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Methylenetetrahydrofolate reductase genotypes and haplotypes associated with susceptibility to colorectal cancer in an eastern Chinese Han population

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ABSTRACT. Methylenetetrahydrofolate reductase (MTHFR) plays an important role in folate metabolism and is involved in DNA synthesis, DNA repair and DNA methylation. The two common functional polymorphisms of MTHFR, C677T and A1298C have been associated with several diseases, including cancer. We made a case-control study to analyze a possible association of MTHFR gene polymorphisms C677T and A1298C with risk for colorectal cancer in an eastern Chinese Han population of 137 patients with a confirmed histopathological diagnosis of CRC and 145 age- and gender-matched controls with no history of cancer. DNA was isolated from peripheral blood samples and the genotypes were determined by PCR-RFLP. The concentrations of folate in plasma were measured by chemiluminescence immunoassay. The MTHFR 677TT genotype had a protective effect against colorectal cancer, with an odds ratio (OR) = 0.467 (95% confidence interval (CI) = 0.225-0.966). The 1298CC genotype was significantly correlated with a reduced risk of colorectal cancer (OR = 0.192; 95%CI = 0.040-0.916). Compared with the MTHFR 677CC and MTHFR 1298 AA genotypes,

for individuals who carried both MTHFR 677CC and 1298CC genotypes, the OR of colorectal cancer was 0.103 (95%CI = 0.012-0.900); among individuals who carried both MTHFR 677TT and 1298AC genotypes, the OR for risk of colorectal cancer was 0.169 (95%CI = 0.044-0.654). MTHFR 677TT+CT genotypes had a significantly lower plasma folate concentration than those with the MTHFR 677CC genotype. MTHFR 1298AC+CC genotypes had a lower plasma folate concentration than those with the MTHFR 1298AA genotype ($P < 0.05$). In conclusion, subjects with the MTHFR 677TT and MTHFR 1298CC genotypes appeared to have a significantly lower risk for colorectal cancer. MTHFR haplotypes 677CC/1298CC and 677TT/1298AC were less common in cases than in controls. These haplotypes, when compared to the most common haplotype 677CC/1298AA, were associated with a decreased risk for colorectal cancer. We conclude that plasma folate level is influenced by MTHFR genotypes.

Key words: Colorectal cancer risk; MTHFR; Genotype; Haplotype

