doi: 10.1111/j.1744-313X.2008.00753.x

The frequency of transforming growth factor-β1 gene polymorphisms in a normal southern Iranian population

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Summary

Several single nucleotide polymorphisms (SNPs) of the transforming growth factor-β1 gene (*TGFB1*) have been reported. Determination of *TGFB1* SNPs allele frequencies in different ethnic groups is useful for both population genetic analyses and association studies with immunological diseases. In this study, five SNPs of *TGFB1* were determined in 325 individuals from a normal southern Iranian population using polymerase chain reaction–restriction fragment length polymorphism method. This population was in Hardy–Weinberg equilibrium for these SNPs. Of the 12 constructed haplotypes, GTCGC and GCTGC were the most frequent in the normal southern Iranian population. Comparison of genotype and allele frequencies of *TGFB* SNPs between Iranian and other populations (meta-analysis) showed significant differences, and in this case the southern Iranian population seems genetically similar to Caucasoid populations. However, neighbour-joining tree using Nei's genetic distances based on TGF-β1 allele frequencies showed that southern Iranians are genetically far from people from the USA, Germany, UK, Denmark and the Czech Republic. In conclusion, this is the first report of the distribution of *TGFB1* SNPs in an Iranian population and the results of this investigation may provide useful information for both population genetic and disease studies.

Introduction

Transforming growth factor-β1 (TGF-β1) is a multifunctional cytokine that plays important roles in modulation of cellular growth and differentiation, immunoregulation and extracellular matrix formation (Smith, 1996; Roberts, 1998; Ling & Robinson, 2002; Wenner & Yan, 2003). TGF-β1 is secreted by many cell types, including peripheral blood mononuclear cells and T regulatory lymphocytes. The human TGF-β1 gene (*TGFB1*) is located on chromosome 19q13 and contains seven exons (Lawrence, 1996; Clark & Coker, 1998).

Several polymorphisms in *TGFB1* have been reported (Cambien *et al*., 1996; Awad *et al*., 1998; Syrris *et al*., 1998). Three polymorphisms have been reported in *TGF-β1* promoter region at positions –988, –800 and –509 (Cambien *et al*., 1996; Awad *et al*., 1998). The –988 variant of TGF-β1 has low frequency and is not included in most studies (Cambien *et al*., 1996). The –800G→A substitution contributes to the lower production of total TGF-β1 in the circulation (Syrris *et al*., 1998). In addition, it has been reported that –509C→T polymorphism is significantly associated with a higher plasma concentration of TGF-β1 (Grainer *et al*., 1999).

A T→C transition at nucleotide (nt) 29 of *TGFB1* results in a Leu→Pro substitution at amino acid position 10 of the signal peptide. This substitution can potentially affect TGF-β1 secretion (Yamada *et al*., 1998; Grainer *et al*., 1999; Yokota *et al*., 2000; Pelletier *et al*., 2000; Dunning *et al*., 2003). In addition, a polymorphism at nt 74G→C that changes codon 25 (Arg→Pro) in the signal sequence has been associated with interindividual variation in the TGF-β1 levels (Awad *et al*., 1998). The 788C→T (Thr263 Ile) polymorphic site is located in the part of the TGF-β1 pro-protein that is cleaved from the active part at the level of amino acid 278. It has been proposed that, activation of latent TGF-β1 is a component in the sequence of events leading to growth regulation by this cytokine (Lyons *et al*., 1990).

The determination of *TGFB1* SNPs allele frequencies in different ethnic groups is useful for both population genetic analyses and association studies with immunological diseases. In this study, five known SNPs of *TGFB1* were determined in 325 individuals from a normal southern Iranian population by polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) method. Allele frequencies, as well as genotype and haplotype distribution of these SNPs in this Iranian population, were compared with other populations. In addition, the genetic

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Received 18 December 2007; revised 18 September 2006, 3 May 2007, 18 December 2007; accepted 4 January 2008

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