

Associations of *FLG* mutations between ichthyosis vulgaris and atopic dermatitis in Han Chinese

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Keywords: atopic dermatitis; filaggrin; ichthyosis vulgaris; mutation.

Filaggrin gene (*FLG*) mutations which cause impaired skin barrier have been considered as predisposing factors for atopic dermatitis (AD) and AD-associated phenotypes (1, 2). In our previous study, we have identified 18 *FLG* mutations in 261 AD patients who met the AD criteria of Hanifin and Rajka and confirmed that *FLG* mutations were strong risk factors for AD in Han Chinese (3). Now we carried out a comprehensive sequencing of *FLG* in 21 unrelated IV patients using an overlapping PCR strategy, which allows the entire *FLG* coding sequence to be sequenced. PCR primers and conditions were described previously by Sandilands et al. (4). The diagnosis of IV accords with clinical features including dry skin, scaling on the extremities, palmoplantar hyperlinearity, keratosis pilaris and early age of onset. Genomic DNA samples from peripheral blood cells of all participants were obtained. Written informed consents were given by all the patients. This study was approved by the medical

ethical committees of Shanghai Jiaotong University, school of medicine, China.

Among the 21 cases of IV patients, nine were male and 12 were female. The average age was 15.05 ± 1.66 years. A total of four types of *FLG* mutations were identified in IV patients, i.e. Q1790X, K4671X, 3321delA and Q2417X (Table 1). Thirteen IV patients were detected with *FLG* mutations and were all heterozygous for those mutations. None of the *FLG* mutations was found in eight IV patients, which did not clinically differ from those mutations carriers. Considering another genetic locus for IV was identified on chromosome 10q22.3–q24.2 in two Chinese families with autosomal-dominant IV (5), we speculated that other candidate genes at the 10q IV locus underlie IV in this group.

Among the 261 AD patients in our previous study, 29 individuals had a compound phenotype AD plus IV. The prevalence of *FLG* mutations in simple AD patients was 29.3% while that in AD patients with concomitant IV was 48.3%

(Table 1). Fourteen out of 18 types of *FLG* mutations were found in simple AD patients and seven were found in compound phenotype AD plus IV.

In our study all the *FLG* mutations found in IV patients were also detected in AD population but not vice versa. It seems that the types of *FLG* mutations are more plentiful in AD patients than in IV patients in Chinese, but further studies with large sample cohort would be needed to confirm it.

Mutation 3321delA was previously identified in Japanese and commonly seen in both Chinese AD patients and IV patients, indicating that it is a common type of *FLG* mutation for both diseases. The other mutation K4671X was also common for AD and IV. Mutation Q2417X, which was previously identified in Singaporean Chinese IV patients (6) was found in one of our IV patients and five simple AD patients and two AD patients with IV. It indicated that this mutation was relatively common for these two diseases. A novel *FLG* mutation 5757del4 was only

The types of *FLG* mutations may be much more plentiful in atopic dermatitis than in ichthyosis vulgaris.

Table 1 The prevalence of *FLG* mutations in patients with AD and IV

<i>FLG</i> mutation	<i>n</i> (%)			<i>FLG</i> mutation	<i>n</i> (%)		
	Simple AD (232)	AD with IV (29)	Simple IV (21)		Simple AD (232)	AD with IV (29)	Simple IV (21)
441delA	1 (0.4)			6950del8	3 (1.3)		
R501X	1 (0.4)			Q2417X	5 (2.2)	2 (6.9)	1 (4.8)
R826X	2 (0.9)			E2422X		3 (10.3)	
3222del4	2 (0.9)			7945delA	1 (0.4)		
3321delA	31 (13.4)	7 (24.1)	7 (33.3)	S2706X	1 (0.4)		
R1140X	1 (0.4)			R4306X		2 (6.9)	
4271delAA	2 (0.9)			K4671X	21 (9.1)	3 (1.0)	4 (19.1)
R1474X		1 (3.4)		Homozygote	7 (3.0)	1 (3.4)	1 (4.8)
Q1790X	3 (1.3)		1 (4.8)	Compound heterozygote	7 (3.0)	5 (17.2)	
5757del4		1 (3.4)		Heterozygote	54 (23.3)	8 (27.6)	12 (57.1)
6834del5	1 (0.4)						

AD, atopic dermatitis; *FLG*, Filaggrin gene.

found in one AD patients with concomitant IV, indicating that it is more likely specific to the compound phenotype AD plus IV or to the family. We think that further studies are indispensable to elucidate the associations between the *FLG* mutations and the two kinds of diseases.

In conclusion, our results suggest that the types of *FLG* mutations may be much more plentiful in AD than in IV. The associations between the *FLG* mutations and different phenotypes, i.e. AD or ichthyosis vulgaris need to be further investigated.

We thank all the patients for their participation. This study was funded by a grant from Science and Technology Commission of Shanghai Municipality (08JC1415900).

Conflict of interest

The authors declare that they have no conflicts of interest.

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Accepted for publication 21 March 2011
Allergy 2011
© 2011 John Wiley & Sons A/S
DOI: 10.1111/j.1398-9995.2011.02597.x

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