

Age and gender differences in the association between MPO 463G>A and lung cancer. Results from the Genetic Susceptibility to Environmental Carcinogens pooled analysis.

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Myeloperoxidase (MPO) is a phase I metabolic enzyme that catalyzes the production of antimicrobial compounds, and converts the metabolites of benzo[a]pyrene from tobacco smoke into highly reactive epoxides. Once released outside the cell, MPO may damage the surrounding tissue through the oxidant properties of its products. A polymorphism in promoter region of MPO (463G>A) has been found to be associated with lung cancer. This polymorphism is also responsible for the creation of a novel estrogen receptor binding site, through which estrogens may increase MPO A allele promoter activity. This may induce gender specific differences in lung cancer risk. Aims of this study were to evaluate the association between MPO polymorphism and lung cancer, and the possible interactions between MPO polymorphism, gender and age. We performed a pooled analysis of 8 studies (2,905 cases and 3,085 controls) from the GSEC data-base. The MPO A allele was protective towards lung cancer (OR for A/G+A/A vs G/G=0.80, 95%CI 0.71-0.90), after adjusting for smoking and race. This effect was still present in males (OR=0.84, 95%CI 0.74-0.95), but not in females (OR=0.91, 95%CI 0.75-1.09). A significant interaction between MPO G/A genotype and age was found among females, with MPO being protective in younger (OR=0.4, 95%CI 0.17-0.94), but not in older women (OR=1.07, 95%CI 0.64-1.77). This analysis suggests that MPO may modify the relationship between estrogens and lung cancer. The significant protective effect of the MPO variant allele disappeared in older females, where exposure to estrogen has been longer in time, but has been discontinued.