Oncology of the chest

Genetic Association Study of CYP1A2 Polymorphisms Identifies Risk Haplotypes in Lung Cancer in Slovak Population.

*E. Halasova[1], A. Dzian[2], M. Skerenova[3], T. Matakova[4], P. Slovakova[5], R. Hruby[6]
[1]Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Department of Medical Biology (Martin, Slovakia)
[2]Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Clinic of Thoracic Surgery (Martin, Slovakia)
[3]University Hospital in Martin, Department of Clinical Biochemistry (Martin, Slovakia)
[4]Comnius University in Bratislava, Jessenius Faculty of Medicine in Martin, Department of Medical Biochemistry (Martin, Slovakia)
[5]Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Biomedical Centre in Martin (Martin, Slovakia)
[6]Hospital in Zilina, Department of Oncology (Zilina, Slovakia)

Objective: Phase I enzymes, including cytochrome P450, family 1, subfamily A, polypeptide 2 (CYP1A2), are involved in the activation of carcinogens, such as polycyclic aromatic hydrocarbons (PAHs), to reactive intermediates that are capable of binding covalently to DNA to form DNA adducts, potentially initiating the carcinogenic process. The aim of present study was to investigate the association of CYP1A2 gene polymorphisms and haplotypes with lung cancer risk.

Material and methods: A case-control study was carried out on 300 lung cancer cases and 333 controls. To investigate three CYP1A2 polymorphisms: rs2422299 (NC_000015.9: g.75033400A>G; 5'UTR of the CYP1A2 gene), rs2470890 (NC_000015.9: g.75047426C>T; c.1548C>T; p.Asn516=) and rs11072508 (NC_000015.9: g.75062397>G; 3'UTR of the CYP1A2 gene) we used high resolution melting analysis (HRM).

Results: We found significant allele associations (rs2470890, rs2422299) with lung cancer risk. We searched for important association under dominant, recessive and additive genetic models for all variants. Genotype association in recessive genetic model was found marginal significance for all three SNPs. Haplotype analysis included five haplotype variants with higher frequency than 1%. Haplotype with highest frequency "acc" was associated with an increased risk of lung cancer development („acc"; 38.7 % vs. 31.5 %; OR 1.378; 95% CI 0.945-2.006). Whereas rare haplotype „gtc" was associated with an increased risk of lung cancer development in the Slovak population. This significant protective effect p = 0.036.

Conclusions: The present study identified risk allele, genotype and haplotype associations for CYP1A2 in lung cancer.

Keywords: cytochrome P450, polymorphisms CYP1A2, haploptypes CYP1A2, lung cancer, Caucasian

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