Breast Cancer Res Treat (2007) 103:71–76
DOI 10.1007/s10549-006-9348-z

EPIDEMIOLOGY

Genetic polymorphism of *XRCC3* Thr^{241}Met and breast cancer risk: case-control study in Korean women and meta-analysis of 12 studies

Sang-Ah Lee · Kyoung-Mu Lee · Sue Kyung Park · Ji-Yeob Choi · Bongcheol Kim · Jinwu Nam · Keun-Young Yoo · Dong-Young Noh · Sei-Hyun Ahn · Daehee Kang

Received: 16 July 2006 / Accepted: 17 July 2006 / Published online: 25 October 2006

Abstract To evaluate the relationship of genetic polymorphism in *XRCC3* Thr^{241}Met and the risk of breast cancer, a hospital-based case-control study was conducted in Korea. Histologically confirmed breast cancer cases (n = 574) and controls (n = 502) with no present or previous history of cancer were recruited from several teaching hospitals in Seoul during 1995–2001. Information on demographic characteristics and other information were collected by interviewed questionnaire. Genetic polymorphisms of *XRCC3* Thr^{241}Met (C > T) was determined by single base extention assay. The frequency of Thr/Thr, Thr/Met, and Met/Met genotype were 89.4, 10.4, 0.2% in cases and 92.3, 7.7, 0.0% in controls, respectively. Genotype distribution in controls fit well to the Hardy–Weinberg equilibrium (P = 0.74). *XRCC3* codon 241 Thr/Met or Met/Met genotype moderately increased the risk of breast cancer (OR = 1.4, 95% CI: 0.87–2.33), but not significant in this study. In the results of meta-analysis using twelve reports, however, Thr/Met or Met/Met genotype increased the risk of breast cancer (OR = 1.08, 95%CI: 1.00–1.17). In conclusion, although the genetic polymorphism of *XRCC3* Thr^{241}Met was unlikely to have a substantial overall association in Korean women, the meta-analysis of studies, including ours, provided that Thr/Met and Met/Met was weakly increased the risk of breast cancer compare to Thr/Thr genotype.

Keywords The genetic polymorphism of *XRCC3* Thr^{241}Met · Breast cancer risk · Case-control study in Korean women · Meta-analysis

S.-A. Lee · S. K. Park · K.-Y. Yoo · D. Kang (✉)
Department of Preventive Medicine, Cancer Research Institute, Seoul National University College of Medicine, 28 Yongon-Dong Chongno-Gu, Seoul 110-799, South Korea
e-mail: dhkang@snu.ac.kr

K.-M. Lee
Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD 20892, USA

J.-Y. Choi
Department of Epidemiology, Roswell Park Cancer Institute, Buffalo, NY 14263, USA

B. Kim · J. Nam
Pan Genomics Co., Ltd., Seoul, South Korea

D.-Y. Noh
Department of Surgery, Seoul National University College of Medicine, Seoul, South Korea

S.-H. Ahn
Department of Surgery, Asan Medical Center, Ulsan University College of Medicine, Seoul, South Korea

Introduction

Exposure to ionizing radiation is a well-established risk factor for breast cancer [1, 2]. Epidemiologic evidences suggest that double-strand break in DNA may contribute to the development of breast cancer from ionizing radiation [3, 4].

X-ray cross-complementing group 3 (XRCC3) is one of protein components involved in homologous recombination repair (HRR) pathway repairing radiation-induced DNA damage. Several polymorphisms such as 4541A > G in 5′-region and Thr^{241}Met have been found in *XRCC3* gene [5]. Kuschel et al. [6] performed genetic association studies in population-

based breast cancer case-control study analyzing polymorphisms in genes involving in homologous recombination (HR: *NBS1, RAD52, RAD51, XRCC2* and *XRCC3*) and non-homologous end-joining (KU70/80 and LIG4), and found strong association between *XRCC3* Thr^{241}Met and breast cancer risk. A number of studies have explored the association between breast cancer and the genetic polymorphism of *XRCC3* Thr^{241}Met [6–16]. However, all studies were conducted for the Caucasian population except one, which was for Chinese population [14].

This study has evaluated the association between genetic polymorphism of *XRCC3* Thr^{241}Met and breast cancer risk in Korean women. Meta-analysis summarizing the previous epidemiological studies is also included in this study.

Methods

Subjects

Approval for this study was obtained from the Committee on Human Research of Seoul National University Hospital. Written informed consent was obtained from all participants. Details of the methods for subject enrollment, collection of peripheral blood, and DAN extraction have been published previously [17, 18], and a brief description is given below. After excluding subjects with previous history of cancer, hysterectomy or oophorectomy, the final study population consisted of 574 cases and 502 controls. DNA was available for 537 cases and 466 controls. Information on demographic characteristics, education, marital status, family history of breast cancer, reproductive and menstruation, life style habits (including smoking and alcohol consumption) were collected using a questionnaire administered by trained interviewers.

Genotyping

DNA was isolated using standard methods from blood drawn into 10 ml heparinized tubes and stored in –70°C until use.

The *XRCC3* Thr^{241}Met genotype was determined by single base extension assay. Polymerase chain reaction (PCR) product was obtained using 500 nM of oligonucleotide primers (P1: 5′-GCC TGG TGG TCA TCG ACT C-3′ and P2: 5′-CTG GCT AAA AAT ACG AGC TC-5′) in a total volume of 20 μl. The amplification conditions were initial denaturation at 95°C for 5 min followed by 35 cycles of 30 s at 94°C and 180 s at 72°C.

Primer extension was performed by combining 1 μl of exonuclease I and alkaline phosphatase treated PCR product with 5 μl single base extension kit, 0.15 pmol extension primer (5′-GCA TCT GCA GTC CCT GGG GGC CA-3′) and 3 μl water. The reaction mixture was incubated at 94°C for 2 min prior to PCR of 25 cycles of 95°C for 5 s, 50°C for 5 s, and 60°C for 5 s. Aliquots of 1 μl SNaPshot product and 9 μl Hi-Di formamide, were combined in 96-well 3100 optical microamp plate, which was loaded onto a 3100 DNA sequencer (Applied Biosystems, Foster city, CA, USA). Reactions were electrophoresed on a 36 cm capillary array at 60°C by using POP4 polymer, dye set ''E'' and Genescan run module ''SNP36POP4_default.'' Electrophoresis data were processed by Genescan Analysis version 3.7 (Applied Biosystems, Foster city, CA, USA). The genotype data could be achieved for 86.4% of the subjects.

Meta-analysis

To collect the literature for meta-analysis, MEDLINE was searched using the following terms for papers published before March 2006: genetic polymorphism, *XRCC3*, double-strand DNA breaks, or homologous recombination repair, and breast cancer risk. Additional articles were identified through the references cited in the first series of articles selected. Articles included in meta-analysis were in English language, with human subjects, published in the primary literature and had no obvious overlap of subjects with other studies. We identified eleven case-control studies that provided information on breast cancer occurrence associated with the *XRCC3* Thr^{241}Met polymorphisms. For meta-analysis, data were combined using both fixed-effects (Mantel–Haenszel) and random-effect (DerSimonian and Laird method) models [19]. Estimate values were based on random-effects model because random-effects model are more appropriate when heterogeneity is present [19]. Heterogeneity among the studies was evaluated by means of the Cochrane Q test [19, 20] and was considered significant at $P < 0.05$. If the test result was negative, a fixed-effects model (Mantel–Haenszel method) was used. On the contrary, if the test result was positive, we used a random-effects model [21] to task the heterogeneity into account. This model assumes that the studies are a random sample of a hypothetical population of studies taking into account within- and between-study variability. Publication bias was assessed by Begg [22] and Egger's test [23]. All the

calculations were performed with computer program STATA Version 8.2 (Stata Corp., College Station, TX, USA).

Statistical analysis

The Hardy–Weinberg equilibrium assumption was assessed using standard maximum likelihood methods. Chi-square tests and Fisher's exact tests used to test whether observed genotype data were consistent with Hardy-Weinberg proportions and to compare the allele frequencies between cases and controls. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by unconditional logistic regression model. The ORs were adjusted for age, body mass index (BMI), education, exposure of lifetime estrogen, and family history of breast cancer. To increase the statistical power, the respective genotypes were divided into two groups in the statistical analyses. All analyses were carried out with the SPSS (version 10.0) statistical software package.

Results

Demographic characteristics of the study population have been previously published [15]. In brief, the mean age was 47.9 (±10.55) in cases and 46.9 (±13.93) in controls (p = 0.180). High education (OR = 2.0, 95% CI: 1.5–2.7), high BMI (OR = 1.5, 95% CI: 1.1–2.0), and family history of breast cancer (OR = 2.4, 95% CI: 1.3–4.4) were significantly different between cases and controls. As the duration of estrogen exposure in their life was longer, the risk of breast cancer was increased ($P < 0.001$).

The frequency of Thr/Thr, Thr/Met and Met/Met genotype were 89.4, 10.4, 0.2% in cases and 92.3, 7.7, 0.0% in controls, respectively. Genotype distribution in controls fit well to the Hardy–Weinberg equilibrium ($P = 0.74$). *XRCC3* codon 241 Thr/Met or Met/Met genotype was moderately increased the risk of breast cancer (OR = 1.4, 95% CI: 0.87–2.33), especially in postmenopausal women (OR = 2.1, 95% CI: 0.93–4.59) (Table 1). However, the association was not statistically significant.

As a result of meta-analysis using ten Caucasian studies and two Asian studies including present study, the Thr/Met or Met/Met genotypes of *XRCC3* Thr^{241}Met polymorphism was positively associated with risk of breast cancer (Thr/Met + Met/Met vs. Thr/Thr; OR = 1.08, 95% CI: 1.00–1.17). The trend was shown little stronger in Asian (OR = 1.29, 95%CI: 0.97–1.70) than Caucasian (OR = 1.07, 95%CI: 0.99–1.16) (Fig. 1); however, the number of Asian study was only two including ours. There was not statistically significant study heterogenesity (Q test $P = 0.07$), and no evidence of publication biases according to the Egger's or Begg's test (data not shown).

Discussion

The genetic polymorphism of *XRCC3* Thr^{241}Met was not significantly associated with breast cancer in Korean women; however, the result of meta-analysis based on twelve studies suggests that the *XRCC3* 241 Met allele is likely to have a substantial overall associated with the risk of breast cancer.

The association is biologically plausible considering the experimental evidence. Matullo et al. [24] observed

Table 1 *XRCC3* (Thr^{241}Met) and breast cancer risk in Korean women

	Case *N* (%)	Control *N* (%)	OR (95% CI)
All women			
Thr/Thr	437 (89.4)	349 (92.3)	1.0
Thr/Met	51 (10.4)	29 (7.7)	1.4 (0.84–2.20)
Met/Met	1 (0.2)	–	–
Thr/Met + Met/Met	52 (10.6)	29 (7.7)	1.4 (0.87–2.33)
Premenopausal women			
Thr/Thr	279 (90.0)	204 (91.5)	1.0
Thr/Met	31 (10.0)	19 (8.5)	1.2 (0.62–2.31)
Met/Met	–	–	–
Thr/Met + Met/Met	31 (10.0)	19 (8.5)	1.1 (0.56–1.99)
Postmenopausal women			
Thr/Thr	158 (88.3)	149 (93.5)	1.0
Thr/Met	20 (11.2)	10 (6.5)	2.0 (0.88–4.41)
Met/Met	1 (0.5)	–	–
Thr/Met + Met/Met	21 (11.7)	10 (6.5)	2.1 (0.93–4.59)

Adjusted for age, BMI, education, exposure of lifetime estrogen, and family history of breast cancer

Author (country)[ref]	genotypes	Cases (%)	Controls (%)
Smith (USA)[7]	*Thr/Met*	47.4	48.0
[114/229][*]	*Met/Met*	17.5	17.0
	Met allele [†]		
Han (USA)[8]	*Thr/Met*	45.1	48.8
[952/1245]	*Met/Met*	14.2	13.7
	Met allele		
Smith (USA)[9]	*Thr/Met*	48.1	41.7
[268/252]	*Met/Met*	13.1	20.2
	Met allele		
Jacobson (Danish)[10]	*Thr/Met*	47.8	46.8
[425/423]	*Met/Met*	13.9	15.4
	Met allele		
Millikan (USA,	*Thr/Met*	46.1	49.0
white only)[11]	*Met/Met*	13.6	12.5
[1254/1132]	*Met allele*		
Figueiredo	*Thr/Met*	46.3	49.8
(Canada)[12]	*Met/Met*	19.2	13.9
[402/402]	*Met allele*		
Webb (Australia)[13]	*Thr/Met*	45.4	47.6
[1445/788]	*Met/Met*	13.7	13.5
	Met allele		
Forsti (Finnish)[15]	*Thr/Met*	35.9	36.9
[223/298]	*Met/Met*	14.3	9.1
	Met allele		
Forsti (Polish)[15]	*Thr/Met*	49.4	43.6
[172/202]	*Met/Met*	8.7	12.4
	Met allele		
Garcia-Closas	*Thr/Met*	47.6	47.5
(USA)[16]	*Met/Met*	15.3	14.4
[2978/2554]	*Met allele*		
Garcia-Closas	*Thr/Met*	45.9	45.5
(Polish)[16]	*Met/Met*	41.3	11.6
[1974/2285]	*Met allele*		
Kushel (ABC-	*Thr/Met*	48.6	46.6
EPIC[**])[6]	*Met/Met*	14.7	13.0
[1242/1052]	*Met allele*		
Zhang (Chian)[14]	*Thr/Met*	36.4	37.1
[220/310]	*Met/Met*	15.0	9.4
	Met allele		
Lee (Korea)[current]	*Thr/Met*	10.4	7.7
[489/378]	*Met/Met*	0.2	0
	Met allele		

		OR (95% CI)
Total	*Thr/Met*	1.02 (0.96-1.07)
	Met/Met	1.11 (0.99-1.24)
	Met allele	1.08 (1.00-1.17)
Caucasians	*Thr/Met*	1.01 (0.95-1.07)
	Met/Met	1.09 (0.97-1.22)
	Met allele	1.07 (0.99-1.16)
Asian	*Thr/Met*	1.19 (0.89-1.60)
	Met/Met	1.78 (1.03-3.08)
	Met allele	1.29 (0.97-1.70)

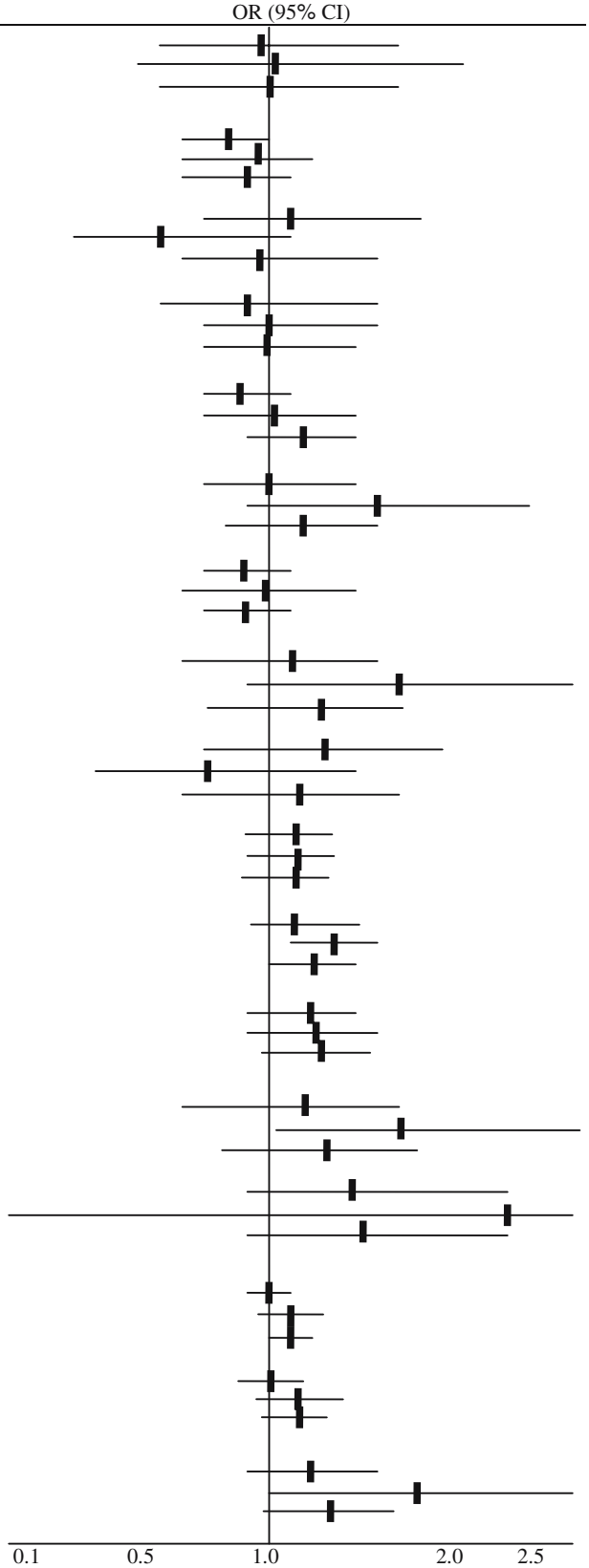

Fig. 1 Meta-analysis of the association between *XRCC3* Thr[241]Met and breast cancer risk using ten Caucasian and two Asian reports

a higher level of DNA adducts in healthy volunteers with Met/Met genotype of *XRCC3* Thr^{241}Met compared with Thr/Thr genotype. *XRCC3* Thr^{241}Met polymorphism change the amino acids coded from one with a neutral hydrophilic hydroxyl group (Thr) to a hydrophobic one with a methyl sulfur group (Met) [6]. The *XRCC3* 241 Met variation is evolutionarily conserved and functional data supports that it could be a risk allele for breast cancer [25, 26]. The impact of this polymorphisms on repair phenotype was studied in 80 healthy subjects [25]; the *XRCC3* 241 Met allele was associated with significant increases in chromosome deletions in X-ray-challenged blood lymphocyte ($P = 0.05$). Chromosome deletion is specific for abnormal repair of X-ray-induced DNA strand breakage, suggested that the *XRCC3* 241 Met allele might be defective in repairing double strand breaks.

A modest association between the homozygote variant genotype for *XRCC3* Thr^{241}Met and breast cancer risk was first reported in the UK [6]; however, subsequent studies were not consistent. *XRCC3* codon 241 Met/Met genotype showed a weak positive association with breast cancer among women in northern Europe [6], Finland [15], Canada [12], China [14], and the United States [9]. No associations were observed among women in Denmark [10], the United States [11], Australia [13], or the Nurses' Health Study [8, 27]. A population-based breast cancer case-control study conducted for 2,592 breast cancer patients and 2,016 controls examined to analyze genetic polymorphisms in homologous recombination (HR) and has found that *XRCC3* Thr^{241}Met are more strongly associated with the risk of breast cancer than other HR genes, such as *XRCC2* and *LIG4* [18]. Smith et al. [7] also defined the role of *XRCC3* in breast cancer development and suggested that the genetic polymorphism may be associated with susceptibility to breast cancer.

The variant allele frequencies ranged from 5 to 45%, with a statistically significant difference in the prevalence of the *XRCC3* 241 polymorphism among different ethnic groups (the prevalence of Met/Met homozygosity was 4.6% in African–Americans, 0.2% in Asians, and 12.4% in Caucasians; $P < 0.001$) [28]. In our study, the Met allele frequency was 4.7%; although the frequency was lower than Caucasian (ranged from 28.5 to 44.9%), but similar and comparable to Asian population (ranged from 3.8 to 18.4%) [14, 28–32].

As a result of meta-analysis, we found that the genetic polymorphism of *XRCC3* Thr^{241}Met was weakly affected to the risk of breast cancer; the Met/Met and Thr/Met was weakly associated with breast cancer compared to Thr/Thr genotype, and this trend was more strongly shown in Asian women. The different of ethnicity, however, must be interpreted with caution because of the lack of power due to the small number of studies and much lower frequency of Met/Met allele compared to Caucasian's. Garcia-Closas et al. examined the meta-analysis of *XRCC3* Thr^{241}Met in Caucasian population using eight published studies, and suggested a small increased in risk for the Met/Met compared to the Thr/Thr genotype (OR = 1.16, 95%CI: 1.04–1.30) similar to that from the present study (OR = 1.09, 95% CI:0.97–1.22).

In conclusion, this results fail to show the association between the genetic polymorphism of *XRCC3* Thr^{241}Met and the risk of breast cancer in Korean women, but the meta-analysis was suggested to weak and positive association between the genetic polymorphism of *XRCC3* Thr^{241}Met and breast cancer risk. However, Smith et al. [9] suggested to potential gene-gene interaction among variant alleles of *XRCC1*, *XRCC3*, and *ERCC4/XPF* in breast cancer risk and to needs for combination of genetic variant of base excision repair (BER), HRR, and nucleotide excision repair (NER) pathways, which play critical roles in repairing various types of DNA damage. Therefore, genetic variants in multiple repair pathways may have a joint or addictive effect on breast cancer risk.

Acknowledgments This study was supported by a grant from the National R&D Program for Cancer Control, Ministry of Health & Welfare, Republic of Korea (0620410–1).

References

1. Wakeford R (2004) The cancer epidemiology of radiation. Oncogene 23:6404–6428
2. Ronckers CM, Erdman CA, Land CE, (2005) Radiation and breast cancer: a review of current evidence. Breast Cancer Res 7:21–32
3. John EM, Kelsey JL (1993) Radiation and other environmental exposures and breast cancer. Epidemiol Rev 15:157–162
4. Holmberg E, Holm LE, Lundell M, Mattsson A, Wallgren A, Karlsson P (2001) Excess breast cancer risk and the role of parity, age at first childbirth and exposure to radiation in infancy. Br J Cancer 85:362–366
5. Parshad R, Price FM, Bohr VA, Cowans KH, Zujewski JA, Sanford K (1996) Deficient DNA repair capacity, a predisposing factor in breast cancer. Br J Cancer 74:1–5
6. Kuschel B, Auranen A, McBride S, Novik KL, Antoniou A, Lipscombe JM, Day NE, Easton DF, Ponder BA, Pharoah PD, Dunning A (2002) Variants in DNA double-strand break repair genes and breast cancer susceptibility. Hum Mol Genet 11(12):1399–1407
7. Smith TR, Miller MS, Lohman K, Lange EM, Case LD, Mohrenweiser HW, Hu JJ (2003) Polymorphisms of XRCC1 and XRCC3 genes and susceptibility to breast cancer. Cancer Lett 190:183–190

8. Han J, Hankinson SE, Ranu H, De Vivo I, Hunter DJ (2004) Polymorphisms in DNA double-strand break repair genes and breast cancer risk in the Nurses' Health Study. Carcinogenesis 25(2):189–195
9. Smith TR, Levine EA, Perrier ND, Miller MS, Freimanis RI, Lohman K, Case LD, Xu J, Mohrenweiser HW, Hu JJ (2003) DAN-repair genetic polymorphisms and breast cancer risk. Cancer Epidemiol Biomarkers Prev 12:1200–1204
10. Jacobsen NR, Nexo BA, Olsen A, Overvad K, Wallin H, Tjonneland A, Vogel U (2003) No association between the DNA repair gene XRCC3 T241M polymorphism and risk of skin cancer and breast cancer. Cancer Epidemiol Biomarkers Prev 12:584–585
11. Millikan RC, Player JS, Decotret AR, Tse CK, Keku T (2005) Polymorphisms in DNA Repair genes, medical exposure to ionizing radiation, and breast cancer risk. Cancer Epidemiol Biomarkers Prev 14(10):2326–2334
12. Figueiredo JC, Knight JA, Briollais L, Andrulis IL, Ozcelik H (2004) Polymorphisms XRCC1-R399Q and XRCC3-T241M and the risk at the Ontario site of the breast cancer family registry. Cancer Epidemiol Biomarkers Prev 13(4): 583–591
13. Webb PM, Hopper JL, Newman B, Chen X, Kelemen L, Giles GG, Southey MC, Chenevix-Trench G, Spurdle AB (2005) Double-strand break repair gene polymorphisms and risk of breast or ovarian cancer. Cancer Epidemiol Biomarkers Prev 14(2):319–323
14. Zhang L, Zhang Z, Yan W (2005) Single nucleotide polymorphisms for DNA repair genes in breast cancer patients. Clin Chim Acta 359:150–155
15. Forsti A, Angelini S, Festa F, Sanyal S, Zhang Z, Grzybowska E, Pamula J, Pekala W, Zientek H, Hemminki K, Kumar R (2004) Single nucleotide polymorphisms in breast cancer. Oncol Rep 11:917–922
16. Garcia-Closas M, Egan KM, Newcomb PA, Brinton LA, Titus-Ernstoff L, Chanock S, Welch R, Lissowska J, Peplonska B, Szeszenia-Dabrowska N, Zatonski W, Bardin-Mikolajczak, Struewing JP (2006) Polymorphisms in DNA double-strand break repair genes and risk of breast cancer: two population-based studies in USA and Poland, and meta-analyses. Hum Genet 119(4):376–388
17. Lee SA, Lee KM, Park WY, Kim B, Nam J, Yoo KY, Noh DY, Ahn SH, Hirvonen A, Kang D (2005) Obesity and genetic polymorphism of ERCC2 and ERCC4 as modifier of risk of breast cancer. Exp Mol Med 37(2):86–90
18. Park SK, Yoo KY, Lee SJ, Kim SU, Ahn SH, Noh DY, Choe KJ, Strickland PT, Hirvonen A, Kang D (2000) Alcohol consumption, glutathione *S*-transferase M1 and T1 genetic polymorphisms and breast cancer risk. Pharmacogenetics 10:301–309
19. Dersimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7:177–188
20. Cohran WG (1983) Adjustments in analysis. In: Moses LE, Mosteller F (eds.), Planning and analysis of observational studies. Wiley, New York, pp 102–108
21. Whitehead A, Whitehead J (1991) A general parametric approach to the meta-analysis of randomized clinical trials. Stat Med 10:1665–1677
22. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50:1088–101
23. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315:629–634
24. Matullo G, Palli D, Peluso M, Guarrera S, Carturan S, Celentano E, Krogh V, Munnia A, Tumino R, Polidoro S, Piazza A, Vineis P (2001) XRCC1, XRCC3, XPD gene polymorphisms, smoking and ^{32}P-DNA adducts in a sample of healthy subjects. Carcinogenesis 9:1437–1445
25. Au WW, Salama SA, Sierra-Torres CH (2003) Functional characterization of polymorphisms in DNA repair genes using cytogenetic challenge assays. Environ Health Perspect 111:1843–1850
26. Savas S, Kim DY, Ahmad MF, Shariff M, Ozcelik H (2004) Identifying functional genetic variants in DNA repair pathway using protein conservation analysis. Cancer Epidemiol biomarkers Prev 13:801–807
27. Han J, Hankinson SE, Zhang SM, DeVivo I, Hunter DJ (2004) Interaction between genetic variations in DNA repair genes and plasma folate on breast cancer risk. Cancer Epidemiol Biomarkers Prev 13:520–524
28. Manuguerra M, Saletta F, Karagas MR, Berwick M, Veglia F, Vineis P, Matullo G XRCC3 and XPD/ERCC2 single nucleotide polymorphisms and the risk of cancer: a HuGE review. Am J Epidemol (Epub ahead of print)
29. Shen H, Wang X, Hu Z, Zhang Z, Xu Y, Hu X, Guo J, Wei Q (2004) Polymorphisms of DNA repair gene XRCC3 Thr241Met and risk of gastric cancer in a Chinese population. Cancer Lett 206:51–58
30. Jin M, Chen K, Song L, Fan CH, Chen Q, Zhu YM, Ma XY, Yao KY (2005) The association of the DNA repair gene XRCC3 Thr241met polymorphism with susceptibility to colorectal cancer in a Chinese population. Cancer Genet Cytogenet 163:38–43
31. Yeh CC, Sung FC, Tang R, Chang-Chieh CR, Hsieh LL (2005) Polymorphisms of the XRCC1, XRCC3, and XPD genes, and colorectal cancer risk: a case-control study in Taiwan. BMC Cancer 5:12–19
32. Ritchey JD, Huang WY, Chokkalingam AP, Gao YT, Deng J, Levine P, Stanczyk FZ, Hsing AW (2005) Genetic variants of DNA repair genes and prostate cancer: a population-based study. Cancer Epidemiol biomarkers Prev 14(7):1703–1709