Reviewer’s report

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

Version: 0 Date: 10 Sep 2017

Reviewer: Kequn Xu

Reviewer's report:

In the present study, the authors demonstrated that, as one of the possible mechanisms of gastric carcinogenesis, chronic inflammation induced by Helicobacter pylori infection can increase the number of tissue stem/progenitor cells, and alter the properties of stem cells toward intestinal metaplasia to cancer. An organoid culture system combined with a Helicobacter pylori-infected gastric cancer model and xenograft model would enable to identify cancer-initiating cells and investigation of inflammation-associated gastric carcinogenesis. You work is of interest but there are some points that need to be addressed.

1. At present, "Helicobacter" should be "Helicobacter pylori ".

2. In Page 1 Line 16, if does "SPEM" mean abbreviation "spasmolytic polypeptide-expressing metaplasia"? It's not clear.

3. What's the difference between tissue or cancer stem cells, progenitor cells or cancer initiating cells? When you mention stem/progenitor cells, you'd better add "tissue" or "cancer" before them because they have different meaning.

4. When you mention "The expression levels of TFF2, MUC2, CD44, DCLK1, and VILLIN in H. felis-infected 12 mice were significantly higher than those in uninfected control mice", it is suggested to make it quantitative rather than just descriptive.

5. After H. felis eradication, the number of cells positive for Villin was significantly reduced while the mRNA expression of Villin in organoid was not significantly down-regulated. Could you give some possible explanation for such phenomenon?

6. In Page 16 Line 14, you mention "...,suggesting that cytokine stimulation may play a role in inducing a genetic throwback from matured cell to the stem/progenitor cell phenotype". Is there any possibility that inflammation cytokines induce the transdifferentiation of stem/progenitor cells rather than a genetic throwback from matured cell to the stem/progenitor cell phenotype, which in turn accelerating proliferation?

7. You mentioned in the discussion that "The mechanism how matured epithelial cells started to express stemness associated genes remains unclear." To my knowledge, in 2004, Houghton
demonstrated that bone marrow-derived cells (BMDCs) might migrate from blood circulation to stomach and possess plasticity to transform into gastric epithelial cells as a result of inflammation, which may further contribute to gastric neoplasia after epithelial metaplasia and dysplasia. What’s your opinion of such synopsis?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Unable to assess

**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.

Unable to assess

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal