Author’s response to reviews

Title: Tumor-infiltrating CD8+ T cells combined with tumor-associated CD68+ macrophages predict postoperative prognosis and adjuvant chemotherapy benefit in resected gastric cancer

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Author’s response to reviews:

Dear Editor:

We are grateful to the professional reviewers for their valuable comments and suggestions which help improve the quality of the paper. We have study the reviewers’ comments carefully and have made modifications and corrections which we hope meet their approval. We have revised the manuscript according to your kind advices and referee’s detailed suggestions. Here below is our description on revision.
Editor Comments:

If we are to consider publication of your manuscript, you will need to go over your manuscript text and rewrite it in original language. It currently contains an unacceptable overlap in text with previously published sources, particularly across the background, methods and discussion sections. If you are not able to improve this, we may be unable to consider it further for publication.

Response: We have rewritten the manuscript in original language to reduce the text overlap rate.

Reviewer reports:

Masaichi Ohira (Reviewer 1): Thank you for giving me the opportunity to review your manuscript again titled, "CD8+Tumor-infiltrating lymphocytes combined with CD68+ tumor-associated macrophages predicts postoperative prognosis and adjuvant chemotherapy benefit in resected gastric cancer".

This manuscript is well written and the author almost answered to my questions and comments courteously. I have one comment to the author.

As I mentioned for the first manuscript, in cancer microenvironment it is common to evaluate M2 macrophage than M1 macrophage or TAM for cancer progression. And CD163 antibody is usually used to evaluate M2 macrophage but not CD68 antibody. I recommend the author should estimate M2 macrophage using CD163 antibody instead of CD68. I hope the author will do the additional immunohistochemical examination using CD163 antibody.

Response: Thanks for your helpful comments. And we also agree that CD163 antibody is usually used to evaluate M2 macrophage. However, which type of macrophage has the greatest influence on the efficacy of chemotherapy for gastric cancer is still largely unknown [1]. CD68 has been widely reported as a specific marker of tumor-associated macrophages in cancer [1, 2, 3]. A recent report found that high amounts of CD68+ macrophages in tumor were associated with melanoma recurrence [3]. More importantly, complex tumor microenvironments are difficult to characterize using a single immune marker [1]. Nakanishi et al found that the CD68+ macrophage/CD57+ cell ratio was strongly correlated with pathological features and prognosis in renal cell carcinoma patients [4]. Therefore, the main purpose of this study was to explore the effect of a combination of TILs and TAMs on the prognosis and efficacy of chemotherapy for GC, rather than the effect of different types of macrophages on prognosis. However, we agreed that tumor-associated macrophages are not simply cells with single markers or restricted M1 or
M2 phenotypes; they are more diverse and heterogeneous. Further studies are required to determine the cross-interaction between diverse tumor-associated macrophages and the tumor microenvironment.

We have added the above contents to the “Discussion” section of the revised manuscript with red mark.

References:


Reviewer 2 (Reviewer 2): PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses one or several testable research questions? (Brief or other article types: is there a clear objective?)

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with sufficient technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately
STATISTICS - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Has the author addressed your concerns sufficiently for you to now recommend the work as a technically sound contribution? If not, can further revisions be made to make the work technically sound?
Yes - current version is technically sound

PEER REVIEWER COMMENTS:
GENERAL COMMENTS: The authors responded adequately and made changes and improved the manuscript especially the discussion section.

ADDITIONAL REQUESTS/SUGGESTIONS:
I still think the title is not accurate and it should be changed. I suggest this title:
"Tumor-infiltrating CD8+ T cells combined with tumor-associated CD68+ macrophages predict postoperative prognosis and adjuvant chemotherapy benefit in resected gastric cancer".
Response: We have revised the title according to your nice suggestion.

There are also minor language mistakes all over the manuscript that should be corrected.
Response: We have re-revised the language and uploaded the editing certificate.

We submit here the revised manuscript as well as a list of changes.
If you have any question about this paper, please don’t hesitate to let me know.
Sincerely yours,

Chang-ming Huang