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Identification of fifteen new psoriasis susceptibility loci highlights the role of innate immunity

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Supplementary Tables

Supplementary Table 1. Description of the 5 datasets used in the meta-analysis

Study	Cases (N)	Controls (N)	Total	λGC
Kiel[1]	474	1,146	1,620	1.09
CASP[2]	1,359	1,400	2,759	1.06
WTCCC2[3]	2,178	5,175	7,353	1.04
PAGE	3,580	5,902	9,482	0.992
GAPC	2,997	9,183	12,180	0.963
TOTAL	10,588	22,806	33,394	1.11

Supplementary Table 2. Description of individual Immunochip samples

'Group' refers to the group that provided the samples and corresponds to the membership of consortia.

Dataset	Population Sample	Group (cases)	Group (controls)	Cases	Controls
PAGE Immunochip	**USA**	UMich/NPF/HFH	UMich/FIMR/NPF	1,351	2,694
	Canada	UToronto/MU	UToronto	362	20
	Estonia	UTartu/EGCUT	EGCUT	1,295	898
	Germany	CAU Kiel	CAU Kiel/KORA/HNR	572	2,290
	Total			3,580	5,902
GAPC Immunochip	**UK**	KCL/Glasgow/Sheffield	WTCCC2	207	4822
	Finland	Helsinki	DILGOM	240	490
	Spain	Barcelona	Barcelona	269	202
	The Netherlands	Nijmegan	Groningen	152	1,107
	Austria	Graz	-	310	0
	Sweden	Gothenburg/Stockholm	-	859	0
	Italy	Rome	Groningen	73	509
	Germany	Erlangen	PopGen	826	1,984
	Ireland	Dublin	Dublin	61	69
	Total			2,997	9,183

Supplementary Table 3. Association results for each of the 5 studies for the most strongly associated SNPs

Showing the 21 known and 15 newly identified loci. The overall OR was calculated using the effective sample size-weighted approach.

Known Loci				Kiel				CASP				WTCCC2				PAGE				GAPC					
SNP	Chr.	Position	Risk/ Non-risk allele	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	Combined P-value	OR (meta)
rs7552167	1	24,518,643	G/A	8.0×10^{-1}	0.86	0.86	1.03 (0.83-1.28)	1.1×10^{-2}	0.88	0.86	1.29 (1.06-1.57)	1.6×10^{-4}	0.89	0.86	1.24 (1.11-1.38)	4.5×10^{-5}	0.87	0.85	1.22 (1.12-1.33)	4.6×10^{-4}	0.88	0.86	1.20 (1.09-1.31)	8.5×10^{-12}	1.21
rs9988642	1	67,726,104	T/C	9.5×10^{-4}	0.95	0.92	1.79 (1.24-2.57)	2.4×10^{-7}	0.95	0.91	1.82 (1.44-2.29)	2.6×10^{-6}	0.95	0.93	1.45 (1.24-1.69)	3.8×10^{-8}	0.95	0.93	1.43 (1.25-1.64)	1.8×10^{-8}	0.96	0.93	1.53 (1.33-1.76)	1.1×10^{-26}	1.52
rs6677595	1	152,590,187	T/C	2.4×10^{-4}	0.68	0.62	1.36 (1.15-1.61)	7.6×10^{-4}	0.68	0.64	1.22 (1.09-1.37)	2.7×10^{-10}	0.71	0.65	1.29 (1.19-1.40)	2.7×10^{-7}	0.67	0.63	1.18 (1.10-1.26)	2.8×10^{-15}	0.70	0.65	1.31 (1.22-1.40)	2.1×10^{-33}	1.26
rs62149416	2	61,083,506	T/C	2.5×10^{-1}	0.67	0.65	1.10 (0.93-1.29)	1.8×10^{-4}	0.68	0.64	1.25 (1.11-1.40)	1.4×10^{-7}	0.69	0.64	1.24 (1.14-1.34)	7.2×10^{-4}	0.66	0.64	1.12 (1.05-1.19)	6.3×10^{-7}	0.67	0.63	1.16 (1.08-1.23)	1.8×10^{-17}	1.17
rs17716942	2	163,260,691	T/C	8.6×10^{-2}	0.90	0.88	1.24 (0.97-1.59)	3.0×10^{-2}	0.88	0.86	1.19 (1.02-1.40)	3.4×10^{-8}	0.90	0.86	1.38 (1.23-1.54)	6.7×10^{-9}	0.90	0.86	1.31 (1.20-1.45)	8.2×10^{-4}	0.88	0.86	1.18 (1.08-1.29)	3.3×10^{-18}	1.27
rs27432	5	96,119,273	A/G	9.8×10^{-2}	0.31	0.28	1.15 (0.97-1.35)	1.3×10^{-1}	0.30	0.28	1.10 (0.97-1.23)	5.2×10^{-8}	0.31	0.27	1.26 (1.16-1.37)	1.1×10^{-5}	0.30	0.27	1.16 (1.09-1.24)	6.4×10^{-10}	0.32	0.28	1.23 (1.15-1.32)	1.9×10^{-20}	1.20
rs1295685	5	131,996,445	G/A	4.2×10^{-1}	0.80	0.78	1.08 (0.89-1.31)	1.5×10^{-6}	0.83	0.78	1.41 (1.22-1.61)	2.1×10^{-2}	0.84	0.82	1.12 (1.02-1.24)	8.6×10^{-3}	0.78	0.78	1.15 (1.06-1.23)	1.9×10^{-4}	0.81	0.80	1.20 (1.11-1.30)	3.4×10^{-10}	1.18
rs2233278	5	150,467,189	C/G	5.3×10^{-2}	0.07	0.05	1.39 (1.00-1.92)	5.5×10^{-8}	0.09	0.06	1.86 (1.48-2.34)	5.5×10^{-11}	0.09	0.06	1.68 (1.44-1.96)	2.7×10^{-14}	0.10	0.06	1.54 (1.37-1.72)	2.8×10^{-14}	0.08	0.05	1.54 (1.37-1.74)	2.2×10^{-42}	1.59
rs12188300	5	158,829,527	T/A	8.1×10^{-6}	0.15	0.11	1.80 (1.39-2.33)	1.9×10^{-7}	0.14	0.10	1.68 (1.38-2.05)	8.6×10^{-14}	0.15	0.11	1.64 (1.44-1.86)	6.9×10^{-21}	0.13	0.08	1.58 (1.43-1.75)	2.1×10^{-13}	0.12	0.09	1.48 (1.34-1.63)	3.2×10^{-53}	1.58
rs4406273	6	31,266,090	A/G	4.2×10^{-42}	0.28	0.11	5.18 (4.04-6.63)	3.1×10^{-53}	0.23	0.11	4.13 (3.41-4.99)	1.3×10^{-229}	0.29	0.09	6.33 (5.66-7.08)	1.8×10^{-169}	0.25	0.09	3.35 (3.06-3.67)	6.9×10^{-265}	0.27	0.09	4.24 (3.88-4.64)	4.5×10^{-723}	4.32
rs33980500	6	111,913,262	T/C	5.8×10^{-5}	0.12	0.07	1.67 (1.31-2.14)	3.3×10^{-4}	0.10	0.07	1.42 (1.17-1.72)	3.5×10^{-15}	0.11	0.07	1.72 (1.50-1.97)	5.2×10^{-10}	0.11	0.08	1.38 (1.25-1.53)	3.6×10^{-19}	0.11	0.07	1.54 (1.39-1.71)	4.2×10^{-45}	1.52
rs582757	6	138,197,824	C/T	5.9×10^{-4}	0.33	0.27	1.34 (1.14-1.59)	6.5×10^{-6}	0.32	0.27	1.31 (1.16-1.47)	3.5×10^{-8}	0.31	0.27	1.26 (1.16-1.37)	1.7×10^{-6}	0.31	0.27	1.17 (1.09-1.25)	4.0×10^{-8}	0.32	0.28	1.22 (1.14-1.31)	2.2×10^{-25}	1.23
rs1250546	10	81,032,532	A/G	3.7×10^{-2}	0.65	0.61	1.19 (1.01-1.39)	4.7×10^{-4}	0.61	0.56	1.21 (1.09-1.35)	1.9×10^{-1}	0.59	0.58	1.05 (0.97-1.14)	1.1×10^{-2}	0.61	0.59	1.09 (1.03-1.16)	4.6×10^{-3}	0.60	0.57	1.09 (1.03-1.16)	6.8×10^{-7}	1.10
rs645078	11	64,135,298	A/C	4.2×10^{-1}	0.63	0.61	1.07 (0.91-1.25)	4.8×10^{-3}	0.64	0.60	1.17 (1.05-1.31)	1.4×10^{-1}	0.62	0.61	1.06 (0.98-1.14)	1.7×10^{-3}	0.63	0.61	1.12 (1.05-1.19)	6.4×10^{-2}	0.62	0.61	1.06 (0.98-1.13)	2.2×10^{-6}	1.09
rs2066819	12	56,750,204	C/T	6.4×10^{-2}	0.95	0.93	1.41 (0.97-2.03)	2.0×10^{-5}	0.96	0.94	1.84 (1.38-2.44)	9.3×10^{-8}	0.95	0.94	1.57 (1.33-1.85)	4.1×10^{-4}	0.94	0.93	1.27 (1.12-1.44)	6.4×10^{-5}	0.95	0.94	1.28 (1.12-1.47)	5.4×10^{-17}	1.39
rs8016947	14	35,832,666	G/T	6.8×10^{-4}	0.64	0.57	1.31 (1.12-1.53)	5.5×10^{-3}	0.59	0.55	1.16 (1.05-1.30)	4.6×10^{-6}	0.61	0.57	1.19 (1.11-1.29)	2.6×10^{-4}	0.59	0.56	1.12 (1.05-1.19)	1.1×10^{-6}	0.60	0.56	1.17 (1.10-1.25)	2.5×10^{-17}	1.16
rs12445568	16	31,004,812	C/T	1.6×10^{-3}	0.43	0.37	1.28 (1.10-1.49)	1.2×10^{-3}	0.40	0.36	1.21 (1.08-1.36)	5.2×10^{-3}	0.40	0.37	1.12 (1.03-1.20)	1.4×10^{-6}	0.41	0.37	1.16 (1.09-1.23)	2.9×10^{-6}	0.40	0.37	1.16 (1.09-1.24)	1.2×10^{-16}	1.16
rs28998802	17	26,124,908	A/G	4.0×10^{-3}	0.20	0.16	1.36 (1.11-1.68)	3.2×10^{-2}	0.18	0.16	1.18 (1.01-1.38)	7.7×10^{-4}	0.18	0.16	1.20 (1.08-1.34)	2.0×10^{-8}	0.16	0.13	1.27 (1.17-1.38)	9.1×10^{-5}	0.16	0.14	1.18 (1.08-1.28)	3.3×10^{-16}	1.22
rs34536443	19	10,463,118	G/C	1.3×10^{-2}	0.97	0.95	1.77 (1.11-2.81)	NA	NA	NA	NA	4.7×10^{-9}	0.97	0.95	1.81 (1.48-2.21)	3.4×10^{-10}	0.98	0.96	1.76 (1.46-2.10)	9.0×10^{-14}	0.98	0.95	2.09 (1.72-2.54)	9.1×10^{-31}	1.88
rs1056198	20	48,556,229	C/T	3.5×10^{-1}	0.59	0.57	1.07 (0.92-1.25)	2.4×10^{-4}	0.63	0.58	1.22 (1.10-1.36)	1.6×10^{-6}	0.63	0.58	1.20 (1.11-1.30)	4×10^{-6}	0.59	0.57	1.17 (1.10-1.25)	4.9×10^{-3}	0.58	0.57	1.11 (1.05-1.18)	1.5×10^{-14}	1.16
rs4821124	22	21,979,289	C/T	1.2×10^{-1}	0.22	0.19	1.17 (0.96-1.41)	8.9×10^{-2}	0.22	0.20	1.12 (0.98-1.29)	5.2×10^{-4}	0.20	0.18	1.19 (1.08-1.31)	2.0×10^{-4}	0.20	0.18	1.16 (1.07-1.25)	8.4×10^{-2}	0.22	0.20	1.06 (0.98-1.14)	3.8×10^{-8}	1.13

Newly Identified Loci				Kiel				CASP				WTCCC2				PAGE				GAPC					
SNP	Chr.	Position	Risk/ Non-risk allele	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	Combined P-value	OR (meta)
rs11121129	1	8,268,095	A/G	9.2×10^{-3}	0.31	0.27	1.25 (1.06-1.47)	3.2×10^{-2}	0.30	0.28	1.14 (1.01-1.29)	9.0×10^{-3}	0.33	0.30	1.11 (1.03-1.20)	1.4×10^{-1}	0.29	0.28	1.06 (0.99-1.13)	2.1×10^{-5}	0.31	0.29	1.20 (1.12-1.28)	1.7×10^{-8}	1.13
rs7536201	1	25,293,084	C/T	1.5×10^{-1}	0.51	0.48	1.12 (0.96-1.32)	3.3×10^{-2}	0.52	0.49	1.12 (1.01-1.25)	1.8×10^{-3}	0.54	0.50	1.13 (1.05-1.21)	1.4×10^{-7}	0.53	0.49	1.16 (1.09-1.23)	3.2×10^{-3}	0.52	0.50	1.11 (1.05-1.18)	2.3×10^{-12}	1.13
rs10865331	2	62,551,472	A/G	4.8×10^{-1}	0.38	0.37	1.06 (0.91-1.23)	2.0×10^{-2}	0.41	0.38	1.14 (1.02-1.27)	5.9×10^{-3}	0.40	0.37	1.11 (1.03-1.20)	6.0×10^{-8}	0.41	0.38	1.19 (1.12-1.26)	6.0×10^{-2}	0.39	0.37	1.08 (1.01-1.15)	4.7×10^{-10}	1.12
rs9504361	6	577,820	A/G	1.5×10^{-2}	0.58	0.54	1.21 (1.04-1.42)	4.0×10^{-2}	0.57	0.54	1.12 (1.01-1.25)	3.6×10^{-5}	0.60	0.55	1.17 (1.09-1.27)	2.8×10^{-2}	0.57	0.55	1.06 (1.00-1.13)	1.7×10^{-5}	0.57	0.54	1.14 (1.07-1.21)	2.1×10^{-11}	1.12
rs2451258	6	159,506,600	C/T	9.4×10^{-1}	0.33	0.33	1.01 (0.86-1.18)	1.3×10^{-2}	0.38	0.34	1.15 (1.03-1.29)	3.2×10^{-3}	0.40	0.37	1.12 (1.04-1.21)	3.9×10^{-4}	0.34	0.33	1.14 (1.07-1.22)	1.3×10^{-2}	0.36	0.35	1.11 (1.04-1.18)	3.4×10^{-8}	1.12
rs2700987	7	37,386,237	A/C	7.8×10^{-2}	0.61	0.57	1.16 (0.98-1.36)	1.8×10^{-2}	0.59	0.56	1.14 (1.02-1.27)	1.4×10^{-5}	0.61	0.56	1.18 (1.10-1.27)	1.2×10^{-2}	0.58	0.57	1.09 (1.02-1.16)	1.5×10^{-2}	0.59	0.57	1.07 (1.01-1.14)	4.3×10^{-9}	1.11
rs11795343	9	32,523,737	T/C	2.3×10^{-3}	0.65	0.59	1.28 (1.09-1.49)	4.7×10^{-3}	0.63	0.60	1.17 (1.05-1.30)	4.8×10^{-4}	0.64	0.60	1.15 (1.06-1.24)	7.2×10^{-5}	0.63	0.60	1.12 (1.05-1.19)	3.9×10^{-2}	0.61	0.60	1.05 (0.99-1.12)	8.4×10^{-11}	1.11
rs10979182	9	110,817,020	A/G	6.9×10^{-3}	0.64	0.59	1.24 (1.06-1.45)	5.9×10^{-2}	0.61	0.59	1.11 (1.00-1.24)	2.4×10^{-3}	0.63	0.59	1.13 (1.04-1.22)	1.3×10^{-2}	0.61	0.59	1.08 (1.02-1.15)	3.2×10^{-3}	0.61	0.59	1.12 (1.06-1.20)	2.3×10^{-8}	1.12
rs4561177	11	109,962,432	A/G	9.0×10^{-1}	0.59	0.60	1.01 (0.87-1.18)	3.8×10^{-2}	0.61	0.59	1.12 (1.01-1.25)	1.6×10^{-4}	0.61	0.57	1.15 (1.07-1.24)	3.1×10^{-5}	0.61	0.58	1.13 (1.07-1.21)	1.1×10^{-5}	0.63	0.58	1.16 (1.09-1.24)	7.7×10^{-13}	1.14
rs3802826	11	128,406,438	A/G	2.3×10^{-1}	0.51	0.48	1.10 (0.94-1.28)	4.2×10^{-2}	0.51	0.48	1.12 (1.00-1.24)	1.7×10^{-2}	0.52	0.50	1.10 (1.02-1.18)	4.0×10^{-4}	0.49	0.47	1.12 (1.06-1.19)	1.3×10^{-4}	0.51	0.49	1.15 (1.08-1.22)	9.5×10^{-10}	1.12
rs367569	16	11,365,500	C/T	2.5×10^{-1}	0.73	0.71	1.11 (0.93-1.31)	6.8×10^{-2}	0.73	0.71	1.12 (0.99-1.27)	2.1×10^{-3}	0.73	0.71	1.14 (1.05-1.24)	4.4×10^{-3}	0.72	0.70	1.10 (1.03-1.18)	3.6×10^{-3}	0.74	0.72	1.15 (1.07-1.23)	4.9×10^{-8}	1.13
rs963986	17	40,561,579	C/G	9.6×10^{-4}	0.19	0.15	1.43 (1.16-1.76)	2.7×10^{-2}	0.17	0.15	1.19 (1.02-1.38)	3.2×10^{-2}	0.17	0.16	1.12 (1.01-1.24)	7.0×10^{-2}	0.16	0.15	1.07 (0.98-1.16)	1.3×10^{-5}	0.18	0.16	1.22 (1.13-1.33)	5.3×10-9	1.15
rs11652075	17	78,178,893	C/T	5.8×10^{-1}	0.52	0.51	1.04 (0.90-1.21)	4.9×10^{-2}	0.53	0.52	1.18 (1.00-1.40)	7.5×10^{-3}	0.52	0.49	1.11 (1.03-1.19)	4.6×10^{-1}	0.52	0.52	1.02 (0.96-1.08)	2.2×10^{-8}	0.55	0.50	1.19 (1.11-1.26)	3.4×10^{-8}	1.11
rs545979	18	51,819,750	T/C	3.8×10^{-2}	0.34	0.30	1.19 (1.01-1.40)	6.9×10^{-3}	0.33	0.30	1.17 (1.04-1.31)	3.1×10^{-4}	0.32	0.29	1.16 (1.07-1.26)	9.6×10^{-3}	0.32	0.30	1.09 (1.02-1.17)	7.2×10^{-4}	0.31	0.29	1.11 (1.04-1.19)	3.5×10^{-10}	1.12
rs892085	19	10,818,092	A/G	3.2×10^{-2}	0.62	0.58	1.19 (1.01-1.39)	1.5×10^{-3}	0.58	0.55	1.27 (1.10-1.48)	1.0×10^{-4}	0.57	0.54	1.16 (1.08-1.26)	2.2×10^{-3}	0.60	0.57	1.10 (1.03-1.17)	4.2×10^{-10}	0.60	0.56	1.20 (1.13-1.28)	3.0×10^{-17}	1.17

Supplementary Table 4. Disease overlap and SNP functional annotation for the known and newly identified SNPs.
The 'disease overlap' is defined as an associated SNP identified in the same region (within 500kb) as the top psoriasis SNP (using NHGRI GWAS catalog and Immunochip results for Celiac disease[4]). Underlined entries have SNPs that are in LD (r^2>0.7) with the identified SNP. *denotes association of the same SNP in the same direction. AD: Atopic dermatitis, AS: Ankylosing spondylitis, BD: Behcet's disease, CD: Crohn's disease, CeD: Celiac disease, IgE: Serum IgE, IgA: Selective Immunoglobulin A deficiency, LE: Leprosy, MS: Multiple Sclerosis, PBC: Primary biliary cirrhosis, RA: Rheumatoid arthritis, SI: Soluble ICAM-1, SLE: Systemic lupus erythematosus, SS: Systemic sclerosis, T1D: Type I Diabetes, UC: Ulcerative colitis. Supplementary Figure 5 shows graphical view of the disease overlap.

SNP	Chr.	Position	Risk/ Non-risk allele	Variant Annotation	Disease Overlap (based on the GWAS catalog)	All genes in locus (+/- 500kb)
Known loci						
rs7552167	1	24,518,643	G/A	4878 bp upstream of IL28RA		LOC100132287;SRRM1;LOC100133331;CNR2;C1orf130;PNRC2;OR4F3;OR4F29; SFRS13A;RPL11;MYOM3;LOC284632;TCEB3;NIPAL3;C1orf128;C1orf201;HMGCL; GALE;IL22RA1;OR4F16;FUCA1;LOC100132062;IL28RA;LYPLA2;GRHL3;RCAN3
rs9988642	1	67,726,104	T/C	454 bp downstream of IL23R	<u>AS</u>, <u>UC</u>, <u>CD</u>, BD, LE, PBC	LOC100132287;LOC100133331;IL23R;GNG12;IL12RB2;MIER1;SLC35D1;C1orf141 ;INSL5;TCTEX1D1;WDR78;OR4F3;OR4F29;SERBP1;GADD45A; OR4F16; LOC100132062
rs6677595	1	152,590,187	T/C	3613 bp downstream of LCE3B		LOC100132287;LOC100133331;FLG;IVL;SPRR4;SPRR3;OR4F3;OR4F29;SPRR1A ;SPRR1B;RPTN;LCE2C;LCE2B;LCE2A;LCE2D;CRCT1;LCE4A;LCE6A;KPRP;FLG2; SMCP;C1orf68;CRNN;OR4F16;SPRR2E;SPRR2D;SPRR2F;SPRR2A;SPRR2B;LOC1 00132062;LCE1F;LCE1D;LCE1E;LCE1B;LCE1C;HRNR;LCE1A; LCE3D; LCE3E;LCE3A;LCE3B;LCE3C;LCE5A
rs62149416	2	61,083,506	T/C	FLJ16341 intron	<u>RA</u>, UC, CD, CeD	REL;USP34;PEX13;KIAA1841;AHSA2;PAPOLG;C2orf74;PUS10;BCL11A
rs17716942	2	163,260,691	T/C	KCNH7 intron	T1D, IgA	SLC4A10;IFIH1;FAP;KCNH7;GCG;GCA;DPP4
rs27432	5	96,119,273	A/G	ERAP1 intron	<u>AS</u>, CD	LNPEP;CAST;RIOK2;ERAP2;ERAP1;LIX1;PCSK1
rs1295685	5	131,996,445	G/A	IL13 3'UTR	IgE, CD, AD, platelet counts, C-reactive protein, eosinophil counts and fibrinogen	IL13; C5orf56; IRF1; ANKRD43; IL4; IL5; AFF4 ;HSPA4; UQCRQ; ZCCHC10; SLC22A4;SLC22A5;CCNI2;GDF9;P4HA2;KIF3A;PDLIM4;SHROOM1; LEAP2; SEPT8;RAD50
rs2233278	5	150,467,189	C/G	TNIP1 5'UTR	SLE, SS, CD	SLC36A3;SLC36A1;SLC36A2;MYOZ3;RBM22;TNIP1;GPX3;ZNF300;IRGM;LOC134 466;ANXA6;CCDC69;SYNPO;FAT2;DCTN4;C5orf62;GM2A
rs12188300	5	158,829,527	T/A	Intergenic	MS, CD, AS, UC	LOC285627;IL12B;UBLCP1;EBF1;RNF145
rs4406273	6	31,266,090	A/G	Intergenic	UC, AS, SS, SLE, Vitiligo, AIDS progression, Grave's Disease, Hepatitis B vaccine response, Follicular lymphoma, CD4:CD8 lymphocyte ratio	MUC21;LY6G6C;LY6G6D;HLA-B; SFTA2; APOM; DPCR1; LY6G5C; PSORS1C2; CLIC1; AIF1; LY6G6E; LY6G6F; LSM2; PSORS1C1; PSORS1C3; LST1; C6orf26; DDAH2 ; C6orf27 ; C6orf25; TNF ; BAT5; BAT2; BAT1; C6orf47; LY6G5B; DDR1; GTF2H4; MSH5; HLA-C; LTA; MCCD1; ATP6V1G2; VARS2; POU5F1; TCF19; NFKBIL1; CCHCR1; SNORA38; VARS; HCP5; CSNK2B; HCG27; HCG22; LTB; MICB;SNORD117;CDSN;C6orf15;HCG26;BAT4;BAT3;NCR3;MICA;SNORD84
rs33980500	6	111,913,262	T/C	missense mutation inTRAF3IP2		TUBE1; REV3L;WISP3;SLC16A10;FYN;TRAF3IP2;C6orf225;KIAA1919
rs582757	6	138,197,824	C/T	TNFAIP3 intron	CeD, RA, UC, SLE	PERP;OLIG3;TNFAIP3;PBOV1;KIAA1244

rs1250546	10	81,032,532	A/G	ZMIZ1 intron	MS, CD, CeD, Vitiligo	LOC283050;ZCCHC24;EIF5AL1;PPIF;MIR1256;ZMIZ1;LOC650623;SFTPA2; SFTPA1
rs645078	11	64,135,298	A/C	RPS6KA4 intron		NRXN2;MACROD1;BAD;SLC22A12;SLC22A11;TRMT112;MARK2;MEN1;RPS6KA4 ;STIP1;MIR1237;KCNK4;FERMT3;TRPT1;SF1;PLCB3;DNAJC4;ESRRA;C11orf20; PPP1R14B;GPR137;COX8A;RASGRP2;CDC42BPG;PYGM;NUDT22;MAP4K2;EHD1; PRDX5;OTUB1;RCOR2;CCDC88B;VEGFB;NAA40;FKBP2;FLRT1
rs2066819	12	56,750,204	C/T	STAT2 intron		ZC3H10;CNPY2;OBFC2B;APOF;SPRYD4;ATP5B;NACA;MYL6B;WIBG;PA2G4; SMARCC2;RNF41;ESYT1;CDK2;SILV;BAZ2A;SLC39A5;MIP;ANKRD52;TIMELESS; CS;ERBB3;RBMS2;PRIM1;SNORD59B;SNORD59A;RAB5B;RPS26;HSD17B6;PAN2; IL23A;SUOX;COQ10A;DGKA;GLS2;RPL41;MYL6;STAT2;PTGES3;IKZF4
rs8016947	14	35,832,666	G/T	Intergenic		KIAA0391;PPP2R3C;BRMS1L;INSM2;NFKBIA;RALGAPA1;PSMA6; C14orf19; FAM177A1;SRP54;BAZ1A
rs12445568	16	31,004,812	C/T	STX1B intron		FBXL19;ITGAX;ITGAL;ITGAM;ITGAD;CTF1;C16orf58;PYCARD;PRSS36;FUS; PYDC1;RNF40;BCKDK;TRIM72;NCRNA00095;PRSS8;MYST1;PRR14;PHKG2; ORAI3; BCL7C; C16orf93; ZNF843; HSD3B7; PRSS53; TGFB1I1; SNORA30; ZNF688; ZNF689; SETD1A; COX6A2; ZNF646; ZNF668; FBRS; ARMC5; MIR762; SRCAP;ZNF629; VKORC1; STX1B;ZNF785;ZNF768;ZNF764;SLC5A2;STX4;ZNF747
rs28998802	17	26,124,908	A/G	NOS2 intron		KSR1;LGALS9;FLJ40504;PYY2;WSB1;NOS2;C17orf108;NLK;PPY2
rs34536443	19	10,463,118	G/C	Missense mutation in *TYK2*	CD, T1D, SI	ATG4D;S1PR2;P2RY11;SLC44A2;ILF3;CDC37;PPAN-P2RY11 ; C19orf38; MRPL4; MIR638; MIR1238; SNORD105; TYK2; ZGLP1; COL5A3; OLFM2; AP1M2; EIF3G; CDKN2D; FDX1L; LOC147727; ANGPTL6; C3P1; KRI1 ;PPAN; MIR199A1; ICAM5; ICAM4 ;ICAM3 ;ICAM1 ;TMED1
rs1056198	20	48,556,229	C/T	*RNF114* intron		TMEM189-UBE2V1; KCNB1; B4GALT5; TMEM189; SLC9A8; CEBPB; UBE2V1; RNF114; SPATA2; SNAI1; PTGIS
rs4821124	22	21,979,289	C/T	966 bp downstream of *UBE2L3*	SLE, CeD*, RA, CD, MS	CCDC116;YDJC;PPIL2;POM121L8P;PI4KAP2;TOP3B;PPM1F;YPEL1;MIR130B; RIMBP3B;MIR301B;SDF2L1;MAPK1;RIMBP3C;HIC2;UBE2L3
Newly Identified Loci						
rs11121129	1	8,268,095	A/G	Intergenic	UC, CeD	LOC100132287;LOC100133331;PARK7;PER3;OR4F3;OR4F29;TNFRSF9;RERE; VAMP3;UTS2;ERRFI1;SLC45A1;CAMTA1;OR4F16;LOC100132062
rs7536201	1	25,293,084	C/T	1583 bp upstream of *RUNX3*	AS, CeD	LOC100132287;CLIC4;SRRM1;RHD;LOC100133331;C1orf130;TMEM57;OR4F3; OR4F29;RUNX3;NIPAL3;C1orf63;TMEM50A;OR4F16;SYF2;LOC100132062;RHCE; RCAN3
rs10865331	2	62,551,472	A/G	Intergenic	AS*	B3GNT2;TMEM17;CCT4;EHBP1;COMMD1;FAM161A
rs9504361	6	577,820	A/G	*EXOC2* intron	CeD, BCC, PSP	IRF4;DUSP22;LOC285768;HUS1B;EXOC2
rs2451258	6	159,506,600	C/T	Intergenic	MS, CeD, CD, RA	RSPH3;EZR;TMEM181;DYNLT1;FNDC1;OSTCL;SYTL3;TAGAP
rs2700987	7	37,386,237	A/C	*ELMO1* intron	PBC, CeD, RA	GPR141;ELMO1;MIR1200
rs11795343	9	32,523,737	T/C	*DDX58* intron		APTX;TOPORS;NDUFB6;DDX58;TAF1L;ACO1;TMEM215
rs10979182	9	110,817,020	A/G	Intergenic		KLF4

rs4561177	11	109,962,432	A/G	1655 bp upstream of *ZC3H12C*		ARHGAP20;RDX;ZC3H12C;FDX1
rs3802826	11	128,406,438	A/G	*ETS1* intron	SLE, CeD	TP53AIP1;ETS1;FLI1;C11orf45;ARHGAP32;KCNJ1;KCNJ5
rs367569	16	11,365,500	C/T	1664 bp downstream of *PRM3*	CeD, T1D, PBC	C16orf75;DEXI;LITAF;ZC3H7A;SNN;SOCS1;FAM18A;CIITA;TNP2;PRM1;PRM3; PRM2;TXNDC11;CLEC16A
rs963986	17	40,561,579		*PTRF* intron	CD, MS	GHDC;KCNH4;FAM134C;LOC100190938;ATP6V0A1;TTC25;CNTNAP1;TUBG1; STAT3;HSPB9;G6PC;ACLY;NKIRAS2;LOC388387;WNK4;DNAJC7;CCDC56;PSME3; PSMC3IP;TUBG2;PLEKHH3;CNTD1;RAB5C;COASY;LOC90586;AOC3;AOC2; NAGLU;STAT5B;STAT5A;BECN1;KAT2A;DHX58;CCR10;HCRT;VPS25;MLX;CNP; RAMP2;EZH1;HSD17B1;PTRF
rs11652075	17	78,178,893		Missense mutation in *CARD14*		CBX2;NPTX1;FLJ35220;CBX8;SLC26A11;LOC100294362;CCDC40;SGSH;RPTOR ;EIF4A3;CBX4;GAA;TBC1D16;CARD14;RNF213;ENPP7
rs545979	18	51,819,750		POLI intron		POLI;MBD2;C18orf26;STARD6;SNORA37;C18orf54
rs892085	19	10,818,092		QTRT1 intron		ATG4D;S1PR2;LDLR;SLC44A2;ILF3;CDC37;C19orf52;C19orf38;MRPL4;KANK2; MIR638;MIR1238;TYK2;DOCK6;ZGLP1;AP1M2;CDKN2D;FDX1L;LOC147727;KRI1; SMARCA4;SPC24;MIR199A1;CARM1;ICAM5;ICAM4;ICAM3;ICAM1;TMED1;QTRT1;K EAP1;RAVER1;YIPF2;MIR1181;S1PR5;PDE4A;DNM2

Supplementary Table 5. Association results for rs892085

The association of rs892085 before and after conditioning on either of two signals in *TYK2*: i) rs12720356, the most significantly associated SNP in this region from a previous study[3]; ii) rs34536443, the most significant SNP in this region

Analysis	P value					
	Kiel	CASP	WTCCC2	PAGE	GAPC	Meta
No conditioning	3.21×10^{-2}	1.48×10^{-3}	1.02×10^{-4}	2.22×10^{-3}	4.18×10^{-10}	2.95×10^{-17}
Conditioning on rs12720356	8.72×10^{-2}	2.88×10^{-3}	2.40×10^{-3}	1.26×10^{-2}	3.68×10^{-8}	7.36×10^{-13}
Conditioning on rs34536443	5.40×10^{-2}	NA	7.70×10^{-4}	9.69×10^{-3}	1.84×10^{-8}	4.22×10^{-12}

Supplementary Table 6. Significant results for the meta-conditional analysis

Signals achieving genome-wide significance when conditioning on the most strongly associated SNPs of the 19 known and 15 new loci that achieve genome-wide significance in this study. Because the strongest SNP in the *TYK2* region was poorly imputed in CASP GWAS, the second strongest SNP (rs2304256) was used in the conditional analysis for this dataset; the CASP GWAS was not included in the conditional meta-analysis for the *TYK2* locus. Underlined shared diseases indicate the indentified SNPs are in high LD (r2>0.7). RAF: Risk Allele Frequency.

SNP	Chr.	Position(bp)	GWAS P-value (meta)	Immunochip P-value (meta)	Combined P-value	Risk/Non-risk alleles	RAF (Case)	RAF (ctrl)	OR (meta)	Notable genes	Disease overlap[c]
rs2111485	2	163,110,536	7.9×10^{-4}	9.5×10^{-6}	2.7×10^{-8}	G/A	0.647	0.610	1.14	*IFIH1*	<u>T1D, IgA</u>
rs2910686	5	96,252,589	2.3×10^{-5}	1.3×10^{-4}	2.0×10^{-8}	C/T	0.442	0.437	1.12	*ERAP2*	<u>CD</u>, AS
rs4379175	5	158,804,928	4.8×10^{-20}	6.9×10^{-22}	9.0×10^{-40}	G/T	0.737	0.678	1.31	*IL12B*	MS, CD, AS, UC
rs13437088	6	31,355,119	2.8×10^{-17}	1.1×10^{-24}	3.1×10^{-40}	T/C	0.342	0.251	1.32	*MICA*	AS, GD[¥]
rs12720356	19	10,469,975	9.7×10^{-6}	1.1×10^{-5}	3.2×10^{-10}	A/C	0.929	0.911	1.25	*TYK2*	<u>CD</u>[*], T1D, SI

[c] AS: Ankylosing spondylitis, CD: Crohn's Disease; GD: Graves' disease, IgA: Selective Immunoglobulin A deficiency, MS: Multiple Sclerosis, SI: Soluble ICAM-1, T1D: Type 1 Diabetes; UC: Ulcerative Colitis. [*]denotes association with the same SNP. [¥] locus also associated with Systemic sclerosis, CD4:CD8 ratio, Vitiligo, AIDS progression, white blood cell types, Dengue shock syndrome, and Nevirapine-induced rash.

Supplementary Table 7. Association results for the most significant SNPs of the 5 significant loci in the conditional analysis for each of the datasets.

				Kiel				CASP				WTCCC2				PAGE				GAPC				
SNP	Chr.	Position	Risk/ Non-risk allele	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	P	RAF (case)	RAF (ctrl)	OR (95% CI)	Combined P-value
rs2111485	2	163,110,536	G/A	$8.5x10^{-2}$	0.67	0.63	1.19 (0.98-1.44)	$1.0x10^{-1}$	0.63	0.60	1.13 (0.98-1.30)	$1.1x10^{-2}$	0.66	0.61	1.11 (1.03-1.21)	$2.3x10^{-2}$	0.64	0.61	1.10 (1.02-1.18)	$6.7x10^{-5}$	0.65	0.61	1.20 (1.11-1.29)	2.7×10^{-8}
rs2910686	5	96,252,589	C/T	$4.9x10^{-3}$	0.46	0.43	1.32 (1.09-1.59)	$1.1x10^{-3}$	0.44	0.41	1.25 (1.09-1.42)	$3.4x10^{-2}$	0.46	0.45	1.09 (1.01-1.18)	$7.7x10^{-3}$	0.44	0.43	1.09 (1.02-1.18)	$5.8x10^{-3}$	0.43	0.44	1.12 (1.04-1.20)	2.0×10^{-8}
rs4379175	5	158,804,928	G/T	$4.3x10^{-4}$	0.76	0.70	1.42 (1.17-1.72)	$4.2x10^{-7}$	0.75	0.67	1.40 (1.23-1.60)	$1.2x10^{-12}$	0.73	0.67	1.35 (1.24-1.46)	$5.6x10^{-12}$	0.75	0.68	1.30 (1.20-1.39)	$2.0x10^{-11}$	0.73	0.68	1.25 (1.16-1.35)	9.0×10^{-40}
rs13437088	6	31,355,119	T/C	$4.0x10^{-2}$	0.34	0.25	1.23 (1.01-1.51)	$2.2x10^{-4}$	0.35	0.26	1.28 (1.12-1.45)	$9.5x10^{-15}$	0.36	0.23	1.44 (1.31-1.58)	$9.6x10^{-11}$	0.33	0.27	1.26 (1.18-1.36)	$1.0x10^{-15}$	0.34	0.25	1.33 (1.23-1.43)	3.1×10^{-40}
rs12720356	19	10,469,975	A/C	$1.7x10^{-2}$	0.95	0.93	1.62 (1.08-2.42)	NA	NA	NA	NA	$1.7x10^{-5}$	0.92	0.90	1.34 (1.17-1.53)	$1.9x10^{-2}$	0.93	0.92	1.18 (1.04-0.74)	$1.1x10^{-4}$	0.94	0.91	1.21 (1.06-1.38)	3.2×10^{-10}

Supplementary Table 8. Epistasis results

Pairwise combinations of psoriasis loci having the strongest evidence for interaction. The p-values and Z-scores are for the interaction terms from the meta-analysis of the epistasis results. The p-values for *LCE-HLA-C* and *ERAP1-HLA-C* remain statistically significant after Bonferroni correction.

Gene1	SNP	Gene2	SNP 2	P-value	Z-score
LCE	rs6677595	*HLA-C*	rs4406273	1.8×10^{-6}	4.78
ERAP1	rs27432	*HLA-C*	rs4406273	2.8×10^{-10}	6.31

Supplementary Table 9. Differential expression analysis results for genes in each of the 39 psoriasis loci identified by the primary or conditional association analysis.

For each locus, a genomic region in strong LD (r^2>0.7) with the most significantly associated SNP was defined using the tag SNP function of PLINK; the tagged regions were then extended by 50 kb on each side. Microarray results[5] for all genes overlapping these extended regions are shown. Results for two-sample tests of differential expression are shown, including the false discovery rate (FDR), fold-change in expression levels (FC), and whether expression is up- or down-regulated in lesional skin (using FDR ≤ 0.05 and FC ≤ 0.67 or ≥ 1.50 as criteria for differential expression).

	Gene	FDR	FC	Differentially expressed
Known loci	*IL28RA*	2.43E-01	0.92	
	LOC284632	9.43E-01	1.02	
	IL22RA1	8.85E-08	1.32	
	IL23R	1.77E-01	1.05	
	IL12RB2	5.99E-49	1.62	Up
	LCE3D	0.00E+00	24.42	Up
	PAPOLG	1.27E-04	0.84	
	REL	2.73E-19	1.74	Up
	PUS10	1.52E-40	1.75	Up
	GCA	1.00E+00	1.02	
	KCNH7	1.00E+00	1.02	
	ERAP1	1.14E-45	0.69	
	ERAP2	5.33E-03	1.21	
	CAST	1.14E-45	0.69	
	KIF3A	1.88E-13	0.73	
	IL13	1.62E-04	1.12	
	IL4	2.53E-01	1.04	
	RAD50	4.24E-06	0.85	
	TNIP1	1.22E-15	1.32	
	ANXA6	1.73E-04	1.11	
	LOC285627	6.54E-01	1.03	
	PSORS1C3	1.84E-01	1.05	
	HCG27	1.54E-01	0.95	
	C6orf15	8.90E-01	1.03	
	POU5F1	1.00E+00	1.02	
	HCG22	4.47E-03	1.09	
	HLA-B	2.26E-15	1.26	
	PSORS1C1	1.00E+00	0.99	
	PSORS1C2	6.72E-04	1.39	
	HLA-C	1.70E-14	1.25	
	CDSN	2.80E-16	2.00	Up
	CCHCR1	7.78E-05	0.90	
	MICA	1.22E-17	0.60	Down
	TCF19	6.08E-30	1.41	
	TRAF3IP2	1.56E-03	1.10	
	TNFAIP3	5.18E-01	1.05	
	STAT2	8.77E-21	1.37	
	SLC39A5	5.39E-03	1.11	
	CS	7.01E-02	0.93	
	IL23A	4.32E-22	1.34	
	RNF41	1.17E-01	0.93	
	OBFC2B	8.28E-05	1.16	
	ANKRD52	1.52E-01	1.05	
	APOF	1.00E+00	1.01	
	COQ10A	1.00E+00	0.99	
	SMARCC2	1.47E-26	0.69	
	PAN2	4.93E-21	0.73	
	CNPY2	9.14E-25	1.30	
	NFKBIA	1.01E-02	1.09	
	PSMA6	4.99E-32	1.35	

	NCRNA00095	1.41E-01	1.05	
	PRSS53	4.92E-120	2.66	Up
	BCKDK	7.01E-25	1.32	
	VKORC1	1.36E-20	1.30	
	MIR762	4.28E-03	0.92	
	STX4	5.95E-07	1.14	
	BCL7C	4.28E-03	0.92	
	FBXL19	6.32E-38	1.43	
	ORAI3	2.59E-19	0.73	
	ZNF646	4.29E-08	1.22	
	SETD1A	1.01E-03	1.11	
	HSD3B7	4.15E-02	0.89	
	MYST1	7.35E-21	0.78	
	PRSS8	4.78E-19	1.80	Up
	ZNF668	2.02E-06	1.15	
	STX1B	3.67E-02	1.07	
	PRSS36	1.12E-04	1.11	
	CTF1	1.00E+00	1.00	
	NOS2	4.78E-25	1.54	Up
	CDC37	3.03E-19	1.26	
	RAVER1	1.00E+00	1.00	
	ICAM4	2.30E-03	1.10	
	MIR1181	3.03E-19	1.26	
	PDE4A	8.49E-25	0.70	
	ICAM3	2.61E-09	1.24	
	ZGLP1	2.38E-02	1.09	
	TYK2	8.31E-02	0.94	
	ICAM1	1.12E-10	1.21	
	FDX1L	3.55E-06	1.17	
	ICAM5	1.28E-03	1.10	
	SLC9A8	5.56E-05	0.90	
	SPATA2	8.65E-21	0.77	
	SNAI1	1.30E-01	1.06	
	RNF114	2.28E-21	0.66	Down
	CCDC116	2.29E-07	0.87	
	PPIL2	2.17E-08	1.18	
	YDJC	2.92E-19	1.26	
	PI4KAP2	2.29E-07	0.87	
	MIR301B	2.29E-07	0.87	
	RIMBP3B	8.97E-33	0.68	
	UBE2L3	6.67E-38	1.39	
	RIMBP3C	8.97E-33	0.68	
	MIR130B	2.29E-07	0.87	
	SDF2L1	1.22E-12	1.34	
New loci	*RUNX3*	1.35E-08	1.20	
	EXOC2	8.20E-11	1.25	
	TAGAP	5.59E-04	1.10	
	ELMO1	1.59E-02	0.87	
	TOPORS	5.18E-05	0.86	
	NDUFB6	3.21E-12	1.20	
	DDX58	7.68E-63	3.30	Up
	ZC3H12C	4.50E-31	1.61	Up
	ETS1	8.93E-11	1.31	
	TNP2	8.77E-01	1.02	
	SOCS1	6.56E-21	1.53	Up
	PRM3	2.78E-04	1.11	
	PRM1	1.00E+00	1.02	
	PRM2	4.80E-03	1.09	
	PTRF	3.73E-36	0.67	Down
	STAT3	1.08E-63	2.13	Up
	ATP6V0A1	1.73E-02	1.14	
	SGSH	9.47E-02	0.94	
	SLC26A11	5.95E-13	0.83	

	CARD14	1.29E-68	2.01	Up
	MBD2	2.50E-08	1.16	
	POLI	6.56E-21	0.54	Down
	STARD6	1.00E+00	1.02	
	SNORA37	7.12E-01	1.03	
	C18orf54	3.55E-02	1.09	
	MIR199A1	3.64E-08	1.21	
	TMED1	1.00E+00	0.99	
	DNM2	2.13E-10	1.18	
	ILF3	1.35E-26	1.37	
	LOC147727	1.00E-08	0.76	
	MIR638	3.64E-08	1.21	
	QTRT1	9.08E-02	1.07	
Conditional Analysis	*IFIH1*	1.14E-50	2.79	Up
	FAP	8.25E-01	1.09	
	LNPEP	9.47E-35	0.73	
	ERAP2	5.33E-03	1.21	
	IL12B	2.70E-14	1.22	
	HLA-B	2.26E-15	1.26	
	MICA	1.22E-17	0.60	Down
	HCG26	7.96E-03	0.91	
	CDC37	3.03E-19	1.26	
	RAVER1	1.00E+00	1.00	
	ICAM4	2.30E-03	1.10	
	KEAP1	7.00E-10	1.18	
	MRPL4	2.44E-44	1.44	
	MIR1181	3.03E-19	1.26	
	PDE4A	8.49E-25	0.70	
	ICAM3	2.61E-09	1.24	
	ZGLP1	2.38E-02	1.09	
	TYK2	8.31E-02	0.94	
	ICAM1	1.12E-10	1.21	
	FDX1L	3.55E-06	1.17	
	ICAM5	1.28E-03	1.10	

Supplementary Table 10. Variance in liability

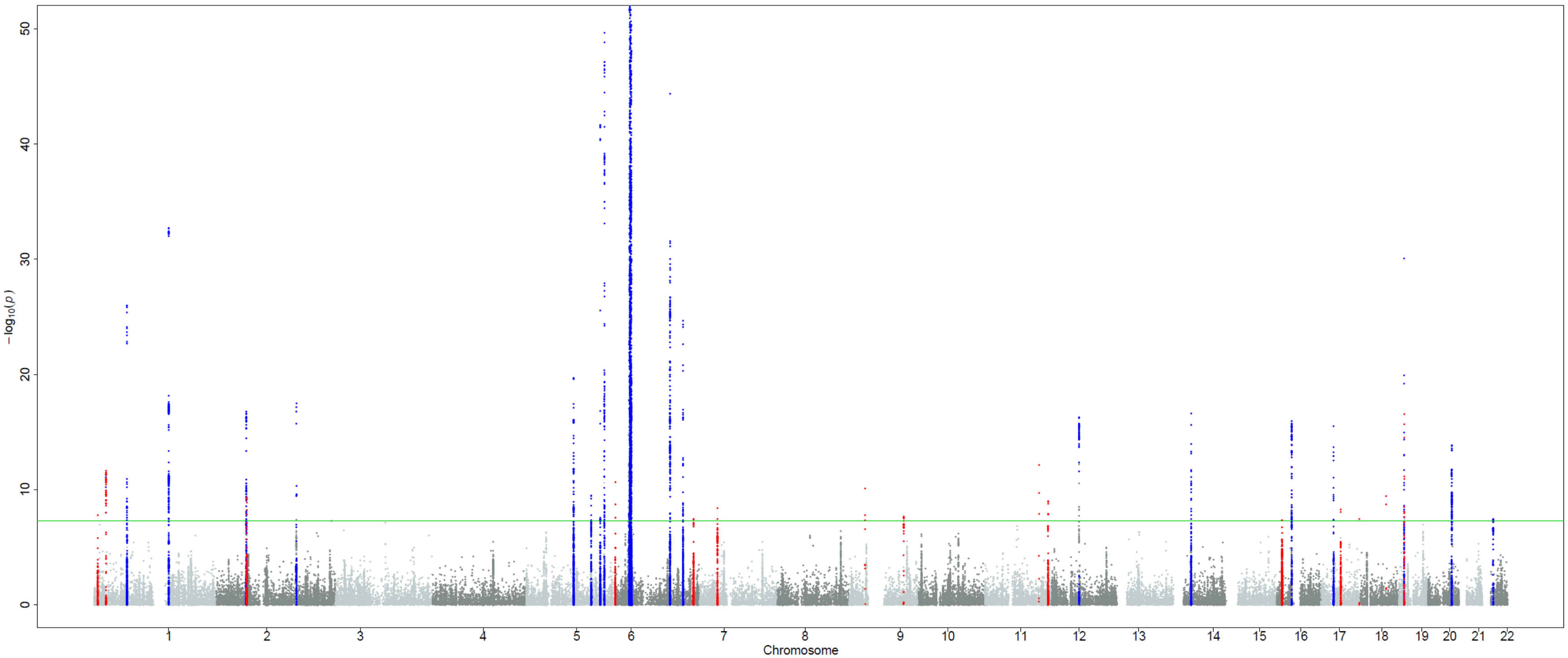
The variance in liability explained by each locus, as determined under a liability model[6]. Prevalence of psoriasis was set as 2% when estimating the variance. Assuming the multiple loci have an additive effect on the risk of psoriasis, the variance in liability explained by the 19 known loci, 15 new loci, and the 5 secondary signals identified by conditional analysis are 11.35%, 1.60%, and 1.36%, respectively.

SNP	Notable nearby genes	Risk allele Freq (case)	Risk allele Freq (control)	OR	RR	Variance in liability
Known loci						
rs7552167	*IL28RA*	0.878	0.858	1.21	1.21	0.14%
rs9988642	*IL23R*	0.952	0.929	1.52	1.51	0.36%
rs6677595	*LCE3D*	0.689	0.64	1.26	1.26	0.40%
rs62149416	*REL*	0.671	0.635	1.17	1.17	0.19%
rs17716942	*IFIH1*	0.891	0.863	1.27	1.27	0.22%
rs27432	*ERAP1*	0.309	0.274	1.2	1.20	0.22%
rs1295685	*IL13/IL4*	0.807	0.798	1.18	1.18	0.14%
rs2233278	*TNIP1*	0.09	0.058	1.59	1.57	0.41%
rs12188300	*IL12B*	0.132	0.095	1.58	1.56	0.62%
rs4406273	*HLA-C*	0.259	0.092	4.32	4.16	6.44%
rs33980500	*TRAF3IP2*	0.108	0.074	1.52	1.51	0.41%
rs582757	*TNFAIP3*	0.315	0.273	1.23	1.23	0.28%
rs2066819	*IL23A/STAT2*	0.948	0.934	1.39	1.38	0.21%
rs8016947	*NFKBIA*	0.6	0.564	1.16	1.16	0.18%
rs12445568	*FBXL19*	0.403	0.368	1.16	1.16	0.17%
rs28998802	*NOS2*	0.17	0.145	1.22	1.21	0.16%
rs34536443	*TYK2*	0.974	0.953	1.88	1.87	0.54%
rs1056198	*RNF114*	0.6	0.573	1.16	1.16	0.18%
rs4821124	*UBE2L3*	0.208	0.189	1.13	1.13	0.08%
New loci						
rs11121129	*SLC45A1*	0.308	0.287	1.13	1.13	0.10%
rs7536201	*RUNX3*	0.528	0.494	1.13	1.13	0.12%
rs10865331	*B3GNT2*	0.404	0.374	1.12	1.12	0.10%
rs9504361	*EXOC2/IRF4*	0.574	0.546	1.12	1.12	0.10%
rs2451258	*TAGAP*	0.362	0.348	1.12	1.12	0.10%
rs2700987	*ELMO1*	0.591	0.564	1.11	1.11	0.09%
rs11795343	*DDX58*	0.628	0.597	1.11	1.11	0.09%
rs10979182	*KLF4*	0.617	0.591	1.12	1.12	0.10%
rs4561177	*ZC3H12C*	0.617	0.581	1.14	1.14	0.14%
rs3802826	*ETS1*	0.505	0.484	1.12	1.12	0.11%
rs367569	*SOCS1*	0.729	0.709	1.13	1.13	0.10%
rs963986	*STAT3,*	0.169	0.154	1.15	1.15	0.08%
rs11652075	*CARD14*	0.53	0.502	1.11	1.11	0.09%
rs545979	*STARD6,POLI,*	0.317	0.291	1.12	1.12	0.09%
rs892085	*ILF3,CARM1*	0.593	0.558	1.17	1.17	0.20%
Conditional analysis loci						
rs2111485	*IFIH1*	0.647	0.61	1.14	1.14	0.13%
rs2910686	*ERAP2*	0.442	0.437	1.12	1.12	0.10%
rs4379175	*IL12B*	0.737	0.678	1.31	1.30	0.51%
rs13437088	*MICA*	0.342	0.251	1.32	1.31	0.48%
rs12720356	*TYK2*	0.929	0.911	1.25	1.25	0.13%

Supplementary Figures

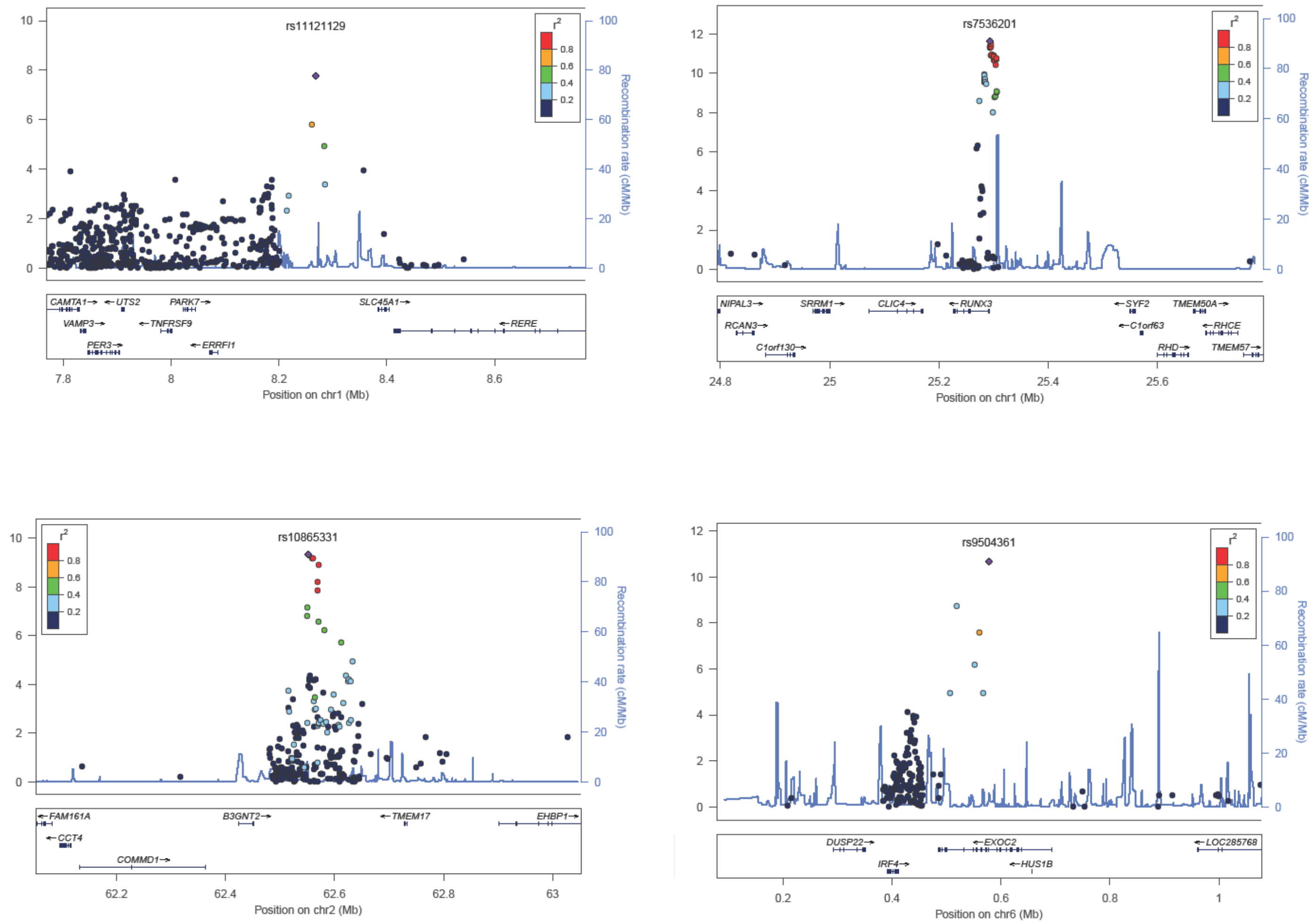
Supplementary Figure 1: Manhattan plot for meta-analysis

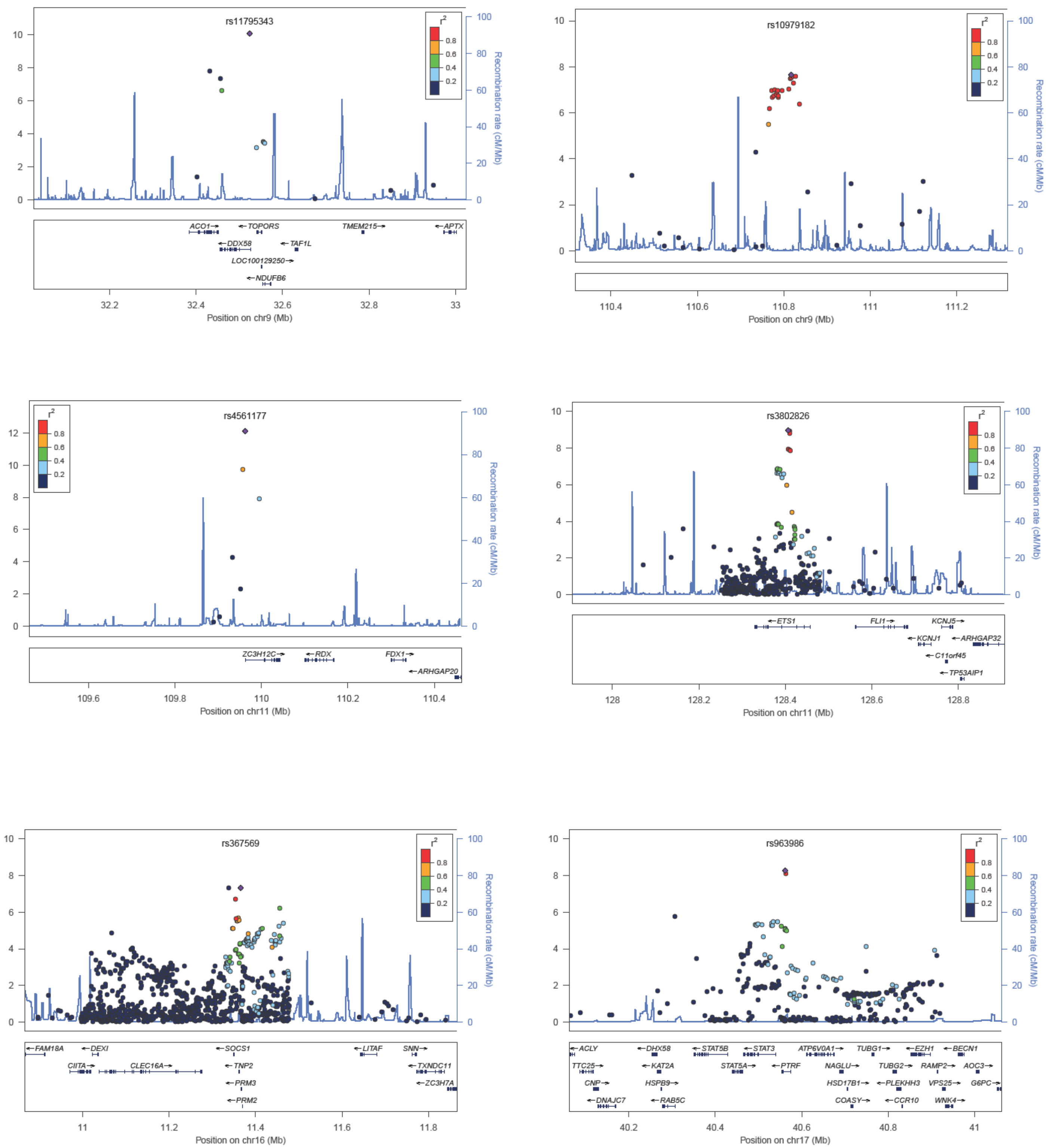
The 34 susceptibility loci that achieve genome-wide significance (above the green line) in the meta-analysis. The 19 known loci are colored blue, and the 15 new loci are colored red. Only SNPs with P-values ≥ 1 x 10^{-50} are shown.



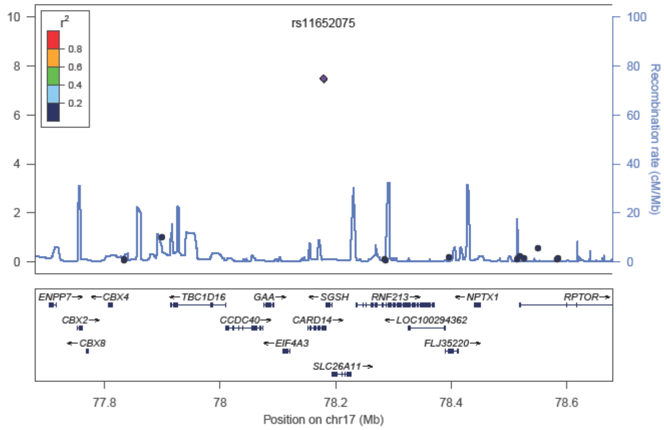
Supplementary Figure 2. Regional association plots

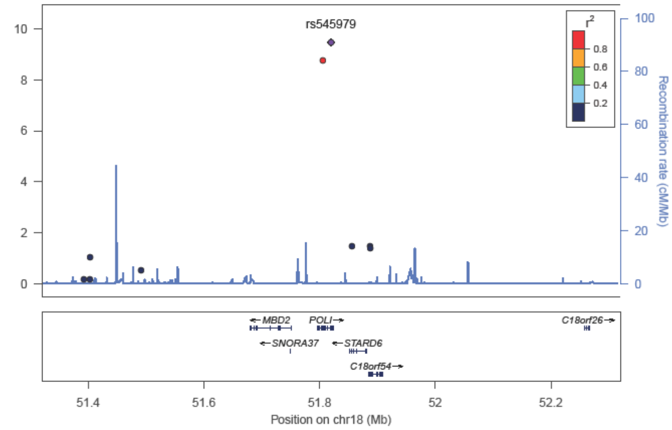
Regional association plots using LocusZoom[7] to show the combined p-values in each of the 15 new loci. The most significant SNP from each locus was used as the index SNP to compute the linkage

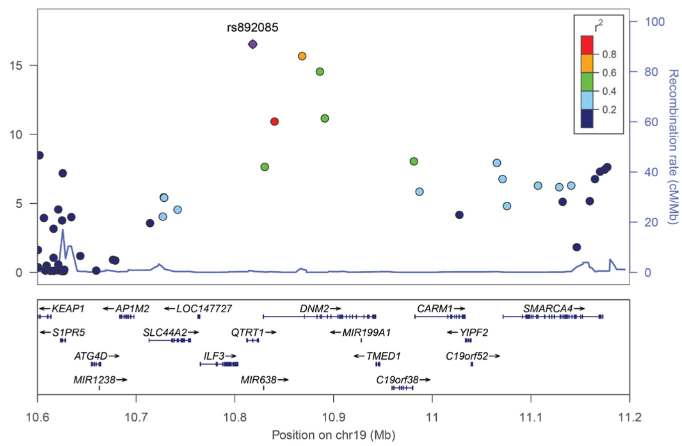




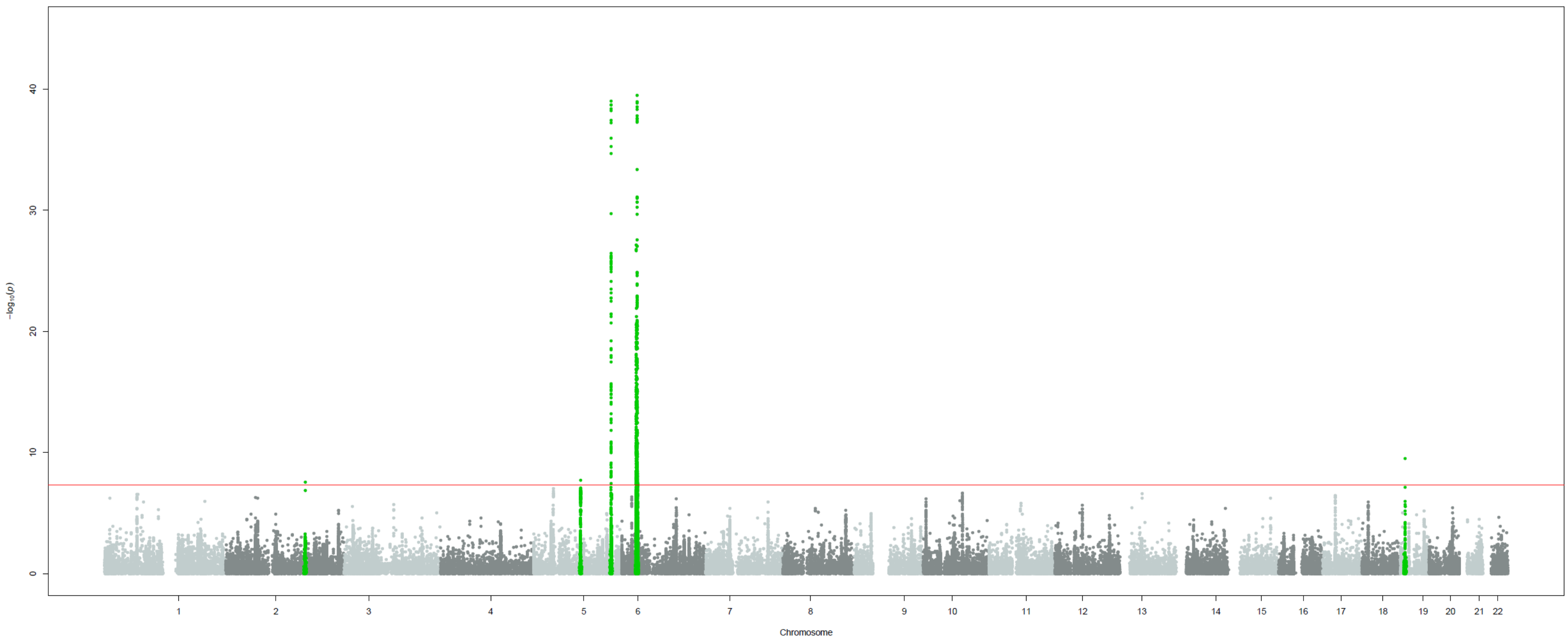
rs11795343
ACO1
TOPORS
TMEM215
APTX
DDX58
TAF1L
LOC100129250
NDUFB6
Position on chr9 (Mb)
rs10979182
Position on chr9 (Mb)
rs4561177
ZC3H12C
RDX
FDX1
ARHGAP20
Position on chr11 (Mb)
rs3802826
ETS1
FLI1
KCNJ5
KCNJ1
ARHGAP32
C11orf45
TP53AIP1
Position on chr11 (Mb)
rs367569
FAM18A
DEXI
SOCS1
LITAF
SNN
CIITA
CLEC16A
TNP2
TXNDC11
PRM3
ZC3H7A
PRM2
Position on chr16 (Mb)
rs963986
ACLY
DHX58
STAT5B
STAT3
ATP6V0A1
TUBG1
EZH1
BECN1
TTC25
KAT2A
STAT5A
PTRF
NAGLU
TUBG2
RAMP2
AOC3
CNP
HSPB9
HSD17B1
PLEKHH3
VPS25
G6PC
DNAJC7
RAB5C
COASY
CCR10
WNK4
Position on chr17 (Mb)
Recombination rate (cM/Mb)


rs11652075
r2
0.8
0.6
0.4
0.2
Recombination rate (cM/Mb)
ENPP7
CBX4
TBC1D16
GAA
SGSH
RNF213
NPTX1
RPTOR
CBX2
CCDC40
CARD14
LOC100294362
CBX8
EIF4A3
FLJ35220
SLC26A11
Position on chr17 (Mb)

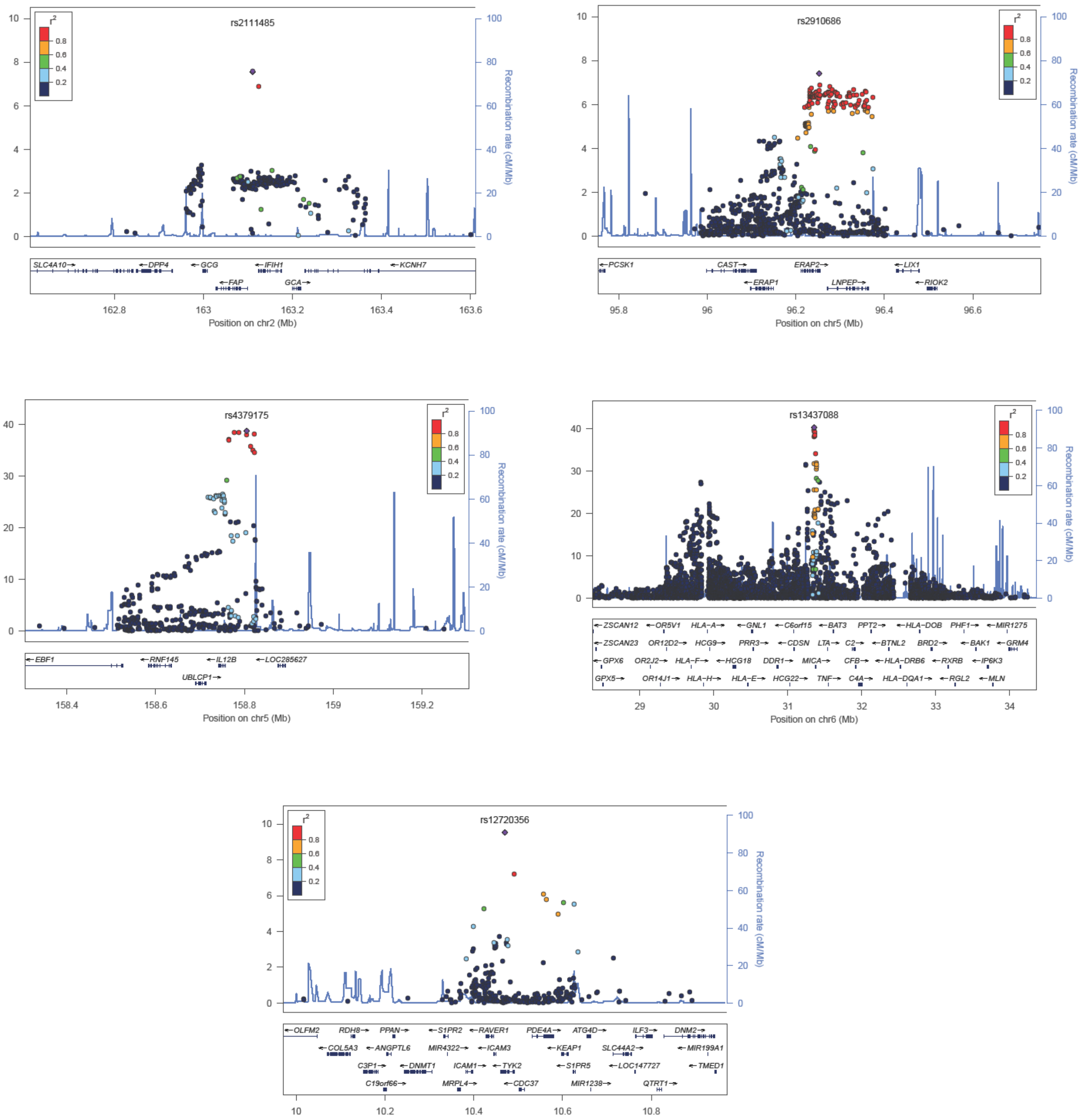

rs545979
r2
0.8
0.6
0.4
0.2
Recombination rate (cM/Mb)
MBD2
POLI
C18orf26
SNORA37
STARD6
C18orf54
Position on chr18 (Mb)


rs892085
r2
0.8
0.6
0.4
0.2
Recombination rate (cM/Mb)
KEAP1
AP1M2
LOC147727
DNM2
CARM1
SMARCA4
S1PR5
SLC44A2
QTRT1
MIR199A1
YIPF2
ATG4D
ILF3
TMED1
C19orf52
MIR1238
MIR638
C19orf38
Position on chr19 (Mb)

Supplementary Figure 3. Manhattan plot for the results of the conditional analysis.
Green dots shown SNPs in the five loci that achieve genome-wide significance ($P=5x10^{-8}$, denoted by red line).



Supplementary Figure. 4. Regional association plots for the significant loci in the conditional meta-analysis.

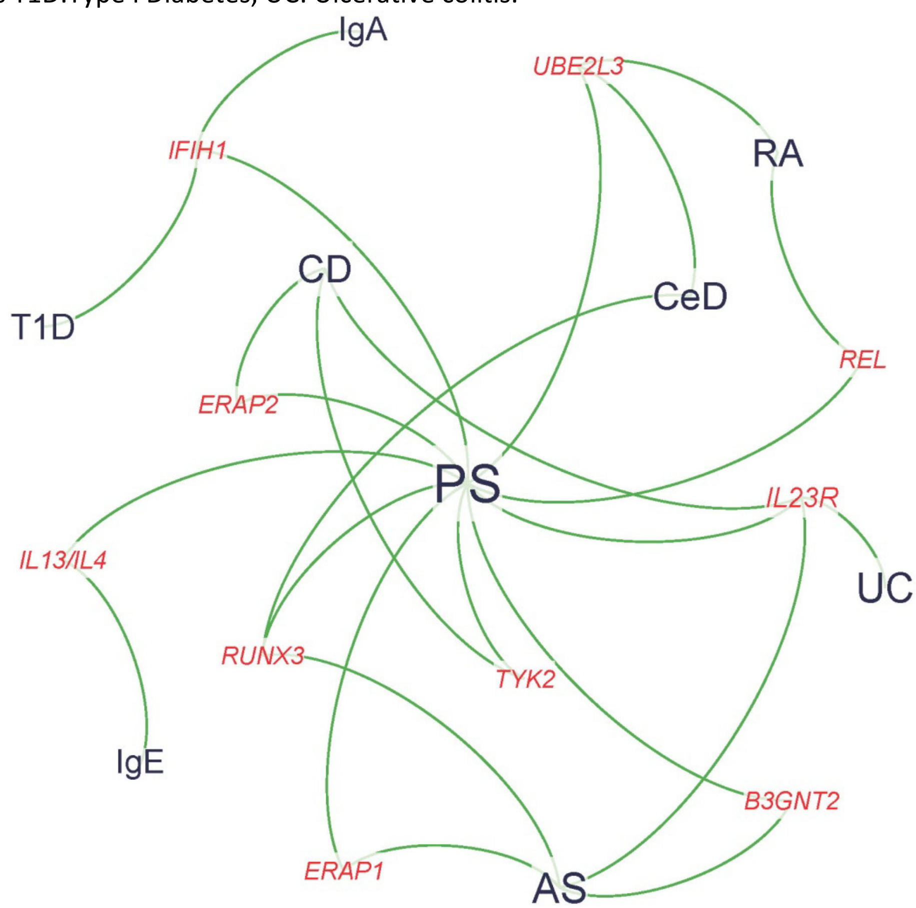


Supplementary Figure 5. Plots illustrating the phenotype overlap for the susceptibility variants listed in Table 1.

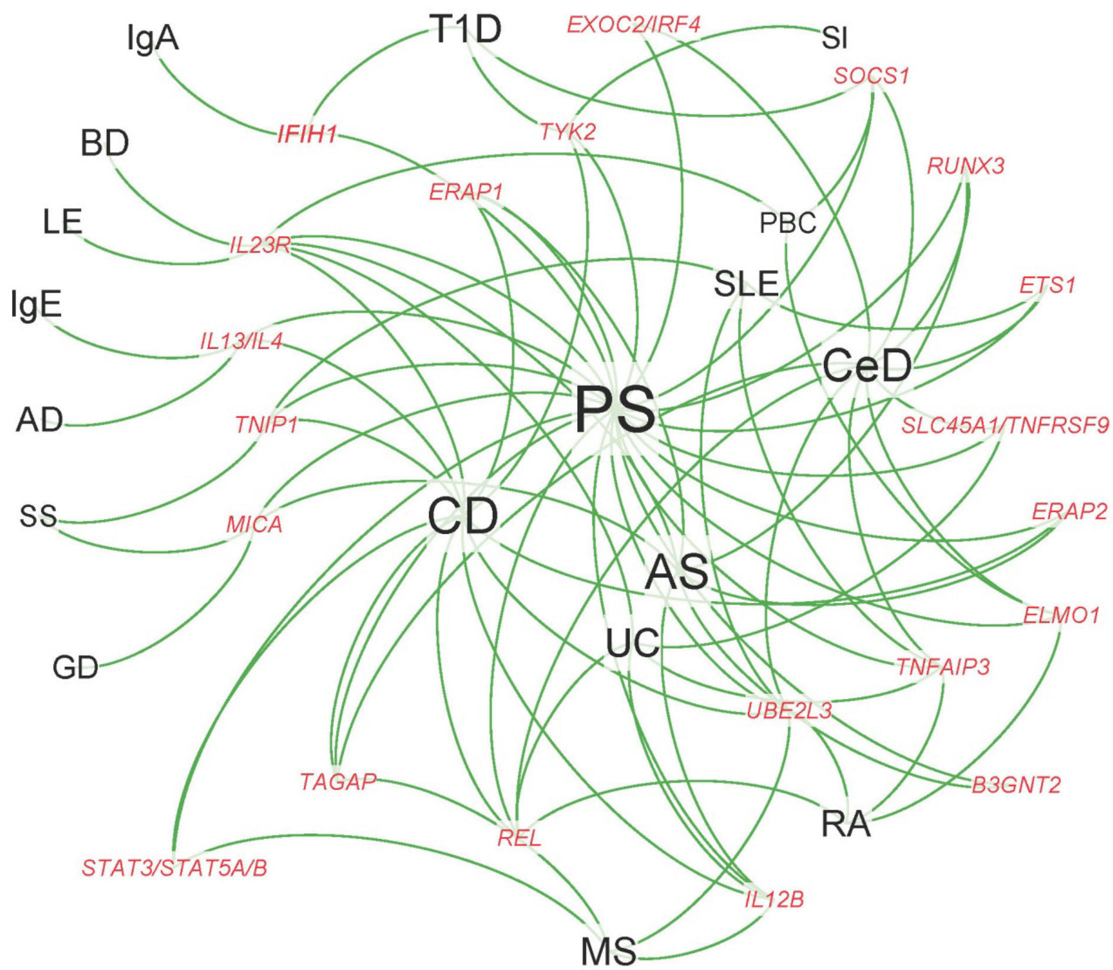
Only disease associations that are listed in the NHGRI GWAS catalog (http://www.genome.gov/gwastudies) and Immunochip results for Celiac disease[4] were included. Genes are shown in red and phenotypes in black. A) Shows the overlap with phenotypes where the identified variant is in LD (r2>0.7) with the identified psoriasis variant. B) Shows all loci shared with phenotypes that have identified variants within 500kb of the identified psoriasis variant for that locus. Phenotypes sharing the most loci with psoriasis are generally more central to the plot, while those sharing only one or two loci are situated on the outside (Plots were produced using Gephi available at http://gephi.org/)[8]. Owing to the number of connections with other phenotypes, the HLA locus was removed from the plot.

AD: Atopic dermatitis, AS: Ankylosing spondylitis, BD: Behcet's disease, CD: Crohn's disease, CeD: Celiac disease, IgE: Serum IgE, IgA: Selective Immunoglobulin A deficiency, LE: Leprosy, MS: Multiple Sclerosis, PBC: primary biliary cirrhosis, PS: Psoriasis, , RA: rheumatoid arthritis, SI: Soluble ICAM-1, SLE: Systemic lupus erythematosus, SS: Systemic sclerosis T1D:Type I Diabetes, UC: Ulcerative colitis.

A.



B.


IgA
T1D
EXOC2/IRF4
SI
SOCS1
BD
IFIH1
TYK2
RUNX3
ERAP1
LE
PBC
IL23R
SLE
ETS1
IgE
IL13/IL4
CeD
PS
AD
TNIP1
SLC45A1/TNFRSF9
SS
ERAP2
MICA
CD
AS
ELMO1
UC
GD
TNFAIP3
UBE2L3
TAGAP
B3GNT2
RA
REL
STAT3/STAT5A/B
IL12B
MS

Supplementary note

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Additional Methods and results

Association Analysis

Logistic regression was used to perform association analysis for the imputed dosages for the GWAS datasets: Kiel (mach2dat[7,9]), CASP (mach2dat), and the WTCCC2 (SNPTESTv2[10]). Linear mixed modeling as implemented in EMMAX[11] was used to perform association analyses for the two Immunochip datasets separately due to its ability to control for population stratification and cryptic relatedness. The Balding-Nicholls algorithm[12] was used to generate the kinship matrix.

Meta-analysis

Sample size weighting was employed to combine P-values across the 5 studies using METAL, employing effective sample sizes[13]. To calculate the meta-odds ratios (ORs) for each SNP, we performed logistic regression analysis for the Immunochip data, using the top ten PCs to adjust for population stratification. The meta-ORs were then calculated as follows:

$$\beta_{weighted} = \frac{\sum_{i=1}^{D} N_i^{eff} \beta_i}{\sum_{i=1}^{D} N_i^{eff}}$$

$$OR_{meta} = e^{\beta_{weighted}}$$

where β_i is the coefficient estimated from the logistic regression analysis, and D is the number of datasets.

Conditional analysis of the newly identified signal at 10.82 Mb on chr19

Conditional analysis was performed to determine if the signal tagged by rs892085 at 10.82 Mb on chromosome 19 is new signal associated with psoriasis. We conditioned on two SNPs from the known locus near *TYK2*: i) the previously identified SNP rs12720356[3]; ii) the current best SNP from our meta-analysis rs34536443. Each conditional analysis was first performed individually for each study (logistic regression framework for the three GWAS; linear mixed model for the Immunochip datasets). Meta-analysis based on the conditional results was then performed using METAL[13]. Since rs34536443 has poor imputation quality (r2=0.17) in the CASP dataset, we excluded this dataset when conditioning on rs34536443. As shown in **Supplementary Table 5**, rs892085 achieves genome-wide significance after conditioning on either of the two *TYK2* SNPs, indicating that it is an independent signal for psoriasis susceptibility.

Conditional analysis

We performed conditional analysis for the 3 GWAS datasets using logistic regression, whereas we used the linear mixed modeling implemented in EMMAX for the two Immunochip datasets. The most strongly associated SNPs from the 19 known loci achieving genome-wide significance in this study and the 15 new loci (**Table 1**) were used as covariates for all five studies. Because the CASP GWAS did not have good imputation quality (r^2>0.3) for SNP rs34536443; the second best SNP in the 19q13.2 region (rs2304256: P_{comb} =1.20×10^{-20}) was used in the conditional analysis of the CASP dataset. We next used METAL to combine the conditional analysis results; for the 19q13.2 region (ie ±500 kb surrounding SNP rs34536443) the meta-analysis excluded the CASP dataset, whereas we used all five datasets for the other regions.

Conditional analysis on the ERAP2 signal

For the follow-up conditional analysis of the *ERAP2* signal, we used only the best ERAP1 SNP (rs27432) as a covariate. Conditioning only on rs27432, the most significant *ERAP1* SNP in the unconditional analysis, continued to support the *ERAP2* signal (P = 3.6 × 10^{-7}). When considered together with the LD results between the 2 SNPs (r2=0.17 and D'=0.75 for PAGE; r2=0.18 and D'=0.76 for GAPC), these suggest the two loci might have opposite effects arising from the same haplotype. To test this, we performed a haplotype association test using the PAGE phased genotypes data for rs27432 and rs2910686. The risk/non-risk alleles for these SNPs are A/G and C/T, respectively, and their haplotype frequencies are: 0.03 (AC), 0.25 (AT), 0.41 (GC), and 0.31 (GT). The haplotype association analysis for ERAP1-ERAP2 was performed using logistic regression, with haplotype counts of AT (ERAP1 risk / ERAP2 nonrisk), GC (ERAP1 nonrisk / ERAP2 risk), and AC (ERAP1 risk / ERAP2 risk) as 3 independent variables, and the top 10 PCs as covariates. We found that the AT (ERAP1 risk / ERAP2 nonrisk) haplotype is strongly associated (P = 3.1 × 10^{-6}), the GC (ERAP1 nonrisk / ERAP2 risk) haplotype is weakly associated (P = 2.7 × 10^{-2}), and the rare AC (ERAP1 risk / ERAP2 risk) haplotype is not associated (P = 0.25), suggesting that the genetic effect of *ERAP2* is masked by *ERAP1*.

Causal SNP lookup

We identified SNPs in strong LD (≥0.9) with the most significant SNP from each of the known and new loci listed in Table 1, including the secondary signals identified by the conditional analysis. LD among SNPs was computed from 379 European-ancestry samples in the 1000 Genomes project (May 21st 2011 version). We then used ANNOVAR[14] to annotate each of these SNPs. All identified SNPs affecting the predicted protein sequence were missense variants; none were nonsense or splicing mutations. SIFT[15] and PolyPhen[16] were used to predict the impact of the mutations on the function of the protein.

Epistasis

We performed an analysis of epistasis using the most significantly associated SNP from each of the 34 loci in **Tables 1** reaching genome-wide significance in this study. Logistic regression was used to model epistasis in the five datasets using a risk allele dosage model; for the PAGE and GAPC datasets the top 10 PCs were included as covariates. For each pair of SNPs, the likelihood ratio test was employed to compute the p-value of the interaction term for each dataset. Epistasis results were combined using METAL, again omitting the CASP dataset for the 19q13.2 region.

Gene expression

We retrieved the SNPs that reside within 500 kb (3 Mb for MHC) of each of the most strongly associated SNPs identified from the known or new loci, including secondary signals from the conditional analysis. Using European-ancestry samples from the 1000 Genomes Project, we then used the tag SNP function from PLINK to identify genomic regions in strong LD (r^2>0.7) with the most significant SNP; we then extended the tagged regions by 50kb on each side. We identified genes overlapping any of the extended regions, and we used false discovery rate (FDR) ≤ 0.05 and fold-change (FC) ≤ 0.67 or ≥ 1.5 to declare genes as differentially expressed in psoriatic skin lesions from a previous microarray experiment[17,18].

eQTL lookup

To check whether any of the 34 genome-wide significant SNPs that were known or new and the 5 secondary signals identified by conditional analysis were eQTLs, we queried the cis-psoriasis eQTL database (in normal and psoriatic skin) compiled by Ding *et al*.[19], and we used $P<1x10^{-7}$ as criteria to look for eQTLs using expression of microarray probesets corresponding to Entrez genes. (available at http://www.sph.umich.edu/csg/junding/eQTL/TableDownload/).

Since the imputation was performed using Hapmap reference panel in Ding *et al*., we performed eQTL analysis using our imputed CASP GWAS data (using 1000 genomes for reference panel) and their corresponding gene expression microarray data (data as described in Ding *et al.*[19]). The significant results are consistent with the cis-psoriasis eQTL database.

Heritability explained by psoriasis-associated SNPs

We estimated the variance in liability (locus-specific heritability)[20] that can be explained by the known, new, and the secondary signals of psoriasis-associated SNPs using the approach described by So *et al*.[6]. We set the prevalence of the disease as 0.02, and calculated risk ratios (RR) from our estimated ORs using an iterative approach[21].

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