J Hum Genet (1999) 44:270–271

BRIEF REPORT — POLYMORPHISM REPORT

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An *Nco*I polymorphism in the human complement component 7 (*C7*) gene

Received: March 25, 1999 / Accepted: April 3, 1999

Abstract A novel polymorphic site has been found in the 3′ untranslated region (UTR) of the human complement component 7 (*C7*) gene. The polymorphic site at 14-bp downstream from the TAG stop codon was either C or A (*Nco* I-digested), with allele frequencies of 0.660 and 0.340. This *Nco*I polymorphism would be useful to perform a DNA marker haplotype study in patients with deficiencies of the complement genes, such as *C6*, *C7*, *C9*, which are located closely on chromosome 5p13.

Key words C7 · *Nco*I · Polymorphism · 3′-UTR

Introduction

The human complement component 7 (C7) is one of five constituents of the membrane attack complex (MAC) of the complement system. The formation of MAC on the target pathogens results in the formation of transmembrane pores that eventually leads to lysis of targets. C7 protein consists of 821 amino acid residues and is structurally similar to the other members of MAC; C6, C8α, C8β, and C9 (DiScipio et al. 1988, Hobart et al. 1995). The genes for *C7*, as well as those for *C6* and *C9*, are located closely on chromosome 5p13 (Setién et al. 1993). Recently, the molecular bases of the deficiencies for these genes have been described (Nishizaka et al. 1996a, 1996b; Kojima et al. 1998; Horiuchi et al. 1998, 1999). In particular, C9 deficiency is very common in Japanese, estimated to be one homozygote in 1000 (Hayama et al. 1989). In the present study, we found an *Nco*I polymorphism in the 3′ untranslated region (UTR) of the *C7* gene. This polymorphism would be useful to perform a DNA marker haplotype study in patients with deficiencies of these complement genes.

Polymorphism and allele frequency

Primers for the polymerase chain reaction (PCR)

For PCR, we used the following primers:
C7-ex17F 5′-CTCCACAATGTACCATTAAGC-3′
C7-ex17R 5′-TGTGCAGATGTTTTCACTCAG-3′

*Nco*I *polymorphism.* The fragment size of the PCR product is 293 bp (Nishizaka et al. 1996b). *Nco*I digestion produces a 293-bp undigested fragment in the A1 allele that lacks the *Nco*I site, while in the A2 allele having the *Nco*I restriction site, two fragments, with lengths of 236 and 57 bp, are generated.

Chromosomal localization. The human *C7* gene has been assigned to chromosome 5p13.

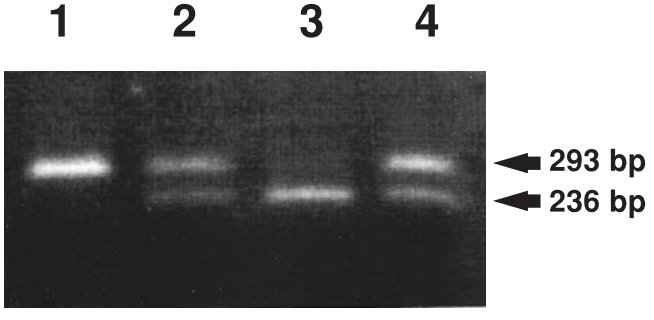

Fig. 1. *Nco*I restriction fragment length polymorphism (RFLP), *Nco*I digests were electrophoresed on 1.5% agarose gel. *Lane 1* indicates a homozygote for A1; *lanes 2 and 4* are heterozygotes for A1/A2; *lane 3* indicates a homozygote for A2. The smaller *Nco*I-digested fragments in the A2 allele (*lanes 2, 3, and 4*) were not clearly observed in this gel condition

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Table 1. Allele frequencies of *Nco*I polymorphisms of the human *C7* gene among 47 Japanese

Allele	Nucleotide	Fragments (bp)	Frequency	Heterozygosity
A1	C	293	0.660	0.468
A2	A	236, 57	0.340	

Mendelian inheritance. Mendelian inheritance was confirmed in two families.

Other comments. The primers, C7-ex17F and C7-ex17R, were intron-based exon-specific primers for exon 17 of the *C7* gene. In the process of screening for *C7* gene mutations in patients with C7 deficiency, using PCR-single-strand conformation polymorphism (SSCP) analysis, we identified this *Nco*I polymorphism. The nucleotide sequence at 14-bp downstream from the TAG stop codon was either C or A (*Nco*I-digested). PCR was carried out in a total volume of 25 μl reaction mixture, containing 1 μg genomic DNA, 2 μM of each primers, 200 μM dNTP, and 2.5 U Taq polymerase, and the standard buffer provided by the manufacturer (Perkin Elmer, Norwalk, CT, USA). Reactions were conducted for 30 cycles consisting of 1 min at 95°C and 2 min at 60°C, using a thermal cycler (PJ2000; Perkin Elmer). After the digestion of the PCR products with *Nco*I, the digests were subjected to 1.5% agarose gel electrophoresis and were visualized with ethidium bromide.

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