Polymorphisms in the microsomal epoxide hydrolase gene: role in lung cancer susceptibility and prognosis

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ABSTRACT

Aims and background. The aim of this study was to investigate the relationship between EPHXI exon 3 Tyr113His and exon 4 His139Arg polymorphisms, predicted microsomal epoxide hydrolase (mEH) activity, and lung cancer development. mEH is a protective enzyme involved in oxidative defences against a number of environmental chemicals and pollutants, but it is also responsible for the xenobiotic activation of carcinogens.

Methods. We investigated the two polymorphisms of the mEH gene (EPHX1) in 58 lung cancer patients and 41 controls using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Results. The exon 3 Tyr113His polymorphism was associated with lung cancer (P <0.001). The frequency of the His113His homozygote genotype in exon 3 was significantly increased in patients compared with controls (P <0.001). In contrast, there was no significant difference in exon 4 polymorphisms between patients and controls. When the exon 3 and 4 polymorphisms were considered together, the combined EPHXI His113His/His139Arg genotype (very low predicted enzyme activity) was found to be associated with an increased risk of lung cancer (P = 0.044, OR = 3.063, CI = 0.932-10.069). We observed that patients with T3 + T4 tumors had an approximately 3-fold higher risk of the Tyr113/His113 genotype than patients with T1 + T2 tumors. Lung cancer patients carrying a heterozygote Tyr113/His113 genotype had a 2-fold increased risk of lymph node metastases (P = 0.051).

Conclusion. These findings suggest that the exon 3 Tyr113His and exon 4 His139Arg polymorphisms of EPHXI may be associated with a increased risk of lung cancer and a worse prognosis. Free full text available at www.tumorionline.it

Key words: microsomal epoxide hydrolase, lung cancer, exons 3 and 4 polymorphism, metastasis.

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