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Editorial

Paradoxical role of *Helicobacter pylori* in Gastric cancer

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In Japan and other countries, *Helicobacter pylori* infection is one of the major causative agents of gastric cancer [1]. Gastric cancer is the second leading cause of cancer mortality worldwide [1,2]. However, interestingly, the prevalence of *H. pylori* does not predict the incidence of gastric cancer [2-4]. For example, the prevalence of *H. pylori* infection is high but that of gastric cancer is low in natives of Bangladesh [3]. Despite similar levels of *H. pylori* infection, the incidence of gastric cancer is seven-fold higher in Japan than in India [4]. Japan has a higher incidence of gastric cancer (age-standardized incidence rate 62.7/100,000) but a lower prevalence of *H. pylori* infection (39.3%) [5]. However, despite the higher prevalence of *H. pylori* infection in Bangladesh (92%) and India (79%), those countries have a lower incidence of gastric cancer (1.6/100,000 and 5.7/100,000, respectively) [5]. In addition, two distinct Colombian populations with a similar incidence of *H. pylori* infection reportedly had different rates of gastric cancer [2].

The eradication of *H. pylori* prevents the progression of gastric cancer in younger people [1]. Kwon et al. [6] reported that both persistent *H. pylori* infection and old age (≥60) are independent risk factors for the increased incidence of metachronous gastric cancer. Many risk factors, including active gastritis such as corpus-predominant gastritis, *H. pylori* infection, and increased age were reported to be involved in the multi-stage carcinogenesis process of gastric cancer [3,4,6,7]. A recent Japanese genome-wide association study (GWAS) on diffuse-type gastric cancer, in which the role of *H. pylori* infection seems limited, identified two genes of interest. These were the prostate stem cell antigen (PSCA) gene encoding a glycosylphosphatidylinositol-anchored cell surface antigen as a gastric cancer-susceptibility gene, and the Mucin 1 (MUC1) gene encoding a cell membrane-bound mucin protein as a gene related to diffuse-type gastric cancer [5]. A GWAS of the Chinese population revealed three additional gastric cancer susceptibility loci: 3q13.31, 5p13.1 and 10q23 [5]. Thus, it seems clear that host genetic factors are associated with gastric cancer susceptibility.

Kodaman et al. [2] reported that human host and *H. pylori* co-evolution determines the risk of gastric disease. They examined the association between the severity of gastric lesions and genomic variation patterns in matched human host and *H. pylori* samples. They found that an interaction between human Amerindian ancestry and *H. pylori* African ancestry accounted for the geographic disparity in the clinical presentation of gastric cancer. That is, African *H. pylori* ancestry was relatively benign in humans of African ancestry but was deleterious in humans of Amerindian ancestry. They concluded that the co-evolution of human and *H. pylori*-modulated disease risk, and the disturbance of the co-evolution of human and *H. pylori* genome can account for the high incidence of gastric disease in the Colombian mountain population [2].

It was reported that the therapeutic efficacy of omeprazole and amoxicillin in the cure rates of *H. pylori* infection and peptic ulcer was increased in patients with a poor-metabolizer genotype for S-mephenytoin 4'-hydroxylase (CYP2C19), by which omeprazole is metabolized in the liver [7]. It is also known that mutations in *H. pylori* 23S rRNA and gyrA genes are associated with resistance to clarithromycin and quinolones, respectively. A high incidence of quinolone resistance was found in clarithromycin-resistant strains of *H. pylori*, in Japanese patients with previous eradication failure [8]. Thus, host as well as *H. pylori* genetic factors are associated with the eradication of *H. pylori* susceptibility.

In conclusion, recent advances in endoscopic diagnosis and serum *H. pylori* antibody-based diagnosis could help with the accurate prediction of *H. pylori* infection status and gastric diseases [7,10,11]. Although the eradication of *H. pylori* and the surveillance of high-risk patients are important for the prevention of gastric cancer [1], study of the co-evolution between humans and *H. pylori* might shed new light on *H. pylori*-induced gastric diseases including gastric cancer.

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