Genetic variants of toll-like receptor 2 and 5, helicobacter pylori infection, and risk of gastric cancer and its precursors in a chinese population.

Abstract:
Genetic polymorphisms of Toll-like receptors (TLR) may influence the outcome of Helicobacter pylori infection and play important roles in gastric carcinogenesis. To screen the genetic variants of TLR2 and TLR5, and evaluate their associations with gastric cancer (GC) and its precursors, a population-based study was conducted in Linqu County, Shandong Province, China. Genetic variants were identified by PCR-based denaturing high-performance liquid chromatography and PCR-restriction fragment length polymorphism analysis in 248 GC cases, 846 subjects with advanced gastric lesions including 350 dysplasia and 496 intestinal metaplasia, and 496 superficial gastritis/mild chronic atrophic gastritis controls. Nine allelic variants each were detected within the promoter and exons of TLR2 and TLR5. Among those, TLR2 c. -196 to -174 del carriers (ins/del+del/del) showed a significantly decreased risk of GC (adjusted OR, 0.66; 95% CI: 0.48-0.90), whereas TLR5 rs5744174 C carriers (TC+CC) had an increased risk of GC (OR, 1.43; 95% CI: 1.03-1.97). Further analysis indicated an elevated risk of GC in subjects with the TLR5 rs5744174 TC+CC genotype and H. pylori infection (OR, 3.35; 95% CI: 2.13-5.26), and a significant interaction between rs5744174 and H. pylori infection was observed (OR, 2.15; 95% CI: 1.12-4.16). These findings suggest that TLR2 c. -196 to
-174 ins> del, TLR5 rs5744174 and interaction between rs5744174 and H. pylori infection were associated with the development of GC. TLR2 and TLR5 polymorphisms may play important roles in the process of H. pylori-related gastric carcinogenesis.