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XRCC2 Polymorphisms and Environmental Factors Predict High Risk of Colorectal Cancer

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Background: This case-control study aimed to analyze the association of *XRCC2* polymorphisms (rs3218408 and rs3218384) with colorectal cancer (CRC) risk. The interaction of *XRCC2* polymorphisms with environmental factors was investigated as well.

Material/Methods: We enrolled 147 CRC patients and 114 healthy individuals into the study. Polymerase chain reaction (PCR)-sequencing method was performed to detect rs3218408 and rs3218384 polymorphisms. Hardy-Weinberg equilibrium (HWE) was checked in the control group. Odds ratio (OR) with 95% confidence interval (CI) represented the risk of CRC. Cross-table method was used in analyzing the interaction effects.

Results: Compared to the control group, the frequency of smokers was much higher in the case group ($P<0.001$). A similar result was observed in drinkers (55.8% *vs.* 40.4%, $P=0.013$). Dietary habits of all subjects were investigated as well, showing that CRC patients ate fewer vegetables than did healthy controls ($P<0.001$). In the analysis of polymorphisms, rs3218408 appeared to be an independent risk factor of CRC (GG: OR=2.048, 95%CI=1.032–4.061; G allele: OR=1.445, 95%CI=1.019–2.049). There were 68 (76.4%) C allele carriers (rs3218384) among smokers, which was higher than the number of G allele carriers ($P<0.001$). A similar outcome was observed for alcohol drinkers ($P=0.048$), which suggests a relationship of rs3218384 with smoking and drinking. Further analysis indicated that interaction of rs3218384 with smoking increased the risk of CRC (GG and smoking: OR=3.250, 95%CI=1.235–8.556; GC+CC and smoking: OR=2.167, 95%CI=1.175–3.996).

Conclusions: We found that rs3218408 was related with increased risk of CRC, and the interaction of rs3218384 with smoking increased the risk of CRC.

MeSH Keywords: Biodegradation, Environmental • Colorectal Neoplasms, Hereditary Nonpolyposis • Genes, vif

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Background

Colorectal cancer (CRC) is one of the most common cancers worldwide. Approximately 60% of the cases occur in developed countries. Incidence rates of CRC are higher in men than in women. The development of CRC results from environmental factors, such as lifestyle, diet, and environmental pollution [1–4], while inter-individual differences in susceptibility to CRC might be brought about by genetic alterations [5]. Polymorphisms in genes belonging to detoxification, metabolic, angiogenesis, and DNA repair pathways have been proved to be linked to CRC risk [6–10]. For instance, Wang et al. reported that SNPs of high-mobility group box-1 (*HMGB1*), an angiogenesis-related gene, showed a significant association with CRC incidence in the Chinese Han population [8]. Investigating gene polymorphisms may provide a novel approach for CRC risk evaluation.

X-ray repair cross-complementing (*XRCC*) 2 is a core component of DNA double-strand breaks (DSBs) repair by homologous recombination repair (HRR) [11–13]. Located on 7q36.1, *XRCC2* encodes a protein of Rad51 family that maintains chromosome stability. *XRCC2* occupies an important position in the HRR pathway of double-stranded DNA through repairing chromosomal deletions, fragmentation, and translocations [14–16]. To date, several *XRCC2* polymorphisms have been identified, such as rs3218536, rs3218499, rs3218408, rs3218384, rs2040639, rs3218550, and rs718282. These polymorphism *loci* were demonstrated to be correlated with cancer risk [17–19]. However, the results might vary due to differences in ethnicity, diet, environment, and lifestyle. Among these SNPs, rs3218408 and rs3218384 are 2 widely studied polymorphisms. The study carried out by Lin et al. reported that *XRCC2* rs3218408 SNP showed an obvious association with risk of breast cancer [20]. Butkiewicz et al. indicated that *XRCC2* rs3218384 polymorphism influences survival of male patients diagnosed with resected non-small cell lung cancer, and showed an interaction with smoking [21]. Based on these studies, we assumed that *XRCC2* rs3218408 and rs3218384 SNPs might be associated with susceptibility to CRC.

Previous studies have proved that the interaction of genetic polymorphisms with environmental factors may increase or inhibit the occurrence of CRC. Jing et al. concluded that *PTEN* rs11202607 polymorphism showed a strong interaction with tea drinking during the development of CRC [22]. *MUTYH*, *OGG1,* and *FEN1* genetic mutations were reported to modify the effect of smoking on colorectal adenoma. Meanwhile, *LIG3* polymorphism modified the effect of alcohol consumption [23]. Liu et al. conducted a 2-stage case-control study and found a strong relationship of *LEPR* polymorphism with CRC risk; the association was strengthened by family history of cancer and cigarette smoking [24].

To date, few studies have focused on the combined effects of *XRCC2* polymorphisms and smoking or alcohol drinking on CRC development. The present study selected *loci* of 2 polymorphisms of *XRCC2* according to previous outcomes and analyzed the effects of genetic polymorphisms on CRC occurrence. The interaction of *XRCC2* polymorphisms and smoking or alcohol drinking during the pathogenesis of CRC was researched.

Material and Methods

Study subjects

We recruited 147 CRC patients from the Oncology Department of Chinese PLA General Hospital from September 2014 to June 2016. The diagnosis of CRC was performed by 2 experienced physicians according to clinical diagnosis, MRI or CT, and histopathological examination. CRC cases caused by familial diseases were removed from the study. The patients included 78 males and 69 females. During the study period, 114 healthy controls were enrolled from the Physical Examination Department of the same hospital from which we recruited the CRC patients. The participants in the control group did not have any tumor history, family history of cancer, genetic diseases, colitis, or Crohn's disease. The controls were frequency-matched with CRC patients by age and sex. Clinical information on each subject was recorded for further analysis. Smoking history was defined as smoking at least 1 cigarette per day for more than 6 months. Drinking history was defined as drinking more than 100 g of alcohol per week for more than 6 months.

All the subjects signed the informed consent before the study, and the study was approved by the Ethics Institute of the hospital.

XRCC2 polymorphisms detection method

We obtained 2 ml of peripheral venous blood from each subject, then anticoagulated it by sodium citrate and stored it at –20°C for later use. Proteinase K-saturated sodium chloride method was used to extract DNA. Polymerase chain reaction (PCR)-sequencing was performed to analyze *XRCC2* polymorphisms (rs3218408 and rs3218384). The PCR reaction parameters were 94°C for 2 min, 35 cycles of 94°C for 15 s, 55°C for 15 s, 72°Cfor 25 s, and then 72°C for 3 min. The 15-μl PCR mixture was composed of 1 μl DNA sample, 10×buffer 1.5 μl, $Mgcl_2$ (25 mM) 1.5 μl, dNTP (10 mM) 0.3 μl, each primer (10 pmol/μl) 0.25 μl, Taq polymerase (5 U/μl) 0.25 μl, and ddH_2O 9.95 μl. The primer sequence is listed in Table 1. PCR products were sequenced by Tiangen Biotech (Beijing) CO., LTD.

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Table 1. Primers sequence.

SNPs	Forward primer (5'-3')	Reverse primer (5'-3')
rs3218408	CTGGGTGACAGAGTGAGACTT	AGAAGAATGGGGAGTGTAAAG
rs3218384	GTGCGCACGCGCGCGGGTGGAC	GCGCCGCCCCAAGCCTCCCAATC

Table 2. Characteristics of subjects.

Characteristics	Case (n=147, %)	Control (n=114, %)	*P* value
Sex			0.774
Male	80 (54.4)	60 (52.6)	
Female	67 (45.6)	54 (47.4)	
Age	657.18±9.26	58.86±9.68	0.165
Education level			0.966
None/elementary	41 (27.9)	31 (27.2)	
Middle or high	58 (39.4)	44 (38.6)	
College or high	48 (32.7)	39 (34.2)	
Smoking			<0.001
Yes	89 (60.5)	41 (36.0)	
No	58 (39.5)	73 (64.0)	
Drinking			0.013
Yes	82 (55.8)	46 (40.4)	
No	65 (44.2)	68 (59.6)	
Vegetable consumption (times/week)			<0.001
<3	65 (44.2)	22 (19.3)	
4–6	43 (29.3)	58 (50.9)	
>6	39 (26.5)	34 (29.8)	

Statistical analysis

All analyses were conducted using SPSS 18.0 software. The differences in basic characteristics between the case and control groups were compared using the χ^2 test. Hardy-Weinberg equilibrium (HWE) was confirmed in the control group with χ^2 method. Interaction of *XRCC2* polymorphisms with smoking and drinking was investigated as well. Odds ratio (OR) and 95% confidence interval (CI) represented the risk of CRC. *P* values less than 0.05 indicated significant differences.

Results

Basic characteristics

As shown in Table 2, the average age of the case group was 57.18 years and 58.86 years in the control group. There was no obvious difference in average age between the 2 groups (*P*=0.165). Education level of each subject was determined by interview and this was found not to be a risk factor for CRC (*P*=0.966). The frequency of smokers was 60.5% in the case group, which was higher than that of the control group (*P*<0.001). Moreover, drinkers formed a relatively greater proportion of CRC patients (55.8%) compared to that of controls (40.4%). Diet was investigated as well, and we found that the case group had more individuals eating vegetables less than 3 times a week compared to the control group (44.2% *vs.* 19.3%).

XRCC2 polymorphisms predicted high risk of CRC

In the subsequent analysis, the relationship of *XRCC2* polymorphisms with CRC risk was evaluated (Table 3). Rs3218408 GG genotype was proved to be a risk factor for CRC (OR=2.048, 95%CI=1.032-4.061). G allele carriers tended to develop CRC (OR=1.445, 95%CI=1.019-2.049) more than T allele carriers

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Table 3. *XRCC2* polymorphisms and CRC risk.

SNPs	Case (n, %)		Control (n, %)		OR (95%CI)	
rs3218408						
TT	42	(28.6)	40	(35.1)	Reference	
TG	62	(42.2)	54	(47.4)	1.093	(0.621–1.926)
GG	43	(29.2)	20	(17.5)	2.048	(1.032–4.061)
Allele						
T	146	(49.7)	134	(58.8)	Reference	
G	148	(50.3)	94	(41.2)	1.445	(1.019–2.049)
rs3218384						
GG	57	(38.8)	46	(40.4)	Reference	
GC	66	(44.9)	50	(43.8)	1.065	(0.624–1.818)
CC	24	(16.3)	18	(15.8)	1.076	(0.522–2.220)
Allele						
G	180	(61.2)	142	(62.3)	Reference	
C	114	(38.8)	86	(37.7)	1.046	(0.732–1.493)

Table 4. *XRCC2* polymorphisms and patients' characteristics.

Characteristics	rs3218408			rs3218384		
	TT	TG+GG	*P* value	GG	GC+CC	*P* value
Sex			0.253			0.305
Male	25	55		28	52	
Female	27	40		29	38	
Age						
Education level			0.786			0.266
None/elementary	12	29		20	21	
Middle or high	18	40		19	39	
College or high	12	36		18	30	
Smoking			0.200			<0.001
Yes	22	67		21	68	
No	20	38		36	22	
Drinking			0.563			0.048
Yes	25	57		26	56	
No	17	48		31	34	
Vegetable consumption (times/week)			0.187			0.356
<3	16	49		22	43	
4–6	14	25		17	26	
>6	12	23		18	21	

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Table 5. Interaction of *XRCC2* polymorphisms with smoking and drinking.

Characteristics	SNPs	Case (n, %)	Control (n, %)	OR	95%CI
Smoking	rs3218384				
No	GG	36 (24.5)	39 (34.2)	Reference	–
	GC+CC	22 (15.0)	34 (29.8)	0.701	0.347–1.414
Yes	GG	21 (14.3)	7 (6.1)	3.250	1.235–8.556
	GC+CC	68 (46.2)	34 (29.8)	2.167	1.175–3.996
Drinking	rs3218384				
No	GG	31 (21.1)	30 (26.3)	Reference	–
	GC+CC	34 (23.1)	38 (33.3)	0.866	0.437–1.714
Yes	GG	26 (17.7)	16 (14.0)	1.573	0.707–3.499
	GC+CC	56 (38.1)	30 (26.3)	1.806	0.925–3.529

did. No remarkable relationship of rs3218384 polymorphism with CRC risk was found in the analysis.

We also analyzed the distribution of *XRCC2* polymorphisms in CRC patients (Table 4). There were 68 (76.4%) C allele carriers (rs3218384) among smokers, was which was significantly higher than the number of G allele carriers ($P<0.001$), and a similar outcome was observed in drinkers ($P=0.048$). All these results indicate associations between rs3218384 polymorphism and smoking and drinking.

Interaction of *XRCC2* polymorphisms with smoking and drinking

Cross-table method was used to check the interaction of *XRCC2* polymorphisms with smoking and drinking (Table 5). There existed a strong association between rs3218384 and smoking, and the interaction enhanced the risk of CRC. No matter what the genotype (rs3218384) was, the smokers showed higher risk of CRC (GG and smoking: OR=3.250, 95%CI=1.235-8.556; GC+CC and smoking: OR=2.167, 95%CI=1.175-3.996). There was no association of rs3218384 with drinking.

Discussion

The DNA repair system ensures the integrity and precision of DNA structure by repairing DNA damage. There are 5 types of repair patterns for DNA damage: mismatch repair (MMR), base excision repair (BER), nucleotide excision repair (NER), damage reverse repair (DRR), and HRR and non-homologous end-joining (NHEJ). HRR is an important pathway for repairing DSBs [25], which might be caused by endogenous or exogenous factors. Any defects in genes of the HRR pathway can block the repair of broken double strands of DNA, thus increasing the occurrence of cancers [26].

XRCC2 is a crucial regulator in the HRR repair of DSBs and shows a pivotal function in tumor progression [13,20]. The occurrence of DSBs activates *ATM* and MRN complex (*RAD50*, *NBS1*, and *MRE11A*) that can initiate the DNA repair process [27]; thus, the response pathway is triggered. Then, *CHEK2* and the breast cancer proteins BRCA1 and BRCA2 are phosphorylated, and, simultaneously, *P53* is activated [28]. Subsequently, the repair of DSBs is performed by HRR or NHEJ pathway. In the HRR pathway, XRCC2 and XRCC3 are crucial for correct chromosome segregation and apoptosis response to DSBs [29]. Perfect repair of DSBs during the DNA replication course contributes to genomic stability. Failure to repair DSBs results in tumor predisposition and carcinogenesis [27,30]. Xu et al. reported that *XRCC2* overexpression inhibits CRC cell apoptosis and promotes cell proliferation [31]. *MiR-7* exhibited inhibitory and promoting effects on CRC cell proliferation and apoptosis, respectively, and the function of which may be due to targeting *XRCC2* [32]. All these reports suggest that *XRCC2* is an important element in the pathogenesis of CRC.

In the subsequent research, *XRCC2* polymorphisms have attracted much attention, and were demonstrated to be related to development of cancers. *XRCC2*-41657C/T polymorphism was identified as a risk factor of CRC in a study by Li [19]. In another study, Krupa suggested that *XRCC2* Arg188His polymorphism increased CRC risk [33]. In the present study, we investigated the effects of *XRCC2* rs3218408 and rs3218384 on risk of CRC. *XRCC2* rs3218408 polymorphism was confirmed as a risk factor of CRC in the present study, supporting by a breast cancer study [27]. Although no relation of rs3218384 with CRC risk was found, its interaction with smoking enhanced the risk of CRC.

Our study is the first to report the interaction of *XRCC2* polymorphisms with environmental factors. However, there are still

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several limitations to the present study. First, the effects of gene-gene interaction on the development of CRC, which was also crucial for the occurrence of CRC, were not investigated in this research. Second, the sample size was relatively small, and only a single Chinese population was included. Third, the influence of *XRCC2* polymorphisms on clinical characteristics of CRC patients was not considered in this study. The genotype of *XRCC2* SNPs might be associated with tumor characteristics, such as tumor location and clinical stage. However, the associations need to be verified in further investigations. Additionally, the molecular mechanisms underlying the regulatory function of *XRCC2* polymorphisms in CRC were not investigated. Molecular pathological epidemiology (MPE) is a relatively new epidemiological area focused at the molecular level. Investigating the known or suspected genetic factors in tumorigenesis may provide new insights into the etiology of cancer [34]. Further well-designed studies will be needed to address the related issues.

Conclusions

XRCC2 rs3218408 polymorphism is an independent risk factor for CRC. rs3218384 is strongly associated with smoking in the pathogenesis of CRC.

References:

1. Doll R, Peto R: The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst, 1981. 66(6): 1191–308
2. Song YK, Park YS, Seon CS et al: Alcohol drinking increased the risk of advanced colorectal adenomas. Intest Res, 2015; 13(1): 74–79
3. Mahfouz EM, Sadek RR, Abdel-Latief WM et al: The role of dietary and lifestyle factors in the development of colorectal cancer: Case control study in Minia, Egypt. Cent Eur J Public Health, 2014l 22(4): 215–22
4. El-Tawil AM: Colorectal cancer and pollution. World J Gastroenterol, 2010; 16(28): 3475–77
5. de Jong MM, Nolte IM, te Meerman GJ et al: Low-penetrance genes and their involvement in colorectal cancer susceptibility. Cancer Epidemiol Biomarkers Prev, 2002; 11(11): 1332–52
6. Zhunussova G, Zhunusbekova B, Djansugurova L: Association between glutathione S-transferase M1 and T1 polymorphisms and colorectal cancer risk in patients from Kazakhstan. Clin Lab, 2015; 61(1–2): 161–68
7. Kim JW, Jeon YJ, Jang MJ et al: Association between folate metabolism-related polymorphisms and colorectal cancer risk. Mol Clin Oncol, 2015; 3(3): 639–48
8. Wang JX, Yu HL, Bei SS et al: Association of *HMGB1* gene polymorphisms with risk of colorectal cancer in a Chinese population. Med Sci Monit, 2016; 22: 3419–25
9. Dong Y, Liu JW, Gao YJ et al: Relationship between DNA repair gene *XPD751* single-nucleotide polymorphisms and prognosis of colorectal cancer. Genet Mol Res, 2015; 14(2): 5390–98
10. Cetinkunar S, Gok I, Celep RB et al: The effect of polymorphism in DNA repair genes RAD51 and *XRCC2* in colorectal cancer in Turkish population. Int J Clin Exp Med, 2015; 8(2): 2649–55
11. Griffin CS, Simpson PJ, Wilson CR, Thacker J: Mammalian recombination-repair genes *XRCC2* and *XRCC3* promote correct chromosome segregation. Nat Cell Biol, 2000; 2(10): 757–61
12. Mohindra A, Hays LE, Phillips EN et al: Defects in homologous recombination repair in mismatch-repair-deficient tumour cell lines. Hum Mol Genet, 2002; 11(18): 2189–200
13. Thacker J, Zdzienicka MZ: The *XRCC* genes: Expanding roles in DNA double-strand break repair. DNA Repair (Amst), 2004; 3(8–9): 1081–90
14. Jones NJ1, Zhao Y, Siciliano MJ, Thompson LH: Assignment of the *XRCC2* human DNA repair gene to chromosome 7q36 by complementation analysis. Genomics, 1995; 26(3): 619–22
15. Thacker J, Tambini CE, Simpson PJ et al: Localization to chromosome 7q36.1 of the human *XRCC2* gene, determining sensitivity to DNA-damaging agents. Hum Mol Genet, 1995; 4(1): 113–20
16. Liu N, Lamerdin JE, Tebbs RS et al: *XRCC2* and *XRCC3*, new human Rad51-family members, promote chromosome stability and protect against DNA cross-links and other damages. Mol Cell, 1998; 1(6): 783–93
17. Curtin K, Lin WY, George R et al: Genetic variants in *XRCC2*: New insights into colorectal cancer tumorigenesis. Cancer Epidemiol Biomarkers Prev, 2009; 18(9): 2476–84
18. Cao J, Luo C, Peng R et al: MiRNA-binding site functional polymorphisms in DNA repair genes *RAD51*, *RAD52*, and *XRCC2* and breast cancer risk in Chinese population. Tumour Biol, 2016 [Epub ahead of print]
19. Li XB, Luo H, Huang J et al: XRCC2 gene polymorphisms and its protein are associated with colorectal cancer susceptibility in Chinese Han population. Med Oncol, 2014. 31(11): 245
20. Lin WY, Camp NJ, Cannon-Albright LA et al: A role for *XRCC2* gene polymorphisms in breast cancer risk and survival. J Med Genet, 2011; 48(7): 477–84
21. Butkiewicz D, Rusin M, Sikora B et al: An association between DNA repair gene polymorphisms and survival in patients with resected non-small cell lung cancer. Mol Biol Rep, 2011; 38(8): 5231–41
22. Jing F, Mao Y, Zhang Z et al: The association of phosphatase and tensin homolog deleted on chromosome 10 polymorphisms and lifestyle habits with colorectal cancer risk in a Chinese population. Tumour Biol, 2014. 35(9): 9233–40
23. Corral R, Lewinger JP, Joshi AD et al: Genetic variation in the base excision repair pathway, environmental risk factors, and colorectal adenoma risk. PLoS One, 2013; 8(8): e71211
24. Liu L, Zhong R, Wei S et al: The leptin gene family and colorectal cancer: Interaction with smoking behavior and family history of cancer. PLoS One, 2013; 8(4): e60777
25. Moynahan ME, Jasin M: Mitotic homologous recombination maintains genomic stability and suppresses tumorigenesis. Nat Rev Mol Cell Biol, 2010; 11(3): 196–207
26. Fayaz S, Fard-Esfahani P, Fard-Esfahani A et al: Assessment of genetic mutations in the *XRCC2* coding region by high resolution melting curve analysis and the risk of differentiated thyroid carcinoma in Iran. Genet Mol Biol, 2012; 35(1): 32–37
27. Phillips ER, McKinnon PJ: DNA double-strand break repair and development. Oncogene, 2007; 26(56): 7799–808
28. Bakkenist CJ, Kastan MB: DNA damage activates ATM through intermolecular autophosphorylation and dimer dissociation. Nature, 2003; 421(6922): 499–506
29. Hinz JM, Helleday T, Meuth M: Reduced apoptotic response to camptothecin in CHO cells deficient in *XRCC3*. Carcinogenesis, 2003; 24(2): 249–53
30. Rodrigue A, Lafrance M, Gauthier MC et al: Interplay between human DNA repair proteins at a unique double-strand break *in vivo*. EMBO J, 2006; 25(1): 222–31
31. Xu K, Song X, Chen Z et al: *XRCC2* promotes colorectal cancer cell growth, regulates cell cycle progression, and apoptosis. Medicine (Baltimore), 2014; 93(28): e294
32. Xu K, Chen Z, Qin C, Song X: miR-7 inhibits colorectal cancer cell proliferation and induces apoptosis by targeting *XRCC2*. Onco Targets Ther, 2014; 7: 325–32
33. Krupa R, Sliwinski T, Wisniewska-Jarosinska M et al: Polymorphisms in *RAD51*, *XRCC2* and *XRCC3* genes of the homologous recombination repair in colorectal cancer – a case control study. Mol Biol Rep, 2011; 38(4): 2849–54
34. Ogino S, Chan AT, Fuchs CS, Giovannucci E: Molecular pathological epidemiology of colorectal neoplasia: An emerging transdisciplinary and interdisciplinary field. Gut, 2011; 60(3): 397–411

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