Methylenetetrahydrofolate reductase C677T polymorphism and predisposition towards esophageal squamous cell carcinoma in a German Caucasian and a northern Chinese population.

PURPOSE: Folate deficiency is considered to increase the risk of developing esophageal cancer. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme involved in folate metabolism. A single C --> T substitution at nucleotide 677 of the MTHFR cDNA influences enzyme activity. The purpose of this study is to compare the association of the MTHFR C677T polymorphism with susceptibility to esophageal squamous cell carcinoma (ESCC).

METHODS: Using real-time PCR and melting curve analysis, the MTHFR C677T genotypes were determined in 430 patients with ESCC (241 German Caucasians and 189 northern Chinese) and 397 unrelated healthy controls (256 German Caucasians and 141 northern Chinese). RESULTS: A significant difference in MTHFR C677T genotype distribution was observed between German Caucasian controls (C/C, 41.8%, C/T, 44.9%, T/T, 13.3%) and northern Chinese controls (C/C, 17.7%, C/T, 38.3%, T/T, 44.0%) (chi(2)=52.19, P<0.001). The distribution of the MTHFR C677T genotypes among German ESCC patients (C/C, 39.0%, C/T, 48.1%, T/T, 12.9%) was not significantly different from that among healthy controls (chi(2)=0.531, P=0.767). In contrast, the frequency of the C/C genotype among Chinese ESCC patients (8.5%)
was significantly lower than among Chinese healthy controls (17.7%) (chi(2)=6.37, P=0.012). The C/C genotype was correlated with a significantly reduced risk for the development of ESCC as compared to the combination of C/T and T/T genotypes (adjusted OR=0.38, 95% CI=0.16-0.88).

CONCLUSIONS: Our results suggest that, in contrast to German Caucasians, the MTHFR 677CC homozygous wild-type plays a protective role in the development of ESCC in the northern Chinese population.