Association between \textit{XPG} polymorphisms and stomach cancer susceptibility in a Chinese population

Yun-Zhi Chen \textsuperscript{a}, Fang Guo \textsuperscript{b}, Hong-Wei Sun \textsuperscript{a}, Hong-Ru Kong \textsuperscript{a}, Sheng-Jie Dai \textsuperscript{a}, Shi-Hao Huang \textsuperscript{a}, Wen-Wei Zhu \textsuperscript{c}, Wen-Jun Yang \textsuperscript{a}, Meng-Tao Zhou \textsuperscript{a}, \textsuperscript{*}

\textsuperscript{a} Department of General Surgery, First Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China
\textsuperscript{b} Department of Gynecology and Obstetrics, People’s Hospital, Wenzhou, Zhejiang, China
\textsuperscript{c} Department of General Surgery, Huashan Hospital, Fudan University Shanghai Cancer Center, Shanghai, China

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Abstract

Xeroderma pigmentosum group G (\textit{XPG}) protein plays an important role in the DNA repair process by cutting the damaged DNA at the 3’ terminus. Previous studies have indicated some polymorphisms in the \textit{XPG} gene are associated with stomach cancer susceptibility. We performed this hospital-based case–control study to evaluate the association of four potentially functional \textit{XPG} polymorphisms (rs2094258 C>T, rs751402 C>T, rs2296147 T>C and rs873601 G>A) with stomach cancer susceptibility. The four single nucleotide polymorphisms (SNPs) were genotyped in 692 stomach cancer cases and 771 healthy controls. Logistic regression analysis was conducted, and odds ratios (ORs) and 95% confidence intervals (CIs) were used to assess the association of interest. Of the studied SNPs, \textit{XPG} rs873601 G>A polymorphism was found to significantly associate with stomach cancer susceptibility (AA versus GG/AG: OR = 1.31, 95% CI = 1.03–1.66, \textit{P} = 0.027). Combined analysis of all SNPs revealed that the individuals with two of risk genotypes had a significantly increased stomach cancer risk (OR = 1.52, 95% CI = 1.13–2.06). In the stratification analysis, the association between the rs873601AA genotype and stomach cancer risk was observed in older group (>59 year), as well as patients with non-cardia stomach cancer. Further combined analysis indicated men, smokers, or non-drinkers more than one risk genotypes had a significantly increased stomach cancer risk. Our results indicate that \textit{XPG} rs873601 G>A polymorphism may be associated with the risk of stomach cancer. Further prospective studies with different ethnicities and large sample sizes are needed to validate our findings.

Keywords: stomach cancer \textbullet \textit{XPG} \textbullet polymorphism \textbullet genetic susceptibility

Introduction

Cancer poses an substantial burden on society worldwide, and the incidence rate of cancer remains rising due to the growth of ageing populations and increasing exposure to well-established risk factors, such as smoking, overweight, and physical inactivity. According to GLOBOCAN estimates, there were approximately 14.1 million new cases and 8.2 million new cancer-related deaths that occurred in 2012 worldwide [1]. Among them, about 951,600 new stomach cancer cases and 723,100 deaths occurred in 2012. Stomach cancer is the third most common cause of cancer-related death, just next to lung cancer and liver cancer that led to 1,589,900 and 745,500 death respectively. The highest risk area involves the Eastern Asia (including China), Central and Eastern Europe, and South America, while the Northern America and most parts of Africa are the lowest risk area [1]. The risk factors of stomach cancer include the consumption of salted and nitrated foods, cigarette smoking, low intake of fresh fruits and vegetables [2]. Overweight and obesity may be a risk factor for residents in Western countries [3], but not for Chinese subjects [4]. \textit{Helicobacter pylori} infection is an important and well-established aetiological factor for stomach cancer in all populations worldwide, and the infected individuals by \textit{H. pylori} show about 3- to 6-fold increased risk of developing stomach cancer [5]. However, even in the regions with a high prevalence of \textit{H. pylori} (e.g., South America, Asia, Africa and Eastern Europe), only a small proportion of individuals eventually develop stomach cancer. Taken together, it suggests that environmental factors are necessary, but not sufficient to cause cancer, and genetic susceptibility may play a critical role in the tumorigenesis of stomach cancer [6].

DNA repair genes play important roles in maintaining the stability and integrity of genome. More than 130 genes are involved in the different DNA repair pathways, including nucleotide excision repair.
Materials and methods

Study population

The current case–control study consisted of 692 stomach cancer cases and 774 healthy controls recruited from the First Affiliated Hospital of Wenzhou Medical University between January 2010 and September 2013. Details of the characteristics of the subjects in this case–control study were described previously [18]. All cases were histologically/pathologically confirmed by two experienced pathologists. All the 774 healthy controls were individuals receiving the health screening in the same hospital, and they were frequency-matched to the cases by gender and age distribution. All of the participants provided written informed consent. This study was approved by the Clinical Research Ethics Committee of Wenzhou Medical University.

DNA extraction and genotyping

Genomic DNA used for the assay was extracted from peripheral blood samples as described previously [16]. We chose the three potentially functional SNPs (rs2094258 C>T, rs2296147 T>C and rs873601G>A) following a previously published protocol [16]. We also chose the rs751402 C>T that is located in the 5’ UTR region which was reported in another study [15]. Taqman real time PCR method was performed to detect the genotypes of the four selected potentially functional SNPs by using a 7900 HT sequence detector system (Applied Biosystems, Foster City, CA, USA). PCR reactions were carried out in 384 wells with a total volume of 5 μl containing 10 ng of genomic DNA for each SNP. At least 10% of the samples were randomly selected and re-genotyped to ensure the accuracy of the analysis.

Statistical analysis

Chi-squared test were performed to examine the differences in the distribution of various characteristics and genotype frequencies between the stomach cancer cases and the healthy controls. Goodness-of-fit chi-squared test was performed to assess the Hardy-Weinberg equilibrium (HWE) for each SNP by comparing observed and expected genotype frequencies. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated to evaluate the strength of the association between these four SNPs and stomach cancer risk by logistic regression. We managed all the statistical analysis by using SAS software (version 9.1; SAS Institute, Cary, NC, USA). A two-sided P-value less than 0.05 was considered to be statistically significant.

Results

Population characteristics

All the stomach cancer cases and healthy controls were from Chinese Han descent. The characteristics of the study population are shown in Table S1. Three samples in controls failed in spite of repeated genotyping tests, thus a total of 692 stomach cancer patients and 771 healthy controls were included in the final analysis. The mean age (±SD) for case and control groups was 59.22 (±11.05) and 59.71 (±11.35) years respectively. Cases consisted of 492 men and 200 women, while healthy controls included 546 men and 225 women. No significant difference was observed in the age and gender distribution between two groups (P = 0.864 and P = 0.906 respectively). Compared to the healthy controls, the stomach cases were more likely to be non-smokers (P < 0.0001), non-drinkers (P = 0.0005) as well as nutrient deficient and with lower BMI (P < 0.0001).

Distributions of selected SNPs and risk of stomach cancer

The genotypes and allele frequencies of the four polymorphisms were shown in Table 1. The observed genotype frequency distributions of the four polymorphisms were in consistent with HWE for controls (P = 0.803 for rs2094258 C>T, P = 0.416 for rs751402 C>T, P = 0.535 for rs2296147 T>C and P = 0.415 for rs873601G>A). The significant differences in genotype frequency distribution were only observed for the rs873601G>A polymorphism between cases and controls. Compared with carriers of the rs873601GG/AG genotypes, carriers of the AA genotype had a significantly increased stomach cancer risk (OR = 1.31, 95% CI = 1.03–1.66, P = 0.027). We also found that the presence of two risk genotypes significantly conferred increased stomach cancer risk (OR = 1.52, 95% CI = 1.13–2.06, P = 0.006, and adjusted OR = 1.44, 95% CI = 1.03–2.01, P = 0.035). Moreover, the risk of developing stomach cancer was also significantly increased among those carrying one or more risk genotypes (OR = 1.32, 95% CI = 1.04–1.69, P = 0.025).
Table 1 Logistic regression analysis of associations between the genotypes of XPG and stomach cancer susceptibility in a Chinese population

| Genotype     | Cases (N = 692) | Controls (N = 771) | P* | Crude OR (95% CI) | P | Adjusted OR (95% CI)† | P† |
|--------------|-----------------|--------------------|----|-------------------|---|----------------------|----|
| rs2094258 C>T |                 |                    |    |                    |   |                      |    |
| CC           | 287 (41.47)     | 291 (37.74)        | 0.296† | 1.00              |   | 1.00                 |    |
| CT           | 304 (43.93)     | 368 (47.73)        | 0.84 (0.67–1.05) | 0.119  | 0.85 (0.68–1.06) | 0.150 |
| TT           | 101 (14.60)     | 112 (14.53)        | 0.91 (0.67–1.25) | 0.577  | 0.92 (0.67–1.26) | 0.601 |
| Additive     |                 |                    | 0.93 (0.80–1.08) | 0.313  | 0.93 (0.80–1.08) | 0.347 |
| Dominant     | 405 (58.53)     | 480 (62.26)        | 0.86 (0.69–1.06) | 0.145  | 0.86 (0.70–1.07) | 0.177 |
| Recessive    | 591 (85.40)     | 659 (85.47)        | 1.01 (0.75–1.35) | 0.970  | 1.00 (0.75–1.35) | 0.980 |
| rs751402 C>T |                 |                    |    |                    |   |                      |    |
| CC           | 286 (41.33)     | 351 (45.53)        | 0.227† | 1.00              |   | 1.00                 |    |
| CT           | 313 (45.23)     | 331 (42.93)        | 1.16 (0.93–1.45) | 0.184  | 1.17 (0.91–1.49) | 0.221 |
| TT           | 93 (13.44)      | 89 (11.54)         | 1.28 (0.92–1.78) | 0.140  | 1.11 (0.77–1.61) | 0.576 |
| Additive     |                 |                    | 1.14 (0.98–1.33) | 0.088  | 1.09 (0.92–1.29) | 0.335 |
| Dominant     | 406 (58.67)     | 420 (54.47)        | 1.19 (0.96–1.46) | 0.106  | 1.15 (0.92–1.45) | 0.226 |
| Recessive    | 599 (86.56)     | 682 (88.46)        | 1.19 (0.87–1.62) | 0.272  | 1.03 (0.73–1.46) | 0.872 |
| rs2296147 T>C |                 |                    |    |                    |   |                      |    |
| TT           | 442 (63.87)     | 475 (61.61)        | 0.464† | 1.00              |   | 1.00                 |    |
| CT           | 217 (31.36)     | 264 (34.24)        | 0.88 (0.71–1.10) | 0.273  | 0.93 (0.73–1.19) | 0.562 |
| CC           | 33 (4.77)       | 32 (4.15)          | 1.11 (0.67–1.83) | 0.688  | 1.38 (0.78–2.44) | 0.268 |
| Additive     |                 |                    | 0.95 (0.80–1.14) | 0.586  | 1.03 (0.84–1.25) | 0.809 |
| Dominant     | 250 (36.13)     | 296 (38.39)        | 0.91 (0.73–1.12) | 0.372  | 0.97 (0.77–1.23) | 0.823 |
| Recessive    | 659 (95.23)     | 739 (95.85)        | 1.16 (0.70–1.90) | 0.566  | 1.41 (0.81–2.48) | 0.227 |
| rs873601G>A  |                 |                    |    |                    |   |                      |    |
| GG           | 172 (24.86)     | 205 (26.59)        | 0.087† | 1.00              |   | 1.00                 |    |
| GA           | 333 (48.12)     | 396 (51.36)        | 1.00 (0.78–1.29) | 0.986  | 1.08 (0.81–1.42) | 0.604 |
| AA           | 187 (27.02)     | 170 (22.05)        | 1.31 (0.98–1.75) | 0.067  | 1.33 (0.96–1.84) | 0.086 |
| Additive     |                 |                    | 1.14 (0.99–1.32) | 0.071  | 1.15 (0.98–1.36) | 0.088 |
| Dominant     | 520 (75.14)     | 566 (73.41)        | 0.449† | 1.10 (0.87–1.39) | 0.450 | 1.15 (0.89–1.50) | 0.287 |
| Recessive    | 505 (72.98)     | 601 (77.95)        | 0.027† | 1.31 (1.03–1.66) | 0.027 | 1.27 (0.97–1.65) | 0.084 |
| Combined effect of risk genotypes |       |                   |   |                   |   |                     |    |
| 0            | 145 (20.95)     | 200 (25.94)        | 0.023† | 1.00              |   | 1.00                 |    |
| 1            | 367 (53.03)     | 408 (52.92)        | 1.24 (0.96–1.60) | 0.099  | 1.20 (0.90–1.60) | 0.211 |
| 2            | 180 (26.01)     | 163 (21.14)        | 1.52 (1.13–2.06) | 0.006  | 1.44 (1.03–2.01) | 0.035 |
Stratification analysis

We further explored the association between XPG polymorphisms and stomach cancer risk in stratification analysis by age, gender, smoking status, pack-year, drinking status, BMI and tumour sites (Table 2). First of all, we only found that the rs873601 AA genotype was shown to significantly increase stomach cancer risk among the older subjects (adjusted OR = 1.54, 95% CI = 1.05–2.25, \( P = 0.028 \)) and the non-cardia subjects (adjusted OR = 1.36, 95% CI = 1.01–1.82, \( P = 0.041 \)). We also observed a borderline significantly increased stomach cancer risk for the men (adjusted OR = 1.37, 95% CI = 1.00–1.89, \( P = 0.052 \)) and ever smokers (adjusted OR = 1.43, 95% CI = 0.95–2.15, \( P = 0.085 \)). We next combined the four SNPs, and found that the presence of one or two risk genotypes was significantly associated with increased stomach cancer risk among men (adjusted OR = 1.40, 95% CI = 1.01–1.93, \( P = 0.043 \)), ever smokers (adjusted OR = 1.83, 95% CI = 1.20–2.80, \( P = 0.005 \)), subjects with pack-years <27 (adjusted OR = 1.83, 95% CI = 1.02–3.23, \( P = 0.045 \)) and never drinkers (adjusted OR = 1.41, 95% CI = 1.02–1.94, \( P = 0.036 \)).

Discussion

In the current hospital-based case–control study, we assessed the association between four potentially functional SNPs in the XPG gene and the risk of stomach cancer in Chinese Han population. We found a significant association between XPG rs873601 G→A polymorphism and stomach cancer susceptibility, especially in older subjects and subjects with non-cardia stomach cancer. We also observed the individuals carrying one or two risk genotypes had a significantly increased stomach cancer risk, especially among ever smokers and men.

XPG gene, also known as ERCC5, is located at 13q33 and consists of 15 exons. There are at least 2430 reported SNPs in the gene region (http://www.ncbi.nlm.nih.gov/SNP). XPG is a structure-specific endonuclease. It participates in both the transcription-coupled repair [19] and the global genomic NER [20] steps, which are critical for correcting the excision repair deficiency. As reported, XPG may also play important roles in other cellular processes, such as RNA polymerase II transcription and transcription-coupled DNA repair [21]. Xeroderma pigmentosum group G can excise damaged oligonucleotide by cleaving the 3' damaged site during NER. The XPF/ERCC1 complex may participate in the 5' incision, and stabilize the binding of DNA repair complex to damaged DNA [22–24].

Polymorphism in the XPG gene may be associated with cancer susceptibility. In a recent study including a total of 279 colorectal cancer (CRC) patients and 884 controls, Du et al. [25] found a significant increased CRC risk for the carriers of XPG rs17655 CG/GG genotypes (OR = 1.39, 95% CI = 1.14–1.69). In the same study, a meta-analysis was also performed on the association of the SNP with CRC risk, with a total of 2649 CRC cases and 2848 controls included. The association between XPG rs17655 and CRC risk was replicated under the dominant model (CG versus CC: OR = 1.35, 95% CI = 1.20–1.51) in the pooled analysis. Thus far, several studies have been carried out to investigate the association between XPG polymorphisms and stomach cancer susceptibility. Hussain et al.[13] performed a population-based study with 196 stomach cancer cases and 397 controls. They found that the rs227869G→C polymorphism was associated with decreased stomach cancer susceptibility, while no association was found for the rs1047768 T→C polymorphism and stomach cancer susceptibility. He et al. [16] genotyped three potentially functional XPG SNPs (rs2094258 C→T, rs2296147 T→C and rs873601G→A) in 1125 stomach cancer cases and 1196 controls. They found carriers of the rs873601 A had a significantly increased stomach cancer risk. Consistently, they also demonstrated that the A allele was significantly associated with reduced mRNA expression level of XPG gene. Duan et al. [15] focused on SNPs in the promoter region of XPG gene and genotyped the rs751402 C→T and rs2296147 T→C polymorphisms in a total of 403 stomach cancer cases and 403 controls. Both of the two polymorphisms were shown to significantly increase stomach cancer risk. In another study with 337 stomach cancer cases and 347 controls, Yang et al. [17] found that the rs2296147 T→C polymorphism was associated with decreased stomach cancer risk, while the rs2094258 C→T polymorphism was associated with increased stomach cancer risk. However, no significant association was found for the rs873601G→A polymorphism. In this study with 692 stomach cancer cases and 771 controls, we found that only the XPG rs873601G→A polymorphism is associated with slightly increased

| Genotype | Cases (N = 692) | Controls (N = 771) | \( P^* \) | Crude OR (95% CI) | \( P^* \) | Adjusted OR (95% CI) | \( P^* \) |
|----------|----------------|-------------------|--------|-----------------|--------|--------------------|--------|
| 0        | 145 (20.95)    | 200 (25.94)       | 1.00   |                 |        | 1.00               |        |
| 1-2      | 547 (79.05)    | 571 (74.06)       | 0.025  | 1.32 (1.04–1.69) | 0.025  | 1.27 (0.97–1.66)   | 0.088  |

*Chi-squared test for genotype distributions between stomach cancer cases and controls.

1Adjusted for age, gender, BMI, smoking and drinking status.

Additive models.

Dominant models.

Recessive models.

OR, odds ratio; CI, confidence interval.

The results were in bold, if the 95% CI excluded 1 or \( P < 0.05 \).
stomach cancer risk. No association with stomach cancer risk was found for the remaining SNPs, which may be partially ascribed to the weak effect of each SNP. Besides, the sample size in this study was moderate and might not be large enough to detect relatively weak association. Moreover, the positive findings by others with smaller sample size may be due to a chance.

Despite the significant findings, several limitations should be addressed. First, the sample size is moderate, with only 692 cases and 771 controls included. The relative small sample size might not be able to reveal some weak gene-disease association and gene-environment interactions. Second, some valuable information on other exposures for individual participants was missing, such as H. pylori infection, occupation and local environmental factors, diet, physical activity. Third, only four potentially functional SNPs were included in this study, and SNPs from the coding and the intron regions that may also be related to stomach cancer risk were omitted. Finally, functional analysis was not performed for the studied SNPs.

In conclusion, this study provided evidence of the associations between four potentially functional SNPs in the XPG gene and the risk of stomach cancer. In particular, we found that the XPG

| Table 2 Stratification analysis of XPG rs873601G>A and risk genotypes with stomach cancer susceptibility |
|--------------------------------------------------|
| Variables                                      | rs873601 (cases/controls) | Adjusted OR* (95% CI) | Risk genotypes (cases/controls) | Adjusted OR* (95% CI) |
| Median age, year                               | GG/GA AA 0/1              | 1.05 (0.72–1.53)      | 0.812 64/92 269/268             | 1.44 (0.97–2.14)      |
| Gender                                         | Females Males             | 1.06 (0.65–1.75)      | 0.810 45/55 155/170             | 1.04 (0.62–1.74)      |
| Smoking status                                 | Never Ever                | 1.43 (0.95–2.15)      | 0.085 47/118 218/292            | 1.83 (1.20–2.80)      |
| Pack-year                                      | 0≤27>27                  | 1.14 (0.80–1.64)      | 0.463 98/82 329/279             | 0.94 (0.65–1.36)      |
| Drinking status                                | Never Ever                | 1.26 (0.92–1.73)      | 0.144 108/140 431/399           | 1.41 (1.02–1.94)      |
| BMI                                            | <18.5 18.5–24.0 >24.0    | 1.76 (0.17–18.58)     | 0.640 13/1 40/4                 | 0.87 (0.08–9.37)      |
| Tumour sites                                   | Cardia Non-cardia         | 1.17 (0.79–1.74)      | 0.433 43/200 156/571            | 1.16 (0.78–1.73)      |
| *Adjusted for age, gender, BMI, smoking and drinking status. OR: odds ratio; CI: confidence interval; BMI: body mass index. The results were in bold, if the 95% CI excluded 1 or P<0.05.
rs873601G>A polymorphism was associated with slightly increased stomach cancer risk in Chinese Han population. In the future, prospective studies with different ethnicities and larger sample size as well as investigations into mechanism are warranted to validate the role of XPG SNPs in stomach cancer carcinogenesis and explore the underlying mechanism.

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References

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin. 2015; 65: 87–108.
2. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. J Clin Epidemiol. 2003; 56: 1–9.
3. Chow WH, Blot WJ, Vaughan TL, et al. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. J Natl Cancer Inst. 1998; 90: 150–5.
4. Tran GD, Sun XD, Abnet CC, et al. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. Int J Cancer. 2005; 113: 456–63.
5. Wadhwa R, Song S, Lee JS, et al. Gastric cancer-molecular and clinical dimensions. Nat Rev Clin Oncol. 2013; 10: 643–55.
6. Holcombe C. Helicobacter pylori: the African enigma. Gut. 1992; 33: 429–31.
7. Wood RD, Mitchell M, Spouros J, et al. Human DNA repair genes. Science. 2001; 291: 1284–9.
8. Friedberg EC. How nucleotide excision repair protects against cancer. Nat Rev Cancer. 2001; 1: 22–33.
9. You JS, Wang M, Lee SH. Biochemical analysis of the damage recognition process in nucleotide excision repair. J Biol Chem. 2003; 278: 7476–85.
10. Cleaver JE. Common pathways for ultraviolet skin carcinogenesis in the repair and replication deficient groups of xeroderma pigmentosum. J Dermatol Sci. 2000; 23: 1–11.
11. Clarkson SG. The XPG story. Biochimie. 2003; 85: 1113–21.
12. Zhu ML, Wang M, Cao ZG, et al. Association between the ERCC5 Asp1104His polymorphism and cancer risk: a meta-analysis. PLoS ONE. 2012; 7: e36293.
13. Hussain SK, Mu LN, Cai L, et al. Genetic variation in immune regulation and DNA repair pathways and stomach cancer in China. Cancer Epidemiol Biomarkers Prev. 2009; 18: 2304–9.
14. Canbay E, Agachan B, Galluoglu M, et al. Possible associations of APE1 polymorphism with susceptibility and HOGG1 polymorphism with prognosis in gastric cancer. Anticancer Res. 2010; 30: 1359–64.
15. Duan Z, He C, Gong Y, et al. Promoter polymorphisms in DNA repair gene ERCC5 and susceptibility to gastric cancer in Chinese. Gene. 2012; 511: 274–9.
16. He J, Qiu LX, Wang MY, et al. Polymorphisms in the XPG gene and risk of gastric cancer in Chinese populations. Hum Genet. 2012; 131: 1235–44.
17. Yang WG, Zhang SF, Chen JW, et al. SNPs of excision repair cross complementing group 5 and gastric cancer risk in Chinese populations. Asian Pac J Cancer Prev. 2012; 13: 6269–72.
18. Sun H, Wu X, Wu F, et al. Associations of genetic variants in the PSCA, MUC1 and PLCe1 genes with stomach cancer susceptibility in a Chinese population. PLoS ONE. 2015; 10: e0117576.
19. Le Page F, Kwoh EE, Avrutskaya A, et al. Transcription-coupled repair of 8-oxoguanine: requirement for XPG, TFIIH, and CSB and implications for Cockayne syndrome. Cell. 2000; 101: 159–71.
20. Hanawalt PC. Controlling the efficiency of excision repair. Mutat Res. 2001; 485: 3–13.
21. Hanawalt PC. Transcription-coupled repair and human disease. Science. 1994; 266: 1957–8.
22. Wakasugi M, Reardon JT, Sancar A. The non-catalytic function of XPG protein during dual incision in human nucleotide excision repair. J Biol Chem. 1997; 272: 16030–4.
23. O’Donovan A, Davies AA, Moggs JG, et al. XPG endonuclease makes the 3’ incision in human DNA nucleotide excision repair. Nure. 1994; 371: 432–5.
24. Friedberg EC. DNA damage and repair. Nature. 2003; 421: 436–40.
25. Du H, Zhang X, Du M, et al. Association study between XPG Asp1104His polymorphism and colorectal cancer risk in a Chinese population. Sci Rep. 2014; 4: 6700.

Conflicts of interest

None.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1 Frequency distribution of selected characteristics in stomach cancer cases and controls.