

Re: Manuscript NO.: 34156

Dear editor,

Thank you for your useful comments and suggestions about our manuscript. We have carefully considered the comments of the reviewer and have revised the manuscript correspondingly.

All responses for these comments are listed below point by point. We are grateful to the reviewers' suggestions which help us to improve the manuscript. Hopefully, this revision would be satisfactory.

**#1. The length of Introduction is too long.**

Response: We thank you for your suggestion and agree with your opinion. We have pruned the introduction section.

**#2. The definition of mild, moderate and severe dysplasia was unclear. The authors should show the definition of grading of dysplasia using HE staining.**

Response: We are very appreciated with your comment and apologized that we should show the definition of grading of dysplasia more clearly. The representative graphs of H&E staining (20×) of various gastric tissues have been added as figure 1.

**#3. The cancer tissue of Figure was only differentiated type cancer. How about undifferentiated type cancer?**

Response: We thank you for your comment. According to Lauren classification [1], all Intestinal-Type gastric cancer are classified to the differentiated type cancer. All the 40 clinical specimens from patients with early gastric cancer included in this study were Intestinal-Type, so no undifferentiated type cancer was included in this study.

[1]: Lauren P. The Two Histological Main Types Of Gastric Carcinoma: Diffuse And So-Called Intestinal-Type Carcinoma. An Attempt at a Histo-Clinical Classification. *Acta Pathol Microbiol Scand.* 1965;64(31-49).

#4. The method about LC-MS/MS was very complicated. The authors should show the method about LC-MS/MS using Schema or Figure.

Response: We thank you for your suggestion and agree with your opinion. We have added Figure 2 to show the method about LC-MS/MS.

#5 There was no statements about the results of LC-MS/MS in Discussion.

Response: We are really appreciated with your suggestion. We have added the discussion about the results of LC-MS/MS: By Label-free combined LC-MC/MC, the expression of 365 proteins based on the tendency of fold change were revealed statistically different between the various stages of GC initiation. Furthermore, we observed that ERGIC1 expression decreased, while DNA-PKcs expression increased gradually along with different stages of GC initiation generally based on the tendency of fold change, suggesting that abnormal ERGIC1 and DNA-PKcs expression may play an important role in GC initiation.

#6 On the end of Abberant expression of DNA-PKcs and ERGIC1 from immunohistochemistry of Results, "----- increased, while DNA-PKcs protein significantly decreased ----- ' was wrong.

Response: We are so sorry about this mistake. It has been revised as "In general, the average immunohistochemistry scores of the DNA-PKcs protein significantly increased, while ERGIC1 protein significantly decreased along with tissue sequence of normal gastric mucosa tissues, mild dysplasia, moderate dysplasia, severe dysplasia, early mucosal gastric cancer.

Once again, we deeply appreciate your comments regarding our manuscript. Should you have any additional questions, please do not hesitate to contact me.

Your sincerely

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