Bacteriology, Epidemiology, and Pathogenesis of *Helicobacter pylori*

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H. pylori is a Gram-negative, spiral, microaerophilic bacterium that infects more than 50% of the human population over the world. The bacterium has been well documented as an etiological agent of most gastro-duodenal maladies like acute and chronic active gastritis, peptic ulcer disease, and atrophic gastritis as well as gastric adenocarcinoma. Infection occurs in early childhood. Once acquired, the infection persists forever during a lifetime despite strong mucosal and serum immune responses to the bacterium, assuming that host immune responses are ineffective in removing the infection.

H. pylori can penetrate to and swim within gastric mucus layer. However, host defense mechanisms cannot reach the intra-mucus, meaning that the control of *H. pylori* infection in gastric mucosa might be difficult to be achieved by the measures against other pathogenic bacterial infections like chemotherapy and vaccination.

When we investigated the *H. pylori*-carrier rate of Korean asymptomatic volunteers aged above 20 years with the bacterial culture, urease test as well as histopathologic examination, most Korean adults are carriers of *H. pylori* resulting in becoming patients of gastritis. Serological investigations showed that *H. pylori* infection begins at infancy and the infection rate reaches up to 50% at 5~6 years of age and 80~90 % at 7 years of age and then maintains the percentage throughout the whole ages of adults. Recently, the carrier-rate is inclined to decrease in childhood.

H. pylori has developed the alpha hemolytic colonies on Mueller-Hinton agar plates supplemented with the bovine blood at ratio of 10% after the 3-day-incubation under 5-10% CO_2 at 37℃. The transition from curved bacilli to coccoid form is pronounced with the prolonged incubation, and lophotricous or amphitricous flagella is also identified by electron microscopy. All *H. pylori* isolates are urease-, catalase-, and oxidase-positive and produce H_2S.

Genome sequences of several *H. pylori* strains were determined. The *H. pylori* Korean strain 51 genome consists of a 3,955 bp cryptic plasmid and a circular chromosome with a size of 1,591,297 bp, which is 76,570 and 52,533 bp smaller than the 26695 and J99 chromosomes, respectively. In the case of strain 52, the total length of the contigs is 1,563,885 bp, which corresponds to 98.3% of the genome of strain 51.

26695 and J99 had 123 (7.7%) and 65 (4.3%) strain-specific genes, respectively. However, of the 1,454 strain 51 genes, only 39 (2.7%) genes were unique. Of these genes, 3 (khp0900, khp1251 and khp1391) were found

exclusively in the Korean strains. About 75-85% of the Korean strains bore these genes. However, none of the 51-specific genes seemed to correlate with particular diseases.

Whole cell proteins of *H. pylori* are displayed in the region of pI 4.0–9.5 with molecular masses from 10 to 100 kDa by two-dimensional electrophoresis, using immobilized pH gradient strips. Of them, 300 genes have been identified by proteomic analysis. The expression levels of CagA, UreB, GroEL, EF–Tu, EF–P, TagD, and FldA showed partly significant difference among gastric disease patterns.

H. pylori shows a strict tropism for the gastric mucosa or sites to generate a chronic gastritis which is a main pathogenesis to develop other gastric disorders like atrophic gastritis, peptic ulcer, dystrophy, and adenocarcinoma. Inflammatory responses are stimulated and persisted by host-bacterial interaction through induction of apotosis, cytokine, and autoimmunity.

Once *H. pylori* migrates to the gastric epithelium, *H. pylori* produces various bacterial proteins including VacA, urease, ADH, and GGT to damage gastric niches. *H. pylori* GGT and ADH induce apoptosis in AGS cells through a mitochondrial pathway, which are the candidate factors provoking cell death in the gastric mucosa. Cell cycle arrest could be observed in the GGT-treated AGS cells at the G1-S phase transition.

H. pylori infection induces the production of various proinflammatory cytokines in gastric mucosa of the host. These cytokines produced in response to *H. pylori* stimulation trigger and maintain the gastric mucosa to be sunk into the inflammatory niches. Of them, IL-8 is most profoundly produced in the gastric epithelium with *H. pylori* infections. *H. pylori* cellular component 26 kDa antigen has been investigated to be responsible for inducing IL-8 production in the gastric lesion.

The autoimmune reaction might be involved in the pathogenesis of chronic gastritis due to *H. pylori* infection. We developed 214 monoclonal antibodies against *H. pylori*. Of them 25 antibodies reacted with ductal cells of the salivary gland, 11 antibodies reacted with renal tubular cells, and 8 antibodies reacted with duodenal epithelial cells. These results might demonstrate that *H. pylori* infection could provoke the autoimmune responses that involves in the pathogenesis of various diseases in other organs.

Inflammation leads to infiltration of netrophil and macrophases/monocytes in the gastric mucosa. These neutrophils and macrophages/monocytes produce oxygen free radicals that could cause DNA damage of the adjacent cells. We measured the 8-OH-dG content of DNA from human gastric mucosa with and without *H. pylori* infection to show that increased DNA damage is associated with *H. pylori* infection. As a result, *H pylori* plays as the major trigger for a sequence of phenotypic changes in the gastric mucosa, progressing from inflammation to superficial gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and finally adenocarcinoma.

Understandings for bacteriology and pathogenesis of *H. pylori* might provide insights for the minimization and eradication of gastric disorders by *H. pylori* infection.