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Large Differences in Testosterone Excretion in Korean and Swedish Men Are Strongly Associated with a UDP-Glucuronosyl Transferase 2B17 Polymorphism

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Context: The reproductive endocrinology in Asians and Caucasians is of great interest in view of large differences in prostate cancer rate and sensitivity to pharmacological male contraception. In addition, interpretation of certain antidoping tests is confounded by interethnic variation in androgen disposition. Uridine diphosphoglucuronosyl transferases have a key role in the homeostasis and metabolism of androgens. Recently a deletion polymorphism was detected in the *UGT2B17* gene.

Objective: The objective of the study was to evaluate the contribution of the UGT2B17 deletion polymorphism to the interindividual and interethnic variation of androgen metabolism and excretion.

Methods and Results: Urine from 122 Swedish and 74 Korean healthy men was analyzed for several androgen glucuronides including testosterone. The distribution of the natural logarithms of urinary testosterone concentrations showed a distinct bimodal pattern in both groups, suggesting a monogenic inheritance. When the UGT2B17 genotypes were compared with urinary testosterone levels, all of the individuals of the UGT2B17 homozygous deletion/deletion genotype had no or negligible amounts of urinary testosterone. The deletion/deletion genotype was seven times more common in the Korean (66.7%) than the Swedish population (9.3%). In addition, the Swedes had significantly higher levels of serum testosterone, compared with the Koreans.

Conclusions: Our results show that the UGT2B17 polymorphism is strongly associated with the bimodal distribution of the testosterone excretion and also with the large differences in testosterone excretion between Koreans and Swedes. **(*J Clin Endocrinol Metab* 91: 687–693, 2006)**

A NUMBER OF conspicuous interethnic differences between Asian and Caucasian men in reproductive endocrinology are still lacking an explanation [see van Houten and Gooren (1) for a review]. For example, the rate of prostate cancer is 2–40 times higher among Caucasian than Asian men (2). Differences between these groups in sensitivity to male contraception regimens have also been described. Thus, Asian men respond to exogenous contraceptive androgens with a higher suppression of spermatogenesis than Caucasian men (3, 4). It is also established that the urinary testosterone to epitestosterone ratio, commonly used in international antidoping test programs, is considerably lower in Asians than Caucasians, leading to difficulties in interpretation of the results. The limited effect of androgen doping on testosterone excretion in Asian populations increases the risk of false-negative results (5).

Much of the current interest in androgen research is focused on the role of testosterone in prostate cancer (6) and the detection and effects of doping to improve the physical achievements in sports (7). Whereas relatively much is known about the function of testosterone and its effects in target organs, little is known about its disposition including urinary excretion.

Testosterone is excreted mainly as glucuronide conjugates (8) after glucuronidation by uridine diphospho (UDP)-glucuronosyl transferases (UGT). These enzymes have a key role in the homeostasis of a number of endogenous molecules including steroid hormones (9), and they facilitate their excretion in bile and urine (9). There are seven members of the UGT2B subfamily. They have a preference for glucuronidation of bile acids, steroids, fatty acids, carboxylic acids, phenols, and carcinogens (9–11). One of these, UGT2B17, was found to be particularly active in androgen glucuronidation (12). A gene deletion in this enzyme gene was recently described (13), and it was further characterized by Wilson *et al.* (14). The physiological consequences of this deletion polymorphism are unknown.

Given this background, we decided to study the urinary excretion pattern and circulating concentrations of testosterone and other androgens in relation to the UGT2B17 genetic polymorphism in nonathlete volunteers of Caucasian and Asian ethnic descent. Our results show that this polymor-

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Abbreviations: Cr, Creatinine; del, deletion; DHT, dihydrotestosterone; ins, insertion; NST, non-SHBG bound testosterone; 17OHP, 17α-hydroxyprogesterone; UDP, uridine diphospho; UDPGA, UDP-glucuronic acid; UGT, uridine diphosphoglucuronosyl-transferase.

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phism is strongly associated with the bimodal distribution of the testosterone excretion as well as the large differences in androgen excretion between Asians and Caucasians. These data may have relevance for understanding the mechanisms behind prostate disease and are of great importance for the antidoping test programs.

Subjects and Methods

Study population and sample selection

Seventy-four unrelated Korean male subjects aged 21–39 yr (mean 26.3 ± 3.5 yr) were recruited among medical students and personnel at Inha University Hospital. Their health status was assessed by medical questionnaire. All subjects in this study participated voluntarily after giving informed consent. The study was approved by the Institutional Review Board at Inha University Hospital and the Ethics Committee at the Karolinska University Hospital. The Caucasian sample included 122 men aged 18.0–20.1 yr (mean 18.9 ± 0.6 yr), who were randomly selected from the Gothenburg Osteoporosis and Obesity Determinants study, which was initiated with the aim to determine both environmental and genetic factors for bone and fat mass, in which study subjects were randomly identified using national population registers, contacted by telephone, and asked to participate in this study. That study was approved by the Ethics Committee at Gothenburg University, and written informed consent was obtained from all participants.

Serum, plasma, and urine

In the Korean population, venous blood was obtained from the cubital vein and collected in EDTA tubes (for DNA and plasma extraction). Plasma was immediately extracted at 4 C and kept frozen at −20 C until analysis. In the Swedish population, whole blood was obtained from the cubital vein and collected in EDTA tubes (for DNA extraction) and gel-containing tubes (for serum extraction). Serum was extracted using standardized procedures, immediately frozen, and stored at −80 C until analysis. The serum and plasma samples were analyzed in the same laboratory using the same assay, and according to the manufacturer of the immunoassay kit for steroid analyses in the circulation (Orion Diagnostica, Espoo, Finland), identical results are obtained in serum and plasma.

Spot urine samples were collected and immediately frozen at −20 C. To minimize any influence of diurnal variation, all blood and urine samples were collected between 1400 and 1930 h.

Urinary steroids

Urinary unconjugated steroids (typically < 1% of glucuronide fraction) + steroid glucuronides were determined by gas chromatography-mass spectrometry after hydrolysis of the conjugates with β-glucuronidase as described (15) with minor modifications (16). Within- and between-assay coefficients of variation were less than 7% and less than 10% for all steroids analyzed.

Serum and plasma testosterone, SHBG, and 17α-hydroxyprogesterone (17OHP) assays

Testosterone was measured by Spectria [^{125}I]-coated tube RIA, and SHBG was measured by [^{125}I] immunoradiometric assay (Orion Diagnostica). Non-SHBG-bound testosterone (NST, sum of unbound + albumin-bound testosterone) was used as an index of biologically active testosterone as proposed by Pardridge (17). Apparent concentrations of NST were calculated from values for total testosterone, SHBG, and a fixed albumin concentration of 42 g/liter by successive approximation using a computer program based on an equation system derived from the law of mass action (18). Additional analysis of 17OHP was performed in subgroups of the populations consisting of 29 Koreans and 22 Swedes by competitive RIA using a commercial kit obtained from CIS Bio International, Gif-sur-Yvette, France (OHP-CT). Detection limits and within- and between-assay coefficients of variation were for testosterone 0.1 nmol/liter, 5.5 and 5.8%; SHBG 1.3 nmol/liter, 2.5 and 6.9%; and 17OHP 0.1 nmol/liter, 7.8 and 10.0%, respectively.

All the serum and plasma samples were analyzed in the same laboratory to avoid interassay variation.

Genotyping of the UGT2B17 deletion

Genotyping was essentially performed as previously described (14). The deletion-specific primers (J markers) and the exon 6-specific primers were used in a standard PCR-protocol (AmpliTaqDNA polymerase, Applied Biosystems, Foster City, CA), and the products were identified in a 2% agarose gel. Due to low DNA concentrations, some of the Swedish samples were analyzed with SYBRGREEN master mix (Applied Biosystems), and the product formations were followed on an ABI Prism 7700. Additionally these products were also confirmed on a gel. In DNA samples from heterozygous individuals [deletion (del)/insertion (ins)], a product from both the reactions appeared, whereas in individuals homozygous for the deletion allele (del/del) and individuals homozygous for UGT2B17 insertion allele (ins/ins), only one product was observed with either the deletion-specific primers or the exon 6 primers.

The number of subjects with DNA samples available for genotyping was 66 Koreans and 86 Swedes.

High-pressure liquid chromatography analysis of testosterone glucuronidation in human liver microsomes

Seventeen human liver tissue samples and DNA were obtained from 14 Caucasian and three Asian human donor livers. The donor samples were genotyped as previously described, and microsomes were prepared according to standard procedure (19).

The microsomes were stored in 50 mM potassium phosphate buffer (pH 7.4) at −80 C until use. The protein concentration was determined spectrophotometrically according to Lowry *et al.* (20).

Incubation samples were performed in duplicates as described by Narayanan *et al.* (21) using 75 μM testosterone as a substrate and 2.5 mM UDPGA as cofactor. The incubation was stopped by addition of 100 μl acetonitrile. The mixture was vortexed and centrifuged at 14,000 rpm for 5 min. The supernatant was removed and 20 μl injected onto a Zorbax SB-CN column (150 × 4.6 mm inner diameter, 5 μm; Agilent Technologies, Palo Alto, CA). The mobile phase consisted of acetonitrile (50 mM) ammonium phosphate buffer (pH 4.5) (30:70).

Peak areas of glucuronide were calculated using a calibration curve that was prepared for each experiment using glucuronide standard solutions. Enzyme activity was expressed as reaction velocity by dividing the amount of product formed by the incubation time and microsomal protein content (nanomoles per milligram per minute). The between-assay coefficient of variation was less than 9%.

Data analyses

The between-subject variability in urine dilution was corrected for by dividing the concentration values by the urinary creatinine (Cr) concentration. All urinary values are expressed as the unconjugated (typically <1% of glucuronide fraction) + the glucuronide conjugated fraction after correction for Cr. When the data were not normally distributed, the data are presented as the median with the 25th and 75th percentiles in parentheses.

Comparisons of hormonal levels were performed according to distribution with Student's two-tailed t test or the Mann-Whitney U test. For categorical variables, the χ^2 test was used.

Results

Urinary steroids and ethnicity

The median value of testosterone excretion was 16 times higher in the Swedish population [5.4 (3.7–7.1) ng/μmol Cr] than the Korean population [0.33 (0.25–0.58) ng/μmol Cr]. The epitestosterone concentrations did not differ between the ethnic groups. Most precursors and metabolites of testosterone investigated were significantly higher in the Swedes, with the exception for etiocholanolone, which was significantly higher in the Koreans (Table 1). Interestingly

TABLE 1. Urinary levels of the glucuronidated and unconjugated fraction of androgen metabolites in healthy men divided by ethnic descent and low and high urinary testosterone excretion phenotypes

	Ethnic descent		Excretion phenotype	
	Koreans (n = 74)	Swedes (n = 122)	Low testosterone (n = 65)	High testosterone (n = 131)
T/EpiT ratio	0.15 (0.08–0.68)	1.8 (1.0–2.6)[c]	0.11 (0.07–0.16)	1.8 (1.1–2.6)[c]
4-Androstenedione	0.13 (0.09–0.17)	0.32 (0.22–0.45)[c]	0.13 (0.09–0.18)	0.30 (0.19–0.45)[c]
5-Androstene-3β,17α-diol	4.4 (3.2–6.7)	6.7 (5.1–8.8)[c]	4.8 (3.4–6.9)	6.4 (4.8–8.7)[c]
Testosterone	0.33 (0.25–0.58)	5.4 (3.7–7.1)[c]	0.29 (0.23–0.40)	5.3 (3.9–7.1)[c]
Epitestosterone	3.0 (1.9–4.1)	3.4 (2.0–5.0)	3.0 (1.9–4.1)	3.4 (2.0–4.8)
Dihydrotestosterone	0.50 (0.23–0.80)	1.2 (0.64–1.8)[c]	0.43 (0.16–0.80)	1.1 (0.57–1.7)[c]
5α-Androstanedione	0.60 (0.40–0.91)	0.96 (0.61–1.6)[c]	0.61 (0.42–0.94)	0.92 (0.55–1.6)[c]
5α-Androstane,3α,17β-diol	4.9 (3.7–6.3)	4.9 (3.6–6.4)	4.4 (3.5–5.9)	5.2 (3.7–6.6)
5β-Androstane,3α,17β-diol	3.74 (2.52–5.83)	10.1 (6.2–15.2)[c]	3.1 (2.4–4.1)	10.4 (6.6–16.1)[c]
Androsterone	218 (171–264)	240 (196–309)[b]	220 (178–252)	243 (189–312)[b]
Etiocholanolone	119 (88.3–182)[b]	99.2 (57.3–158)	116 (87.0–159)	108 (61.3–170)
11β-OH Androsterone	62.9 (48.1–94.8)	82.5 (61.5–114)[c]	66.0 (51.2–97.3)	79.3 (57.3–110)[a]
11β-OH Etiocholanolone	4.3 (1.56–12.5)	23.0 (6.9–40.7)[c]	4.5 (1.8–14.4)	18.4 (5.7–36.3)[c]

Results are medians (in ng/μmol Cr) with the 25th and 75th percentiles in *parentheses.* Low and high testosterone excretion phenotypes are explained by the bimodal excretion pattern. In Koreans 74.3% and in Swedes 6.6% belonged to the low urinary testosterone excretion group, whereas 25.7% and 93.4% of the Koreans and Swedes, respectively, belong to the high testosterone excretion group.

[a] $P < 0.05$; [b] $P < 0.01$; [c] $P < 0.001$.

5β-androstane-3α,17β-diol excretion was 2.7 times higher in Swedes than Koreans, whereas no difference was found for 5α-androstane-3α,17β-diol. There were no differences between the ethnic groups in Cr excretion.

The distribution of the natural logarithms of urinary testosterone/Cr concentrations showed a distinct bimodal pattern in both the Korean and Swedish population (Fig. 1A). However, the distribution into the low- and high-excretion mode differed markedly. In Koreans, 74.3% and in Swedes 6.6% belonged to the low urinary testosterone excretion group, whereas 25.7 and 93.4% of the Koreans and Swedes belonged to the high testosterone excretion group. The urinary concentrations of androgens in the low and high testosterone excretion groups are listed in Table 1.

Serum testosterone, SHBG, and ethnicity

Compared with the Koreans, the Swedish population had significantly higher concentrations of total testosterone (18.0 ± 5.3 *vs.* 14.4 ± 4.6 nmol/liter, $P < 0.001$) and SHBG (20.2 ± 6.2 *vs.*18.2 ± 6.2 nmol/liter, $P = 0.030$). The NST also differed significantly between the two ethnic groups [13.4 ± 3.9 for Swedes and 10.8 ± 3.2 for Koreans ($P < 0.001$)] (Fig. 1B).

The NST correlated with the urinary testosterone in both Swedes (r = 0.35, $P < 0.001$) and Koreans (r = 0.39, $P < 0.001$). Similarly, total testosterone correlated significantly with SHBG in both Swedes (r = 0.28, $P = 0.002$) and Koreans (r = 0.52, $P < 0.001$).

UGT2B17 deletion genotypes

We screened 66 of the Koreans and 86 of the Swedes for presence or absence of the *UGT2B17* gene. The results in Table 2 show that the distribution of the genotypes was significantly different between these two ethnic groups (H_0, test for independence between genotype and ethnic background; $\chi^2 = 57.5$, 2 *df*, $P < 0.001$). The del/del genotype is 7.2 times more common among the Koreans than the Swedes (66.7 and 9.3%, respectively).

All of the Koreans and Swedes with the del/del genotype had unmeasurable or negligible amounts of urinary testosterone (Fig. 2, *left panel*). The genotype also significantly affected the excretion of dihydrotestosterone (DHT) (Fig. 2, *right panel*), although a large part of the samples (25% in the del/del, 26% in the ins/del, and 10% in the ins/ins group) had DHT glucuronide levels below the detection limit. The proportion of the samples that had unmeasurable levels of DHT was similar in both ethnic groups.

Serum hormones and genotype

In the subgroup analyzed for 17OHP, the levels of this steroid were significantly lower in the Korean del/del individuals (2.0 ± 0.7, n = 19) than the combined ins/del and ins/ins Koreans (2.7 ± 0.9, n = 10) ($P = 0.027$) and nonsignificantly reduced in the del/del Swedes (3.3 ± 1.3, n = 7), compared with the combined ins/del and ins/ins Swedes (4.2 ± 1.7, n = 15). The serum levels of testosterone, NST, and SHBG did not differ between the genotypes of the same ethnic descent.

In vitro testosterone glucuronide formation using human liver microsomes

Among the Caucasian liver donors, four had the del/del genotype, four were ins/del, and six belonged to the ins/ins genotype. Two of the Asian samples were del/del, whereas one had the ins/ins genotype. There was a significantly higher formation of testosterone glucuronide in human liver microsomes having one or two copies of the *UGT2B17* gene, compared with microsomes with the del/del genotype ($P = 0.038$) (Fig. 3). There was no difference in glucuronidation rate between the ins/del and the ins/ins genotype or between the ethnic groups within the same genotype.

Discussion

This work provides a genetic correlate for the conspicuous and large difference in testosterone excretion between Caucasians and Asians. We show for the first time that both Asian and Caucasian men can be divided into two subgroups ac-

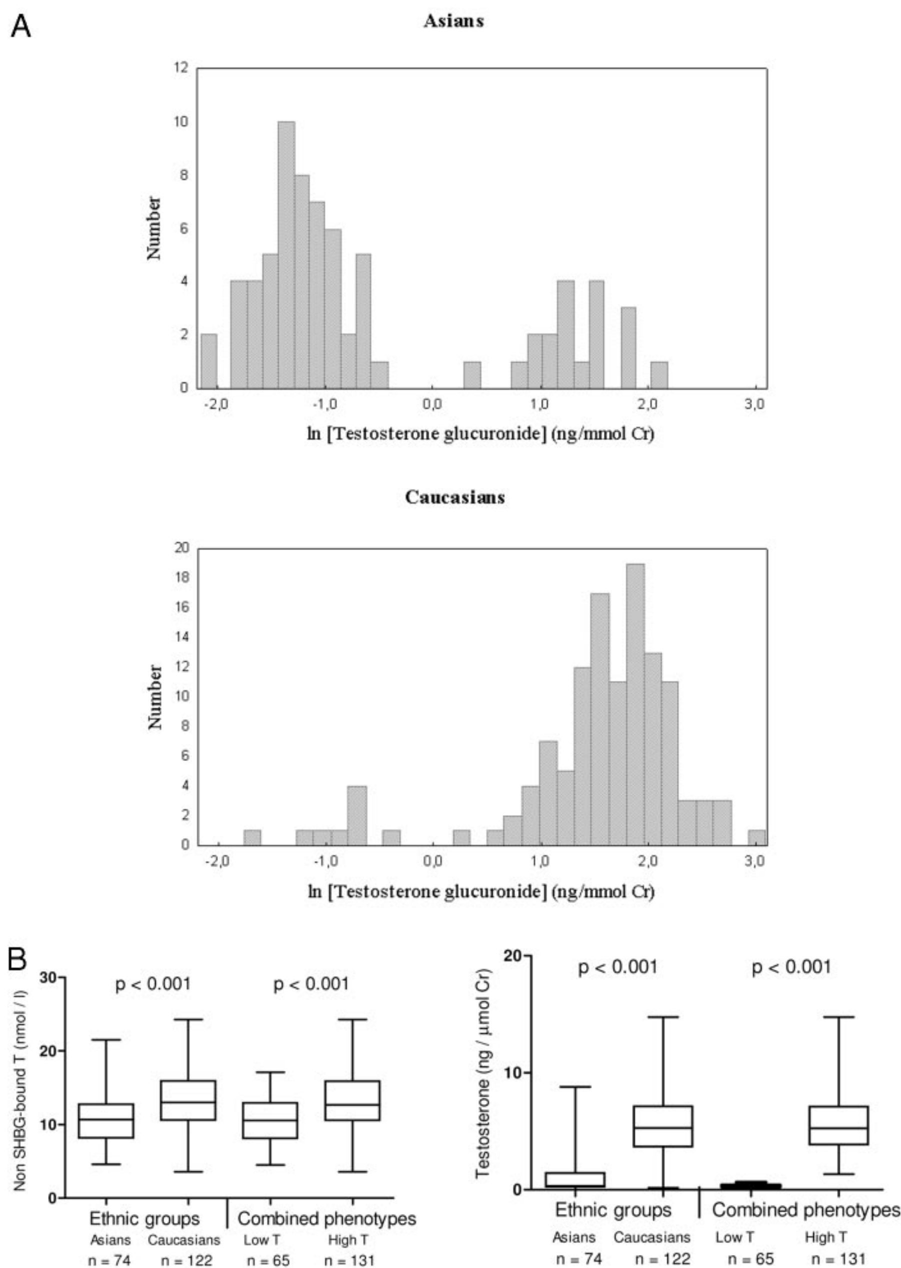

FIG. 1. A, Frequency distribution of natural logarithms of urinary unconjugated + glucuronide conjugated testosterone (nanograms per micromole Cr) in a Korean (n = 74) (*upper panel*) and Swedish (n = 122) (*lower panel*) population of healthy men. B, Serum levels of NST (nanomoles per liter) (*left panel*) and urinary unconjugated + glucuronide conjugated testosterone levels (nanograms per micromole Cr) (*right panel*) in Swedish, Koreans, and combined low and high urinary testosterone excretion phenotypes.

cording to their urinary testosterone levels (Fig. 1A). The bimodal distribution suggests a monogenic inheritance pattern. This assumption is strongly supported by our results, as all of the individuals of the UGT2B17 homozygous del/del genotype had no or negligible amounts of testosterone in their urine. This genotype is devoid of the enzyme gene (13, 14). There were three Asian individuals that were heterozygotes and one Asian that was homozygous for the ins/ins, yet they had negligible amounts of urinary testosterone. We have no explanation for this, but the possibility of other functional mutations in the UGT2B17 gene cannot be ruled out. Absence of the *UGT2B17* gene was seven times more common in the Korean than the Swedish population sample.

TABLE 2. UGT2B17 genotype distribution

	del/del % (n)	del/ins % (n)	ins/ins % (n)
Koreans	66.7 (44)	22.7 (15)	10.6 (7)
Swedes	9.3 (8)	39.5 (34)	51.2 (44)

It has been suggested that the low concentration of testosterone in male urine is a result of its rapid and complete conversion to the ultimate urinary metabolites (androsterone and etiocholanolone) due to higher specific enzyme activity toward testosterone (22). However, our results show that the low urinary testosterone excretion group, in addition to significantly lower levels of androsterone, also had significantly lower amounts of several investigated urinary testosterone metabolites (Table 1). Thus, it is conceivable that the low excretion is due to slow formation of androgen glucuronides.

We did not measure the glucuronidated fraction of testosterone in serum, but this fraction is also likely to be lower

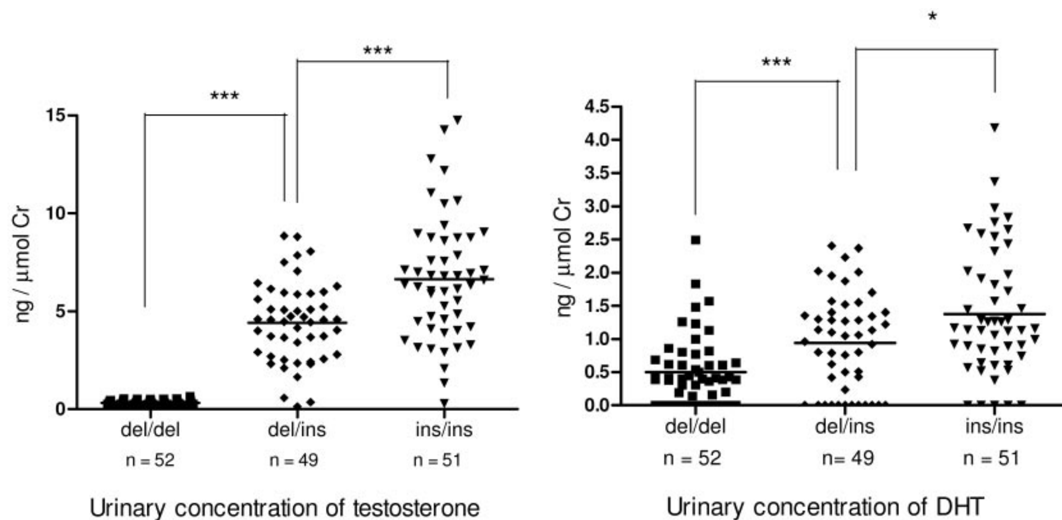

FIG. 2. Relation between urinary unconjugated + glucuronide conjugated testosterone glucuronide (nanograms per micromole Cr) (*left panel*) and urinary unconjugated + glucuronide conjugated DHT (nanograms per micromole Cr) (*right panel*) and UGT2B17 genotype in the combined Swedish and Korean population samples. Significances of differences are denoted (*, $P < 0.05$; and ***, $P < 0.001$).

in the Korean population considering the low urinary levels of testosterone glucuronide.

The serum levels of total testosterone, SHBG, and NST were also significantly higher in Caucasians, although the difference was not as large as for the urinary levels (Fig. 1B). The method used for calculating NST (17, 18) also enables the calculation of free testosterone. Recently it was shown that the method may overestimate the concentration of free testosterone, when compared with values measured by physicochemical methods (23). However, as far as we know from the literature, no corresponding comparisons have been undertaken for NST. Comparative studies on plasma levels of androgens in Asians and Caucasians have generated inconsistent results. Most investigators were unable to demonstrate a difference in serum concentrations of bioavailable testosterone (24–26), whereas one group (27) found even higher serum testosterone levels in Chinese men, compared with Caucasians. In contrast, de Jong *et al.* (28) and Heald *et al.* (29) found a slight difference, consistent with our findings. Lower levels of testosterone metabolites such as androsterone glucuronide and androstanediol glucuronide were observed in plasma of Asian subjects (24, 25). This finding was interpreted as a sign of lower androgen load, which may contribute to the lower incidence of prostate cancer in Asians. Their findings may be due to a larger proportion of UGT2B17 del/del genotypes among Asians, which we demonstrate in this work.

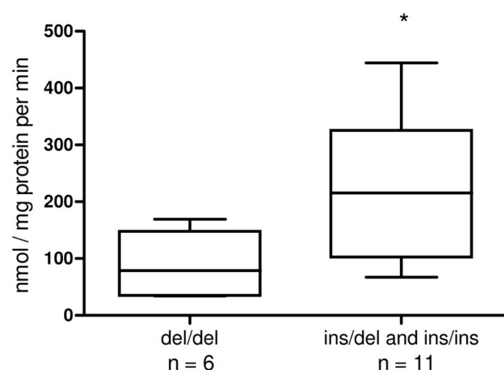

FIG. 3. Relation between testosterone glucuronidation rate and UGT2B17 genotype in microsomes from different human livers. Testosterone was used as a substrate and UDPGA as a cofactor. *, $P < 0.05$.

Seventy-five percent of circulating 17OHP is of testicular origin in healthy adult males. Theoretically, a decreased metabolism of testosterone is compatible with normal circulating testosterone concentrations provided the testicular testosterone synthesis is reduced. Other testicular steroids, such as 17OHP, being affected by the defective metabolism would then be present at subnormal concentrations (30). Consistent with this, serum 17OHP was significantly decreased in the Korean and combined ethnic del/del subjects. Unfortunately, we had access to only seven Swedish del/del samples, which makes it difficult to interpret the serum data. Further studies are needed to elucidate whether 17OHP levels and testicular activity are associated with the gene-deletion.

We found a positive correlation between serum testosterone and SHBG. This indicates that the UGT2B17 deletion does not seem to affect the hypothalamic-pituitary-testicular axis to any great extent (31) because such a correlation was also present in the Koreans in whom 67% had the del/del genotype.

We measured the glucuronidated moiety of steroids in urine. Only a minor part of the urinary testosterone is excreted as sulfate conjugates (8). However, it cannot be ruled out that there is a compensatory increase in sulfate conjugation of testosterone in subjects with low urinary testosterone. On the other hand, in a comparison of urinary sulfate and glucuronide conjugates of testosterone and epitestosterone, Borts and Bowers (32) found that both the sulfate and glucuronide conjugates of testosterone were lower in a Chinese than a Caucasian unselected population sample.

The UGT2B enzymes have a distinct, but overlapping, specificity toward different steroids (12). Turgeon *et al.* (12)

compared the enzymatic activity of UGT2B4, 2B7, 2B15, and 2B17 *in vitro* toward a number of different substrates including steroids. They found that UGT2B17 showed the highest activity toward testosterone and DHT and, surprisingly, also etiocholanolone. Our data are consistent with these results (12) except etiocholanolone that was not excreted at a lower rate in the del/del subjects. UGT2B15 was shown to have a low activity toward testosterone and a somewhat higher activity toward DHT (12). A $D^{85}Y$ polymorphism in the UGT2B15 gene increased the maximal velocity 2-fold for DHT and 5α-androstane-3α,17β-diol (33), the more active Y^{85} allele being more common in Caucasians (32.2%) than Asians (18.7%) (34). We did not study this polymorphism, but it is possible that it may have contributed to the interindividual and interethnic variation in glucuronidation of DHT and perhaps also testosterone. On the other hand, the urinary levels of 5α-androstane-3α,17β-diol, which is one of the major substrates of UGT2B15, were equal in Koreans and Swedes. Hence, it is unlikely that the UGT2B15 $D^{85}Y$ polymorphism had any considerable impact on our results.

Further support that the UGT2B17 del/del genotype is associated with a compromised testosterone conjugation capacity was obtained in our *in vitro* experiments using human liver microsomes (Fig. 3). We found that the del/del genotype was associated with a significantly lower glucuronidation rate. The residual basal rate of glucuronidation in the del/del genotype specimens may be explained by the presence of other UGT enzymes with testosterone glucuronidating activity *in vitro* (35) but with lower quantitative importance than UGT2B17.

Interestingly the UGT2B17 protein has been shown to have a more rapid turnover than other UGT2B enzyme proteins (12), which may have affected our results.

Our *in vitro* experiments demonstrating a basal rate of testosterone glucuronidation in the del/del genotype may seem inconsistent with the unmeasurable or negligible levels of glucuronide-conjugated testosterone in urine of the del/del subjects. However, it is important to note that the mutual contribution to the testosterone glucuronidation of the liver and extrahepatic organs, such as the prostate, is unknown.

It is conceivable that androgens play a pivotal role in prostate carcinogenesis. Therefore, androgen deprivation by inhibition of their synthesis and/or receptor interaction (36, 37) is the mainstay in treatment of prostate cancer. Environmental (38) and dietary (39) factors may explain only a minor part of the large difference in prostate cancer incidence between Asians and Caucasians (2). Because the UGT2B17 del/del genotype subjects had negligible levels of testosterone in their urine, this enzyme seems to be the most important one for testosterone glucuronidation *in vivo*. The genetic influence on glucuronidation activity in steroid target organs has not been studied. However, it is likely that genetically polymorphic testosterone glucuronidation is present in the basal cells of the prostate, in which UGT2B17 appears to be one of the most important glucuronic acid conjugating enzymes (40). Thus, the UGT2B17 deletion is important to study in relation to the prostate cancer rate.

In conclusion, the UGT2B17 deletion polymorphism, which is 7.2 times more common in our Asian, compared with our Caucasian, population sample group, provides a monogenic explanation for the low urinary testosterone excretion in Asian populations. A direct consequence of this is that the commonly used testosterone to epitestosterone ratio, used to detect testosterone abuse, would be more useful if taking the genetic constitution into account, particularly in Asians because the del/del trait is extremely common in this group. The importance of the polymorphism for the risk of prostate cancer is uncertain but certainly warrants further investigations.

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