Format for ANSWERING REVIEWERS

May 5, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 18119-review.doc).

Title: High expression of CD11c indicates favorable prognosis in patients with gastric cancer

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 18119

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) In the figure 1, the authors have provided the evidence of differential expression of CD11c in normal and gastric cancer tissues. It should be worth to add further description of the main finding in this figure in the text (3.1).

Answer: We have revised this section according to the suggestions of the reviewer.

(2) As claimed and written by the authors in the discussion, CD11c is predominantly expressed in DCs cells as well as in some macrophages, NK and activated T cells. First: it is essential to show images with higher magnification in Figure 1. Second: serial sections staining should be performed by including markers for immune cells (DCs, macrophages, NK and activated T cells). This staining will provide evidence of the CD11c distribution during the tumor progression. As least, this experiment will clearly show whether CD11c is specifically expressed in immune cells during the tumor progression.

Answer:

1. We have shown images with higher magnification in Figure 1.
2. Thanks for your suggestion ,and we will further exact the CD11c distribution during the tumor progression by serial sections staining in the research for the next phase.

(3) If the authors have frozen tissues from patients, it would be worth to access the CD11c expression level by immunoblot

Answer: Thanks for your advice, we will collect enough proper gastric carcinoma specimens to access the CD11c expression level by Western blot.

(4) The authors' should proofread the paper for clarity and continuity in some sections; In addition, the authors' should rewrite several sentences, particularly in the Introduction, as they are either unclear or run-on (i.e. – Lines 3-7 of the introduction; Lines 15-18; Line 23); Authors should provide company's name and place for reagents. The authors fail to describe the statistical analyses used in the comparisons of the quantitative PCR results.

Answer: Thanks for your advice, and we have revised this section depending on the suggestions of the reviewer. And we describe the statistical analyses of qRT-PCR in Figure legends.

(5) The data presented in this manuscript contradicts with several recently published papers (Okita et. al., J Surg Res. 2014 Jan;186(1):192-200. and Chen et. al. Int J Clin Exp Pathol. 2014 Oct 15;7(11):8304-11.), which suggests that high CD11c has a worse prognosis. However, these data were not mentioned in the discussion. Contrasting these data in the discussion, and explaining their impact on this work would help contextualize the role of CD11c in gastric cancer.

Answer: Chen et. al. Int J Clin Exp Pathol. 2014 Oct 15;7(11):8304-11.-reported that CD11c content was decreased in cancer tissue and peripheral blood in gastric cancer patients compared with controls. Above-mentioned controls include normal gastric tissues and peripheral blood of donors.

Okita et. al., J Surg Res. 2014 Jan;186(1):192-20-reporten that $CD11b^+$DCs were associated with unfavorable prognosis, and almost all the $CD11b^+$DCs expressed CD11c. While the authors didn't describe the number of tumor-infiltrating $CD11b^+$DCs.

Given to above-mentioned various results, We consider as the authors did not completely distinguish $CD11b^+$ cells between macrophages and DCs on account of the similar characteristics in inducing immune tolerance between $CD11b^+$ DCs and tumor-associated M2 macrophages

(6) Abstract: Authors should be more accurate in the conclusion. They should indicate that low expression of CD11c was associated with the death and relapse risk of patients with gastric cancer but it was not an independent factor. In addition, Cd11c should be presented as an “alternative” prognostic indicator.

Answer: We have revised the "Abstract" according to the suggestion.

(7) Results. 3.4. Cox model analysis. Please, explain model 1, 2, 3 and 4. Please include the following result: ”Data reveal that stage IV is related with increased death and relapse hazard”.

Answer: Model 1 and 3 represent the death and relapse hazard of patients with CD11c high expression compared with the reference group (patients with CD11c low expression) after the adjustments of gender, age, tumor location, histological type, pathological grade and UICC stage , respectively. And model 2 and 4 respect the death and relapse hazard of patients with CD11c high expression compared with the reference group

(8) Discussion: A decrease of CD11c in gastric cancer has recently been observed (Chen et al., Function and subsets of dendritic cells and natural killer cells were decreased in gastric cancer. Int J Clin Exp Pathol 7(11):8304-11). This outcome should be discussed taking into account the present data.

Answer: The paper mentioned that a decrease of CD11c in gastric cancer compared with normal gastric tissue samples, while we revealed that CD11c expression levels were decreased gradually from UICC stage I to stage IV, and overexpression of CD11c in gastric cancer compared with gastritis and gastric polyps, respectively.

(9) English is poor and needs improvement.

Answer: We appreciate your comments, then we will strengthen our English learning.

(10) Introduction is not sufficient. It should be increased by writing about cancer (one paragraph) with the citation of the following references. -Heterocyclic Scaffolds: Centrality in Anticancer Drug Development, Curr. Drug Target, In Press (2015). -Glutamic acid and its derivatives: Candidates for rational design of anticancer drugs, Future Med. Chem., 5, 961-978 (2013). -Curcumin-I Knoevenagel’s condensates and their Schiff’s bases as anticancer agents: Synthesis, pharmacological and simulation studies, Bioorg. & Med. Chem., 21: 3808-3820 (2013). -Platinum Compounds: A hope for future cancer chemotherapy, Anti-Cancer Agents Med. Chem., 13: 296-306 (2013). -Thalidomide: A Banned Drug Resurged into Future Anticancer Drug, Current Drug Ther, 7:

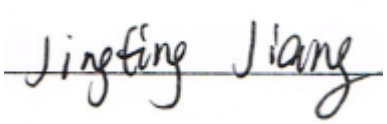
13-23 (2012). -Cancer Scenario in India with Future Perspectives, Cancer Therapy, 8: 56-70 (2011). -Social aspects of cancer genesis, Can. Ther., 8: 6-14 (2011). Imran Ali, Nano anti-cancer drugs: Pros and cons and future perspectives, Current Cancer Drug Targets, 11, 131-134 (2011). -Advances in nano drugs for cancer chemotherapy, Current Cancer Drug Targets, 11, 135-146 (2011). -Natural Products: Human Friendly Anti-Cancer Medications, Egyp. Pharm. J., 9: 133-179 (2010).

Answer: Thanks for your advice, and we have revised this section depending on the suggestions.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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