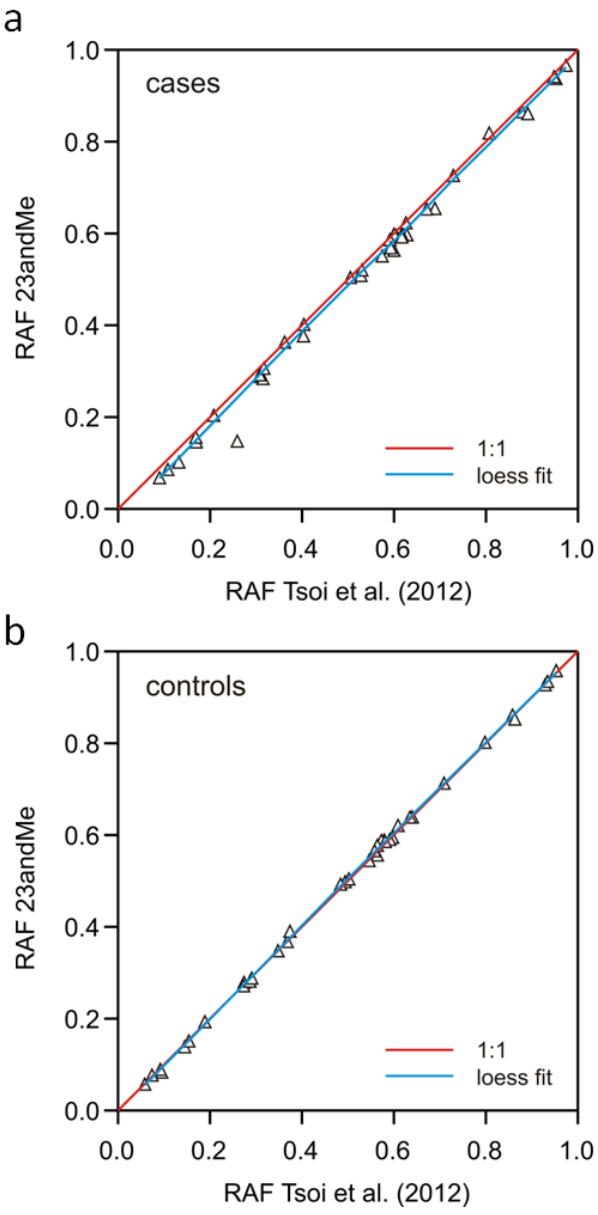
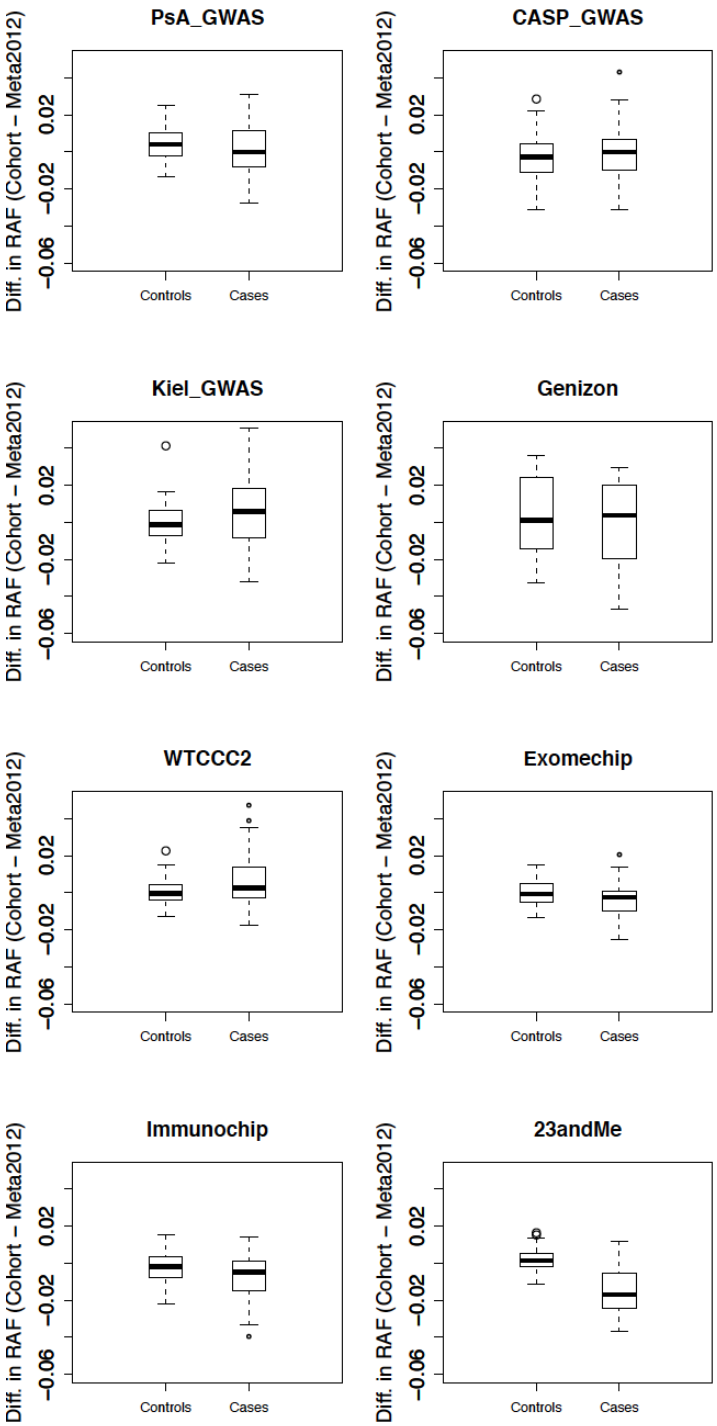
Supplementary Information

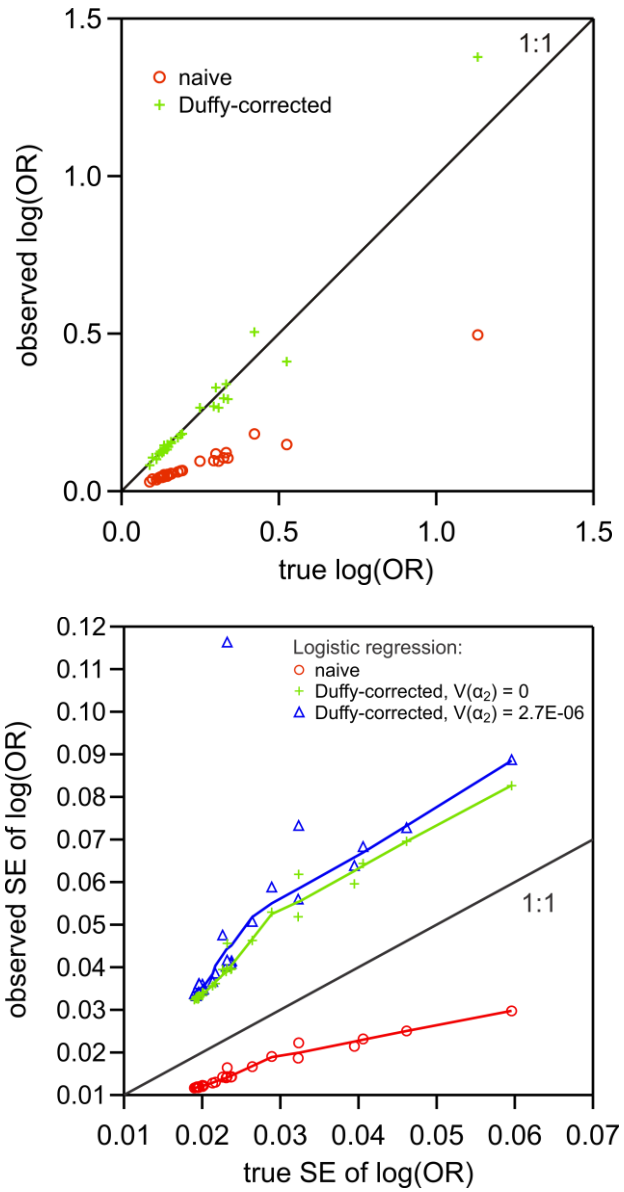
Supplementary Figures



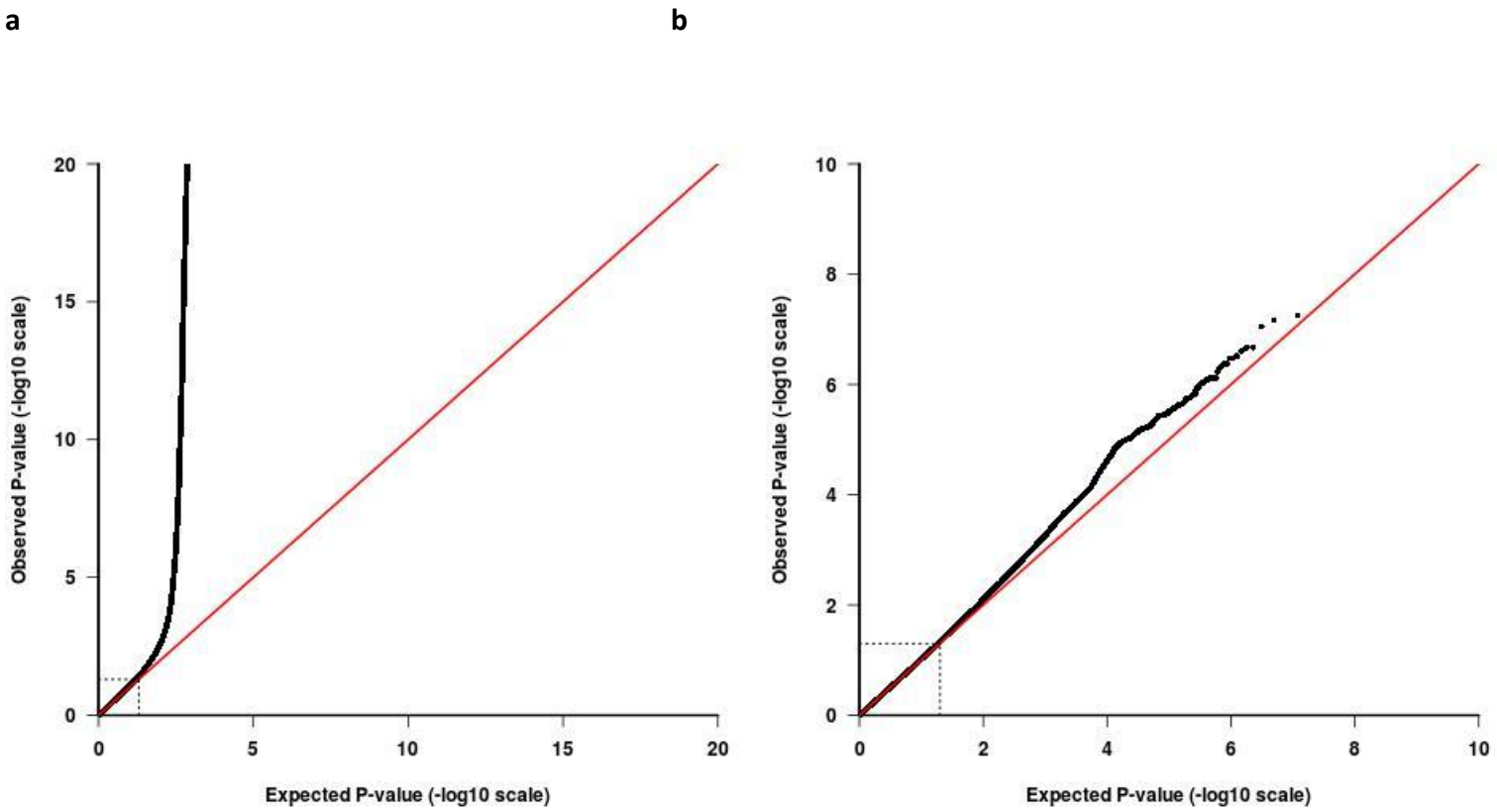
Supplementary Figure 1. Risk allele frequencies (RAFs) for the known psoriasis loci estimated in the 23andMe cohort versus those estimated from our previous study (Tsoi et al., 2012. *Nat Genet*) in cases (a) and controls (b). The loess fit is shown in blue, and the expected 1:1 relationship is shown in red.



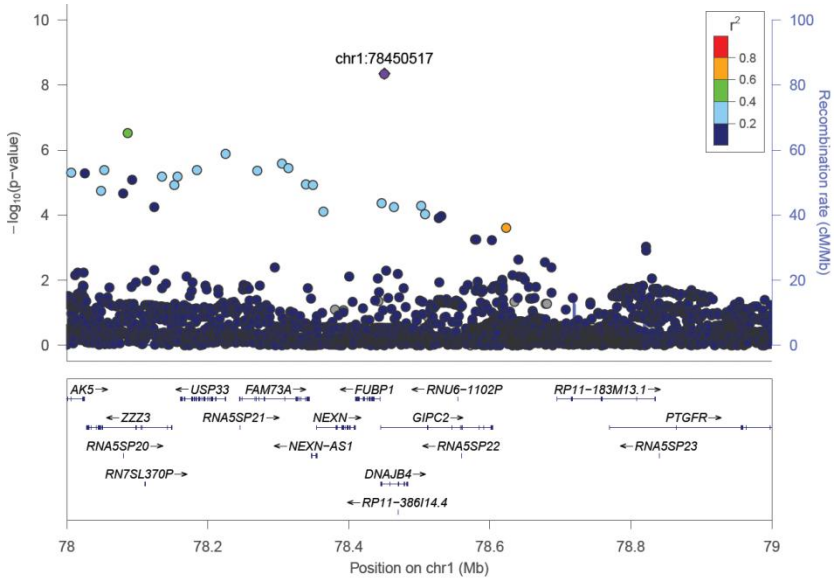
Supplementary Figure 2. Boxplots showing differences in risk allele frequencies (RAFs) estimated in the different cohorts versus those estimated in the meta-analysis of Tsoi et al, 2012. *Nat Genet*. The RAFs estimated from the meta-analysis were used as they represent the results of the previous largest genetic study of psoriasis in European-origin individuals.

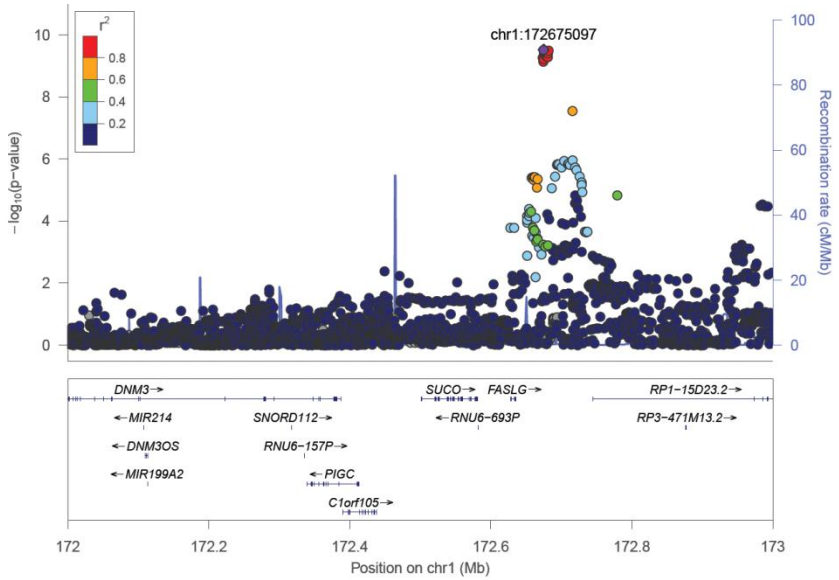


Supplementary Figure 3. Duffy-adjusted ORs and standard errors. (Top) Using ORs estimated from independent cohorts for known loci, the Duffy adjustment could correct the downward bias of ORs estimator in the 23andMe cohort. The results were based on simulation of misclassified data described in Materials and methods. (Bottom) Duffy-adjusted standard errors of the ln(OR), illustrating that correction for misclassification increases the standard error (blue and green vs. red), and the increase is greater when uncertainty for the estimator of the misclassification parameter α_2 is accounted for (blue vs. green).



Supplementary Figure 4. QQ plots for the meta-analysis. a) all markers; b) markers outside previously known psoriasis susceptibility regions.


chr1:78450517
r²
0.8
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
AK5
USP33
FAM73A
FUBP1
RNU6−1102P
RP11−183M13.1
ZZZ3
RNA5SP21
NEXN
GIPC2
PTGFR
RNA5SP20
NEXN−AS1
RNA5SP22
RNA5SP23
RN7SL370P
DNAJB4
RP11−386I14.4
Position on chr1 (Mb)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r²
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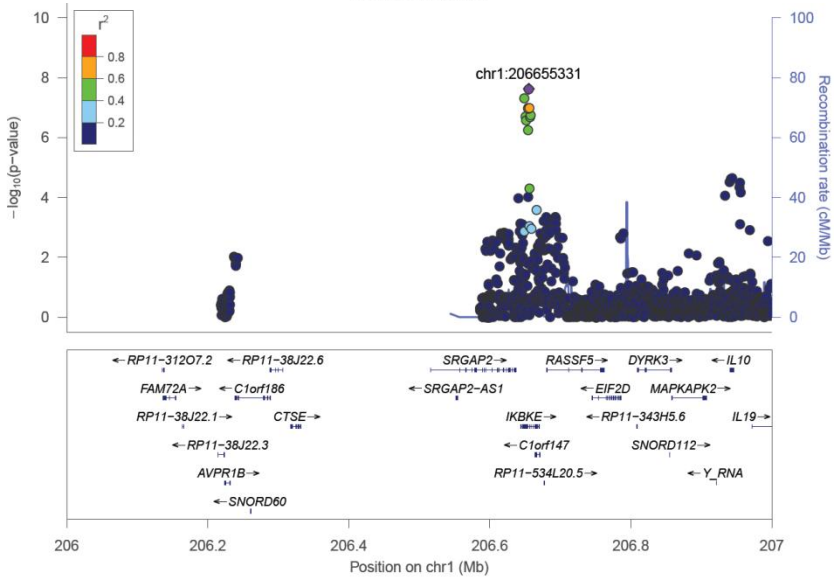
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
DNM3
SUCO
FASLG
RP1−15D23.2
MIR214
SNORD112
RNU6−693P
RP3−471M13.2
DNM3OS
RNU6−157P
MIR199A2
PIGC
C1orf105
Position on chr1 (Mb)


chr1:206655331
r²
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0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
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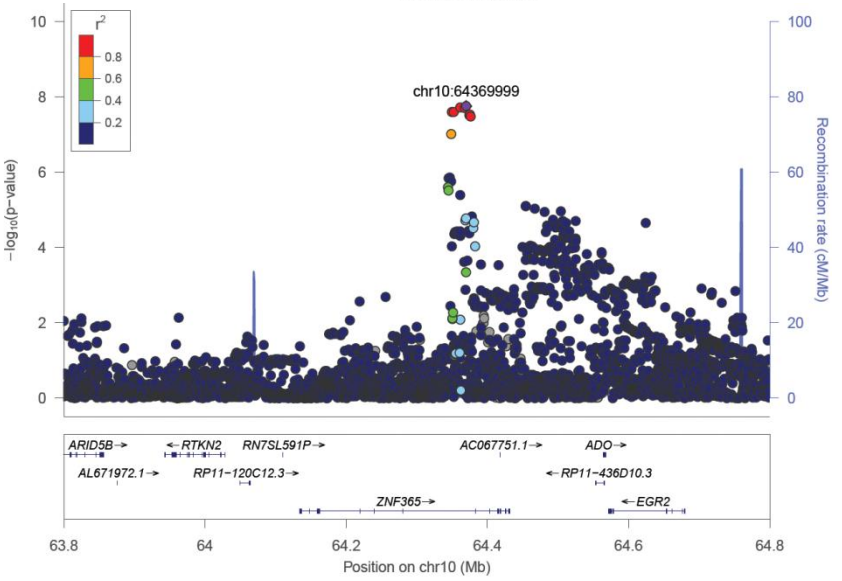
RP11−38J22.6
SRGAP2
RASSF5
DYRK3
IL10
FAM72A
C1orf186
SRGAP2−AS1
EIF2D
MAPKAPK2
RP11−38J22.1
CTSE
IKBKE
RP11−343H5.6
IL19
RP11−38J22.3
C1orf147
SNORD112
AVPR1B
RP11−534L20.5
Y_RNA
SNORD60
Position on chr1 (Mb)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r²
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0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
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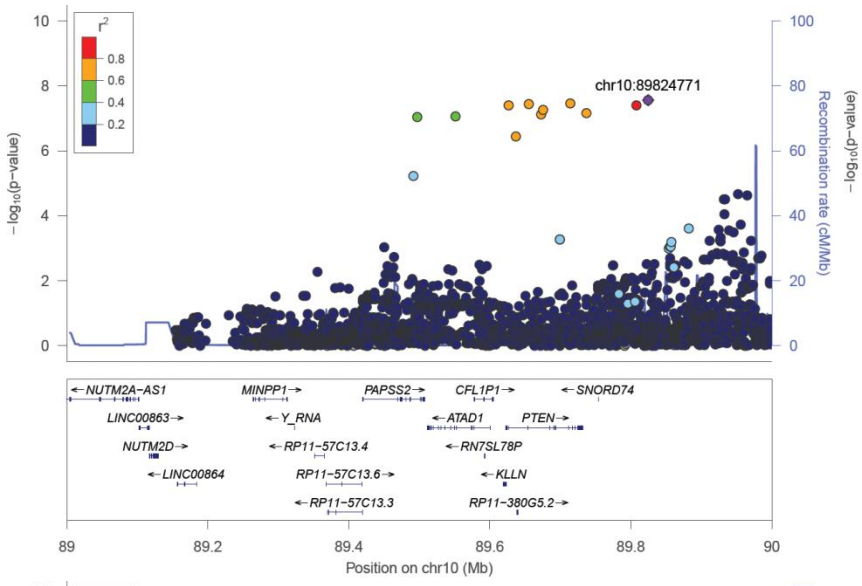
RTKN2
RN7SL591P
AC067751.1
ADO
AL671972.1
RP11−120C12.3
RP11−436D10.3
ZNF365
EGR2
Position on chr10 (Mb)


chr10:89824771
r²
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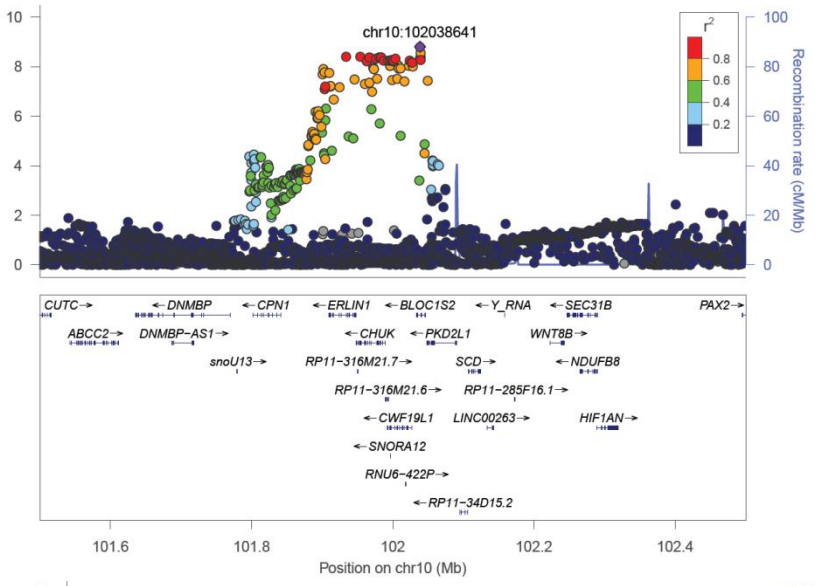
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
NUTM2A−AS1
MINPP1
PAPSS2
CFL1P1
SNORD74
LINC00863
Y_RNA
ATAD1
PTEN
NUTM2D
RP11−57C13.4
RN7SL78P
LINC00864
RP11−57C13.6
KLLN
RP11−57C13.3
RP11−380G5.2
Position on chr10 (Mb)


chr10:102038641
r²
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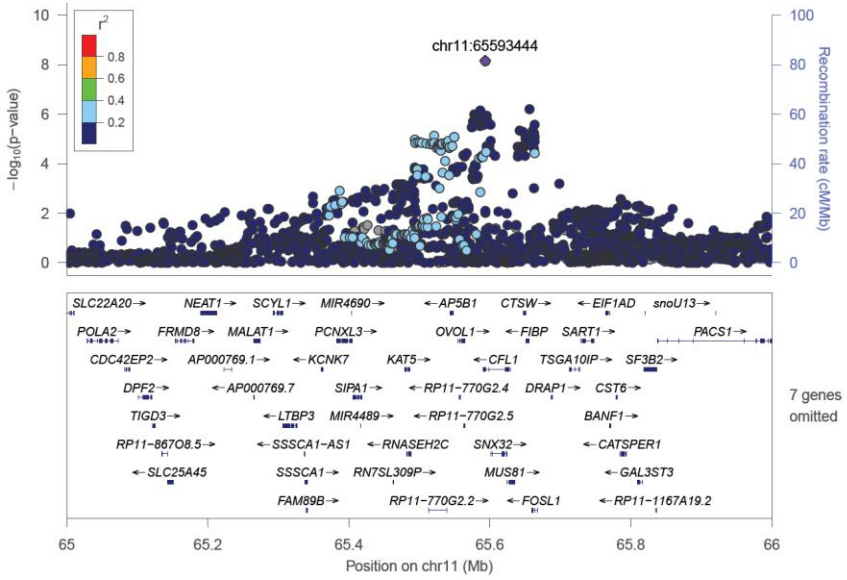
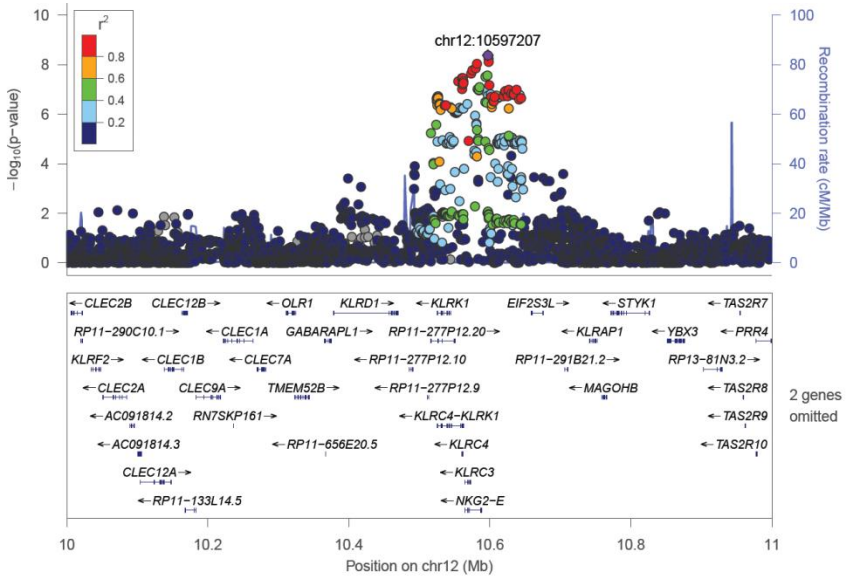
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
CUTC
DNMBP
CPN1
ERLIN1
BLOC1S2
Y_RNA
SEC31B
PAX2
ABCC2
DNMBP−AS1
CHUK
PKD2L1
WNT8B
snoU13
RP11−316M21.7
SCD
NDUFB8
RP11−316M21.6
RP11−285F16.1
CWF19L1
LINC00263
HIF1AN
SNORA12
RNU6−422P
RP11−34D15.2
Position on chr10 (Mb)


chr11:65593444
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
SLC22A20
NEAT1
SCYL1
MIR4690
AP5B1
CTSW
EIF1AD
snoU13
POLA2
FRMD8
MALAT1
PCNXL3
OVOL1
FIBP
SART1
PACS1
CDC42EP2
AP000769.1
KCNK7
KAT5
CFL1
TSGA10IP
SF3B2
DPF2
AP000769.7
SIPA1
RP11−770G2.4
DRAP1
CST6
TIGD3
LTBP3
MIR4489
RP11−770G2.5
BANF1
RP11−867O8.5
SSSCA1−AS1
RNASEH2C
SNX32
CATSPER1
SLC25A45
SSSCA1
RN7SL309P
MUS81
GAL3ST3
FAM89B
RP11−770G2.2
FOSL1
RP11−1167A19.2
7 genes
omitted
Position on chr11 (Mb)


chr12:10597207
r²
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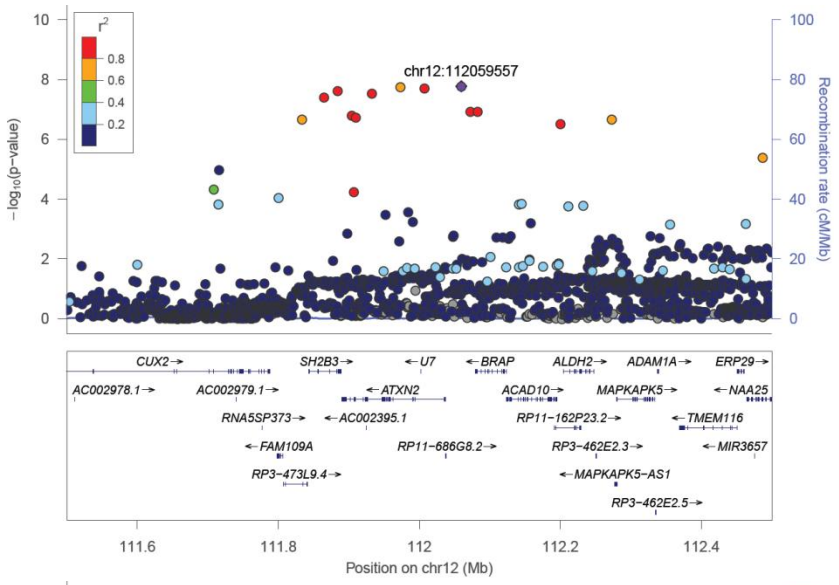
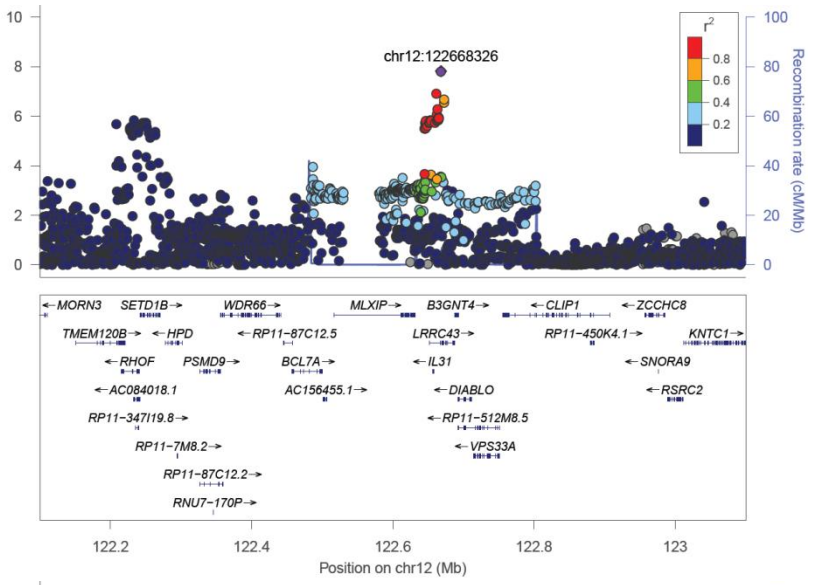
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
CLEC2B
CLEC12B
OLR1
KLRD1
KLRK1
EIF2S3L
STYK1
TAS2R7
RP11−290C10.1
CLEC1A
GABARAPL1
RP11−277P12.20
KLRAP1
YBX3
PRR4
KLRF2
CLEC1B
CLEC7A
RP11−277P12.10
RP11−291B21.2
RP13−81N3.2
CLEC2A
CLEC9A
TMEM52B
RP11−277P12.9
MAGOHB
TAS2R8
AC091814.2
RN7SKP161
KLRC4−KLRK1
TAS2R9
AC091814.3
RP11−656E20.5
KLRC4
TAS2R10
CLEC12A
KLRC3
RP11−133L14.5
NKG2−E
2 genes
omitted
Position on chr12 (Mb)


chr12:112059557
r²
0.8
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
CUX2
SH2B3
U7
BRAP
ALDH2
ADAM1A
ERP29
AC002978.1
AC002979.1
ATXN2
ACAD10
MAPKAPK5
NAA25
RNA5SP373
AC002395.1
RP11−162P23.2
TMEM116
FAM109A
RP11−686G8.2
RP3−462E2.3
MIR3657
RP3−473L9.4
MAPKAPK5−AS1
RP3−462E2.5
111.6
111.8
112
112.2
112.4
Position on chr12 (Mb)


chr12:122668326
r²
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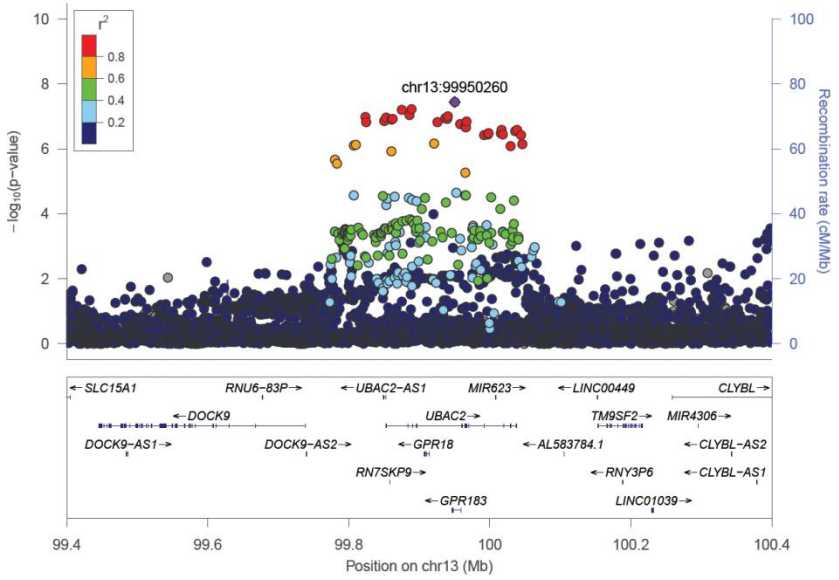
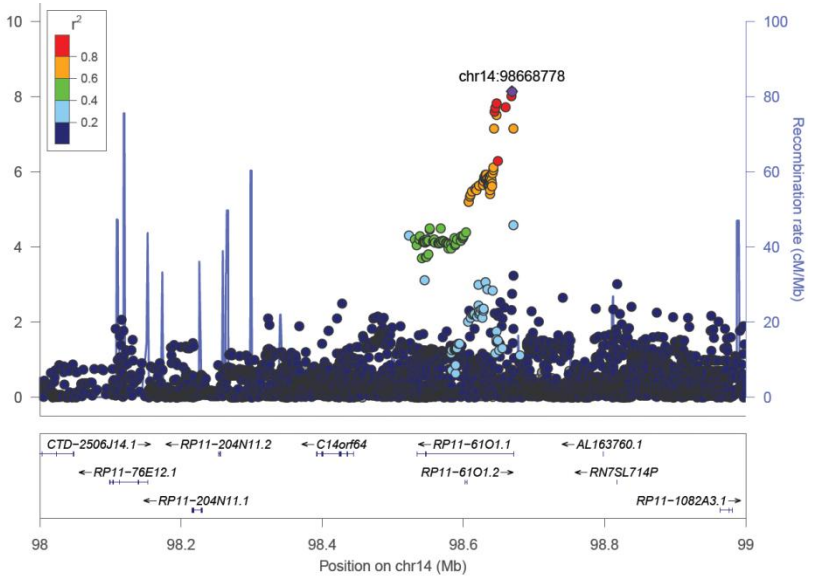
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
MORN3
SETD1B
WDR66
MLXIP
B3GNT4
CLIP1
ZCCHC8
TMEM120B
HPD
RP11−87C12.5
LRRC43
RP11−450K4.1
KNTC1
RHOF
PSMD9
BCL7A
IL31
SNORA9
AC084018.1
AC156455.1
DIABLO
RSRC2
RP11−347I19.8
RP11−512M8.5
RP11−7M8.2
VPS33A
RP11−87C12.2
RNU7−170P
122.2
122.4
122.6
122.8
123
Position on chr12 (Mb)


chr13:99950260
r²
0.8
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
SLC15A1
RNU6−83P
UBAC2−AS1
MIR623
LINC00449
CLYBL
DOCK9
UBAC2
TM9SF2
MIR4306
DOCK9−AS1
DOCK9−AS2
GPR18
AL583784.1
CLYBL−AS2
RN7SKP9
RNY3P6
CLYBL−AS1
GPR183
LINC01039
99.4
99.6
99.8
100
100.2
100.4
Position on chr13 (Mb)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r²
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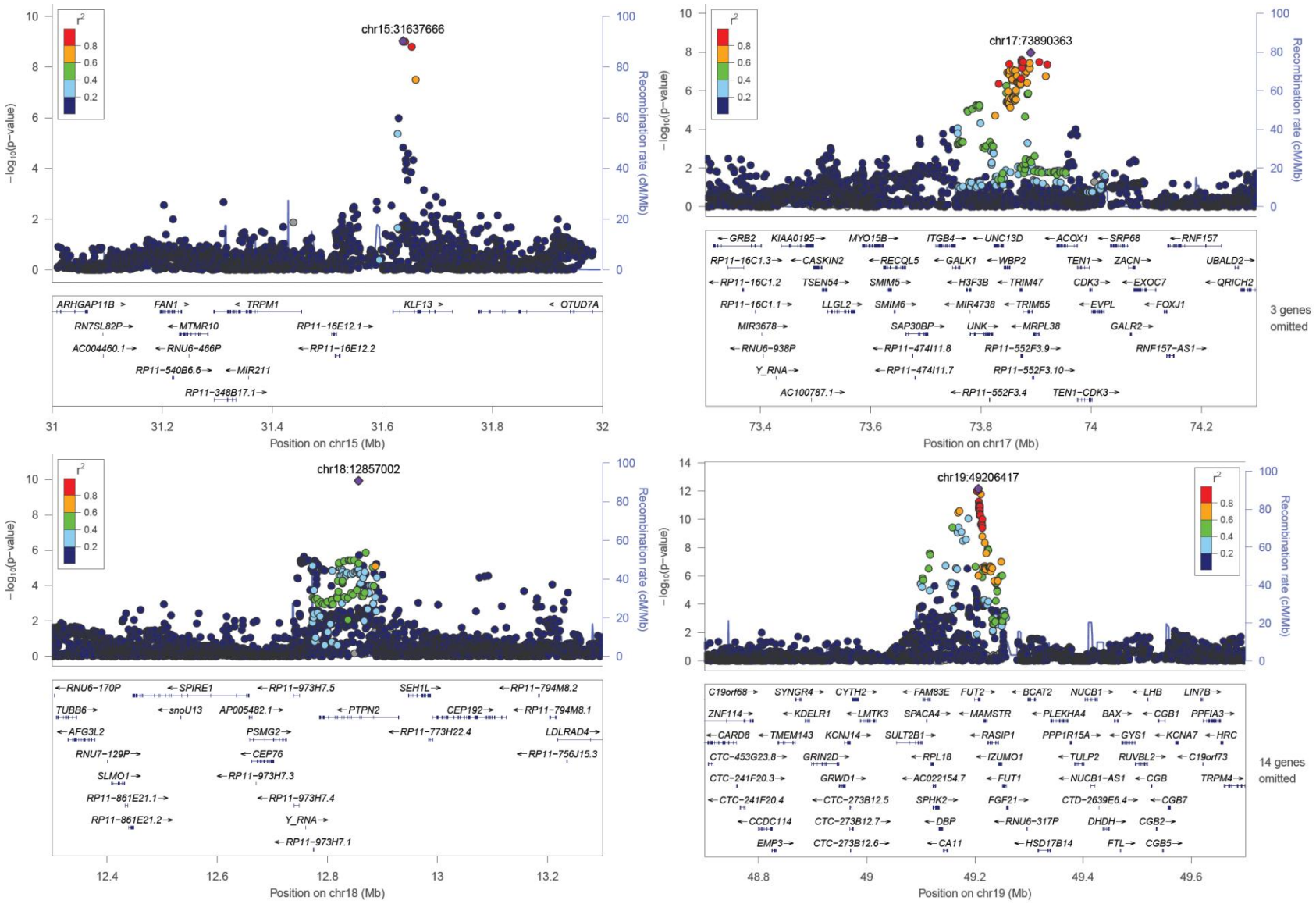
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
CTD−2506J14.1
RP11−204N11.2
C14orf64
RP11−61O1.1
AL163760.1
RP11−76E12.1
RP11−61O1.2
RN7SL714P
RP11−204N11.1
RP11−1082A3.1
98
98.2
98.4
98.6
98.8
99
Position on chr14 (Mb)


chr15:31637666
chr17:73890363
chr18:12857002
chr19:49206417
r²
0.8
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
ARHGAP11B→ FAN1→ ←TRPM1 KLF13→ ←OTUD7A
RN7SL82P→ ←MTMR10 RP11−16E12.1→
AC004460.1→ ←RNU6−466P ←RP11−16E12.2
RP11−540B6.6→ ←MIR211
RP11−348B17.1→
Position on chr15 (Mb)
←GRB2 KIAA0195→ MYO15B→ ITGB4→ ←UNC13D ←ACOX1 ←SRP68 ←RNF157
RP11−16C1.3→ ←CASKIN2 ←RECQL5 ←GALK1 ←WBP2 TEN1→ ZACN→ UBALD2→
←RP11−16C1.2 TSEN54→ SMIM5→ ←H3F3B ←TRIM47 CDK3→ ←EXOC7 ←QRICH2
RP11−16C1.1→ LLGL2→ SMIM6→ ←MIR4738 ←TRIM65 ←EVPL ←FOXJ1
MIR3678→ SAP30BP→ UNK→ ←MRPL38 GALR2→
←RNU6−938P ←RP11−474I11.8 RP11−552F3.9→ RNF157−AS1→
Y_RNA→ ←RP11−474I11.7 RP11−552F3.10→
AC100787.1→ ←RP11−552F3.4 TEN1−CDK3→
3 genes omitted
Position on chr17 (Mb)
←RNU6−170P ←SPIRE1 ←RP11−973H7.5 SEH1L→ ←RP11−794M8.2
TUBB6→ ←snoU13 AP005482.1→ ←PTPN2 CEP192→ ←RP11−794M8.1
←AFG3L2 PSMG2→ ←RP11−773H22.4 LDLRAD4→
RNU7−129P→ ←CEP76 ←RP11−756J15.3
SLMO1→ ←RP11−973H7.3
RP11−861E21.1→ ←RP11−973H7.4
RP11−861E21.2→ Y_RNA→
←RP11−973H7.1
Position on chr18 (Mb)
C19orf68→ SYNGR4→ CYTH2→ ←FAM83E FUT2→ ←BCAT2 NUCB1→ ←LHB LIN7B→
ZNF114→ ←KDELR1 ←LMTK3 SPACA4→ ←MAMSTR ←PLEKHA4 BAX→ ←CGB1 PPFIA3→
←CARD8 ←TMEM143 KCNJ14→ SULT2B1→ ←RASIP1 PPP1R15A→ ←GYS1 ←KCNA7 ←HRC
CTC−453G23.8→ GRIN2D→ ←RPL18 ←IZUMO1 ←TULP2 RUVBL2→ ←C19orf73
CTC−241F20.3→ GRWD1→ ←AC022154.7 ←FUT1 ←NUCB1−AS1 ←CGB TRPM4→
←CTC−241F20.4 ←CTC−273B12.5 SPHK2→ ←FGF21 CTD−2639E6.4→ ←CGB7
←CCDC114 CTC−273B12.7→ ←DBP ←RNU6−317P DHDH→ CGB2→
EMP3→ CTC−273B12.6→ ←CA11 ←HSD17B14 FTL→ CGB5→
14 genes omitted
Position on chr19 (Mb)

Supplementary Figure 5. Regional association plots for 16 new psoriasis loci identified in this cohort. The y-axis represents the –log10 p-values of the meta-analysis results (left) and recombination rate (right). Build 37 (GRCh37) was used to generate these plots

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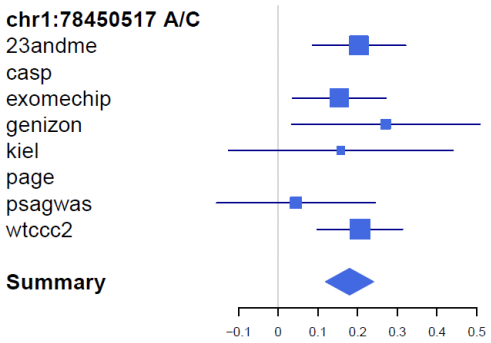
chr1:78450517 A/C
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
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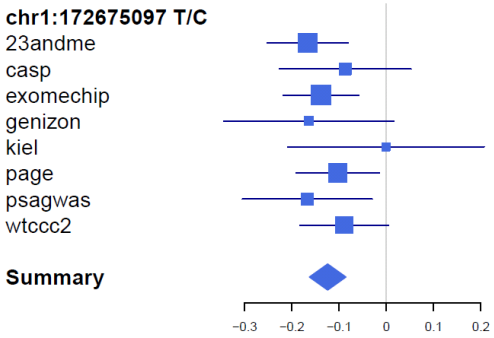
0.1
0.2
0.3
0.4
0.5


chr1:172675097 T/C
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
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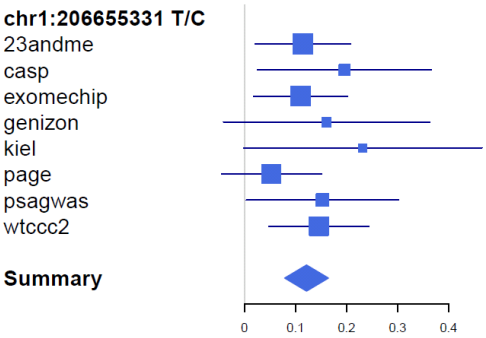
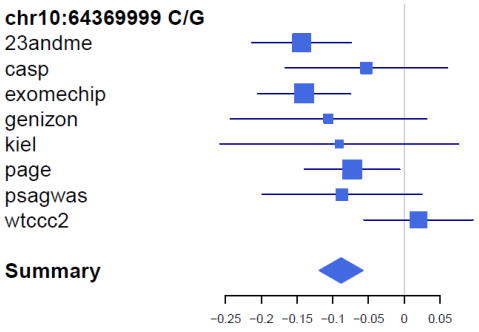
−0.2
−0.1
0
0.1
0.2


chr1:206655331 T/C
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
0
0.1
0.2
0.3
0.4


chr10:64369999 C/G
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
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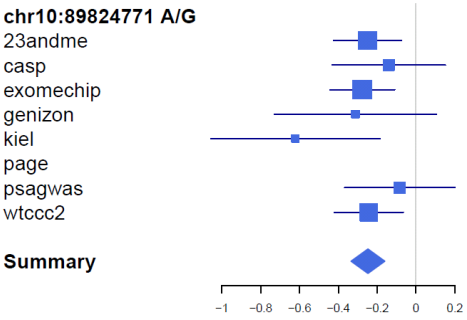
−0.2
−0.15
−0.1
−0.05
0
0.05


chr10:89824771 A/G
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
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−0.6
−0.4
−0.2
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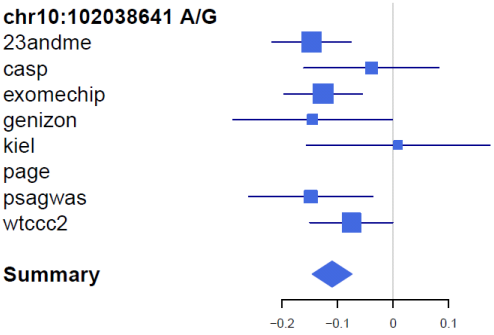
chr10:102038641 A/G
23andme
casp
exomechip
genizon
kiel
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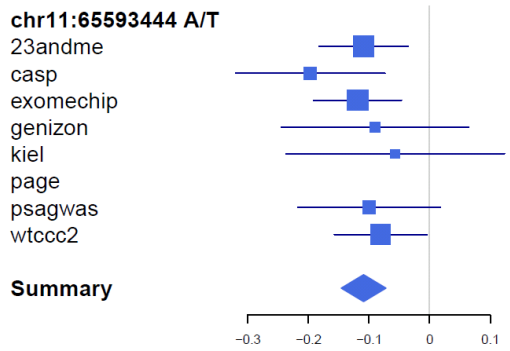
0
0.1


chr11:65593444 A/T
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
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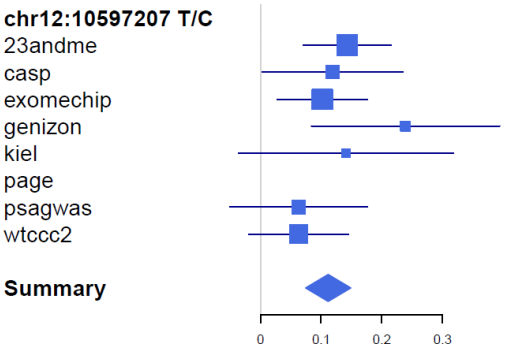
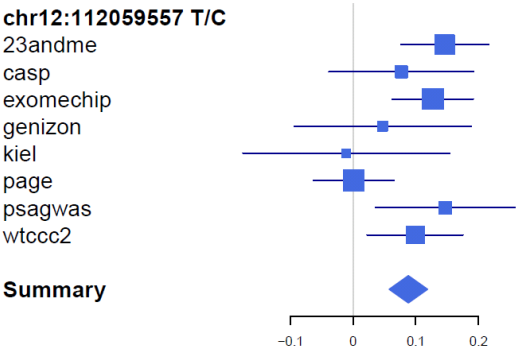
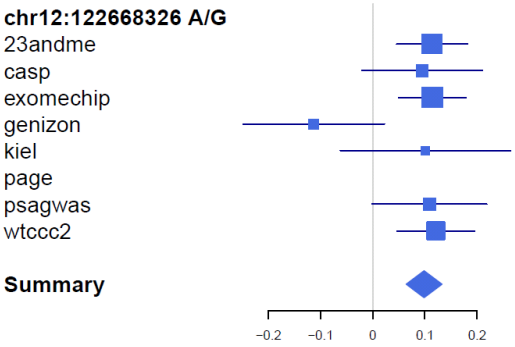
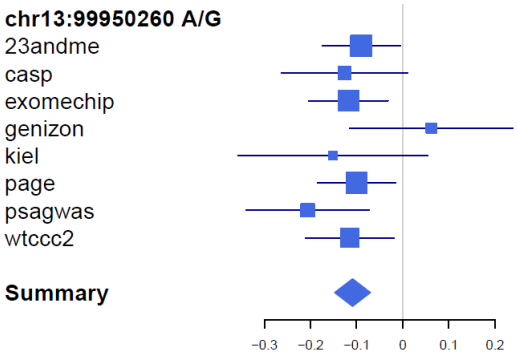
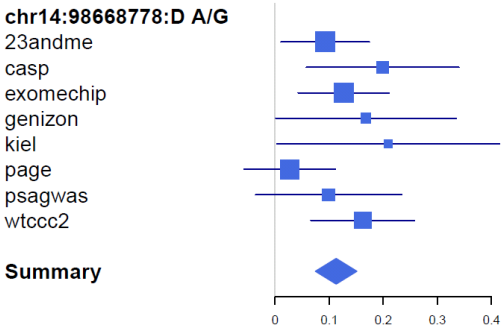
−0.2
−0.1
0
0.1

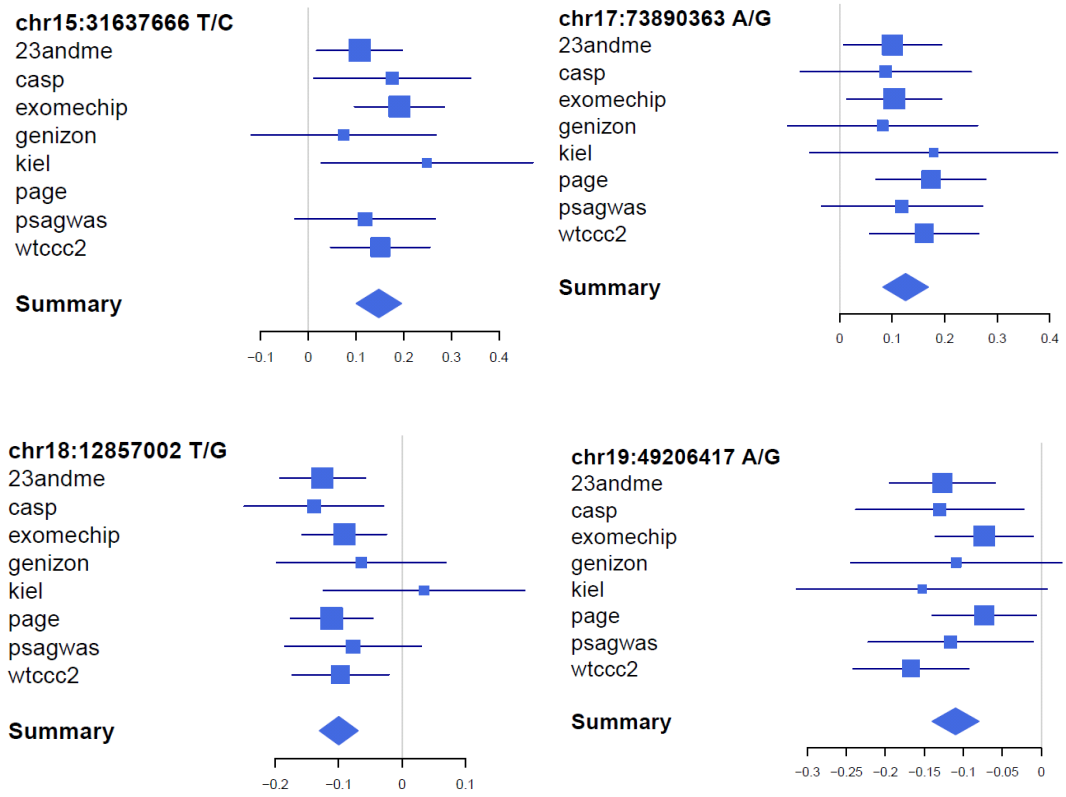

chr12:10597207 T/C
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
0
0.1
0.2
0.3


chr12:112059557 T/C
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
−0.1
0
0.1
0.2

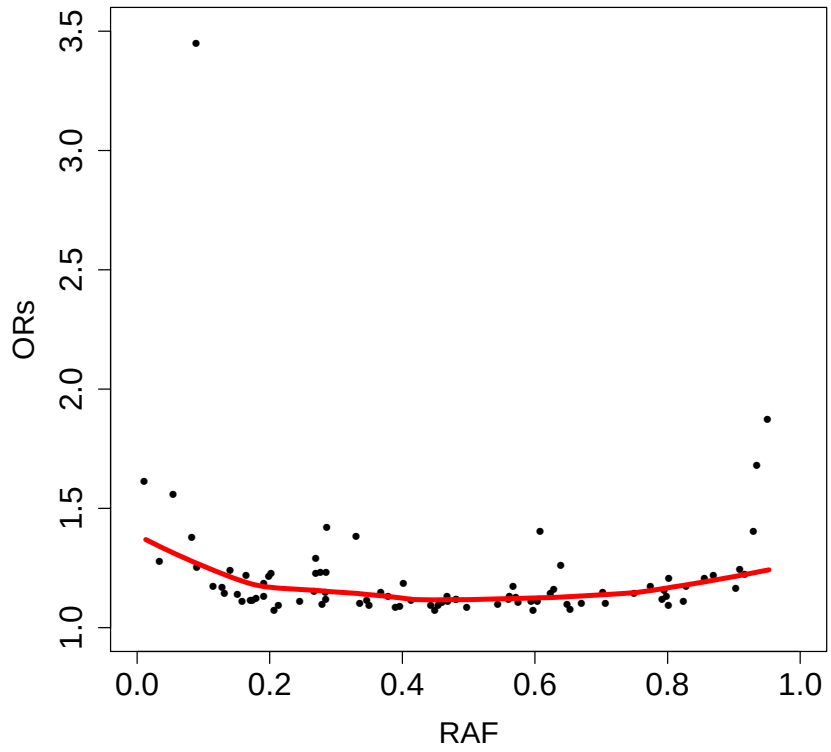

chr12:122668326 A/G
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
−0.2
−0.1
0
0.1
0.2


chr13:99950260 A/G
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
−0.3
−0.2
−0.1
0
0.1
0.2

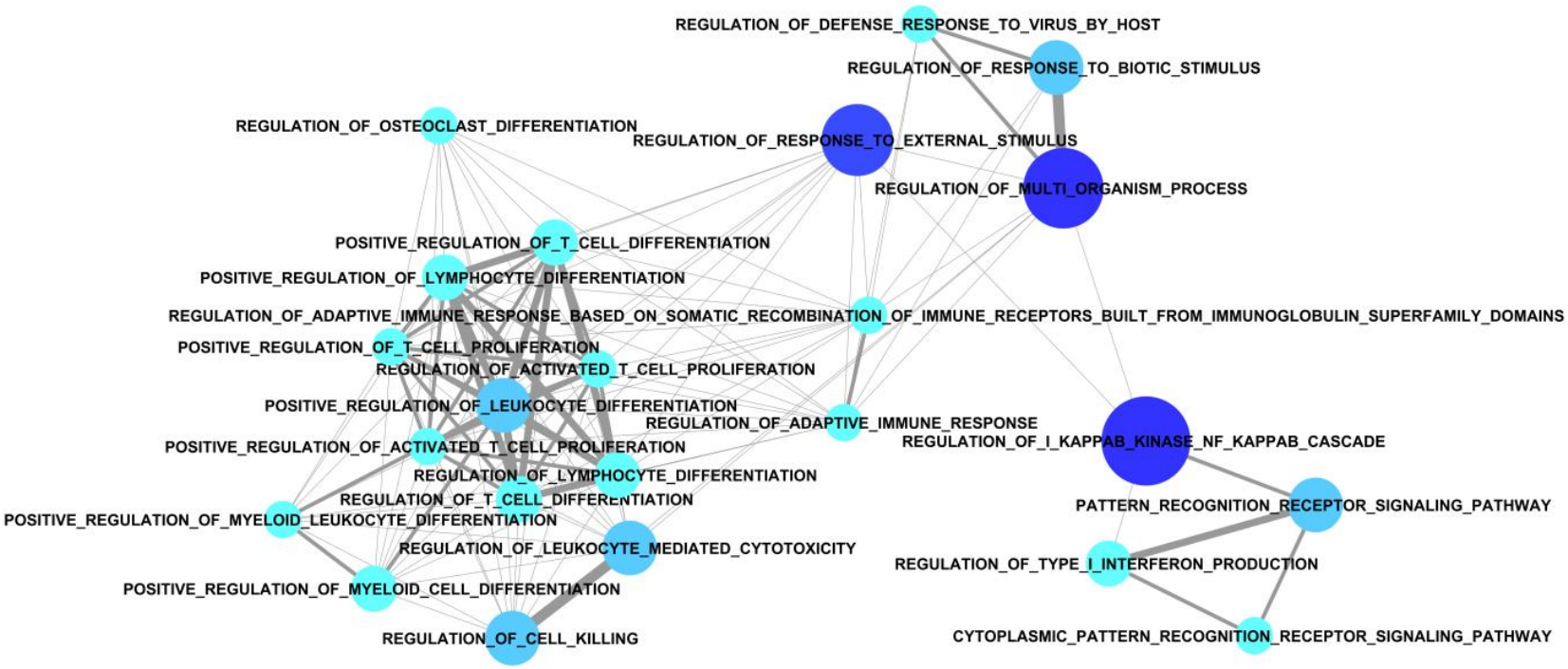

chr14:98668778:D A/G
23andme
casp
exomechip
genizon
kiel
page
psagwas
wtccc2
Summary
0
0.1
0.2
0.3
0.4



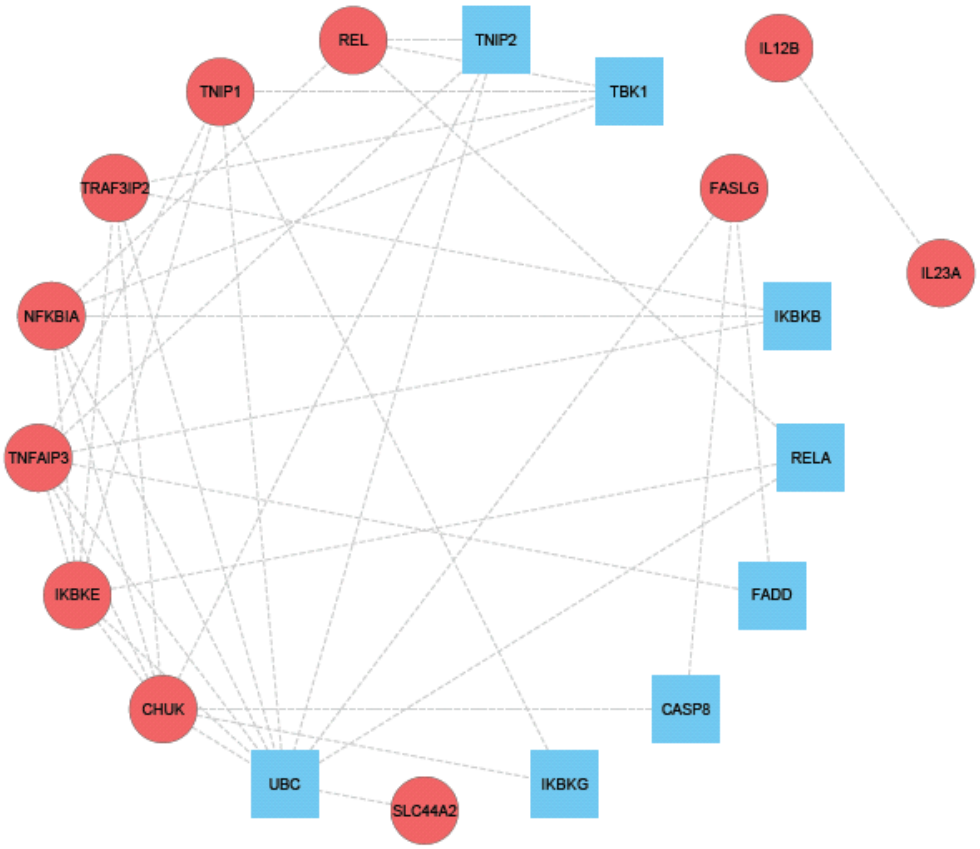
Supplementary Figure 6. Forest plots for the 16 novel loci to illustrate the betas and 95% confidence intervals for each cohort and the meta-analysis. The effect and non-effect alleles are shown after the marker positions for each locus. The x-axes denote the effect sizes.



Supplementary Figure 7. Effect sizes (odds ratios, OR) versus risk allele frequencies (RAF) for all loci.



Supplementary Figure 8. Enriched functions with genes overlapped with other enriched function. This is the reproduction of Figure 2a with node labels. Enriched functions (nodes) among the associated loci identified using MEAGA. For illustration purposes, only functions with at least four genes overlapping with other enriched functions are shown. The size of the nodes and the width of the edges correlate with the number of overlapped disease-loci and the number of shared disease-loci, respectively. Blue color represents higher number of overlapped loci and red color represents lower number of overlapped loci.



Supplementary Figure 9. Genes from the enriched function ("Regulation of I-κB kinase/NFκB cascade") which has one of the highest number of associated loci-overlapped genes. Red color represents genes from the associated loci, and blue color represents genes from the enriched function that have interactions with associated loci.

Supplementary Table

Supplementary Table 1. Datasets used in the meta-analysis. The number of cohort-defined cases/controls after quality control are listed.

Cohort	Number of defined cases after QC	Number of defined controls after QC	Effective Sample size*	Number of well-imputed markers ($r^2 \geq 0.7$)	Dataset Genomic Inflation factor
PsA GWAS	1,430	1,417	2,847	10,752,852	1.03
CASP GWAS[1]	1,352	1,389	2,741	8,748,985	1.02
Kiel GWAS[2]	464	1,135	1,317	8,920,790	1.05
Genizon GWAS[2]	761	993	1,723	9,046,475	1.02
WTCCC2 GWAS[3]	2,178	5,175	6,131	10,582,016	1.04
Exomechip w/ GWAS content	3,863	4,028	7,888	8,394,884	1.02
PAGE Immunochip[4]	3,181	7,406	8,901	757,723	1.02
23andMe GWAS	*5,803*[#]	*265,226*[#]	7,950	11,134,041	1.05
TOTAL	19,032	286,769	39,498		

[#]Estimated numbers of true cases and controls based on self-reported data and misclassification estimation (see Methods)

*The effective sample size for each cohort with dermatologist-defined cases was computed as: $4/(1/N_{case}+1/N_{control})$; the 23andMe GWAS uses self-reported information to define cases, and we determined the effective sample size using misclassification adjustment simulated data and the asymptotic relative efficiency approach (see **Methods**).

Supplementary Table 2. Summary statistics for previously identified loci. EA: effect allele; NEA: non-effect allele. Direction represents whether the EA increases (+) or decreases (-) the risk of psoriasis.

Chr	Position	EA	NEA	Beta	p-value	Direction
1	8286009	a	g	0.1208	4.26E-10	++++++++
1	24518206	t	c	-0.1512	4.82E-16	-?------
1	25291010	a	t	-0.1407	2.93E-19	--------
1	67713346	t	c	0.3904	2.46E-29	++++++++
1	69788482	t	g	-0.0682	0.0001644	-----+--
1	152591953	c	g	0.1771	1.63E-27	++++++++
1	197757846	c	g	-0.1005	3.53E-07	--------
2	61072183	a	t	0.1665	2.33E-26	++++++++
2	62560332	a	g	0.1157	2.78E-13	++++++++
2	163167746	c	g	0.3105	1.07E-24	++++++++
3	16996623	a	g	-0.1198	2.22E-14	--------
3	101647309	t	g	-0.1061	8.37E-11	--------
3	189662658	a	g	0.1394	4.95E-09	++++++?+
5	40370724	a	c	-0.1215	1.41E-05	--------
5	96118852	c	g	-0.1444	4.37E-18	--------
5	131996445	a	g	-0.196	4.91E-23	--------
5	150469973	a	g	0.4863	9.79E-59	++++++++
5	158829527	a	t	-0.5294	2.92E-84	--------
6	577820	a	g	0.091	4.60E-09	-+++++++
6	20689945	a	g	0.1676	6.40E-19	++++++++
6	30916259	a	g	1.1598	5.58e-325	++++++++
6	111929862	t	g	0.3475	1.93E-42	++++++++
6	138197824	t	c	-0.1765	1.04E-25	--------
6	159506600	t	c	-0.1109	5.82E-12	---+----
7	37385365	a	g	0.0995	1.91E-10	++++++++
9	32523737	t	c	0.0918	2.84E-09	++++++++
9	110792282	t	c	0.1004	9.15E-10	++++++++
10	75601596	t	c	-0.127	1.90E-15	--------
10	81043743	a	g	0.1062	1.72E-11	++++++++
11	64053157	t	g	0.0953	1.10E-08	++++++++
11	109962432	a	g	0.1239	9.32E-16	++++++++
11	128391937	t	c	0.1426	8.69E-15	++++++++
12	56741228	a	g	-0.3421	3.79E-25	--------
13	40745693	a	g	-0.2019	1.21E-07	------?-
13	45321731	a	c	-0.0972	1.18E-08	--------
14	35839236	c	g	0.1521	1.92E-19	++++++++
16	11354091	a	g	0.1367	9.84E-16	++++++++

16	31021078	t	c	0.1275	1.13E-15	+++-++++
17	26124908	a	g	0.2118	9.23E-23	++++++++
17	40536396	t	c	-0.1024	1.84E-10	--------
17	78175483	t	c	0.1015	1.27E-08	++++++?+
18	51816394	t	c	0.1214	1.04E-12	++++++++
19	10463118	c	g	-0.6762	3.39E-43	-?-?----
19	10886206	t	g	-0.0994	2.00E-10	--------
20	48574454	a	g	-0.1462	6.52E-21	--------
21	36488822	t	c	-0.1181	6.10E-08	---+----
22	21974703	c	g	0.1377	6.81E-13	++++++++

Supplementary Table 3. Detailed information regarding the new loci identified in this study. The "Meta p without 23andMe" column shows the p-values of the meta-analysis including all but the 23andMe dataset. The "Meta P value (wo/adj)" and "Meta P value (w/adj)" illustrate the meta-analysis results without and with the Duffy's adjustment, respectively. The "Direction" column indicates the direction of the meta-analysis-identified risk allele in each dataset (P: PsA GWAS; C: CASP GWAS; K: Kiel GWAS; G: Genizon GWAS; W: WTCCC2; E: Exomechip; I: PAGE Immunochip; M: 23andMe GWAS).

Chr	Pos	Marker	Meta p without 23andMe	Meta P value (wo/adj)	Meta OR (wo/adj)	Meta P value (w/adj)	Heterogeneity p-value (w/adj)	OR(w/adj)	Direction (PCKGWEIM)	Nearby genes
1	78450517	rs34517439	1.19E-06	4.95E-08	1.10	4.43E-09	0.72	1.18	+?++++?+	*FUBP1*
1	172675097	rs12118303	2.07E-07	7.17E-10	1.08	3.02E-10	0.8	1.12	++++++++	*FASLG*
1	206655331	rs41298997	4.01E-07	1.09E-06	1.07	2.37E-08	0.78	1.13	++++++++	*IKBKE*
10	64369999	rs2944542	1.35E-05	3.27E-09	1.06	1.76E-08	7.8E-02	1.08	++++-+++	*ZNF365*
10	89824771	rs76959677	1.37E-06	7.49E-07	1.14	2.75E-08	0.59	1.28	++++++?+	*PTEN, KLLN, SNORD74*
10	102038641	rs61871342	2.63E-06	1.93E-09	1.07	1.56E-09	0.44	1.10	++-+++?+	*CHUK*
11	65593444	rs118086960	4.65E-07	2.63E-07	1.06	6.89E-09	0.82	1.12	++++++?+	*CFL1, FIBP, FOSL1*
12	10597207	rs11053802	4.01E-06	9.09E-09	1.07	4.17E-09	0.49	1.11	++++++?+	*KLRK1, KLRC4*
12	112059557	rs11065979	1.38E-05	2.41E-09	1.06	1.67E-08	6.09E-02	1.08	++-+++++	*BRAP, MAPKAPK5*
12	122668326	rs11059675	2.77E-06	1.23E-07	1.06	1.50E-08	0.13	1.10	+++-++?+	*IL31*
13	99950260	rs9513593	2.75E-07	3.12E-06	1.06	3.60E-08	0.29	1.12	+++-++++	*UBAC2, RN7SKP9*
14	98668778	rs142903734	7.08E-08	1.08E-06	1.06	7.15E-09	0.34	1.12	++++++++	*RP11-61O1.1*
15	31637666	rs28624578	4.15E-08	8.00E-07	1.07	9.22E-10	0.80	1.18	++++++?+	*KLF13*
17	73890363	rs55823223	8.39E-08	1.61E-06	1.07	1.06E-08	0.94	1.15	++++++++	*TRIM47, TRIM65*
18	12857002	rs559406	5.72E-08	7.05E-10	1.06	1.19E-10	0.75	1.10	++-+++++	*PTPN2*
19	49206417	rs492602	4.24E-10	2.23E-11	1.07	6.57E-13	0.62	1.11	++++++++	*FUT2*

Supplementary Table 4. Information for the independent signals used to construct Figure 1 and used for the regulatory element enrichment analysis. RA: risk allele; NRA: non-risk allele.

	RA	NRA	OR	MAF
chr1:8273177	G	T	1.15	0.29
chr1:24518643	G	A	1.21	0.14
chr1:25297184	A	G	1.14	0.47
chr1:67702526	T	G	1.68	0.06
chr1:67705574	T	C	1.12	0.40
chr1:67619259	G	T	1.11	0.34
chr1:69788482	G	T	1.12	0.25
chr1:152593549	T	C	1.26	0.36
chr2:61083506	T	C	1.17	0.37
chr2:62552321	A	G	1.14	0.38
chr2:163110536	G	A	1.41	0.39
chr2:163128824	T	C	1.30	0.27
chr3:16996035	G	A	1.12	0.48
chr3:101663555	A	G	1.14	0.20
chr5:40370724	C	A	1.17	0.09
chr5:96120170	G	A	1.24	0.29
chr5:96290647	T	C	1.09	0.39
chr5:131996669	C	T	1.16	0.20
chr5:150466690:D	G	A	1.56	0.06
chr5:158826310	G	C	1.22	0.20
chr5:158748012	C	T	1.21	0.19
chr5:158829527	T	A	1.26	0.09
chr5:158812417	C	T	1.15	0.29
chr5:158871681	T	A	1.23	0.08
chr5:158839745	T	C	1.10	0.35
chr6:515393	C	T	1.12	0.42
chr6:31251924	T	C	3.45	0.09
chr6:31353651:I	C	A	1.39	0.33
chr6:29803526	T	G	1.43	0.29
chr6:31249217	A	G	1.23	0.20
chr6:31431820	C	T	1.12	0.17
chr6:31457362	C	A	1.19	0.20
chr6:29555585	A	G	1.15	0.25
chr6:32392757	A	G	1.62	0.01
chr6:31264823	A	G	1.22	0.17
chr6:29923554	T	C	1.19	0.40
chr6:31553151:D	A	G	1.23	0.13

chr6:111929862	T	G	1.38	0.09
fachr6:111580561	C	A	1.10	0.28
chr6:138197824	C	T	1.23	0.27
chr6:159492044	T	C	1.18	0.13
chr7:37386237	A	C	1.13	0.44
chr9:32523737	T	C	1.11	0.40
chr9:110792282	T	C	1.15	0.37
chr10:75599127	A	G	1.12	0.44
chr10:81032532	A	G	1.11	0.42
chr11:64115137	C	T	1.12	0.39
chr11:109973130	C	A	1.18	0.43
chr11:128406438	A	G	1.12	0.48
chr12:56744422	G	A	1.41	0.07
chr12:56497903	T	C	1.10	0.35
chr14:35839236	C	G	1.24	0.28
chr14:35840257	C	T	1.16	0.27
chr16:11365500	C	T	1.11	0.29
chr16:31006972	T	C	1.16	0.37
chr17:26124908	A	G	1.24	0.14
chr17:26096473	A	C	1.12	0.35
chr17:40563017	A	G	1.14	0.15
chr17:78178830	A	G	1.09	0.50
chr18:51791375	C	G	1.12	0.29
chr19:10463118	G	C	1.88	0.05
chr19:10469975	A	C	1.25	0.09
chr19:10886206	G	T	1.14	0.44
chr20:48582769	A	C	1.13	0.43
chr20:48642702	T	C	1.12	0.16
chr22:21925017	G	A	1.14	0.19
chr1:197671115	T	C	1.10	0.22
chr3:189615475	C	A	1.10	0.20
chr6:20678430	C	G	1.18	0.22
chr13:40333369	T	C	1.08	0.34
chr13:45334194	C	T	1.09	0.40
chr21:36470865	T	C	1.08	0.21
chr1:78450517	A	C	1.18	0.12
chr1:172675097	C	T	1.12	0.17
chr1:206655331	T	C	1.13	0.18
chr10:64369999	G	C	1.08	0.40
chr10:89824771	G	A	1.28	0.04
chr10:102038641	G	A	1.10	0.45

chr11:65593444	T	A	1.12	0.47
chr12:10597207	T	C	1.11	0.33
chr12:112059557	T	C	1.08	0.45
chr12:122668326	A	G	1.10	0.46
chr13:99950260	G	A	1.12	0.18
chr14:98668778:D	A	G	1.12	0.21
chr15:31637666	T	C	1.18	0.17
chr17:73890363	A	G	1.15	0.13
chr18:12857002	G	T	1.10	0.45
chr19:49206417	G	A	1.11	0.46

Supplementary Table 5. Heritability explained (%) by known loci using GCTA. Heritability explained by psoriasis loci determined by (the phenotypic variance explained by psoriasis loci) / (phenotypic variance explained by genotyped markers in the corresponding cohort).

Psoriasis Prevalence	Cohort		
	PAGE	Exomechip (full)	WTCCC2
2%	13/24.7 = 52.6	11/46.4 = 23.7	16.3/74.2 = 22
2.5%	13.8/26.2 = 52.7	11.7/49.2 = 23.8	17.3/78.7 = 22
3%	14.5/27.6 = 52.5	12.3/51.8 = 23.7	18.2/82.8 = 22

Supplementary Table 6. Enriched functions identified by MEAGA.

Enriched Functions	# genes in functions	# of overlapped genes	# of connected graph	pval	False Discovery Rate	Genes
POSITIVE_REGULATION_OF_CELL_FATE_COMMITMENT	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_T_HELPER_1_TYPE_IMMUNE_RESPONSE	20	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
NEGATIVE_REGULATORS_OF_RIG_I_MDA5_SIGNALING	22	4	1	≤2.00E-05	≤2.08E-02	DDX58;IFIH1;TNFAIP3;IKBKE
REGULATION_OF_TYPE_I_INTERFERON_PRODUCTION	70	6	1	≤2.00E-05	≤2.08E-02	CHUK;DDX58;IFIH1;IKBKE;NFKBIA;TNFAIP3
POSITIVE_REGULATION_OF_NATURAL_KILLER_CELL_ACTIVATION	18	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;STAT5A
REGULATION_OF_NK_T_CELL_ACTIVATION	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_MYELOID_CELL_DIFFERENTIATION	63	6	3	≤2.00E-05	≤2.08E-02	ETS1;IL12B;IL23A;IL23R;RUNX1;STAT5A
POSITIVE_REGULATION_OF_T_HELPER_1_TYPE_IMMUNE_RESPONSE	9	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_ACTIVATION_OF_JANUS_KINASE_ACTIVITY	7	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_OSTEOCLAST_DIFFERENTIATION	15	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_ACTIVATION_OF_JANUS_KINASE_ACTIVITY	7	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_LEUKOCYTE_MEDIATED_CYTOTOXICITY	33	7	4	≤2.00E-05	≤2.08E-02	ICAM1;IL12B;IL23A;IL23R;KLRK1;NOS2;STAT5A
REGULATION_OF_ACTIVATION_OF_JAK2_KINASE_ACTIVITY	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_CELL_FATE_COMMITMENT	25	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT5_PROTEIN	18	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_INTERLEUKIN_17_PRODUCTION	11	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_T_HELPER_17_TYPE_IMMUNE_RESPONSE	7	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_T_HELPER_17_TYPE_IMMUNE_RESPONSE	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_MEMORY_T_CELL_DIFFERENTIATION	7	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_INTERLEUKIN_10_PRODUCTION	29	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_GRANULOCYTE_MACROPHAGE_COLONY_STIMULATING_FACTOR_PRODUCTION	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_MEMORY_T_CELL_DIFFERENTIATION	5	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R

REGULATION_OF_INTERLEUKIN_17_PRODUCTION	18	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_DEFENSE_RESPONSE_TO_VIRUS_BY_HOST	23	5	3	≤2.00E-05	≤2.08E-02	DDX58;IL12B;IL23A;IL23R;TNFAIP3
POSITIVE_REGULATION_OF_ACTIVATED_T_CELL_PROLIFERATION	18	5	3	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4;STAT5A
POSITIVE_REGULATION_OF_ACTIVATION_OF_JAK2_KINASE_ACTIVITY	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
NEGATIVE_REGULATION_OF_INTERLEUKIN_10_PRODUCTION	7	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_NK_T_CELL_ACTIVATION	5	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
CYTOPLASMIC_PATTERN_RECOGNITION_RECEPTOR_SIGNALING_PATHWAY	31	5	1	≤2.00E-05	≤2.08E-02	CHUK;DDX58;IFIH1;NFKBIA;TNFAIP3
REGULATION_OF_CELL_KILLING	36	7	4	≤2.00E-05	≤2.08E-02	ICAM1;IL12B;IL23A;IL23R;KLRK1;NOS2;STAT5A
POSITIVE_REGULATION_OF_ALPHA_BETA_T_CELL_ACTIVATION	44	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
CYTOSOLIC_DNA_SENSING_PATHWAY	56	4	1	≤2.00E-05	≤2.08E-02	CHUK;DDX58;NFKBIA;IKBKE
REGULATION_OF_MULTI_ORGANISM_PROCESS	216	10	2	≤2.00E-05	≤2.08E-02	DDX58;ELMO1;FYN;IL12B;IL23A;IL23R;ILF3;NOS2;TNFAIP3;TNIP1
REGULATION_OF_NATURAL_KILLER_CELL_ACTIVATION	24	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;STAT5A
TRAF3_DEPENDENT_IRF_ACTIVATION_PATHWAY	12	3	1	≤2.00E-05	≤2.08E-02	DDX58;IFIH1;IKBKE
PATTERN_RECOGNITION_RECEPTOR_SIGNALING_PATHWAY	132	7	1	≤2.00E-05	≤2.08E-02	CHUK;DDX58;IFIH1;IKBKE;NFKBIA;TNFAIP3;TNIP1
DEFENSE_RESPONSE_TO_GRAM_NEGATIVE_BACTERIUM	18	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;NOS2
POSITIVE_REGULATION_OF_NATURAL_KILLER_CELL_PROLIFERATION	6	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_ACTIVATED_T_CELL_PROLIFERATION	25	5	3	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4;STAT5A
POSITIVE_REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT5_PROTEIN	16	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4
REGULATION_OF_GRANULOCYTE_MACROPHAGE_COLONY_STIMULATING_FACTOR_PRODUCTION	10	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_T_HELPER_17_CELL_DIFFERENTIATION	5	4	2	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT3_PROTEIN	27	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT1_PROTEIN	12	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
REGULATION_OF_NATURAL_KILLER_CELL_PROLIFERATION	7	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_INTERLEUKIN_12_PRODUCTION	24	3	1	≤2.00E-05	≤2.08E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_DEFENSE_RESPONSE_TO_VIRUS_BY_HOST	15	4	2	≤2.00E-05	≤2.08E-02	DDX58;IL12B;IL23A;IL23R

REGULATION_OF_RESPONSE_TO_BIOTIC_STIMULUS	87	7	2	4.00E-05	3.19E-02	DDX58;ELMO1;FYN;IL12B;IL23A;IL23R;TNFAIP3
TRAF6_MEDIATED_IRF7_ACTIVATION	25	3	1	4.00E-05	3.19E-02	DDX58;IFIH1;IKBKE
REGULATION_OF_TYROSINE_PHOSPHORYLATION_OF_STAT3_PROTEIN	32	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;SOCS1
REGULATION_OF_ALPHA_BETA_T_CELL_DIFFERENTIATION	41	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_LYMPHOCYTE_DIFFERENTIATION	65	6	3	4.00E-05	3.19E-02	BAD;IL12B;IL23A;IL23R;IL4;STAT5A
REGULATION_OF_T_HELPER_CELL_DIFFERENTIATION	22	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;IL4
REGULATION_OF_RESPONSE_TO_EXTERNAL_STIMULUS	387	9	2	4.00E-05	3.19E-02	IL12B;IL23A;IL4;PLAU;PSMA6;PTEN;STAT5A;TNFAIP3;TNIP1
REGULATION_OF_ALPHA_BETA_T_CELL_ACTIVATION	60	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;IL4
POSITIVE_REGULATION_OF_INTERLEUKIN_10_PRODUCTION	16	3	2	4.00E-05	3.19E-02	IL12B;IL23A;IL4
REGULATION_OF_CD4_POSITIVE__ALPHA_BETA_T_CELL_DIFFERENTIATION	28	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;IL4
REGULATION_OF_CD4_POSITIVE__ALPHA_BETA_T_CELL_ACTIVATION	30	4	2	4.00E-05	3.19E-02	IL12B;IL23A;IL23R;IL4
REGULATION_OF_T_CELL_DIFFERENTIATION	82	6	3	6.00E-05	4.53E-02	BAD;IL12B;IL23A;IL23R;IL4;STAT5A
POSITIVE_REGULATION_OF_T_CELL_DIFFERENTIATION	54	6	4	6.00E-05	4.53E-02	BAD;IL12B;IL23A;IL23R;IL4;STAT5A
HAIR_FOLLICLE_MORPHOGENESIS	27	4	2	6.00E-05	4.53E-02	RUNX1;RUNX3;SNAI1;TP63
REGULATION_OF_OSTEOCLAST_DIFFERENTIATION	41	5	3	6.00E-05	4.53E-02	ESRRA;IL12B;IL23A;IL23R;IL4
REGULATION_OF_I_KAPPAB_KINASE_NF_KAPPAB_CASCADE	194	11	2	6.00E-05	4.53E-02	CHUK;FASLG;IKBKE;IL12B;IL23A;NFKBIA;REL;SLC44A2;TNFAIP3;TNIP1;TRAF3IP2
REGULATION_OF_TRANSCRIPTION_FACTOR_IMPORT_INTO_NUCLEUS	67	4	2	8.00E-05	5.52E-02	DDX58;IL12B;IL23A;NFKBIA
NEGATIVE_REGULATION_OF_TYPE_I_INTERFERON_PRODUCTION	34	4	1	8.00E-05	5.52E-02	DDX58;IFIH1;IKBKE;TNFAIP3
POSITIVE_REGULATION_OF_LEUKOCYTE_DIFFERENTIATION	97	7	3	8.00E-05	5.52E-02	BAD;IL12B;IL23A;IL23R;IL4;RUNX1;STAT5A
POSITIVE_REGULATION_OF_T_CELL_PROLIFERATION	69	5	3	8.00E-05	5.52E-02	IL12B;IL23A;IL23R;IL4;STAT5A
POSITIVE_REGULATION_OF_MYELOID_LEUKOCYTE_DIFFERENTIATION	37	5	3	8.00E-05	5.52E-02	IL12B;IL23A;IL23R;RUNX1;STAT5A
REGULATION_OF_INTERLEUKIN_12_PRODUCTION	44	4	2	8.00E-05	5.52E-02	IL12B;IL23A;IL23R;REL
HAIR_CYCLE_PROCESS	74	4	1	1.00E-04	6.69E-02	RUNX1;RUNX3;SNAI1;TP63
MOLTING_CYCLE	77	4	1	1.00E-04	6.69E-02	RUNX1;RUNX3;SNAI1;TP63
HAIR_FOLLICLE_DEVELOPMENT	74	4	1	1.00E-04	6.69E-02	RUNX1;RUNX3;SNAI1;TP63
MOLTING_CYCLE_PROCESS	74	4	1	1.00E-04	6.69E-02	RUNX1;RUNX3;SNAI1;TP63

HAIR_CYCLE	77	4	1	1.00E-04	6.69E-02	RUNX1;RUNX3;SNAI1;TP63
POSITIVE_REGULATION_OF_TISSUE_REMODELING	21	2	1	1.20E-04	7.70E-02	IL12B;IL23A
REGULATION_OF_T_CELL_MEDIATED_IMMUNITY	35	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_ADAPTIVE_IMMUNE_RESPONSE_BASED_ON_SOMATIC_RECOMBINATION_OF_IMMUNE_RECEPTORS_BUILT_FROM_IMMUNOGLOBULIN_SUPERFAMILY_DOMAINS	45	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
POSITIVE_REGULATION_OF_T_CELL_MEDIATED_CYTOTOXICITY	14	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
REGULATION_OF_T_CELL_MEDIATED_CYTOTOXICITY	17	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
REGULATION_OF_LYMPHOCYTE_DIFFERENTIATION	107	6	3	1.40E-04	8.62E-02	BAD;IL12B;IL23A;IL23R;IL4;STAT5A
POSITIVE_REGULATION_OF_ADAPTIVE_IMMUNE_RESPONSE	48	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
CHRONIC_MYELOID_LEUKEMIA	73	5	1	1.40E-04	8.62E-02	CHUK;NFKBIA;BAD;STAT5A;RUNX1
POSITIVE_REGULATION_OF_T_CELL_MEDIATED_IMMUNITY	26	3	1	1.40E-04	8.62E-02	IL12B;IL23A;IL23R
ACTIVATION_OF_NF_KAPPAB_IN_B_CELLS	18	3	1	1.60E-04	9.49E-02	CHUK;NFKBIA;REL
REGULATION_OF_ADAPTIVE_IMMUNE_RESPONSE	92	5	2	1.60E-04	9.49E-02	IL12B;IL23A;IL23R;IL4;TNFAIP3
RIG_I_MDA5_MEDIATED_INDUCTION_OF_IFN_ALPHA_BETA_PATHWAYS	44	4	1	1.60E-04	9.49E-02	DDX58;IFIH1;TNFAIP3;IKBKE
REGULATION_OF_ADAPTIVE_IMMUNE_RESPONSE_BASED_ON_SOMATIC_RECOMBINATION_OF_IMMUNE_RECEPTORS_BUILT_FROM_IMMUNOGLOBULIN_SUPERFAMILY_DOMAINS	84	5	2	1.60E-04	9.49E-02	IL12B;IL23A;IL23R;IL4;TNFAIP3

Supplementary Table 7. Enrichment results for regulatory regions among the independent psoriasis signals in different cell types.

Cell types	Enrichment p	Obs	Exp	Obs/Exp
Th1	2.23E-22	52	18.74	2.78
Th0	1.82E-20	52	19.74	2.63
CD25-_IL17+_Th17_stim	1.32E-17	48	19.09	2.51
CD45RA_CD8	1.66E-16	43	16.72	2.57
CD25-_IL17-_Th_stim_MACS	1.89E-16	49	20.57	2.38
CD45RO_CD8	5.72E-16	50	21.64	2.31
GM12878	2.27E-15	50	21.84	2.29
CD25-_CD45RO+_mem	5.23E-15	44	18.19	2.42
CD25+_CD127-_Treg	1.07E-13	44	19.09	2.30
Th2	2.39E-13	44	19.04	2.31
CD25-_CD45RA+_naive	1.08E-12	43	19.21	2.24
adult_CD14	7.70E-12	49	23.88	2.05
adult_CD20	4.95E-11	41	18.96	2.16
B_Cell_Centroblast	1.59E-09	40	19.36	2.07
Mobilized_CD34	3.63E-08	38	19.74	1.92
colonic_mucosa	1.98E-07	45	25.42	1.77
Duodenum_mucosa	1.12E-06	43	24.96	1.72
chondrogenic_dif_cells	1.50E-06	46	27.60	1.67
K562	1.78E-06	36	19.97	1.80
anterior_caudate	2.58E-06	46	27.97	1.64
HSMM-myotube	1.48E-05	46	29.10	1.58
kidney	1.55E-05	41	25.06	1.64
Pancreatic_Islets	4.51E-05	40	25.25	1.58
substantia_nigra	5.08E-05	39	24.39	1.60
hippocampus_middle	5.18E-05	42	26.82	1.57
NH-Osteoblast	6.92E-05	42	27.11	1.55
Liver1	9.07E-05	40	25.77	1.55
mid_frontal_lobe	4.47E-04	40	26.94	1.48
AdiposeNuclei	4.84E-04	40	27.07	1.48
inferior_temporal_lobe	9.85E-04	39	26.87	1.45
cingulate_gyrus	2.72E-03	37	26.27	1.41
angular_gyrus	4.38E-03	37	26.74	1.38
HepG2	1.12E-02	29	20.99	1.38

Supplementary Table 8. Number of markers in strong LD ($r^2 \geq 0.8$) with the most significant marker of each novel locus that overlap with enhancers in different cell/tissue types.

Novel loci (GRCh37)	Nearby genes	Th17	CD8+ (naive)	Th0	Th2
chr1:78450517	*FUBP1*	1	0	0	0
chr1:172675097	*FASLG*	4	0	1	1
chr1:206655331	*IKBKE*	0	0	0	0
chr10:64369999	*ZNF365*	1	0	1	0
chr10:89824771	*PTEN, KLLN, SNORD74*	1	1	0	0
chr10:102038641	*CHUK*	2	2	1	1
chr11:65593444	*CFL1, FIBP, FOSL1*	0	0	0	0
chr12:10597207	*KLRK1, KLRC4*	0	7	0	0
chr12:112059557	*BRAP, MAPKAPK5*	2	0	2	2
chr12:122668326	*IL31*	0	0	1	7
chr13:99950260	*UBAC2, RN7SKP9*	19	17	14	18
chr14:98668778:D	*RP11-61O1.1*	6	5	7	7
chr15:31637666	*KLF13*	4	4	4	4
chr17:73890363	*TRIM47, TRIM65*	11	7	10	6
chr18:12857002	*PTPN2*	0	0	1	1
chr19:49206417	*FUT2*	0	0	0	0

Novel loci (GRCh37)	Nearby genes	HSMM	Inferior temporal lobe	K562	Kidney	Liver	Mid-frontal lobe	NH osteoblast	Pancreatic Islets	Substantia nigra
chr1:78450517	*FUBP1*	1	1	0	1	0	0	1	1	0
chr1:172675097	*FASLG*	0	0	0	0	0	0	0	0	0
chr1:206655331	*IKBKE*	0	0	0	0	0	0	0	0	0
chr10:64369999	*ZNF365*	3	0	0	0	0	0	2	1	1
chr10:89824771	*PTEN, KLLN, SNORD74*	0	1	0	1	1	1	0	1	1
chr10:102038641	*CHUK*	2	1	1	2	1	1	1	4	1
chr11:65593444	*CFL1, FIBP, FOSL1*	0	0	0	0	0	0	0	0	0
chr12:10597207	*KLRK1, KLRC4*	0	3	0	0	0	0	0	0	0
chr12:112059557	*BRAP, MAPKAPK5*	3	5	5	4	3	5	4	7	5
chr12:122668326	*IL31*	3	0	0	0	0	0	3	0	1
chr13:99950260	*UBAC2, RN7SKP9*	5	2	5	8	11	4	9	7	7
chr14:98668778:D	*RP11-61O1.1*	0	0	0	0	0	0	0	0	0
chr15:31637666	*KLF13*	2	4	1	4	4	4	0	4	4
chr17:73890363	*TRIM47, TRIM65*	6	11	5	9	9	11	6	11	11
chr18:12857002	*PTPN2*	0	0	0	0	0	0	0	0	0
chr19:49206417	*FUT2*	0	0	0	0	0	0	0	0	0

Novel loci (GRCh37)	Nearby genes	Adipose	Angular gyrus	Anterior caudate	Chondrogenic diff	Cingulate gyrus	Colonic mucosa	Duodenum mucosa	HepG2	Hippocampus middle
chr1:78450517	*FUBP1*	0	0	1	1	1	0	0	1	1
chr1:172675097	*FASLG*	0	0	0	0	0	0	0	0	0
chr1:206655331	*IKBKE*	0	0	0	0	0	0	0	0	0
chr10:64369999	*ZNF365*	0	0	0	0	0	0	0	0	1
chr10:89824771	*PTEN, KLLN, SNORD74*	1	1	1	0	1	1	1	0	1
chr10:102038641	*CHUK*	3	1	1	1	1	2	1	2	1
chr11:65593444	*CFL1, FIBP, FOSL1*	0	0	0	0	0	0	0	0	0
chr12:10597207	*KLRK1, KLRC4*	0	0	3	5	0	0	0	1	0
chr12:112059557	*BRAP, MAPKAPK5*	3	5	6	3	5	4	2	1	4
chr12:122668326	*IL31*	0	0	0	3	0	0	0	0	1
chr13:99950260	*UBAC2, RN7SKP9*	9	2	9	3	6	13	10	2	10
chr14:98668778:D	*RP11-61O1.1*	0	0	1	0	0	0	0	0	0
chr15:31637666	*KLF13*	4	4	4	0	4	4	4	0	4
chr17:73890363	*TRIM47, TRIM65*	10	11	11	10	11	10	9	10	12
chr18:12857002	*PTPN2*	0	0	1	0	0	0	0	0	0
chr19:49206417	*FUT2*	0	0	0	0	0	0	0	0	0

Supplementary Table 9. Drugs targeting genes from the susceptibility loci

Locus	Gene Target	DrugBank	PharmGKB
Novel Loci			
chr1:78450517	*FUBP1*	MGI-114	NA
chr10:89824771	*PTEN*	NA	carboplatin; cisplatin
chr10:102038641	*CHUK*	Aminosalicylic Acid; Mesalazine; Acetylcysteine; Sulfasalazine	NA
chr11:65593444	*CFL1*	Lauryl Dimethylamine-N-Oxide	NA
chr17:73890363	*ACOX1*	(3R)-3-HYDROXYDODECANOIC ACID; Flavin adenine dinucleotide	NA
chr19:49206417	*BCAT2*	Pyridoxal Phosphate; N-[O-Phosphono-Pyridoxyl]-Isoleucine; Pyridoxamine-5'-Phosphate; Alpha-ketoisovalerate; L-Leucine; L-Glutamic Acid; L-Isoleucine	NA
chr19:49206417	*CA11*	Zonisamide	NA
known loci			
chr1:67726104	*IL23R*	NA	celecoxib
chr2:163260691	*KCNH7*	Terazosin; Ibutilide; Miconazole; Doxazosin; Prazosin	NA
chr2:163260691	*GCA*	Guanosine-5'-Diphosphate	NA
chr5:96119273	*CAST*	Calcium	NA
chr5:131996445	*IL4*	NA	aspirin
chr5:150467189	*GPX3*	Glutathione	NA
chr5:158829527	*IL12B*	5-Mercapto-2-Nitro-Benzoic Acid; CNTO 1275; ABT-874; humanized SMART Anti-IL-12 Antibody	NA
chr6:31266090	*HLA-C*	NA	ustekinumab; lamotrigine; methazolamide; phenytoin
chr6:31266090	*HLA-B*	N-Formylmethionine	trichloroethylene; interferons; flucloxacillin; acetazolamide; clozapine; dapsone; methazolamide; ribavirin
chr6:111913262	*FYN*	Dasatinib; 1-Methoxy-2-[2-(2-Methoxy-Ethoxy]-Ethane	NA
chr6:138197824	*TNFAIP3*	NA	methotrexate
chr9:32523737	*NDUFB6*	NADH	NA
chr10:75599127	*CAMK2G*	1-tert-butyl-3-(3-methylbenzyl)-1H-pyrazolo[3,4-d]pyrimidin-4-amine; Bosutinib	NA

chr10:75599127	*PLAU*	6-[(Z)-Amino(Imino)Methyl]-N-[4-(Aminomethyl)Phenyl]-4-(Pyrimidin-2-Ylamino)-2-Naphthamide; 6-[N-(1-Isopropyl-3,4-Dihydro-7-Isoquinolinyl)Carbamyl]-2-Naphthalenecarboxamidine; 6-[N-(4-(Aminomethyl)Phenyl)Carbamyl]-2-Naphthalenecarboxamidine; Trans-6-(2-Phenylcyclopropyl)-Naphthalene-2-Carboxamidine; 6-[N-(1-Isopropyl-1,2,3,4-Tetrahydro-7-Isoquinolinyl)Carbamyl]-2-Naphthalenecarboxamidine; 6-Chloro-2-(2-Hydroxy-Biphenyl-3-Yl)-1h-Indole-5-Carboxamidine; 1-[4-(2-oxo-2-phenylethyl)phenyl]guanidine; (2R)-1-(2,6-dimethylphenoxy)propan-2-amine; 6-[N-(4-Ethyl-1,2,3,4-Tetrahydro-6-Isoquinolinyl)Carbamyl]-2-Naphthalenecarboxamidine; CRA_8696; 8-(Pyrimidin-2-Ylamino)Naphthalene-2-Carboximidamide; Plasmin; 4-(2-aminoethoxy)-N-(3-chloro-5-piperidin-1-ylphenyl)-3,5-dimethylbenzamide; 4-(2-aminoethoxy)-N-(2,5-diethoxyphenyl)-3,5-dimethylbenzamide; 4-(2-aminoethoxy)-N-(3-chloro-2-ethoxy-5-piperidin-1-ylphenyl)-3,5-dimethylbenzamide; 2-(2-HYDROXY-BIPHENYL)-1H-BENZOIMIDAZOLE-5-CARBOXAMIDINE; 6-FLUORO-2-(2-HYDROXY-3-ISOBUTOXY-PHENYL)-1H-BENZOIMIDAZOLE-5-CARBOXAMIDINE; 6-FLUORO-2-[2-HYDROXY-3-(2-METHYL-CYCLOHEXYLOXY)-PHENYL]-1H-INDOLE-5-CARBOXAMIDINE; N-(4-CARBAMIMIDOYL-3-CHORO-PHENYL)-2-HYDROXY-3-IODO-5-METHYL-BENZAMIDE; 6-[(Z)-AMINO(IMINO)METHYL]-N-[3-(CYCLOPENTYLOXY)PHENYL]-2-NAPHTHAMIDE; Urokinase; 2-(2-Hydroxy-5-Methoxy-Phenyl)-1h-Benzoimidazole-5-Carboxamidine; Thieno[2,3-B]Pyridine-2-Carboxamidine; Benzamidine; CRA_10655; [2,4,6-Triisopropyl-Phenylsulfonyl-L-[3-Amidino-Phenylalanine]]-Piperazine-N'-Beta-Alanine; 4-Iodobenzo[B]Thiophene-2-Carboxamidine; 7-Methoxy-8-[1-(Methylsulfonyl)-1h-Pyrazol-4-Yl]Naphthalene-2-Carboximidamide; 4-(2-AMINOETHOXY)-3,5-DICHLORO-N-[3-(1-METHYLETHOXY)PHENYL]BENZAMIDE; 2-Amino-5-Hydroxy-Benzimidazole; Amiloride; 2-(2-Hydroxy-Phenyl)-1h-Benzoimidazole-5-Carboxamidine; N-(1-Adamantyl)-N'-(4-Guanidinobenzyl)Urea; 6-(N-Phenylcarbamyl)-2-Naphthalenecarboxamidine	NA
chr10:81032532	*PPIF*	L-Proline; Cyclosporine; 7-AMINO-4-METHYL-CHROMEN-2-ONE; 1-Methoxy-2-[2-(2-Methoxy-Ethoxy]-Ethane	NA
chr11:64135298	*ESRRA*	Troglitazone; 1-CYCLOHEXYL-N-{[1-(4-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}METHANAMINE	NA
chr11:64135298	*PRDX5*	Diminazene; Auranofin; Benzoic Acid	NA
chr11:64135298	*RPS6KA4*	Riboflavin Monophosphate	NA
chr11:64135298	*BAD*	ABT-263	NA
chr12:56750204	*IL23A*	ABT-874	NA
chr12:56750204	*CS*	Nitromethyldethia Coenzyme A; Oxaloacetate Ion; Trifluoroacetonyl Coenzyme A; Alpha-Fluoro-Carboxymethyldethia Coenzyme a Complex; Malate Ion; Coenzyme A; Citric Acid	NA
chr14:35832666	*NFKBIA*	Acetylsalicylic acid	NA
chr14:35832666	*PSMA6*	(3AR,6R,6AS)-6-((S)-((S)-CYCLOHEX-2-ENYL)(HYDROXY)METHYL)-6A-METHYL-4-OXO-HEXAHYDRO-2H-FURO[3,2-C]PYRROLE-6-CARBALDEHYDE; N-[(1R)-1-(DIHYDROXYBORYL)-3-METHYLBUTYL]-N-(PYRAZIN-2-YLCARBONYL)-L-PHENYLALANINAMIDE	NA
chr16:31004812	*PRSS53*	NA	warfarin; phenprocoumon; fluindione

chr16:31004812	*VKORC1*	Warfarin; Menadione; Acenocoumarol; Dicoumarol; Phenindione; Phenprocoumon	fluindione; coumarin
chr16:31004812	*STX4*	NA	warfarin; phenprocoumon
chr17:26124908	*NOS2*	Aminoguanidine; S-Ethylisothiourea; (3R)-3-[(1,2,3,4-tetrahydroisoquinolin-7-yloxy)methyl]-2,3-dihydrothieno[2,3-f][1,4]oxazepin-5-amine; 1-(6-CYANO-3-PYRIDYLCARBONYL)-5',8'-DIFLUOROSPIRO[PIPERIDINE-4,2'(1'H)-QUINAZOLINE]-4'-AMINE; KD7040; N,N-dimethylarginine; L-Citrulline; 7-Nitroindazole; 4r-Fluoro-N6-Ethanimidoyl-L-Lysine; N-[2-(4-AMINO-5,8-DIFLUORO-1,2-DIHYDROQUINAZOLIN-2-YL)ETHYL]-3-FURAMIDE; ACCLAIM; Ethylisothiourea; N-(3-(Aminomethyl)Benzyl)Acetamidine; 4-(1,3-BENZODIOXOL-5-YLOXY)-2-[4-(1H-IMIDAZOL-1-YL)PHENOXY]-6-METHYLPYRIMIDINE; (3S)-1-(1,3-BENZODIOXOL-5-YLMETHYL)-3-[4-(1H-IMIDAZOL-1-YL)PHENOXY]PIPERIDINE; 7,8-Dihydro-L-Biopterin; 5-(4'-AMINO-1'-ETHYL-5',8'-DIFLUORO-1'H-SPIRO[PIPERIDINE-4,2'-QUINAZOLINE]-1-YLCARBONYL)PICOLINONITRILE; 4-(1H-IMIDAZOL-1-YL)PHENOL; Dexamethasone; N-[2-(1,3-BENZODIOXOL-5-YL)ETHYL]-1-[2-(1H-IMIDAZOL-1-YL)-6-METHYLPYRIMIDIN-4-YL]-D-PROLINAMIDE; N-[2-(6-AMINO-4-METHYLPYRIDIN-2-YL)ETHYL]-4-CYANOBENZAMIDE; ETHYL 4-[(4-METHYLPYRIDIN-2-YL)AMINO]PIPERIDINE-1-CARBOXYLATE; L-Thiocitrulline; Thiocoumarin; 1-[4-(AMINOMETHYL)BENZOYL]-5'-FLUORO-1'H-SPIRO[PIPERIDINE-4,2'-QUINAZOLIN]-4'-AMINE; (6r,1'r,2's)-5,6,7,8 Tetrahydrobiopterin; N-(4-(2-((3-Chlorophenylmethyl)Amino)Ethyl)Phenyl)-2-Thiophecarboxamidine; 6-Nitroindazole; L-Arginine; N-Omega-Hydroxy-L-Arginine; ETHYL 4-[(4-CHLOROPYRIDIN-2-YL)AMINO]PIPERIDINE-1-CARBOXYLATE; 7,8-Dihydrobiopterin; 5-Nitroindazole; Miconazole; N-Omega-Propyl-L-Arginine; 4-({4-[(4-methoxypyridin-2-yl)amino]piperidin-1-yl}carbonyl)benzonitrile; (2S)-2-methyl-2,3-dihydrothieno[2,3-f][1,4]oxazepin-5-amine; 4-(1,3-BENZODIOXOL-5-YLOXY)-2-[4-(1H-IMIDAZOL-1-YL)PHENOXY]PYRIMIDINE; Triflusal; 3-Bromo-7-Nitroindazole	isoniazid; rifampin; doxorubicin
chr17:40561579	*STAT3*	NA	interferons
chr17:78178893	*GAA*	Acarbose; AT2220; Miglitol	NA
chr19:10463118	*TYK2*	3-{(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]piperidin-1-yl}-3-oxopropanenitrile; 2-(1,1-DIMETHYLETHYL)9-FLUORO-3,6-DIHYDRO-7H-BENZ[H]-IMIDAZ[4,5-F]ISOQUINOLIN-7-ONE	NA
chr19:10463118	*ICAM1*	Hyaluronan; Natalizumab	NA
chr19:10463118	*PDE4A*	PDE4; Theophylline; AN2728; Dyphylline; Roflumilast; 4-[8-(3-nitrophenyl)-1,7-naphthyridin-6-yl]benzoic acid; Iloprost; Enprofylline; Drotaverine; Pentoxifylline; Oxtriphylline; Piclamilast; Ibudilast; (4R)-4-(3-butoxy-4-methoxybenzyl)imidazolidin-2-one; Tofisopam; Ketotifen; Dipyridamole	NA

Supplementary Note

Annotated functions of notable candidate genes within newly identified psoriasis susceptibility loci

FUBP1 **(1p31.1):** *FUBP1* encodes a single stranded DNA-binding protein that modulates c-Myc mRNA levels. As a transcription factor c-Myc controls the expression of about 10% of cellular genes, including those essential for cell proliferation, differentiation and apoptosis [5-8]. FUBP1 also directly represses the cell cycle inhibitor p21 [9], which also plays an important role in myeloid cell differentiation with loss of p21 inhibiting both DC and macrophage differentiation [10].

FASLG **(1q24.3)*:*** *FASLG* encodes Fas ligand (CD95), a type-II transmembrane protein that belongs to the tumor necrosis factor (TNF) family. Fas ligand/receptor interactions play an important role in the regulation of the immune system [11]. Although apoptosis is the most studied outcome of Fas:Fas ligand binding [11], Fas receptor engagement includes promotion of inflammatory responses in cell such as macrophages [12], dendritic cells [13,14], and keratinocytes [15]. The Fas:Fas ligand system may interact with NF-κB via A20 (*TNFAIP3*) [16], a known risk gene for psoriasis [1].

IKBKE **(1q32.1)*:*** IKBKE encodes IKKε, which belongs to the IκB kinase family, and is essential for regulation of antiviral signaling pathways. IKKε is activated downstream of cytosolic RNA/DNA sensors, and mediates phosphorylation and activation of transcription factors, including IRF3 and IRF7, and NF-κB [17-19].

ZNF365 (10q21.2): *ZNF365* encodes a zinc-finger binding protein. It is induced by DNA double-strand breakage and is involved in the homologous recombination pathway and maintains genome integrity during DNA replication. It has been reported to be a susceptibility locus for Crohn's disease [20], and atopic dermatitis [21].

PTEN, KLLN, (10q23.31): *PTEN* is a tumor suppressor that inhibits cell proliferation through inactivation of the PI3 kinase/Akt pathway. Keratinocyte-specific Pten deficiency in mice results in epidermal hyperplasia and hyperkeratosis [22]. PTEN has been reported to be suppressed in psoriatic skin compared to normal skin [23]. *KLLN* is a high-affinity DNA-binding protein, downstream of p53 and necessary for p53-induced apoptosis [24].

CHUK **(10q24.31):** CHUK encodes IKK1/IKKα. It is one of three core proteins of the IKK complex and has a critical role in regulating NF-κB activity. It has been reported to have an important role in inflammatory responses [25,26] and epidermal differentiation [27].

CFL1, FIBP, FOSL1 **(11q13.1):** *CFL1* encodes for cofilin, which is a widely distributed intracellular actin-modulating protein and may have a role in regulating dendritic and T-cell migration and T-cell activation [28,29]. *FIBP* encodes for acidic fibroblast growth factor (aFGF) intracellular binding protein. It is mainly found in the nucleus and thought to be involved in the intracellular function of aFGF [30]. *FOSL1* is a member of the AP-1 transcription factor and has been shown to have a role in endothelial assembly into capillary tubes [31].

KLRK1, KLRC4 **(12p13.2):** *KLRK1* encodes NKG2D, a killer cell lectin-like receptor. It is an activating receptor that triggers natural killer (NK) cell CD8+ T-cells, but is normally absent from CD4+ T-cells. NKG2D is also present on most gamma-delta T-cells. Its ligands are stress induced proteins such as MICA [32]. *KLRC4* encodes NKG2F. It is expressed intracellularly in NK cells but is unable to bind with CD94 and has been thought to be a vestigial gene product [33].

BRAP, MAPKAPK5 (12q24.12): *BRAP* may function as a cytoplasmic retention protein and play a role in the cytoplasmic translocation of p21 [34],. *MAPKAP5* encodes a protein kinase regulated by p38. It is activated in response to cellular stress and pro-inflammatory cytokines [35] and is involved in tumor suppression, cell motility and cell cycle regulation [36].

***IL31* (12q24.31):** *IL31* encodes IL-31, which is a member of the IL-6 cytokine family. It is thought to be mainly a Th2– derived cytokine that has been implicated in the pathogenesis of atopic dermatitis [37] and promotes Th2-driven inflammation [38].

***UBAC2* (13q32.3):** UBAC2 has an ubiquitin-associated domain and is predicted to be involved in ubiquitination processes [39]. Polymorphisms in this gene have been associated with Bechet's disease [39] and cutaneous basal and squamous cell carcinoma [40]. The function of the protein encoded by UBAC2 is not known.

***RP11-61O1.1* (14q32.2):** *RP11-61O1.1* encodes a novel lincRNA., whose function is currently unknown.

***KLF13* (15q13.3)**: *KLF13* encodes for Kruppel-like factor 13, and belongs to a family of transcription factors that have C2H2 motif. KLF13 is the dominant regulator of the chemokine RANTES (CCL5) in T-cells [41] and has a role in regulating IL-4 expression in CD4+T-cells [42].

***TRIM47, TRIM65* (17q25.1)**: *TRIM47* and *TRIM65* encode tripartite motif-containing protein 47 and 65.. Over 60 TRIM proteins are known and many of these are induced by type I and type II interferons and play a crucial role in pathogen-recognition and anti-viral responses [43]. Members of the TRIM family interact with RIG1/DDX58 a previously implicated risk gene for psoriasis [4].

***PTPN2* (18p11.21):** *PTPN2* encodes protein-tyrosine phosphatase, T-cell. PTPN2 has various roles in T-cell biology. Loss of *PTPN2* in the T-cell compartment leads to enhanced induction of Th1 and Th17 cells along with impaired induction of regulatory T-cells [44]. *PTPN2* is a critical mediator of peripheral tolerance by restraining CD8+ T-cell responses after antigen-cross-presentation [45].

***FUT2* (19q13.33):** *FUT2* encodes alpha – (1,2) fucosyltransferase with has a role in glycosylation of proteins. It regulates expression of the Lewis ABO blood group antigens on the surface of epithelial cells [46] and determines the secretion status of the ABO antigens. Risk variants in *FUT2* have been associated with Crohn's disease [47,48].

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