

Dear Editors and Reviewers,

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "*Silencing Bmi-1 enhances the senescence and decreases the metastasis of human gastric cancer cell*" (ESPS Manuscript NO: 4411).

We found the reviewers' comments most helpful. We have studied their comments carefully and have made modification and correction which we hope meet with your approval.

We greatly appreciate both your help and that of the reviewers' concerning improvement to this paper. We hope that the revised manuscript is now suitable for publication.

We are sending the revised manuscript according to the comments of the reviewers. Revised parts are marked in red.

Thank you very much for your consideration and looking forward to hearing back from you.

Sincerely,

Fenglan Gao

Reviewed by 00556405: This study demonstrated that the inhibition of Bmi-1 gene expression can increase gastric cancer cell senescence and inhibit invasive behavior in a well-accepted boyden chamber model. The data presented in this manuscript are quite good and very supportive of the hypothesis tested. There is the sense that the paper is more "wordy" than necessary and could easily be reduced by 20% but this is not a major criticism.

Response: Modified

Reviewed by 00289643: May you perform the same silencing experiments to other gastric cancer cell line?

Response: Thanks for your suggestion. We will further investigate the mechanism.

Reviewed by 00505507: The present study focused on the role of Bmi in the cell senescence and metastasis. It would help to understand the mechanism of Bmi contribution to cancer progression.

Comments 1. There are a lot of mistakes in the manuscript. For example, the legend of figure 4 "the levels of Bmi-1 mRNA by Western blot ", as we know western blot is the method to detect the protein level not the mRNA.

Response: Corrected

2. The authors should show the Bmi expression level in gastric cancer and the reason why they chose BGC823 cell line as their experimental cells.

Response: BGC823 cell line is commonly used as in vitro model for gastric cancer.

3. In the discussion part, the authors repeated their methods and results. They should discuss the significance of their study or what new brought by their study.

Response: Modified

4. Regarding of the senescence, at least, the author should measure the growth curve or proliferation ratio before and after shRNA transfection.

Response: In fact, the data of this study can clarify the senescence. Thus growth curve or proliferation ratio before and after shRNA transfection was not measured.

5. Boyden chamber assay is the invasion assay; it needs more exams to conclude on the influence on metastasis.

Response: Boyden chamber assay is the metastasis assay.