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Human glutathione S-transferase polymorphisms associated with prostate cancer in the Brazilian population

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ABSTRACT

Objective: To evaluate the influence of polymorphisms in GSTA1, GSTM1, GSTT1, and GSTP1 in the risk of developing Prostate Cancer (PCa) in a population of Rio de Janeiro and compare the distribution of allele and genotype frequencies of the polymorphisms analyzed in the present study population with other regions in the country and different ethnic groups.

Materials and Methods: We analyzed a sample of the Brazilian population, comprising 196 patients with PCa treated by the urology services of the Brazilian National Cancer Institute (INCA) and Mario Kroeff Hospital (HMK), and 208 male blood donors from the Clementino Fraga Filho Hospital, Federal University of Rio de Janeiro (UFRJ). The polymorphisms were determined in DNA, extracted from peripheral blood leucocytes using the Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP).

Results: Our results showed that the distribution of polymorphisms can vary significantly according to the Brazilian region and ethnic groups. The distribution of allele and genotype frequencies of the polymorphism GSTA1 was statistically different between cases and controls. Genotypes (A / B + B / B) were associated with protection (OR = 0.61, 95 % CI = 0.40-0.92) for PCa in comparison to genotype A / A.

Conclusion: The distribution of genotype frequencies of the polymorphism GSTA1 was statistically different between the case and control groups (p = 0.023), and the presence of genotypes A / B and B / B suggests a protective role against the risk of PCa compared to genotype A / A. This is the first study that reports the genotypic frequency of this polymorphism and its association with PCa in a Brazilian population sample.

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INTRODUCTION

Prostate Cancer (PCa) is the second most common type of cancer in men (1). The incidence of PCa may vary among different ethnic groups and countries. The lowest rates are found in the Asian countries and the highest in the USA, Canada, Sweden, Australia, and France (2). In

Brazil, 68,800 new cases of PCa are estimated for 2014 (3).

The etiology of the PCa is still poorly understood and the lack of consistent results for markers of high penetrance suggests that susceptibility to PCa possibly involves the effects of multiple factors, including the interaction of low-penetrance genes associated with exposure to environmental factors (4). The biochemical basis for genetic susceptibility to environmental risks has been related to mutations in genes involved in the elimination of carcinogenic compounds in the body (5). Several polymorphic genes encoding enzymes involved in the biotransformation of carcinogens have been studied as potential modifiers of risk of prostate cancer, including genes of the family of glutathione S-transferases (GSTs) (6). GSTs are enzymes involved in phase II xenobiotic metabolism, characterized by the combination of hydrophobic and electrophilic compounds with glutathione, leading to more soluble compounds that can be excreted.

The GSTA1 (ID: 2938; 6p12.1) gene has two alleles, GSTA1 * A and GSTA1 * B, with 3 (three) SNPs (Single Nucleotide Polymorphisms) apparently linked (-567T, -69C, -52G and -567G, -69T, -52A, respectively). Although much is known about the polymorphism, the exact mechanism of how it affects gene expression has not been fully clarified yet, but it is known that the exchange of base G at A position -52 gene prevents binding of transcription factor (Sp1) of the promoter site, resulting in lower expression of the gene GSTA1 (7). Polymorphisms associated with decreased expression of the GSTA1 enzyme can lead to a buildup of carcinogens in the body and increase the risk of developing cancer (8). The GSTM1 (ID: 2944; 1p13.3) gene is polymorphic and has three allelic variants GSTM1 *0, GSTM1 *A, and GSTM1 *B, which have been widely investigated in various types of cancer (9-11).

Alleles GSTM1 *A and GSTM1 *B encode metabolically active enzymes. The difference between these two alleles is the exchange of a base G to C, the coding region at position 534 (G534C), so that there is a substitution of lysine for asparagine (Asn → Lys). This exchange does not affect the enzymatic function (12). The null allele, GSTM1 *0, is the result of deletion of the gene GSTM1 due to fusion of two homologous regions flanking the gene. Interest in GSTM1 has been stimulated by studies that suggest that homozygosity for GSTM1 *0 is associated with an increased risk for various cancers, due to no protein expression (13-15). Similar to GSTM1 *0, the GSTT1 (ID: 2952; 22q11.2) gene also has a null allele (GSTT1 *0). Despite the deficiency in the metabolism of carcinogenic compounds due to gene deletion, there is controversy about which allele (GSTT1 *0 or GSTT1 positive) would be at risk for cancer because unlike GSTM1, GSTT1 can play a role in both detoxification and activation processes (16).

The GSTP1 (ID: 2950; 11q13.2) gene has a G → A transition at nucleotide 313, causing a variation of isoleucine for valine at codon 105 (17). The substitution Ile105Val alters the kinetic properties of the enzyme with possible functional alteration in the detoxification process, which, in the event of prolonged exposure to carcinogens, could cause irreversible damage to DNA, favoring carcinogenesis (14,18). This polymorphism has been extensively investigated, and studies have revealed that the genotype GSTP1 105 Val / Val may be associated with increased risk for PCa (5,19,20).

We conducted a case-control study to investigate the influence of GSTA1 (rs 3957357), GSTM1, GSTT1, and GSTP1 I105V (rs 1695) genetic polymorphisms in the susceptibility to prostate cancer. Additionally, we developed a descriptive observational profile of these polymorphisms in a sample of the population of Rio de Janeiro and its comparison with other regions of the country and different ethnic groups.

MATERIALS AND METHODS

Subjects

The case group consisted of 196 adult patients between 42-80 years of age (mean 61.3 ± 7.00) who were diagnosed with prostate cancer, confirmed by histological examination, and treated at the Urology Services of the Brazilian National Cancer Institute (INCA) and of Mario Kröeff Hospital (HMK), 110 and 86 individuals, respectively, between February 2006 and September 2008. The control group consisted of 208 men aged between 43-86

years (mean 58.0 ± 7.78) recruited at the blood bank of INCA (66 individuals) and at the blood bank of Clementino Fraga Filho Hospital, Federal University of Rio de Janeiro (UFRJ) (142 individuals), from July 2006 to March 2009. All participants were given an explanation of the nature of the study, and informed consent was obtained. This study was approved by the ethics committee of INCA (registration# 091/05). All institutions are mapped in the city of Rio de Janeiro. The sample power was calculated based on Zar, 1999 (21).

Genotype analysis

To determine the genetic polymorphisms, samples were collected from peripheral blood in EDTA tubes properly identified. The genomic DNA extraction was performed from lymphocytes from whole blood, following the protocol with phenol and chloroform (22). All polymorphisms were determined in genomic DNA using PCR following protocols previously described (Table-1). GSTA1 and GSTP1 I105V polymorphisms were determined by Polymerase Chain Reaction and Restriction Fragment Length Polymorphism (PCR-RFLP). The technique of allele-specific PCR was applied to determine the GSTM1 polymorphism with three primers: one common, specific for the intron 6 (sense), and the other two for the exon 7 (antisense), specific to the alleles GSTM1 * A and GSTM1 * B. A fragment of the β-globin with 268 bp (primer forward CAA CTT CAT CCA CGT TCA CC and primer reverse GAA GAG CCA AGG ACA GGT AC) was co-amplified as internal control of the PCR reactions for GSTM1 and GSTT1. Negative controls containing all reagents in the reaction, except DNA, were included in all reactions in order to detect possible contamination of reagents. DNA products were separated by electrophoresis in a 1.5% agarose gel, at 80V in 1X TAE buffer (Tris-Acetate-EDTA). The identification of the DNA fragments after the enzymatic digestion was performed in 10% polyacrylamide gels at 180V in 1X TBE buffer (Tris-Borate-EDTA) (23). In all digestions DNAs from positive controls (holders of the enzyme cleavage site) were included to verify the success of the reaction. After electrophoresis, the gels were stained with ethidium bromide and visualized under ultraviolet (UV) light. DNA fragment sizes were estimated by comparison with pBR322/Hae III molecular weight marker (Uniscience® Brazil) (Figure-1).

Statistical analysis

Calculations of allele frequencies were performed using the maximum likelihood method. Tests for Hardy-Weinberg and the heterogeneity of the samples were made by using the chi-square tests (χ^2). The statistical program Epi Info version 6.0 was used to estimate the hazard ratio with a confidence interval of 95%. The chi-square (χ^2) was also used to compare the frequencies of the alleles found in this study with the frequencies observed in other populations (literature data).

RESULTS

All polymorphisms were in Hardy-Weinberg equilibrium in the case and in the control populations (Table-2). Table-3 shows the analysis of the association between GSTA1, GSTM1, GSTT1, and GSTP1 I105V polymorphisms and the risk for PCa. Interestingly, the results showed a statistically significant protective association between GSTA1 genotypes A / B + B / B and PCa (OR = 0.61, 95% IC 0.40 - 0.92, p = 0.018).

The analysis of the genotype distribution of GSTM1, GSTT1, and GSTP1 Ile105Val polymorphisms showed that the case and control populations were homogeneous with respect to these polymorphisms. Thus, the two groups were assembled (cases + controls) to form a single larger and more representative group of the population that was used for comparisons with literature data. GSTA1 for polymorphism allele frequency in comparison with the other populations was performed using only the control group, since the samples (cases and controls) were not homogenous. For GSTM1 and GSTT1 polymorphism comparison among the different ethnic groups, analysis of phenotypes (positive and null) was performed because the inability to distinguish between homozygous and heterozygous genotypes for the technique used did not allow us to count genes (Table-4).

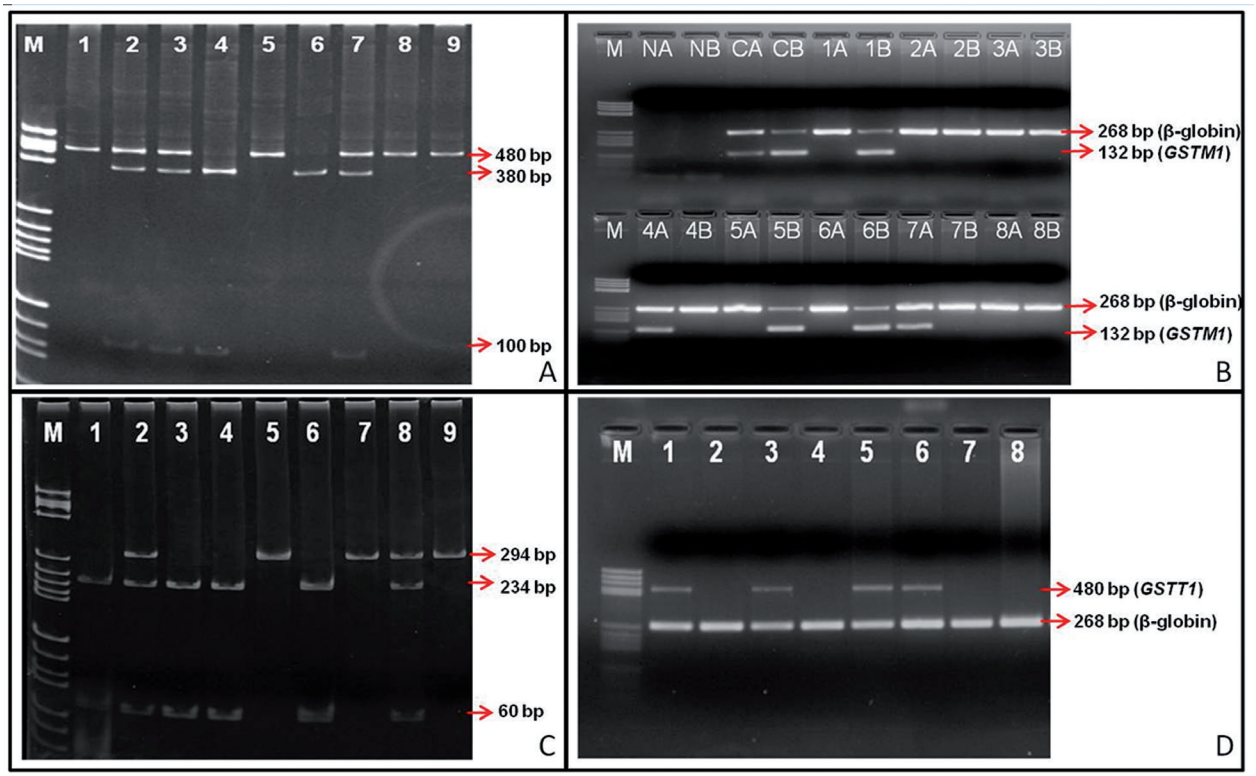
The allele frequencies of GSTA1 (only the control group) and GSTT1 polymorphisms showed no statistically significant difference when compared

Table 1 - Conditions established after standardization of the techniques of PCR, allele-specific PCR and PCR-RFLP for the determination of polymorphisms GSTA1, GSTP1 I105V, GSTT1 and GSTM1.

		GSTA1 C-69T (rs 3957357)	GSTP1 I105V (rs 1695)	GSTT1 null	GSTM1 null
Technique		PCR-RFLP	PCR-RFLP	PCR	PCR allele-specific
Reference		14	36	37	38
Oligonucleotide Sequence (5`at 3`)*		F - TGT TGA TTG TTT GCC TGA AAT T R - GTT AAA CGC TGT CAC CCG TCC T	F - TCC TTC CAC GCA CAT CCT CT R - AGC CCC TTT CTT TGT TCA GC	F - TTC CTT ACT GGT CCT CAC ATC TC R - TCA CCG GAT CAT GGC CAG CA	F - GCT TCA CGT GTT ATG AAG GTT C RA - TTG GGA AGG CGT CCA AGC GC RB - TTG GGA AGG CGT CCA AGC AG
Amplification conditions **	Reaction buffer	1 X	1 X	1 X	1 X
	$MgCl_2$	2 mM	2 mM	2 mM	2 mM
	dNTP	200µM	200 µM	200 µM	200 µM
	Oligonucleotide 10 pmol each		10 pmol each	10 pmol each	10 pmol each
	Taq DNA pol.	2U	1U	2U	2U
	Final volume	25 µL	25 µL	20 µL	25 µL
Amplicom		480 bp	294 bp	480 bp	480 bp
Cycling	Initial Denaturation	94ºC - 5min	94°C – 30s	94°C – 5 min	94°C – 2,5 min.
	Denaturation	94ºC/1min	94°C/30 s	94°C/1min 30 cycles	94°C/45 s 5 cycles
	Annealing	64ºC/1min 35	68°C/30s(-1°C for cycle)	60°C/1min	57°C/1min
	Extension	72ºC/1min. cycles	20 cycles	72°C/2min	72°C/2min
	Denaturation		72°C/30 s 97°C/ 30 s		94°C/ 30 s 30 cycles
	Annealing		51°C/ 30 s		57°C/ 30 s
	Extension		10 cycles 72°C/ 30 s		72°C/45s (-3s for cycle)
	Final Extension	72ºC – 5min.	72°C – 10 min.	72°C – 10 min.	72°C – 10 min.
Restriction enzyme ***		*Ear* I (10U)	*BsmA* I (3U)	-	-
Effect of SNP on the DNA sequence		Creation of restriction site	Creation of restriction site	-	-
Fragments wild-type allele		480 bp	294 bp	-	-
Fragments mutant allele		380 e 100 bp	234 e 60 bp	-	-
Digestion Temperature		37ºC	37°C	-	-
Digestion time		20 h	20h	-	-

*** F**= Foward; **R=** Reverse ; **RA**= Reverse allele GSTM1*A; **RB**= Reverse allele GSTM1*B. ** Taq DNA polimerase e Buffer Biotools [50mM KCl, 2mM $MgCl_2$, 20mM $(NH4)_2SO_4$, 75mM Tris-HCl, pH 9,0]; *** Restriction enzyme of New England BioLabs; 1U = 1 unit = enzyme amount capable of digesting 1 mg of DNA; bp = base pair.

Figure 1 - Electrophoresis profile of polymorphisms GSTA1, GSTM1, GSTT1 and GSTP1.



M = molecular weight marker pBR322/Hae III, **A)** Gel of 10% polyacrylamide with the GSTA1 products digested by Ear I. Lanes 1, 5, 8, and 9 = homozygous for the wild type allele (A / A), 2, 3, and 7 = heterozygous (A / B) 4, and 6 = homozygous for the mutant allele (B / B). **B)** Gel 2.5% agarose with GSTM1 amplification products by allele-specific PCR. NA and NB = negative control; CA and CB = positive for the A and B alleles (genotype A / B) controls; 2, 3 and 8 = homozygous for the null allele (GSTM1 0/0); 1, 5 and 6 = negative for allele A and allele B for the positive (B phenotype / -) individuals; Lanes 4, 7 = positive for individuals negative for allele A and B (phenotype A / -). **C)** Gel to 10% polyacrylamide with the products of digestion with GSTP1 by BSMA I. Sample 5, 7 and 9 = homozygous for the wild type allele (Ile / Ile) 2 and 8 = heterozygous (Ile / Val), 1, 3, 4 and 6 = homozygous for the mutant allele (Val / Val) individuals. **D)** Agarose gel 2.5% with GSTT1 amplification products. Lanes 2, 4, 7, and 8 = homozygous for the null allele (null genotype) individuals; 1, 3, 5, and 6 = subjects with at least one active allele for the gene GSTT1 (T / T or T / 0).

to the frequencies of different populations of Caucasians and African-Americans, differing only in the Japanese population. The frequency of GSTM1 genotype frequencies varied significantly in Caucasians, African-Americans, and Asians while the allele frequency of the GSTP1 I105V polymorphism was unique, and showed a statistically significant difference in relation to the frequencies observed in other ethnic groups, with the exception of another population, the city of Sao Paulo (Table-4).

DISCUSSION

The metabolism of xenobiotic compounds is one of the most versatile mechanisms for cell protection. GSTs belong to a multigene family of dimeric enzymes that catalyze the conjugation of a number of carcinogens and endogenous compounds. Furthermore, studies suggest that GSTs are involved in the intracellular transport of steroid hormones (24). The cumulative exposure over a lifetime to androgens, androgen metabolites, and carcinogenic products can develop PCa in men who are genetically predisposed (25). Thus, the identification of genetic markers that are actually associated with initiation and progression of prostate tumors would enable the identification of men at risk for PCa, allowing the development of preventive strategies for this cancer.

This study presents the first data on the frequency of GSTA1*A (-567T, -69C, -52G) and GSTA1*B (-567G, -69T, -52A) polymorphisms in

Table 2 - Analysis of Hardy-Weinberg equilibrium for the genetic sample of controls and patients with PCa polymorphisms.

Genotypes	Observed	Expected	χ^2_1	p
Controls				
GSTA1 A/A	76	79.147		
A/B	99	92.706	0.917	0.338
B/B	24	27.147		
GSTM1 0/0	87	83.830		
A/ -	70	73.171	1.393	0.238
B/ -	32	35.171		
A/B	15	11.829		
GSTP1 I/I	85	85.043		
I/V	96	95.914	0.000	0.999
V/V	27	27.043		
Patients				
GSTA1 A/A	99	101.434		
A/B	84	79.133	0.741	0.389
B/B	13	15.433		
GSTM1 0/0	80	81.205		
A/ -	88	86.795	0.285	0.593
B/ -	21	19,795		
A/B	7	8.205		
GSTP1 I/I	73	76.563		
I/V	99	91.875	1.179	0.277
V/V	24	27.562		

χ^2_1 = chi-square with one degree of freedom.

a Brazilian population. The analyses revealed that the genotype frequencies were significantly different between cases and controls (p = 0.023), suggesting an association between the GSTA1 polymorphism and the risk of PCa (OR = 0.61, 95% CI = 0.40 to 0.92) (Table-2). Previously, a case--control study (190 patients with PCa and 294 controls) in Japan found no statistically significant association in the overall analysis (14). However, after conducting an analysis stratified by smoking, they observed among smokers a higher risk for PCa associated with genotypes A / B and B / B (OR = 1.72, 95% CI = 1.01 to 2.72). It was reported that a GSTA1 enzyme is efficient in the detoxification of compounds derived from tobacco, such as 2-amino-1-methyl-6-phenylimidazo [4,5-β] pyridine (PhIP) (26). Therefore, GSTA1 possibly plays an important role in protecting DNA against compounds derived from tobacco. Although this observation requires further study, the effect of smoking may be more important for susceptible populations such as those with a higher frequency

Table 3 - Analysis of association between genetic polymorphisms and the risk of Prostate Cancer.

Genotypes	Cases	Controls	OR(IC 95%)	P (Yates)
GSTA1 A/A	99	76	1	
A/B	84	99	0.65 (0.42 – 1.01)	0.056
B/B	13	24	0.42 (0.19 – 0.92)	0.028
A/B + B/B	97	123	0.61 (0.40 – 0.92)	0.018
GSTM1 Positive	116	117	1	
Null	80	87	0.93 (0.61 - 1.41)	0.787
GSTT1 Positive	161	161	1	
Null	35	47	0.74 (0.44 - 1.25)	0.289
GSTP1 I/I	73	85	1	
I/V	99	96	1.20 (0.77 - 1.87)	0.455
V/V	24	27	1.04 (0.52 - 2.04)	0.956

of GSTA1 genotypes A / B or B / B. Unfortunately, we do not have data on tobacco use to perform analyses similar to those of Komiya et al. (14). Association studies with prostate cancer GSTA1 are rare, but they were also conducted for other types of cancer. A recent study found an association of the A / A genotype with the risk of gastric cancer in the Vietnamese population (OR = 4.3, 95% CI = 1.2 to 17) (27). Genotypes related to reduced expression of GSTA1 (GSTA1 A / B and B / B) were associated with breast cancer, especially among women smokers (OR = 1.89, 95% CI = 1.09 - 3.25) and those with lower consumption of cruciferous vegetables (OR = 1.73, 95% CI = 1.10 to 2.72) (28).

Little is known about the influence of the GSTA1 polymorphism in the prostate. However, the observation that the expression of this enzyme is increased in situations involving oxidative stress and proliferative hyperplasia associated with chronic inflammation (29) and is reduced in tumors of the prostate intraepithelial reinforce the idea of the possible GSTA1 involvement in carcinogenesis of prostate cancer (30).

In the present study, the distribution of genotype frequencies for GSTM1, GSTT1, and GSTP1 I105V polymorphisms showed no differences between the groups of cases and controls. Risk analysis detected no statistically significant association between these polymorphisms and prostate cancer, suggesting that they do not influence the risk of developing PCa in the Brazilian population (Table-2). For GSTT1 and GSTP1 I105V polymorphisms, some previous studies also reported no association with PCa corroborating our results (6,14,31-33). We found only one study in the Brazilian population, conducted in Sao Paulo, which examined the relationship of GSTT1 and GSTP1 I105V polymorphisms with the risk of PCa (32). The authors also looked at variables such as dietary habits, alcohol consumption, smoking, skin color, among other factors in 225 subjects (125 patients with PCa and 100 patients with benign prostatic hyperplasia (BPH), used as controls). Even after stratification of the population for these variables, Lima et al. (32) found no association of these polymorphisms with PCa. A meta-analysis (33) involving 22 studies with the GSTT1 polymorphism (totaling 4,564 cases and 4,552 controls) and 24 studies with the GSTP1 I105V polymorphism (totaling 5,301 cases and 5,621 controls) also showed no association of these polymorphisms with PCa (OR = 1.05, 95% CI = 0.86 to 1.27 and OR = 1.06, 95% CI = 0.91 to 1.24, respectively). Significant associations of alleles GSTT1 and GSTP1 * 0 * 105V

Table 4 - Comparison of allelic polymorphisms of GSTA1, GSTM1, GSTT1 and GSTP1 I105V in the study population and different populations

GSTA1			
Population (nº of alelles)	**GSTA1*A (%)**	**GSTA1*B (%)**	**p**
This study ** (398)	251 (63)	147 (37)	-
Caucasians[a] (EUA) (162)	92 (57)	70 (43)	0.166
Afro-Americans[a] (EUA) (126)	81 (64)	45 (36)	0.804
Japanese[b] (588)	526(89)	62 (11)	< 0.001
GSTP1 I105V			
Population (nº of alelles)	**Ile (%)**	**Val (%)**	**p**
This study* (808)	511 (63)	297(37)	-
Rio de Janeiro[c] (Brazil) (1182)	813 (69)	369 (31)	0.01
São Paulo (Brazil)[d] (442)	303 (68)	139 (32)	0.06
Caucasians[e] (Eslováquia) (456)	333 (73)	123 (27)	<0.001
Afro-Americans[f] (EUA) (1144)	646 (57)	498 (43)	0.003
Japonese[b] (582)	493 (85)	89 (15)	<0.001
Genotype GSTM1			
Population (nº of individuals)	**POSITIVE (%)**	**NULL (%)**	**p**
This study* (400)	233 (58)	167 (42)	-
Rio de Janeiro[c] (Brazil) (591)	342 (58)	249 (42)	0.905
São Paulo[d] (Brazil) (221)	120 (54)	101 (46)	0.341
Caucasians[g] (Portugual) (325)	157 (48)	168 (52)	0.007
Afro-Americans[f] (EUA) (578)	441 (76)	137 (24)	<0.001
Japonese[b] (474)	224 (47)	250 (53)	<0.001
Genotype GSTT1			
Population (nº of individuals)	**POSITIVE (%)**	**NULL (%)**	**p**
This study* (404)	322 (80)	82 (20)	-
Rio de Janeiro[c] (Brazil) (591)	441 (75)	150 (25)	0.062
São Paulo[d] (Brazil) 221	178 (80)	43 (20)	0.802
Caucasians[g] (Portugual) (329)	254(77)	75 (23)	0.412
Afro-Americans[f] (EUA) (584)	482 (83)	102 (17)	0.261
Japonese[b] (288)	149 (52)	139(48)	<0.001

Reference population; **Reference population = control group in this study; [a]39; b14; c16; d40; e20; f6; g41.

with PCa were detectable only after correlation with other factors. For example, Komiya et al. (14) showed an association between PCa and the GSTT1 null genotype, only when the sample was stratified for smokers and non-smokers. The association was observed for the group of smokers: OR = 1.68, 95% CI = 1.06 to 2.68. Regarding the GSTP1 I105V polymorphism, Lavender et al. (6) showed that the genotype Val / Val was significantly associated with PCa only when considered in conjunction with the positive GSTM1 genotype (OR = 2.11, 95% CI = 1.07 to 4.16). Another study (31) showed that the Val / Val genotype was associated with an increased risk of PCa (OR = 1.85, 95% CI = 1.19 to 2.89) in Americans exposed to aromatic hydrocarbons (PAH). For the GSTM1 polymorphism, for example, Agalliu et al. (34) found an increased risk of PCa for the GSTM1 null genotype in U.S. Caucasians (OR = 1.54, 95% CI = 1.19 to 2.01). Subsequently, a meta-analysis of a sample of 4,564 cases and 5,464 controls also showed an increase of 1.3 times the risk for PCa (OR = 1.33, 95% CI = 1.15 to 1.55) in individuals with the GSTM1 null genotype (33).

The differences observed in susceptibility studies can be attributed to several factors such as sample size, differences in exposure to biological, chemical, or physical differences in genetic profile and among populations. The evaluation of the combined effects of other susceptibility factors, including other polymorphisms, in a larger study population, could help determine the actual genetic role in the development of PCa.

Variations in the frequencies of polymorphisms in the same population and among different ethnic groups (Table-3) reinforce the importance of being careful in planning epidemiological studies on the role of these polymorphisms in modulating susceptibility to cancer and other diseases. Our results show that GST genotype frequencies in the human population differ among ethnic and geographic groups. Interestingly, the observed frequencies quoted for the Brazilian population are average values of the frequencies found in Caucasians and Africans (Table-3), corroborating data on the mixing of these two dominant groups in southeastern Brazil (35).

Studies in other regions of the country and with a larger sample size are needed to confirm our results; however, we believe that the identification of the genotypic profile of the sample certainly contributes important information for the identification and reassessment of the role of these polymorphisms in a Brazilian population.

CONCLUSIONS

This is the first study that reports the genotypic frequency of the GSTA1 polymorphism and its association with PCa in a Brazilian population cohort. The distribution of genotype frequencies for GSTM1, GSTT1, and GSTP1 I105V polymorphisms were not associated with risk of prostate cancer in the study sample. The distribution of allele and genotype frequencies of GSTA1, GSTM1, GSTT1 and GSTP1 I105V polymorphisms was statistically different from that of most of the populations compared, showing that a deeper study more specific to the Brazilian population is necessary to design preventive strategies to fight PCa and therapeutic follow-up differentiated from those for other populations.

ABBREVIATIONS

FIOCRUZ = Fundação Oswaldo Cruz
GSTA1 = glutathione S-transferase Alpha 1
GSTM1 = glutathione S-transferase Mu 1
GSTP1 = glutathione S-transferase Pi 1
GSTT1 = glutathione S-transferase Theta 1
HMK = Mario Kroeff Hospital
INCA = Brazilian National Cancer Institute
PCa = Prostate cancer
PCR = Polymerase Chain Reaction
PCR-RFLP = Restriction Fragment Length Polymorphism
SNP = Single Nucleotide Polymorphisms

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CONFLICT OF INTEREST

None declared.

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