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PREVALENCE OF G6721T POLYMORPHISM OF *XRCC7* IN AN IRANIAN POPULATION

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ABSTRACT

Genetic polymorphism G6721T (rs.7003908) in gene encoding DNA-dependent protein kinase (DNA-PKcs, encoded by the *XRCC7* gene) has been defined. In order to get more insight into the genetic structure of Iranian population the present study was carried out on Iranian Persian population living in Shiraz (Fars province, southwest Iran). The total study subjects consisted of 935 (195 males, 740 females) unrelated healthy individuals. Genotypes of *XRCC7* G6721T were detected by PCR-RFLP based method. There was no significant difference between males and females for the *XRCC7* polymorphism (χ^2=1.275, df=2, P=0.529). Prevalence of the G allele was 0.473 (95 % CI: 0.441-0.505) in our sample. The study population was at Hardy-Weinberg equilibrium for the *XRCC7* polymorphism (χ^2=0.980, df=1, P=0.323). The allelic frequency of the G allele showed high frequency in Iranian population compared to other populations.

Keywords: Iran, polymorphism, population genetics, *XRCC7*

INTRODUCTION

DNA-dependent protein kinase (DNA-PKcs, encoded by the *XRCC7* gene, MIM:600899, NM_001469) is recruited to DNA double-strand break (DSB) sites by the Ku70/Ku80 heterodimer to form the active DNA-PK complex (Gottlieb and Jackson 1993). DNA-PK activity is activated by binding to free DNA ends and catalyzes rejoining of DSB (Hartley et al., 1995). Thus, DNA-PK activity is essential for non-homologous end joining and V(D)J recombination. Deficiencies in DNA-PK activity are clinically significant. Mice with inactivated components of DNA-PK show severe combined immunodeficiency as well as ionizing radiation hypersensitivity (Singleton et al., 1997; Ferguson et al., 2000).

The genetic G6721T polymorphism of *XRCC7* (rs.7003908), in intron 8, may regulate splicing and cause mRNA instability (Sipley et al., 1995). The association between G6721T polymorphism of *XRCC7* and cancers has been studied (Wang et al., 2004, 2008; Hirata et al., 2006, 2007; Liu et al., 2007; Gangwar et al., 2009).

Iran has one of the most heterogeneous populations of the world (Amirshahi et al., 1989; Walter et al., 1991; Rafiee et al., 2010). The distribution of serum proteins, blood groups, and red cell enzymes in Iranian populations has been studied by different investigators (Amirshahi et al., 1989; Walter et al., 1991). Very recently we had reported the frequencies of some genetic polymorphisms from several Iranian populations using DNA analysis (Saadat et al., 2004a-c, 2007; Saadat and Dadbine-Pour 2005; Saadat 2006, 2010; Bazrgar et al., 2008; Mohamadynejad and Saadat 2008; Masoudi et al., 2009).

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Since genetic polymorphism of *XRCC7* and cancer susceptibility varies in different ethnic groups and no report is available on the prevalence of G6721T polymorphism of *XRCC7* in Iranian population, and also to get more insight into the genetic structure of Iranian population, the present study was carried out on healthy individuals.

MATERIALS AND METHODS

Subjects

The present study was performed in Shiraz (Fars province, southern Iran). The total study subjects consisted of 935 (195 males, 740 females) unrelated adult healthy blood donors. All individuals were healthy as assessed by medical history. The mean age (SD; Min–Max) of the participants was 39.2 (9.2; 23-50) years.

Informed consent was obtained from each subject before the study. The study was approved by the institutional review board at our department.

DNA extraction and genotyping analysis

Genomic DNA was extracted from whole blood samples. Genotypic analysis for the polymorphism of *XRCC7* was determined by PCR-RFLP assay, as described previously (Wang et al., 2004).

To test for contamination, negative controls (tubes containing the PCR mixture, without the DNA template) were incubated in every run. Any sample with ambiguous result due to low yield was retested and a random selection of 15 % of all samples was repeated. No discrepancies were discovered upon replicate testing.

Statistical analysis

A Chi-square test was performed for *XRCC7* polymorphism to determine if the sample groups demonstrated Hardy-Weinberg equilibrium. The difference in genotypic frequencies between sex groups was determined using the Chi-square test of goodness of fit. A probability of $P<0.05$ was considered statistically significant. All P-values were two-tailed.

RESULTS AND DISCUSSION

Genotypic frequencies of *XRCC7* among study population are shown in Table 1. There were no significant gender differences for the *XRCC7* polymorphism (χ^2=1.275, df=2, P=0.529). Prevalence of the G allele for the total study group was 0.473 (95 % CI: 0.441-0.505) (Table 2). The study population was at Hardy-Weinberg equilibrium (χ^2=0.980, df=1, P=0.323).

Table 1: Distribution of the G7621T *XRCC7* genotypes among healthy blood donors in Shiraz population (southern Iran)

Genotypes	Females	Males	Total
TT	212	55	267
TG	362	89	451
GG	166	51	217
Total	740	195	935

Table 2: Allelic frequency for the *XRCC7* G7621T polymorphism among healthy blood donors in Shiraz population (southern Iran)

Alleles	Females	Males	Total
G	0.469	0.490	0.473
T	0.531	0.510	0.527

Table 3 shows the prevalence of the G allele in several populations using published articles or data presented on NCBI Entrez SNP (www.ncbi.nlm.nih.gov/projects/snp). The frequency of the polymorphic allele varies among populations, suggesting an ethnic distribution (Wang et al., 2004, 2008; Hirata et al., 2006, 2007; Liu et al., 2007; Gangwar et al., 2009).

Table 3: Distribution of the G allele of *XRCC7* G7621T polymorphism among African, Asian and Caucasian populations

Country/ethnicity	(%)	References
West Africa	0.317	NCBI Entrez SNP
African/African American	0.271	NCBI Entrez SNP
Japan	0.276	Hirata et al., 2007
Japan	0.289	Hirata et al., 2006
China	0.203	Liu et al., 2007
China	0.279	Wang et al., 2008
East Asia	0.281	NCBI Entrez SNP
India	0.448	Gangwar et al., 2009
USA	0.387	Wang et al., 2004
Hispanic	0.326	NCBI Entrez SNP
Caucasians	0.425	NCBI Entrez SNP
Caucasians	0.355	NCBI Entrez SNP
Iran	0.473	Present study

There were significant differences in terms of the G allele frequency between the three major ethnic groups (Wang et al., 2004, 2008; Hirata et al., 2006, 2007; Liu et al., 2007; Gangwar et al., 2009). The frequency of the G allele was about 38 % among Caucasians (Wang et al., 2004; NCBI Entrez SNP). The prevalence of the G allele was lower among Africans and Asian populations (Hirata et al., 2006, 2007; Liu et al., 2007; Wang et al., 2008; NCBI Entrez SNP). The allelic frequency of the G in our sample (about 47 %) seems to be more similar to the Caucasians than to Asians. The G allele showed high frequency in Iranian (=47.1 %) and Indian (=44.8 %) populations (Gangwar et al., 2009; present study). We know that both Indian and Iranian ethnic groups biologically belong to Caucasoid. Our present data showed high similarity between these two populations for the prevalence of the G allele.

Previous reports for other genetic polymorphisms, such as *GSTM1*, *GSTT1*, *GSTO2*, *XRCC1*, *CC16* and *GRIN1*, showed intermediate frequency of the Iranian gene pool showed in comparison with European Caucasians and Asians (Saadat et al., 2004a-c, 2007; Saadat and Dadbine-Pour 2005; Saadat 2006, 2010; Bazrgar et al., 2008; Mohamadynejad and Saadat 2008; Masoudi et al., 2009). However the present study on the *XRCC7* polymorphism did not coincide with this conclusion. Some evolutionary forces may be responsible for this difference.

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DISCLOSURE STATEMENT

No competing financial interests exist.

REFERENCES

Amirshahi P, Sunderland E, Farhud DD, Tavakoli SH, Daneshmand P, Papiha SS. Serum proteins and erythrocyte enzymes of populations in Iran. Hum Hered 1989; 39:75-80.

Bazrgar M, Karimi M, Fathzadeh M, Senemar S, Peiravian F, Shojaee A et al. Apolipoprotein E polymorphism in Southern Iran: E4 allele in the lowest reported amounts. Mol Biol Rep 2008;35:495-9.

Ferguson DO, Sekiguchi JM, Chang S, Frank KM, Gao Y, DePinho RA et al. The non-homologous end-joining pathway of DNA repair is required for genomic stability and the suppression of translocations. Proc Natl Acad Sci USA 2000;97:6630-3.

Gangwar R, Ahirwar D, Mandhani A, Mittal RD. Do DNA repair genes OGG1, XRCC3 and XRCC7 have an impact on susceptibility to bladder cancer in the North Indian population? Mutat Res 2009; 680:56-63.

Gottlieb TM, Jackson SP. The DNA-dependent protein kinase: Cell 1993;72: 131-42.

Hartley KO, Gell D, Smith GC, Zhang H, Divecha N, Connelly MA et al. DNA-dependent protein kinase catalytic subunit: a relative of phosphatidylinositol 3-kinase and the ataxia telangiectasia gene product. Cell 1995;82:849-56.

Hirata H, Hinoda Y, Matsuyama H, Tanaka Y, Okayama N, Suehiro Y et al. Polymorphisms of DNA repair genes are associated with renal cell carcinoma. Biochem Biophys Res Commun 2006;342: 1058-62.

Hirata H, Hinoda Y, Tanaka Y, Okayama N, Suehiro Y, Kawamoto K et al. Polymorphisms of DNA repair genes are risk factors for prostate cancer. Eur J Cancer 2007;43:231-7.

Liu Y, Zhang H, Zhou K, Chen L, Xu Z, Zhong Y et al. Tagging SNPs in non-homologous end-joining pathway genes and risk of glioma. Carcinogenesis 2007; 28:1906-13.

Masoudi M, Saadat I, Omidvari S, Saadat M. Genetic polymorphisms of *GSTO2*, *GSTM1*, and *GSTT1* and risk of gastric cancer. Mol Biol Rep 2009;36:781-4.

Mohamadynejad P, Saadat M. Genetic polymorphisms of *XRCC1* (at codons 194 and 399) in Shiraz population (Fars province, southern Iran). Mol Biol Rep 2008; 35:669-72.

Rafiee L, Saadat I, Saadat M. Glutathione S-transferase genetic polymorphisms (*GSTM1*, *GSTT1* and *GSTO2*) in three Iranian populations. Mol Biol Rep 2010;37: 155-8.

Saadat M. Genetic polymorphisms of glutathione S-transferase T1 (*GSTT1*) and susceptibility to gastric cancer, a meta-analysis. Cancer Sci 2006;97:505-9.

Saadat M. Association between the G1001C polymorphism of N-methyl-D-aspartate receptor NR1 subunit gene (*GRIN1*) and susceptibility to schizophrenia, a meta-analysis of the literatures. EXCLI Journal 2010;9:11-6.

Saadat M, Dadbine-Pour A. Influence of polymorphism of glutathione S-transferase M1 on systolic blood pressure of normotensive individuals. Biochem Biophys Res Commun 2005;326:449-54.

Saadat M, Bahaoddini A, Mohabatkar H. Polymorphisms of glutathione S transferase M1 and T1 modulate blood pressure of individuals chronically exposed to natural sour gas containing sulfur compounds. Biochem Biophys Res Commun 2004a; 316:749-52.

Saadat M, Farvardin-Jahromi M, Saadat H. Null genotype of glutathione S-transferase M1 is associated with senile cataract susceptibility in non-smoker females. Biochem Biophys Res Commun 2004b;319: 1287-91.

Saadat M, Saadat I, Saboori Z, Emad A. Combination of *CC16*, *GSTM1*, and *GSTT1* genetic polymorphisms is associated with asthma. J Allergy Clin Immunol 2004c;113:996-8.

Saadat M, Mobayen F, Farrashbandi H. Genetic polymorphism of glutathione S-transferase T1: a candidate genetic modifier of individual susceptibility to schizophrenia. Psychiatry Res 2007;153:87-91.

Singleton BK, Priestley A, Steingrimsdottir H, Gell D, Blunt T, Jackson SP et al. Molecular and biochemical characterization of xrs mutants defective in Ku80. Mol Cell Biol 1997;17:1264-73.

Sipley JD, Menninger JC, Hartley KO, Ward DC, Jackson SP, Anderson CW. Gene for the catalytic subunit of the human DNA-activated protein kinase maps to the site of the XRCC7 gene on chromosome 8. Proc Natl Acad Sci USA 1995;92:7515-9.

Walter H, Farhud DD, Danker-Hopfe H, Amirshahi P. Investigations on the ethnic variability of the ABO blood group polymorphism in Iran. Z Morphol Anthropol 1991;78:289-306.

Wang LE, Bondy ML, Shen H, El-Zein R, Aldape K, Cao Y et al. Polymorphisms of DNA repair genes and risk of glioma. Cancer Res 2004;64:5560-3.

Wang SY, Peng L, Li CP, Li AP, Zhou JW, Zhang ZD et al. Genetic variants of the XRCC7 gene involved in DNA repair and risk of human bladder cancer. Int J Urol 2008;15:534-9.