Brief Report

Associations between interleukin-13, interleukin-4 and their receptor gene polymorphisms and susceptibility to atopic dermatitis in a Chinese Han population

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Abstract

Background: Atopic dermatitis (AD) is a common skin condition that occurs due to a combined effect of immune dysregulation, skin barrier dysfunction, changes in the cutaneous microbiome, and genetic factors. Recent data from both clinical trials and real-world studies indicate that dupilumab, a biological agent that inhibits interleukin 4 receptor-α is an effective drug in the treatment of AD, which further suggests the important role of IL-13 and IL-4 in the pathogenesis of AD.

Objectives: To assess the association between gene polymorphisms of IL-13, IL-13 receptor, IL-4, and IL-4 receptor and susceptibility to AD.

Methods: The single nucleotide polymorphisms (SNPs) of the above-mentioned genes were detected by single base extension (SNaPshot) assay. The association between these SNPs and AD risk was analysed using SPSS software.

Results: Two hundred and seventy-one subjects including 130 patients with AD and 141 healthy controls were enrolled. There were statistical differences between AD patients and controls in genotype distribution at rs2265753, rs6646259, and rs2254672 of the IL-13 receptor gene (P all < 0.001). Subjects with CG at rs2265753, AG at rs6646259 and TG at rs2254672 had increased risks for AD (P all < 0.001), and subjects with GG at rs2265753, rs6646259, and rs2254672 had reduced risks for AD (P all < 0.001).

Limitation: This was a single-centre and single-race study, with a relatively small sample size.

Conclusions: Findings from this study show that rs2265753, rs6646259 and rs2254672 of the IL-13 receptor gene are associated with susceptibility to AD.

Key words: Atopic dermatitis, IL-14, IL-13, single nucleotide polymorphism, receptor

Introduction

Atopic dermatitis (AD) is a common skin disease that usually begins during infancy. The lesions of AD are characterised by pruritic erythematous, papules, papulovesicles, and lichenification which may become excoriated and tend to have a flexural distribution such as the neck, cubital fossa, and popliteal fossa. AD generally occurs due to a combined effect of immune dysregulation, skin barrier dysfunction, alterations in the skin bacterial microbiome, and genetic factors.[1] Genetic factors are very important in the pathogenesis of AD, which is supported by the facts that the concordance rate for AD is much higher in identical twins than in fraternal twins,[2] AD patients or their first-degree relatives often have a history of atopic diseases, such as AD, allergic rhinitis,

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allergic conjunctivitis, asthma, food allergy, and eosinophilic esophagitis. Recent studies have shown that more than 70 genes may be related to the pathogenesis of AD.[3]

Recent data from both clinical trials and real-world studies indicate that dupilumab, a biological agent targeting interleukin 4 receptor-α is a very effective drug for the treatment of AD, emphasising the role of IL-13 and IL-4 in the pathogenesis.[4] The objective of this study was to evaluate the association between IL-13, IL-4, and their receptor gene polymorphisms and the susceptibility to AD in a Chinese Han population.

Methods

Study population

The required sample size was calculated using the Raosoft sample size calculator,[5] based on a significance level of 5%, confidence interval of 90%, population size of 2,00,000, and the prevalence of each mutation [Table 1]. Inclusion criteria were a confirmed diagnosis of AD based on Hanifin and Rajka criteria, absence of other skin diseases, and Chinese Han ethnicity. Patients with mixed ethnicities were excluded. All patients were enrolled from October 2021 to July 2022 in Xiamen Children's Hospital. Healthy controls were enrolled from children undergoing a routine physical examination in the same hospital, and all of them had no personal and/or family history of AD, allergic rhinitis, asthma, and other allergic diseases based on the questionnaire and previous diagnoses. The study was approved by the Ethics Committee of Xiamen Children's Hospital (Approval no. [2022]04) and all patients and controls signed informed consent before data collection.

Primer design, data collection, and genotyping

Blood was collected from each patient and control and immediately stored at –80°C. We searched the website of The National Center for Biotechnology Information (NCBI) to identify Single Nucleotide Polymorphisms (SNPs) in IL-13, IL-4, and their receptor genes, reviewed relevant literature, and in total choose 12 SNPs from the four genes as listed, IL-13 -rs3091307, rs2054, and rs1800925, IL-13 receptor - rs2265753, rs6646259 and rs2254672, IL-4 - rs2243250, rs2227284 and rs2243274 and IL-4 receptor - rs1801275, rs1805010 and rs1805011. Genotypes of samples were detected by SNaPshot assay, polymerase chain reaction (PCR) primers used for amplification, and minisequencing primers used for SNaPshot reactions of the 12 gene regions as shown in Table 2.

Table 1: The required sample size calculated using Raosoft sample size calculator

SNP	Minor allele	Minor allele frequency	Sample size required
rs3091307[6]	G	0.213	182
rs2254672[6]	G	0.407	261
rs2265753[6]	G	0.408	262
rs20541[6]	A	0.360	250
rs1800925[7]	T	0.215	183
rs2243250[8]	T	0.165	149
rs2227284[8]	T	0.341	243
rs1805011[8]	C	0.173	155
rs1801275[9]	G	0.188	166
rs1805010[9]	G	0.500	271
rs6646259	A	0.500*	271
rs2243274	G	0.500*	271

*We used 50% because there is no data available on atopic dermatitis (AD) patients.

Statistical analysis

SPSS 21.0 software was applied to analyse all the experimental data. The age of the patients and controls were analysed by Student's t-test. The gender of the two groups and the deviation of Hardy–Weinberg equilibrium (HWE) were analysed by the chi-square test. Differences in allelic frequency and genotypic distribution including dominant, codominant, over dominant, and recessive genetic models between AD patients and healthy controls were evaluated using logistic regression analyses, and the odd ratios (OR) with the 95% confidence interval (95% CI) were obtained accordingly.

Results

We enrolled 130 patients with AD (64 males and 66 females, mean age 39.74 ± 31.49 months) and 141 healthy controls (72 males and 69 females, mean age 41.45 ± 29.68 months) less than 18 years of age. No significant differences were observed concerning gender and age between patients and controls ($P > 0.05$). All 271 samples were successfully genotyped for the selected 12 SNPs, and they did not deviate from the distribution of Hardy–Weinberg equilibrium [Table 3]. Representative electropherograms of the 12 SNPs are shown in Figure 1. Table 3 lists the minor allele frequency of the 12 SNPs with a 95% CI level. Table 4 lists the allele and genotype frequencies of the 12 SNPs in the AD patient group and the control group. There were no statistically significant differences between AD patients and controls in genotype and allele frequencies at SNPs of IL-13, IL-4, and IL-4 receptor genes. There were no statistically significant differences between AD patients and controls in allele frequencies at SNPs of the IL-13 receptor gene. There were statistically significant differences between AD patients and controls in genotype distribution at rs2265753, rs6646259, and rs2254672 of the IL-13 receptor gene (P all < 0.001). Subjects with CG at rs2265753, AG at rs6646259, and TG at rs2254672 had increased risks for AD (P all < 0.001), and subjects with GG at rs2265753, rs6646259, and rs2254672 had reduced risks for AD (P all < 0.001).

Discussion

As most patients with AD have eosinophilia and elevated serum total IgE, AD is currently considered to be a Th2 cells-mediated inflammatory disease. In the Th2 inflammatory process of AD, Th2 cells-derived cytokines, especially IL-4 and IL-13 play a crucial role because both can stimulate

Table 2: PCR primers used for the amplification and minisequencing primers used for the SNaPshot reactions of the 12 gene regions

PCR primers used for the amplification of the 12 gene regions

Genes	SNPs	Primer sequence	Product (bp)
IL-4	rs2243250	F: AAGGGCTTCCTTATGGGTAAGG R:GCATCTTGGAAACTGTCCTGTC	208
	rs2227284	F:CTGTCTGAGGAACAGCAAAGTG R:GAACTGCTTAGGGAGTGACTCA	386
	rs2243274	F:AAGGAGATTCTCACTCCGCATC R:TCTCAGTCAGGTTCTGCTCTTG	345
IL-13	rs3091307	F:AGATACAGAGGTGTTATAGTG R:AGTTCCTGAGCATTCTTG	343
	rs20541	F:CTTCCGTGAGGACTGAATGAGA R:CACAGGCTGAGGTCTAAGCTAA	360
	rs1800925	F:TGGGTAGGGGAGAAATCTTGAC R:ACGTGTCTGGCCCCTTTAAT	360
IL-4R	rs1805010	F:ATCTGTCCTCACATCCGTGATC R:CTTCCTCCTGCTGTTGCTATGA	393
	rs1805011	F:AGATCAGCAAGACAGTCCTCTG R:AGGAACAGGCTCTCTGTTAGC	202
	rs1801275	F:AGAGTCCAGACAACCTGACTTG R:CTTGAGAAGGCCTTGTAACCAG	394
IL-13R	rs2265753	F:CATTTGAGGAGAGACTCCCAGT R:CCAAGTCAGTTCTTCACTCAGC	329
	rs6646259	F:AGCCTGGACCTCTATTACTCCT R:TCGTTGAAGAGGCTGTTGGT	356
	rs2254672	F:GTCATCATTCCCTTCGACAGC R:GGCCTAGCACAAACCAAAGAC	257

Minisequencing primers used for the SNaPshot reactions of the 12 gene regions

Genes	SNPs	Primer sequence
IL-4	rs2243250	TTTTTTTTTTTTTTTTTTTTTTTTTTCACCTAAACTTGGGAGAACATTGT
	rs2227284	TTTTTTTTTTAGCTCTCTTTGGTAAATAGGAAAT
	rs2243274	TTTTTTTTTTTTTTTTAAAATGTCTTAGCTCCTCACTTGG
IL-13	rs3091307	TTTTTTTTTTTTTTTTTTTTGTTTGTGTTTATTCCATTGTTTTCA
	rs20541	TTTTTTTTTTTTTTTTTTTTTTTTTTTTGCTTTCGAAGTTTCAGTTGAAC
	rs1800925	TTTTTTTTTTTTTTTTTTTTCCTTTTCCTGCTCTTCCCTC
IL-4R	rs1805010	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTCCTCCGTTGTTCTCAGGGA
	rs1805011	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGACTTCCAGGAGGGAAGGG
	rs1801275	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTCCCCCACCAGTGGCTATC
IL-13R	rs2265753	TTTTTTTTTTTTTTTTTTTTTTTTTTTGCCATGGCCTGCGTGAT
	rs6646259	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTTGTCGCGGACACTCCATA
	rs2254672	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTCCACTGCCCCTAACAGCCTA

Note: A-adenine, C-cytosine, T-thymine and G-guanine.

eosinophil recruitment and IgE production, and contribute to decreased antimicrobial peptide production, increase keratinocyte proliferation and impairment of skin barrier function.[10]

In most patients with AD, the serum total IgE level is significantly elevated. Therefore, IL-4 has long been considered the most critical cytokine involved in the pathogenesis of AD, because it plays a crucial role in the regulation of IgE synthesis. However, in recent years, strong evidence has shown that IL-13 is more important than IL-4 in AD inflammation.[11–13]

In recent years, advances in biologics also suggest that IL-13 plays a more important role than IL-4 in the pathogenesis of AD. As mentioned above, clinical and real-world data indicate that dupilumab which blocks the biological functions of both IL-4 and IL-13 has shown very good efficacy in the treatment of AD.[4] Lebrikizumab and tralokinumab which blocks the biological function of IL-13 alone, have also shown promising efficacy in the treatment of AD,[14,15] and tralokinumab has been approved by FDA for the treatment of moderate to severe AD in 2022.[16] However, till date there is no evidence to prove that a biological agent that exclusively blocks IL-4 is effective in the treatment of AD.

In recent years, studies have increasingly focused on the relationship between genetic factors and susceptibility to AD. These studies have shown that more than 70 genes could be involved in the pathogenesis of AD, especially the filaggrin

Table 3: Hardy–Weinberg equilibrium test and minor allele frequency with 95% CI level of the 12 SNPs

	Hardy–Weinberg equilibrium test					Minor allele frequency with 95% CI		
SNPs	**Genotype distribution**			χ^2	***P***	**Minor allele**	**Minor allele frequency**	**95% CI**
rs2265753	CC	CG	GG	4.08	0.13	G	0.446	0.385–0.507
	48	48	34					
rs6646259	AA	AG	GG	3.19	0.20	G	0.419	0.359–0.480
	51	49	30					
rs2254672	TT	TG	GG	4.97	0.08	G	0.423	0.363–0.484
	52	46	32					
rs3091307	AA	AG	GG	2.94	0.23	G	0.219	0.169–0.270
	75	53	2					
rs20541	GG	AG	AA	1.19	0.55	A	0.362	0.303–0.420
	49	68	13					
rs1800925	CC	CT	TT	0.63	0.73	T	0.188	0.141–0.236
	84	43	3					
rs2243250	TT	CT	CC	0.01	1.00	C	0.185	0.137–0.232
	86	40	4					
rs2227284	TT	GT	GG	0.27	0.87	G	0.131	0.090–0.172
	99	28	3					
rs2243274	AA	AG	GG	0.00	1.00	G	0.192	0.144–0.241
	85	40	5					
rs1801275	AA	GA	GG	0.24	0.89	G	0.169	0.123–0.215
	91	34	5					
rs1805010	GG	GA	AA	0.88	0.65	A	0.477	0.416–0.538
	32	72	26					
rs1805011	AA	CA	CC	0.25	0.99	C	0.073	0.041–0.105
	112	17	1					

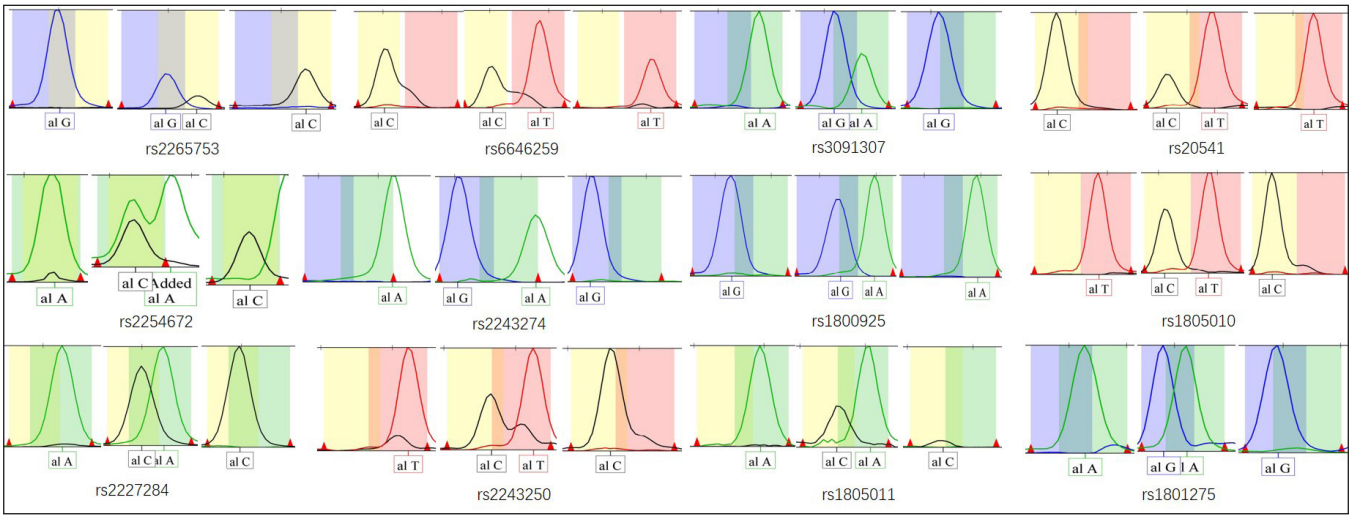

Figure 1: Representative electropherograms of the 12 Single Nucleotide Polymorphisms (SNPs). Peaks of different colors indicates different alleles (Blue peak: G; Black peak: C; Green peak: A; Red peak: T). The overlapping peaks at rs 2254672 means alleles C and A at the same site but in different color.

gene.[3] Because IL-13 plays a crucial role in the pathogenesis of AD, the polymorphism of IL-13 and its receptor genes could be associated with the genetic susceptibility and severity of AD. In recent years, many researchers have shown that the SNPs of the IL-13 gene, such as rs20541, rs1800925, rs3091307, and rs1295685 are associated with AD. The association between rs20541 and AD susceptibility and total serum IgE level in a German population was reported by Liu *et al*.[17] Lee *et al*. reported that rs20541 and rs1295685 of the IL-13 gene showed significant associations with AD risk and the total serum IgE level.[7] The frequency of allele and genotypes of rs1800925 was found to be associated with the incidence and severity of AD, and total serum IgE level in Polish patients in the research of Gleń *et al*.[18] In a research

Table 4: Genotypes and alleles frequencies of the 12 SNPs in AD patients and normal controls

SNP	Genetic model	Genotype/allele	Patients N = 130(%)	Controls N = 141(%)	Logistic regression	
					OR (95% CI)	*P* value
IL-13R						
rs2265753	Codominant	CC	48 (36.9)	62 (44)	1	<0.001
		CG	48 (36.9)	14 (9.9)	0.226 (0.112–0.457))	
		GG	34 (26.2)	65 (46.1)	1.480 (0.845–2.592)	
	Dominant	CC	48 (36.9)	62 (44)	1	0.238
		CG+GG	82 (63.1)	79 (65.1)	0.746(0.458–1.214)	
	Recessive	CC+CG	96 (73.8)	76 (53.9)	1	0.001
		GG	34 (26.2)	65 (46.1)	2.415 (1.447–4.031)	
	Over dominant	CC+GG	82 (63.1)	127 (90.1)	1	<0.001
		CG	48 (36.9)	14 (9.9)	0.188 (0.098–0.363)	
	Alleles	C	144 (55.4)	138 (48.9)	1	0.133
		G	116 (44.6)	144 (51.1)	1.295 (0.924–1.186)	
rs6646259	Codominant	AA	51 (39.2)	66 (48.8)	1	<0.001
		AG	49 (37.7)	13 (9.2)	0.205 (0.101–0.418)	
		GG	30 (23.1)	62 (44.0)	1.597 (0.904–2.820)	
	Dominant	AA	51 (39.2)	66 (48.8)	1	0.208
		AG+GG	79 (60.8)	75 (53.2)	0.734 (0.453–1.189)	
	Recessive	AA+AG	100 (76.9)	79 (56.0)	1	<0.001
		GG	30 (23.1)	62 (44.0)	2.616 (1.545–4.428)	
	Over dominant	AA+GG	81 (62.3)	128 (90.1)	1	<0.001
		AG	49 (37.7)	13 (9.1)	0.168 (0.086–0.329)	
	Alleles	A	151 (58.1)	145 (51.4)	1	0.120
		G	109 (41.9)	137 (48.6)	1.309 (0.932–1.838)	
rs2254672	Codominant	TT	52 (40)	63 (44.7)	1	<0.001
		TG	46 (35.4)	13 (9.2)	0.233 (0.114–0.478)	
		GG	32 (24.6)	65 (46.1)	1.677 (0.957–2.936)	
	Dominant	TT	52 (40)	63 (44.7)	1	0.436
		TG+GG	78 (60.0)	78 (55.3)	0.825 (0.509–1.338)	
	Recessive	TT+TG	98 (75.4)	76 (57.6)	1	<0.001
		GG	32 (24.6)	65 (42.4)	2.619 (1.559-–4.339)	
	Over dominant	TT+GG	84 (64.6)	128 (90.8)	1	<0.001
		TG	46 (35.4)	13 (9.2)	0.185 (0.094–0.364)	
	Alleles	T	150 (57.7)	139 (49.3)	1	0.050
		G	110 (42.3)	143 (50.7)	1.403 (0.999–1.969)	
IL-13						
rs3091307	Codominant	AA	75 (57.7)	91 (64.5)	1	0.139
		AG	53 (40.8)	44 (31.2)	0.684 (0.414–1.132)	
		GG	2 (1.5)	6 (4.3)	2.473 (0.485–12.610)	
	Dominant	AA	75 (57.7)	91 (64.5)	1	0.248
		AG+GG	55 (42.3)	50 (35.5)	0.749 (0.459–1.223)	
	Recessive	AA+AG	128 (98.5)	135 (95.7)	1	0.176
		GG	2 (1.5)	6 (4.3)	2.844 (0.564–14.351)	
	Over dominant	AA+GG	77 (59.2)	97 (68.8)	1	0.101
		AG	53 (40.8)	44 (31.2)	0.659 (0.400–1.086)	
	Alleles	A	203 (78.1)	226 (80.1)	1	0.555
		G	57 (21.9)	56 (19.9)	0.882 (0.583–1.336)	
rs20541	Codominant	GG	49 (37.7)	64 (45.4)	1	0.434
		AG	68 (52.3)	64 (45.4)	0.721 (0.435–1.194)	
		AA	13 (10.0)	13 (9.2)	0766 (0.326–1.799)	
	Dominant	GG	49 (37.7)	64 (45.4)	1	0.199
		AG+AA	81 (62.3)	77 (54.6)	0.728 (0.448–1.183)	

(*Continued*)

Table 4: (Continued)

SNP	Genetic model	Genotype/allele	Patients N = 130(%)	Controls N = 141(%)	Logistic regression	
					OR (95% CI)	*P* value
	Recessive	GG+AG	117 (90.0)	128 (90.8)	1	0.828
		AA	13 (10.0)	13 (9.2)	0.914 (0.407–2.052)	
	Over dominant	AA+GG	62 (47.7)	77 (54.6)	1	0.255
		AG	68 (52.3)	64 (45.4)	0.758 (0.470–1.222)	
	Alleles	A	94 (36.2)	90 (31.9)	1	0.298
		G	166 (63.8)	192 (68.1)	1.208 (0.846–1.725)	
rs1800925	Codominant	CC	84 (64.6)	94 (66.7)	1	0.938
		CT	43 (33.1)	44 (31.2)	0.914 (0.547–1.527)	
		TT	3 (2.3)	3 (2.1)	0.894 (0.176–4.548)	
	Dominant	CC	84 (64.6)	94 (66.7)	1	0.722
		CT+TT	46 (35.4)	47 (33.3)	0.913 (0.553–1.508)	
	Recessive	CC+CT	127 (97.7)	138 (97.9)	1	0.920
		TT	3 (2.3)	3 (2.1)	0.920 (0.182–4.643)	
	Over dominant	CC+TT	87 (66.9)	97 (68.8)	1	0.742
		CT	43 (33.1)	44 (31.2)	0.918 (0.551–1.529)	
	aAlleles	C	211 (81.2)	232 (82.3)	1	0.737
		T	49 (18.8)	50 (17.7)	0.928 (0.600–1.435)	
IL-4						
rs2243250	Codominant	TT	86 (66.1)	91 (64.5)	1	0.818
		CT	40 (30.8)	45 (31.9)	1.063 (0.633–1.785)	
		CC	4 (3.1)	5 (3.6)	1.575 (0.365–6.792)	
	Dominant	TT	86 (66.1)	91 (64.5)	1	0.780
		CT+CC	44 (33.9)	50 (35.5)	1.074 (0.651–1.772)	
	Recessive	TT+CT	126 (96.9)	136 (96.4)	1	0.830
		CC	4 (3.1)	5 (3.6)	1.158 (0.304–4.409)	
	Over dominant	CC+TT	90 (69.2)	96 (68.1)	1	0.839
		CT	40 (30.8)	45 (31.9)	1.055 (0.631–1.763)	
	Alleles	C	48 (18.5)	55 (19.5)	1	0.757
		T	212 (81.5)	227 (80.5)	0.934 (0.608–1.437)	
rs2227284	Codominant	TT	99 (76.2)	115 (81.6)	1	0.382
		GT	28 (21.5)	25 (17.7)	0.769 (0.421–1.404)	
		GG	3 (2.3)	1 (0.7)	0.287 (0.029–2.803)	
	Dominant	TT	99 (76.2)	115 (81.6)	1	0.275
		GT+GG	31 (23.8)	26 (18.4)	0.722 (0.402–1.298)	
	Recessive	GG	3 (2.3)	1 (0.7)	1	0.276
		GT+TT	127 (97.7)	140 (99.3)	3.307 (0.340–32.199)	
	Over dominant	GG+TT	102 (78.5)	116 (82.3)	1	0.430
		GT	28 (21.5)	25 (17.7)	0.785 (0.430–1.432)	
	Alleles	T	226 (86.9)	255 (90.4)	1	0.197
		G	34 (13.1)	27 (9.6)	0.704 (0.412–1.203)	
rs2243274	Codominant	AA	85 (65.4)	89 (63.1)	1	0.872
		AG	40 (30.8)	45 (31.9)	1.074 (0.639–1.806)	
		GG	5 (3.8)	7 (5.0)	1.337 (0.409–4.375)	
	Dominant	AA	85 (65.4)	89 (63.1)	1	0.698
		AG+GG	45 (34.6)	52 (39.9)	1.104 (0.671–1.815)	
	Recessive	GG	5 (3.8)	7 (5.0)	1	0.655
		AG+AA	125 (96.2)	134 (95.0)	0.766 (0.237–2.475)	
	Over dominant	AA+GG	90 (69.2)	96 (68.1)	1	0.568
		AG	40 (30.8)	45 (31.9)	1.160 (0.697–1.932)	
	Alleles	A	210 (80.8)	223 (79.1)	1	0.624
		G	50 (19.2)	59 (20.9)	1.111 (0.729–1.693)	

SNP	Genetic model	Genotype/allele	Patients N = 130(%)	Controls N = 141(%)	Logistic regression	
					OR (95% CI)	*P* value
IL-4R						
rs1801275	Codominant	AA	91 (70.0)	103 (73.1)	1	0.440
		GA	34 (26.2)	36 (25.5)	0.935 (0.541–1.617)	
		GG	5 (3.8)	2 (1.4)	0.353 (0.067–1.866)	
	Dominant	AA	91 (70.0)	103 (73.1)	1	0.578
		GA+GG	39 (30)	38 (26.9)	0.861 (0.508–1.460)	
	Recessive	GG	5 (3.8)	2 (1.4)	1	0.208
		GA+AA	125 (96.2)	139 (98.6)	2.780 (0.530–14.585)	
	Over dominant	AA+GG	96 (73.8)	105 (74.5)	1	0.907
		GA	34 (26.2)	36 (25.5)	0.968 (0.562–1.668)	
	Alleles	A	216 (83.1)	242 (85.8)	1	0.379
		G	44 (16.9)	40 (14.2)	0.811 (0.509–1.293)	
rs1805010	Codominant	GG	32 (24.6)	33 (23.4)	1	0.473
		GA	72 (55.4)	71 (50.4)	0.956 (0.532–1.719)	
		AA	26 (20.0)	37 (26.2)	1.380 (0.686–2.775)	
	Dominant	GG	32 (24.6)	33 (23.4)	1	0.816
		GA+AA	98 (75.4)	108 (76.6)	1.069(0.612–1.867)	
	Recessive	AA	26 (20.0)	37 (26.2)	1	0.224
		GA+GG	104 (80.0)	104 (73.8)	0.703 (0.397–1.243)	
	Over dominant	GG+AA	58 (44.6)	70 (49.6)	1	0.407
		GA	72 (55.4)	71 (50.4)	0.817 (0.507–1.318)	
	Alleles	G	136 (52.3)	137 (48.6)	1	0.386
		A	124 (47.7)	145 (51.4)	1.161 (0.828–1.626)	
rs1805011	Codominant	AA	112 (86.2)	120 (85.8)	1	0.964
		CA	17 (13.1)	20 (14.2)	1.098 (0.547–2.202)	
		CC	1 (0.7)	1 (0.0)	0.933 (0.058–15.101)	
	Dominant	AA	112 (86.2)	120 (85.8)	1	0.806
		CA+CC	18 (13.8)	21 (14.2)	1.089 (0.552–2.150)	
	Recessive	CC	1 (0.7)	1 (0.0)	1	0.954
		CA+AA	129 (99.3)	140 (100.0)	1.085 (0.067–17.530)	
	Over dominant	AA+CC	113 (86.9)	121 (85.8)	1	0.791
		CA	17 (13.1)	20 (14.2)	1.099 (0.548–2.203)	
	Alleles	A	241 (92.7)	260 (92.9)	1	0.828
		C	19 (7.3)	22 (7.1)	1.073 (0.567–2.032)	

by Namkung *et al*., there were significant differences in the genotypic and allelic distributions of rs20541, rs3091307, rs2254672 and rs2265753 between AD patients and normal controls in a Korean population.[6] In recent years, many studies have also shown that gene polymorphisms of IL-4 and IL-4 receptor are also related to AD susceptibilities, such as rs2243250, rs2243248, rs2243274 and rs2227284 of IL-4,[19–21] and rs1805015, rs1805010, rs1805011 and rs1801275 of IL-4R.[22–25]

Limitations

This was a single-centre and single-race study with a small sample size. We did not apply the Bonferroni correction in the present study to control the multiple comparisons.

Conclusions

This study researched the association between the polymorphism of IL-4 and IL-13, and their receptor genes, and the genetic susceptibility of AD patients in a Chinese Han Population. The results suggested that the rs2265753, rs6646259, and rs2254672 of the IL-13 receptor gene are associated with susceptibility to AD. Subjects with CG at rs2265753, AG at rs6646259, and TG at rs2254672 had increased risks for AD, while patients with GG at rs2265753, rs6646259 and rs2254672 showed a protective effect. These findings may have a role in the development of future precision therapy and targeted drugs in the treatment of AD. Other functional SNPs of the IL-13 receptor gene need to be explored. Large-scale, multi-centric studies including patients from different ethnicities are required to further

clarify the role of the IL-13 receptor gene in the pathogenesis of AD.

Ethical approval

This research/study is approved by the Institutional Review Board at the Ethics Committee of Xiamen Children's Hospital, number [2022]04, dated 12 May 2021.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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