Reviewer’s report

Title: Helicobacter-induced Gastric Inflammation Alters the Properties of Gastric Tissue Stem/Progenitor Cells

Version: 0 Date: 12 Sep 2017

Reviewer: Guifang Xu

Reviewer's report:

This article by Shibata et al want to clarify the changes in epithelial stem/progenitor cells after chronic inflammation. This is an interesting research. The three-dimensional gastric epithelial cell culture system has been utilized. However, the precise mechanism has not been clarified. In this study only explained some phenomenons by mRNA expression and IHC analysis. According to current results, I think the authors can not come to the conclusions.

Major

1. The 3D organoid culture was from mice either infected, treated with MNU, or untreated control after 4 days of culture, then, organoids were injected subcutaneously into mice and the 6 tumorigenicity and histological changes were analyzed after 2 months (page 7 line 3-7). Only the 4 days culture is enough to form organoid? We know the 3D organoid culture from the tumor tissue need long time can do the further research.

2. In the methods about "3-dimentional organoid culture of gastric epithelial cells", the mice were killed, the mouse gastric corpus was removed and cut into approximately 1-mm2 pieces. The gastric epithelial tissues were washed only by PBS, during the procedure, any antibiotics has not been used, how to avoid the cell contamination? In the previous study of prostate cancer, primocin was used during the cell culture[Unno K et al. Oncotarget. 2017 Apr 19;8(31):51264-51276. ].

3. This study only examined the stem cell markers such as Cd44, Dclk1...only the mRNA expression and IHC analysis have been analyzed. Just like the author explained the gastric cancer stem cells marker is not very specific. So I think the following conclusion "chronic inflammation induced by Helicobacter infection increased the number of tissue stem/progenitor cells, which acquired stemness properties, and altered the direction of differentiation toward intestinal metaplasia to cancer." cannot been drown (page 3 line 7-9).

4. Figure 2D should select a picture which can show the whole area, not the regional part. I think the MUC4 expression trend may be clear and more convincing.
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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