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Original Article

Association between ERCC1 rs3212986 and ERCC2 rs13181 gene polymorphisms in NER pathway and the risk of bladder cancer in a Chinese population

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Abstract: We conducted a case-control study to investigate the association of ERCC1 (rs3212986) and ERCC2 (rs13181) gene polymorphisms with the susceptibility to bladder cancer. A total of 194 bladder cancer patients and 240 control subjects were recruited from the Zhumadian City Center Hospital between March 2012 and March 2014. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was taken to genotype ERCC1 rs3212986 and ERCC2 rs13181. A significant difference was found between the genotype distributions of ERCC1 rs3212986 between the two groups by chi-square test (χ^2 = 6.01, *P* = 0.04). Unconditional logistic regression analyses showed that subjects carrying the CC genotype of ERCC1 rs3212986 were associated with a higher risk of developing bladder cancer than those carrying the AA genotype, and the adjusted OR (95% CI) was 2.05 (1.10-3.83) (*P* = 0.01). Moreover, we found that the CC genotype of ERCC1 rs3212986 had 1.8 fold risk of bladder cancer compared to the AA+AC genotype (OR = 1.80, 95% CI = 1.01-3.21; *P* = 0.03). However, we did not find any significant association between the ERCC2 rs13181 polymorphism and susceptibility to bladder cancer. In conclusion, we suggest that the ERCC1 rs3212986 gene polymorphism influences the development of bladder cancer in co-dominant and recessive models.

Keywords: ERCC1 rs3212986, ERCC2 rs13181, polymorphism, bladder cancer

Introduction

Bladder cancer (BC) is one of the most common cancers worldwide, and it is estimated that there were one million new cases of bladder cancer in 2012 (178,101 cases, 1.3% of the total), making it the eleventh most common malignancy in both sexes worldwide [1]. The development of bladder cancer is involved in various environmental risk factors, such as chemical carcinogens resulting from tobacco use and occupational exposure [2-5], however, the exact etiology remains poorly understood. Not all patients with exposure to chemical carcinogens develop bladder cancer during their life-time, which suggested that genetic factors contribute to the development of this cancer. Many single-nucleotide polymorphisms (SNPs) have been reported to be associated with the bladder carcinogenesis, such as matrix metalloproteinase gene 1, 2 and 7, cyclooxygenase-2, transforming growth factor-β1 and TP53 [6-10].

These chemical carcinogens may cause DNA damage through inactivation of enzymes, and thus induce DNA strand breaks and base damage that can result in severe mutations leading to cancers [11]. Nucleotide excision repair (NER) pathway is one of the most important DNA repair process involved in maintaining genome integrity. Excision Repair cross complementation group 1 (ERCC1) and ERCC2 are two DNA repair genes, and their products are located on chromosome 19q13.3 [12]. Polymorphisms in DNA repair gene could modify the function and/or proficiency of DNA repair, and thus influence inter-individual variation of DNA repair capacity [13, 14]. Previous studies have investigated the association between ERCC1 and ERCC2 gene polymorphisms and development of several kinds of cancers, but the results

Table 1. PCR primers and restriction enzymes for ERCC1 rs3212986 and ERCC2 rs13181 genes

SNP	Location	Primer sequences	Restriction enzyme	Fragment size
ERCC1 rs3212986	3'UTR	5'-TGAGCCAATTCAGCCACT-3'	*M*boII	380 bp
		5'-TAGTTCCTCAGTTTCCCG-3'		
ERCC2 rs13181	Exon23	5'-CTGCTcAGCTGAGAGACGCTG-3'	*P*stI	161 bp
		5'-AAGACCTTCTAGCACCACCG-3'		

Table 2. Demographic characteristics of the study subjects

Variables	Patients	%	Controls	%	Chi-square test	*P* value
Sex						
Male	143	73.71	145	60.42		
Females	51	26.29	95	39.58	8.49	0.003
Age						
< 50	85	43.81	121	50.42		
≥ 50	109	56.19	119	49.58	1.88	0.17
BMI						
< 25	154	79.38	201	83.75		
≥ 25	40	20.62	39	16.25	1.38	0.24
Tobacco smoking						
Never	119	61.34	176	73.33		
Ever	75	38.66	64	26.67	7.09	0.01
Alcohol drinking						
Never	122	62.89	169	70.42		
Ever	72	37.11	71	29.58	2.75	0.10
A family history of cancer						
No	179	92.27	224	93.33		
Yes	15	7.73	16	6.67	0.18	0.67

are inconclusive [10, 15-19]. Therefore, we conducted a case-control study to investigate the association of ERCC1 (rs3212986) and ERCC2 (rs13181) gene polymorphisms with the susceptibility to bladder cancer.

Material and methods

Patients

Bladder cancer patients were recruited from the Zhumadian City Center Hospital between March 2012 and March 2014. Initially, 214 bladder cancer patients were diagnozed and histopathologically confirmed by two pathologists. Patients who had received chemotherapy or radiotherapy before participating in this study, or patients who had suffered from other malignant cancer and recurrent cancer as well as serious kidney or liver diseases were excluded. Ultimately, 194 patients were included into our study, and the participation rate was 85.3%.

A total of 254 subjects were randomly selected from individuals who underwent a regular health examination at the Zhumadian City Center Hospital between March 2012 and March 2014. Control subjects who had a history of cancer and urinary system diseases were excluded from this study. Ultimately, 240 control subjects were recruited for analysis, with a participation rate of 94.49%. Blood samples (5 mL) and signed informed consent forms were collected from all patients and controls before their participation in the study. The protocol of this project was approved by the Ethics Committee of the Zhumadian City Center Hospital.

The demographic characteristics were collected using a self-designed questionnaire, such as sex, age, alcohol drinking, tobacco smoking, body mass index (BMI), and a family history of cancer in the first relatives. Similarly, subjects who had drunk alcoholic beverages at least once a week for more than one year previously were defined as drinkers. Tobacco smoking dose was estimated as 'pack-years' (PY = number of packs of 20 cigarettes per days for one year).

DNA extraction and SNPs genotyping

The collected blood samples were kept in ethylene diamine tetra-acetic acid (EDTA)-coated tubes. The blood samples were stored at -20°C until required. Genomic DNA was isolated from peripheral blood leukocytes using a TIANamp Blood DNA Kit (Tiangen Biotech, Beijing, China) according to the manufacturer instructions, and genomic DNA was stored at -20°C until required. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was

Table 3. Genotype distributions of ERCC1 rs3212986 and ERCC2 rs13181 genes between bladder cancer patients and control subjects

IL-17	Patients	%	Controls	%	P for HWE	χ^2 test	*P* value	Minor allele frequency	
	N = 194		N = 240		In controls			In database	In controls
ERCC1 rs3212986									
AA	71	36.60	109	45.42					
AC	87	44.85	104	43.33					
CC	36	18.56	27	11.25	0.77	6.01	0.04	0.2951	0.3292
ERCC2 rs13181									
CC	96	49.48	128	53.33					
CA	81	41.75	99	41.25					
AA	17	8.76	13	5.42	0.27	2.05	0.36	0.2366	0.2604

Table 4. Association between ERCC1 rs3212986 and ERCC2 rs13181 polymorphisms and bladder cancer risk

IL-17	Patients	%	Controls	%	OR (95% CI)[1]	*P* value
	N = 194		N = 240			
ERCC1 rs3212986						
Co-dominant						
AA	71	36.6	109	45.42	1.0 (Ref.)	-
AC	87	44.85	104	43.33	1.28 (0.83-1.98)	0.23
CC	36	18.56	27	11.25	2.05 (1.10-3.83)	0.01
Dominant						
AA	71	36.6	109	45.42	1.0 (Ref.)	-
AC+CC	123	63.41	131	54.58	1.44 (0.96-2.16)	0.06
Recessive						
AA+AC	158	81.45	213	88.75	1.0 (Ref.)	-
CC	36	18.56	27	11.25	1.80 (1.01-3.21)	0.03
ERCC2 rs13181						
Co-dominant						
CC	96	49.48	128	53.33	1.0 (Ref.)	-
CA	81	41.75	99	41.25	1.09 (0.72-1.65)	0.67
AA	17	8.76	13	5.42	1.74 (0.75-4.10)	0.15
Dominant						
CC	96	49.48	128	53.33	1.0 (Ref.)	-
CA+AA	98	50.51	112	46.67	1.17 (0.78-1.73)	0.43
Recessive						
CC+CA	177	91.23	227	94.58	1.0 (Ref.)	-
AA	17	8.76	13	5.42	1.68 (0.74-3.86)	0.17

[1]Adjusted for sex, age and tobacco smoking.

taken to genotype ERCC1 rs3212986 and ERCC2 rs13181. The primers for PCR were designed using Sequenom Assay Design 3.1 software (San Diego, CA, USA), PCR fragments of the investigated polymorphisms were subsequently digested with their specific restriction enzyme (**Table 1**). The amplification reaction were began with an initial denaturation at 95°C for 5 min, followed by 35 cycles of denaturation at 94°C for 60 s, annealing at 60°C for 60 s, and extension at 72°C for 60 s, with final extension at 72°C for 10 min. Digestion products were separated by electrophoresis on ethidium bromide stained agarose gel and visualized under UV light.

Statistical method

All statistical analyses were conducted using the SPSS® statistical package, version 16.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Means of quantitative variables were compared between groups using Student T-test after log transformation to obtain normal distribution, while distributions of categorical variables were compared by chi-square test. Hardy-Weinberg equilibrium (HWE) was examined using a Chi-square (χ^2) test with one degree of freedom. Unconditional logistic regression was conducted to assess the effects of ERCC1 rs3212986 and ERCC2 rs13181 polymorphisms on the risk of bladder cancer and the results are expressed as ORs and 95% CIs. All *P*-values were two sided, and $P < 0.05$ was considered statistically significant.

Results

The demographic characteristics of the study subjects are presented in **Table 2**. Compared with the control subjects, patients with bladder cancer were more likely to be males (χ^2 = 8.49, *P* = 0.003) and have a habit of tobacco smoking (χ^2 = 7.09, *P* = 0.01). No significant difference was found between bladder cancer patients and control subjects in terms of age (χ^2 = 1.88, *P* = 0.17), BMI (χ^2 = 1.38, *P* = 0.24), alcohol drinking (χ^2 = 2.75, *P* = 0.10) and a family history of cancer (χ^2 = 0.18, *P* = 0.67).

The genotype distributions of ERCC1 rs3212986 and ERCC2 rs13181 genes between bladder cancer patients and control subjects were described in **Table 3**. The genotype distributions of ERCC1 rs3212986 and ERCC2 rs13181 did not deviate from Hardy-Weinberg equilibrium, and the *P* values for HEW were 0.77 and 0.27, respectively. A significant difference was found in the genotype distributions of ERCC1 rs3212986 between the two groups by chi-square test (χ^2 = 6.01, *P* = 0.04). The minor allele frequencies of ERCC1 rs3212986 and ERCC2 rs13181 were close to those in the National Center for Biotechnology Information SNP database (http://www.ncbi.nlm.nih.gov/snp/).

The association between ERCC1 rs3212986 and ERCC2 rs13181 polymorphisms and bladder cancer risk was shown in **Table 4**. Unconditional logistic regression analyses showed that subjects carrying the CC genotype of ERCC1 rs3212986 were associated with a higher risk of developing bladder cancer than those carrying the AA genotype, and the adjusted OR (95% CI) was 2.05 (1.10-3.83) (*P* = 0.01). Moreover, we found that the CC genotype of ERCC1 rs3212986 had 1.8 fold risk of bladder cancer compared to the AA+AC genotype (OR = 1.80, 95% CI = 1.01-3.21; *P* = 0.03). However, we did not find any significant association between the ERCC2 rs13181 polymorphism and susceptibility to bladder cancer.

Discussion

Genetic susceptibility to disease has attracted increasing attention in recent years, and gene polymorphisms that are involved in various diseases are of particular interest. DNA damage caused by several exogenous or endogenous factors needs efficient DNA repair to restore genomic integrity, and the process of DNA repairing is involves many DNA repair genes. NER is an important mechanism of the DNA repair pathway, and this pathway has a role in maintaining genomic integrity through removing DNA interstrand crosslinks [20, 21]. Both products of ERCC1 and ERCC2 genes are two key rate-limiting enzymes acting in the NER process.

ERCC1 is a subunit of the NER complex, and it has interaction with XPA, XPF and/or RPA, guiding the 5' cleavage activity in the NER pathway [22, 23]. Cells from ERCC1-deficient mice usually present a high mutation frequency, an elevated level of genomic instability and a reduced frequency of S-phase-dependent illegitimate chromosome exchange, a response adopted by rodent cells to prevent the accumulation of DNA double strand breaks [24]. The ERCC2 protein is located at chromosome 19q13.3, possesses both single strand DNA-dependent ATPase and 5'-3' DNA helicase activities and participates in DNA unwinding during NER [25-27]. Polymorphisms in the ERCC2 gene have a role in decreasing the helicase activity, and causing in a lower DNA repair capacity of NER pathway as well as influencing cancer susceptibility. Therefore, potentially functional ERCC1 and ERCC2 SNPs may affect cellular DNA repair capacity and thus contribute to the development of cancers. In our study, we demonstrated that the CC genotype of ERCC1 rs3212986 was associated with a higher risk of developing bladder cancer compared to the wide-type genotype.

Previous studies have reported the association between ERCC1 rs3212986 and ERCC2 rs13181 variants and development of several kinds of cancer, such as colorectal cancer, lung cancer, breast cancer and glioma [28-33]. Zhou et al. conducted a study with 1,752 Caucasian lung cancer patients and 1358 controls, and they showed that ERCC1 rs3212986 polymorphism may modify the association between lung cancer risk [28]. Zhang et al. showed that polymorphism in ERCC1 rs3212986 gene was not associated with the risk of glioma in a Chinese population [29]. Pei et al. performed a study with 417 breast cancer patients and 417 control subjects, and they did not find a significant association between ERCC1 rs3212986 and the risk of breast cancer [30]. Hou et al. conducted a case-control study in a Chinese population, and they found that ERCC1 rs3212986 polymorphism is correlated with risk

of colorectal cancer in a Chinese population [31]. Wu et al. conducted a meta-analysis with 30 studies, and suggested that the ERCC2 rs13181 may be associated with an increased risk of lung cancer in Caucasian populations [32]. Xu et al. reported that ERCC2 rs13181 polymorphism contributed to the development of glioma in a Chinese population [33]. The discrepancies of the above mentioned studies may be explained by different cancers, populations, source of patients and controls and sample sizes.

Several previous studies have reported role of ERCC1 rs3212986 and ERCC2 rs13181 polymorphisms in the susceptibility to bladder cancers, but the results are inconclusive [18, 19, 34]. Matullo et al. suggested that XPD-ERCC1 region may modify the bladder cancer risk in a British population [34]. Chang et al. found that ERCC2 rs13181 polymorphism may be responsible for bladder carcinogenesis, and help in early detection and prediction of bladder cancer [18]. Li et al. conducted a meta-analysis with 11 studies, and they reported that ERCC2 rs13181 polymorphism may contribute to bladder cancer susceptibility in Caucasians [19]. In our study, we only found a significant association between ERCC1 rs3212986 and risk of bladder. Therefore, further studies with large sample size are greatly needed to confirm our findings.

In conclusion, we suggest that the ERCC1 rs3212986 gene polymorphism influences the development of bladder cancer in co-dominant and recessive models. Further well-designed, multicenter studies with a large sample size would be very helpful to verify our findings.

Disclosure of conflict of interest

None.

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References

[1] International Agency for Research on Cancer. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/Pages/fact_sheets_population.aspx.

[2] Cohen SM, Johansson SL. Epidemiology and etiology of bladder cancer. Urol Clin North Am 1992; 19: 421-8.

[3] Brennan P, Bogillot O, Cordier S, Greiser E, Schill W, Vineis P, Lopez-Abente G, Tzonou A, Chang-Claude J, Bolm-Audorff U, Jockel KH, Donato F, Serra C, Wahrendorf J, Hours M, T'Mannetje A, Kogevinas M, Boffetta P. Cigarette smoking and bladder cancer in men: a pooled analysis of 11 case-control studies. Int J Cancer 2000; 86: 289-294.

[4] Feki-Tounsi M, Khlifi R, Mhiri MN, Rebai A, Hamza-Chaffai A. Cytogenetic damage in the oral mucosa cells of bladder cancer patients exposed to tobacco in Southern Tunisia. Environ Sci Pollut Res Int 2014; 21: 12922-7.

[5] Feki-Tounsi M, Olmedo P, Gil F, Khlifi R, Mhiri MN, Rebai A, Hamza-Chaffai A. Cadmium in blood of Tunisian men and risk of bladder cancer: interactions with arsenic exposure and smoking. Environ Sci Pollut Res Int 2013; 20: 7204-13.

[6] Tao L, Li Z, Lin L, Lei Y, Hongyuan Y, Hongwei J, Yang L, Chuize K. MMP1, 2, 3, 7, and 9 Gene Polymorphisms and Urinary Cancer Risk: A Meta-Analysis. Genet Test Mol Biomarkers 2015; 19: 548-55.

[7] Wan GX, Chen P, Yu XJ, Di QS, Yu YD, Lei JH, Tai YY, Cao FJ. Cyclooxygenase-2 polymorphisms and bladder cancer risk: a meta-analysis based on case-control studies. Int J Clin Exp Med 2015; 8: 3935-45.

[8] Gautam KA, Pooja S, Sankhwar SN, Sankhwar PL, Goel A, Rajender S. c.29C>T polymorphism in the transforming growth factor-β1 (TGFB1) gene correlates with increased risk of urinary bladder cancer. Cytokine 2015; 75: 344-8.

[9] Hosen MB, Salam MA, Islam MF, Hossain A, Hawlader MZ, Kabir Y. Association of TP53 gene polymorphisms with susceptibility of bladder cancer in Bangladeshi population. Tumour Biol 2015; 36: 6369-74.

[10] Akhmadishina LZ, Giliazova IR, Kutlyeva LR, Korytina GF, Kochetova OV, Urmantsev MF, Izmaĭlova SM, Izmaĭlov AA, Kunsbaeva GB, Zagidullin AA, Haliullin AA, Pavlov VN, Viktorova TV, Husnutdinova EK. DNA repair XRCC1, XPD genes polymorphism as associated with the development of bladder cancer and renal cell carcinoma. Genetika 2014; 50: 481-90.

[11] Hoeijmakers JH. Genome maintenance mechanisms for preventing cancer. Nature 2001; 411: 366-374.

[12] Smith JS, Tachibana I, Pohl U, Lee HK, Thanarajasingam U, Portier BP, Ueki K, Ramaswamy S, Billings SJ, Mohrenweiser HW, Louis DN, Jenkins RB. A transcript map of the chromosome 19q-arm glioma tumor suppressor region. Genomics 2000; 64: 44-50.

[13] Goode EL, Ulrich CM, Potter JD. Polymorphisms in DNA repair genes and associations with can-

cer risk. Cancer Epidemiol Biomarkers Prev 2002; 11: 1513-1530.
[14] Lunn RM, Helzlsouer KJ, Parshad R, Umbach DM, Harris EL, Sanford KK, Bell DA. XPD polymorphisms: effects on DNA repair proficiency. Carcinogenesis 2000; 21: 551-5.
[15] Ricceri F, Guarrera S, Sacerdote C, Polidoro S, Allione A, Fontana D, Destefanis P, Tizzani A, Casetta G, Cucchiarale G, Vineis P, Matullo G. ERCC1 haplotypes modify bladder cancer risk: a case-control study. DNA Repair (Amst) 2010; 9: 191-200.
[16] Ramaniuk VP, Nikitchenko NV, Savina NV, Kuzhir TD, Rolevich AI, Krasny SA, Sushinsky VE, Goncharova RI. Polymorphism of DNA repair genes OGG1, XRCC1, XPD and ERCC6 in bladder cancer in Belarus. Biomarkers 2014; 19: 509-16.
[17] Li SX, Dai QS, Chen SX, Zhang SD, Liao XY, Deng X, Chi HB, Li FJ, Zhu JH, Jiang YY. Xeroderma pigmentosum complementation group D (XPD) gene polymorphisms contribute to bladder cancer risk: a meta-analysis. Tumour Biol 2014; 35: 3905-15.
[18] Chang CH, Wang RF, Tsai RY, Wu HC, Wang CH, Tsai CW, Chang CL, Tsou YA, Liu CS, Bau DT. Significant association of XPD codon 312 single nucleotide polymorphism with bladder cancer susceptibility in Taiwan. Anticancer Res 2009; 29: 3903-7.
[19] Li C, Jiang Z, Liu X. XPD Lys (751) Gln and Asp (312) Asn polymorphisms and bladder cancer risk: a meta-analysis. Mol Biol Rep 2010; 37: 301-9.
[20] Neumann AS, Sturgis EM, Wei Q. Nucleotide excision repair as a marker for susceptibility to tobacco-related cancers: a review of molecular epidemiological studies. Mol Carcinogenesis 2005; 42: 65-92.
[21] Wu Q, Christensen LA, Legerski RJ, Vasquez KM. Mismatch repair participates in error-free processing of DNA interstrand crosslinks in human cells. EMBO Rep 2005; 6: 551-7.
[22] Volker M, Mone MJ, Karmakar P, van Hoffen A, Schul W, Vermeulen W, Hoeijmakers JH, van Driel R, van Zeeland AA, Mullenders LH. Sequential assembly of the nucleotide excision repair factors in vivo. Mol Cell 2001; 8: 213-24.
[23] Sijbers AM, de Laat WL, Ariza RR, Biggerstaff M, Wei YF, Moggs JG, Carter KC, Shell BK, Evans E, de Jong MC, Rademakers S, de Rooij J, Jaspers NG, Hoeijmakers JH, Wood RD. Xeroderma pigmentosum group F caused by a defect in a structure-specific DNA repair endonuclease. Cell 1996; 86: 811-22.
[24] Melton DW, Ketchen AM, Nunez F, Bonatti-Abbondandolo S, Abbondandolo A, Squires S, Johnson RT. Cells from ERCC1-deficient mice show increased genome instability and a reduced frequency of S-phase-dependent illegitimate chromosome exchange but a normal frequency of homologous recombination. J Cell Sci 1998; 111: 395-404.
[25] Sung P, Bailly V, Weber C, Thompson LH, Prakash L, Prakash S. Human xeroderma pigmentosum group D gene encodes a DNA helicase. Nature 1993; 365: 852-5.
[26] de Boer J, Hoeijmakers JH. Nucleotide excision repair and human syndromes. Carcinogenesis 2000; 21: 453-60.
[27] Hou R, Liu Y, Feng Y, Sun L, Shu Z, Zhao J, Yang S. Association of single nucleotide polymorphisms of ERCC1 and XPF with colorectal cancer risk and interaction with tobacco use. Gene 2014; 548: 1-5.
[28] Zhou W, Liu G, Park S, Wang Z, Wain JC, Lynch TJ, Su L, Christiani DC. Gene-smoking interaction associations for the ERCC1 polymorphisms in the risk of lung cancer. Cancer Epidemiol Biomarkers Prev 2005; 14: 491-6.
[29] Zhang N, Lin LY, Zhu LL, Wu F, Wen H, Pan D, Huang YC, Chen DQ. ERCC1 polymorphisms and risk of adult glioma in a Chinese population: a hospital-based case-control study. Cancer Invest 2012; 30: 199-202.
[30] Pei XH, Yang Z, Lv XQ, Li HX. Genetic variation in ERCC1 and XPF genes and breast cancer risk. Genet Mol Res 2014; 13: 2259-67.
[31] Hou R, Liu Y, Feng Y, Sun L, Shu Z, Zhao J, Yang S. Association of single nucleotide polymorphisms of ERCC1 and XPF with colorectal cancer risk and interaction with tobacco use. Gene 2014; 548: 1-5.
[32] Wu HY, Ding LY. Comprehensive assessment of the association between XPD rs13181 polymorphism and lung cancer risk. Tumour Biol 2014; 35: 8125-32.
[33] Xu Z, Ma W, Gao L, Xing B. Association between ERCC1 C8092A and ERCC2 K751Q polymorphisms and risk of adult glioma: a meta-analysis. Tumour Biol 2014; 35: 3211-21.
[34] Matullo G, Guarrera S, Sacerdote C, Polidoro S, Davico L, Gamberini S, Karagas M, Casetta G, Rolle L, Piazza A, Vineis P. Polymorphisms/haplotypes in DNA repair genes and smoking: a bladder cancer case-control study. Cancer Epidemiol Biomarkers Prev 2005; 14: 2569-78.