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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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