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

Zelal Erkisi[1], Ilhan Yaylim-Eraltan[1], Akif Turna[2], Uzay Görmüs[1], Hakan Camlica[3], and Turgay Isbir[4]

[1]Department of Medicine, Institute of Experimental Medical Research, University of Istanbul, Istanbul; [2]Department of Thoracic Surgery, Yedikule Teaching Hospital for Chest Diseases and Thoracic Surgery, Istanbul; [3]Division of Cancer Epidemiology and Biostatistics, Institute of Oncology, University of Istanbul, Istanbul; [4]Department of Medical Biology, Medical Faculty, Yeditepe University, Istanbul, Turkey

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 *EPHX1* His113His113/His139His139 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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Correspondence to: Prof Dr Turgay Isbir, Yeditepe University, Inönü Mah. Kayışdağı Cad. 26 Ağustos Yerle imi, 34755 Kadiköy – Istanbul, Turkey.
Tel/fax +90-0216-5780000;
e-mail tisbir@superonline.com

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