Author's response to reviews

Title: Predictive Value of Preoperative Serum CCL2, CCL18, and VEGF for the Patients with Gastric Cancer

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Author's response to reviews: see over
Dear editor and reviewer

We are very grateful to your and the reviewers’ critical comments and thoughtful suggestions. Based on these comments and suggestions, we have made careful responses and revised our original manuscript. All changes made to original manuscript are documented in the space provided.

Once again, we appreciate your comments and advice very much, which are valuable in enhancing the quality and impact of our work.

Sincerely yours

Dr. Yanong Wang

Here are our responses to the reviewers’ comments one-by-one.

**Reviewer’s comments and our responses**

**Reviewer 1**

**Comment 1** The title is a little indistinct, please summarise it more clearly

**Response** We have changed the title

**Comment 2** You should note corresponding stage of Gastric Cancer while examining the serum biological markers

**Response** We have notes the corresponding stage of patients in the part of results
Comment 3  Much more information about both Gastric Cancer patients and the normal people should be declared, such as age, gender, and with or without other disease

Response  We have added the information about patients and the normal people in the part of results

Comment 4  As Tonouchi et al. have reported, the serum concentration of CCL-2 in patients with carcinoma was lower than that in controls, how to explain the opposite results?

Response  We have added the explanation about this opposite results in discussion.

Comment 5  There are some spelling mistakes

Response  We have corrected the spelling mistakes

Reviewer 2

Comment 1  The findings presented in this study are interesting and look convincing. However, it does not achieve a high enough priority for publication at this time in the viewpoint of novelty. Although they claim that this is the first paper reporting roles of CCL2, CCL18, and VEGF in progression of gastric cancer, it has already demonstrated that CCL and/or VEGF were hallmarks of gastric cancer development (Yoshie O et al. Cancer Res. 2006 Feb 15;66(4):2181-7; Xing YN et al. Hum Pathol. 2012 Dec;43(12):2299-307; Kakeji Y et al. Surgery. 2002 Jan;131(1 Suppl):S48-54.). Moreover, serum levels of these chemokines and growth factor has been already examined in several malignant tumors, even if the cells are not gastric cancer as the authors describes in this manuscript (Zohny SF, et al. Med Oncol
2010;27(4):1246-1253). Thus, this paper shows similar results as already demonstrated data. Certainly, they showed combined CCL2 & VEGF had superior sensitivity and specificity of prediction, but it looks like that organ specificity is lacking. I can’t identify the diagnosis of patient who shows high level of serum CCL2 and VEGF as gastric cancer, because other types of organ, such as ovary and colon should be good candidates as described previously. Thus, the authors surly need to show the data demonstrating the specificity of CCL2 and VEGF to predict the presence of gastric cancer or discuss about it. It might be useful to combine the existing specific markers for gastric cancer in addition to their results.

**Response**  It was well known that some serum biomarkers were very specific for some kinds of cancer, such as AFP in liver cancer, PSA in prostate cancer. But it was disappointed that there were still no specific serum biomarkers for most of the cancers, it was the same for gastric cancer. In this study, we found that CCL2 and VEGF were useful for diagnosis of gastric cancer. However, we realised that there were some limitations in our study.

**Comment 2** Materials and Methods

Page 5, line 17: -80 °C is typed incorrectly.

**Response** We have corrected it

**Comment 3**

Table

The authors claim the serum levels of chemokine ligands and VEGF was significantly related with clinicopathological factors, but don't show the data. This is an important
point in the manuscript and it would be highly preferable to show the data as tables.

**Response** We have added a table

**Changes to original manuscript:**

I have used bold print to highlight the modifications in the revised manuscript.