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Aberrant DNA methylation of the *P16*, *MGMT*, and *hMLH1* genes in combination with the methylenetetrahydrofolate reductase C677T genetic polymorphism and folate intake in gastric cancer

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ABSTRACT. Epidemiological studies have indicated that folate metabolism is correlated with increased risk of gastric cancer. Since methylenetetrahydrofolate reductase (MTHFR) is an important enzyme involved in folate metabolism, in this study, we examined whether polymorphisms and haplotypes of *MTHFR* are correlated with the risk of gastric cancer. The polymorphisms *MTHFR* C677T and *MTHFR* A1298C were genotyped by polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP) analysis in 285 patients and 570 healthy controls. Association analyses based on binary logistic regression were conducted to determine the odds ratio (OR) and its 95% confidence interval (95%CI) for each genotype. The *MTHFR* 677TT genotype was significantly related with a reduced risk of gastric cancer (OR = 0.60, 95%CI = 0.39-0.92) compared to the CC genotype. Similarly, the *MTHFR* 1298CC genotype was significantly

associated with a decreased risk of cancer (OR = 0.52, 95%CI = 0.32-0.81). Haplotype analysis showed that the TC haplotype was associated with a reduced risk of gastric cancer compared to the most common haplotype, CA (OR = 0.28, 95%CI = 0.12-0.60). Our results suggest that the *MTHFR* C677T and *MTHFR* A1298C polymorphisms are related to gastric cancer susceptibility in the Chinese population.

Key words: Methylenetetrahydrofolate reductase; Gastric cancer; Susceptibility; Haplotype analysis

