

Respiratory allergy	Cross-sectional Cohort	↑ : 25 N : 41		
Respiratory illness	Cross-sectional Cohort	↑ : 25, 41 N : 57	↑ : 158 N : 9	
Pneumonia	Cohort	↑ : 42 N : 66		
Bronchial hyperresponsiveness	Cross-sectional Cohort	↑ : 132 N : 8		
Cough	Cross-sectional Case-control			
Chronic bronchitis emphysema	Cohort	↑ : 36 N : 82		
Chronic obstructive pulmonary disease	Cross-sectional Cohort	↑ : 9 N : 82		
Chronic lung diseases	Cross-sectional Cohort	↑ : 192 N : 82		
History of tuberculosis	Cross-sectional Cohort	↑ : 33, 82, 193 N : 82		
RSV bronchiolitis	Cohort	↑ : 194 N : 195		
Lower respiratory tract illness	Cohort	↑ : 196 N : 195		
Respiratory disease in infancy	Cross-sectional Cohort	↑ : 196 N : 82		
Transient tachypnoea of newborn or respiratory distress syndrome	Cohort	↑ : 198 (during pregnancy) N : 66, 197		
Adenoidectomy and/or tonsillectomy	Cohort	↑ : 199 N : 82		
Adenoidectomy	Cross-sectional Cohort	↑ : 198 (during pregnancy) N : 66		
Otitis media	Case-control Cohort	↑ : 199 N : 80 (asthma or wheezing)		
Parotitis	Cross-sectional Cohort	↑ : 199 N : 80 (asthma or wheezing)		
Fever	Cross-sectional Cohort	↑ : 199 N : 80 (asthma or wheezing)		
Flu	Case-control Cohort	↑ : 7 N : 200		
Cold lasting 3+ days	Cross-sectional Cohort	↑ : 7 N : 200		
Dyspnea	Cross-sectional Cohort	↑ : 7 N : 200		
Gastroesophageal reflux disease	Case-control Cohort	↑ : 7 N : 200		
Acute gastroenteritis	Cross-sectional Cohort	↑ : 7 N : 200		
Stomach ulcer	Case-control Cohort	↑ : 7 N : 200		
Diarrhoea lasting 3+ days	Cross-sectional Cohort	↑ : 7 N : 200		
Depression	Case-control Cohort	↑ : 7 N : 200		
Illness or health problems in first week of life	Cohort	↑ : 7 N : 200		
Infantile colic	Cohort	↑ : 7 N : 200		
Rash	Cohort	↑ : 7 N : 200		
Exanthema subitum	Cross-sectional Cohort	↑ : 7 N : 200		
Viral warts	Case-control Cohort	↑ : 7 N : 200		
Arthritis	Case-control Cohort	↑ : 7 N : 200		
Hypertension	Case-control Cohort	↑ : 7 N : 200		
Infection				
Infection	Cohort	↑ : 32 (ever) N : 32 (DD)		
Total number of infections	Cohort	↑ : 32 (ever) N : 32 (DD)		
Respiratory infection	Cohort	↑ : 32 (ever) N : 32 (DD)		
	Case-control Cohort	↑ : 32 (ever) N : 32 (DD)		

Cross-sectional	N : 12	↑ : 19 (infection before 5 yrs), 51 (childhood and adolescent onset)			
Upper respiratory tract infections		N : 51 (adult onset)	N : 82		N : 82
Lower respiratory infection		N : 82, 193			
Ear infection	↑ : 202	↑ : 39, 202	N : 93		N : 93
Gastrointestinal infection		↑ : 203			
Viral infection		↑ : 202	N : 201		
		↓ : 202	N : 197		
Hepatitis A virus		N : 77 (wheeze+asthma)			
Hepatitis B virus		↓ : 204	↓ : 204		↓ : 204
Hepatitis C virus		N : 204	N : 204		N : 204
Herpes		N : 204	N : 204		N : 204
Herpes simplex	↓ : 202	↓ : 292			
Herpes simplex virus type 1		↓ : 204	N : 93		
Herpes simplex virus type 2		N : 204			
Measles		N : 202	N : 205		
	N : 77, 206	↓ : 77 (<3 y, wheeze+asthma)	↑ : 207		↑ : 207
		N : 77 (>3 y, wheeze+asthma)	N : 93		
		↑ : 207			
Rubella		N : 77 (wheeze+asthma)	↓ : 93		
Epstein-Barr virus	N : 77, 206	N : 77 (wheeze+asthma)			N : 208 (suspected)
Mumps	N : 208	N : 77 (wheeze+asthma)	N : 66		
Varicella	N : 77, 206	N : 77 (wheeze+asthma)			
Bacterial infections		N : 77 (wheeze+asthma)	N : 209		↓ : 209
Chlamydia pneumoniae		N : 202			
		↓ : 209			
		N : 118			
		N : 210			
	↑ : 210 (prior infection)	N : 77 (wheeze+asthma)			
	N : 210 (acute infection)	N : 77 (wheeze+asthma)			
Pertussis	N : 77	N : 77 (wheeze+asthma)			
Helicobacter pylori	N : 77	N : 77 (wheeze+asthma)			
Salmonellosis	↓ : 211	↓ : 211	↓ : 211		↓ : 211
Scarlet fever	N : 207				
Geohelminth	↓ : 212 (exercise-induced)	N : 129	N : 212		N : 212
	N : 170, 212				
Helminth		N : 213			
Malaria		↑ : 58	↑ : 58		
Hookworm		N : 58	N : 58		
Ascaris		↑ : 214			
Worm		N : 58	N : 58		
Toxocara		↓ : 28	↓ : 28		
Trichuris		↑ : 58	↑ : 58		
Parasite egg in stool					N : 29
Parasite presence		↑ : 58	↑ : 58		

Hormon replacement therapy	Cross-sectional	↑ : 18, 226	↑ : 226 N : 18		↑ : 226
Oral contraceptive	Cohort	↑ : 80 (asthma or wheezing), 227 (without asthma) ↓ : 227 (with asthma)	N : 80		
Paracetamol	Cross-sectional	N : 18	↑ : 228 ↑ : 225		N : 228
Salicylate	Case-control				
Trimethoprim/co-trimox.	Case-control				N : 223
Medical/health related factor					
Admitted to hospital for infection	Cohort			N : 66	
Visits to the GP in previous year	Case-control		↑ : 8		
Referral/hospitalization in previous year	Case-control		N : 8		
Blood pressure	Cross-sectional				↓ : 95 (diastolic) N : 95 (systolic) ↓ : 95 (DD + reported)
Heart rate	Cross-sectional		N : 97		
Catch-up growing	Cohort		N : 40 (in first 3 mo)		↓ : 66 (before 6 mo)
Child care/day care	Cohort		↑ : 229		
Child psychological risk	Cohort		N : 57		
Neonatal hospital admission	Cross-sectional	↑ : 92	N : 22		
Expulsion of intestinal worms	Cohort		↑ : 61		N : 61
Physical examination	Cross-sectional		N : 230		
Life events	Case-control		N : 230		
Life satisfaction	Cohort		N : 230		
Stress	Cohort		N : 230		
Neuroticism	Cross-sectional	↑ : 15	N : 230		
Extroversion	Cohort		N : 230		
Nitric oxide levels in exhaled air	Cross-sectional		↑ : 230 (women) N : 230 (men)		
Early age at menarche	Cohort	N : 231	N : 230		
Number of pregnancies	Cross-sectional	N : 60	↑ : 231		
Number of live births	Cross-sectional	N : 60	↑ : 227		
Mechanical ventilation	Cohort		N : 60		N : 60
Threatened abortions	Case-control		N : 97		↓ : 60 (allergic conjunctivitis)
Total IgE					
Mite, cockroach, cat, dog, egg, milk, soy, wheat, fish, or peanut	Cohort	↑ : 79, 232	↑ : 229, 233 (at 10 y: in cord serum) N : 233 (at 4 y: in cord serum)		↑ : 43 N : 79
Specific IgE					
Mite, cockroach, cat, dog, egg, milk, soy, wheat, fish, or peanut	Case-control	↑ : 44			
Mite, cockroach, cat, or dog	Case-control	↑ : 44			
Ascaris lumbricoides	Case-control	N : 44			
Timothy grass	Cohort				↑ : 42
Chlamydia pneumoniae	Case-control				↓ : 234 (self-reported)
Cat dander	Cross-sectional				↑ : 19

Cladosporium	Cross-sectional	↑ : 19			
Dermatophagoides pteronyssinus	Cross-sectional	↑ : 19			
Food	Case-control	↑ : 47 (grass pollen asthma)			
IgG	Cohort	N : 234 (current)			
Sensitization (skin prick test)					
Alternaria	Cohort	N : 235	N : 235		N : 235
Animal	Case-control	↑ : 47 (grass pollen asthma)			
Cat	Cohort	N : 235	↑ : 235		N : 235
Cladosporium herbarum	Cohort	N : 235	N : 235		N : 235
Cod	Cohort	N : 235	N : 235		N : 235
Cockroach	Cross-sectional	↑ : 170			
Dog	Cohort	N : 235	N : 235		N : 235
Egg	Cohort	N : 235	N : 235		↑ : 235
Grass pollen	Cohort	N : 235	↑ : 235		↑ : 235
Milk	Cohort	N : 235	N : 235		N : 235
Mites	Cohort	↑ : 235	↑ : 235		N : 235
Molds	Case-control	↑ : 47 (grass pollen asthma)			
Peanut	Case-control	N : 47 (grass pollen asthma)			
Soya	Cohort	N : 235	↑ : 235		N : 235
Wheat	Cohort	N : 235	N : 235		N : 235
Dermatophagoides pteronyssinus	Cross-sectional	↑ : 170			
Dermatophagoides pteronyssinus, cockroach, cat, Alternaria tenuis, mixed grasses and mixed trees	Cohort	↑ : 32	↑ : 43		
Birch, timothy, mugwort, cat, dog, horse, Dermatophagoides pteronyssinus,					
Dermatophagoides farinae, Cladosporium, and Alternaria					
Silk					
Reported food intolerance					
	Cohort	↑ : 83 (reported)			
		N : 83 (DD)			
Blood test					
Lead level	Cohort	N : 237			
Dichlorodiphenyldichloroethylene	Cohort	↑ : 238 (cord serum)			
HDL cholesterol	Cross-sectional	N : 239	N : 239		N : 239
Estradiol	Case-control	N : 240 (serum)	↑ : 240 (serum)		↑ : 240 (serum)
Haemoglobin	Case-control	N : 241 (serum at early pregnancy)	N : 241 (serum at early pregnancy)		N : 241 (serum at early pregnancy)
Ratio of progesterone/estradiol	Cohort	N : 43	N : 43		
	Case-control	N : 241 (serum at early pregnancy)	N : 241 (serum at early pregnancy)		N : 241 (serum at early pregnancy)
Breast milk					
Progesterone	Case-control	N : 241 (serum at early pregnancy)	N : 241 (serum at early pregnancy)		N : 241 (serum at early pregnancy)
soluble CD14	Cohort	↓ : 242 (without maternal atopy)	N : 242		
		N : 242 (with maternal atopy)			

Others

Oil-fire smoke (Gulf War)	Cross-sectional	↑ : 243
Parenting difficulties	Cohort	↑ : 229
Source of water	Cohort	
(Well vs piped)	Case-control	N : 58
(River vs piped))	Case-control	↓ : 58
(Spring vs piped)	Case-control	↓ : 58

↑ : significant positive association

↓ : significant inverse association

N : not statistically significant

DD: Doctor-diagnosed

Table 2. Dietary factors and allergic diseases

Factors	Outcome		
	Wheeze	Asthma	Atopic dermatitis
Dietary intake			
Total energy/calories			Allergic rhinitis (Hay fever)
Brown bread		N : 84	
Miso	N : 30	N : 244	N : 245
Miso soup		↓ : 30	N : 245
Soy product			↓ : 245
Boiled soybeans			N : 245
Tofu			N : 245
Tofu products			N : 245
Fermented soybeans			N : 245
Vegetable		↓ : 48	N : 245
Green, leafy vegetables		N : 20	
Fruit			↑ : 58
Fruit and vegetable		N : 20	
		↑ : 23 (women)	
		N : 23 (men)	
Citrus/kiwi fruit			N : 247
			↓ : 247
Fish			
Meat		N : 248	
Meat products		N : 248	
Butcher's meats		N : 71	
Chicken, meat, or fish		N : 20	
Liver		↑ : 71	
Eggs		N : 248	↑ : 71
		N : 20	
Milk		↓ : 48	
		N : 248	
		N : 20	
		N : 30	
Semi-skimmed milk		N : 68	
Unpasteurized milk	N : 30		↓ : 68
Whole milk	N : 30		
Milk products	↓ : 30		
Cheese		N : 248	
Butter	↓ : 30	↓ : 30 (current)	
		N : 30 (ever)	
		N : 248	
Margarine			N : 249
		N : 30	
		↑ : 248	
			N : 249
Margarine only (vs exclusive butter)			↑ : 249 (men)
Margarine and butter (vs exclusive butter)			N : 249 (women)
			↑ : 250 (allergic rhinitis)
			N : 250 (hay fever)
Vegetable oils			N : 250
			N : 248

Linoleic acid	Cohort		N : 264		N : 264
Arachidonic acid	Cohort		N : 264		N : 264
Trans fatty acid	Cohort		↓ : 264		↓ : 264
n-6/n-3	Cohort		↑ : 264		↑ : 264
Linoleic acid/Alpha-Linolenic acid	Cohort		N : 264		N : 264
Eicosapentaenoic acid/Arachidonic acid	Cohort		N : 264		N : 264
In blood					
Selenium	Cross-sectional		N : 265 (serum)		N : 265 (serum)
β-Carotene	Cross-sectional	N : 246 (plasma)	N : 265 (serum)		N : 265 (serum)
Vitamin A	Cross-sectional	↑ : 246 (plasma)			
Vitamin E	Cross-sectional	N : 246 (plasma)	N : 265 (serum)		N : 265 (serum)
Vitamin C	Cross-sectional	N : 246 (plasma)	↓ : 265 (serum)		↓ : 265 (serum)
Saturated fatty acids	Cross-sectional		↓ : 266 (plasma)		↓ : 266 (plasma)
Monounsaturated fatty acids	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Oleic acid	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Polyunsaturated fatty acids (PUFA)	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
n-3	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Docosahexaenoic acid	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
α-Linolenic acid	Cross-sectional		↑ : 266 (plasma: asthma)		↑ : 266 (plasma: asthma)
Eicosapentaenoic acid	Cross-sectional		N : 266 (plasma: current, DD)		N : 266 (plasma: current, DD)
n-6	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Gamma-Linolenic acid	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Eicosadienoic acid	Cross-sectional		↑ : 266 (plasma: asthma, DD)		↑ : 266 (plasma: asthma, DD)
Eicosatrienoic acid	Cross-sectional		N : 266 (plasma: current)		N : 266 (plasma: current)
Docosapentaenoic acid	Cross-sectional		↑ : 266 (plasma)		↑ : 266 (plasma)
Linoleic acid	Case-control		N : 266 (plasma)		N : 266 (plasma)
Arachidonic acid	Cross-sectional	↓ : 257 (serum)	↓ : 257 (serum)		↓ : 257 (serum)
Arachidonic acid	Cohort		N : 266 (plasma)		N : 266 (plasma)
Arachidonic acid	Case-control		↑ : 257 (serum)		↑ : 257 (serum)
PUFA: 22:4 n-6	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Trans fatty acid	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
n-6/n-3	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)
Arachidonic acid/eicosapentaenoic acid	Cross-sectional		N : 266 (plasma)		N : 266 (plasma)

↑ : significant positive association

↓ : significant inverse association

N : not statistically significant

DD: Doctor-diagnosed

Table 3. Family history and allergic diseases

Factors	Outcome				
	Design	Wheeze	Asthma	Atopic dermatitis	Allergic rhinitis (Hay fever)
Family history					
Asthma	Cohort	↑ : 32 N : 81	↑ : 32, 135		
	Case-control		↑ : 6		
	Cross-sectional	↑ : 18, 50, 55, 92	↑ : 18, 19, 55, 136 N : 25	N : 27	
Atopy or allergy	Cohort	N : 81			
	Case-control	↑ : 44 (among <2 y)			
	Cross-sectional	N : 44 (among 2-12 y) ↑ : 9	↑ : 9 (ever), 136 N : 9 (DD) ↑ : 48		N : 9
Asthma/allergy	Case-control				
Atopic dermatitis	Cross-sectional			↑ : 27	
Allergic rhinitis	Cross-sectional			N : 27	
Chronic bronchitis	Cross-sectional			N : 27	
emphysema					
Household tuberculosis	Cross-sectional	N : 9	↑ : 9 N : 9		↑ : 9 (current, ever) N : 9, 9 (DD)
Parental history					
Allergy or atopy	Cohort		↑ : 74, 118 N : 41	↑ : 43	↑ : 125 (hay fever and/or asthma)
	Case-control				
	Cross-sectional		↑ : 24, 41, 136	↑ : 61 ↑ : 24	↑ : 24 N : 29 ↑ : 61 N : 16
Asthma	Case-control		↑ : 61		
	Cross-sectional	↑ : 16	↑ : 93, 136	N : 16, 93	
Asthma and/or allergies	Case-control		↑ : 167		
	Cross-sectional	N : 16	↑ : 51	↑ : 16, 28, 93	N : 16
Atopic dermatitis	Cohort			↑ : 16	↑ : 76
Rhinitis or hayfever	Cross-sectional	N : 16	↑ : 93	N : 93	↑ : 16
Maternal history					
Allergy or atopy	Cohort	N : 30	↑ : 30, 38	↑ : 43	↑ : 26
	Cross-sectional		N : 26	N : 26	
Asthma	Cohort	↑ : 31, 186 (persistent and late onset wheezing) N : 33, 56, 164 (transient wheezing)	↑ : 39, 40, 259	N : 43	
	Case-control		↑ : 46, 84, 167		
	Cross-sectional	↑ : 9, 14, 17	↑ : 9, 52, 132 N : 9, 14	↑ : 16	↑ : 9, 16
Atopic dermatitis	Cohort		↑ : 46	↑ : 43	
	Case-control				
	Cross-sectional	↑ : 16 N : 164		↑ : 16, 93 ↑ : 43	↑ : 16
Rhinitis or hayfever	Cohort				
	Case-control		N : 46		

Paternal history					
Allergy or atopy	Cross-sectional	↑ : 92 N : 16		↑ : 16, 93 N : 16	↑ : 16
	Cohort	↑ : 30	↑ : 30 (ever) N : 30 (current)	↑ : 43	
Asthma	Case-control Cohort	N : 164	↑ : 37	↑ : 43	
	Case-control		↑ : 46, 167		
	Cross-sectional Cohort		↑ : 132	↑ : 43	
Atopic dermatitis	Case-control		N : 46		
	Cross-sectional Cohort	N : 164		↑ : 93 ↑ : 43	
Rhinitis or hayfever	Case-control		↑ : 46		↑ : 93
	Cross-sectional	↑ : 92			
in siblings					
Asthma	Cross-sectional		↑ : 93	↑ : 93	
Atopic dermatitis	Cross-sectional			N : 93	
Rhinitis or hayfever	Cross-sectional		↑ : 93		↑ : 93

↑ : significant positive association

↓ : significant inverse association

N : not statistically significant

DD: Doctor-diagnosed

アトピー性皮膚炎の遺伝的要因系統的レビュー

分担研究者 三宅 吉博 福岡大学医学部公衆衛生学助教授
分担研究者 田中 景子 福岡大学医学部公衆衛生学助手

研究要旨

結果因子としてアトピー性皮膚炎に限定し、症例対照研究により遺伝子多型とアトピー性皮膚炎との関連の検討された論文を系統的に調べた。「(“atopic eczema” OR “atopic dermatitis”) AND human AND polymorphism」という検索式で130件の論文を抽出した。タイトルと要約を検討し、49編の原著論文を今回のレビューの対象とした。49編中19編が日本人を対象とした報告であった。計47の遺伝子が検討されていた。IL13は4編の論文で統計学的に有意な関連を認めた。IL4Rは3編の論文で統計学的に有意な関連を認めた。CMA1とCD14は2編の論文で統計学的に有意な関連を認めた。1編の論文のみ有意な関連を認めた遺伝子はTAP1、IL4、TGFB1、TAP2、IL12B、CARD15、SPINK5、CSF2、GSTP1、KLK7、IL18、NOD1、IL1RL1、IL12RB1、NAT2であった。OberとHoffjanによる系統的レビューでは、6編以上の論文で関連を認めた遺伝子は25ある。今回のレビューの結果とあわせて、今後の遺伝要因解析の優先順位を決定すべきである。

研究協力者

清原 千香子
九州大学大学院医学研究院予防医学分野
講師

A. 研究目的

アレルギー疾患に関連する遺伝子の発見のため、全世界で多大な努力がなされている。OberとHoffjanによる系統的レビューによると、2つ以上の独立した研究集団でアレルギー疾患やアトピーと関連の認められた遺伝子は79ある（Genes and Immunity. 2006; 7: 95-100）。

今回、特に結果因子としてアトピー性皮膚炎に限定し、症例対照研究により遺伝子多型とアトピー性皮膚炎との関連の検討された論文を系統的に調べた。

B. 研究方法

Medlineにおいて、「(“atopic eczema” OR “atopic dermatitis”) AND human AND polymorphism」という検索式で130件の論文を抽出した。タイトルと要約を検討し、症例対照研究の手法を用いた49編の原著論文を今回のレビューの対象とした。

C. 結果

Table 1に49編の論文の方法と結果をまとめた。49編中19編が日本人を対象とした報告であった。計47の遺伝子が検討されていた。Table 2に関連の有無を示す。IL13は4編の論文で統計学的に有意な関連を認めた。IL4Rは3編の論文で統計学的に有意な関連を認めた。CMA1とCD14は2編の論文で統計学的に有意な関連を認めた。1編の論文のみ有意な関連を認めた遺伝子はTAP1、IL4、TGFB1、TAP2、IL12B、CARD15、SPINK5、CSF2、GSTP1、KLK7、IL18、NOD1、IL1RL1、IL12RB1、NAT2であった。その他の遺伝子は、有意な関連を認めなかった。

D. 考察

アトピー性皮膚炎においては、遺伝要因の解析をした症例対照研究は数少なく、なんら結論は得られない。

OberとHoffjanによる系統的レビューでは、6編以上の論文で関連を認めた遺伝子は25ある。今回のレビューの結果とあわせて、今後の遺伝子解析の優先順位を決定すべきである。

E. 結論

アトピー性皮膚炎と関連する遺伝要因の解

析は十分になされておらず、さらなる研究が必要である。

F. 研究発表

1) 論文発表

なし。

2) 学会発表

なし。

G. 知的財産権の出願・登録状況

1) 特許取得

なし。

2) 実用新案登録

なし。

3) その他

なし。

H. 文献

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Table 1. Evidence table for epidemiological studies on association between genetic factors and atopic dermatitis

Ref.No.	Authors	Year	Country	Type	Subjects	Age	Association with allele or genotype																																																					
1	Hashimoto, et al.	2005	Japan	Case-control	Cases: 45/23 (M/F) Controls: 22/10 (M/F)	20-49 18-32	Codon 54 of MBL gene. <table border="1"> <thead> <tr> <th>Genotype</th> <th>AD (n=68)</th> <th>Control (n=32)</th> </tr> </thead> <tbody> <tr> <td>G/G</td> <td>48 (70.4%)</td> <td>26 (81.2%)</td> </tr> <tr> <td>G/A</td> <td>16 (23.5)</td> <td>6 (18.8)</td> </tr> <tr> <td>A/A</td> <td>4 (6.1)</td> <td>0 (0)</td> </tr> </tbody> </table> <table border="1"> <thead> <tr> <th>Allele</th> <th>AD (n=68)</th> <th>Control (n=32)</th> </tr> </thead> <tbody> <tr> <td>G</td> <td>112 (82.3%)</td> <td>58 (90.6%)</td> </tr> <tr> <td>A</td> <td>24 (17.7%)</td> <td>6 (9.4)</td> </tr> </tbody> </table> No differences	Genotype	AD (n=68)	Control (n=32)	G/G	48 (70.4%)	26 (81.2%)	G/A	16 (23.5)	6 (18.8)	A/A	4 (6.1)	0 (0)	Allele	AD (n=68)	Control (n=32)	G	112 (82.3%)	58 (90.6%)	A	24 (17.7%)	6 (9.4)																																
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2	Makarova, et al.	2005	Russia	Case-control	Cases: 87 Controls: 101	1-15	Distribution of NAT2 Genotypes. <table border="1"> <thead> <tr> <th rowspan="2">Accountable factors</th> <th colspan="2">Significance of differences</th> </tr> <tr> <th>χ^2</th> <th>P</th> </tr> </thead> <tbody> <tr> <td>Genotypes</td> <td></td> <td></td> </tr> <tr> <td>C481T</td> <td>3.24</td> <td>0.078</td> </tr> <tr> <td>G590A</td> <td>4.61</td> <td>0.0996</td> </tr> <tr> <td>C481T and G590A (double heterozygote;OR:0.43)</td> <td>34.95</td> <td>0.0005</td> </tr> <tr> <td>Sex and genotypes</td> <td></td> <td></td> </tr> <tr> <td>C481T</td> <td>7.33</td> <td>0.3953</td> </tr> <tr> <td>G590A</td> <td>9.68</td> <td>0.2076</td> </tr> <tr> <td>C481T and G590A</td> <td>51.12</td> <td>0.0069</td> </tr> <tr> <td>Smoking and genotypes</td> <td></td> <td></td> </tr> <tr> <td>C481T</td> <td>12.74</td> <td>0.0789</td> </tr> <tr> <td>G590A</td> <td>10.91</td> <td>0.1425</td> </tr> <tr> <td>C481T and G590A</td> <td>53.07</td> <td>0.0042</td> </tr> <tr> <td>Sex, smoking, and genotypes</td> <td></td> <td></td> </tr> <tr> <td>C481T</td> <td>23.69</td> <td>0.1655</td> </tr> <tr> <td>G590A</td> <td>26.24</td> <td>0.9454</td> </tr> <tr> <td>C481T and G590A</td> <td>98.29</td> <td>0.0038</td> </tr> </tbody> </table>	Accountable factors	Significance of differences		χ^2	P	Genotypes			C481T	3.24	0.078	G590A	4.61	0.0996	C481T and G590A (double heterozygote;OR:0.43)	34.95	0.0005	Sex and genotypes			C481T	7.33	0.3953	G590A	9.68	0.2076	C481T and G590A	51.12	0.0069	Smoking and genotypes			C481T	12.74	0.0789	G590A	10.91	0.1425	C481T and G590A	53.07	0.0042	Sex, smoking, and genotypes			C481T	23.69	0.1655	G590A	26.24	0.9454	C481T and G590A	98.29	0.0038
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3	Hoffjan, et al.	2005	Germany	Case-control	Cases: 180/114 (M/F) Controls: 131/81 (M/F)	12 (0.5-72) 59 (22-87)	Genotype frequencies of the TLR6 Ser249Pro polymorphism <table border="1"> <thead> <tr> <th>TLR6 Ser249Pro</th> <th>Controls</th> <th>Asthma adults</th> <th>Asthma children</th> <th>AD</th> </tr> </thead> <tbody> <tr> <td></td> <td>N = 212</td> <td>N = 68</td> <td>N = 132</td> <td>N = 294</td> </tr> <tr> <td>Pro/Pro</td> <td>75</td> <td>28</td> <td>32</td> <td>108</td> </tr> <tr> <td>Pro/Ser</td> <td>104</td> <td>32</td> <td>72</td> <td>138</td> </tr> <tr> <td>Ser/Ser</td> <td>33</td> <td>8</td> <td>28</td> <td>48</td> </tr> <tr> <td>p-value</td> <td>.</td> <td>n.s.</td> <td>0.07</td> <td>n.s.</td> </tr> </tbody> </table>	TLR6 Ser249Pro	Controls	Asthma adults	Asthma children	AD		N = 212	N = 68	N = 132	N = 294	Pro/Pro	75	28	32	108	Pro/Ser	104	32	72	138	Ser/Ser	33	8	28	48	p-value	.	n.s.	0.07	n.s.																							
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4	Takahashi, et al.	2005	Japan	Case-control	Cases: 189/193 (M/F) Controls: 658	30.2 (16-65) 18-83	Genotype frequencies in Japanese AD cases and controls for IL12RB1 SNPs at nucleotide positions -111 and -2. <table border="1"> <thead> <tr> <th>Polymorphism</th> <th>Genotype</th> <th>AD (n = 382) (%)</th> <th>Controls (n = 658) (%)</th> <th>OR (95% CI)</th> </tr> </thead> <tbody> <tr> <td rowspan="3">-111A/T</td> <td>AA</td> <td>221 (59.7)</td> <td>396 (61.5)</td> <td>1.00</td> </tr> <tr> <td>AT</td> <td>113 (30.5)</td> <td>221 (34.3)</td> <td>0.92 (0.69-1.21)</td> </tr> <tr> <td>TT</td> <td>36 (9.7)</td> <td>27 (4.2)</td> <td>2.39 (1.41-4.04)</td> </tr> <tr> <td rowspan="3">-2C/T</td> <td>CC</td> <td>232 (63.2)</td> <td>415 (65.5)</td> <td>1.00</td> </tr> <tr> <td>CT</td> <td>105 (28.6)</td> <td>198 (31.2)</td> <td>0.95 (0.71-1.26)</td> </tr> <tr> <td>TT</td> <td>30 (8.2)</td> <td>21 (3.3)</td> <td>2.55 (1.43-4.57)</td> </tr> </tbody> </table>	Polymorphism	Genotype	AD (n = 382) (%)	Controls (n = 658) (%)	OR (95% CI)	-111A/T	AA	221 (59.7)	396 (61.5)	1.00	AT	113 (30.5)	221 (34.3)	0.92 (0.69-1.21)	TT	36 (9.7)	27 (4.2)	2.39 (1.41-4.04)	-2C/T	CC	232 (63.2)	415 (65.5)	1.00	CT	105 (28.6)	198 (31.2)	0.95 (0.71-1.26)	TT	30 (8.2)	21 (3.3)	2.55 (1.43-4.57)																						
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Frequency of CMAI SNP genotypes and haplotypes in atopic eczema and controls. Genotype, haplotype frequencies

SNP ID	Location and genotypes	Atopic eczema	Control numbers	Total study population
rs1800875	5' flanking			
	AA	26.8	28.8	28.5
	AG	44.8	48.6	48.0
	GG	28.4	22.6	23.5
rs1956923	OR	(OR: 1.91 [95% CI: 1.25-2.86])		
	5' flanking			
	CC	54.8	55.4	55.3
	CT	36.1	38.7	38.4
rs5244	TT	9.1	5.9	6.3
	5' flanking			
	CC	5.1	3.9	4.1
	CT	33.5	30.6	31.0
rs5246	TT	61.4	65.5	64.9
	Exon 3			
	CC	0	0	0
	CG	0.8	1.3	1.2
rs5247	GG	99.2	98.7	98.8
	Exon 3			
	AA	94.0	95.7	95.5
	AG	6.0	4.3	4.5
rs5248	GG	0	0	0
	Intron 4			
	AA	83.4	85.2	85.0
	AG	16.6	14.1	14.4
rs5250	GG	0	0.7	0.6
	3' flanking			
	CC	74.8	77.8	77.4
	CT	22.8	21.1	21.4
	TT	2.4	1.1	1.2
	A-C-T-G-A-A-C	46	50.5	49.9
	G-C-C-G-A-A-T	13.5	11.5	11.8
	G-C-C-G-A-G-C	8	7.5	7.6
	G-T-T-G-A-A-C	26.5	24.6	24.9

Association between ST2-26999 G/A SNP and AD

	Controls (n=614)	AD (n=452)	χ^2	P-value	OR	95% CI
-26999G/A						
GG	223	106	20.20		1.86	
GA	279	240	(0.0000070)		(1.42-2.45)	
AA	112	106	(0.000049)			

Haplotype structures and frequencies in ST2 distal promoter

Haplotype	Haplotype frequency	χ^2	P-value	OR
-27639, -26999	Case			
	Control			
A, G	0.56	0.48	13.00	0.0012
G, A	0.41	0.50	15.14	0.0004
G, G	0.025	0.019	0.85	0.35

Haplotype structures and frequencies in ST2

HaplotypeID	Haplotype frequency	-27639	-26999	744	2992	5283	5860	11147
	Case							
	Control							
Haplotype A	0.41	0.5	G	A	C	T	A	C
Haplotype B	0.33	0.32	A	G	C	C	G	A
Haplotype C	0.13	0.12	A	G	A	T	A	C

Haolotype1/others: $\chi^2=17.5$; $P=0.000028$; OR=1.45.
 Haolotype2/others: $\chi^2=0.15$; $P=0.703$; OR=1.04.
 Haolotype3/others: $\chi^2=0.57$; $P=0.451$; OR=1.1.