Polymorphisms in the DNA repair gene *XRCC1* associated with basal cell carcinoma and squamous cell carcinoma of the skin in a Korean population

Sang Yoon Kang,[1,2] Kwang Gil Lee,[4] Wooseung Lee,[6] Jeong Yun Shim,[3] Seung Il Ji,[1] Ki Wha Chung,[7] Yoon Kyu Chung[5] and Nam Keun Kim[1,8]

[1]Institute for Clinical Research, [2]Department of Plastic and Reconstructive Surgery, [3]Department of Pathology, Bundang CHA General Hospital, College of Medicine, Pochon CHA University, Seongnam, 463-712, South Korea; [4]Department of Pathology, [5]Department of Plastic and Reconstructive Surgery, Wonju College of Medicine, Yonsei University, Wonju, 220-701, South Korea; [6]Department of Health Care, Seoul Medical Center, Seoul; [7]Department of Biological Science, College of Natural Sciences, Kongju National University, Kongju, 314-701, South Korea

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DNA in most cells is regularly damaged by endogenous and exogenous mutagens. Unrepaired damage can result in apoptosis or may lead to unregulated cell growth and cancer. Inheritance of genetic variants at one or more loci results in reduced DNA repair capacity. This hospital-based case-control study examined whether polymorphisms in the DNA repair gene X-ray repair cross-complementing groups 1 (*XRCC1*) (Arg194Trp[C > T], Arg280His[G > A] and Arg399Gln[G > A]) play a role in susceptibility to skin cancer. We genotyped these polymorphisms for 212 histopathologically confirmed skin cancer cases (*n* = 114 basal cell carcinoma, *n* = 98 squamous cell carcinoma) and 207 age- and sex-matched healthy control cases in Korea. We found that individuals with the Arg/Gln and Arg/Gln + Gln/Gln genotypes at *XRCC1* Arg399Gln(G > A) had an approximately 2-fold increased risk of basal cell carcinoma compared to individuals with the Arg/Arg genotype (adjusted odds ratio [AOR] = 2.812, 95% confidence interval [CI] 1.32–5.98, and AOR = 2.324, 95% CI 1.11–4.86). However, we observed that the *194Trp* allele of the Arg194Trp(C > T) polymorphism was inversely associated with squamous cell carcinoma risk (Trp/Trp, AOR = 0.06, 95% CI 0.006–0.63). Our data suggest that the Arg194Trp and Arg399Gln polymorphisms may be differentially associated with skin cancer risk. (*Cancer Sci* 2007; 98: 716–720)

DNA repair enzymes have been reported to play an important role in the carcinogenesis of several cancers.[1–5] DNA repair enzymes are involved in repairing damaged DNA and at least four pathways operate on specific types of DNA damage: the BER,[6–8] NER,[9] DSBR[10,11] and MMR[12] pathways. Enzymes involved in BER include XRCC1, those involved in NER include XPC, XPD, ERCC1, those involved in DSBR include BRCA1, BRCA2 and XRCC3, and those involved in MMR include MLH1, MSH2, PMS2 and MSH6. Polymorphisms of DNA repair genes may also alter protein function and the capacity to repair damaged DNA, which may be associated with risk of developing cancer.[1–3] Cancers such as breast cancer,[13–15] prostate cancer,[16] lung cancer,[17] acute myeloblastic leukemia,[18] colon cancer,[19] stomach cancer[20,21] and SCC of the head and neck[22] are associated with DNA repair gene polymorphisms, and skin cancer is associated with polymorphisms in *XRCC1*, *XPD* and *XRCC3*.[23–26]

Various SNP are known to occur in *XRCC1*[1,3,5,27,28] and they are thought to cause the occurrence of skin cancer through altering the function of BER. *In vivo* and *in vitro*, the *XRCC1* gene repairs chromosomes directly by acting on SSB or indirectly through the BER pathway. Cells deficient in the *XRCC1* gene are known to be susceptible to a wide variety of genotoxins and subsequently sustain translocations and loss of chromosomes.[2,29]

Nelson *et al*. reported that in BCC and SCC, the homozygous variant genotype of *XRCC1* Arg399Gln(G > A) had a statistically significant reduced risk of cancer.[30] They observed, however, that the risk of SCC increased 6.8 times in patients with more than two times of lifetime sunburn exposure. Winsey *et al*. reported that in individuals with the variant *T* allele of Thr241Met(C > T), the risk of melanoma increased 2.4 times.[26] Han *et al*. reported that the risk of cancer decreases in SCC patients with *XRCC1* Arg194Trp(C > T) and Arg399Gln(G > A) homozygous mutant types.[10] But they also reported that in patients with *XRCC1* Arg399Gln(G > A), lifetime sunburn exposure of more than four times is a risk factor for SCC.

Skin cancer is increasing with the lengthening of people's life spans, environmental pollution and destruction of the ozone layer. Of all skin cancers, BCC and SCC occur most frequently. In the present study we test whether the *XRCC1* polymorphisms are associated with an increased risk of SCC and BCC of the skin in the Korean population.

Materials and methods

Study population. The study population was composed of 212 patients (mean age ± SD, 68.98 ± 12.6 years; age range, 36–100 years) with skin cancer (114 BCC, 98 SCC) and 207 control subjects (mean age ± SD, 46.42 ± 16.6 years; age range, 21–85 years). Patients with skin cancer were enrolled and recruited from February 1998 to August 2004 in the Department of Plastic and Reconstructive Surgery of Bundang CHA General Hospital and Department of Plastic and Reconstructive Surgery of Yonsei Wonju Christian Hospital. These hospitals are located in close proximity to each other. Their latitudes are between 37 and 38′N.

We subcategorized the patients according to the location of cancer lesions and sun exposure time. The frequencies of SCC were: head and neck, 65.9%; body, 8.5%; and limb, 12.7%. Those of BCC were: head and neck, 95.9%; body, 2.7%; and limb, 0.9%. Irrespective of BCC and SCC, compared to the control group patients with outdoor jobs and sun exposure times of more than 4 h/day had a higher proportion of skin cancer (4.6 vs 51.6% and 4.5 vs 46.9%, respectively). All of the cases underwent skin cancer surgery and were histologically confirmed.

The controls (*n* = 207) were healthy individuals without any history of premalignant skin lesions or other malignant disorders who visited Bundang CHA General Hospital. The institutional review board of Bundang CHA General Hospital approved this genetic study in January 1998. All of the patients and controls

[8]To whom correspondence should be addressed. E-mail: nkkim@cha.ac.kr

Abbreviations: AFB_1, afflatoxin B_1; AOR, adjusted odds ratio; BCC, basal cell carcinoma; BER, base excision repair; CI, confidence interval; DSBR, double-strand-break repair; MMR, mismatch repair; NER, nucleotide excision repair; OR, odds ratio; PCR, polymerase chain reaction; SCC, squamous cell carcinoma; SNP, single nucleotide polymorphism; SSB, single-strand binding protein; XRCC1, X-ray repair cross-complementing groups 1.

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Table 1. Odds ratios (OR) and 95% confidence interval (CI) of the *XRCC1* polymorphisms Arg194Trp(C > T), Arg280His(G > A) and Arg399Gln(G > A) in squamous cell carcinoma and basal cell carcinoma

Genotype	Controls (%)	Squamous cell carcinoma			Basal cell carcinoma		
		Cases (%)	OR (95% CI)	AOR (95% CI)	Cases (%)	OR (95% CI)	AOR (95% CI)
Codon 194							
Arg/Arg	90 (43.7)	57 (59.4)	1.0 (–)	1.0 (–)	54 (47.4)	1.0 (–)	1.0 (–)
Arg/Trp	98 (47.6)	34 (35.4)	0.548 (0.33–0.91)	0.617 (0.25–1.51)	51 (44.7)	0.867 (0.54–1.40)	0.847 (0.41–1.76)
Trp/Trp	18 (8.7)	5 (5.2)	0.438 (0.15–1.25)	0.06 (0.006–0.63)	9 (7.9)	0.833 (0.35–1.99)	0.248 (0.05–1.21)
Arg/Trp + Trp/Trp	116 (56.3)	39 (40.6)	0.531 (0.32–0.87)	0.490 (0.21–1.17)	60 (52.6)	0.862 (0.54–1.37)	0.727 (0.36–1.48)
Allele frequency (Trp)	0.33	0.23	–	–	0.30	–	–
Codon 280							
Arg/Arg	169 (82.0)	73 (76.0)	1.0 (–)	1.0 (–)	90 (78.9)	1.0 (–)	1.0 (–)
Arg/His	35 (17.0)	21 (21.9)	1.389 (0.76–2.55)	1.470 (0.46–4.71)	23 (20.2)	1.234 (0.69–2.22)	1.198 (0.46–3.12)
His/His	2 (1.0)	2 (2.1)	2.315 (0.32–16.76)	10.098 (0.55–183.67)	1 (0.9)	0.938 (0.08–10.50)	0.000011 (–)
Arg/His + His/His	37 (18.0)	23 (24.0)	1.439 (0.80–2.59)	1.720 (0.57–5.19)	24 (21.1)	1.218 (0.69–2.16)	1.145 (0.44–2.96)
Allele frequency (His)	0.09	0.13	–	–	0.11	–	–
Codon 399							
Arg/Arg	108 (52.7)	48 (19.5)	1.0 (–)	1.0 (–)	39 (34.8)	1.0 (–)	1.0 (–)
Arg/Gln	85 (41.5)	38 (39.2)	1.006 (0.60–1.68)	1.370 (0.57–3.31)	69 (61.6)	2.248 (1.38–3.65)	2.777 (1.30–5.92)
Gln/Gln	12 (5.9)	11 (11.3)	2.063 (0.85–5.00)	1.036 (0.18–5.84)	4 (3.6)	0.923 (0.28–3.03)	0.374 (0.05–2.64)
Arg/Gln + Gln/Gln	97 (47.3)	49 (50.5)	1.137 (0.70–1.84)	1.388 (0.58–3.30)	73 (65.2)	1.08 (1.30–3.35)	2.289 (1.09–4.80)
Allele frequency (Gln)	0.27	0.31	–	–	0.34	–	–

AOR, adjusted odds ratio.

were Korean and they gave informed consent prior to enrolment in the study.

Genetics analysis. Genomic DNA was extracted from peripheral blood leukocytes using the G-DEX blood extraction kit (Intron, Seongnam, Korea). The nucleotide changes were determined by PCR–restriction fragment length polymorphism analysis using the isolated genomic DNA as a template. The forward and reverse primers for the *XRCC1* Arg194Trp(C > T) polymorphism used were 5′-GCC CCG TCC CAG GTA-3′ and 5′-AGC CCC AAG ACC CTT TCA CT-3′, respectively. PCR reactions were run for 35 cycles: 94°C for 60 s, 61°C for 60 s and 72°C for 60 s, and the products were digested with the restriction endonuclease *Msp*I (New England Biolabs, Beverly, MA, USA) at 37°C for 16 h.

The primer sequences used to detect the *XRCC1* Arg280His (G > A) polymorphism were 5′-TGG GGC CTG ATT GCT GGG TCT G-3′ and 5′-CAG CAC CAC TAC CAC ACC CTG AAG G-3′. DNA was amplified for 35 cycles and each cycle comprised denaturing at 94°C for 30 s, annealing at 64°C for 30 s and extension at 72°C for 30 s. The PCR products were detected after incubation with a restriction endonuclease, *Rsa*I (New England Biolabs) at 37°C for 16 h. The PCR products were visualized by gel electrophoresis. PCR for the *XRCC1* Arg399Gln (*G* > A) polymorphism was carried out using primers 5′-CCA AGT ACA GCC AGG TCC TA-3′ and 5′-AGT CTG ACT CCC CTC CGG AT-3′. DNA was amplified for 35 cycles comprising denaturing at 94°C for 30 s, annealing at 62°C for 30 s and extension at 72°C for 30 s. The PCR products were detected after incubation with the restriction endonuclease *Msp*I at 37°C for 16 h.

Statistical analysis. For statistical analysis, we used SPSS for Windows, version 11.0 (SPSS, Chicago, IL, USA) to calculate the AOR and 95% CI. All adjusted models included age, sex, smoking, occupation and sun exposure time per day.

Results

Polymorphisms of *XRCC1* codons 194, 280 and 399 and skin cancer risk. The *XRCC1* gene polymorphisms Arg194Trp(C > T), Arg280His(*G* > A) and Arg399Gln(*G* > A) were investigated, and their genotype distributions and allele frequencies in BCC and SCC patients and controls are shown in Table 1. When the *XRCC1* 194Arg/Arg(CC) genotype was used as the reference group, a significantly decreased risk for SCC was associated with Trp/Trp(TT) (AOR = 0.06, 95% CI 0.006–0.63), whereas for the Arg280His(G > A) and Arg399Gln(G > A) polymorphsims in SCC patients, there were no statistically significant differences in cancer development between controls and cases (Table 1).

When the *XRCC1* 399Arg/Arg(GG) genotype was used as the reference group, a significantly increased risk for BCC was associated with Arg/Gln(GA) (AOR = 2.777, 95% CI 1.30–5.92) and Arg/Gln(GA) + Gln/Gln(AA) (AOR = 2.289, 95% CI 1.09–4.80), whereas for the 194Arg/Trp(C > T) and 280Arg/His(*G* > A) polymorphsims in BCC patients, there were no statistically significant differences in cancer development between the controls and cases (Table 1).

Combination analysis of *XRCC1* codons 194, 280 and 399 polymorphisms. Among combination genotypes of DNA repair genes in all of the non-melanoma skin cancer, the combination genotype of 399Arg/Arg(GG) and 194Arg/Trp + Trp/Trp(CT + TT) showed a statistically significant difference in cancer development (OR = 0.528, 95% CI 0.30–0.87; Table 2). Among 399Arg/Gln and 280Arg/His combination types, 399Arg/Arg + Arg/Gln (GG + GA) + *XRCC1*280Arg/His + His/His(GA + AA) genotype showed a statistically significant difference (OR = 1.600, 95% CI 1.09–2.35; Table 2). However, these two combined genotypes showed no significant risk for skin cancer when being adjusted by conventional risk factors such as smoking, occupation and sun exposure time (Table 2). However, the combination genotype of Arg194Trp (C > T) and Arg280His(G > A) showed no statistically significant difference (data not shown).

Haplotype analysis. Eight haplotypes were distinguished by the six alleles of *XRCC1*. When the cases of SCC and BCC were compared with controls, T-G-G ($P = 0.0012$), T-G-A ($P = 0.0011$) and C-A-A ($P = 0.0077$) showed statistically significant differences and T-A-G ($P = 0.0502$) showed marginal statistical significance (Table 3). There were significant differences in frequency distributions between cases and controls for one (T-G-G, $P = 0.0137$) of eight haplotypes in SCC and six (C-G-G, $P = 0.0009$; C-G-A, $P = 0.0264$; T-G-G, $P < 0.0001$; T-G-A, $P < 0.0001$; T-A-G, $P = 0.0183$ and C-A-A, $P = 0.0095$) of eight haplotypes in BCC of the skin (Table 3).

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Table 2. Combination analysis of *XRCC1* Arg194Trp(C > T), Arg280His (G > A) and Arg399Gln(G > A) polymorphisms in relation to skin cancer

Genotype	Controls (%)	Cases (%)	OR (95% CI)	AOR (95% CI)
Codon 399/Codon 280				
GG/GG + GA	105 (52.0)	92 (40.4)	1.0 (–)	1.0 (–)
GA + AA/GG + GA	97 (48.0)	136 (59.6)	1.600 (1.09–2.35)	1.704 (0.91–3.20)
Codon 399/Codon 194				
GG/CC	38 (34.7)	48 (51.1)	1.0 (–)	1.0 (–)
GG/CT + TT	69 (65.3)	46 (48.9)	0.528 (0.30–0.93)	0.540 (0.21–1.38)

Combined Arg194Trp(C > T)/Arg280His(G > A) genotypes showed no statistically significant difference. AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

Table 3. Frequencies of *XRCC1* Arg194Trp(C > T), Arg280His(G > A) and Arg399Gln(G > A) haplotypes in squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) of the skin

Haplotype	Frequency			
	Controls	Cases	SCC	BCC
C-G-G	0.3285	0.3833	0.3729	0.4761*
C-G-A	0.2493	0.2468	0.2747	0.1648*
T-G-G	0.3017	0.2049*	0.2050*	0.0931*
C-A-G	0.095	0.0721	0.1148	0.0830
T-G-A	0.0184	0.0645*	0.0172	0.1511*
T-A-G	2.31E-07	0.0099	0.0000	0.0145*
C-A-A	1.46E-12	0.0184*	0.0084	0.0175*
T-A-A	7.10E-03	3.36E-08	7.00E-03	2.45E-19

*$P < 0.05$.

Discussion

Many studies have shown that genes play a very important role in repairing damaged DNA from endogenous and exogenous mutagens and in maintaining genetic stability. Mutagenesis may result in reduced DNA repair capacity and can lead to an increased risk of cancer.[31–33] There are at least four different DNA repair pathways. Among the many repair genes, the *XRCC1*, *XPD*, *XRCC3* and *ERCC1* polymorphisms are reported to be associated with skin cancer. Of these, *XRCC1* was observed to be involved in both melanoma and non-melanoma skin cancer.[26,30]

The enzymatic function of XRCC1 is not yet known, but it is known to function as a nucleating factor that codes for poly(adenosine diphosphate[ADP]-ribose) polymerase (PARP) recognizing DNA damage,[34] APE1 involving glycosylases and gap filling,[35] DNA polymerase-β and DNA ligase III.[36] After all, *XRCC1* plays an important role in repairing damaged sites, acting as an endonuclease or a scaffold after the damaged base is removed,[37] and three types of polymorphisms, including R194W, R280H and R399Q, are often reported in epidemiological studies concerning this gene.[26,30]

In the present study we observed two significant results. First, the risk of SCC decreased with the 194Arg/Trp(CT) variant genotype, and second, the risk of BCC increased with the 399Arg/Gln(GA) variant genotype. In addition, we observed that the Arg280His polymorphism, combined with the Arg399Gln genotypes, could be a risk factor for skin cancers (Table 2). Furthermore, we delineated the association of skin cancers with allele haplotypes (Table 3). Interestingly, in BCC, the C-G-G haplotype, a normal allele combined haplotype, increased the risk of cancer development. Moreover, against our expectations in SCC that no allele haplotypes would increase the risk of cancer development, we found that the T-G-G haplotype actually lowered it.

Among the polymorphisms of Arg194Trp(C > T) in SCC, the Trp/Trp(TT) type (AOR = 0.06) showed reduced risk of cancer development (Table 1). Lunn *et al*. studied individual capabilities of removing AFB_1 DNA adducts according to Arg194Trp(C > T) genotypes, and reported that those with the *194Trp(T)* allele had a higher ability than those with the *194Arg(C)* allele, which is consistent with our data (AOR = 0.490; Arg/Arg[CC] vs Arg/Trp + Trp/Trp[CT + TT]).[38] However, Han *et al*. reported that in Americans with SCC, individuals with the *194Trp(T)* allele had a higher risk of cancer development. Consequently, studies with a larger population are needed to elucidate the association between *XRCC1* Arg194Trp(C > T) polymorphism and skin cancer development.[10]

The Arg194Trp(C > T) polymorphism in BCC was not associated with any statistically significant differences in cancer development, although it was reported that in Caucasians the Arg194Trp(C > T) polymorphism lowers the risk of cancer development in bladder, lung, breast and stomach as well as BCC.[1] The Arg194Trp(C > T) polymorphism was not shown to have any statistically significant association with BCC development in Koreans. Other studies on Caucasian populations did not show any association with BCC, bladder cancer, lung cancer, breast cancer or stomach cancer.[1] The Arg399Gln(G > A) polymorphism was positively associated with increased development of BCC in Arg/Gln(GA) and Arg/Gln + Gln/Gln(GA + AA) types, but not of SCC. This result with BCC was consistent with the study of Lunn *et al*., which showed increased development of BCC due to remarkably decreased enzymatic ability to eliminate AFB_1 DNA adducts in individuals with the *399Gln(A)* allele.[38]

In contrast, Han *et al*. proposed that Arg399Gln(G > A) reduces the risk of SCC only in groups with lifetime sunburn exposure of more than five times or with continuous sunlight exposure, but increases the risk in groups without such skin cancer risks.[10] They also proposed that in BCC and melanoma there was no such correlation. However, Nelson *et al*. reported that Arg399Gln(G > A) suppresses cancer development when there is less than three times sunburn, but it significantly increases cancer development when there is three or more times sunburn.[30] These studies are not consistent regarding the effect of sunburn, even though sun exposure, which causes DNA damage through UV light, is accepted as an important factor in skin cancer development. We analyzed and compared the study groups according to their jobs, that is, whether they had indoor or outdoor jobs. In the control group, only a few people had outdoor jobs (4.6%) whereas in the patient group, more than half of the people had outdoor jobs (51.6%) ($P < 0.0001$). The proportions of sun exposure times of >4 h per day were 4.5% in control group, 51.4% in SCC patients and 43.2% in BCC patients, respectively, with the significantly lower value in control group ($P < 0.001$). In SCC group, the locations of cancer were: head and neck, 65.9%; limb, 12.8%; and trunk, 8.5%. After an additional adjustment for smoking, occupations and sun exposure time for Arg194Trp(C > T) of SCC, the OR for Arg/Trp(CT) became statistically insignificant, increasing from 0.548 (95% CI 0.33–0.91) to 0.617 (95% CI 0.25–1.51). The OR of Trp/Trp(TT) also became statistically significant, decreasing from 0.439 (95% CI 0.15–1.25) to 0.06 (95% CI 0.006–0.63) (Table 1). Sex, smoking, occupation and sun exposure did not

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Table 4. Genotype distribution of *XRCC1* polymorphisms in controls by ethnic differences

Genotype	American Whites[38] (*n* = 169) (%)	American Blacks[38] (*n* = 98) (%)	Chinese[42] (*n* = 210) (%)	Taiwanese[40] (*n* = 264) (%)	Korean (*n* = 207) (%)
Codon 194					
Arg/Arg	150 (88.8)	89 (90.8)	85 (40.5)	125 (47.3)	90 (43.7)
Arg/Trp	18 (10.7)	9 (9.2)	104 (49.5)	120 (45.5)	98 (47.6)
Trp/Trp	1 (0.6)	0 (0.0)	21 (10.0)	19 (2.7)	18 (8.7)
Codon 280					
Arg/Arg	159 (94.1)	94 (95.9)	177 (84.7)	212 (80.3)	169 (82.0)
Arg/His	10 (5.9)	4 (4.1)	32 (15.3)	50 (18.9)	35 (17.0)
His/His	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	2 (1.0)
Codon 399					
Arg/Arg	65 (38.5)	67 (68.4)	117 (56.3)	132 (50.0)	108 (52.7)
Arg/Gln	83 (49.1)	27 (27.6)	80 (38.3)	108 (40.9)	85 (41.5)
Gln/Gln	21 (12.4)	3 (3.1)	11 (5.3)	24 (9.1)	12 (5.9)

show any statistical significance individually, but when they were combined and adjusted accordingly, they showed statistical significance (Table 1). Inferring from this, we can say that additional conventional risk factors had the greatest effect on the polymorphism Arg194Trp(C > T) of SCC.

According to the studies of Han *et al*.[10] and Nelson *et al*.[30] on the American population, the homozygous variant Arg399Gln(G > A) showed decreased development of SCC, but in our study, there was no significant association between them in the Korean population. Our study showed that Arg280His(G > A) was not associated with either BCC or SCC. Arg280His(G > A) has been reported as not being associated with bladder cancer,[39] esophageal cancer[40] or head and neck cancer in Koreans.[41] The Arg280His(G > A) polymorphism is not useful as a biomarker as it was reported to have little association with cancer.[1,2,39–41] In case of the combined genotype of XRCC1399/280 and XRCC1399/194, it persistently showed statistical significance after being adjusted for age and sex (data not shown); however, it no longer showed any statistical significance after being adjusted for smoking, occupation and sun exposure (Table 2).

We next looked at the individual alleles' genotype ratios among different populations. For *XRCC1194Trp(T)*, its allele ratio was 0.06–0.09 in Americans, 0.27–0.35 in Chinese and 0.33 in Koreans, which showed that the allele ratio was similar between Asian populations (Table 3).[38,42] As for *XRCC1*280His(A), its allele ratios were 0.03–0.04 in Americans, 0.08–0.11 in Chinese and 0.09 in Koreans, and the allele ratios for *XRCC1*399Gln(A) were 0.37 in Americans, 0.24–0.30 in Chinese and 0.28 in Koreans. So there was a racial difference in the frequency of these three alleles. Among them the *194Trp(T)* allele showed the greatest racial difference.

Polymorphisms of *XRCC1* and increased cancer risk are not confined to skin cancer. They are known to be associated with other cancers including SCC of the head and neck,[22] bladder cancer, breast cancer, uterine leiomyoma,[43] hepatocellular carcinoma[44] and lung cancer. Therefore, further studies are needed to delineate the association between polymorphisms of DNA repair genes and the risk of cancer development.

The Arg280His(G > A) polymorphism, reported to be associated with skin cancers, was shown to be associated with neither BCC nor SCC of the skin in Koreans. The Arg280His(G > A) polymorphism alone had no effect on the development of skin cancers (BCC and SCC); however, when combined with Arg399Gln(G > A), it was a risk factor for them (data not shown). Interestingly, when the Arg399Gln(G > A) genotypes were combined with the *XRCC1* Arg194Trp(C > T) genotypes, it worked as a protective factor against skin cancers. Regrettably, as we had no data for the Japanese population, we could not compare the skin cancer incidence of Koreans with that of the Japanese population. However, we observed that the frequency of genotypes in Koreans was very similar to those in the Chinese and Taiwanese populations (Table 4). In conclusion, for Koreans, of the *XRCC1* gene polymorphisms, the Arg399Gln(G > A) genotype increased the risk of BCC of the skin and the Arg194Trp(C > T) genotype decreased the risk of SCC of the skin. Consequently these genotypes could be used as biomarkers for the estimation of skin cancer (BCC and SCC) risk.

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