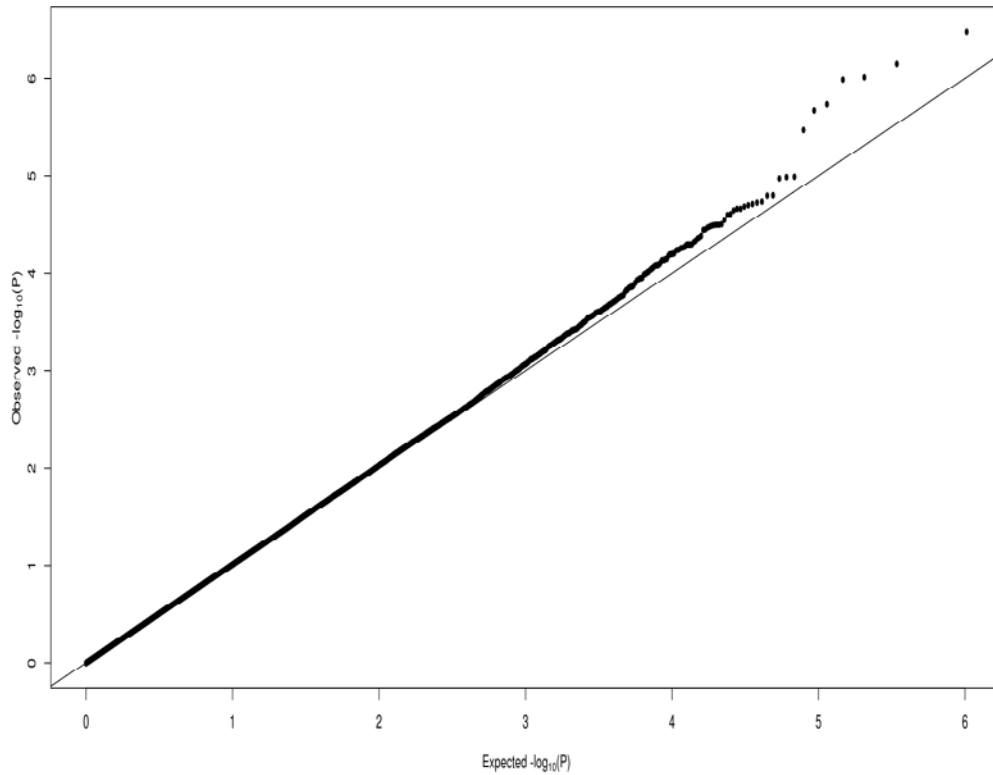


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A novel role for cilia function in atopy: *ADGRV1* and *DNAH5* interactions

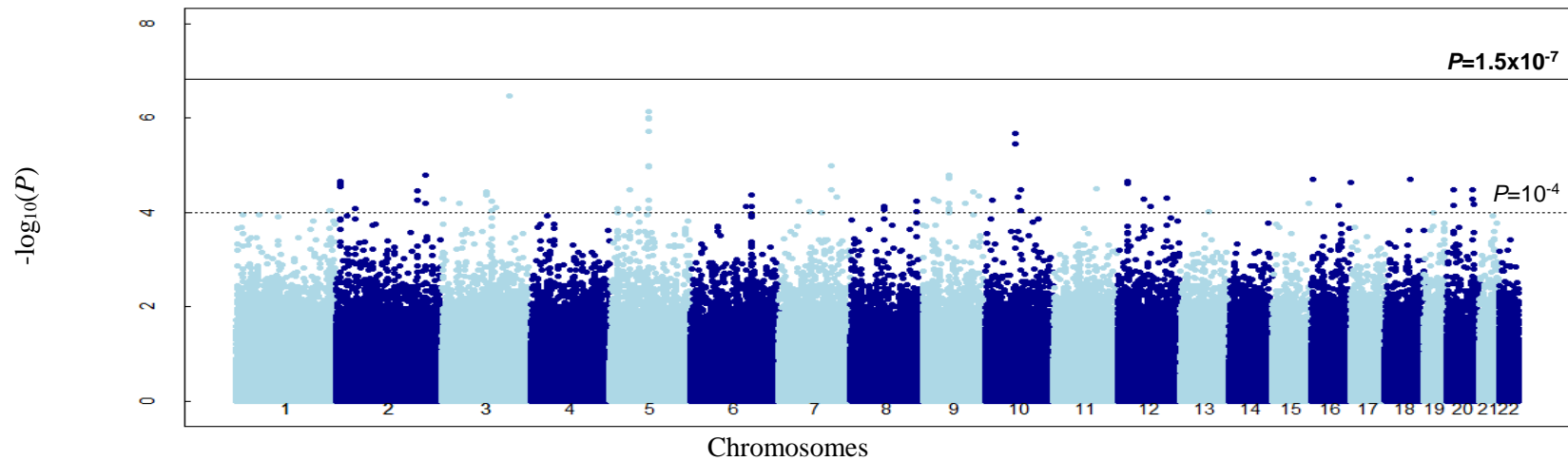
Pierre-Emmanuel Sugier^{a,b}, MSc, Myriam Brossard^{a*}, PhD, Chloé Sarnowski^{a*}, PhD, Amaury Vaysse^a, PhD, Andréanne Morin^{c,d}, MSc, Lucile Pain^d, MSc, Patricia Margaritte-Jeannin^a, PhD, Marie-Hélène Dizier^a, PhD, William O.C.M. Cookson, MD, D.Phil.^e, Mark Lathrop^c, PhD, Miriam F. Moffatt, D.Phil.^e, Catherine Laprise^{d‡}, PhD, Florence Demenais^{a‡}, MD, Emmanuelle Bouzigon^{a‡}, MD, PhD

Figure E1: Quantile-quantile plot of GWAS results of atopy in the stage 1 EGEA dataset



Quantile-quantile (QQ) plot for the association of atopy with 501,167 genotyped SNPs that passed quality control (QC) in the stage 1 EGEA dataset. The dots represent the distribution of observed $-\log_{10}(P)$ values against the expected $-\log_{10}(P)$ values from a theoretical chi-square distribution. The straight line represents the theoretical distribution of expected $-\log_{10}(P)$ values under the null hypothesis of no association. There was no evidence of any systematic bias: the genomic inflation factor (λ) was equal to 1.017.

Figure E2: Manhattan plot of GWAS results for atopy in the stage 1 EGEA dataset



The y axis shows the $-\log_{10} P$ -values of the association test of individuals SNPs with atopy in the stage 1 EGEA dataset and the x axis shows the SNP chromosomal positions. The solid horizontal line indicates the genome-wide significance level ($P=1.5 \times 10^{-7}$); the dotted horizontal line indicates the suggestive association level ($P=10^{-4}$) to select SNPs for follow-up in stage 2 SLSJ and MRC datasets.

Table E1. Descriptive statistics of EGEA, SLSJ and MRC datasets

	EGEA			SLSJ			MRC		
	Non-atopics N=735	Atopics N=925	<i>P</i> *	Non-atopics N=497	Atopics N=641	<i>P</i> *	Non-atopics N=340	Atopics N=106	<i>P</i> *
Sex (male), n (%)	329 (44.8)	539 (58.3)	<10 ⁻⁴	205 (41.3)	317 (49.5)	5.9x10 ⁻³	117 (34.4)	68 (64.2)	<10 ⁻⁴
Age (yrs), mean (SD)	35.9 (16.7)	27.5 (15.7)	<10 ⁻⁴	45.1 (23.4)	32.5 (18.4)	<10 ⁻⁴	19.6 (14.7)	12.7 (4.3)	<10 ⁻⁴
Asthma, n (%)	114 (16.0)	514 (56.3)	<10 ⁻⁴	144 (29.0)	405 (63.2)	<10 ⁻⁴	84 (24.7)	93 (87.7)	<10 ⁻⁴
Indoor allergens [†] , n (%)	-	720 (78.0)		-	481 (75.0)		-	83 (78.3)	
Outdoor allergens [‡] , n (%)	-	512 (55.5)		-	497 (77.5)		-	56 (52.8)	
Molds [§] , n (%)	-	320 (34.8)		-	95 (14.8)		-	13 (12.3)	

**P*-values for tests of distribution of each feature (sex, age, asthma) between atopic and non-atopic subjects in each dataset (chi-square test for sex and asthma; Wilcoxon-Mann-Whitney test for age).

[†]Indoor allergens included house dust mite, cockroach and cat in EGEA; house dust mite, dust and cat in SLSJ; dust mite and cat in MRC.

[‡]Outdoor allergens included timothy grass, olive, birch, ragweed and pellitory in EGEA; herbs, trees and animals in SLSJ; timothy grass in MRC.

[§]Molds included *Alternaria*, *Aspergillus* and *Cladosporium* in EGEA; *Alternaria*, *Aspergillus*, *Cladosporium*, *Hormodendrum* and *Penicillium* in SLSJ; *Aspergillus* and *Cladosporium* in MRC.

Table E2. Loci showing suggestive association with atopy at $P \leq 10^{-4}$ in the stage 1 EGEA dataset and followed-up in stage 2 SLSJ and MRC datasets

SNP	Chr*	Position (kb)	Nearest genes (kb distance) [†]	Alleles [‡]	EAF [§]	Stage 1		Stage 2						Overall Meta-Analysis	
						EGEA (N=1,660)		SLSJ (N=1,138)		MRC (N=446)		Meta-Analysis		OR (95% CI)	P_{meta}^{**}
						OR (95% CI)	$P^{††}$	OR (95% CI)	$P^{††}$	OR	$P^{††}$	OR (95% CI)	P_{stage2}^{**}		
rs1252146	1	237 154	<i>MTR (87);RYR2 (51)</i>	C/T	0.31	1.41 (1.19;1.67)	8.9x10 ⁻⁵	0.75 (0.60;0.93)	8.9x10 ⁻³	1.03 (0.68;1.58)	0.88	0.80 (0.66;0.97)	0.02	1.10 (0.97;1.25)	0.15
rs9428818	1	239 172	<i>ZP4 (1 118);CHRM3 (620)</i>	C/T	0.08	1.74 (1.32;2.29)	8.9x10 ⁻⁵	1.60 (1.07;2.41)	2.3x10 ⁻²	1.07 (0.52;2.21)	0.86	1.46 (1.02;2.08)	0.04	1.63 (1.31;2.02)	1.3x10 ⁻⁵
rs13409750	2	7 610	<i>RNF144A (425);LINC00299 (538)</i>	C/T	0.80	0.64 (0.53;0.79)	2.5x10 ⁻⁵	1.05 (0.84;1.32)	0.66	0.95 (0.63;1.45)	0.83	1.03 (0.84;1.26)	0.78	0.82 (0.71;0.94)	5.9x10 ⁻³
rs7567384	2	7 611	<i>RNF144A (426);LINC00299 (537)</i>	C/T	0.80	0.65 (0.53;0.79)	2.8x10 ⁻⁵	1.05 (0.84;1.32)	0.66	0.96 (0.63;1.45)	0.84	1.03 (0.85;1.25)	0.77	0.82 (0.71;0.95)	6.8x10 ⁻³
rs1561574	2	7 647	<i>RNF144A (463);LINC00299 (501)</i>	C/T	0.15	1.60 (1.29;2.00)	2.2x10 ⁻⁵	1.07 (0.83;1.37)	0.6	1.13 (0.73;1.75)	0.57	1.08 (0.87;1.35)	0.46	1.32 (1.13;1.54)	4.3x10 ⁻⁴
rs3819892	2	37 510	<i>PRKD</i>	G/T	0.86	0.63 (0.50;0.79)	8.1x10 ⁻⁵	1.09 (0.81;1.48)	0.56	0.89 (0.46;1.7)	0.72	1.05 (0.80;1.39)	0.71	0.78 (0.65;0.93)	5.7x10 ⁻³
rs10497664	2	186 260	<i>ZNF804A (456);FSIP2(343)</i>	G/T	0.41	1.38 (1.18;1.61)	5.5x10 ⁻⁵	0.89 (0.74;1.08)	0.24	0.79 (0.54;1.14)	0.21	0.87 (0.74;1.03)	0.11	1.11 (0.99;1.25)	0.06
rs13006333	2	186 268	<i>ZNF804A (464);FSIP2 (335)</i>	G/T	0.43	1.38 (1.18;1.61)	3.4x10 ⁻⁵	0.89 (0.74;1.08)	0.23	0.76 (0.52;1.11)	0.16	0.86 (0.73;1.02)	0.09	1.12 (1.00;1.25)	0.05
rs12328639	2	211 676	<i>CPSI (132);ERBB4 (564)</i>	A/G	0.19	1.50 (1.23;1.84)	6.4x10 ⁻⁵	1.11 (0.89;1.39)	0.35	1.04 (0.64;1.69)	0.88	1.10 (0.90;1.34)	0.36	1.29 (1.12;1.48)	4.8x10 ⁻⁴
rs1016403	2	211 704	<i>CPSI (161);ERBB4 (536)</i>	A/G	0.16	1.60 (1.29;1.99)	1.6x10 ⁻⁵	1.17 (0.92;1.48)	0.19	1.01 (0.63;1.63)	0.95	1.14 (0.92;1.40)	0.23	1.35 (1.16;1.56)	9.9x10 ⁻⁵
rs2689860	3	801	<i>CHLI (349);CNTN6 (334)</i>	A/C	0.63	1.37 (1.18;1.59)	5.1x10 ⁻⁵	0.83 (0.68;1.02)	7.9x10 ⁻²	1.10 (0.77;1.57)	0.60	0.89 (0.75;1.06)	0.20	1.14 (1.02;1.28)	0.02
rs445518	3	28 004	<i>EOMES (240);CMC1 (279)</i>	C/T	0.32	0.71 (0.61;0.84)	6.5x10 ⁻⁵	1.21 (0.99;1.47)	6.6x10 ⁻²	1.08 (0.75;1.55)	0.69	1.17 (0.99;1.40)	0.07	0.90 (0.80;1.02)	0.09
rs1007368	3	93 961	<i>NSUN3 (115);EPHA6 (2 573)</i>	A/G	0.87	1.59 (1.28;1.99)	4.2x10 ⁻⁵	0.99 (0.71;1.40)	0.98	1.37 (0.75;2.48)	0.30	1.07 (0.80;1.44)	0.63	1.38 (1.16;1.65)	3.8x10 ⁻⁴
rs1584930	3	93 962	<i>NSUN3 (116);EPHA6 (2 572)</i>	A/G	0.13	0.62 (0.50;0.78)	3.6x10 ⁻⁵	1.00 (0.71;1.41)	1	0.73 (0.4;1.33)	0.31	0.92 (0.69;1.25)	0.61	0.72 (0.60;0.86)	3.1x10 ⁻⁴
rs3900940	3	108 148	<i>MYH15</i>	C/T	0.68	1.39 (1.18;1.64)	9.3x10 ⁻⁵	0.93 (0.74;1.16)	0.51	1.20 (0.84;1.73)	0.32	1.00 (0.82;1.21)	0.98	1.21 (1.07;1.37)	3.1x10 ⁻³
rs11917965	3	108 189	<i>MYH15</i>	A/C	0.41	0.72 (0.62;0.85)	5.9x10 ⁻⁵	1.05 (0.85;1.29)	0.66	0.81 (0.57;1.15)	0.24	0.98 (0.82;1.17)	0.83	0.83 (0.74;0.93)	1.6x10 ⁻³
rs7633227	3	116 831	<i>LSAMP-AS4 (180);IGSF11 (1 789)</i>	C/T	0.62	0.73 (0.62;0.85)	7.9x10 ⁻⁵	0.97 (0.79;1.18)	0.73	1.13 (0.77;1.65)	0.54	1.00 (0.84;1.19)	0.98	0.84 (0.75;0.94)	3.2x10 ⁻³
rs4681369	3	147 419	<i>FLJ30375 (279);AGTRI (997)</i>	G/T	0.20	0.62 (0.51;0.74)	3.4x10 ⁻⁷	1.01 (0.80;1.29)	0.91	1.03 (0.69;1.54)	0.89	1.02 (0.83;1.25)	0.87	0.77 (0.67;0.89)	2.3x10 ⁻⁴
rs795540	5	13 818	<i>DNAH5</i>	C/T	0.56	0.73 (0.62;0.85)	8.3x10 ⁻⁵	1.02 (0.84;1.23)	0.86	0.95 (0.67;1.35)	0.76	1.00 (0.85;1.18)	0.99	0.85 (0.75;0.95)	4.4x10 ⁻³
rs17194068	5	39 821	<i>DAB2 (396);PTGER4 (859)</i>	A/G	0.28	1.44 (1.21;1.70)	3.3x10 ⁻⁵	0.81 (0.66;1.00)	5.1x10 ⁻²	0.87 (0.6;1.26)	0.45	0.82 (0.69;0.99)	0.04	1.11 (0.98;1.26)	0.11
rs7711329	5	65 126	<i>NLN (1);ERBB2IP (96)</i>	C/T	0.19	0.68 (0.56;0.83)	8.3x10 ⁻⁵	1.07 (0.83;1.37)	0.61	1.07 (0.65;1.77)	0.80	1.07 (0.85;1.33)	0.57	0.82 (0.71;0.95)	8.7x10 ⁻³
rs10942608	5	90 083	<i>ADGRV1</i>	C/T	0.23	0.71 (0.60;0.84)	8.2x10 ⁻⁵	0.99 (0.81;1.21)	0.92	0.75 (0.49;1.16)	0.19	0.94 (0.78;1.13)	0.52	0.81 (0.71;0.92)	8.4x10 ⁻⁴
rs4244205	5	90 189	<i>ADGRV1</i>	A/G	0.41	0.71 (0.61;0.83)	1.1x10 ⁻⁵	0.83 (0.68;1.01)	6.0x10 ⁻²	0.87 (0.62;1.24)	0.45	0.84 (0.70;1.00)	0.04	0.76 (0.68;0.86)	3.8x10 ⁻⁶
rs4916829	5	90 195	<i>ADGRV1</i>	T/G	0.35	0.70 (0.61;0.83)	1.0x10 ⁻⁵	0.94 (0.78;1.16)	0.59	0.88 (0.59;1.31)	0.52	0.93 (0.75;1.18)	0.44	0.79 (0.70;0.89)	1.2x10 ⁻⁴
rs4916831	5	90 212	<i>ADGRV1</i>	A/G	0.44	0.67 (0.58;0.79)	1.0x10 ⁻⁶	0.72 (0.59;0.89)	2.3x10 ⁻³	0.81 (0.58;1.14)	0.23	0.75 (0.63;0.89)	1.2x10 ⁻³	0.71 (0.63;0.79)	6.8x10 ⁻⁹
rs10060641	5	90 213	<i>ADGRV1</i>	T/C	0.38	0.67 (0.58;0.79)	7.2x10 ⁻⁷	0.85 (0.68;1.04)	0.11	0.79 (0.54;1.16)	0.22	0.83 (0.69;1.00)	0.05	0.74 (0.66;0.83)	4.3x10 ⁻⁷
rs12054681	5	90 218	<i>ADGRV1</i>	C/A	0.37	0.68 (0.58;0.79)	9.7x10 ⁻⁷	0.87 (0.70;1.06)	0.18	0.75 (0.5;1.12)	0.16	0.84 (0.70;1.01)	0.06	0.74 (0.66;0.84)	7.8x10 ⁻⁷
rs949787	5	90 251	<i>ADGRV1</i>	G/T	0.28	0.72 (0.61;0.84)	5.5x10 ⁻⁵	0.79 (0.66;0.96)	1.9x10 ⁻²	0.83 (0.56;1.23)	0.36	0.80 (0.67;0.95)	0.01	0.76 (0.67;0.85)	3.2x10 ⁻⁶
rs12522571	5	90 259	<i>ADGRV1</i>	A/G	0.22	0.66 (0.56;0.78)	1.9x10 ⁻⁶	0.90 (0.73;1.12)	0.36	0.75 (0.46;1.23)	0.25	0.88 (0.72;1.07)	0.19	0.74 (0.65;0.85)	7.4x10 ⁻⁶
rs7769042	6	106 156	<i>PREP (305);PRDM1 (378)</i>	A/G	0.57	1.38 (1.18;1.62)	7.4x10 ⁻⁵	1.14 (0.93;1.39)	0.21	0.61 (0.43;0.87)	0.01	0.98 (0.82;1.16)	0.79	1.18 (1.05;1.33)	5.9x10 ⁻³
rs12660166	6	120 894	<i>MIR3144 (557);C6orf170 (507)</i>	C/T	0.25	0.70 (0.59;0.84)	7.4x10 ⁻⁵	1.11 (0.87;1.42)	0.41	0.95 (0.62;1.45)	0.80	1.07 (0.86;1.32)	0.55	0.83 (0.73;0.95)	7.2x10 ⁻³
rs12194792	6	121 085	<i>MIR3144 (348);C6orf170 (316)</i>	C/T	0.58	1.37 (1.18;1.60)	4.3x10 ⁻⁵	0.90 (0.74;1.09)	0.27	1.04 (0.69;1.58)	0.83	0.92 (0.78;1.10)	0.36	1.16 (1.03;1.30)	0.01
rs1880617	7	53 138	<i>POM121L12 (33);FLJ45974 (585)</i>	G/T	0.39	1.36 (1.17;1.59)	9.5x10 ⁻⁵	1.02 (0.81;1.27)	0.89	0.85 (0.57;1.25)	0.40	0.97 (0.80;1.18)	0.77	1.19 (1.06;1.35)	4.3x10 ⁻³
rs12530936	7	91 187	<i>FZD1 (289);MTERF (315)</i>	C/T	0.13	0.64 (0.51;0.80)	9.9x10 ⁻⁵	0.86 (0.63;1.17)	0.34	0.83 (0.43;1.6)	0.57	0.85 (0.65;1.13)	0.27	0.72 (0.60;0.85)	1.8x10 ⁻⁴
rs10279056	7	115 847	<i>TFEC (176);TES (4)</i>	A/G	0.57	1.40 (1.20;1.62)	1.0x10 ⁻⁵	0.90 (0.74;1.10)	0.30	1.05 (0.75;1.48)	0.77	0.94 (0.79;1.11)	0.45	1.17 (1.05;1.31)	4.9x10 ⁻³
rs17138756	7	116 135	<i>TES (236);CAV2 (4)</i>	A/G	0.10	0.58 (0.45;0.75)	3.4x10 ⁻⁵	0.99 (0.77;1.28)	0.95	0.93 (0.51;1.7)	0.83	0.98 (0.78;1.24)	0.89	0.77 (0.65;0.92)	3.9x10 ⁻³
rs10253511	7	130 797	<i>MKLN1</i>	C/T	0.91	0.59 (0.46;0.76)	4.8x10 ⁻⁵	0.88 (0.61;1.25)	0.46	1.97 (0.82;4.74)	0.13	0.98 (0.71;1.37)	0.92	0.71 (0.58;0.87)	1.6x10 ⁻³
rs4237038	8	61 731	<i>CHD7</i>	A/G	0.25	1.44 (1.20;1.73)	7.3x10 ⁻⁵	0.97 (0.80;1.18)	0.77	1.08 (0.7;1.67)	0.74	0.99 (0.83;1.18)	0.89	1.19 (1.05;1.35)	7.6x10 ⁻³
rs10957162	8	61 758	<i>CHD7</i>	A/G	0.27	1.44 (1.20;1.72)	8.5x10 ⁻⁵	0.99 (0.82;1.21)	0.95	0.98 (0.63;1.51)	0.92	0.99 (0.83;1.18)	0.92	1.19 (1.05;1.35)	7.3x10 ⁻³
rs7357565	8	134 817	<i>ST3GALI (233);ZFAT (673)</i>	A/G	0.51	0.73 (0.62;0.86)	9.7x10 ⁻⁵	1.00 (0.82;1.22)	1	0.63 (0.41;0.96)	0.03	0.92 (0.77;1.10)	0.36	0.81 (0.72;0.91)	3.9x10 ⁻⁴

rs4399592	8	134 824	<i>ST3GAL1 (240);ZFAT (666)</i>	C/T	0.65	1.41 (1.19;1.66)	5.8x10 ⁻⁵	1.00 (0.81;1.22)	0.99	1.67 (1.11;2.52)	0.01	1.11 (0.92;1.33)	0.27	1.26 (1.12;1.43)	2.1x10 ⁻⁴
rs1408793	9	12 628	<i>PTPRD (2 000);TYRP1 (65)</i>	A/C	0.21	0.68 (0.57;0.82)	5.1x10 ⁻⁵	0.94 (0.73;1.21)	0.62	1.67 (1.02;2.72)	0.04	1.06 (0.85;1.32)	0.62	0.81 (0.71;0.94)	5.00x10 ⁻³
rs1433831	9	18 869	<i>ADAMTSL1</i>	A/G	0.34	0.72 (0.61;0.84)	5.7x10 ⁻⁵	1.13 (0.91;1.41)	0.27	0.79 (0.54;1.14)	0.20	1.03 (0.85;1.24)	0.78	0.83 (0.74;0.94)	4.0x10 ⁻³
rs2309394	9	71 671	<i>FXN</i>	A/G	0.56	0.72 (0.61;0.85)	8.4x10 ⁻⁵	1.02 (0.84;1.24)	0.83	1.49 (1.01;2.18)	0.04	1.1 (0.93;1.30)	0.27	0.88 (0.78;0.99)	0.04
rs9314854	9	71 686	<i>FXN</i>	C/T	0.52	1.37 (1.18;1.61)	6.3x10 ⁻⁵	1.18 (0.97;1.44)	9.9x10 ⁻²	0.85 (0.56;1.28)	0.43	1.11 (0.93;1.33)	0.24	1.25 (1.11;1.41)	1.6x10 ⁻⁴
rs7870295	9	71 686	<i>FXN</i>	A/G	0.55	1.42 (1.21;1.66)	1.6x10 ⁻⁵	1.15 (0.94;1.40)	0.17	0.79 (0.52;1.19)	0.25	1.07 (0.89;1.28)	0.46	1.25 (1.11;1.41)	2.0x10 ⁻⁴
rs4745580	9	71 690	<i>FXN</i>	C/T	0.55	1.41 (1.21;1.65)	1.9x10 ⁻⁵	1.16 (0.95;1.41)	0.14	1.19 (0.78;1.79)	0.42	0.89 (0.75;1.07)	0.21	0.8 (0.71;0.90)	1.5x10 ⁻⁴
rs7859021	9	71 694	<i>FXN</i>	A/G	0.48	0.73 (0.63;0.86)	8.6x10 ⁻⁵	0.84 (0.69;1.02)	7.5x10 ⁻²	1.14 (0.65;1.99)	0.64	1.02 (0.73;1.44)	0.89	1.41 (1.15;1.72)	1.1x10 ⁻³
rs2771064	9	103 921	<i>PLPPRI</i>	A/G	0.89	1.68 (1.30;2.16)	6.4x10 ⁻⁵	0.96 (0.63;1.48)	0.86	1.20 (0.82;1.75)	0.35	1.19 (1.00;1.42)	0.05	0.90 (0.80;1.02)	0.09
rs13286744	9	117 444	<i>TMEM268 (35);TNFSF15 (103)</i>	C/T	0.42	0.71 (0.60;0.84)	3.6x10 ⁻⁵	1.19 (0.98;1.45)	8.7x10 ⁻²	0.88 (0.49;1.57)	0.66	1.17 (0.87;1.57)	0.31	1.46 (1.19;1.79)	2.4x10 ⁻⁴
rs12000625	9	126 686	<i>DENND1A</i>	A/C	0.93	1.78 (1.35;2.34)	4.4x10 ⁻⁵	1.29 (0.91;1.82)	0.15	0.95 (0.58;1.57)	0.85	0.86 (0.67;1.10)	0.22	1.20 (1.02;1.41)	0.03
rs17515236	10	9 540	<i>GATA3 (1 423);CELF2 (1 507)</i>	A/G	0.87	1.57 (1.26;1.95)	5.4x10 ⁻⁵	0.83 (0.63;1.10)	0.2	0.86 (0.51;1.45)	0.57	0.73 (0.54;0.97)	0.03	1.24 (1.05;1.47)	0.01
rs11005971	10	59 649	<i>MIR3924 (584);IPMK (302)</i>	C/T	0.15	1.64 (1.33;2.01)	3.4x10 ⁻⁶	0.68 (0.48;0.96)	2.7x10 ⁻²	1.13 (0.67;1.9)	0.65	1.38 (1.03;1.84)	0.03	0.80 (0.68;0.95)	0.01
rs7101032	10	59 672	<i>MIR3924 (607);IPMK (279)</i>	C/T	0.85	0.61 (0.49;0.74)	2.1x10 ⁻⁶	1.50 (1.07;2.12)	2.0x10 ⁻²	0.69 (0.38;1.26)	0.23	0.89 (0.67;1.17)	0.41	1.24 (1.01;1.54)	0.04
rs12771265	10	71 411	<i>C10orf35 (18);COL13A1 (150)</i>	A/G	0.52	1.38 (1.19;1.61)	3.2x10 ⁻⁵	0.87 (0.72;1.05)	0.14	1.04 (0.71;1.52)	0.85	0.90 (0.76;1.07)	0.22	1.14 (1.02;1.28)	0.02
rs4746906	10	71 516	<i>C10orf35 (122);COL13A1 (45)</i>	C/T	0.16	1.53 (1.24;1.90)	9.1x10 ⁻⁵	0.93 (0.74;1.17)	0.52	0.73 (0.44;1.21)	0.22	0.89 (0.72;1.10)	0.28	1.16 (1.00;1.35)	0.05
rs618929	11	96 229	<i>JRKL (102);CNTN5 (2 662)</i>	A/G	0.54	1.39 (1.19;1.63)	3.2x10 ⁻⁵	0.81 (0.66;1.00)	4.7x10 ⁻²	1.23 (0.87;1.76)	0.24	0.90 (0.75;1.08)	0.27	1.16 (1.03;1.30)	0.02
rs4475974	12	18 262	<i>RERGL (19);PIK3C2G (152)</i>	G/T	0.60	0.71 (0.61;0.83)	2.5x10 ⁻⁵	1.05 (0.86;1.29)	0.62	0.73 (0.5;1.06)	0.10	0.97 (0.81;1.16)	0.73	0.81 (0.72;0.92)	7.1x10 ⁻⁴
rs4457807	12	18 306	<i>RERGL (63);PIK3C2G (109)</i>	A/G	0.39	0.70 (0.60;0.83)	2.2x10 ⁻⁵	1.09 (0.92;1.29)	0.32	1.16 (0.78;1.72)	0.45	1.10 (0.94;1.29)	0.23	0.89 (0.79;0.99)	0.04
rs10783599	12	54 186	<i>CALCOCO1 (65);HOXC13 (147)</i>	A/G	0.32	1.39 (1.18;1.62)	5.1x10 ⁻⁵	0.80 (0.66;0.97)	2.0x10 ⁻²	1.24 (0.81;1.89)	0.33	0.86 (0.72;1.02)	0.09	1.11 (0.99;1.25)	0.07
rs7315435	12	69 284	<i>CPM</i>	A/G	0.80	1.45 (1.21;1.75)	7.4x10 ⁻⁵	1.03 (0.80;1.34)	0.81	1.04 (0.64;1.69)	0.87	1.03 (0.82;1.30)	0.77	1.27 (1.10;1.47)	1.1x10 ⁻³
rs2434080	12	106 454	<i>C12orf75 (689);NUAK1 (3)</i>	A/G	0.59	0.72 (0.62;0.85)	5.0x10 ⁻⁵	1.04 (0.84;1.28)	0.73	0.90 (0.58;1.41)	0.66	1.01 (0.84;1.22)	0.90	0.83 (0.74;0.94)	2.4x10 ⁻³
rs1327751	13	75 282	<i>LINC00347 (150);TBC1D4 (577)</i>	C/T	0.11	1.64 (1.28;2.11)	9.7x10 ⁻⁵	1.05 (0.74;1.47)	0.79	0.89 (0.52;1.52)	0.67	1.00 (0.75;1.33)	0.99	1.33 (1.10;1.60)	3.2x10 ⁻⁴
rs8030108	15	98 056	<i>SPATA8 (726);ARRDC4 (448)</i>	C/T	0.44	0.74 (0.64;0.86)	6.4x10 ⁻⁵	1.02 (0.84;1.23)	0.84	1.37 (0.94;1.99)	0.10	1.08 (0.91;1.28)	0.36	0.87 (0.78;0.97)	0.02
rs13338087	16	4 105	<i>ADCY9</i>	G/T	0.39	1.41 (1.20;1.65)	2.0x10 ⁻⁵	0.84 (0.69;1.02)	8.4x10 ⁻²	0.84 (0.56;1.25)	0.39	0.84 (0.70;1.00)	0.05	1.12 (1.00;1.26)	0.05
rs12929999	16	76 915	<i>MIR4719 (13);MON1B (309)</i>	C/T	0.19	1.49 (1.22;1.81)	7.2x10 ⁻⁵	1.09 (0.85;1.40)	0.5	0.94 (0.62;1.43)	0.78	1.05 (0.85;1.30)	0.66	1.27 (1.10;1.47)	1.2x10 ⁻³
rs11647758	16	89 094	<i>CBFA2T3 (51);ACSF3 (66)</i>	C/T	0.82	1.53 (1.26;1.86)	2.3x10 ⁻⁵	1.10 (0.88;1.38)	0.38	1.04 (0.66;1.64)	0.86	1.09 (0.89;1.33)	0.39	1.3 (1.13;1.49)	2.7x10 ⁻⁴
rs2571225	18	55 462	<i>ATP8B1</i>	C/T	0.72	0.68 (0.57;0.81)	2.0x10 ⁻⁵	0.96 (0.78;1.18)	0.67	0.69 (0.47;1.03)	0.07	0.89 (0.74;1.07)	0.22	0.77 (0.68;0.88)	8.3x10 ⁻⁵
rs6056732	20	9 577	<i>PAK5</i>	A/C	0.91	0.56 (0.42;0.73)	3.2x10 ⁻⁵	0.73 (0.52;1.03)	7.0x10 ⁻²	0.55 (0.28;1.06)	0.07	0.68 (0.51;0.93)	0.01	0.61 (0.50;0.75)	2.5x10 ⁻⁶
rs6056733	20	9 577	<i>PAK5</i>	A/G	0.12	1.62 (1.28;2.06)	7.2x10 ⁻⁵	1.28 (0.98;1.67)	7.2x10 ⁻²	1.80 (1.06;3.07)	0.03	1.37 (1.08;1.74)	0.01	1.49 (1.26;1.77)	3.7x10 ⁻⁶
rs8117366	20	52 365	<i>ZNF217 (65);BCAS1 (439)</i>	G/T	0.81	1.51 (1.24;1.84)	3.2x10 ⁻⁵	0.94 (0.73;1.21)	0.64	1.47 (0.88;2.46)	0.14	1.03 (0.82;1.29)	0.81	1.28 (1.11;1.49)	9.5x10 ⁻⁴
rs6013784	20	52 365	<i>ZNF217 (65);BCAS1 (439)</i>	C/T	0.21	0.68 (0.57;0.82)	5.2x10 ⁻⁵	1.08 (0.84;1.40)	0.54	0.68 (0.41;1.13)	0.14	0.99 (0.79;1.24)	0.91	0.79 (0.68;0.91)	1.3x10 ⁻³
rs4389378	20	54 592	<i>CBLN4 (12);MC3R (232)</i>	A/G	0.24	0.72 (0.62;0.85)	6.8x10 ⁻⁵	0.93 (0.75;1.15)	0.51	1.12 (0.76;1.63)	0.57	0.97 (0.80;1.17)	0.77	0.82 (0.72;0.92)	1.1x10 ⁻³

*Chr is the chromosome number where the SNP is located

†The gene where the SNP is located is indicated otherwise the genes on either side of the SNP are indicated together with the distance between the SNP and gene boundary (using Build 37.3)

‡Baseline/Effect allele

§Effect allele frequency

||OR is the Odds Ratio associated with the effect allele under an additive model. 95% CI is the 95% confidence interval associated with the Odds Ratio.

††P is the P-value associated with the Wald test statistic of SNP effect

**P_{stage2} is the P-value associated with the Wald test of meta-analyzed SNP effect in the stage 2 datasets (SLSJ and MRC)

‡‡P_{meta} is the P-values associated with the Wald test of meta-analyzed SNP effect in the three datasets (EGEA, SLSJ & MRC)

Table E3. List of genes (gene set-2) tested for their relationship with *ADGRV1* (gene set-1) using GRAIL

Gene symbol*	Nearest SNP (kb distance) †	Cytogenetic Band	Position (kb) ‡	GWAS <i>P</i> -values in EGEA	<i>P</i> _{GRAIL}
<i>CHD7</i>	rs4237038	8q12	61,731	7.3x10 ⁻⁵	3.2x10⁻³
<i>ATP8B1</i>	rs2571225	18q21	55,462	2.0x10 ⁻⁵	0.016
<i>DNAH5</i>	rs795540	5p15	13,818	8.3x10 ⁻⁵	0.084
<i>NDUFAF7</i>	rs3819892 (34)	2p22	37,510	8.1x10 ⁻⁵	1
<i>PRKD3</i>	rs3819892	2p22	37,510	8.1x10 ⁻⁵	1
<i>MYH15</i>	rs3900940	3q13	108,148	9.3x10 ⁻⁵	1
<i>NLN</i>	rs7711329 (1)	5q12	65,126	8.3x10 ⁻⁵	1
<i>PDE1C</i>	rs11763324	7p14	32,171	2.3x10 ⁻⁵	1
<i>POM121L12</i>	rs1880617 (33)	7p12	53,138	9.5x10 ⁻⁵	1
<i>TES</i>	rs10279056 (4)	7q31	115,847	1.0x10 ⁻⁵	1
<i>CAV2</i>	rs17138756 (4)	7q31	116,135	3.4x10 ⁻⁵	1
<i>LINC-PINT</i>	rs10253511 (3)	7q32	130,797	4.8x10 ⁻⁵	1
<i>MKLN1</i>	rs10253511	7q32	130,797	4.8x10 ⁻⁵	1
<i>ADAMTSL1</i>	rs1433831	9p22	18,869	5.7x10 ⁻⁵	1
<i>FXN</i>	rs2309394	9q21	71,671	8.4x10 ⁻⁵	1
<i>PRKACG</i>	rs2309394 (42)	9q21	71,671	8.4x10 ⁻⁵	1
<i>TJP2</i>	rs7859021 (42)	9q21	71,694	8.6x10 ⁻⁵	1
<i>PLPPR1</i>	rs2771064	9q31	103,921	6.4x10 ⁻⁵	1
<i>TMEM268</i>	rs13286744 (36)	9q32	117,444	3.6x10 ⁻⁵	1
<i>DENND1A</i>	rs12000625	9q33	126,686	4.4x10 ⁻⁵	1
<i>JMJD1C</i>	rs10995495	10q21	65,062	4.7x10 ⁻⁵	1
<i>C10orf35</i>	rs12771265 (18)	10q22	71,411	3.2x10 ⁻⁵	1
<i>COL13A1</i>	rs4746906 (46)	10q22	71,516	9.1x10 ⁻⁵	1
<i>RERGL</i>	rs4475974 (19)	12p12	18,262	2.5x10 ⁻⁵	1
<i>CPM</i>	rs7315435	12q15	69,284	7.4x10 ⁻⁵	1
<i>MDM2</i>	rs7315435 (45)	12q15	69,284	7.4x10 ⁻⁵	1
<i>NUAK1</i>	rs2434080 (3)	12q23	106,454	5.0x10 ⁻⁵	1
<i>ADCY9</i>	rs13338087	16p13	4,105	2.0x10 ⁻⁵	1
<i>PAK5</i>	rs6056732	20p12	9,577	3.2x10 ⁻⁵	1
<i>CBLN4</i>	rs4389378 (12)	20q13	54,592	6.7x10 ⁻⁵	1

*Genes are located at most 50 kb apart from SNPs having $P \leq 10^{-4}$ in the stage 1 EGEA dataset

†The distance (in kilobases; build 37.3) of nearest SNP to each gene is indicated in parentheses when the SNP lies outside of a gene.

‡SNP position in kilobases (Build 37.3)

Table E4. Number of SNP pairs tested for the three selected gene pairs and multiple-testing corrected threshold

Gene set 1	Gene set 2	Number of SNP pairs tested	Effective number of independent SNP pairs tested	Total effective number of independent SNP pairs tested*
<i>ADGRV1</i>	<i>CHD7</i>	808	110	688
<i>ADGRV1</i>	<i>ATP8B1</i>	1450	223	
<i>ADGRV1</i>	<i>DNAH5</i>	3066	355	

*The total effective number of independent SNP pairs tested is estimated by the sum of the effective number of independent SNP pairs tested by gene pair over all gene pairs examined.

The multiple-testing corrected threshold is thus equal to the 5% type I error divided by the total effective number of independent SNP pairs tested ($T=7.3 \times 10^{-5}$).

Table E5A. Stratified analysis on asthma for the *ADGRVI* SNP significantly associated with atopy at the genome-wide level

SNPs	Gene*	Alleles [†]	MAF [‡]	Group	Stage 1		Stage 2		Overall Meta-Analysis	
					OR (95% CI) [§]	P_{value}	OR (95% CI) [§]	P_{stage2} ^{**}	OR (95% CI) [§]	P_{meta} ^{††}
rs4916831	<i>ADGRVI</i>	A/G	0.44	Asthmatics	0.67 (0.48-0.92)	0.01	0.69 (0.53-0.89)	3.9×10^{-3}	0.68 (0.56-0.83)	1.4×10^{-4}
				Non-asthmatics	0.69 (0.57-0.84)	1.8×10^{-4}	0.72 (0.55-0.94)	1.4×10^{-2}	0.70 (0.60-0.82)	7.8×10^{-6}
				P_{Cochran} ^{‡‡}		0.86		0.82		0.82

Table E5B. Stratified analysis on asthma for the interacting *ADGRVI/DNAH5* SNP pair significantly associated with atopy

SNPs	Genes*	Alleles [†]	MAF [‡]	Group	Stage 1		Stage 2		Overall Meta-Analysis	
					Interaction Effect		Interaction Effect		Interaction Effect	
					OR (95% CI) [§]	P_{int}	OR (95% CI) [§]	$P_{\text{stage2-int}}$ ^{**}	OR (95% CI) [§]	$P_{\text{meta-int}}$ ^{††}
rs17554723	<i>ADGRVI</i>	A/G	0.33	Asthmatics	0.77 (0.47-1.24)	0.28	0.73 (0.48-1.12)	0.15	0.74 (0.54-1.02)	0.07
rs2134256	<i>DNAH5</i>	T/C	0.25	Non-asthmatics	0.64 (0.46-0.89)	7.3×10^{-3}	0.53 (0.34-0.82)	4.2×10^{-3}	0.60 (0.46-0.78)	1.1×10^{-4}
					P_{Cochran} ^{‡‡}	0.55		0.29		0.30

The two groups contained 1,354 asthmatics (628, 549, 177 for EGEA, SLSJ and MRC respectively) and 1,849 non-asthmatics (997, 583, 269 for EGEA, SLSJ and MRC)

*Gene symbol

[†]Major allele/Minor allele

[‡]Minor allele frequency

[§]OR is the Odds-Ratio for single SNP effect (Table E5A) or interaction between SNPs (Table E5B) associated with atopy assuming an additive model. 95% CI is the 95% Confidence Interval of the OR.

^{||} P and P_{int} are the P -values associated with the Wald test of SNP effect (Table E5A) and interaction effect (Table E5B).

^{**} P_{stage2} and $P_{\text{stage2-int}}$ are the P -values associated with the Wald test of meta-analyzed single SNP effect (Table E5A) and interaction between SNPs (Table E5B) in the stage 2 datasets (SLSJ and MRC).

^{††} P_{meta} and $P_{\text{meta-int}}$ are the P -values associated with the Wald test of meta-analyzed single SNP effect (Table E5A) and interaction between SNPs (Table E5B) in the three datasets (EGEA, SLSJ and MRC).

^{‡‡} P_{Cochran} is the P -value associated with the Cochran's Q test for homogeneity between the two groups of asthmatic and non-asthmatic subjects.

Table E6. Functional annotations of *ADGRV1* and *DNAH5* SNPs

Gene	SNP	Position on chromosome 5	Variant Location	r ² with the significant SNP(s) in our analysis	Regulatory elements			
					Promoter	Enhancer	DNaseI hyper	Transcription factor binding sites
					histones marks	histones marks	sensitivity site	
<i>ADGRV1</i>	rs4916831	90,916,459	intronic	-	No	No	No	SOX, TCF12
	rs4637585	90,889,700	intronic	0.8	No	Yes (lung)	No	DBX, FOXO, GATA, MEF2, NCX, PAX, PDX, SOX, ZFP
	rs10045202	90,890,830	intronic	0.8	No	No	No	NERF1A
	rs4244205	90,893,069	intronic	0.8	No	No	No	DOBOX4
	rs4580808	90,894,483	intronic	0.82	No	Yes (lung)	No	PAX4, SREBP, SIN3AK20
	rs4496735	90,894,600	intronic	0.82	No	No	No	EVII, OSF2, SIX5
	rs10035307	90,906,182	intronic	0.83	No	No	No	FOX, SP2
	rs6858917	90,909,376	intronic	0.96	No	Yes (skin, lung)	No	AHR, CTCF, RAD21, SMAD
	rs6889986	90,911,582	intronic	0.99	No	Yes (lung)	No	ARID3A, CDX, DBX1, FOXL1, HOXB13, HOXB9, HOXD10, MEF2, NCX, PBX1, POU2F2, POU3F2, SOX, TATA, TEF, ZFP105
	rs10078568	90,915,831	intronic	0.8	No	No	No	CDX
	rs17554723	90,793,497	intronic	-	No	No	No	-
	rs11745546	90,794,895	intronic	1	No	No	No	CCNT2, E2F, MZF1
	rs13186025	90,827,511	intronic	0.8	No	No	No	DMRT2, HDAC2
<i>DNAH5</i>	rs2134256	13,768,544	intronic	-	No	No	No	SMC3, TCF12
	rs6862904	13,750,128	intronic	0.83	No	No		MRG, NRSF, PBX3, TGIF1, ZNF143
	rs11745096	13,750,128	intronic	0.84	Yes (blood)	Yes (blood)	No	-
	rs34789506	13,757,027	intronic	0.93	No	No	No	GR
	rs11742383	13,762,604	intronic	0.95	No	No	No	GR
	rs13156606	13,765,320	intronic	0.93	No	No	No	BATF, HDAC2, IRF
	rs60499013	13,772,775	intronic	0.94	No	No	No	CDX, DMRT2, DMRT3, DBX1, FOXA, HDAC2, HOXA10, HOXB13, HOXD10, NF, PAX, STAT

The *ADGRV1* rs4916831 SNP is significantly associated with atopy; the *ADGRV1* rs17554723 and *DNAH5* rs2134256 SNPs show significant interaction in atopy. These three SNPs and their proxies ($r^2 \geq 0.8$, using the 1,000 Genomes project database) were mapped to regulatory elements using the HaploReg v4.1 tool (<http://archive.broadinstitute.org/mammals/haploreg/haploreg.php>)