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TGF-β1 gene polymorphisms

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Key words: allergy; asthma; gene; polymorphism; TGF.

● ASTHMA, hay fever, and eczema are part of a syndrome of allergic diseases known as atopy. Genome-wide screens, linkage analysis, and studies of polymorphisms in candidate genes have all identified genetic factors likely to contribute to the allergic pathogenesis (1). Recently, some studies have indicated a role for TGF-beta in the etiopathogenesis of allergic diseases, and its increased levels were found in asthmatic and rhinitis patients. The coding gene is located on chromosome 19q13.1–13.3 (2), and several polymorphic variants have been identified in this gene. The C/T base exchange in position –509, which is present in a region of the promoter associated with negative transcription regulation, was previously shown to be associated with elevated total serum IgE levels (3). The aim of our study was to determine whether atopic asthma or other atopic diseases (or possibly related phenotypes) are associated with selected mutations (polymorphisms) in the TGF-beta 1 gene also in the highly homogeneous Czech population.

Caucasian subjects of exclusively Czech ethnicity ($n=288$) were included in this study. DNA taken from subjects with clinically manifested asthma and other atopic diseases ($n=170$, 90 men and 80 women, aged 25.4 ± 11.5 years [mean $\pm$ SD]) and reference ethnically and age-matched unrelated subjects ($n=118$, 61 men and 57 women, aged 29.3 ± 7.9 years) was examined for base substitutions in the TGF-beta 1 gene.

Atopy (defined as enhanced IgE responsiveness) was recognized by specific IgE (>0.35 kU/l) or a positive skin prick test to any one or more allergens, as described previously (4).

Project approval was granted by the local ethics committee at the Medical Faculty, MU Brno, and written informed consent for genetic analysis was obtained from all subjects.

After DNA extraction, three polymorphisms located in the 5' region at position –988 (C/A), –800 (G/A), and –509 (C/T) and two polymorphisms located at codons 10 (L10P) and 25 (R25P) of exon 1 were investigated by PCR methods, as described earlier (5).

The TGF-beta 1 –988 A variant was not present in our subjects (all patients and reference subjects had only the CC genotype for this mutation). We found no association between any of the four polymorphisms in the TGF-beta 1 gene and clinical manifestation of atopic diseases ($P>0.05$ in all cases) (Table 1). In atopic subjects, there were no significant associations among TGF-beta 1 genotypes and a number of quantitative traits investigated in our study, including total serum IgE levels (TGF –509: wild type [CC genotype] – IgE: 294 ± 50.9 [mean $\pm$ SEM], heterozygote [CT] – IgE:

Table 1. Genotype distributions (%) and allele frequencies of four polymorphisms in TGF-beta 1 gene

		–800G/A polymorphism					
		GG (%)	GA (%)	AA (%)	G allele	A allele	P
Atopic patients	($n=170$)	153 (90.0)	16 (9.4)	1 (0.6)	0.947	0.053	
Reference group	($n=118$)	100 (84.7)	18 (15.3)	0 (0)	0.924	0.076	>0.05
		–509C/T polymorphism					
		CC (%)	CT (%)	TT (%)	C allele	T allele	P
Atopic patients	($n=170$)	85 (50.0)	66 (38.8)	19 (11.2)	0.694	0.306	
Reference group	($n=118$)	63 (53.4)	43 (36.4)	12 (10.2)	0.716	0.284	>0.05
		+869 T/C (L10P) polymorphism					
		TT (%)	TC (%)	CC (%)	T allele	C allele	P
Atopic patients	($n=167$)	65 (38.9)	71 (42.5)	31 (18.6)	0.602	0.398	
Reference group	($n=117$)	46 (39.3)	51 (43.6)	20 (17.1)	0.611	0.389	>0.05
		+915 G/C (R25P) polymorphism					
		GG	GC	CC	G allele	C allele	P
Atopic patients	($n=167$)	143 (85.6)	23 (13.8)	1 (0.6)	0.925	0.075	
Reference group	($n=117$)	98 (83.8)	19 (16.2)	0 (0)	0.919	0.081	>0.05

P values refer to both genotype and allele distribution.

323.7 ± 66.1 and base substitution [TT] – IgE: 243.7 ± 62.2, $P > 0.05$), selected specific IgE levels, and skin test responses to aeroallergens (data not shown). The polymorphisms were strongly associated with one another.

TGF-beta 1 is a cytokine that is constitutively expressed in the healthy airways but that also mediates a complex mix of pro- and anti-inflammatory activities. In contrast to some previous studies which found associations of polymorphisms in the TGF-beta 1 gene with atopic diseases or related phenotypes (3, 6), we found no association of five selected polymorphisms in this gene with clinically manifested atopic asthma or other allergies. None of the polymorphisms were associated with total serum IgE, selected specific IgE, pulmonary function tests, and other phenotypic markers of atopic predisposition. Therefore, our results do not confirm previously published data on the association of the TGF-beta 1 – 509 C/T polymorphism with increased serum total IgE levels (3). In conclusion, our results indicate that the mentioned polymorphisms of the TGF-beta 1 gene do not influence susceptibility to atopic diseases and related phenotypes, at least in the Czech population.

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Environmental allergens in Kuwait

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Key words: allergen; cat; cockroach; dog; exposure; mite; passive.

● THE level of exposure to indoor allergens outside the home has been investigated in many developed countries (1–3), but not in the developing ones. Allergic diseases were extremely rare in Kuwait until the mid-1950s (4). Since then,

however, the prevalence seems to have rapidly increased (e.g., within the 3-year period 1982–5, childhood asthma admissions had increased from 8.8% to 14.9% of emergency admissions [5]).

Cat allergen was found in more than 50% of public buildings.

The prevalence rates of wheeze ever, current wheeze, and physician-diagnosed asthma in the ISAAC study in Kuwait were 25.9%, 16.1%, and 14.5%, respectively (6).

This study investigated the levels of mite, cat, dog, and cockroach allergen in public places in Kuwait. Dust samples ($n = 110$) were collected from 20 mosques, 10 restaurants, 15 nurseries, six family practices, five hospitals, 10 cinemas, and 12 schools. Der p 1, Der f 1, Fel d 1, Can f 1, and Bla g 2 were measured by mAb-based ELISAs.

Der f 1 was below the limits of detection in all the samples, and Der p 1 was detected in one sample only. Can f 1 was above the detection limit in 14 samples (eight mosques, four cinemas, and two restaurants) (Table 1). Bla g 2 was detected in 39 samples. However, Fel d 1 was detected in more than half of the samples (62 out of 110), and the highest levels were found in cinemas.

Fel d 1 in public places ($n = 110$; median 0.30 $\mu\text{g/g}$, range 0.06–1.62) was compared with the levels found in homes in the same area (15 homes with a cat [median 0.72 $\mu\text{g/g}$, range 0.10–700.0] and 274 homes without cats [median 0.18 $\mu\text{g/g}$, range 0.04–11.60]; Mann-Whitney U test). Fel d 1 from public places was significantly higher than in homes without cats ($P = 0.002$). However, levels in homes with cats were significantly higher than those found in public places ($P = 0.007$).

This is the first study to investigate the levels of indoor allergens in public places in the Middle East. In contrast to the