Null Results in Brief

A Polymorphism in the *UDP-Glucuronosyltransferase 2B15* Gene ($D^{85}Y$) Is Not Associated with Prostate Cancer Risk

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Introduction

UGT,[2] a family of Phase II detoxification enzymes, catalyzes the transfer of the glucuronyl group from uridine diphosphoglucuronic acid to many substrates, including steroid hormones (1). Glucuronidation, an irreversible step in the pathway of steroid metabolism, converts steroids into polar, water soluble derivatives and may alter the levels of active androgens in steroid target tissues, such as the prostate. UGT2B15, a member of the UGT2B subfamily, is expressed in the liver as well as in several extrahepatic tissues, including the prostate, and is responsible for the glucuronidation of androgens (2).

In the human *UGT2B15* gene, a guanine-to-thymine single bp polymorphism has been identified that results in an amino acid change from aspartate (D^{85}) to tyrosine (Y^{85}) at position 85 (2). UGT2B15(D^{85}) and UGT2B15(Y^{85}) have similar substrate specificities. However, UGT2B15(Y^{85}) has a 2-fold higher V_{max} than UGT2B15(D^{85}) for C19 steroids, such as 5α-androstane-3α,17β-diol and dihydrotestosterone (3).

Because UGT2B enzymes play an important role in steroid metabolism and excretion, we investigated the association of the UGT2B15($D^{85}Y$) polymorphism and prostate cancer in a case control study of 190 patients with histologically verified, previously untreated prostate cancer and 190 age-matched control patients with BPH.

Materials and Methods

Study Population. Our case control study was conducted at the University of Vienna from October 1998 to January 2001. Cases were Caucasian patients (n = 190) with previously untreated, histologically verified prostate cancer. The control group (n = 190) consisted of Caucasian men with lower urinary tract symptoms because of BPH, in whom prostate cancer was excluded either clinically or histologically. Written consent was obtained from all participants, and the protocol was approved by the institutional review board at the University of Vienna. The details of the study population have been described previously (4). Controls were matched to the cancer patients on the basis of age (±2 years). The mean age was 65.9 years for prostate cancer cases and 66.5 years for controls; the median for both groups was 66 years.

Genotyping. Mononuclear cells were isolated by Ficoll-Paque (Amersham Pharmacia Biotech, Arlington Heights, IL) gradient centrifugation. Genomic DNA was extracted from mononuclear cells, using QIAmp Blood Kit (Qiagen Hilden, Germany). The UGT2B15 genotypes were determined by an oligonucleotide ligation assay as described by Lampe *et al.* (5).

Statistical Analysis. Analysis of data were performed using the computer software SPSS (Version 6.0.1 for Windows) and Epi Info (Version 6.04c). We used uncorrected χ^2 test to calculate *P*s and Cornfield 95% CLs for ORs. Whenever 95% CLs would not include unity, the corresponding OR was considered to be significantly different from unity.

Results

The UGT2B15($D^{85}Y$) genotype frequencies are presented in Table 1. The genotype frequencies were in Hardy Weinberg equilibrium. There was no difference in the prevalence of the UGT2B15(Y^{85}/Y^{85}) genotype between prostate cancer cases (27%) and controls (26%). Neither the UGT2B15(Y^{85}/Y^{85}) (OR = 1.2, 95% CL = 0.65–2.22) genotype nor the UGT2B15(D^{85}/Y^{85}) (OR = 1.25, 95% CL = 0.73–2.15) genotype was associated with prostate cancer risk.

Study Limitation. A potential limitation of our study is the hospital-based study design as BPH is also under steroid hormone control. On the other hand, using a population-based control of men in their 60s and 70s, it can be assumed that this control group is contaminated with undetected prostate cancer cases. Additionally, it is almost impossible to collect a population in this age group without BPH because the incidence of this disease is between 70 and 80% (6).

Statistical Power. We had 80% power to detect as statistically significant an OR of 2.2 when comparing the UGT2B15(D^{85}/Y^{85}) and UGT2B15(Y^{85}/Y^{85}) genotypes to the UGT2B15(D^{85}/D^{85}) genotype.

Conclusion

In this case control study of Caucasians, we could not observe an association between the UGT2B15($D^{85}Y$) polymorphism and prostate cancer. To date, only one study concerning the prevalence of the genetic polymorphism in UGT2B15 in healthy individuals from the Seattle area exists (5). They found a high prevalence of the variant allele (Y^{85}) in Caucasians; the allele frequency of 50% was nearly the same as in our control group.

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[2] The abbreviations used are: UGT, UDP-glucuronosyltransferase; BPH, benign prostatic hyperplasia; OR, odds ratio; CL, confidence limit.

Table 1 Association between prostate cancer risk and UGT2B15(D^{85}Y) polymorphism

UGT2B15 genotype	No. of controls (%) $n = 190$	No. of cases (%) $n = 190$	OR (95% CL)	*P*
UGT2B15(D^{85}/D^{85})	47 (25)	40 (21)	1.00 (reference)	
UGT2B15(D^{85}/Y^{85})	93 (49)	99 (52)	1.25 (0.73–2.15)	0.39
UGT2B15(Y^{85}/Y^{85})	50 (26)	51 (27)	1.20 (0.65–2.22)	0.54

Although glucuronidation of steroids by UGT enzymes is an important mechanism by which the levels of steroids are regulated in steroid target tissues, our data indicate that UGT2B15(D^{85}Y) polymorphism cannot be considered as a susceptibility marker for prostate cancer. However, because UGT2B15 enzymes are also involved in glucuronidation of numerous phytochemicals, this polymorphism could contribute to interindividual variability in chemopreventive effects (5).

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