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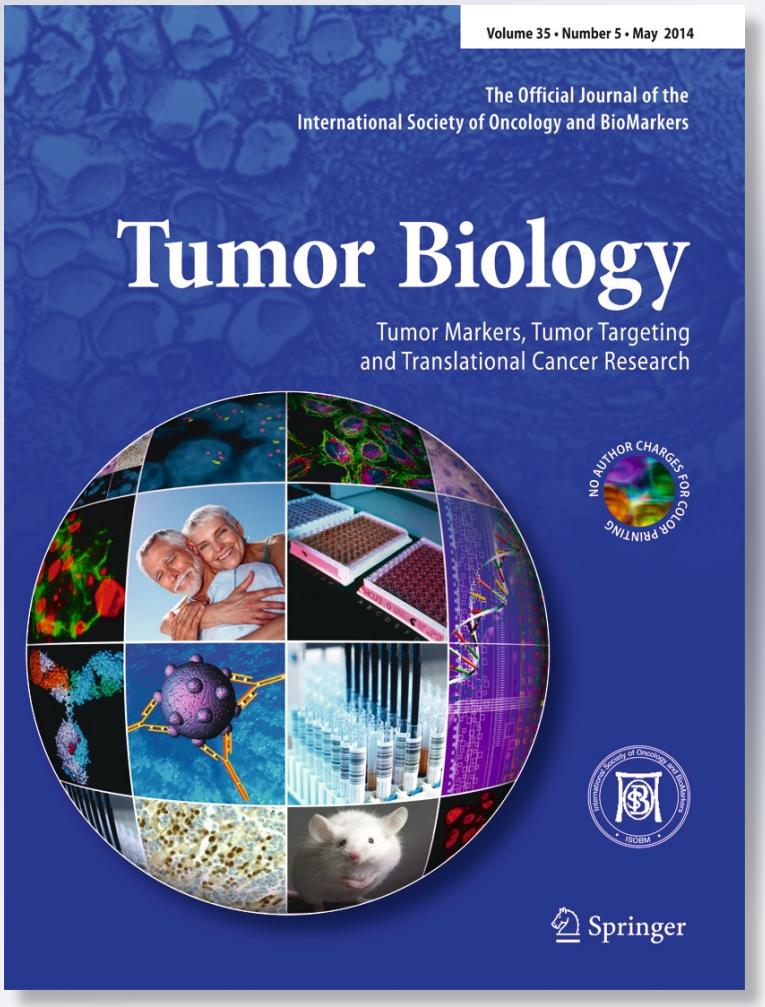

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RESEARCH ARTICLE

Association between X-ray repair cross-complementing group 1 Arg194Trp polymorphism and prostate cancer risk

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Abstract X-ray repair cross-complementing group 1 (XRCC1) plays an important role in the maintenance of the genomic integrity. Previous studies on the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk reported conflicting results. To get a more precise assessment of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk, we performed a meta-analysis of previously published studies. Eligible studies were searched in PubMed, Embase, and China National Knowledge Infrastructure (CNKI) databases. Nine studies with a total of 5,407 subjects were finally included into the meta-analysis. Odds ratio (OR) with 95 % confidence interval (95 %CI) was used to assess the association. Overall, there was no obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk (Trp vs. Arg: OR=1.02, 95 %CI 0.84–1.25, *P*=0.824; TrpTrp vs. ArgArg: OR=1.17, 95 %CI 0.83–1.66, *P*=0.374; TrpTrp/ArgTrp vs. ArgArg: OR=1.00, 95 %CI 0.79–1.28, *P*=0.990; TrpTrp vs. ArgArg/ArgTrp: OR=1.20, 95 %CI 0.85–1.68, *P*=0.301). Subgroup analysis according to ethnicity also detected no significant association in both Asians and Caucasians. In conclusion, the meta-analysis suggests that there is no obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk.

Keywords XRCC1 · Prostate cancer · Meta-analysis

Introduction

Prostate cancer is the most common cancer in men worldwide and it has caused serious damages to human health [1, 2]. There are several risk factors associated with prostate cancer, such as tobacco smoking and drinking alcohol [2, 3]. In addition, it is no doubt that genetic factors also play vital roles in the development of prostate cancer [4, 5]. Environmental carcinogens can result in DNA damages, which finally lead to the development of prostate cancer [6, 7]. DNA repair system aims to maintain genomic integrity and constantly challenge the environmental insults and replication errors [6–8]. X-ray repair cross-complementing group 1 (XRCC1) plays an important role in the maintenance of the genomic integrity [9, 10]. There are several common single nucleotide polymorphisms in the XRCC1 gene, and XRCC1 Arg194Trp, Arg280His, and Arg399Gln polymorphisms are the three most studied ones [11, 12]. XRCC1 Arg194Trp polymorphism is a C to T substitution at exon 6, which further results in an amino acid change from Arg to Trp [11, 12]. There were many studies performed to assess the associations of XRCC1 genetic polymorphisms with prostate cancer, but previous studies on the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk reported conflicting results [13–20]. To get a more precise assessment of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk, we performed a meta-analysis of previously published studies.

Methods

Search strategy and study selection

Eligible studies were searched in PubMed, Embase, and China National Knowledge Infrastructure (CNKI) databases. We used the combination of the following search terms: ('X-ray repair cross-complementing group 1', 'XRCC1' or 'Arg194Trp') and ('prostate cancer' or 'prostate carcinoma'). All included studies must meet the following inclusion

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criteria: (1) Case–control studies, (2) assessing the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk, and (3) providing the genotype frequencies of XRCC1 Arg194Trp polymorphism. When duplicated studies were published from the same sample, only the study with the most complete data was included in the meta-analysis.

Data extraction

The data extraction was performed according to a standard protocol. The following information was extracted from each included study: first author, year of publication, country, ethnicity, genotyping methods, characteristics of the sample population, source of the sample population, and genotype frequencies of cases and controls.

Statistical analysis

The odds ratio (OR) with corresponding 95 % confidence interval (95 %CI) was used to examine the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk. The association was assessed by the following models: the allelic model, the homozygote model, the dominant model, and the recessive model. Heterogeneity among the studies was assessed using the I^2 statistic method [21]. Either the random effects model (DerSimonian–Laird method) or the fixed effects model (Mantel–Haenszel method) was used to calculate pooled OR in the presence or absence of heterogeneity, respectively [22, 23]. Subgroup analysis was further performed for the Asian and Caucasian populations. Finally, potential publication bias was evaluated by visual analysis of the funnel plot. All statistical analyses were performed with the STATA version 11.0 software (Stata Corporation, College Station, TX, USA).

Results

Studies characteristics

From the search, 49 abstracts of publications were found. After excluding those irrelevant studies, nine studies with a total of 5,407 subjects were finally included into the meta-analysis [13–20]. Those nine studies were from eight publications [13–20]. Of those nine studies, five studies were performed in Asians [13, 14, 18–20], three studies were from Caucasians [15–17], and one study was from other population [16]. In addition, the controls were from healthy populations in three studies, and the controls were from hospitals in the five studies left.

Meta-analysis

The main results of the meta-analysis of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk were shown in Table 1. Overall, there was no obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk (Trp vs. Arg: OR=1.02, 95 %CI 0.84–1.25, P=0.824; TrpTrp vs. ArgArg: OR=1.17, 95 %CI 0.83–1.66, P=0.374; TrpTrp/ArgTrp vs. ArgArg: OR=1.00, 95 %CI 0.79–1.28, P=0.990; TrpTrp vs. ArgArg/ArgTrp: OR=1.20, 95 %CI 0.85–1.68, P=0.301) (Table 1, Figs. 1, 2, and 3).

Subgroup analysis by ethnicity was performed in order to determine the source of heterogeneity among the studies and to assess the effect of race on the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk. Subgroup analysis according to ethnicity detected no significant association in both Asians and Caucasians (Table 1).

Publication bias

Potential publication bias was evaluated by visual analysis of the funnel plot. Visual analysis of the funnel plots did not present any evidence of obvious asymmetry for any genetic model in the overall meta-analysis of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk. Therefore, there was no obvious risk of publication bias in the meta-analysis.

Discussion

It has been well-accepted that DNA repair systems in human body play a critical role in the maintenance of genomic integrity. In addition, DNA repair system aims to maintain genomic integrity and constantly challenge the environmental insults and replication errors. XRCC1 plays an important role in the maintenance of the genomic integrity. Previous studies on the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk reported conflicting results. To get a more precise assessment of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk, we performed the present meta-analysis. Nine studies with a total of 5,407 subjects were finally included into the meta-analysis. Overall, there was no obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk (Trp vs. Arg: OR=1.02, 95 %CI 0.84–1.25, P=0.824; TrpTrp vs. ArgArg: OR=1.17, 95 %CI 0.83–1.66, P=0.374; TrpTrp/ArgTrp vs. ArgArg: OR=1.00, 95 %CI 0.79–1.28, P=0.990; TrpTrp vs. ArgArg/ArgTrp: OR=1.20, 95 %CI 0.85–1.68, P=0.301) (Table 1). Subgroup analysis according to ethnicity also detected no significant association in both Asians and Caucasians. Thus, the meta-analysis suggests that there is no

Table 1 Meta-analysis of the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk

Groups	Study (subject)	OR [95 %CI]	*P* value	I^2 (%)
All populations				
Trp versus Arg	9 (5,407)	1.02 [0.84–1.25]	0.824	52.8
TrpTrp versus ArgArg	9 (5,407)	1.17 [0.83–1.66]	0.374	29.7
TrpTrp/ArgTrp versus ArgArg	9 (5,407)	1.00 [0.79–1.28]	0.990	56.5
TrpTrp versus ArgArg/ArgTrp	9 (5,407)	1.20 [0.85–1.68]	0.301	10.0
Asians				
Trp versus Arg	5 (1,849)	1.18 [0.89–1.57]	0.260	65.3
TrpTrp versus ArgArg	5 (1,849)	1.44 [0.78–2.67]	0.240	50.1
TrpTrp/ArgTrp versus ArgArg	5 (1,849)	1.16 [0.78–1.73]	0.453	72.9
TrpTrp versus ArgArg/ArgTrp	5 (1,849)	1.30 [0.90–1.89]	0.161	27.4
Caucasians				
Trp versus Arg	3 (3,329)	0.87 [0.71–1.06]	0.167	0.0
TrpTrp versus ArgArg	3 (3,329)	0.94 [0.35–2.50]	0.900	0.0
TrpTrp/ArgTrp versus ArgArg	3 (3,329)	0.86 [0.69–1.06]	0.155	0.0
TrpTrp versus ArgArg/ArgTrp	3 (3,329)	0.99 [0.39–2.50]	0.984	0.0

OR odds ratio; *95 %CI* 95 % confidence interval

obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk.

The XRCC1 protein is a very important part of DNA repair system, and the joint effects of XRCC1 and other proteins can promote the repair of DNA. Since the dysfunction of DNA repair system can result in the development of cancer, genetic mutations in the XRCC1 gene are suggested to alter host's susceptibility to prostate cancer. There are several common single nucleotide polymorphisms in the XRCC1 gene, and XRCC1 Arg194Trp, Arg280His, and Arg399Gln polymorphisms are the three most studied ones [24–26]. XRCC1 Arg194Trp polymorphism is a C to T substitution at exon 6, which further results in an amino acid change from Arg to Trp [24–26]. In the present meta-analysis, we only assessed the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk and failed to identify an obvious

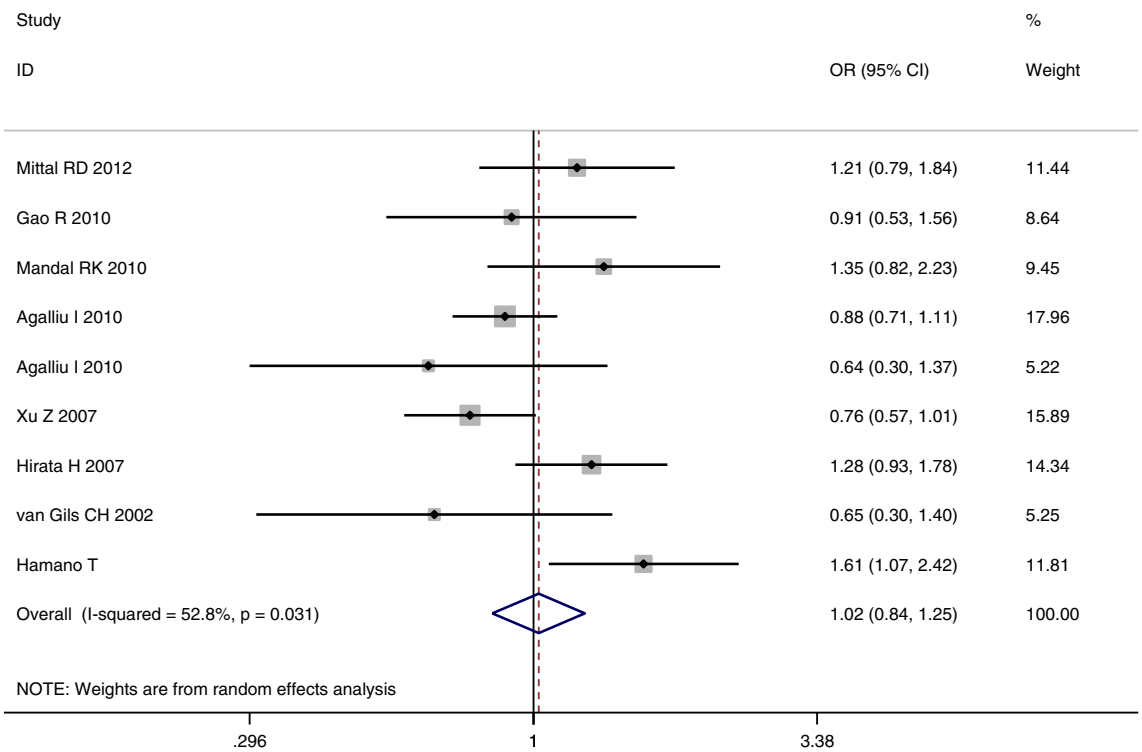

Fig. 1 Forest plot for the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk under the allelic model

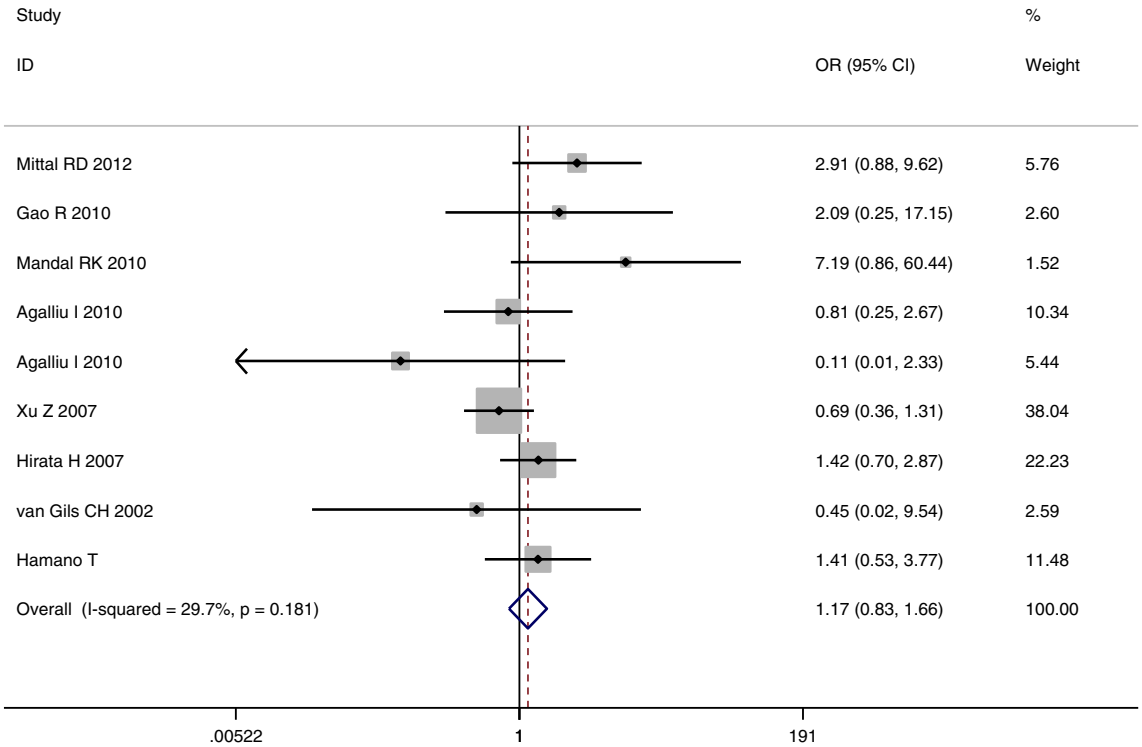

Fig. 2 Forest plot for the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk under the homozygote model

association. However, the associations of other XRCC1 polymorphisms with prostate cancer risk are not assessed in the present meta-analysis, and those associations need further studies.

However, there were several limitations in the meta-analysis. Firstly, there were only nine studies with a total of 5,407 subjects that were finally included into the meta-analysis. The limited number of studies may increase the risk

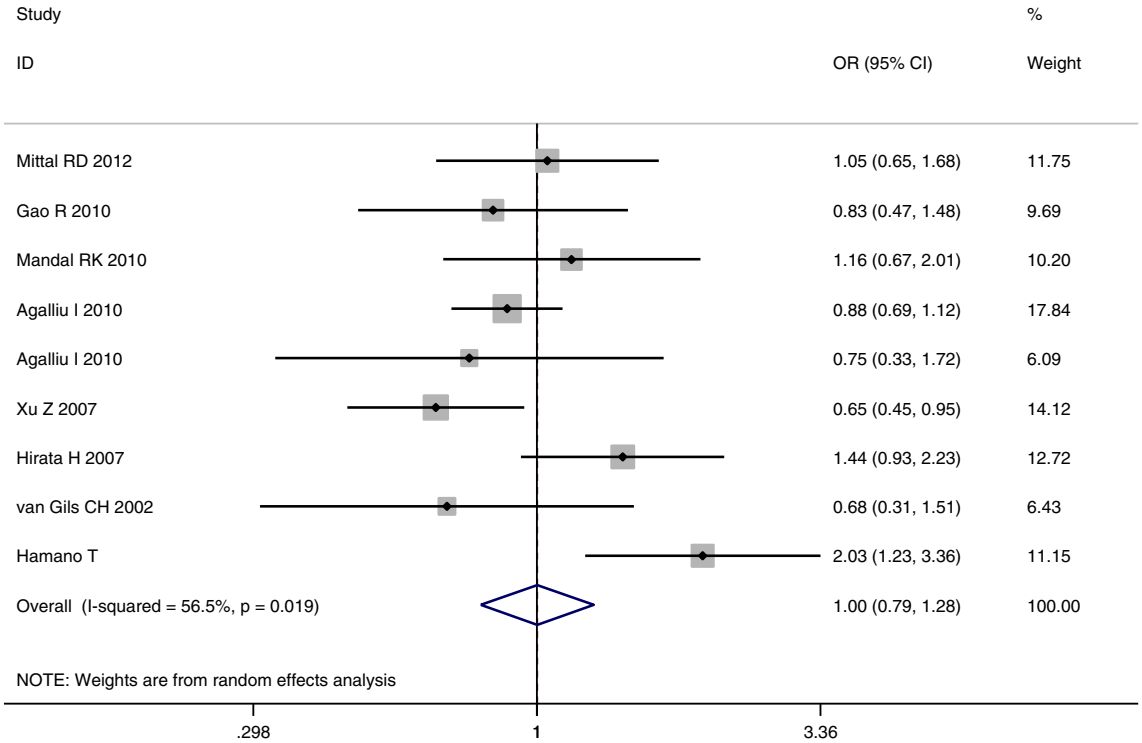

Fig. 3 Forest plot for the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk under the dominant model

of bias in the meta-analysis, especially in the subgroup analysis by race. Thus, more studies with large samples are needed. Secondly, the eligibility criteria for inclusion of cases and controls were different between the included studies. The controls in most studies were selected from non-cancer individuals, while the controls in other studies were from healthy individuals. Finally, the ORs from most studies were not adjusted for other confounding factors, such as age and smoking. It is no doubt that the confounding factors may have some effects on the association between XRCC1 Arg194Trp polymorphism and prostate cancer risk. Therefore, studies with good design are needed in the future, and ORs adjusted for other confounding factors need reporting.

In conclusion, the meta-analysis suggests that there is no obvious association between XRCC1 Arg194Trp polymorphism and prostate cancer risk. Besides, more studies with good design and large samples are needed in the future.

Conflicts of interest None

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012;62:10–29.
2. Pienta KJ, Smith DC. Advances in prostate cancer chemotherapy: a new era begins. CA Cancer J Clin. 2005;55:300–18. quiz 23-5.
3. Kasper JS, Liu Y, Giovannucci E. Diabetes mellitus and risk of prostate cancer in the health professionals follow-up study. Int J Cancer. 2009;124:1398–403.
4. McCracken M, Olsen M, Chen Jr MS, Jemal A, Thun M, Cokkinides V, et al. Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Korean, and Japanese ethnicities. CA Cancer J Clin. 2007;57:190–205.
5. Amankwah EK, Sellers TA, Park JY. Gene variants in the angiogenesis pathway and prostate cancer. Carcinogenesis. 2012;33:1259–69.
6. Shiloh Y, Ziv Y. The atm protein kinase: regulating the cellular response to genotoxic stress, and more. Nat Rev Mol Cell Biol. 2013;14:197–210.
7. Schipler A, Iliakis G. DNA double-strand-break complexity levels and their possible contributions to the probability for error-prone processing and repair pathway choice. Nucleic Acids Res. 2013;41:7589–605.
8. Goodarzi AA, Jeggo PA. The repair and signaling responses to DNA double-strand breaks. Adv Genet. 2013;82:1–45.
9. Horton JK, Watson M, Stefanick DF, Shaughnessy DT, Taylor JA, Wilson SH. Xrcc1 and DNA polymerase beta in cellular protection against cytotoxic DNA single-strand breaks. Cell Res. 2008;18:48–63.
10. Caldecott KW. Xrcc1 and DNA strand break repair. DNA Repair (Amst). 2003;2:955–69.
11. Harms C, Salama SA, Sierra-Torres CH, Cajas-Salazar N, Au WW. Polymorphisms in DNA repair genes, chromosome aberrations, and lung cancer. Environ Mol Mutagen. 2004;44:74–82.
12. Bartsch H, Dally H, Popanda O, Risch A, Schmezer P. Genetic risk profiles for cancer susceptibility and therapy response. Recent Results Cancer Res. 2007;174:19–36.
13. Xu Z, Hua LX, Qian LX, Yang J, Wang XR, Zhang W, et al. Relationship between xrcc1 polymorphisms and susceptibility to prostate cancer in men from Han, Southern China. Asian J Androl. 2007;9:331–8.
14. Hamano T, Matsui H, Ohtake N, Nakata S, Suzuki K. Polymorphisms of DNA repair genes, xrcc1 and xrcc3, and susceptibility to familial prostate cancer in a Japanese population. Asia Pac J Clin Oncol. 2008;4:21–6.
15. Gao R, Price DK, Dahut WL, Reed E, Figg WD. Genetic polymorphisms in xrcc1 associated with radiation therapy in prostate cancer. Cancer Biol Ther. 2010;10:13–8.
16. Agalliu I, Kwon EM, Salinas CA, Koopmeiners JS, Ostrander EA, Stanford JL. Genetic variation in DNA repair genes and prostate cancer risk: results from a population-based study. Cancer Causes Control. 2010;21:289–300.
17. van Gils CH, Bostick RM, Stern MC, Taylor JA. Differences in base excision repair capacity may modulate the effect of dietary antioxidant intake on prostate cancer risk: an example of polymorphisms in the xrcc1 gene. Cancer Epidemiol Biomarkers Prev. 2002;11:1279–84.
18. Mandal RK, Gangwar R, Mandhani A, Mittal RD. DNA repair gene X-ray repair cross-complementing group 1 and xeroderma pigmentosum group d polymorphisms and risk of prostate cancer: a study from north India. DNA Cell Biol. 2010;29:183–90.
19. Hirata H, Hinoda Y, Tanaka Y, Okayama N, Suehiro Y, Kawamoto K, et al. Polymorphisms of DNA repair genes are risk factors for prostate cancer. Eur J Cancer. 2007;43:231–7.
20. Mittal RD, Mandal RK, Gangwar R. Base excision repair pathway genes polymorphism in prostate and bladder cancer risk in north Indian population. Mech Ageing Dev. 2012;133:127–32.
21. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–60.
22. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst. 1959;22:719–48.
23. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7:177–88.
24. Ginsberg G, Angle K, Guyton K, Sonawane B. Polymorphism in the DNA repair enzyme xrcc1: utility of current database and implications for human health risk assessment. Mutat Res. 2011;727:1–15.
25. Liu F, Li B, Wei Y, Yan L, Wen T, Zhao J, et al. Xrcc1 genetic polymorphism arg399gln and hepatocellular carcinoma risk: a meta-analysis. Liver Int. 2011;31:802–9.
26. Karahalil B, Bohr VA, Wilson 3rd DM. Impact of DNA polymorphisms in key DNA base excision repair proteins on cancer risk. Hum Exp Toxicol. 2012;31:981–1005.