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Original Article

ERCC2 Lys751Gln genetic variation is associated with the susceptibility to gastric cancer in a Chinese population

Xiangji Lu[1,2], Xiaohong Wang[2], Lijun Liu[3], Jinlong Yu[1], Qiang Li[1], Yanwei Gao[4], Kai Wu[2], Zonghai Huang[1]

[1]Department of General Surgery, Zhujiang Hospital of Southern Medical University, Guangzhou, China; [2]The First Surgical Department, The Armed Police General Hospital of Inner Mongolia, Hohhot, China; [3]Department of Radiology, The First Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China; [4]The Second Department of Oncology, Inner Mongolia People's Hospital, Hohhot, China

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Abstract: We conducted a case-control study to investigate the role of *ERCC2* Lys751Gln and *ERCC2* Asp312Asn polymorphisms in the development of gastric cancer in a Chinese population. A total of 240 patients with pathologically proven gastric cancer and 240 control subjects were recruited between January 2013 and December 2014. Genotyping of *ERCC2* Lys751Gln and *ERCC2* Asp312Asn was carried out by the method of polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). All the statistical analyses were done by using SPSS version 17.0 (SPSS Inc. Chicago, USA). By chi-square test, we found significant differences in the genotype distributions of *ERCC2* Lys751Gln between gastric cancer patients and control subjects (χ^2=4.52, *P* value =0.03). By multivariate logistic regression analysis, we observed that individuals carried the GG genotype of *ERCC2* Lys751Gln were correlated with an increased risk of gastric cancer when compared with the TT genotype (OR=2.25, 95% CI=1.18-4.36). Individuals carried the G allele of *ERCC2* Lys751Gln was associated with a higher risk of gastric cancer compared to the T allele (OR=1.46, 95% CI=1.10-1.93). However, no significant association was observed between *ERCC2* Asp312Asn polymorphism and risk of developing gastric cancer. In conclusion, our study indicates that the *ERCC2* Lys751Gln polymorphism is associated with an increased risk of gastric cancer in the Chinese population, which suggests that this gene variation could affect the etiology of this cancer.

Keywords: *ERCC2* Lys751Gln, *ERCC2* Asp312Asn, polymorphism, gastric cancer, Chinese population

Introduction

Gastric cancer is a highly lethal cancer, with increasing incidence worldwide [1]. Poor understanding on molecular mechanisms underlying tumorigenesis of gastric cancer leads to lack of effective treatment [2]. Intensive studies focus on identification of gastric cancer related genes [3-5]. Many transcription factors, such as caudal-related homeobox family genes, have been demonstrated to participate in gastric cancer tumorigenesis and progression [6-8]. However, molecular pathogenesis of gastric cancer is not fully understood. Thus, it is necessary to identify novel molecular targets involved in gastric cancer tumorigenesis.

The excision repair cross-complementing rodent repair deficiency group 2 (*ERCC2*) gene is located on chromosome 19q13.2-13.3, and contains 23 exons and spans approximately 54,300 bp [9]. *ERCC2* encodes an evolutionarily conserved helicase, a subunit of the core transcription factor IIH (TFIIH) that is involved in normal transcription and in nucleotide excision repair of DNA by opening the DNA helix around damage [9]. Polymorphisms of *ERCC2* gene are involved in regulating the gene expression, and they could contribute to the differences between individuals in the susceptibility to, and severity of, a disease. *ERCC2* rs13181 (Lys751Gln) polymorphism is a T to G substitution at the 751 locus, and *ERCC2* rs1799793 (Asp312Asn) polymorphism is a G to A substitution at the 312 locus, and the two gene polymorphism could influence the activity and expression of the encoded protein. Previous studies have reported that *ERCC2* rs13181 and *ERCC2* rs1799793 polymorphisms are involved

Table 1. The primers and restriction enzymes of *ERCC2* Lys751Gln and Asp312Asn

ERCC2	SNP	Primers (5'-3')	PCR product size	Restriction enzyme
Lys751Gln	rs13181	GTCACCTGACTTCATAAGACC TCTCCCTTTCCTCTGTTCTCTG	348 bp	*Pst*I
Asp312Asn	rs1799793	AGGATCAAAGAGACAGACGAG TCTGCGAGGAGACGCTATCAG	211 bp	*Sty*I

in the susceptibility to several kinds of cancers, such as lung cancer, gastric cancer and prostate cancer [10-14]. A number of epidemiologic studies have been conducted to investigate whether there is an association between the *ERCC2* Lys751Gln and Asp312Asn polymorphisms and gastric cancer risk in the past decade [12-16]. However, the results of these studies are conflicting, possibly because of the relatively small size of published studies or there being only a small effect of the polymorphism on gastric cancer risk. In our study, we conducted a case-control study to investigate the role of *ERCC2* Lys751Gln and *ERCC2* Asp312Asn polymorphisms in the development of gastric cancer in a Chinese population.

Subjects and methods

Patients

Patients with pathologically proven gastric cancer (n=240) were recruited from the department of the First Surgical Department, the Armed Police General Hospital of Inner Mongolia in the period between January 2013 and December 2014. All the gastric cancer patients received gastrointestinal endoscopy and were confirmed by pathological examination. The control group consisted of 240 subjects without malignant cancer, and all the control subjects were recruited from individuals for regular health check-up. None of the control subjects were presence of malignant tumor, and the control subjects were recruited simultaneously from similar geographic areas and matched with patients with respect to age and gender. Study subjects who had had a history of acute or chronic infection disease, cancers, or end-stage liver or kidney diseases were excluded from our hospital.

The main information of the gastric cancer patients were as follows: mean age was 64.30±10.64 years, and mean body mass index (BMI) was 25.45±2.24 kg/m^2. Males accounted for 67.50% of the patients, and 62.50% of the gastric cancer patients had infected with *Helicobacter pylori*. The main information of the control subjects were as follows: mean age was 63.76±10.25 years; BMI was 23.67±2.60 kg/m^2. Males represented 67.50% of the patients, and 37.08% of the gastric cancer patients had infected with *Helicobacter pylori*.

Cases and controls were interviewed using a standardized questionnaire including sociodemographic characteristics, such as age, gender, BMI, tobacco smoking and alcohol consumption. The clinical data were collected from medical records, such as *Helicobacter pylori*, Lauren's classification, and TNM stage. The *Helicobacter pylori* infection was tested using serology. All individuals voluntarily participated in the study and gave their informed consent prior to participating into our study. The project was approved by the Ethics Committee of the Armed Police General Hospital of Inner Mongolia.

DNA extraction and genotyping

Five ml peripheral blood was collected from patients with gastric cancer and control subjects after recruiting into this study. The collected blood samples were kept in a refrigerator at -20°C until using. The DNA was isolated from peripheral blood sample using a Blood Mini Kit (TIANGEN Co. Limited, Beijing, China). Genotyping of *ERCC2* Lys751Gln and *ERCC2* Asp312Asn was carried out by the method of polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). All primers and PCR conditions used are described in **Table 1**. The *ERCC2* Lys751Gln and *ERCC2* Asp312Asn were amplified as follows: denaturation at 95°C for 10 min, and then 40 cycles of 95°C for 10 s, 60°C for 20 s, and 72°C for 10 s. The PCR fragments of the investigated polymorphisms were subsequently digested with their specific restriction enzyme. Digestion products were separated by electrophoresis on ethidium bromide stained agarose gel and visualized under UV light.

Table 2. The demographic and lifestyle information of study subjects

Variables	Patients N=240	%	Controls N=240	%	*t* test or χ^2-test	*P* value
Age, years	64.30±10.64		63.76±10.25		0.57	0.29
Gender						
Female	78	32.50	78	32.50		
Male	162	67.50	162	67.50	0.00	1.00
BMI, kg/m^2	25.45±2.24		23.67±2.60		8.04	<0.001
Alcohol consumption						
No	136	56.67	152	63.33		
Yes	104	43.33	88	36.67	2.22	0.14
Tobacco drinking						
No	149	62.08	157	65.42		
Yes	91	37.92	83	34.58	0.58	0.45
Helicobacter pylori						
Negative	90	37.50	151	62.92		
Positive	150	62.50	89	37.08	31.01	<0.001
TNM stage at diagnosis						
I-II	132	55.00				
III-IV	108	45.00				
Lauren classification						
Intestinal	105	43.75				
Diffuse	135	56.25				

Statistical analysis

The demographic and lifestyle data between gastric cancer patients and control subjects were compared using Chi-square (χ^2) test or independent sample t-test. Whether the genotype frequencies of *ERCC2* Lys751Gln and Asp312Asn confirm with the Hardy-Weinberg equilibrium (HWE) was assessed using a χ^2-test with one degree of freedom. The genotype frequencies of *ERCC2* Lys751Gln and Asp312Asn between gastric cancer patients and control subjects were compared using χ^2-test. The multiple logistic regression analysis was performed to assess the association between *ERCC2* Lys751Gln and Asp312Asn polymorphisms and gastric cancer risk. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated after adjustment for potential confounding factors. All the statistical analyses were done by using SPSS version 17.0 (SPSS Inc. Chicago, USA). A *P*-value <0.05 at 95% confidence interval (CI) was taken as statistically significant.

Results

The demographic and lifestyle information of the included gastric cancer patients and control subjects were shown in **Table 2**. By Chi-square test, the gastric cancer patients and control subjects were comparable with respect to age (t=0.57, P=0.29), gender (χ^2=0.00, P=1.00), alcohol consumption (χ^2=2.22, P=0.14) and tobacco drinking (χ^2=0.58, P=0.45). However, no significant difference was found between gastric cancer patients and controls in terms of BMI (t=8.04, P<0.001) and Helicobacter pylori (χ^2=31.01, P<0.001).

In gastric cancer patients, 97 (40.42%), 107 (44.58%) and 36 (15.00%) cases carried TT, TG and GG genotypes, respectively; 128 (53.33%), 92 (38.33%) and 19 (7.92%) cases carried GG, GA and AA genotypes, respectively. In control subjects, 121 (50.42%), 99 (41.25%) and 20 (8.33%) cases carried the TT, TG and GG genotypes, respectively; 136 (56.67%), 88 (36.67%) and 16 (6.67%) carried the GG, GA and AA genotypes, respectively. By chi-square test, we found significant differences in the genotype distributions of *ERCC2* Lys751Gln between gastric cancer patients and control subjects (χ^2=4.52, *P* value =0.03), but no significant difference was observed in the genetic distributions of *ERCC2* Asp312As (**Table 3**). The genotype frequencies of *ERCC2* Lys751Gln and Asp312Asn did not deviated with Hardy-Weinberg Equilibrium in patients and controls (P>0.05).

By multivariate logistic regression analysis, we observed that individuals carried the GG genotype of *ERCC2* Lys751Gln were correlated with an increased risk of gastric cancer when compared with the TT genotype (OR=2.25, 95% CI=1.18-4.36) (**Table 4**). Individuals carried the G allele of *ERCC2* Lys751Gln was associated with a higher risk of gastric cancer compared to the T allele (OR=1.46, 95% CI=1.10-1.93). However, no significant association was observed between *ERCC2* Asp312Asn poly-

Table 3. Genotype distribution of *ERCC2* Lys751Gln and Asp312Asn between gastric cancer patients and control subjects

ERCC	Patients N=240	%	Controls N=240	%	Chi-square test	*P* value	P for Hardy-Weinberg Equilibrium	
							In patients	In controls
Lys751Gln								
TT	97	40.42	121	50.42				
TG	107	44.58	99	41.25				
GG	36	15.00	20	8.33	7.52	0.02	0.47	0.97
Asp312Asn								
GG	128	53.33	136	56.67				
GA	92	38.33	88	36.66				
AA	19	7.92	16	6.67	0.59	0.75	0.67	0.73

Table 4. Association between *ERCC2* Lys751Gln and Asp312Asn polymorphisms and risk of developing gastric cancer

ERCC	Patients N=240	%	Controls N=240	%	OR (95% CI)[1]	*P* value
Lys751Gln						
TT	97	40.42	121	50.42	1.0 (Ref.)	-
TG	107	44.58	99	41.25	1.35 (0.90-2.01)	0.13
GG	36	15.00	20	8.33	2.25 (1.18-4.36)	0.01
Allele						
T	301	62.71	341	71.045	1.0 (Ref.)	-
G	179	74.58	139	28.955	1.46 (1.10-1.93)	0.01
Asp312Asn						
GG	128	53.33	136	56.67	1.0 (Ref.)	-
GA	92	38.33	88	36.67	1.11 (0.75-1.65)	0.59
AA	19	7.92	16	6.67		
Allele						
G	348	72.50	360	75.01	1.0 (Ref.)	-
A	130	27.09	120	25.01	1.12 (0.83-1.51)	0.44

[1]Adjusted for age, gender, BMI and *Helicobacter pylori* infection.

morphism and risk of developing gastric cancer.

We further analyzed the correlation between *ERCC2* Lys751Gln and Asp312Asn polymorphisms and risk of gastric cancer stratified by BMI, alcohol consumption, tobacco drinking, and *Helicobacter pylori* infection. However, we did not observed the *ERCC2* Lys751Gln and Asp312Asn polymorphisms had interaction with the BMI, alcohol consumption, tobacco drinking, and *Helicobacter pylori* infection (P>0.05).

Discussion

In the present study, we investigated the association between two common functional genetic variations in *ERCC2* (Lys751Gln and Asp312Asn) and the risk of gastric cancer in a Chinese population. We observed that GG genotype and G allele of *ERCC2* Lys751Gln were associated with an increased susceptibility to the risk of gastric cancer. However, *ERCC2* Asp312Asn did not observe any significant association with the development of gastric cancer in the Chinese population.

DNA damage caused by several exogenous or endogenous factors needs efficient DNA repair to restore genomic integrity, which is involves a number of DNA repair genes. Recently, many studies have indicated that single nucleotide polymorphisms (SNPs) in DNA repair genes might be associated with the development of gastric cancer, such as APE1, XRCC1, XRCC2 and XRCC3 [17-20]. Nucleotide excision repair is an important mechanism of the DNA repair pathway, maintaining genomic integrity by removing DNA interstrand crosslinks. ERCC2 gene products are important rate-limiting enzymes during the nucleotide excision repair process, which is involved in maintaining genomic integrity by removing DNA interstrand crosslinks [21, 22]. The ERCC2 protein possesses both single strand DNA-dependent ATPase and 5'-3' DNA helicase activities and participates in DNA unwinding during NER [23, 24]. Polymorphisms in the ERCC2 gene reduce-

helicase activity, lower DNA repair capacity, and increase cancer susceptibility [25, 26].

The *ERCC2* Lys751Gln polymorphism may cause a defect in nucleotide excision repair. The role of insufficient DNA repair in carcinogenesis has been extensively studied [27-34]. Guo et al. conducted a meta-analysis with 21 case-control studies and revealed that *ERCC2* Lys751Gln genetic polymorphisms contribute to the susceptibility to esophageal cancer [28]. Kabzinski et al. conducted a study in a Polish population, and found that *ERCC2* Lys751Gln and Asp312Asn polymorphisms may be associated with an increased risk of colorectal cancer [29]. Joo et al. reported that *ERCC2* Lys751Gln was associated with cervical cancer in the Korean population [30]. Michalska et al. reported that *ERCC2* Lys751Gln genetic polymorphism may be a risk factor for the development of ovarian carcinoma [31]. Zhao et al. conducted a case-controls study with 246 pancreatic cancer patients and 246 controls and indicted that *ERCC2* Lys751Gln polymorphisms contribute to the development of pancreatic cancer [33]. Sun and Zhang et al. conducted a meta-analysis with 5961 cases and 8669 subjects and reported that *ERCC2* Lys751Gln polymorphisms did not play a role in the pathogenesis of melanoma in Caucasian populations [32]. Akhmadishina et al. conducted a case-control study with 468 cancer patients and 351 healthy individuals, and reported that *ERCC2* Lys751Gln did not contribute to the pathogenesis mechanisms of bladder cancer [27]. Sun and Tan et al. reported that *ERCC2* Lys751Gln polymorphism could not influence the risk of larynx cancer in a Chinese population.

Several studies regarding the correlation between *ERCC2* Lys751Gln polymorphism and gastric cancer have revealed inconclusive results [13, 15, 16, 35]. Zhang et al. and Engin et al. conducted case-control studies in a Chinese population and a Turkish population, and they reported that *ERCC2* Lys751Gln did not contribute to the etiology of gastric cancer [13, 15]. However, Long et al. and Yin et al. indicated that *ERCC2* Lys751Gln polymorphism might be a biomarker of gastric cancer susceptibility in Chinese population [16, 35]. The discrepancies of these results might be caused by differences in ethnicities, selection of patients and controls and sample size.

In conclusion, our study indicates that the *ERCC2* Lys751Gln polymorphism is associated with an increased risk of gastric cancer in the Chinese population, which suggests that this gene variation could affect the etiology of this cancer. Further large sample size studies are required to confirm our findings.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Zonghai Huang, Department of General Surgery, Zhujiang Hospital of Southern Medical University, Guangzhou 510-280, China. Tel: +86-20-62782402; Fax: +86-20-6278242; E-mail: huangzonghh@sina.com

References

[1] Shah MA, Kelsen DP. Gastric cancer: A primer on the epidemiology and biology of the disease and an overview of the medical management of advanced disease. J Nat Compr Cancer Netw 2010; 8: 437-447.

[2] Compare D, Rocco A, Nardone G. Risk factors in gastric cancer. Eur Rev Med Pharmacol Sci 2010; 14: 302-308.

[3] Lynch HT, Grady W, Suriano G, Huntsman D. Gastric cancer: New genetic developments. J Surg Oncol 2005; 90: 114-133.

[4] Aung P, Oue N, Mitani Y, Nakayama H, Yoshida K, Noguchi T, Bosserhoff A, Yasui W. Systematic search for gastric cancer-specific genes based on sage data: Melanoma inhibitory activity and matrix metalloproteinase-10 are novel prognostic factors in patients with gastric cancer. Oncogene 2006; 25: 2546-2557.

[5] Sun W, Wu Y, Yu X, Liu Y, Song H, Xia T, Xiao B, Guo J. Decreased expression of long noncoding RNA ac096655. 1-002 in gastric cancer and its clinical significance. Tumor Biol 2013; 34: 2697-2701.

[6] Sakakura C, Hagiwara A, Miyagawa K, Nakashima S, Yoshikawa T, Kin S, Nakase Y, Ito K, Yamagishi H, Yazumi S. Frequent downregulation of the runt domain transcription factors runx1, runx3 and their cofactor cbfb in gastric cancer. Int J Cancer 2005; 113: 221-228.

[7] Li Q, Zhang N, Jia Z, Le X, Dai B, Wei D, Huang S, Tan D, Xie K. Critical role and regulation of transcription factor foxm1 in human gastric cancer angiogenesis and progression. Cancer Res 2009; 69: 3501-3509.

[8] Li T, Lu Y, Zhao X, Guo H, Liu C, Li H, Zhou L, Han Y, Wu K, Nie Y. Microrna-296-5p increases proliferation in gastric cancer through repres-

sion of caudal-related homeobox 1. Oncogene 2014; 33: 783-793.
[9] Coin F, Marinoni JC, Rodolfo C, Fribourg S, Pedrini AM, Egly JM. Mutations in the XPD helicase gene result in XP and TTD phenotypes, preventing interaction between XPD and the p44 subunit of TFIIH. Nat Genet 1998; 20: 184-188.
[10] Mirecka A, Paszkowska-Szczur K, Scott RJ, Górski B, van de Wetering T, Wokołorczyk D, Gromowski T, Serrano-Fernandez P, Cybulski C, Kashyap A, Gupta S, Gołąb A, Słojewski M, Sikorski A, Lubiński J, Dębniak T. Common variants of xeroderma pigmentosum genes and prostate cancer risk. Gene 2014; 546: 156-61.
[11] Lee MS, Liu CY, Su L, Christiani DC. Polymorphisms in ERCC1 and ERCC2/XPD genes and carcinogen DNA adducts in human lung. Lung Cancer 2015; 89: 8-12.
[12] Yuan T, Deng S, Chen M, Chen W, Lu W, Huang H, Xia J. Association of DNA repair gene XRCC1 and XPD polymorphisms with genetic susceptibility to gastric cancer in a Chinese population. Cancer Epidemiol 2011; 35: 170-4.
[13] Engin AB, Karahalil B, Engin A, Karakaya AE. DNA repair enzyme polymorphisms and oxidative stress in a Turkish population with gastric carcinoma. Mol Biol Rep 2011; 38: 5379-86.
[14] Chen Z, Zhang C, Xu C, Li K, Hou R, Li D, Cheng X. Effects of selected genetic polymorphisms in xeroderma pigmentosum complementary group D on gastric cancer. Mol Biol Rep 2011; 38: 1507-13.
[15] Zhang CZ, Chen ZP, Xu CQ, Ning T, Li DP, Hou RP. Correlation of XPD gene with susceptibility to gastric cancer. Ai Zheng 2009; 28: 1163-7.
[16] Long XD, Ma Y, Huang YZ, Yi Y, Liang QX, Ma AM, Zeng LP, Fu GH. Genetic polymorphisms in DNA repair genes XPC, XPD, and XRCC4, and susceptibility to Helicobacter pylori infection-related gastric antrum adenocarcinoma in Guangxi population, China. Mol Carcinog 2010; 49: 611-8.
[17] Gong H, Li H, Zou J, Mi J, Liu F, Wang D, Yan D, Wang B, Zhang S, Tian G. The relationship between five non-synonymous polymorphisms within three XRCC genes and gastric cancer risk in a Han Chinese population. Tumour Biol 2015; [Epub ahead of print].
[18] Li H, Zou J, Mi J, Wei X, Zhao D, Zhang S, Tian G. Association of APE1 gene Asp148Glu variant with digestive cancer: a meta-analysis. Med Sci Monit 2015; 21: 2456-66.
[19] Bashir H, Majid S, Hamid R, Farooq R, Wani HA, Shoib S, Bhat AA. Polymorphism of the XRCC3 gene and risk of gastric cancer in a Kashmiri population: a case-control study. Eur J Cancer Prev 2015; 24: 167-75.
[20] Gok I, Baday M, Cetinkunar S, Kilic K, Bilgin BC. Polymorphisms in DNA repair genes XRCC2 and XRCC3 risk of gastric cancer in Turkey. Bosn J Basic Med Sci 2014; 14: 214-8.
[21] Neumann AS, Sturgis EM and Wei Q. Nucleotide excision repair as a marker for susceptibility to tobacco-related cancers: a review of molecular epidemiological studies. Mol Carcinog 2005; 42: 65-92.
[22] Wu Q, Christensen LA, Legerski RJ and Vasquez KM. Mismatch repair participates in error-free processing of DNA interstrand crosslinks in human cells. EMBO Rep 2005; 6: 551-557.
[23] Sung P, Bailly V, Weber C, Thompson LH, Prakash L, Prakash S. Human xerodermapigmentosum group D gene encodes a DNA helicase. Nature 1993; 365: 852-855.
[24] de Boer J and Hoeijmakers JH. Nucleotide excision repair and human syndromes. Carcinogenesis 2000; 21: 453-460.
[25] Zhang J, Gu SY, Zhang P, Jia Z, Chang JH. ERCC2 Lys751Gln polymorphism is associated with lung cancer among Caucasians. Eur J Cancer 2010; 46: 2479-2484.
[26] Xue H, Lu Y, Lin B, Chen J, Tang F, Huang G. The effect of XPD/ERCC2 polymorphisms on gastric cancer risk among different ethnicities: a systematic review and meta-analysis. PLoS One 2012; 7: e43431.
[27] 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.
[28] Guo XF, Wang J, Lei XF, Zeng YP, Dong WG. XPD Lys751Gln polymorphisms and the risk of esophageal cancer: an updated meta-analysis. Intern Med 2015; 54: 251-9.
[29] Kabzinski J, Przybylowska K, Dziki L, Dziki A, Majsterek I. An association of selected ERCC2 and ERCC5 genes polymorphisms, the level of oxidative DNA damage and its repair efficiency with a risk of colorectal cancer in Polish population. Cancer Biomark 2015; 15: 413-23.
[30] Joo J, Yoon KA, Hayashi T, Kong SY, Shin HJ, Park B, Kim YM, Hwang SH, Kim J, Shin A, Kim JY. Nucleotide excision repair gene ERCC2 and 5 variants increase risk of uterine cervical cancer. Cancer Res Treat 2015; [Epub ahead of print].
[31] Michalska MM, Samulak D, Romanowicz H, Sobkowski M, Smolarz B. An association between single nucleotide polymorphisms of Lys751Gln ERCC2 gene and ovarian cancer in polish women. Adv Med 2015; 2015: 109593.

[32] Sun Y, Zhang H, Ying H, Jiang W, Chen Q. A meta-analysis of XPD/ERCC2 Lys751Gln polymorphism and melanoma susceptibility. Int J Clin Exp Med 2015; 8: 13874-8.
[33] Zhao F, Shang Y, Zeng C, Gao D, Li K. Association of single nucleotide polymorphisms of DNA repair genes in NER pathway and susceptibility to pancreatic cancer. Int J Clin Exp Pathol 2015; 8: 11579-86.
[34] Sun Y, Tan L, Li H, Qin X, Liu J. Association of NER pathway gene polymorphisms with susceptibility to laryngeal cancer in a Chinese population. Int J Clin Exp Pathol 2015; 8: 11615-21.
[35] Yin QH, Liu C, Hu JB, Meng RR, Li L, Wang YJ. XPD Lys751Gln and Asp312Asn polymorphisms and gastric cancer susceptibility: a meta-analysis of case-control studies. Asian Pac J Cancer Prev 2013; 14: 231-6.