Xenobiotic metabolising enzymes: influence of polymorphism on oesophageal cancer susceptibility

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Squamous cell carcinoma of the oesophagus is one of the most common cancers among black male South Africans. The importance of genetic factors in determining individual susceptibility to cancer is becoming clearer. Xenobiotic metabolising enzymes are an important part of cellular enzymatic defense against endogenous and exogenous chemicals, many of which have carcinogenic potential. These enzymes are classified into phase I and phase II. During detoxification of harmful substances, an imbalance between phase I drug metabolism and phase II detoxification may contribute to the development of several diseases and this imbalance is a result of genetic polymorphism. Genetic variants of phase I enzymes result in reduced, abolished or increased enzyme activity therby impairing bioactivation, whereas polymorphic variants in phase II often result in impaired detoxification. Several detoxification genes were investigated for their possible role in the development of oesophageal cancer. These included CYP3A5, CYP2E1, ALDH2 and GSTs amongst patients and control individuals in South Africa. In comparing patients with controls, some allelic variants and genotype combinations were associated with either increased or decreased risk for esophageal cancer. the CYP3A5 homozygous mutated genotypes were associated with decreased risk while wild type CYP3A5 was associated with increased risk for the development of squamous cell carcinoma of the oesophagus. Furthermore different South African population groups had different genetic profiles thereby having a different predisposition to oesophageal cancer.