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Advances in Gastric Carcinogenesis Related to *Helicobacter Pylori*

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Abstract
Helicobacter pylori (H. pylori), a Gram-negative bacterium, has been classified as a Group I carcinogen by the World Health Organization. It represents the most significant modifiable risk factor for gastric cancer (GC), particularly the intestinal subtype. Although global infection rates are on the decline, its role in gastric oncogenesis remains prominent, especially in areas with elevated incidence rates. This review consolidates current insights into the molecular and immunological pathways through which *H. pylori* contributes to gastric tumorigenesis, with a focus on epigenetic modulation, host-microbe interactions, and the influence of the gastric microbiota. Chronic inflammation, instigated by *H. pylori* infection, advances through the Correa cascade, culminating in neoplastic transformation. Principal virulence determinants, including CagA and VacA, compromise epithelial barriers and initiate oncogenic signaling networks such as NF-κB, STAT3, Wnt/β-catenin, and Hippo/YAP. The infection is also associated with extensive epigenetic remodeling, notably promoter hypermethylation of tumor suppressor genes like CDH1, and regulation of non-coding RNAs (including miRNAs, lncRNAs, and circRNAs). Sustained colonization drives immune polarization toward Th1 and Th17 responses, promotes immune escape mechanisms such as PD-L1 overexpression, and alters the composition of the gastric microbiome. Recent findings highlight the potential role of non-*H. pylori* microbial species in supporting tumor progression. While eradication of *H. pylori* lowers the risk of gastric cancer, it does not confer complete protection, particularly in individuals with pre-existing mucosal alterations or microbial dysbiosis. The development of *H. pylori*-associated gastric cancer is a multifactorial process, shaped by microbial virulence, host genetics, epigenetic shifts, and immune dynamics. A deeper understanding of these interrelated mechanisms is crucial for refining preventive measures, diagnostic accuracy, and therapeutic approaches.
Keywords: *Helicobacter pylori*, gastric cancer, microbiome, carcinogenesis