

Null Results in Brief

No Association between *GPX Pro*¹⁹⁸Leu 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 that 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, among them hydrogen peroxide (1). Hydrogen peroxide accumulation may directly or through reaction products, such as hydroxyl radicals, cause oxidative stress and oxidative DNA damage. Glutathione peroxidase is part of the defense system that neutralizes hydrogen peroxide. Heterozygous and homozygous carriers of the variant allele of the *GPX Pro*¹⁹⁸Leu polymorphism are at 1.8-fold (95% confidence interval 1.2-2.8) and 2.3-fold (95% confidence interval 1.3-3.8) higher risk of lung cancer, respectively (2). Homozygous carriers of the variant allele are at 1.9-fold (95% confidence interval 1.0-3.6) increased risk of breast cancer (3). The amino acid substitution decreased the enzymatic activity of glutathione peroxidase in a cell line overexpressing the mutant protein compared with the same cell line overexpressing similar amounts of the wild-type enzyme (3). It is therefore conceivable that the polymorphism could increase the risk of basal cell carcinoma if UV-A-induced oxidative DNA damage is involved in skin carcinogenesis.

To investigate the possibility of an association between *GPX Pro*¹⁹⁸Leu polymorphism and risk of basal cell carcinoma, we studied 317 cases and 317 controls, all recruited from the Danish "Diet, Cancer, and Health" cohort.

Materials and Methods

This nested case-control study was undertaken within the Danish "Diet, Cancer, and Health" prospective cohort (4). Cases were 317 participants who developed basal cell carcinoma during follow-up. The 317 controls were matched on age at inclusion into the cohort (half-year intervals) and sex (5). The controls were cancer free at the age at diagnosis of the case.

The *GPX Pro*¹⁹⁸Leu polymorphism (rs#1050450) was genotyped by real-time PCR on a Sequence Detection System ABI 7700 (Applied Biosystems, Nærum, Denmark) as described (2). 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 (6). 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, SAS release 6.12 (SAS Institute, Inc., Cary, NC), on Unix platform was used for statistical analyses.

Results and Discussion

The allele frequencies of the variant *T* allele for *GPX Pro*¹⁹⁸Leu (0.312 and 0.304 for cases and controls, respectively) were close to the allele frequency for Finnish men of 0.36 (2). 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). Age at diagnosis of basal cell carcinoma did not modify the association between genotype and cancer risk (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 of the controls, we had a 94% chance of detecting a 1.8-fold higher incidence rate comparing the wild-type homozygote and the other two genotypes (two-sided, $P = 0.05$; ref. 2).

The lack of effect of the polymorphism in this study may reflect that gene-environment interactions are required, for which the environmental exposures are not present in Denmark, or that the gene is not important for development of basal cell carcinoma.

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Table 1. Distribution of *GPX Pro*¹⁹⁸*Leu* Genotypes and Risk of Basal Cell Carcinoma

	<i>GPX Pro</i> ³²⁶ <i>Leu</i> Genotypes		
	CC (Pro/Pro)	CT (Pro/Leu)	TT (Leu/Leu)
Cases	150	136	31
Controls	151	139	27
Odds ratio (95% confidence interval)	1.00*	0.96 (0.69-1.34)	1.21 (0.68-2.16)

*The CC genotype served as reference category.

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