Reviewer’s report

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

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Reviewer: Yong Sung Kim

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

The manuscript by Hong et al., presents evidence that the hypermethylated genes under the influence of retroelement methylation in the HP-positive gastric mucosae are demethylated in the gastric cancers influenced by LOH. Initially, to delineate the CpG methylation patterns of CpG-island-containing and -lacking genes in view of the retroelements, the methylation status were examined in the transitional-CpG sites of CpG-island-containing genes and CpG-island-lacking genes in HP-negative and HP-negative gastric mucosae or additional gastric cancer tissues using MSP. They observed the CpG-island-containing genes were hypermethylated depending on the proximity to the nearest retroelement in the HP-positive gastric mucosa and the CpG-island-lacking genes were similarly methylated independent on HP infection. And they also found that both the methylation level of CpG-island-containing and -lacking genes tended to be decreased according to LOH-level-dependent manner in gastric cancers.

Overall this is an impressive body of work on the different epigenetic regulation of genes between CpG-island-containing house-keeping and -lacking stomach specific genes during gastric carcinogenesis connecting to LOH event. The result may provide an insight to understand the mechanism of epigenetic regulation for the dynamic changes of methylation on different class of gene during gastric carcinogenesis.

Comments:

Authors said that hypermethylated genes in HP-positive gastric mucosa are demethylated in gastric cancers. They examined the HP infection in gastric mucosae samples but not in gastric cancer samples. If the HP infection is examined in gastric cancer samples and the methylation status is compared between HP positive and negative, their opinion may be clearer. How do you think about it?

Introduction section: the concept of the transitional-CpG sites has to be defined for reader, though it has been described in the previous publications.

Page 7: In subsection of Collection of tissue samples, HP-positive or -negative cases tested were described as each 50 cases. But actually authors analyzed
with 100 HP-positive and 100 HP-negative cases to examine the methylation status, respectively. Correction is needed.

Page 8: In lane, ‘1,040’ µl may be a misprint. Correction is needed.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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