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Original Article

The association between XRCC1 polymorphism and laryngeal cancer susceptibility in different ethnic groups in Xinjiang, China

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Abstract: Reduction in DNA repair capacity is associated with increased rates of birth defects, cancer, and accelerated aging. According to some earlier studies, genetic polymorphisms in DNA repair genes might influence the repair activities of the enzymes predisposing individuals to cancer risk. Owing to the presence of these genetic variants, inter-individual and ethnic differences in DNA repair capacity have been observed in various populations. Polymorphisms in DNA repair genes and differences in repair capacity between individuals have been widely reported in different cancers. We conducted a case-control study to examine the role of genetic polymorphisms in XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), Arg280His (rs25489), Arg194Trp (rs1799782) in the risk of laryngeal cancer in different ethnic groups in Xinjiang. This study included 58 laryngeal cancer patients and 120 healthy controls age- and sex-matched without cancer. The genotypes of XRCC1Gln632Gln (rs3547), Arg399Gln (rs25487), Arg280His (rs25489) and Arg194Trp (rs1799782) were analyzed by PCR-RFLP, and the odds ratio (OR) and 95% confidence interval (CI) were calculated using an unconditional logistic regression model. C/T (hybrid) and T/T (mutant) genotypes of XRCC1 Arg280His (rs25489) revealed no statistical significance in the risk of laryngeal cancer ($P>0.05$), whereas the genotypes of XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), Arg280His (rs25489), Arg194Trp (rs1799782) showed a higher risk than the controls ($P<0.01$) in Han, Uygur, and Kazak nations. In conclusion, the current study suggests that XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), and Arg194Trp (rs1799782) polymorphisms may be associated with laryngeal cancer risk in the Han, Uygur, and Kazakh populations in Xinjiang. Individuals carrying genotype Arg/Gln+Gln/Gln showed a greater risk than those carrying Arg/Arg for laryngeal cancer in the Han, Uygur and Kazakh ethnic groups, and the odds ratios are 1.47, 1.32, and 0.77.

Keywords: XRCC1, polymorphism, laryngeal cancer

Introduction

Head and neck cancer (HNC) is the fifth most common cancer worldwide; it is associated with low survival and high morbidity when diagnosed at an advanced stage [1], accounting for almost 500,000 newly diagnosed cancer cases per year [2]. Laryngeal cancer is one of the largest subgroups of head and neck cancers [3], with approximately 156,000 new laryngeal cancer patients and 83,000 deaths from laryngeal cancer in 2012 worldwide [4]. The incidence of laryngeal cancer varies considerably across different populations, suggesting that many environmental and lifestyle risk factors are involved in laryngeal cancer development, such as exposure to carcinogens in the work environment, and infection with the human papilloma virus and the Epstein-Barr virus [5, 6]. In fact, many studies have indicated that heritable factors contribute to the development of laryngeal cancer, including methylene tetrahydrofolate reductase, epidermal growth factor-like domain 7/Egfl7, nucleotide excision repair pathway gene, matrix metalloproteinase 11, P14, B-cell translocation gene 1, special AT-rich sequence-binding protein 1 and 2, DNA repair gene, and cyclin-dependent kinase [7-13]. The majority of the laryngeal cancer cases are males [14]. The most common histopathological type of laryngeal

cancer is squamous cell carcinoma (85-90%), reflecting the cancer's origin in the squamous cells of the laryngeal epithelium [15, 16]. It can develop in any part of the larynx. Genetic polymorphisms in DNA repair genes which lead to amino acid substitution may lead to a differential capacity to repair DNA damage. This effect has been found to be associated with increased genetic instability and carcinogenesis [17]. Genetic variation plays a critical role in most diseases; however, gene-environment interactions may also be important in various ways, either by risk due to individual or population genotypes or by differential gene risk based on exposure [18, 19]. The exposure of cells to physical and chemical agents, including ionizing radiation and other toxic chemicals, results in DNA damage, potentially causing the loss of genetic integrity and an elevated cancer risk. The integrity of the damaged DNA is typically restored by the action of certain DNA repair enzymes [20, 21].

Earlier studies have shown that X-ray repair cross-complementing group 1 (XRCC1) protein functions in a complex with many other components to facilitate BER and single-strand break-repair processes, and it plays an important role in base excision repair (BER) and single-strand break repair (SSBR), upon exposure to endogenous reactive oxygen species, ionizing radiation or alkylating agents [22, 23]. The BER pathway mainly removes non-bulky base adducts produced by methylation, oxidation, or reduction by ionizing radiation or oxidative damage [24]. Several SNPs in XRCC1 have been identified, and three coding polymorphisms were detected at codons 194 (Arg>Trp), 280 (Arg>His) and 399 (Arg>Gln) in several kinds of cancer [25-27]. In this study, we conducted a case-control study to examine the role of genetic polymorphisms in XRCC1 at codons 632 (Gln/Gln), 194 (Arg>Trp), 280 (Arg>His) and 399 (Arg>Gln) with the risk of LC. We also investigated whether there is a link between the clinicopathological variables with the XRCC1 gene polymorphisms and its role in modulating the risk of LC.

Materials and methods

Patients

Blood samples were obtained from 58 patients with laryngeal squamous cell cancer from the Department of Otolaryngology-Head and Neck Surgery, First Affiliated Hospital of Xinjiang Medical University, Urumqi, China from 2013-2017 and 120 cancer-free age- and sex-matched controls. The patients and controls ranged in age from 40 to 80 years (mean age - standard deviation, 62±6.75 years and 58±7.14 years), with 49 males, 9 females (including 28 Hans, 16 Uygurs, and 14 Kazaks). Tumor types and stages were determined by experienced pathologists, and all of them were diagnosed as squamous cell carcinoma. According to UICC staging, there were 18 cases of T1N0M0, 15 cases of T2N0-1M0, 17 cases of T3N0-2M0, 8 cases of T4N0-2M0, 21 cases of glottic type, 26 cases of superglottic type, and 11 cases of subglottic type.

Data of all LC patients and controls were obtained from face-to-face interviewers with patients and controls, medical records, and pathology reports. All patients and controls were informed about this study and their willingness to participate in this study was recorded on a predesigned questionnaire. The collection and use of blood samples for this study were previously approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University.

In order to evaluate whether the polymorphisms were associated with the progression of larynx cancer, individuals were categorized into groups according to the cancer staging system of the *TNM Classification of Malignant Tumours*.

Main reagents and instruments

A whole blood genomic extraction kit was purchased from Tiangen Biochemical Technology Beijing Co., LTD. A DK-8D electric thermostat was purchased from Shanghai Jinghong Experimental Equipment Co., LTD. A gel imager was purchased from Shanghai Peiqing Technology Co., LTD. A centrifuge model 5810R was purchased from Eppendorf (Germany). A BG-Power 300 electrophoresis meter was purchased from Beijing Biotechnology Co., LTD. The primers were purchased from Shanghai Sangon Biotechnology Co., LTD. A PCR buffer was purchased from TAKARA, Japan. A PCR Marker was purchased from NEW ENGLAND Biolabs. BIOWEST agarose was purchased from Shanghai Xiayi Industrial Co., LTD. SNaPshot Multiples were purchased from ABI, America. A 5X Sequencing Buffer was purchased from ABI, America. SAP was purchased from Promega,

Table 1. Correlation between XRCC1 genotype frequencies and LSCC in Han

Genotype	Case	Control	OR	95% CI
Arg/Arg	10 (62.5%)	25 (53.2%)	1	
Arg/Gln	4 (25%)	19 (40.4%)	1.90	0.52-7.00
Gln/Gln	2 (12.5%)	3 (6.4%)	0.60	0.09-4.15
Arg/Gln+Gln/Gln	6 (37.5%)	22 (46.8%)	1.47	0.46-4.69

P<0.05, compared with control group.

Table 2. Correlation between XRCC1 genotype frequencies and LSCC in Uygur

Genotype	Case	Control	OR	95% CI
Arg/Arg	15 (53.6%)	14 (46.7%)	1	
Arg/Gln	12 (42.9%)	15 (50%)	1.34	0.47-3.83
Gln/Gln	1 (3.6%)	1 (3.3%)	1.07	0.06-18.82
Arg/Gln+Gln/Gln	13 (46.4%)	16 (53.3%)	1.32	0.47-3.70

P<0.05, compared with control group.

Table 3. Correlation between XRCC1 genotype frequencies and LSCC in Kazakh

Genotype	Case	Control	OR	95% CI
Arg/Arg	7 (50.0)	22 (56.4)	1	
Arg/Gln	6 (42.9)	14 (35.9)	0.74	0.21-2.67
Gln/Gln	1 (7.1)	3 (7.7)	0.95	0.09-10.71
Arg/Gln+Gln/Gln	7 (50.0)	17 (43.6)	0.77	0.23-2.63

P<0.05, compared with control group.

America. DNA polymerase was purchased from Qiagen, Germany.

DNA extraction and genotype analysis

Genomic DNA was isolated from peripheral blood lymphocytes using a Qiagen blood mini kit (Qiagen, Germany) according to the manufacturer's protocol. The genotypes of XRCC1 at codons 632 (Gln/Gln), 194 (Arg>Trp), 280 (Arg> His), and 399 (Arg>Gln) were analyzed by a polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay. The positive and reverse primer sequences of the XRCC1 at codon rs1799782 were 3'-CCAGCCCCCTCTACCCTCA-5' and 3'-TTCCCCAGTTCCCTGTGAAG-5', respectively. At codon rs25489, the positive and reverse primers were 3'-GAAGGATCTTCCCCAGCTCCTC-5' and 3'-GTTGACCCCCAGTGGTGCTAAC-5', respectively. At codon rs25487, the positive and reverse primers were 3'-TTGCCCAGCACAGGATAAGGA-5' and 3'-TGCCAACACCCCCAAGTACAG-5', respectively. At codon rs3547, the positive and reverse primers were 3'-ACGGAGGTGCCCAGCATTCTT-5' and 3'-TCGTCCCCGATGGATCTACAGT-5', respectively. The conditions of PCR were set as follows: one cycle of initial denaturation at 95°C for 2 min; 11 cycles of denaturation at 94°C for 20 s, annealing at 64.5°C for 30 s, and extension at 72°C for 90 s; 24 cycles of denaturation at 94°C for 20 s, annealing at 59°C for 30 s, and extension at 72°C for 1.5 min; and a final one cycle of extension at 72°C for 2 min.

Statistical analysis

The statistical differences between cases and controls were analyzed by a Chi-square test. The Hardy-Weinberg equilibrium (HWE) was tested by Fisher's exact test for each SNP in the controls. Conditional regression models were used to calculate the strength of the association between XRCC1 gene polymorphisms and laryngeal cancer risk, and the results were expressed using Odds Ratio (OR) and 95% confidence interval (CI). The link between the clinicopathologic variables with the XRCC1 gene polymorphisms was assessed by conditional regression models. Statistical significance was set at P<0.05. Odds ratios (OR) and 95% confidence intervals (CI) were also calculated. Statistical analyses were performed using SPSS 21.0 software.

Results

A total of 58 LC cases and 120 control subjects were included in this study with prior consent (**Table 1**). The mean ages of the LC patients and the control subjects were 62±6.75 years and 58±7.14 years, respectively. Out of the 58 LC cases, 49 were males and 9 were females. The patients ranged in age from 40 to 80 years (mean age - standard deviation, 62±6.75 years) and included 28 Hans, 16 Uygurs, and 14 Kazaks. According to UICC staging, there were 18 cases of T1N0M0, 15 cases of T2N0-1M0, 17 cases of T3N0-2M0, 8 cases of T4N0-2M0, 21 cases of glottic type, 26 cases of superglottic type, and 11 cases of subglottic type.

Table 4. Site rs25489 XRCC1 SNP associated with laryngeal cancer susceptibility analysis

Genotype	Case	Control	OR	95% CI
Han XRCC1 rs25489				
C/C	16 (100%)	40 (51.1%)	1	
C/T	0 (0%)	7 (14.9%)	NA	0.00-NA
T/T	0 (0%)	7 (14.9%)	NA	0.00-NA
C/T-T/T	0 (0%)	7 (14.9%)	NA	0.00-NA
Kazakh XRCC1rs25489				
C/C	14 (100%)	31 (79.5%)	1	
C/T	0 (0%)	8 (20.5%)	NA	0.00-NA
T/T	0 (0%)	8 (20.5%)	NA	0.00-NA
C/T-T/T	0 (0%)	8 (20.5%)	NA	0.00-NA
Uygur XRCC1 rs25489				
C/C	24 (78.6%)	24 (80%)	1	
C/T	6 (21.4%)	6 (20%)	0.92	0.26-3.27
T/T	6 (21.4%)	6 (20%)	0.92	0.26-3.27
C/T-T/T	6 (21.4%)	6 (20%)	0.92	0.26-3.27

P>0.05, compared with control group.

Table 5. Site rs3547 XRCC1 SNP associated with laryngeal cancer susceptibility analysis

Genotype	Case	Control	OR	95% CI
Han XRCC1 rs3547				
C/C	8 (50%)	24 (51.1%)	1	
C/T	4 (25%)	20 (42.5%)	1.11	0.33-3.74
T/T	2 (12.5%)	3 (6.4%)	0.50	0.07-3.55
C/T-T/T	6 (37.5%)	23 (48.9%)	0.96	0.31-2.98
Kazakh XRCC1 rs3547				
C/C	9 (64.3%)	22 (56.4%)	1	
C/T	4 (28.6%)	17 (43.6%)	1.74	0.46-6.62
T/T	1 (7.1%)	0 (0%)	0.00	0.00-NA
C/T-T/T	5 (35.7%)	17 (43.6%)	1.39	0.39-4.92
Uygur XRCC1 rs3547				
C/C	24 (85.7%)	28 (93.3%)	1	
C/T	4 (14.3%)	2 (6.7%)	1.74	0.46-6.62
T/T	0 (0%)	0 (0%)	0.00	0.00-NA
C/T-T/T	4 (14.3%)	2 (6.7%)	1.74	0.46-6.62

P<0.05, compared with control group.

Characteristics of included subjects

The genotype frequencies of XRCC1 in the three different ethnic groups in Xinjiang are shown in **Tables 1-3**. Genotype frequencies of Arg/Arg, Arg/Gln, Gln/Gln, and Arg/Gln+Gln/Gln showed statistical significance between the cases and controls in the three different groups, P<0.05. The individuals carrying genotype Arg/Gln+Gln/Gln showed a higher risk than Arg/Arg for laryngeal cancer in the Han, Uygur, and Kazakh groups, with odds ratios at 1.47, 1, 32, and 0.77 (**Tables 1-3**).

In this study, in LC cases of three different ethnic groups, we did not find any significant association between XRCC1 Arg280His (rs25489) C/T (hybrid) and T/T (mutant) polymorphisms and LC risk compared with the control group (P>0.05) (**Table 4**). The frequencies of the other three SNPs XRCC1 Gln632Gln (rs3547) C/T (hybrid) and T/T (mutant), Arg399Gln (rs25487), C/T (hybrid) and T/T (mutant) Arg194Trp (rs1799782) G/A (hybrid) and A/A (mutant) showed a significantly higher risk than the controls, P< 0.01. The individuals carrying the genotype rs3547 C/T and T/T, rs25487 C/T and T/T, rs1799782 G/A and A/A in the Han, Kazakh and Uygur groups showed a significantly higher risk for LC than the individuals who carry the genotype rs3547 C/C, rs25487 C/C and rs1799782 G/G, and the odds ratios are increased 0.96, 1.39, 1.74; 1.47, 0.77, 1.32; 1.49, 1.56, 1.51 (**Tables 4-7**).

Figure 1 shows patterns of LD in the XRCC1 gene. The SNPs of XRCC1 shows different patterns in three different nations. In the Han and Kazakh groups, there is a linkage between rs25487, rs25489 and rs1799782, but in the Uygur group, there is a linkage between rs3547, rs25487, and rs25489. From this result we found that the Han group reveals a positive result in the XRCC1 SNP block, but the Uygur and Kazakh groups were all negative. With the distribution of the genotype of four SNPs using the SNaPshot method, we found the peak representing the genotype XRCC1 rs25487 C/T (hybrid) and T/T (mutant), rs3547 C/T (hybrid) and T/T (mutant), rs1799782 G/A and A/A significantly

Table 6. Site rs25487 XRCC1 SNP associated with laryngeal cancer susceptibility analysis

Genotype	Case	Control	OR	95% CI
Han XRCC1 rs25487				
C/C	10 (62.5%)	25 (53.2%)	1	
C/T	4 (25%)	19 (40.4%)	1.90	0.52-7.00
T/T	2 (12.5%)	3 (6.4%)	0.60	0.09-4.15
C/T-T/T	6 (37.5%)	22 (46.8%)	1.47	0.46-4.69
Kazakh XRCC1 rs25487				
C/C	7 (50%)	22 (56.4%)	1	
C/T	6 (42.9%)	14 (35.9%)	0.74	0.21-2.67
T/T	(7.1%)	3 (7.7%)	0.95	0.09-10.71
C/T-T/T	7 (50%)	17 (43.6%)	0.77	0.23-2.63
Uygur XRCC1 rs25487				
C/C	15 (53.6%)	14 (46.7%)	1	
C/T	12 (42.9%)	15 (50%)	1.34	0.47-3.83
T/T	(3.6%)	1 (3.3%)	1.07	0.06-18.82
C/T-T/T	13 (46.4%)	16 (53.3%)	1.32	0.47-3.70

P<0.05, compared with control group.

Table 7. Site rs1799782 XRCC1 SNP associated with laryngeal cancer susceptibility analysis

Genotype	Case	Control	OR	95% CI
Han XRCC1 rs1799782				
G/G	11 (68.8%)	28 (59.6%)	1	
G/A	3 (18.8%)	18 (38.3%)	2.36	0.58-9.63
A/A	2 (12.5%)	1 (2.1%)	0.20	0.02-2.39
G/A-A/A	5 (31.2%)	19 (40.4%)	1.49	0.45-4.99
KazakhXRCC1 rs1799782				
G/G	10 (71.4%)	24 (61.5%)	1	
G/A	3 (21.4%)	14 (35.9%)	1.94	0.46-8.28
A/A	1 (7.1%)	1 (2.6%)	0.42	0.02-7.34
G/A-A/A	4 (28.6 %)	15 (38.5%)	1.56	0.41-5.89
UygurXRCC1 rs1799782				
G/G	15 (53.6 %)	13 (43.3%)	1	
G/A	13 (46.4%)	15 (50%)	1.33	0.47-3.81
A/A	0 (0%)	2 (6.7%)	NA	0.00-NA
G/A-A/A	13 (46.4 %)	17 (56.7%)	1.51	0.54-4.25

P<0.05, compared with control group.

higher than the wild type in all three groups (Han, Kazakh and Uygur), reveals statistically significance, P<0.05. The result of the XRCC1 genotype SNPs in three different nations is basically the same with gene haplotypes (**Figure 2**). All these results showed different genotype distributions in these three ethnic groups.

Discussion

The mortality rate of LC remains high, with a 5-year survival rate of approximately 65% [28]. Smoking is one of the most important risk factors for laryngeal cancer, and heavy, chronic consumption of alcohol is another important risk. When combined, these two factors appear to have a synergistic effect [29, 30]. Although smoking and the consumption of alcohol can cause laryngeal cancer, the specific carcinogenic mechanisms are unclear [29-31]. There is growing evidence that cancer can be initiated by DNA damage caused by radiation and environmental chemical agents [32]. Due to the metabolites of tobacco and alcohol, DNA damage can occur as a result of oxidative stress, alkylation, bulky adducts and strand breaks. Moreover, altered DNA repair mechanisms can increase the risk of developing laryngeal cancer [33, 34]. To the best of our knowledge, this is the first report on polymorphisms in XRCC1 susceptibility to LC in these three different ethnic groups in the Xinjiang area.

It is reported that since there is increasing evidence that genetic variation leads to different DNA repair capacities in the human population, thus gene polymorphisms can play a critical role in an individual's genetic susceptibility to cancer [35]. Mutations in XRCC1 gene may cause decrease or loss of DNA repair capacity and confer variation in development of many malignant tumors.

In this case-control study, we investigated the role of XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), Arg280His (rs25489), Arg194Trp (rs1799782) polymorphisms in the develop-

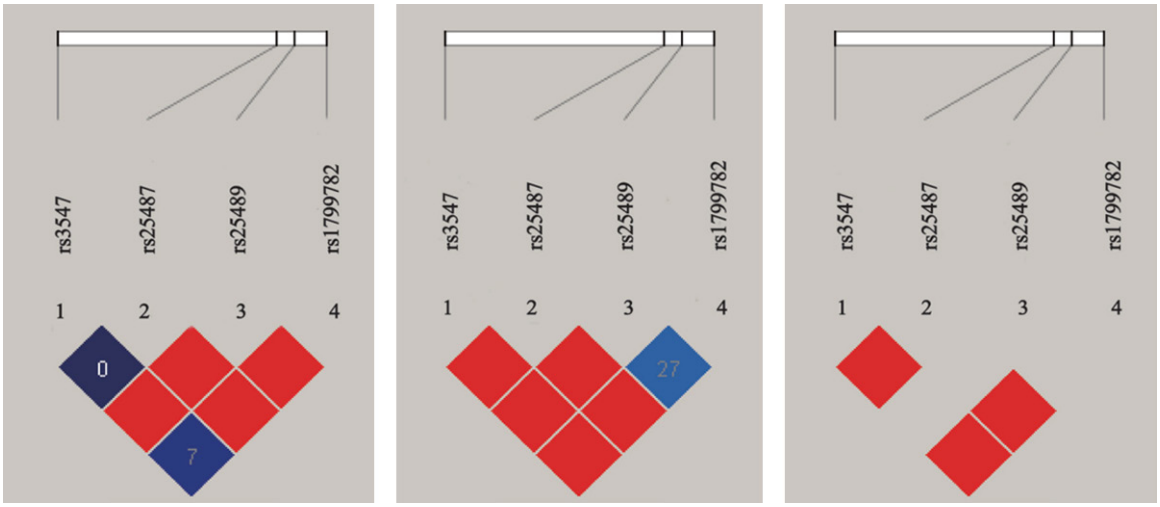

Figure 1. Overall XRCC1 genotype SNPs LD drawing of the three ethnic groups. The first one is for Han overall cases, the middle one for Uygur overall cases, and the last one is for Kazakh overall cases.

ment of LSCC. Our study found that the polymorphisms of XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), Arg280His (rs25489), and Arg194Trp (rs1799782) showed association and differentiation with LC in the Han, Uygur and Kazakh ethnic groups, the mutation of genotype Gln632Gln, Arg399Gln, Arg194Trp may increase the risk of LC, but the mutation of Arg280His showed no association with LC in these three groups.

The results of this study also indicated the rs25487 C/T (hybrid) and T/T (mutant), rs3547 C/T (hybrid) and T/T (mutant), rs1799782 G/A and A/A were significantly higher than the wild type in all three nations (Han, Kazakh and Uygur). They were correlated with a higher risk of laryngeal cancer. The genotype and genotype frequencies in the Han group showed a significant difference from the Uygur and Kazakh groups.

Several studies have reported on the association between XRCC1 polymorphisms and development of several types of cancer, including non-small-cell lung cancer, gastric cancer, cervical cancer, hepatocellular carcinoma, pancreatic cancer, ovarian cancer, colorectal cancer, and thyroid cancer [36-46]. Liu et al. [47] observed a significant relationship between the XRCC1 Arg399Gln polymorphism and risk of cervical cancer in a meta-analysis comprising 2051 cervical cancer patients and 2919 control subjects. Han et al. [42] reported, in a case-control study comprising 245 patients with non-small cell lung cancer and 257 healthy controls, that the XRCC1 Arg399Gln polymorphism influences cancer risk in a Chinese population. Xu et al. [44] observed a significant association between the XRCC1 Arg280His polymorphism and the risk of hepatocellular carcinoma in a meta-analysis comprising 1848 patients with hepatocellular carcinoma and 1969 controls. However, Liu et al. [36] reported the lack of any association between the XRCC1 Arg399Gln polymorphism and gastric cancer risk, based on a meta-analysis comprising 3278 gastric cancer patients and 6243 controls. These studies have shown that the XRCC1 polymorphisms may play an important role in imparting susceptibility to cancer development.

Zhao et al. have reported that XRCC1 Arg194Trp polymorphism has an increased gastric cancer risk in the Asian population [27]. Xu et al. have suggested that the XRCC1 Arg194Trp polymorphism is a genetic risk factor for glioma, especially in the Asian population [48]. However, some studies did not find a significant association between XRCC1 polymorphisms and cancer risk. Dong et al. found no association between the XRCC1 gene polymorphism and bladder cancer risk [49]. Rim Khlifi et al. [50] found a significant association between the XRCC1 399Gln genotype and the risk of laryngeal cancer in the Tunisian population. Some reports showed a similar trend in cancer risk to

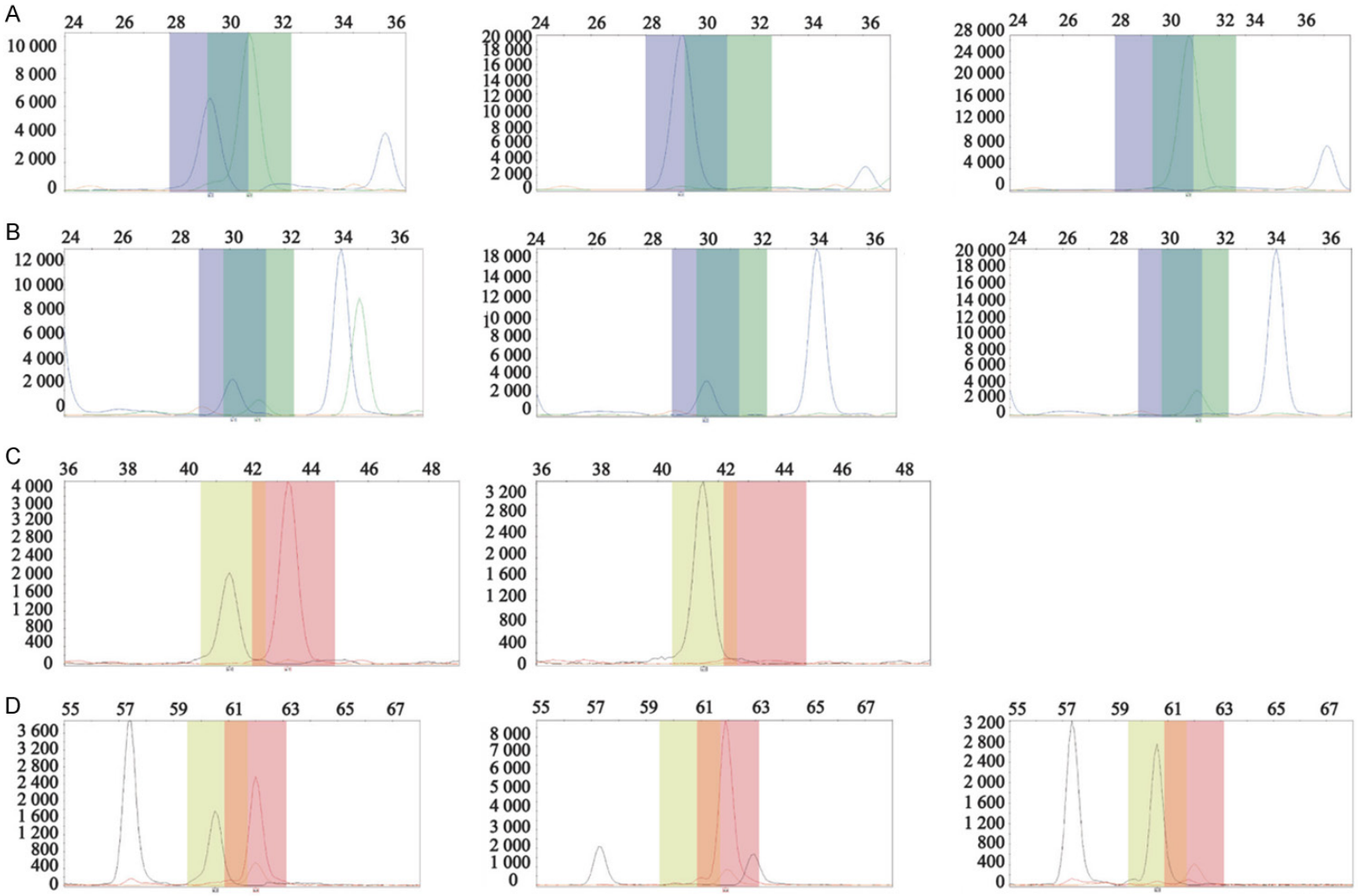

Figure 2. Gel electrophoresis and unit type dotted peak shape. The orange peak is the size standard, and the blue, green, red and black peaks respectively extend to join the ddGTP, ddATP, ddTTP and ddCTP extensions of product, below the peak of allele. (If using an extension of primer that is positive, it is compatible with the bases of a stretch to join; if it is the opposite, with an extension to join the complementary bases). A. rs25487 genotype C/T, C/C, T/T; B. rs3547 genotype C/T, C/C, T/T; C. rs25489 genotype C/T, C/C; D. rs1799782 genotype G/A, A/A, G/G.

the XRCC1 399 polymorphisms in Saudi, Chinese, and Japanese populations [51]. In contrast, a European population did not show an association with the XRCC1 399 polymorphism in lung cancer patients [52] or in bladder cancer patients [53].

The divergence in results from different studies on the XRCC1 polymorphisms could be elucidated by differences in populations, cancer types, sample size and study design.

Therefore, further studies are greatly needed to confirm our findings.

In conclusion, the current study suggests that XRCC1 Gln632Gln (rs3547), Arg399Gln (rs25487), and the Arg194Trp (rs1799782) polymorphisms may be associated with LC risk in the Han, Uygur and Kazakh ethnic groups, but no association was found between polymorphism XRCC1 Arg280His (rs25489) and LC risk, and the genotype and genotype frequencies in Han showed a significant difference with the Uygur and Kazakh ethnic groups, but life style, and living conditions may affect the result. Further large-sample studies are needed to confirm the role of XRCC1 polymorphisms in the development of LC risk.

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Disclosure of conflict of interest

None.

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