LETTER TO THE EDITOR (RESPONSE)

Cag A status of *Helicobacter pylori* infection and p53 gene mutations in gastric adenocarcinoma

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Dear Sir,

We thank Magalhães et al. for their interest in our study and for reminding us of the complexity inherent in the interpretation of our results (1). We agree that a single measurement of *Helicobacter pylori* infection status, no matter what assay method and type of biological specimen are used, cannot represent a cumulative exposure of the gastric mucosa to the bacteria. The situation is compounded by the fact that pathological changes in the gastric epithelium caused by *H. pylori* infection in turn affects the validity of serological tests as surrogate markers of long-term infection. Gastric histopathology and *H. pylori* infection both evolve over time and interdependently, which makes it very difficult, if not impossible, for us to design a scientifically more sound and yet feasible study to address the hypothesis we attempted to test in our study.

It has been suggested that a stronger association of gastric cancer risk with CagA positivity than with *H. pylori* may merely indicate the superiority of anti-CagA antibody to anti-*H. pylori* antibody as a reliable marker of persistent *H. pylori* infection, particularly where CagA+ strains are prevalent (2). If that is the case, combining *H. pylori*+ and *H. pylori*+/CagA− subjects into a single group in our data analysis may have in effect made a comparison between *H. pylori*+ and *H. pylori*+ subjects rather than between CagA− and CagA+ subjects. Another challenge is the difficulty of identifying a sufficient number of *H. pylori*+ and CagA− subjects with gastric cancer. If essentially all the cancer patients are CagA+, as is the case for the study population of Magalhães et al., differences in p53 mutation frequency between CagA+ and CagA− subjects cannot be assessed, whether the CagA− group includes *H. pylori*− or not.

Common to all observational studies, results of one study are subject to further corroboration or refutation by subsequent studies. From a scientific point of view, researchers could look for robust findings that are observed consistently despite idiosyncrasies of various studies or attempt to identify particular characteristics of each study population including other risk factors that might contribute to the differences in findings across studies. However, logistical and practical constraints could limit our further pursuit in either direction.

References
