Association of NAD(P)H: quinone oxidoreductase 1 (NQO1) C609T polymorphism with esophageal squamous cell carcinoma in a German Caucasian and a northern Chinese population.

Abstract:

NAD(P)H: quinone oxidoreductase 1 (NQO1) is an antioxidant enzyme, important in the detoxification of environmental carcinogens. A single base substitution (C --> T) polymorphism at nucleotide 609 (null-allele) of NQO1 gene impairs stability and function of the NQO1 protein. To investigate the association of this NQO1 polymorphism with susceptibility to esophageal squamous cell carcinoma (ESCC), the NQO1 C609T genotypes were determined by PCR-RFLP analysis in 450 patients with ESCC (257 German Caucasians and 193 northern Chinese) and 393 unrelated healthy controls (252 German Caucasians and 141 northern Chinese). Additionally, NQO1 protein expression was determined by immunohistochemistry in a subset of 74 ESCC (50 German, 24 Chinese). A significant difference in NQO1 C609T genotype distribution was observed between Caucasian healthy controls (C/C, 73.4%; C/T, 25.0%; T/T, 1.6%) and Chinese healthy controls (C/C, 34.0%; C/T, 49.7%; T/T, 16.3%) (chi^2 = 68.40, P< 0.001). The NQO1 T/T genotype significantly increased the risk for developing ESCC in both Caucasian subjects (OR = 4.62, 95% CI = 1.54-13.86) and Chinese subjects (OR = 1.81, 95% CI = 1.04-3.15), compared with the combined C/C and C/T genotypes. In Chinese subjects, this increased susceptibility was
pronounced in patients with family history of upper gastrointestinal cancers (OR = 2.18, 95% CI = 1.14-4.17). Immunohistochemical analysis showed NQO1 protein expression in 53 carcinomas, whereas 21 carcinomas were negative. Negativity for NQO1 expression correlated strongly with the NQO1 genotype, being present in 8.6% of cases with C/C, 22.2% of cases with C/T and 100% of cases with T/T genotype (chi(2) = 16.60, P< 0.001). In summary, the association of the NQO1 C609T polymorphism with ESCC in genetically distinct populations makes a strong argument for its importance in carcinogenesis of ESCC in the German Caucasian and the northern Chinese population.