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Glutathione S-transferase polymorphisms influence the level of oxidative DNA damage and antioxidant protection in humans.

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Abstract

Glutathione S-transferase genotypes GSTT1, GSTM1, GSTP1 were characterised in 155 middle-aged men and compared with parameters of oxidative stress at the level of DNA and lipids, with antioxidant enzymes, and with plasma antioxidants in smokers and non-smokers. Smokers had on average significantly lower levels of Vitamin C, beta-carotene and beta-cryptoxanthin and higher amounts of oxidised purines and pyrimidines in lymphocyte DNA. The GSTM1 null genotype was associated with elevated glutathione as well as with higher Vitamin C concentration in plasma. Vitamin C was higher in GSTT1+ compared with GSTT1 null--as was glucose-6-phosphate dehydrogenase activity. The homozygous GSTP1 a/a genotype was associated with significantly higher levels of GST activity measured in lymphocytes, in comparison with the b/b genotype. Using multifactorial statistical analysis we found significant associations between smoking, GSTP1 genotype, plasma Vitamin C, and purine base damage in lymphocyte DNA. The difference in Vitamin C plasma levels between smokers and non-smokers was seen only with the GSTP1 b/b genotype. This group accounted also for most of the increase in purine oxidation in smokers. In contrast, the link between smoking and oxidised pyrimidines in DNA was seen only in the GSTT1 null group. It seems that polymorphisms in the phase II metabolising enzyme glutathione S-transferase may be important determinants of commonly measured biomarkers.

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