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T. C. T. M. van der Pouw Kraan, *et al.*

Science **286**, 1647b (1999);

DOI: 10.1126/science.286.5445.1647b

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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).

T. C. T. M. van der Pouw Kraan

*CLB, Lab Experimental and
Clinical Immunology
AMC University of Amsterdam
Plesmanlaan 125
1066 CX Amsterdam, Netherlands
E-mail: c.vd.pouw@cable.a2000.nl*

L. A. Aarden

*CLB, Lab Experimental and
Clinical Immunology
AMC University of Amsterdam
Plesmanlaan 125
1066 CX Amsterdam, Netherlands
E-mail: l_aarden@clb.nl*

C. L. Verweij

*Department of Rheumatology
Leiden University Medical Center
PO Box 9600
2300 RC Leiden, Netherlands
E-mail: verweij_c@mail2.medfac.leidenuniv.nl*

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7 July 1999; accepted 23 August 1999

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.

Kathleen M. Gillespie

*Karen L. Anderson
Peter W. Mathieson
University of Bristol
Academic Renal Unit
Southmead Hospital
Westbury-on-Trym
Bristol, BS10 5NB, UK
E-mail: p.mathieson@bris.ac.uk*

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23 August 1999; accepted 28 October 1999