Peer Review File

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Review Comments

The authors investigated expression of narcissus peudonarcissus lection and mannose receptor positive macrophages predict progression and prognosis of patients with gastric cancer. The manuscript was well written and very interesting. However, the following comments should be addressed.

Major comments

1. In figure1, the images were very important to show us the expression of NPL and MR. Please show us the clearer images and point out where you focused on.

Answer: we fully agree. we offer the original pictures in the reviewed version of the manuscript as required. “On which, stars represented positive gastric gland epithelial cells. Arrows indicated positive macrophages in cancerous interstitial tissue and the triangles showed positive cancerous cells.” in the revised version of the manuscript, please see page 27 lines 15-17.

2. Not only overall survival but also disease specific survival (or disease-free survival) should be discussed.

Answer: Many thanks for your comments.

Usually, OS is used as an end point which is simply obtained through talking to the inpatients during hospitalization or calling either patients or their relatives outside the hospital. There is usually little difficulty in confirming the date of death, and obviously, the time of death has its own independent causality. However, DFS is less used as an end point to survey in pathological data analysis, because of inconvenience in tracing the patients with the disease recurrence and in determining death cause of tumor-loaded patients. In this study, we only focused our attention on the effect of expression of mannose and mannose receptor in tumor tissues on overall survival of patients with gastric cancer under a relative standardization, and did not involve postoperative factors, based on the previous investigation [1]. It was true that during our follow-up, we found that many patients had irregular re-examination problems, so sometimes we cannot find the disease recurrence in the first place, which will bias the statistical results.

3. The long-term outcomes should be shown with at least median follow up period of five years.

Answer: We’d like to thank our reviewer very much for his valuable comments. We fully agree with your suggestions. However, there were literatures available in the PubMed, setting the median survival time for patients of gastric cancer for 23.1-27.4

months [2]. In this manuscript, we evaluated effect of expression of mannose and mannose receptor in tumor tissues on the survival time of the patients with gastric cancer through a retrospective study. The median survival time of the patients in the manuscript was 27 months. With regard to statistical analysis of the data, we followed a previous investigation [3], in which the patients were followed up only for 35 months.

4. How many cases underwent post-surgical chemotherapy?

Answer: We feel sorry for not having mentioned the description on postoperative therapy in the patients in the original version of the manuscript. A paragraph is added: "All the patients received a conventional postoperative chemotherapy modality, i.e. postoperative intravenous infusion of oxaliplatin plus oral tegafur, three weeks per course, eight courses under adjuvant treatment, and 6 courses under palliative treatment. Dosages were supplied according to body weight and body surface area of the patients" in the reviewed version of the manuscript, see page 7, lines 5-10.

5. Liu Deng-Rui was previously published in IJBM in 2017 'Mannose receptor as a potential biomarker for gastric cancer: a pilot study'. The paper showed high mannose receptor expression indicated the poor prognosis for gastric cancer. Therefore, I think this is not first study.

Answer: We fully agree. As one of the most potential markers in gastric cancer, clinical and biological value of mannose receptor has been widely investigated. Also, the previous investigation that the reviewer mentions was one of the references we cited in our manuscript [Reference 15 in the text and here in the letter to the reviewers [6]] in the original version of our manuscript. However, most of previous manuscripts analyzed single factor effect of either MR or NPL on consequences of patients with gastric cancer. In this manuscript, we highlighted a concurrent association analysis on expression of mannose receptors and its ligand NPL in gastric cancer tissues and therefore, saying that this is the first time evaluate potential relationship between both the biomarkers and their biological effects on clinical characteristics in the advanced gastric cancer.

6. Helicobacter pylori is well known as a risk factor of gastric cancer. Therefore, H. pylori should be added in the clinical parameters in table 4.

Answer: We agree. We feel very sorry for having missed this description on the patients in the original version of our manuscript. In fact, we took a careful enrollment limit for the patients and we only focused our attention on those patients without *Helicobacter pylori infection history* in order to avoid any potential biases [4]. And reasonably a paragraph, "Fifty Chinese patients with primarily advanced gastric adenocarcinoma, who had negative Helicobacter pylori infection history and full data of clinical pathological observation, were carefully recruited in this study as described elsewhere [38].", is added into the reviewed version of the manuscript, please see page 6, lines 20-23.

7. Limitation should be discussed clearly.

Answer: we agree. A paragraph is added in the reviewed version of the manuscript. “There were several potential shortages in this study, for example, 1) the panel of patients selected was relatively limited. Increasing numbers of clinical cases would be able to more objectively evaluate relationship of MR and NPL in gastric cancer tissues and 2) the methodology was relatively simple. Based on our previous data in which a significant serological expression of mannose in gastric cancer patients was found [4], we identified the histological localization of mannose in the identical patients with gastric cancer, as described by the previous investigation [5]. Potential target proteins rich in NPL in the gastric cancer tissues would be worth exploring further”. Please see page 16, lines 2-10.

8. Please make space before [the number of reference].

Answer: we agree. Spaces have been left before each reference in the reviewed version of the manuscript.

References

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