Reviewer's report

Title: Association between Helicobacter pylori cagA-related genes and clinical outcomes in Colombia and Japan

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Reviewer: Richard Ferrero

Reviewer's report:

General comments:
Watada and colleagues have investigated correlations between novel candidate virulence genes with cagA, a marker of more virulent Helicobacter pylori strains, and the association of these novel genes with clinical outcomes in Colombian and Japanese populations. From previous microarray studies, the authors identified nine genes as being significantly correlated with the presence of cagA; they selected four of these for examination in 177 Colombian and 169 Japanese H. pylori strains. The key finding of the work was the identification of two genes (jhp0045 and jhp0046) as markers for gastric cancer in cagA-positive cases in Colombia, but not for cases of gastric cancer in Japan. Although this is a relatively modest observation it does illustrate the limitations of using cagA-positivity alone as a predictor for more severe forms of H. pylori-associated disease. Furthermore, the work identifies additional bacterial factors that may be important as promoters of gastric carcinogenesis and also demonstrates how the etiology of this disease may vary between different human populations. The authors need to address the specific comments below.

Major compulsory revisions:
None

Minor essential revisions:
1) (Throughout) The manuscript needs to be edited by a native English speaker.
2) (pg 8) The authors should give as much information as possible on the different genes/ORFs i.e. Are these conserved hypothetical genes? In which of the sequenced H. pylori genomes are these genes found? The authors also need to address why they investigated two of the ORFs (jhp0967 and jhp0951), which are associated with duodenal ulcer (DU) disease, when it is commonly accepted that DU and gastric cancer are mutually exclusive diseases.
3) (pg 23) From “eye balling” of the numbers, it seems surprising that there is a significant association between the carriage of jhp0045 and jhp0046 in H. pylori strains and gastric cancer development (32.6% and 37%, respectively) when compared with gastritis (11.4% and 18.2%, respectively), yet there is no association with duodenal ulcer disease (28.6% and 28.6%, respectively).

Discretionary revisions:
4) (pg 20) What are PZ1 and PZ2?

5) (Tables 3 and 4) For consistency, the data in the two tables should be presented in the same order. i.e. Japanese strains then those from Columbia.

**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.

**Declaration of competing interests:**

I declare that I have no competing interests.