Null Results in Brief

Lack of Association between *CCND1* G870A Polymorphism and Risk of Esophageal Squamous Cell Carcinoma[1]

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Introduction

ESCC,[3] like most malignant tumors, is primarily a consequent of abnormal cell proliferation induced by uncontrolled cell cycle. Cyclin D1 plays an important role in the transition from G_1 to S phase of the cell cycle and has oncogenic properties. Overexpression of this protein is thought to be related to the development of a variety of tumors, including ESCC (1). The gene encoding cyclin D1, *CCND1*, has a common G870A polymorphism at codon 242 in exon 4 that increases the frequency of alternate splicing, leading to an altered protein (2). The altered cyclin D1 does not contain the sequences involved in protein turnover and, thus, may have a longer acting half-life. It has been suggested that this polymorphism in the *CCND1* gene confers susceptibility to certain cancers (3–5).

In this study, we analyzed DNA samples from a hospital-based case-control study in a Chinese population to test the hypothesis that the *CCND1* G870A polymorphism may be a genetic risk modifier for ESCC.

Materials and Methods

This study included 321 patients with ESCC and 345 age- and gender-matched healthy controls. Patients were consecutively recruited from January 1998 to December 2000 at the Cancer Hospital, Chinese Academy of Medical Sciences (Beijing, China). Population controls were accrued from a database of nutritional survey conducted in the same regions. Most of the cases and controls have been characterized in a molecular epidemiological study described elsewhere (6). The *CCND1* G870A genotypes were determined by PCR-restriction fragment length polymorphism method as described previously (4). The ORs and their 95% CIs calculated by unconditional logistic regression models and adjusted for age, sex, and smoking status were used to estimate risk of ESCC for the *CCND1* polymorphism.

Results and Discussion

The allele frequencies for *CCND1* 870G and 870A were 0.424 and 0.576, respectively, among controls and 0.457 and 0.543, respectively, among cases with ESCC. The distribution of three *CCND1* G870A genotypes among cases were not significantly different from that among controls and, thus, the polymorphism did not associated with risk of ESCC (Table 1). In addition, no evidence for interaction between the polymorphism and tobacco smoking was observed.

Table 1 *CCND1* G870A genotypes in cases and controls and their association with the risk of esophageal cancer

Genotype	Cases (n = 321)		Controls (n = 345)		OR (95% CI)[a]
	n	(%)	*n*	(%)	
GG	68	(21.2)	58	(16.8)	1.00
GA	157	(48.9)	177	(51.3)	0.80 (0.53–1.21)
AA	96	(29.9)	110	(31.9)	0.80 (0.51–1.25)

[a] ORs and 95% CIs were calculated by logistic regression model with the *GG* genotype as the reference group and adjusted for age, gender, and smoking status.

Although this study had sufficient power (80%) to detect risk >1.8, we observed no association between the *CCND1* G870A polymorphism and risk of ESCC. These results indicate that the *CCND1* G870A genotypes themselves may not be involved in the predisposition to develop ESCC. However, in this study, we did not assay other genetic variations of cell cycle related proteins such as retinoblastoma and p21, which interact with cyclin D1 and also play key roles in cell cycle regulation. Without such information, we cannot exclude the possibility that the *CCND1* G870A polymorphism may confer susceptibility to ESCC via functional interaction with other genetic polymorphisms. Therefore, the results of this study highlight the need for additional studies on polygene analysis.

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[3] The abbreviations used are: ESCC, esophageal squamous cell carcinoma; OR, odds ratio; CI, confidence interval.

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