Null Results in Brief

No Association between *OGG1* Ser^{326}Cys and Risk of Basal Cell Carcinoma

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Introduction

Skin cancer is the most frequent type of cancer in the Western World, and the strongest known risk factor is exposure to UV light. The high-energy UV-B and UV-C light only constitute a small fraction of the total UV light in sunlight. UV-B and UV-C light induce pyrimidine dimers, which are repaired by nucleotide excision repair. The majority of the UV light in sunlight is UV-A light. UV-A light is absorbed in keratinocytes, giving rise to formation of reactive oxygen species (1). Formation of reactive oxygen species may directly or through reaction products cause oxidative stress and oxidative DNA damage. *OGG1* encodes 8-oxo-guanine glycosylase, a key enzyme in repair of 8-oxo-guanine and other oxidative DNA damages. Carriers of the variant allele of polymorphism *OGG1* Ser^{326}Cys are at relatively high risk of esophageal cancer, lung cancer, and prostate cancer (2), whereas no association has been found with risk of breast cancer (3). It is not clear whether the amino acid substitution affects the catalytic properties of the enzyme, because the catalytic activity was similar in Ser^{326} and Cys^{326} variants of *OGG1* measured in human lymphocytes from 34 individuals (4). On the other hand, the *OGG1* Ser^{326} wild-type protein complemented a defective *Escherichia coli fpg* mutant better than the Cys^{326} mutant protein (5). Moreover, the polymorphism is tightly linked to other polymorphisms in *OGG1*. It is therefore conceivable that carriers of the variant allele of the polymorphism could be at increased risk of basal cell carcinoma given that UV-A-induced oxidative DNA damage is involved in skin carcinogenesis.

To investigate the possibility of an association between the polymorphism *OGG1* Ser^{326}Cys and risk of basal cell carcinoma, we studied 319 cases and 319 controls all recruited from the Danish ''Diet, Cancer and Health'' cohort.

Materials and Methods

This nested case-control study was undertaken within the Danish prospective cohort ''Diet, Cancer and Health'' (6). Cases were 319 participants who developed basal cell carcinoma during follow-up. The 319 controls were matched to cases as described previously for a breast cancer case-control study on women (7), except that controls were matched to cases on age at inclusion into the cohort (half-year intervals) and sex and that both men and women were included in the study. The control was cancer-free at the age at diagnosis of the case.

The *OGG1* Ser^{326}Cys polymorphism (rs1052134) was genotyped by real-time PCR on a Sequence Detection System ABI 7700 (Applied Biosystems, Nærum, Denmark) as described (3). Controls were included in each run, and repeated genotyping of a random 10% subset yielded 100% identical genotypes.

A nested case-control study design was used (7). Due to the sampling design, the odds ratio was estimated using matched logistic regression; thus, only known discordant pairs contribute to this analysis. The procedure PHREG in SAS release 6.12 (SAS Institute, Inc., Cary, NC) on Unix platform was used for statistical analyses.

Results and Discussion

The allele frequency of the variant *G* allele for *OGG1* Ser^{326}Cys was 0.280 for cases and 0.279 for controls. This is close to the allele frequency of 0.24 among postmenopausal Danish women (3). The genotype distribution in the control group was in Hardy-Weinberg equilibrium. There was no association between genotype and risk of basal cell carcinoma (Table 1). No consistent effect measure modification from sex and age was observed (results not shown).

The design in this study is relatively strong for two reasons: the study is fairly large and cases and controls were carefully matched, being recruited from the same cohort of 57,053 Danes. Given the sample size and the allele frequencies among the controls, we had a 97% chance of detecting a 1.75-fold increase of the rate between the wild-type homozygote and the other two genotypes (two sided, $P = 0.05$).

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Table 1. Distribution of *OGG1* Ser^{326}Cys genotypes and risk of basal cell carcinoma

	OGG1 Ser^{326}Cys Genotypes		
	CC (Ser/Ser)	*CG* (Ser/Cys)	*GG* (Cys/Cys)
Cases	169	121	29
Controls	167	125	27
Odds ratio	1.00*	0.98	1.09
(95% confidence interval)		(0.70-1.37)	(0.59-2.03)

*The *CC* genotype served as reference category.

OGG1 Ser^{326}Cys is a risk factor for several cancer forms including lung cancer, esophageal cancer, and prostate cancer (2), but to our knowledge this is the first study on basal cell carcinoma. The lack of association observed in this study may reflect that gene-environment interactions are required, for which the environmental exposures are not present in Denmark, or that *OGG1* is not important for development of basal cell carcinoma.

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