearing from you, thank you!

Best Regards,
Yours Sincerely,

Leisheng Zhang, MD,
Department of General Surgery, Gansu Provincial Hospital,
204 West Donggang R.D., Lanzhou, 730000, China,
leisheng_zhang@163.com,
ORCID ID: <https://orcid.org/0000-0001-6540-0943>;
Hui Cai and Tiankang Guo