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Letter

Biomarker in *Helicobacter pylori* infection: the standoff condition?

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Dear Editor,

We read with great interest the recent publication by Ramis IB et al, who investigated *Helicobacter pylori* virulence factors in Brazilian dyspeptic patients[1]. It has been firmly shown that no reliable diagnostic biomarkers exist to predict a specific disease outcome after primary colonization of *H. pylori*, although this has become an interesting area of research on this important microorganism worldwide. Many studies had been conducted to test/validate proper disease-related biomarkers of *H. pylori.* Recent findings based on sequencing and proteomic technologies have suggested new determinants as virulence factors that are disease-specific for *H. pylori*[2,3]. Ramis IB et al found that *cagA/cagE/babA*$_2$*/vacAm*$_1$*s*$_1$*/iceA*$_1$ was a significant biomarker among only 15% (4/26) of their entire investigated population[1]. Indeed, the conclusion in this study is based on a very small number of *H. pylori* strains (57 isolates), which cannot serve as a proper sample size from which to draw a comprehensive conclusion. Furthermore, the presence of a gene alone is not sufficient to suggest that it is a virulence factor. Gene expression analysis or proteomic tests are needed to identify true biomarkers of *H. pylori* that are associated with certain gastroduodenal diseases. Undeniably, additional *in vitro* and *in vivo* studies are necessary to elucidate the relationship between the *H. pylori* cagE gene and pathologic findings. It may be advisable to design a prospective study with different samples from other originating populations, and larger groups will be required to enhance the preliminary hypothesis stated in the current study. Moreover, it has been broadly recognized that gastroduodenal diseases are quite complicated outcomes of a variety of parameters, including environmental factors and host genetics. Additional in-depth studies are required to define a true biomarker for *Helicobacter pylori*-associated gastroduodenal disorders. Another controversial issue in the field of *H. pylori* biomarker and disease research is whether physicians can use this type of data in clinical trials. While characterizing accurate *H. pylori* biomarkers associated with certain diseases seems difficult, new, full-genome sequencing studies may answer unsolved related issues in the near future.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Authors' reply: Biomarker in *Helicobacter pylori* infection: the standoff condition?

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Dear Editor,

In our paper, we concluded that *cagE* could be a risk biomarker for gastric lesions and may contribute to a better evaluation of the pathogenic potential of *Helicobacter pylori* and, in particular, the diversity of factors involved in the relationship between gastric diseases and *H. pylori* colonization/ infection. Thus, we have been studying new biomarkers for *H. pylori,* patient susceptibility, and environmental factors. Our results suggest only that *cagE,* like *cagA, vacA, iceA*, or *babA2*, could be related to the virulence of *H. pylori.*

Our hypothesis, in agreement with Dr. Abadi et al and others, is that a combination of patient and microorganismal genetics and environmental conditions determine the actual risk of gastric diseases related to *H. pylori* colonization/infection.

With respect to sequencing, transcriptome, and proteomic studies, sequencing of the genomes of the main strains circulating in each region is necessary because of the high genetic diversity found in both the host and the microorganism. Indeed, studies on gene expression should also consider different aspects of the regulation of these genes, such as the identification of the inducers?

Obviously, this is a complex issue, and more highly refined studies are required to confirm or reject some hypotheses. Finally, it is important to highlight that recent studies have shown that *H. pylori* colonization/infection should be eradicated with caution because some diseases, such as gastro-esophageal reflux and allergy, may be related to *H. pylori* eradication. Our study is not the final word but rather contributes to progress in the knowledge obtained from the search for a putative biomarker of microorganism pathogenicity and the inferred relationship with gastric disease.