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Polymorphisms in base-excision & nucleotide-excision repair genes & prostate cancer risk in north Indian population

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***Background & objectives*: Genetic variation in the DNA repair genes might be associated with altered DNA repair capacities (DRC). Reduced DRC due to inherited polymorphisms may increase the susceptibility to cancers. Base excision and nucleotide excision are the two major repair pathways. We investigated the association between two base excision repair (BER) genes (*APE1* exon 5, *OGG1* exon 7) and two nucleotide excision repair (NER) genes (*XPC* PAT, *XPC* exon 15) with risk of prostate cancer (PCa).**

***Methods*: The study was designed with 192 histopathologically confirmed PCa patients and 224 age matched healthy controls of similar ethnicity. Genotypes were determined by amplification refractory mutation specific (ARMS) and PCR-restriction fragment length polymorphism (RFLP) methods.**

***Results*: Overall, a significant association in NER gene, *XPC* PAT Ins/Ins (I/I) genotype with PCa risk was observed (Adjusted OR- 2.55, 95%CI-1.22-5.33, *P*=0.012). *XPC* exon 15 variant CC genotypes presented statistically significant risk of PCa (Adjusted OR- 2.15, 95% CI-1.09-4.23, *P*=0.026). However, no association was observed for polymorphism with BER genes. Diplotype analysis of *XPC* PAT and exon 15 revealed that the frequency of the D-C and I-A diplotype was statistically significant in PCa. The variant genotypes of NER genes were also associated with high Gleason grade.**

***Interpretation & conclusions*: The results indicated that there was a significant modifying effect on the association between genotype *XPC* PAT and exon 15 polymorphism and PCa risk which was further confirmed by diplotype analysis of *XPC* PAT and exon 15 in north Indian population.**

Key words Bone metastatis - DNA repair gene - Gleason score - polymorphism - prostate cancer

Prostate cancer (PCa) is the most common malignancy in men and the second leading cause of cancer mortality in western countries[1]. In India, it is the sixth most commonly diagnosed cancer in men[2]. It is well established that genetic factors also play an important role in the pathogenesis of PCa[3]. Therefore, there is an increasing interest in the role that genetic variants such as single nucleotide polymorphic (SNPs) variants play in PCa risk.

Deficient DNA repair capacity is known to be a cancer predisposing factor[4]. DNA damage induced by reactive oxygen species (ROS) may be repaired by the base excision repair (BER) pathway. Human *OGG1* (also known as 8-oxoguanine glycosylase) is a DNA glycosylase that performs the initial step of recognizing the 8-oxo-dG damage and the subsequent step of hydrolyzing the N-glycosyl bond, which releases the damaged base but leaves a site of base loss

[apurinic (AP) site] in the DNA. Apurinic/apyrimidinic endonuclease I (APE1) then cleaves the AP site and assembles pol b onto AP sites and allows pol b and ligase III to complete the DNA repair process[5]. However, genetic variants in BER have not been well studied in PCa. Two studies have reported an association between the *OGG1* Ser326Cys polymorphism and PCa but the results are ambiguous[6,7]. Although one of the common polymorphisms T>G transversion (Asp>Glu; rs1130409) of *APE1* has shown association with various neoplasm such as the lung, stomach, head and neck[8].

The xeroderma pigmentosum complementation group C (XPC) protein plays a key role in nucleotide excision repair (NER) pathway. The functional DNA-binding domains of XPC interact with HR23B to form a complex that recognizes and binds to the sites of DNA damage[9]. Deficiency in XPC has been implicated in tumourigenesis. More than 100 polymorphic variants in the *XPC* gene have been identified and the two most common polymorphisms are Lys939Gln (*XPC* A33512C, rs2228001) and a poly (AT) insertion/deletion polymorphism (*XPC* PAT I/D) in intron 9 which have been associated with risks of many human malignancies, including cancers of lung, bladder, breast, oesophagus, skin, oral cavity, and head and neck[10]. A potential rationale behind these gene-cancer risk associations is that these genetic variants may result in alterations in phenotypes like DNA repair capacity (DRC).

In this study, we investigated whether functional variants of BER (*APE1* exon 5*, OGG1* exon 7) and NER (*XPC* PAT and exon 15) genes play any role in the pathogenesis of PCa.

Material & Methods

Study subjects: The study subjects were enrolled consecutively in department of Urology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow between January 2006 to February 2009. The participants were unrelated individuals of similar ethnicity from Lucknow and other adjoining cities of north India. All symptomatic men for lower urinary tract infection (LUTS) suspected to have PCa based on serum prostate specific antigen (PSA) >4 ng/ml and/or abnormal digital rectal examination (DRE), had transrectal systematic ultrasound-guided needle biopsies. The primary end point was the histologic presence of adenocarcinoma of the prostate in the biopsy specimen. Tumour grade was evaluated in PCa samples by the Gleason scoring system[11]. The two most common pattern of growth (well differentiated and poorly differentiated) were combined to a score. The patients were then divided in two groups - Gleason total <7 (less aggressive disease) and Gleason total ≥7 (highly aggressive disease). A total of 192 histologically confirmed PCa patients were enrolled for the study. Bone scan was conducted in patients suspected for bone metastasis. A total of 224 cancer free, unrelated, age matched healthy control individuals of similar ethnicity, randomly selected from general population from Lucknow and adjoining areas, were recruited from individuals attending PCa screening programmes. PSA was done in all the control individuals. Individuals with total PSA >4 ng/ml and/or any irregularity in DRE, or with history of cancer were excluded from the study. Serum PSA was assayed by sandwich ELISA using CanAg PSA kit, Sweden. The study was approved by the Ethical Committee Review Board of the Institute and informed written consent was obtained from each participant.

DNA extraction and genotype analysis: Standard venipuncture was used to collect five ml of peripheral blood in EDTA tubes. Genomic DNA was extracted from the stored peripheral blood by salting out method[12]. Genotyping were performed using amplification refractory mutation specific (ARMS) PCR methodology for *OGG1* exon 7 (C>G) and *APE1* exon 5 (T>G)[13,14]. Polymerase chain reaction (PCR) were used to amplify regions of *XPC*-PAT[15]. *XPC* exon 15 (A>C) was genotyped by PCR-RFLP method using *PvuII* (New England Biolabs, Beverly, MA, USA) restriction enzyme, as shown in Figs 1-4 respectively. All the four gene polymorphisms were successfully genotyped in 224 controls and 192 PCa patients.

Quality control procedures: Precise quality control procedures were applied during the genotyping process. As a negative control, PCR mix without DNA sample was used to ensure contamination free PCR product. Samples that failed to genotype were scored as missing and subjected to repetition. Ten per cent of samples from patients and controls were repeated to evaluate the quality of genotyping which showed 100 per cent concordance. Genotyping was performed without knowledge of the case or control status.

Diplotype analysis: Diplotype was constructed and the frequencies assessed using the maximum-likelihood method, using an expectation - maximization algorithm by performing 100,000 permutations through software

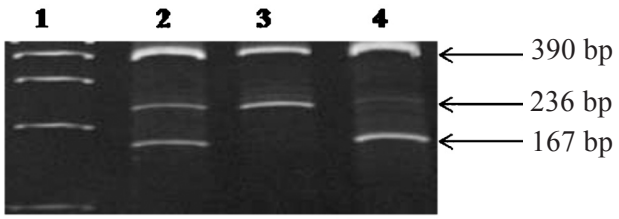

Fig. 1. Representative gel picture of *APE1* (C>G) polymorphism. Lane 1: 100bp ladder, Lane 2: hetero (TG), Lane 3: wild (TT), Lane 4: variant (GG).

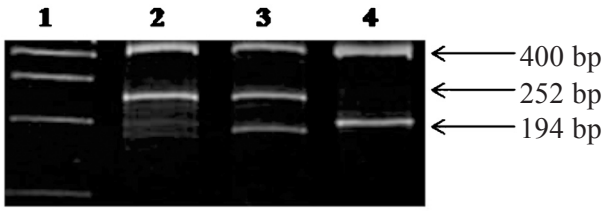

Fig. 2. Representative gel picture of *OGG1* (C>G) polymorphism. Lane 1: 100bp ladder, Lane 2: wild (CC), Lane 3: hetero (CG), Lane 4: variant (GG).

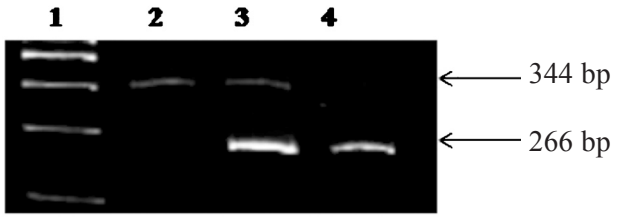

Fig. 3. Representative gel picture of *XPC* PAT polymorphism. Lane 1: 50bp ladder, Lane 2: Variant (I/I), Lane 3: Hetero (I/D), Lane 4: wild (D/D).

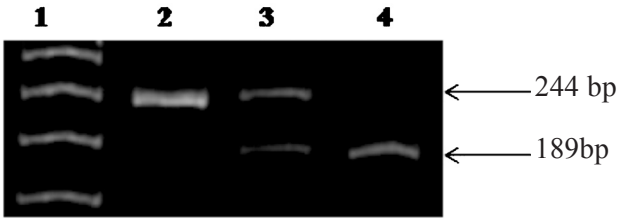

Fig. 4. Representative gel picture of *XPC* exon 15 (A>C) polymorphism. Lane 1: 50bp ladder, Lane 2: wild (AA), Lane 3: hetero (AC), Lane 4: variant (CC).

Arlequin (Version 2.0, Switzerland). Odds ratio (OR) was calculated using unconditional logistic regression for risk diplotype taking the wild-type diplotype as reference.

Statistical analyses: Power of study was calculated using Quanto program version 1.1 (*http://hydra.usc.edu/gxe*) with input of the following variables: case- control study design, significance level <0.05 (2 sided), model of inheritance=log additive, minor allele frequency=0.26 (minor allele frequency of *APE1* exon 5 which was the lowest in all of the four polymorphism), genetic effect OR <0.6 or >1.6. Present study achieved 80 per cent of power which was sufficient to consider OR of <0.6 or >1.6. Chi-square analysis was used to assess deviation from Hardy-Weinberg's Equilibrium (HWE) and to compare the genotype/allele/diplotype frequency between PCa and controls. Odds ratios were obtained by unconditional logistic regression analysis and adjusted for age as a continuous variable. Statistical significance was set at $P<0.05$. All the statistical analysis were performed with the SPSS software, version 11.5 (SPSS, Chicago, IL, USA).

Results

Demographical and clinical details of study subjects: A total of 416 individuals (192 PCa and 224 controls) were analyzed in the study. There was no significant difference between age of the patients (62.6±8.9 yr) and healthy controls (59.1±10.4 yr) and smoking habits. As expected, there was statistically significant difference ($P<0.001$) between serum PSA of PCa patients (221±57.4 ng/ml) and controls (2.3±0.8 ng/ml);

Table I. Clinical and demographic details of study subjects

	Controls (n=224)	PCa (n=192)
Age (yr) (mean ± SD)	59.1 ± 10.4	62.6 ± 8.9
Total PSA ng/ml (mean± SD)	2.3 ± 0.8	221 ± 57.4**
Demographic details		
	n (%)	n (%)
Cigarette/bidi smoking*		
Non smokers	156 (70.0)	125 (65.4)
Smokers	67 (30.0)	66 (34.6)
Clinical details		
	n (%)	n (%)
Bone metastasis		
Bone Mets (-)	--	91 (47.3)
Bone Mets (+)	--	80 (41.8)
Bone Scan not done		21 (10.9)
Gleason grade		
<7	--	106 (55.2)
≥7	--	86 (44.8)

*Numbers may not add to the total because of some missing data
PCa, prostate cancer; PSA, prostate-specific antigen
**$P<0.001$ compared to controls

Table II. Association between DNA repair gene polymorphisms and PCa risk

	Controls n (%)	Patients n (%)	OR (95%CI)Adj.	*P* value	OR (95%CI) Crude	*P* value
APE1 exon5						
TT	118 (52.7)	106 (55.2)	1.00 (Reference)		1.00 (Reference)	
TG	94 (42.0)	71 (37.0)	0.80 (0.53-1.21)	0.295	0.84 (0.56-1.26)	0.401
GG	12 (5.3)	15 (7.8)	1.34 (0.59-3.00)	0.474	1.39 (0.62-3.10)	0.420
TG+GG	106 (47.3)	86 (44.8)	0.87 (0.59-1.29)	0.496	0.90 (0.61-1.33)	0.606
T allele	330 (73.7)	283 (73.7)			1.00 (Reference)	
G allele	118 (26.3)	101 (26.3)	----------		0.99 (0.73-1.36)	0.990
OGG1 exon7						
CC	116 (51.8)	96 (50.0)	1.00 (Reference)		1.00 (Reference)	
CG	95 (42.4)	82 (42.7)	1.03 (0.69-1.54)	0.863	1.04 (0.69-1.55)	0.837
GG	13 (5.8)	14 (7.3)	1.22 (0.54-2.74)	0.628	1.30 (0.58-2.90)	0.520
CG + GG	108 (48.2)	96 (50.0)	1.05 (0.71-1.55)	0.798	1.07 (0.73-1.57)	0.716
C allele	327 (73.0)	274 (71.4)			1.00 (Reference)	
G allele	121(27.0)	110 (28.6)	----------		1.08 (0.80-1.47)	0.599
XPC PAT						
D/D	124 (55.3)	103 (53.6)	1.00 (Reference)		1.00 (Reference)	
D/I	88 (39.3)	63 (32.8)	0.84 (0.55-1.28)	0.425	0.86 (0.56-1.30)	0.484
I/I	12 (5.4)	26 (13.6)	2.55 (1.22-5.33)	0.012	2.60 (1.25-5.42)	0.010
D/I+I/I	100 (44.7)	119 (46.4)	1.29 (0.87-1.91)	0.191	1.32 (0.89-1.94)	0.159
D Allele	336 (75.0)	269 (70.1)			1.00 (Reference)	
I Allele	112 (25.0)	115 (29.9)	----------		1.28 (0.94-1.74)	0.111
XPC exon15						
AA	114 (50.9)	93 (48.4)	1.00 (Reference)		1.00 (Reference)	
AC	94 (42.0)	71 (37.0)	0.92 (0.60-1.39)	0.697	0.92 (0.61-1.39)	0.714
CC	16 (7.1)	28 (14.6)	2.15 (1.09-4.23)	0.026	**2** 2.14 (1.09-4.20)	0.026
AC + CC	110 (49.1)	99 (51.6)	1.08 (0.73-1.60)	0.673	1.10 (0.75-1.62)	0.618
A allele	322 (71.9)	257 (66.9)			1.00 (Reference)	
C allele	126 (28.1)	127 (33.1)	----------		1.26 (0.93-1.69)	0.122

OR adjusted (adj.) for age

55.2 per cent patients had <7 and 44.8 per cent patients had >7 Gleason grade at the time of diagnosis, 41.8 per cent of patients were diagnosed to have bone metastasis (Table I).

Association of APE1, OGG1 and XPC genotype variants with PCa risk: The genotypic distributions of these gene polymorphisms in the controls were in HWE. To evaluate the association between genetic variant with risk of PCa, BER genes *APE1* exon 5, *OGG1* exon 7 and NER gene *XPC* genotype frequency distribution was compared in the PCa and control group (Table II). Overall, individuals carrying the G-G (Glu/Glu) of *APE1* and G-G (Cys/Cys) homozygous genotype of *OGG1* did not demonstrate any significant risk associated with PCa. The genotype frequency distribution of *XPC* PAT and *XPC* exon 15 revealed significant association with PCa risk. *XPC* PAT insertion (II) genotype showed 2.5 fold [Adjusted (Adj.) OR-2.55, 95% CI-1.22-5.33, *P*=0.012] increased risk with PCa and variant genotype CC of *XPC* exon 15 showed 2.1 fold (Adj.OR-2.15, 95%CI-1.09-4.23, *P*=0.026) increased risk. However, no significant association was observed in case of alleles in these two gene polymorphism. Further, to elucidate the combined

Table III. Diplotype frequencies of *XPC* PAT and *XPC* exon 15 gene polymorphisms

Diplotype	Controls n (%)	Patients n (%)	OR (95%CI)	*P* value
D-A	256 (57.2)	179 (46.6)	1.00 (Reference)	
D-C	79 (17.8)	90 (23.5)	1.62 (1.14-2.32)	0.007
I-A	66 (14.6)	78 (20.2)	1.69 (1.15-2.47)	0.007
I-C	47 (10.4)	37 (9.7)	1.12 (0.70-1.80)	0.622

influence of these polymorphisms, we constructed *XPC* PAT and *XPC* exon 15 diplotype (Table III). Diplotype results showed that D of *XPC* PAT and C of exon 15, diplotype (D-C) was associated with 1.6 folds (OR-1.62, 95%CI- 1.14-2.32, *P*=0.007) and I of *XPC* PAT-A of *XPC* exon 15; (I-A) demonstrated association with increased risk of PCa (OR- 1.69, 95%- 1.15-2.47, *P*=0.007), respectively.

Analysis of APE1, OGG1 and XPC gene polymorphism with risk for higher Gleason grades: For genotypic comparison the patients with different Gleason grades were sub-categorized in to two groups (Low grade <7, High grade ≥7) based on degree of differentiation between cells. The genotypes frequencies of *APE1* exon 5 and *OGG1* exon 7 were analysed between the control and high Gleason group. Marginally significant risk was associated with combined genotype (CG+GG) of *OGG1* in higher grades of Gleason score of PCa disease, when OR was adjusted with age, significance was lost. In *XPC* PAT the variant genotype I/I demonstrated 2.8-fold increased risk (Adj.OR-2.88, 95%CI 1.22-6.79, *P*=0.015) with high Gleason grade of PCa patients. Similarly, combined genotype DI+II also showed 1.9 fold increased risk (Adj. OR-1.95, 95% CI 1.17-3.25, *P*=0.010) (Table IV).

Analysis of APE1, OGG1 and XPC polymorphism with risk for bone metastasis: Association between the *APE1, OGG1* and *XPC* gene variants and the risk associated with bone metastasis was also investigated. The PCa patients were stratified in to two groups, one with positive and the other with negative bone metastasis. No association of these polymorphism was observed with PCa bone metastasis (Table V).

Table IV. Association between DNA repair gene polymorphisms and tumour grade

	Gleason <7 (Low) n (%)	Gleason ≥7 (High) n (%)	Control vs. High		Control vs. High	
			OR (95%CI) Adj.	*P* value	OR (95%CI) Crude	*P* value
APE1 exon 5						
TT	63 (59.5)	43 (50.0)	1.00 (Reference)		1.00 (Reference)	
TG	33 (31.1)	38 (44.2)	1.05 (0.62-1.77)	0.831	1.10 (0.66-1.85)	0.692
GG	10 (9.4)	5 (5.8)	1.10 (0.36-3.32)	0.861	1.14 (0.38-3.43)	0.811
TG+GG	43 (40.5)	43 (50.0)	1.35 (0.81-2.24)	0.237	1.40 (0.85-2.31)	0.181
OGG1 exon 7						
CC	54 (50.9)	42 (48.9)	1.00 (Reference)		1.00 (Reference)	
CG	43 (40.6)	39 (45.3)	1.12 (0.67-1.88)	0.652	1.13 (0.67-1.89)	0.632
GG	9 (8.5)	5 (5.8)	0.97 (0.32-2.92)	0.959	1.06 (0.35-3.16)	0.914
CG+GG	52 (49.1)	44 (51.1)	1.61 (0.96-2.67)	0.066	1.64 (0.99-2.72)	0.054
XPC PAT						
D/D	57 (53.8)	46 (53.5)	1.00 (Reference)		1.00 (Reference)	
D/I	36 (34.0)	27 (31.4)	0.81 (0.46-1.40)	0.460	0.82 (0.47-1.43)	0.497
I/I	13 (12.3)	13 (15.1)	2.88 (1.22-6.79)	0.015	2.92 (1.24-6.86)	0.014
DI+II	49 (46.3)	40 (46.5)	1.95 (1.17-3.25)	0.010	1.99 (1.19-3.31)	0.008
XPC exon15						
AA	45 (42.5)	48 (55.8)	1.00 (Reference)		1.00 (Reference)	
AC	45 (42.5)	26 (30.2)	0.64 (0.37-1.12)	0.121	0.65 (0.37-1.13)	0.134
CC	16 (15.0)	12 (14.0)	1.80 (0.78-4.11)	0.163	1.78 (0.78-4.04)	0.168
AC+CC	61 (57.5)	38 (44.2)	1.63 (0.98-2.72)	0.057	1.66 (1.00-2.76)	0.049

Table V. ORs and 95% CIs for PCa in relation to *APE1, OGG1* and *XPC* gene polymorphism by positive metastasis and negative metastasis status

	Metastasis (-) ve n (%)	Metastasis (+) ve n (%)	OR (95% CI) Adj.	*P* value	OR (95% CI) Crude	*P* value
APE1 exon 5						
TT	44 (48.3)	50 (62.5)	1.00 (Reference)		1.00 (Reference)	
TG	41 (45.1)	24 (30.0)	0.54 (0.28-1.01)	0.073	0.51 (0.27-0.98)	0.044
GG	6 (6.6)	6 (7.5)	0.94 (0.28-3.16)	0.920	0.88 (0.26-2.92)	0.835
TG+GG	47 (51.7)	30 (37.5)	0.83 (0.44-1.55)	0.571	0.80 (0.43-1.47)	0.476
OGG1 exon 7						
CC	41 (45.1)	40 (50.0)	1.00 (Reference)		1.00 (Reference)	
CG	41 (45.1)	36 (45.0)	0.92 (0.49-1.74)	0.816	0.90 (0.48-1.68)	0.741
GG	9 (9.8)	4 (5.0)	0.48 (0.13-1.70)	0.257	0.45 (0.13-1.59)	0.220
CG+GG	50 (54.9)	40 (50.0)	1.07 (0.58-1.97)	0.816	1.04 (0.57-1.91)	0.876
XPC PAT						
D/D	43 (47.2)	49 (61.2)	1.00 (Reference)		1.00 (Reference)	
D/I	34 (37.4)	24 (30.0)	0.63 (0.32-1.24)	0.184	0.61 (0.31-1.20)	0.157
I/I	14 (15.4)	7 (8.8)	0.44 (0.16-1.20)	0.111	0.43 (0.16-1.18)	0.105
DI+I I	48 (51.8)	21 (38.8)	1.01 (0.55-1.86)	0.954	1.01 (0.55-1.84)	0.974
XPC exon 15						
AA	41 (45.1)	41 (51.3)	1.00 (Reference)		1.00 (Reference)	
AC	36 (39.5)	29 (36.3)	0.81 (0.42-1.56)	0.532	0.80 (0.41-1.54)	0.516
CC	14 (15.4)	10 (12.4)	0.73 (0.29-1.86)	0.520	0.71 (0.28-1.79)	0.473
AC+CC	50 (54.9)	39 (48.7)	1.01 (0.55-1.86)	0.954	1.01 (0.55-1.84)	0.974

Interaction of APE1, OGG1 and XPC polymorphism with smoking habit in PCa: The gene-smoking interaction was evaluated to study the modulation of PCa risk with respect to *APE1, OGG1* and *XPC* gene polymorphisms. The PCa patients were grouped in to non smoker (never smoked) and smokers (smoking more than 5 yr). On analyzing the genotype frequency between these two groups for susceptibility to PCa, none of the polymorphisms demonstrated association (data not shown).

Discussion

Multiple repair mechanisms have been evolved in humans to minimize the consequences of DNA damage, preserving genomic integrity. The DNA repair pathways like BER and NER repair specific types of lesions, and individuals with a suboptimal repair capacity may have higher susceptibility to PCa.

In the present study, we did not find evidence to support such an association between the variant genotype GG (Glu/Glu) of *APE1* and GG (Cys/Cys) genotype of *OGG1* in the aetiology of PCa. Some earlier studies showed that the *APE1* variant (Glu) genotype did not affect the frequency of X-ray or ultraviolet-induced chromosome aberrations[16]. However, many studies have investigated the association between *APE1* T>G (Glu/Glu) and cancer risks; conversely, the findings were varied among different ethnic populations and different cancer types. Agachan *et al*[17] found that the GG genotype was associated with the risk of lung cancer in a Turkey population, whereas others[18,19] did not observe any association with PCa and bladder cancer. Although *OGG1* is abundantly expressed in prostate tissue, initially the *OGG1* 326Ser enzyme was shown to have higher activity than the 326Cys variant enzyme[20]. Several studies have shown that the frequency of the *OGG1*

G>C polymorphism depends on race and ethnicity. Our finding is consistent with the result of a previous study of *OGG1* G>C polymorphism in PCa risk[21]. But our results contradict the findings of another study, in which a significantly elevated risk of PCa was observed[7].

We observed that individuals with *XPC* PAT Ins/Ins and *XPC* exon 15 CC genotypes were at significant increased risk of PCa. A recent meta-analysis of 34 case-control studies by Zhang *et al*[10] showed *XPC* Lys939Gln allele C and *XPC* PAT I allele to be associated with lung, breast, bladder, colorectal, oesophageal, and other cancer risks. Therefore, it can be speculated that functional variation of *XPC* may influence the individual susceptibility of PCa. Qiao *et al*[22] studied *XPC* genotype-related DRC using a host-cell re-activation assay and found that healthy subjects with the homozygous variant genotype of the PAT polymorphism (I/I) exhibited lower DRC as compared to wild-type carriers (D/D), and has been proposed as a useful biomarker to identify individuals at increased risk for developing cancer. Blankenburg *et al*[23] reported that *XPC* PAT and exon 15 polymorphisms are associated with risk of melanoma, while Hirata *et al*[24] reported significantly reduced risk of PCa with *XPC* Lys939Gln (CC) genotype. Interestingly, diplotype of *XPC* PAT and exon 15 (D-C, p- 0.007; I-A, p-0.007) demonstrated increased risk with PCa[24]. Gleason grade is generally used to categorize the patients based on cell differentiation. We observed significant association of *XPC* PAT with high Gleason grade of PCa. This indicated that these polymorphisms may have a role in the initiation of PCa. We did not find significant association of these two polymorphisms (*APE1* and *OGG1*) with high Gleason grade of PCa. However, there was no association either with bone metastasis in PCa. Thus, the interactions among genetic polymorphisms in NER pathway genes may affect the DNA damage repair capacity and contribute to increased PCa risk.

In conclusion, our results suggested that the *XPC* PAT and *XPC* exon 15 polymorphisms may be a risk for PCa in north Indian population. Moreover, the diplotype analysis of *XPC* PAT and *XPC* exon 15 was also found to be associated with PCa risk. Further studies are warranted to validate these observations with large sample size and diverse ethnicity.

Conflict of interest: The authors report no conflicts of interest.

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