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BRIEF REPORT — POLYMORPHISM REPORT

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Human C-reactive protein (*CRP*) 1059G/C polymorphism

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Abstract We found a novel G → C change at nucleotide 1059 within exon 2 of the *CRP* gene encoding the C-reactive protein. The *CRP* 1059G/C polymorphism could be detected by digestion with endonuclease *Mae*III. The frequency of the *CRP* 1059C allele was 0.109 in Caucasians, but it was absent from Canadian Oji-Cree. Because of the importance of the *CRP* gene product in inflammation and its recent association with ischemic heart disease syndromes, this polymorphism may be useful in the association studies of atherosclerosis and its related phenotypes.

Key words Atherosclerosis · Inflammation · Risk factor

Introduction

Human C-reactive protein (CRP) was originally observed in the plasma of patients with acute infections and was found to react with the C polysaccharide of the pneumococcus (Tillett and Francis, 1930). It is an acute-phase reactant, because of a pronounced rise in concentration, up to 1000-fold or more, after tissue injury or inflammation. Acute-phase reactant CRP is produced in the liver, while CRP that is detectable on lymphocytes is produced by those cells (Kuta and Baum 1986). Based on in-vitro and in-vivo experiments, CRP appears to recognize both foreign pathogens and damaged host cells and can initiate their elimination by interacting with humoral and cellular effector systems in the blood (Kilpatrick and Volanakis 1991).

Recent experiments suggest that CRP may also be related to the development of atherosclerosis, since the development of coronary atherosclerosis in certain patients seems to be associated with a relapsing inflammatory process occurring within the coronary intima (Ridker 1999). Also, CRP has been associated with atherosclerosis-related phenotypes, such as measures of obesity, insulin resistance, and subclinical atherosclerosis (Hak et al. 1999). Thus, the *CRP* gene is an important candidate gene for atherosclerosis and some of its related phenotypes. In the course of DNA sequencing of all of the coding regions and the 5′- and 3′-untranslated regions of the *CRP* gene in a Canadian subject with diabetes and early coronary heart disease, we identified a novel, previously unreported G → C change at nucleotide 1059, which is contained within exon 2.

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Polymorphism and allele frequency

Primers for the polymerase chain reaction (PCR). For PCR, we used the following primers:
CRP-1059F 5′-GATCTGTGTGATCTGAGAAACCTCT-3′
CRP-1059R 5′-GAGGTACCAGAGACAGAGACGTG-3′

*Mae*III *polymorphism.* The PCR product size was 744 bp. Digestion of the less common 1059C allele produced two smaller fragments, with sizes of 434 and 310 bp. Digestion of the more common 1059G allele produced three fragments, with sizes of 310, 233, and 201 bp.

Chromosomal localization. The human *CRP* gene was mapped to chromosome 1q21 (Floyd-Smith et al. 1986).

Mendelian inheritance. Mendelian inheritance was confirmed in two large families.

Other comments. Nucleotide 1059 is within exon 2, but is silent at the amino acid level (CTG → CTC, Leu → Leu). Target DNA was amplified using an initial melting temperature of 94°C for 5 min, followed by 30 cycles of 94°C for 30 s, 57°C for 30 s, and 72°C for 30 s. A final 72°C extension step for 10 min terminated the process. The fragments were visualized in 2% agarose gels.

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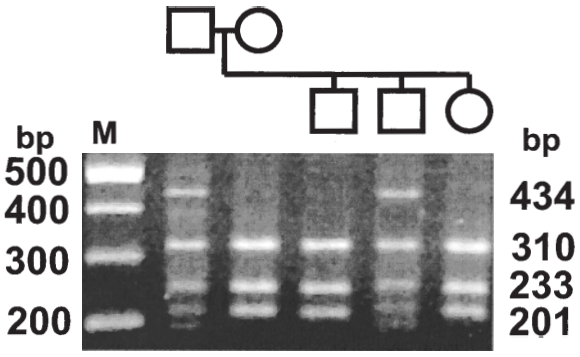

Fig. 1. *Mae*III restriction fragment length polymorphism (RFLP) detecting *CRP* 1059G/C polymorphism. *Mae*III digests were electrophoresed in 2% agarose gels. *Pedigree structure* indicates familial relationships between samples. *M* indicates molecular weight marker. *Numerals on left side* correspond to molecular weight marker band sizes. *Numerals on right side* correspond to fragment sizes

Table 1. Allele frequencies of *CRP* 1059G/C polymorphism as detected by *Mae*III

Allele	Nucleotide	Fragments (bp)	Frequency	
			Caucasian (n = 64)	Oji-Cree (n = 32)
1059G	G	434 + 310	0.891	1.0
1059C	C	310 + 233 + 201	0.109	0.0

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