



Single nucleotide polymorphism in the *RECQL5* gene increased osteosarcoma susceptibility in a Chinese Han population

Y.Z. Dong, Y.X. Huang and T. Lu

Department of Orthopedics,
The First Affiliated Hospital of Xinxiang Medical College, Weihui, China

Corresponding author: Y.Z. Dong
E-mail: dongy_zhen@yeah.net

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ABSTRACT. In this study, we investigated the association between a *RECQL* genetic polymorphism and osteosarcoma in a Chinese population. We selected rs820196 in the *RECQL5* gene and genotyped 185 patients with osteosarcoma and 201 age- and gender-matched non-cancer controls. We found that the CC genotype was more frequent in the osteosarcoma group compared to the control group ($P = 0.011$). We also found that the C allele was more common in osteosarcoma patients than that in control subjects ($P = 0.004$). Our results suggested that the *RECQL5* genetic polymorphism was associated with osteosarcoma in a Chinese population.

Key words: Osteosarcoma; Polymorphism; *RECQL5*

INTRODUCTION

Osteosarcoma (OS) is the most common malignancy in bone and is most frequently observed in children and young adults (Dorfman and Czerniak, 1995). The exact mechanisms of osteosarcoma are largely unknown, but many studies have suggested that multiple genetic and environmental factors play important roles in OS carcinogenesis. Patients with localized OS at presentation have a 60-80% rate of long-term survival, while metastatic disease carries a poorer prognosis (Kager et al., 2003; Mirabello et al., 2009). Previous studies suggested that OS is a complex disease resulting from the interaction between environmental factors and genetics (Zhou et al., 2014; Wang et al., 2014).

Recently, studies have indicated that DNA damage leads to genomic instability, cancer transformation, or cell death (Bohr, 2008). The *RECQ* family is a highly conserved group of DNA helicases required to maintain genome stability and integrity, which plays important roles in DNA replication and repair pathways including mismatch repair, nucleotide excision repair, and direct repair (Sharma et al., 2006; Hu et al., 2007). Therefore, *RECQL5* has been reported to be associated with several cancers, and genetic polymorphisms may increase the risk of human cancers (Hu et al., 2007; Pellatt et al., 2012). *RECQL5* is one member of the *RECQL* family. The relationship between the polymorphism and OS is not understood. In the present study, we investigated the association between *RECQL5* gene polymorphisms and OS in a Chinese population.

MATERIAL AND METHODS

Study population

Written informed consent was obtained from each participant. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Xinxiang Medical College.

A total of 185 patients diagnosed with OS (7-44 years of age) and 201 healthy subjects (10-45 years of age) were included in the present study. All subjects were recruited from the First Affiliated Hospital of Xinxiang Medical College between March 2001 and March 2012. The cancer-free controls were matched with OS patients with regards to gender, age, and residence area.

Genotyping

Genomic DNA was extracted from peripheral blood leukocytes using a DNA extraction Kit (Beijing Biotek Co. Ltd., Beijing, China). Genotyping was confirmed by TaqMan method as described previously (Li et al., 2009).

Statistical analyses

All statistical analyses were conducted using the Statistical Package for Social Sciences software (SPSS, Windows version release 15.0; SPSS Inc., Chicago, IL, USA). Hardy-Weinberg equilibrium in allele and genotype distribution was assessed by using the chi-squared (χ^2) test. The odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated by unconditional logistic regression and utilized to evaluate the potential associations between *RECQL5* genetic variants and OS risk. Statistical significance was established at $P < 0.05$.

RESULTS

We enrolled 185 OS patients and 201 healthy control subjects. The general characteristics of the 2 groups are shown in Table 1. There were no significant differences between OS patients and cancer-free controls in gender, age, tumor location, and metastasis.

Table 1. Clinical characteristics of osteosarcoma cases and controls.

Characteristics	Cases [N (%)]	Controls [N (%)]	P value
Number	185	201	
Gender (male)	97 (52.4)	101 (50.2)	0.634
Age (years)	32.3 ± 12.1	33.1 ± 12.4	0.565
Tumor location			
Long tubular bones	121 (65.4)	-	
Axial skeleton	64 (34.6)	-	
Metastasis			
Yes	84 (45.4)	-	
No	101 (54.6)	-	

The genotype distribution showed no significant difference from Hardy-Weinberg equilibrium values (data not shown). We found that the CC genotype in rs820196 was more frequent in the OS group than in the control group. We also found that the C allele of rs820196 was more common in the OS patients than in control subjects (OR = 1.87, 95%CI = 1.21-1.97; P = 0.001; Table 2).

Table 2. Genotype distribution of *RECQL5* SNP between cases and controls.

SNPs	Genotype and allele	Osteosarcoma (N = 185)	Control (N = 201)	OR (95%CI)	P value
rs820196	CC	30 (0.162)	18 (0.090)		0.005
	CT	96 (0.519)	102 (0.507)		
	TT	59 (0.319)	81 (0.403)		
	C	156 (0.422)	138 (0.338)	1.87 (1.21-1.97)	
	T	214 (0.578)	264 (0.338)		

DISCUSSION

In this study, we found that the *RECQL5* gene polymorphism was associated with OS risk in a Chinese population. Previous studies indicated that *RECQL5* plays a role in DNA replication, DNA repair, homologous recombination, and RNA polymerase II-mediated transcription (Pellatt et al., 2012). Additionally, the *RECQL5* polymorphism was reported to be associated with colon cancer (Pellatt et al., 2012). However, the relationship between the *RECQL5* polymorphism and OS is unknown. To clarify the relationship between the *RECQL5* genetic polymorphism and OS, we performed a case-control study to genotype 1 single nucleotide polymorphism in the *RECQL5* gene in a Chinese population. We found that the genotype distribution for rs820196 was significantly different between OS patients and control subjects. This suggested that subjects with the C allele of rs820196 increased the susceptibility to OS.

There were several limitations to this study. The sample size was relatively small, which may have affected the power of the statistical analysis; additionally, we did not perform a functional study to examine the mechanism of how genetic polymorphisms in *RECQL5* affect OS risk.

In conclusion, our findings suggest that OS is associated with the *RECQL5* gene polymorphism in a Chinese Han population.

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