The bacterial factors and strain diversity in *H. pylori*-related gastrointestinal disorders

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As with many infectious diseases, only a fraction of people infected with *Helicobacter pylori* develop clinical disease and host genetics, host immune response and bacterial virulence factors appear to play critical roles. There has been considerable interest in putative *H. pylori* virulence factors and, while several have been identified, it is not clear whether they act independently or in concert. Disease associations have been proposed for the *cag* pathogenicity island (PAI), *vacA*, *dupA* and genes encoding outer membrane proteins (OMPs) such as *oipA* and *babA*. Especially our group found four important novel findings about virulence factors; 1) relation between number of *cagA* second repeat regions and gastric cancer (e.g., J Clin Microbiol 1998 and Gastroenterology 1999), 2) relation between *oipA* (outer inflammatory protein) and gastric injury (e.g., PNAS 2000, Gastroenterology 2002a, Gastroenterology 2002b, Gastroenterology 2004, Mol Biol Cell 2005, Infect & Immun 2005, and Cancer Research 2006), 3) relation between *dupA* (duodenal ulcer promoting) and duodenal ulcer diseases (Gastroenterology 2005) and 4) relation between expression levels of BabA and clinical outcomes (Clin Gastroenterol Hepatol 2006). *H. pylori* with more than three repeat regions in the 3´ region of the *cagA* gene were associated with enhanced histologic injury and with reduced survival in acidic conditions. It is hypothesized that these variants arise within the stomach. Using human biopsy specimens as well as mice models, we also found that *oipA* functional status was related to clinical presentation, *H. pylori* density and gastric inflammation. We found that *dupA* is a novel marker associated with an increased risk for duodenal ulcer and reduced risk for gastric atrophy and cancer both in Asian and Western countries. Finally, we found that quantitation of BabA expression revealed that Lewis-b non-binding low BabA expressing strains are rather associated with higher levels of mucosal injury and clinical outcome. Here I review the recent novel findings for roles of the putative virulence factors in *H. pylori*-related gastrointestinal disorders.