Reviewer’s report

Title: The overmethylated genes in Helicobacter pylori-infected gastric mucosa are demethylated in gastric cancers

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Reviewer: Rommel Burbano

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Major Compulsory Revisions:
- The authors should clarify the number of gastric cancer samples used on the paper. In Methods section, they mention n=70 (48 males and 22 females). However, in page 9 of the manuscript they cited “40 duplicated DNAs of the same tissue, 48 pairs of 1-cm-adjacent tissues...”
- There is no information regarding the histological type of the gastric cancer samples used in the manuscript. Is there any difference in the methylation status according to the histopathological type?
- In pages 10 and 11, the authors classified on or no chromosome lost in diffuse-type of gastric cancer as LOH-B (baseline level) and as LOH-L (low level) in intestinal and mixed type. Why?
- The authors concluded that “concurrent methylation of multiple CpG-island genes initiates and sustains the adaptive differentiation of newly fixed stem cell in the gastric mucosa infected with H. pylori”. However, no comment about stem cells is made in the methods or results sections. How the authors conclude such information about stem cells? Is there any marker that was used to check if the cells used in DNA extraction were newly fixed stem cells?

Minor Essentials Revisions:
- The authors checked for H. pylori status of non-cancerous tissue samples. How is the H. pylori status of the gastric cancer tissue samples? Is there any difference in the methylation status between gastric cancer tissue samples H. pylori positive and H. pylori negative?
- The authors should explain the 5-level and 10-level classification (including the intermediary status) of methylation status. In a previous paper (Hong et al., 2009), they explain the 5-level. I believe that a better explanation should improve the manuscript;
- The first paragraph of the Results section is about results of a previous paper. Please, transfer it to the Discussion section. However, if they are results of the current manuscript (although similar of the obtained previously), please cite the methodology used in the Methods section;
- The last paragraph of page 13 should be transferred to Methods section;
- In page 13, 1st and 2nd lines, the authors can substitute 20 percent for 20%;
- In page 14, lines 14-17: The authors say that PGC and TFF1 are stomach-specific genes weakly active when compared with the two master stomach-specific genes. In which tissue? The authors also say that those genes are densely methylated in bone marrow. And in the stomach?

- Is there any microsatellite in which the authors observed LOH more frequently? And how about LOH and histologic type?

- In page 18, please change H202 for H2O2 (there is a zero instead of an “O”).

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests