Cytochrome P450 2E1 and Glutathione S-transferase Polymorphisms in Oesophageal Cancer risk amongst South Africans

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Squamous cell carcinoma of the oesophagus is among the most common cancers among black South African males. The importance of genetic factors in determining individual susceptibility to cancer is becoming clearer. During detoxification of harmful substances, imbalances between phase I drug metabolism and phase II detoxification may contribute to the development of several diseases. Polymorphic variants in genes coding for the phase I enzymes lead to increased levels of bioactive compounds; whereas polymorphic variants in phase II enzymes often result in impaired detoxification. Several detoxification genes were investigated for their possible role in the development of oesophageal cancer. These included three CYP2E1 polymorphisms [the *Rsa* I (-1053C>T), *Pst* I (-1293G>A) and *Dra* I (7632T>A)], homozygous deletions of GSTM1 and GSTT1 and two single nucleotide polymorphisms in GSTP1 (313A>G, 341C>T). In comparing South African patients with controls, the CYP2E1 *Dra* I heterozygous genotype was associated with increased risk for the development of oesophageal squamous cell carcinoma ($P<0.001$) after adjusting for age, sex, smoking and alcohol consumption. The combination of the two GSTP1 mutations results in four alleles, *GSTP1*A, *B, *C* and **D*. The *GSTP1*X/*X* (combined *GSTP1*B/*B, *B/*C* and **D/*D*) was significantly associated with increased risk for oesophageal cancer ($P<0.001$). The *GSTM1*0/*0* genotype was significantly associated with decreased risk for oesophageal cancer ($P=0.001$).