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Short Communication

Helicobacter Pylori Infection Leads to Colorectal Cancer Development: A Major Scientific Debate

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Etiology of colorectal cancer (CRC) is complex and remains incompletely understood, even though a number of genetic and environmental risk factors are yet to be fully established. Globally CRC is the third most common cancer and the fourth leading cause of cancer-related death. Several studies have suggested that chronic infection with *Helicobacter pylori* (*H. pylori*) in the gastric mucosa is an established strong risk factor for gastric cancer. It may also be associated with a moderately increased risk of CRC development. *H. pylori* is a gram-negative pathogenic bacterium (Figure 1) usually located on the surface of the stomach epithelium. *H. pylori* infection is one of the most widely spread infectious diseases in humans. It can cause chronic gastritis, peptic ulcer disease and gastric malignancies.

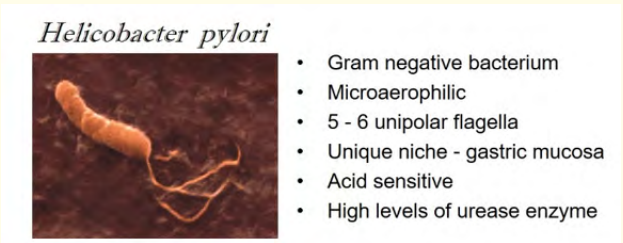

Figure 1

The prevalence of *H. pylori* infection markedly varies in different countries. Increased prevalence rates are seen in some developing countries, while lower rates have been found in many developed countries. Moreover, the prevalence rates may vary significantly in different geographic regions or ethnic populations of a single country. However, the variation in *H. pylori* infection rate in CRC patients of different origin has not been established yet. Studies with colorectal endoscopy restricted the possibilities of more specific analyses of key determinants viz. age, sex, cancer site, stages of CRC risk. Thus, *H. pylori* infection may considered to be the major cause for the development of CRC. *H. pylori* infection is also one of the most common causes of hypergastrinemia and chronic atrophic gastritis. The chronic atrophic gastritis generally result in intestinal overgrowth of microflora during progression of CRC. It is also linked with gastric carcinoma and lymphoma. The pathological reason involves the persistent colonization of *H. pylori* and inflammation of the gastric mucosa for CRC development. Hence, evidence concerning the role of *H. pylori* infection in the development of CRC remains controversial till date. To assess the direct association between *H. pylori* sero-positivity and the risk of CRC, a large population-based study should be done considering the potential virulence factors of the infectious agent, and potential variation of risk with respect to age, sex, and cancer stage.

The cytoxin-associated gene (CagA) secreted by *H. pylori* often results in the development of chronic atrophic gastritis and ultimately hypergastrinemia. Its role in CRC development remains unclarified. CagA+ strain of *H. pylori* infection (Figure 2) are associated with CRC stage and lymph node metastasis. Furthermore, hypergastrinemia has been reported to be associated with increased risk of colorectal malignancy.

The direct connection between *H. pylori* infection and hypergastrinemia in the development of colorectal carcinogenesis with many controversial results has been now a matter of scientific debate. It has been suggested that the association between *H. pylori* infection and CRC risk may be due to excessive and prolonged release of gastrin among those who are infected. The G-cells of the gastric antrum, duodenum and pancreas produces a 17-amino acid polypeptide hormone called gastrin. It is considered to serve as a growth factor of normal colonic epithelium and required for the secretion of gastric juice from the parietal cells of the stomach. Gastrin is a putative trophic factor for the colonic mucosa that may stimulate tumor growth. Gastrin has been established to exert carcinogenic effect to the epithelium of both the colon and rectum. It is known that gastrin triggers proliferation of colonic mucosa through activation of its receptors. These receptors have been shown to

be expressed early in the adenocarcinoma and also in advanced neoplastic tissues. Whether gastrin is implicated in the ability of cancer cells to metastasize to the lymph nodes requires further research. The exact mechanism through which gastrin acts in the progression of colorectal carcinogenesis remains a matter of dispute. Recent reports have suggested that gastrin is produced and secreted by the malignant intestinal cells. It works in tissue cells via autocrine or paracrine pathways. Mounting evidences showed controversial findings, not being able to either reject or clearly support a direct correlation between *H. pylori* infection with CRC and elevated gastrin levels in infected cells. Another strong conflict remains till date is the possible connection between the levels of gastrin and CRC stage. The expression of inflammatory mediators like COX-2, IL-8 is under control of gastrin. Thus, CRC development can be prevented by inhibition of these mediators.

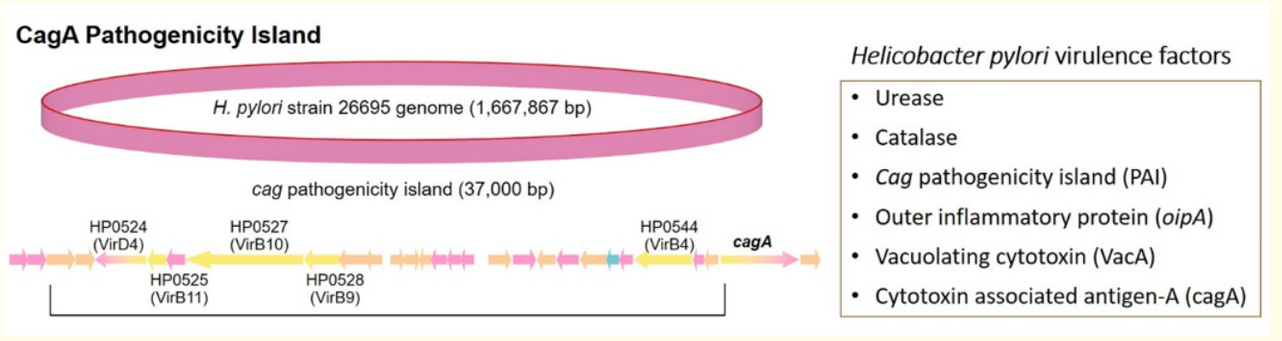

Figure 2

To conclude, oncologists are crucially concerned about the connection between *H. pylori* infection and colorectal cancer development from both diagnostic and therapeutic point of view (Figure 3). Although, it is well accepted that *H. pylori* strains that express the cytoxin-associated gene (CagA+) are associated to even greater increase of local and systemic inflammation compared to CagA- strains. More studies need to be performed in order to either confirm or reject the association between *H. pylori* infection and CRC development.

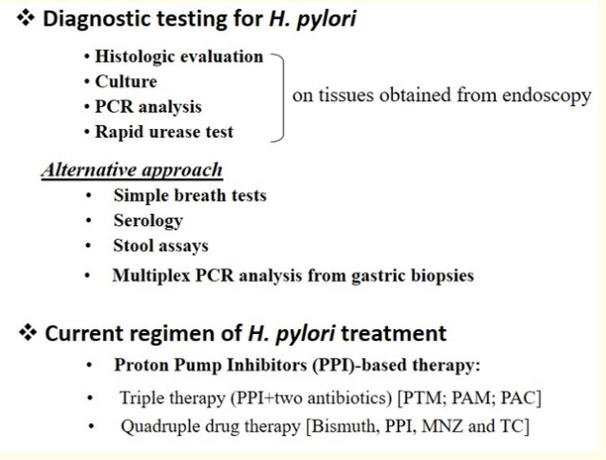

Figure 3

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