

번호 10-2

제 목	국문	폐암 발생에 있어 glutathione S-transferase(GST) M1 , GSTT1, and CYP2E1의 유전적 다형성의 상호작용			
	영문	Interaction of genetic polymorphisms of glutathione S-transferase (GST) M1 , GSTT1, and CYP2E1 in development of lung cancer			
저 자 및 소 속	국문	강대희 ^o , 이승준, 최인미, 이영주, 최승호, 김영환, 조수현			
	영문	Kang DH ^{o1} , Lee SJ ² , Choi IM ¹ , Lee YJ ¹ , Choi SH, Kim YW, Cho SH ¹ ¹ Departments of Preventive Medicine and Internal Medicine, Seoul National University College of Medicine, Institute of Environmental Medicine, SNUMRC; ² Department of Internal Medicine, Hallym University College of Medicine			
분 야	보건관리 () 역 학 (○) 환 경 ()	발 표 자	일반회원 (○) 전 공 의 ()	발표 형식	구 연 (○) 포스터 ()
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1. 연구 목적

The association between genetic polymorphisms of glutathione S-transferase (GST) M1 and GSTT1 with lung cancer have been reported in populations with various ethnic background. However, the results are inconclusive. The results of previous studies on the association between CYP2E1 polymorphisms and lung cancer are also still controversial. A hospital based case-control study has been conducted to evaluate the role of genetic polymorphisms of GSTM1, GSTT1, and CYP2E1 in development of lung cancer.

2. 연구 방법

Two hundred and nineteen histologically confirmed lung cancer patients and 173 patients with no present or previous history of systemic illnesses, who visited the urology department, were recruited from Seoul National University Hospital during February 1997-May 1999. Information on demographic characteristics and smoking was collected. GSTM1 and GSTT1 genetic polymorphism were determined for 215 lung cancer cases and 166 controls by multiplex PCR. CYP2E1 genetic polymorphisms were determined for 206 cases and 149 controls by PCR followed by RsaI enzyme digestion. Adjusted odds ratios and 95% confidence intervals were estimated by unconditional logistic regression model. Twenty nine women cases were excluded for the analysis since controls were all men.

3. 연구 결과

More numbers of cases than controls are ever-smokers (94% for cases, 82% for controls, $p=0.001$ by chi-square test) and the average pack-years among ever-smokers was higher in cases than in controls (38 PY for cases, 30 PY for controls, $p=0.004$ by t-test). For patients with all lung cancer combined, neither GSTM1 or GSTT1 null genotype increased the risk (OR: 1.1, 95% CI: 0.7-1.7, for GSTM1; OR: 0.8, 95% CI: 0.5-1.2, for GSTT1). Men with at least one variant c2 alleles of CYP2E1 (c1/c2 or c2/c2 genotype) was not associated with increased risk of all lung cancer compared with homozygous wild type (c1/c1 genotype) (OR: 1.2, 95% CI: 0.8-1.9). When the OR was calculated by histology type, the OR of null GSTM1 with squamous cell cancer was 1.6 (95% CI: 0.9-2.8) and the OR of c2/c2 or c1/c2 genotype with small cell cancer was 1.8 (95% CI: 0.8-4.3). When the interactive effect of GSTM1 and GSTT1 was evaluated, the risk of development of squamous cell cancer in both null polymorphisms of GSTM1 and GSTT1 increased 2.2 fold compared with one (either GSTM1 or GSTM1) or null genotype (OR: 2.2, 95% CI: 1.2-4.2) when data were adjusted for age and smoking by the multiple logistic analysis.

4. 고찰

These results indicated that both null genotypes of GSTM1 and GSTT1 is associated with the increased risk of development of squamous cell lung cancer in men. The interactive effects with other genotypes (e.g., N-acetyl transferases, CYP1A1, etc.) presumably involved in lung carcinogenesis are currently being assessed in more numbers of study subjects (This project was supported in part by SNUMRC research grant).