Hum Genet. 2005 Mar;116(4):247-54. Epub 2005 Jan 6.

Methylenetetrahydrofolate reductase (MTHFR) and susceptibility for (pre)neoplastic cervical disease.

Zoodsma M, Nolte IM, Schipper M, Oosterom E, van der Steege G, de Vries EG, te Meerman GJ, van der Zee AG.

Source

Department of Gynecology, University Medical Center Groningen, Hanzeplein 1, 30.001, 9700 RB, Groningen, The Netherlands.

Abstract

Methylenetetrahydrofolate reductase (MTHFR) is a critical enzyme regulating the metabolism of folate and methionine. The potential influence of MTHFR activity on DNA methylation and on the availability of uridylates and thymidylates for DNA synthesis and repair presents MTHFR as a candidate for being a cancer-predisposing gene. In the present study, we have examined a large study population to determine whether the C677T polymorphism at the MTHFR locus affects susceptibility for cervical cancer or its precursor, cervical intraepithelial neoplasia (CIN). In addition, we have investigated whether this polymorphism is causal, and not merely associated, by typing microsatellite markers in the region surrounding the MTHFR gene. A total of 311 CIN and 695 cervical cancer patients and 115 family-based and 586 unrelated controls was analysed. Association analysis showed a decreased cervical cancer risk for individuals heterozygous or homozygous for the T-allele, both for squamous cell carcinoma (heterozygous odds ration [OR] 0.66 [0.51-0.86]; homozygous OR 0.76 [0.49-1.16]) and adenocarcinoma (heterozygous OR 0.71 [0.49-1.03]; homozygous OR 0.34 [0.14-0.81]). No difference was found for high grade CIN (heterozygous OR 1.03 [0.76-1.40]; homozygous OR 0.91 [0.54-1.55]). A microsatellite haplotype containing the C allele was associated with an increased risk for cervical cancer and CIN (both among squamous cell carcinomas, adenocarcinomas and CIN II-III; OR = 2.61 [1.59-4.27]). Our study thus lends further support to the hypothesis that the MTHFR C677T polymorphism is involved in susceptibility cervical cancer but also illustrates that, despite the large sample size analysed, still larger studies are needed to establish fully the nature of this association.

PMID:
15635481
[PubMed - indexed for MEDLINE]