RESEARCH ARTICLE

Genetic Polymorphisms of Glutathione S-transferase M1 and Prostate Cancer Risk in Asians: A Meta-analysis of 18 Studies

Zheng-Hui Hu, Yi-Wei Lin, Xin Xu, Hong Chen, Ye-Qing Mao, Jian Wu, Yi Zhu, Xiang-Lai Xu, Li-Ping Xie*

Abstract

Background: Many studies have investigated associations between the glutathione S-transferase M1 (GSTM1) null polymorphism and risk of prostate cancer, but the impact of GSTM1 in people who live in Asian countries is still unclear owing to inconsistencies across results. Methods: We searched the PubMed, Web of Science, Scopus, Ovid and CNKI databases for studies of associations between the GSTM1 null genotype and risk of prostate cancer in people who live in Asian countries, and estimated summary odds ratios (ORs) with 95% confidence intervals (95% CIs). Results: A total of 18 case-control studies with 2,172 cases and 3,258 controls were included in this meta-analysis, which showed the GSTM1 null genotype to be significantly associated with increased risk of prostate cancer in people who live in Asian countries (random-effects OR=1.74, 95% CI1.44-2.09, *P*<0.001). Similar results were found in East Asians (OR=1.41; 95% CI: 1.12–1.78; *P*=0.004) and Caucasians in Asia (OR=2.19; 95% CI: 1.85-2.60; *P*<0.001). No evidence of publication bias was observed. Conclusions: This meta-analysis of available data suggested that the GSTM1 null genotype does contribute to increased risk of prostate cancer in people who live in Asian countries.

Keywords: Glutathione-S-transferase M1 - prostate cancer - gene polymorphism - meta-analysis

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Introduction

Prostate cancer (PCa) is the most common malignancy among men in industrialized countries and with a worldwide incidence of 25.3 per 100 000 (Jemal et al., 2008). The reported incidence in Asia is much lower than that in Western countries. For example, the incidence in the African-American population is 60 times that of the Chinese population of Han nationality, so the research of pathogenesis of PCa from genetic and geographic aspects has important significance (Quinn et al., 2002; Bono, 2004; Pu et al., 2004).

Glutathione S-transferases (GSTs) are generally detoxifying enzymes, active in the detoxification of a wide variety of potentially toxic and carcinogenic electrophiles by conjugating them to glutathione. The GSTM1 gene, a member of the μ class of the GST gene family, catalyzes the detoxification of certain carcinogenic polycyclic aromatic hydrocarbon compounds. Thus its inactive form will cause lower detoxification, and that maybe the risk for cancer. For this reason GSTM1 is one of the most extensively studied genes concerning polymorphism and cancer risk. GSTM1 null genotype has been reported to be associated with cancers of the gastric (Masoudi et al., 2009; Garcia-Gonzalez et al., 2012; Zhu et al., 2012), colorectum (Ye et al., 2003) , bladder (Garcia-Closas et al., 2005; McGrath et al., 2006), lung (Ada et al., 2012; Lopez-Cima et al., 2012), breast (Oliveira et al., 2010; de Aguiar et al., 2012), head and neck (Suzen et al., 2007; Nosheen et al., 2010).

Many studies have investigated the association between GSTM1 null genotype and risk of prostate cancer, but the impact of GSTM1 null genotype on prostate cancer in people who live in Asian countries was still unclear owing to the obvious inconsistence among those studies. We present herein the results of a meta-analysis of published data investigating the association between GSTM1 null genotype and risk of prostate cancer to shed some light on these contradictory results and to decrease the uncertainty of the effect size of the estimated risk.

Materials and Methods

Literature search

We performed a systematic search of the PubMed, Web of Science, Scopus,Ovid and CNKI databases to identify studies on GSTM1 null genotype and prostate cancer published before Oct 2012. The following search strategy was performed by consecutively entering the combined free words: 'GSTM1' or 'Glutathione S-transferases', 'prostate', 'carcinoma' or 'cancer' or'tumor', 'PCa'. The reference lists of reviews and retrieved articles were

*Department of Urology, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China *For correspondence: xielp@zjuem.zju.edu.cn*

handsearched at the same time. We did not consider abstracts or unpublished reports. All studies on GSTM1 null genotype and prostate cancer were included. No language restrictions were applied. All non-English articles were translated if necessary.

Study eligibility

Eligibility criteria included the following: (1) case–control design with the genotyping of men with and without prostate cancer, concentrating upon polymorphisms in GSTM1; (2) an appropriate description of GSTM1 polymorphisms in prostate cancer cases and prostate cancer-free controls, provided information on genotype frequency; (3) cases with prostate cancer were eligible regardless of whether they had a first-degree relative with prostate cancer or not, regardless of tumor stage; (4) controls were eligible if they were male, with or without BPH, or other diseases; (5) results expressed as odds ratio (OR); (6) studies with a 95% CI for OR, or sufficient data to calculate these numbers; (7) the population is in Asia. While for the exclusion criteria, we provided as follows: (1) review articles and editorial; (2) case reports; (3) preliminary result was not on GSTM1 or outcome was not prostate cancer; (4) studies that used GSTM1 polymorphisms to predict survival in prostate cancer; (5) if multiple publications from the same study group occurred, we selected only the most complete paper for our final analysis.

Data Extraction

Two investigators independently extracted data, and disagreements were resolved through consensus. The extracted data included first author's name, year of publication, the country of origin, ethnicity, characteristics of cases and controls, source of controls, demographics, genotyping method, and the genotype distribution of cases and controls for the GSTM1 polymorphism. The frequency of GSTM1 null genotype was extracted or calculated for cases and controls. All data were extracted from published articles, and we did not contact individual authors for further information.

Statistical Analyses

The odds ratio (OR) was used as thematic of choice. Based on the individual ORs, the pooled OR was estimated. We did not pool the adjusted ORs because studies either did not adjust for confounders, or the adjustments were not comparable among them. To determine whether to use the fixed- or random-effects model, we measured statistical heterogeneity between and within groups using the Q

Table 1. Characteristics of Studies Included in the Meta-analysis

Study (author, year)	Study period	Population (country)	Genotyping method	No. of cases (control source)	No. of controls	Null of cases	Null of controls
Murata, 2001	1995-1996	East Asians (Japan)	PCR	115	200 (BPH)	57	85
Nakazato, 2003	DNR	East Asians (Japan)	PCR	81	105 (Hospital)	38	53
Guan, 2005	2001-2003	East Asians (China)	PCR	83	115 (Hospital)	48	48
Aktas, 2004	1999-2002	Caucasian (Turkey)	PCR	100	107 (BPH)	19	14
Komiya, 2005	1992-2002	East Asians (Japan)	PCR-RFLP	190	294 (Healthy)	93	157
Lai, 2005	DNR	East Asians (Taiwan,China)	PCR	96	121 (Hospital)	57	55
Wang, 2005	DNR	East Asians (China)	PCR	81	50 (Hospital)	44	40
Vijayalakshmi, 2005	DNR	Caucasian (India)	PCR	75	100 (Hospital)	18	15
Srivastava, 2005	2001-2004	Caucasian (India)	PCR	127	144 (Hospital)	70	51
Yang, 2006	2003-2005	East Asians (China)	PCR	163	202 (Hospital)	99	112
Silig, 2006	2002	Caucasian (Turkey)	PCR-RFLP	152	169 (Hospital)	98	52
Mittal, 2006	2003-2005	Caucasian (India)	PCR	54	105 (BPH)	30	35
Li, 2008	2001-2004	East Asians (China)	PCR	208	230 (Hospital)	121	96
Kwon, 2011	DNR	East Asians (South Korea)	PCR	166	327 (Hospital)	90	125
Ashtiani, 2011	DNR	Caucasian (Iran)	PCR	110	100(Healthy)+99(BPH)	50	10(Healthy)+47(BPH)
Kumar, 2011	DNR	Caucasian (India)	PCR	57	53(Healthy)+46(BPH)	34	15(Healthy)+21(BPH)
Thakur, 2011	2003-2006	Caucasian (India)	PCR	150	172(Healthy)+150(BPH)	87	62(Healty)+82(BPH)
Safarinejad, 2011	DNR	Caucasian (Iran)	PCR	168	336 (Healthy)	72	94

DNR, data not reported; PCR, polymerase chain reaction; RFLP, restriction fragment length polymorphism

Table 2. Summary of Odds Ratios (OR) with Confidence Interval (CI) in the Meta-analysis

Null versus present	Studies	Odds ratio		Model	Heterogeneity	
		OR (95 % CI)	P_{OR}		I^2 (%)	$P_{heterogeneity}$
Total studies	18(5430)	1.74(1.44–2.09)	<0.001	Random	60	0.001
Subgroup analyses by ethnicity						
Caucasians	9(2573)	2.19(1.85–2.60)	<0.001	Fixed	22.2	0.246
East Asians	9(2857)	1.41(1.12–1.78)	0.004	Random	55.1	0.023
Subgroup analyses by control source						
Healthy	5(1613)	2.33(1.21–4.49)	0.011	Random	88.2	<0.001
Hospital	10(2835)	1.81(1.41–2.32)	0.008	Random	59.7	<0.001
BPH	6(1299)	1.37(1.09–1.73)	0.007	Random	31.5	0.008

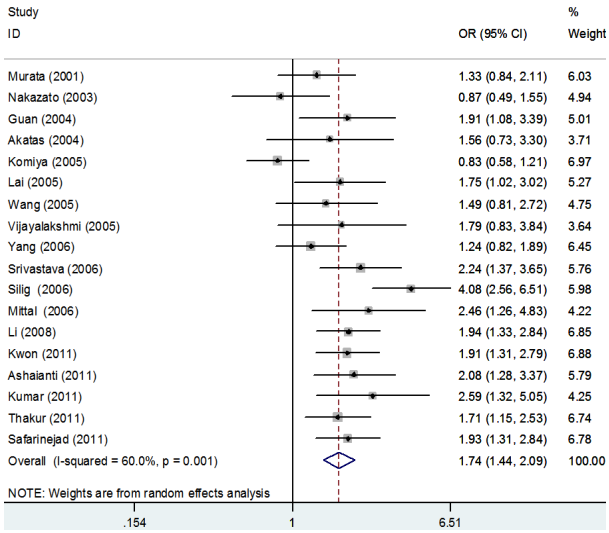

Figure 1. Forest Plots Showed Associations Between GSTM1 Null Genotype and Risk of Prostate Cancer

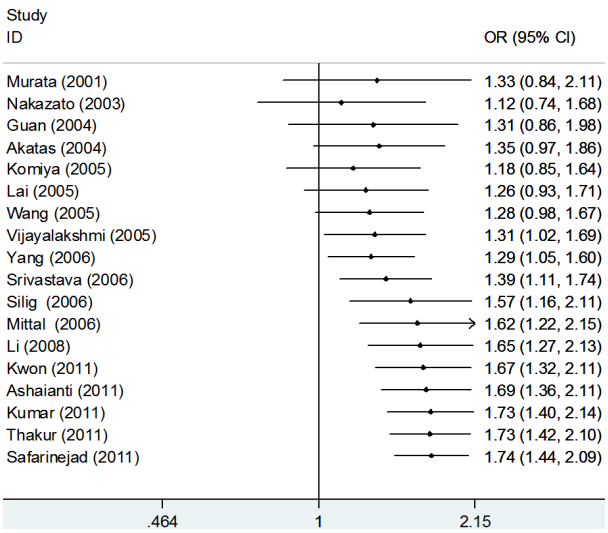

Figure 2. Forest Plots Showed Results of the Cumulative Meta-analysis (The random effects pooled odds ratio with the corresponding 95% confidence interval at the end of each information step was shown)

statistic, $P<0.05$ was considered statistically significant. We used fixed-effects methods if the result of the Q test was not significant. Otherwise, we calculated pooled estimates and confidence intervals assuming a random-effects model.

While publication bias was not expected, we assessed this possibility using Begg's funnel plots and Egger's bias test . We also performed a cumulative meta-analysis to provide a framework for updating a genetic effect from all studies and to measure how much the genetic effect changes as evidence accumulated and found the trend in estimated risk effect. In cumulative meta-analysis, studies were chronologically ordered by publication year, and then the pooled ORs were obtained at the end of each year. To validate the credibility of outcomes in this meta-analysis, sensitivity analysis was performed by sequential omission of individual studies.

For additional analyses, subgroup analyses were performed by grouping studies that showed similar characteristics, such as ethnicity, control source. The ethnic subgroups were categorized into two ethnic groups: Caucasian, and East Asian, while the control source subgroups were considered as three groups: (1) hospital controls (patients recruited within a hospital setting); (2) healthy controls (healthy blood donors or individuals selected through population-based sampling methods); (3) BPH (patients diagnosed benign prostatic hyperplasia).

Analyses were conducted using Stata version 11.0 (Stata Corporation) and all of the *P* values generated were two tailed.

Results

Characteristics of included studies

Excluding overlapping data, we identified 18 eligible reports. All reports selected prostate cancer patients based on a histologic diagnosis from biopsy or prostatectomy. Among the eligible studies, three articles contained separate data on two different control groups (Ashtiani et al., 2011; Kumar et al., 2011; Thakur et al., 2011). One article provided data on both blood and tissue samples from the same subjects (Mittal et al., 2006), to avoid overlapping, only the data of blood samples were included. Thus, a total of 18 case-control studies with 2172 cases and 3258 controls were included into this meta-analysis. All included studies were English language literature except for two Chinese language literatures (Guan et al., 2005; Wang et al., 2005). Of these studies, 9 reported on Caucasians, and 9 reported on East Asians. Studies were carried out in Japan (Murata et al., 2001; Nakazato et al., 2003; Komiya et al., 2005), China (Guan et al., 2005; Lai et al., 2005; Wang et al., 2005; Yang et al., 2006; Li et al., 2008), India (Vijayalakshmi et al., 2005; Srivastava et al., 2005; Mittal et al., 2006; Thakur et al., 2011; Kumar et al., 2011), South Korea (Kwon et al., 2011), Iran (Ashtiani et al., 2011; Safarinejad et al., 2011) and Turkey (Aktas et al., 2004; Silig et al., 2006). A list of details abstracted from the studies included in the meta-analysis is provided through Table 1.

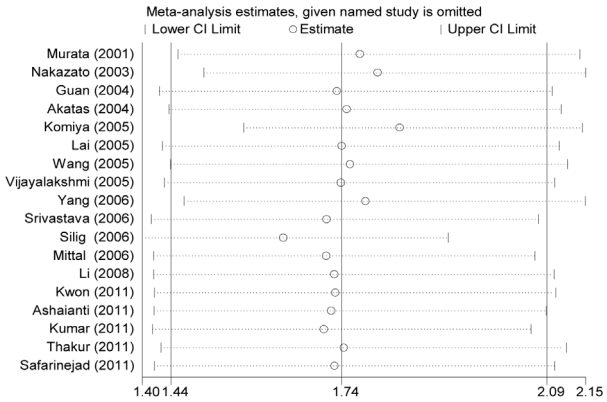

Figure 3. Sensitivity Analyses by Sequential Omission of Individual Studies

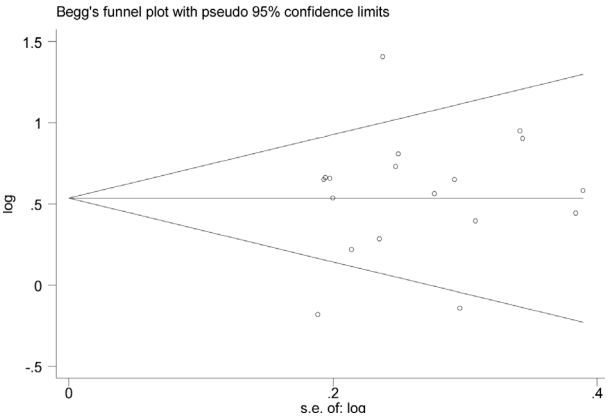

Figure 4. Begg's Funnel Plot for Assessing the Publication bias Risk (P_{Begg}=0.65)

Main results

There was obvious heterogeneity among in the meta-analysis of total 18 studies (I^2=60 %), thus the random-effects model was used. Meta-analysis showed GSTM1 null genotype was associated increased risk of prostate cancer (OR=1.74, 95% CI 1.44–2.09, *P*<0.001) (Figure 1).

This analysis is based on pooling of data from a number of different ethnic groups (Table 2). Subgroups analyses in the different ethnic groups were therefore conducted. Similar results were found in East Asians (OR=1.41; 95% CI: 1.12–1.78; *P*=0.004) and Caucasians (OR=2.19; 95% CI: 1.85–2.60; *P*<0.001). By considering control source subgroups ,in healthy controls, the OR was 2.33 (95% CI: 1.21–4.49; *P*<0.001), compared to 1.81 (95% CI: 1.41–2.32; *P*<0.001) in hospital controls, and 1.37 (95% CI: 1.09–1.73; *P*=0.007) in BPH controls.

The cumulative meta-analyses for total 18 studies showed a trend of more obvious association as information accumulated (Figure 2).

Sensitivity Analyses and Publication Bias

Sensitivity analyses by sequential omission of individual studies did not significantly alter the overall combined ORs (Figure 3). In the funnel plot analysis of publication bias (contrast of null genotype plotted against the present), the shape of the funnel plot seems symmetrical, both Begg's test (*P*=0.65) (Figure 4) and Eggar's test (*P*=0.51) showed no evidence of publication bias.

Discussion

Many studies have investigated the association between GSTM1 null genotype and risk of prostate cancer, but the impact of GSTM1 null genotype on prostate cancer risk in people who live in Asian countries is unclear owing to the obvious inconsistence among those studies. Our meta-analysis of 2172 prostate cancer cases and 3258 controls from 18 case–control studies provides evidence that the GSTM1 null genotype is associated with a increase in the risk of prostate cancer in Asian population.

GSTM1 null genotype also has been extensively studied for many other cancers. To explore the exact association between GSTM1 polymorphisms and gastric cancer risk, Zhu et al. conducted a meta-analysis of 38 published genetic association studies including 6605 gastric cancer cases and 11,311 controls. This meta-analysis indicated that GSTM1 null genotype might be associated with increased gastric cancer risk in Asians,while it did not provide an evidence of confirming association between GSTM1 polymorphism and gastric cancer in Caucasians (Zhu et al., 2012).

GSTM1 have broad and overlapping substrate specificities, and the genetic polymorphisms of these enzymes are attractive candidates for cancer susceptibility, as reduced ability to remove potential carcinogens may result in mutation in key tumor suppressor genes.Earlier molecular epidemiologic studies have suggested that allelic (deletion or null) variants of GSTM1 genes are associated with failure to express GST proteins, which may lead to less effective detoxification of potential carcinogens and increased susceptibility to cancer (Board, 1981; Pemble et al., 1994; Spurdle et al., 2001). Mavis et al. examined Gst gene expression and Gst promoter DNA methylation in normal murine prostates and Transgenic Adenocarcinoma of Mouse Prostate (TRAMP) tumors,and demonstrate that reduced Gst gene expression is a common event in primary tumors arising in the TRAMP model, reminiscent of human prostate cancer (Mavis et al., 2009).

Our results showed GSTM1 null genotype was associated with increased risk of prostate cancer in people who live in Asian countries. In subgroup analysis of Caucasians and East Asians, there were also obvious associations between GSTM1 null genotype and increased risk of prostate cancer.

Similar results were found in different control source subgroups (healthy,in the hospital and BPH). However,compared to the subgroups of healthy controls (OR 2.33) and hospital controls (OR 1.81),the BPH controls' estimate magnitude was drown down (OR 1.37). One possible reason was that BPH may be also affected by the same polymorphism, but susceptibility to prostate enlargement is a different issue than susceptibility to prostate cancer.

Cumulative meta-analysis and sensitivity analysis were also performed. Sensitivity analyses by sequential omission of individual studies did not materially alter the significance of pooled ORs. Sensitivity analysis and publication bias analysis suggest that it is highly unlikely that the findings may be due to chance (Type 1 error) or bias favoring publication of 'positive' studies. Thus, these

findings support the concept of GSTM1 null genotype as a genetic susceptibility factor of PCa in people who live in Asian countries.

Wei et al. (2012) evaluated the association between GSTM1 null polymorphism and PCa risk from 36 Case-Control studies,and draw a conclusion that GSTM1 null allele was a low-penetrant risk factor for Pca among East Asians (Chinese,Japanese and Korean). Their article mainly discussed the possible role of ethnic differences in genetic backgrounds,while we want to investigate the situation in the region of Asia, so to explore the assosiation between the gene polymorphism and PCa risk in this region is also significant.

As with all meta-analyses, our analysis has limitations that must be considered when interpreting the findings. Firstly, most eligible studies were published papers written in English, only two were Chinese. Thus, some inevitable publication bias may exist in the results, although the funnel plots as well as Egger's linear regression tests indicated no remarkable publication bias in the meta-analysis. Secondly, only published studies were included in the meta-analysis; therefore, publication bias may have occurred. Further studies should search thoroughly to obtain as many papers as possible, especially the unpublished ones in remote countries. Thirdly, no prospective studies have addressed this association between GSTM1 null genotype and prostate cancer risk, and all included studies followed a retrospective case–control design. Thus, owing to the limitations of case–control design, we can not exclude the possibility of undetected bias. Future prospective studies can investigate whether routine screening for the presence of the GSTM1 null genotype may improve prediction of prostate cancer risk. Finally, gene-gene and gene-environmental factors interactions were not addressed in this meta-analysis for the lack of sufficient data.

In conclusion, this present meta-analysis supports a significant association between GSTM1 null genotype and risk of prostate cancer in Asians. Larger and more rigorous analytical studies will be required to generate a more robust result in the future.

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References

Ada AO, Kunak SC, Hancer F, et al (2012). Association between GSTM1, GSTT1, and GSTP1 polymorphisms and lung cancer risk in a Turkish population. *Mol Biol Rep*, **39**, 5985-93.

Aktas D, Hascicek M, Sozen S, Ozen H, Tuncbilek E (2004). CYP1A1 and GSTM1 polymorphic genotypes in patients with prostate cancer in a Turkish population. *Cancer Genet Cytogenet*, **154**, 81-5.

Ashtiani ZO, Hasheminasab SM, Ayati M, Goulian BS, Modarressi MH (2011). Are GSTM1, GSTT1 and CAG repeat length of androgen receptor gene polymorphisms associated with risk of prostate cancer in Iranian patients? *Pathol Oncol Res,* **17**, 269-75.

Board PG (1981). Biochemical genetics of glutathione-S-transferase in man. *Am J Hum Genet*, **33**, 36-43.

Bono AV (2004). The global state of prostate cancer: epidemiology and screening in the second millennium. *BJU Int*, **94**, 1-2.

de Aguiar ES, Giacomazzi J, Schmidt AV, et al (2012). GSTM1, GSTT1, and GSTP1 polymorphisms, breast cancer risk factors and mammographic density in women submitted to breast cancer screening. *Rev Bras Epidemiol*, **15**, 246-55.

Garcia-Closas M, Malats N, Silverman D, et al (2005). NAT2 slow acetylation, GSTM1 null genotype, and risk of bladder cancer: results from the Spanish Bladder Cancer Study and meta-analyses. *Lancet*, **366**, 649-59.

Garcia-Gonzalez MA, Quintero E, Bujanda L, et al (2012). Relevance of GSTM1, GSTT1, and GSTP1 gene polymorphisms to gastric cancer susceptibility and phenotype. *Mutagenesis*, **27**, 771-7.

Guan TY, Li M, Na YQ (2005). [Polymorphism of metabolic gene and genetic susceptibility to prostate cancer]. *Zhonghua Wai Ke Za Zhi*, **43**, 1467-70.

Jemal A, Siegel R, Ward E, et al (2008). Cancer statistics, 2008. *CA Cancer J Clin*, **58**, 71-96.

Komiya Y, Tsukino H, Nakao H, et al (2005) Human glutathione S-transferase A1, T1, M1, and P1 polymorphisms and susceptibility to prostate cancer in the Japanese population. *J Cancer Res Clin Oncol*, **131**, 238-42.

Kumar V, Yadav CS, Datta SK, et al (2011). Association of GSTM1 and GSTT1 polymorphism with lipid peroxidation in benign prostate hyperplasia and prostate cancer: a pilot study. *Dis Markers*, **30**, 163-9.

Kwon DD, Lee JW, Han DY, et al (2011). Relationship between the Glutathione-S-Transferase P1, M1, and T1 Genotypes and Prostate Cancer Risk in Korean Subjects. *Korean J Urol*, **52**, 247-52.

Lai MT, Chen RH, Tsai FJ, Wan L, Chen WC (2005) Glutathione S-transferase M1 gene but not insulin-like growth factor-2 gene or epidermal growth factor gene is associated with prostate cancer. Urol Oncol 23, 225-9

Li M, Guan TY, Li Y, Na YQ (2008). Polymorphisms of GSTM1 and CYP1A1 genes and their genetic susceptibility to prostate cancer in Chinese men. *Chin Med J (Engl)*, **121**, 305-8.

Lopez-Cima MF, Alvarez-Avellon SM, Pascual T, Fernandez-Somoano A, Tardon A (2012). Genetic polymorphisms in CYP1A1, GSTM1, GSTP1 and GSTT1 metabolic genes and risk of lung cancer in Asturias. *BMC Cancer*, **12**, 433.

Masoudi M, Saadat I, Omidvari S, Saadat M (2009). Genetic polymorphisms of GSTO2, GSTM1, and GSTT1 and risk of gastric cancer. *Mol Biol Rep*, **36**, 781-4.

Mavis CK, Morey Kinney SR, Foster BA, Karpf AR (2009). Expression level and DNA methylation status of glutathione-S-transferase genes in normal murine prostate and TRAMP tumors. *Prostate*, **69**, 1312-24.

McGrath M, Michaud D, De Vivo I (2006). Polymorphisms in GSTT1, GSTM1, NAT1 and NAT2 genes and bladder cancer risk in men and women. *BMC Cancer,* **6**, 239.

Mittal RD, Mishra DK, Mandhani A (2006). Evaluating polymorphic status of glutathione-S-transferase genes in blood and tissue samples of prostate cancer patients. *Asian Pac J Cancer Prev,* **7**, 444-6.

Murata M, Watanabe M, Yamanaka M, et al (2001). Genetic polymorphisms in cytochrome P450 (CYP) 1A1, CYP1A2,

CYP2E1, glutathione S-transferase (GST) M1 and GSTT1 and susceptibility to prostate cancer in the Japanese population. *Cancer Lett*, **165**, 171-7.

Nakazato H, Suzuki K, Matsui H, et al (2003). Association of genetic polymorphisms of glutathione-S-transferase genes (GSTM1, GSTT1 and GSTP1) with familial prostate cancer risk in a Japanese population. *Anticancer Res*, **23**, 2897-902.

Nosheen M, Ishrat M, Malik FA, Baig RM, Kayani MA (2010). Association of GSTM1 and GSTT1 gene deletions with risk of head and neck cancer in Pakistan: a case control study. *Asian Pac J Cancer Prev,* **11**, 881-5.

Oliveira AL, Rodrigues FF, Santos RE, et al (2010). GSTT1, GSTM1, and GSTP1 polymorphisms and chemotherapy response in locally advanced breast cancer. *Genet Mol Res*, **9**, 1045-53.

Pemble S, Schroeder KR, Spencer SR, et al (1994). Human glutathione S-transferase theta (GSTT1), cDNA cloning and the characterization of a genetic polymorphism. *Biochem J*, **300**, 271-6.

Pu YS, Chiang HS, Lin CC, et al (2004). Changing trends of prostate cancer in Asia. *Aging Male*, **7**, 120-32.

Quinn M, Babb P (2002). Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part II: individual countries. *BJU Int*, **90**, 174-84.

Safarinejad MR, Shafiei N, Safarinejad SH (2011). Glutathione S-transferase gene polymorphisms (GSTM1, GSTT1, GSTP1) and prostate cancer, a case-control study in Tehran, Iran. *Prostate Cancer Prostatic Dis*, **14**, 105-13.

Silig Y, Pinarbasi H, Gunes S, et al (2006). Polymorphisms of CYP1A1, GSTM1, GSTT1, and prostate cancer risk in Turkish population. *Cancer Invest,* **24**, 41-5.

Spurdle AB, Webb PM, Purdie DM, et al (2001). Polymorphisms at the glutathione S-transferase GSTM1, GSTT1 and GSTP1 loci: risk of ovarian cancer by histological subtype. *Carcinogenesis*, **22**, 67-72.

Srivastava DS, Mandhani A, Mittal B, Mittal RD (2005). Genetic polymorphism of glutathione S-transferase genes (GSTM1, GSTT1 and GSTP1) and susceptibility to prostate cancer in Northern India. *BJU Int,* **95**, 170-3.

Suzen HS, Guvenc G, Turanli M, et al (2007). The role of GSTM1 and GSTT1 polymorphisms in head and neck cancer risk. *Oncol Res*, **16**, 423-9.

Thakur H, Gupta L, Sobti RC, et al (2011). Association of GSTM1T1 genes with COPD and prostate cancer in north Indian population. *Mol Biol Rep*, **38**, 1733-9.

Vijayalakshmi K, Vettriselvi V, Krishnan M, et al (2005). Polymorphisms at GSTM1 and GSTP1 gene loci and risk of prostate cancer in a South Indian population. *Asian Pac J Cancer Prev*, **6**, 309-14.

Wang YL, Jiang J, Wang LF, Liu YF (2005). Polymorphisms of glutathione-S-transferase genes GSTM1 and GSTT1 and prostate cancer risk in Chinese population. *Acta Acadiemiae Midicinae Militaris Tertiae*, **27**, 1039-41.

Wei B, Xu Z, Zhou Y, et al (2012). Association of GSTM1 Null Allele with Prostate Cancer Risk: Evidence from 36 Case-Control Studies. *PLoS One*, **7**, e46982.

Yang J, Wu HF, Zhang W, et al (2006). Polymorphisms of metabolic enzyme genes, living habits and prostate cancer susceptibility. *Front Biosci,* **11**, 2052-60.

Ye Z, Parry JM (2003). A meta-analysis of 20 case-control studies of the glutathione S-transferase M1 (GSTM1) status and colorectal cancer risk. *Med Sci Monit*, 9, SR83-91.

Zhu Y, He Q, Wang J, Pan HF (2012). The association between GSTM1 polymorphism and gastric cancer risk: a meta-analysis. *Mol Biol Rep*, **39**, 685-91.