Polymorphism in the IL-13 Promoter

Interleukin-13 (IL-13) has received considerable attention as a central mediator in allergic responses (1). The existence of inter-individual differences in IL-13 production capacity, together with the association of the 5q31-35 region—which includes the gene for IL-13, with atopy and asthma (2)—prompted speculation about the presence of functionally relevant polymorphism in the IL-13 gene. In their search for genetic heterogeneity in the IL-13 gene, Anderson et al. (3) analyzed the IL-13 promoter region from -1039 to +80 in 129 individuals (33 healthy and 96 with minimal-change nephropathy). Single-strand conformation analysis indicated the absence of polymorphisms, a finding that caused Anderson et al. (3) to doubt the significance of the IL-13 promoter as a susceptibility locus for atopy or for any associated conditions. Similar findings were reported by Wills-Karp and Rosenwasser in a response (4).

We examined the IL-13 promoter region from -1360 to -108 in 208 individuals (107 healthy and 101 with allergic asthma). At position -1055, immediately adjacent to a consensus NFAT binding site, we identified a C to T transition polymorphism. Analysis of the distribution of the -1055 C to T polymorphism revealed an increased frequency of the homozygous TT genotype in the allergic asthma group (13/101) compared to the nonatopic individuals (2/107) (RR 6.9, P = 0.002). Moreover, the -1055 TT genotype is associated with altered regulation of IL-13 production and increased binding of nuclear proteins, indicating its functional significance. Therefore, our data argue in favor of a role of the IL-13 promoter as a susceptibility locus in allergic asthma (5).

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Response: We were intrigued to learn that van der Pouw Kraan et al. have identified a polymorphism in the IL-13 promoter at a position just outside the region that we had previously studied (1). We have now examined this region in our populations and can confirm the presence of the -1055 C to T polymorphism in caucasoids in the United Kingdom. Using single-strand conformation polymorphism analysis and sequencing, we have studied 67 individuals with minimal-change nephropathy and 59 healthy controls. The allele frequencies of -1055 T were 16/134 (11.9%) and 16/118 (13.5%), respectively, with two TT homozygotes in the minimal-change patients and one TT in the control group (no statistically significant difference between the two groups).

Van der Pouw Kraan et al. do not quote the allele frequencies in their populations and base their conclusion that this polymorphism is a susceptibility locus for allergic asthma on a high incidence of the homozygous TT genotype in their asthmatic subjects. Our results confirm the rarity of the TT genotype in another European caucasoid population but do not support a role for the -1055 polymorphism in predisposition to a different atopy-related disease, namely, minimal-change nephropathy.

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