IV. 약물유전체학

한국인 방광암 발생에서 CYP2E1과 NQO1 유전자 다형성의 영향

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Genetic polymorphisms of NQO1 & CYP2E1 and risk of bladder cancer

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Cytochrome P450 2E1 (CYP2E1) and NAD(P)H:quinone oxidoreductase (NQO1) catalyze the activation of some environmental procarcinogen present in tobacco smoke, such as nitrosoamine. Although the association of genetic polymorphisms in NAT1 and NAT2 with bladder cancer have been reported, a limited numbers of studies have indicated the association of CYP2E1 and NQO1 with bladder cancer, particularly in Asian population. A hospital based case-control study was conducted in South Korean male, consisting of 218 histologically confirmed prevalent bladder cancer cases and 201 controls without cancer or systemic illness to evaluate the association between genetic polymorphisms of CYP2E1 (RsaI) and NQO1 (HinfI) and development of bladder cancer.

A PCR-RFLP method was used for the genotyping and statistical evaluations were performed by unconditional logistic regression model.

The risk of bladder cancer increased as the amount of smoking increased (p for trend=0.000). The frequency of CYP2E1 c1/c1 genotype in bladder cancer patients (57.9%) was significantly higher than in the controls (47.5%) (OR=1.9, 1.2-3.0). In case of NQO1, C/C genotypes in patients (45.8%) was higher than in the controls (37.8%) (OR=1.7, 95% CI=1.0-2.7). There were significant associations between smoking and CYP2E1, NQO1 genetic polymorphisms; heavy smokers (more than 25 pack year) with CYP2E1 c1/c1 genotype have 5.4-fold increased risk in development of bladder cancer (95% CI=1.4-21.4)

compared to non and light smokers with c2 allele and heavy smokers with NQO1 C/C genotype have 5.2-fold increased risk (95% CI=2.4-11.4) compared to non and light smokers with T allele.

Our findings suggest that genetic polymorphisms of CYP2E1 (Rsal, c1/c1) and NQO1 (HinfI, C/C) may play important role for development of bladder cancer among Korean men. Moreover, the results indicate that the associations between the genetic polymorphisms of CYP2E1, NQO1 and smoking are also important risk factors for bladder cancer.