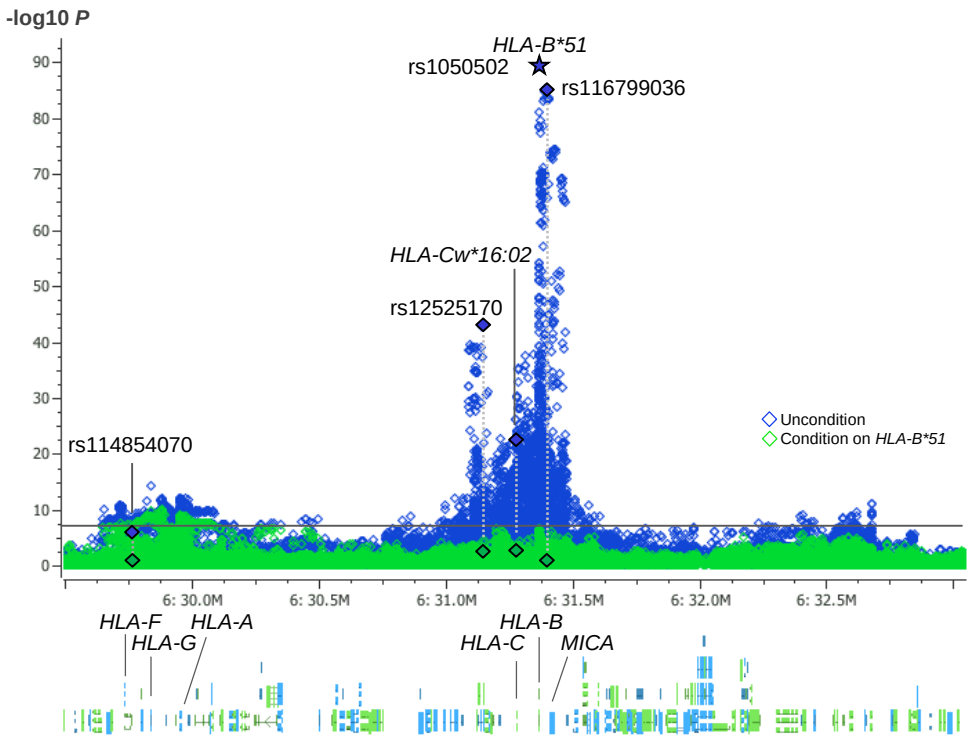
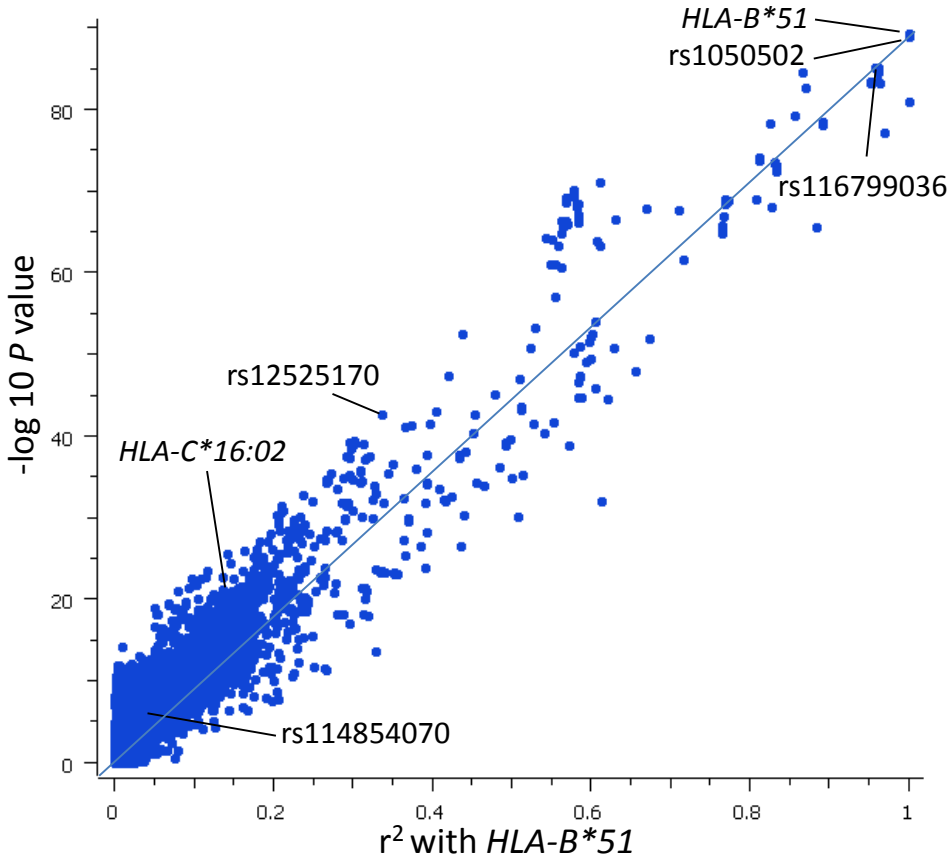


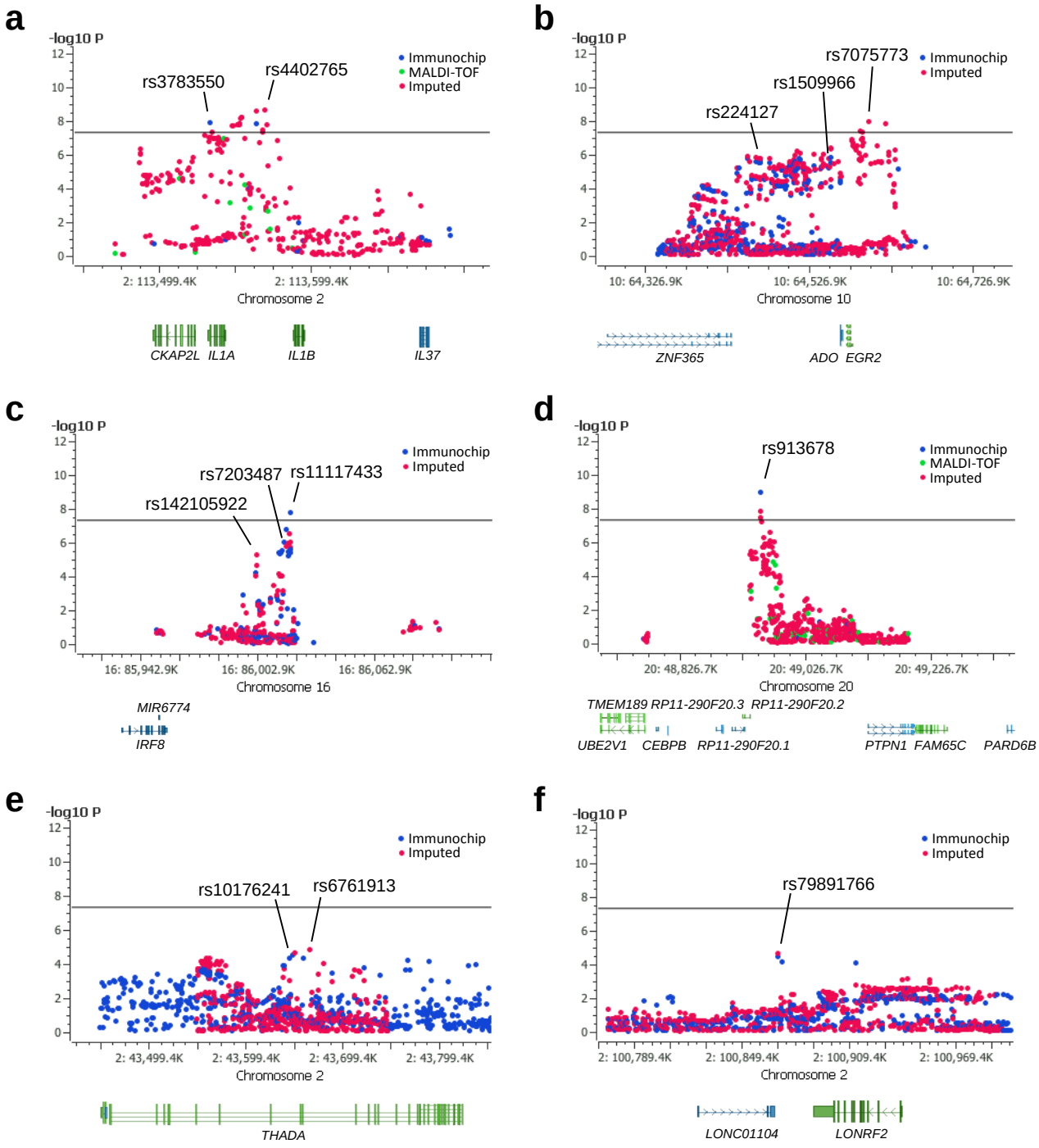
Supplementary Figure 1: Genetic association of imputed markers and HLA types in the MHC region.

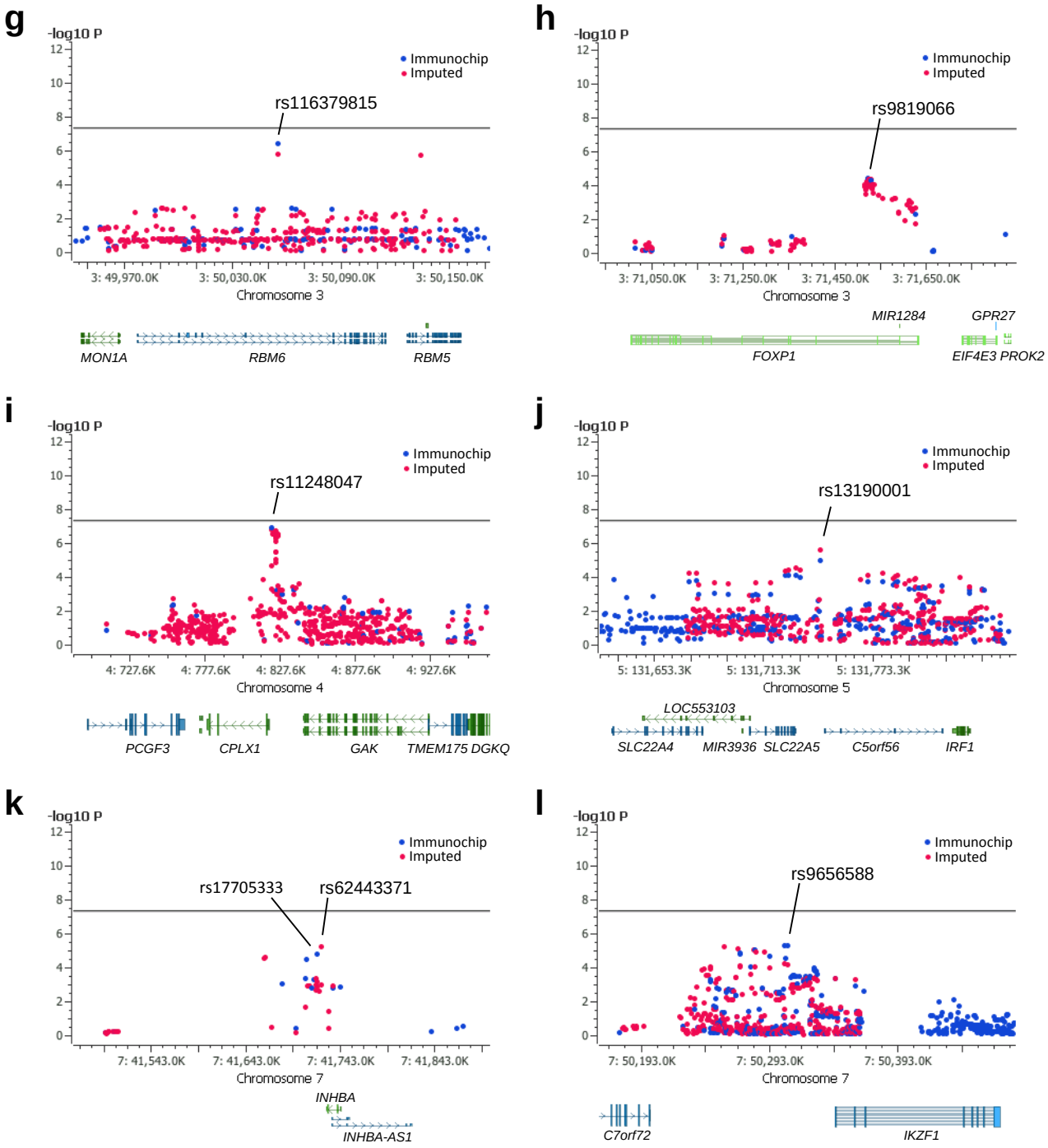
The solid line indicates the threshold for genome-wide significance ($P = 5\times10^{-8}$). Build 37/hg19 was applied for the map positions. *HLA-B*51* showed the strongest association with Behçet's disease ($P = 5.67\times10^{-90}$). Four markers reported in the previous Immunochip study[17] were labeled. The *P*-value for rs116799036 was 1.3×10^{5} fold higher (less significant) than the *P*-value for *HLA-B*51*. In addition, disease associations of the four reported independent markers were fully attenuated after conditioning on *HLA-B*51*.

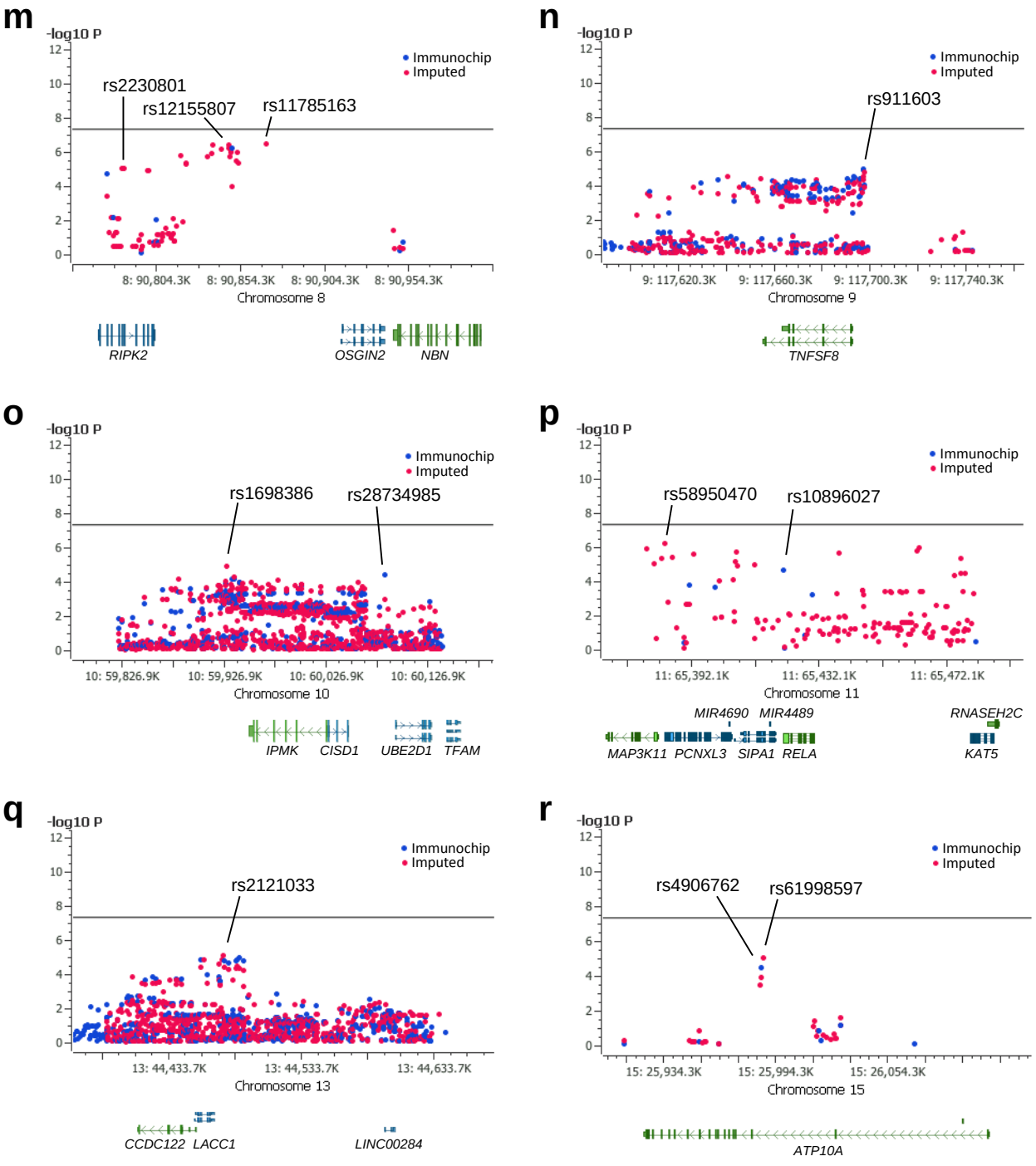


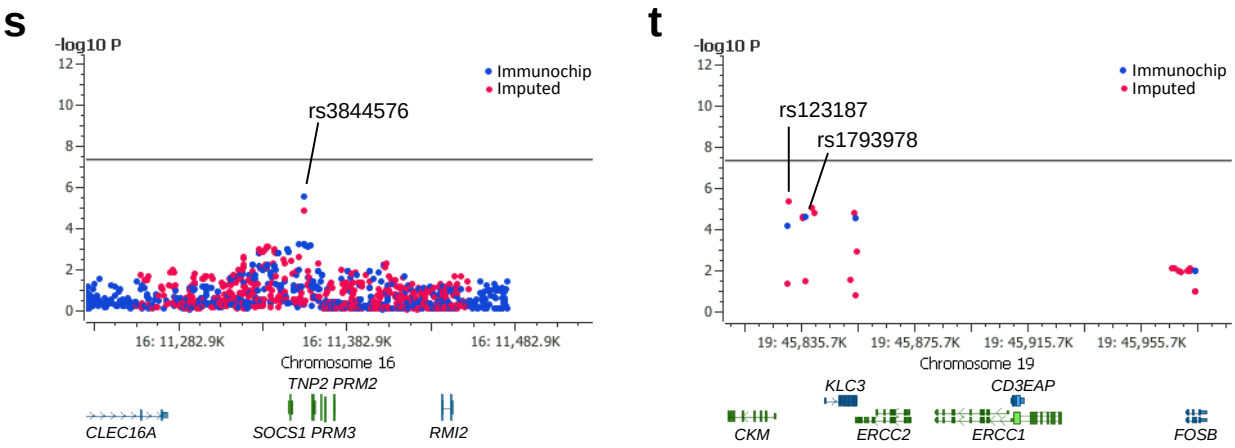
Supplementary Figure 2: HLA region marker associations are highly correlated with their LD with *HLA-B*51*.

53,936 Markers located in the MHC region (28 - 34 Mb in Chromosome 6) and HLA types were analyzed.


a
-log10 P
rs3783550
rs4402765
Immunochip
MALDI-TOF
Imputed
2: 113,499.4K
2: 113,599.4K
Chromosome 2
CKAP2L
IL1A
IL1B
IL37
b
-log10 P
rs7075773
rs1509966
rs224127
Immunochip
Imputed
10: 64,326.9K
10: 64,526.9K
10: 64,726.9K
Chromosome 10
ZNF365
ADO
EGR2
c
-log10 P
rs7203487
rs11117433
rs142105922
Immunochip
Imputed
16: 85,942.9K
16: 86,002.9K
16: 86,062.9K
Chromosome 16
MIR6774
IRF8
d
-log10 P
rs913678
Immunochip
MALDI-TOF
Imputed
20: 48,826.7K
20: 49,026.7K
20: 49,226.7K
Chromosome 20
TMEM189
RP11-290F20.3
RP11-290F20.2
UBE2V1
CEBPB
RP11-290F20.1
PTPN1
FAM65C
PARD6B
e
-log10 P
rs10176241
rs6761913
Immunochip
Imputed
2: 43,499.4K
2: 43,599.4K
2: 43,699.4K
2: 43,799.4K
Chromosome 2
THADA
f
-log10 P
rs79891766
Immunochip
Imputed
2: 100,789.4K
2: 100,849.4K
2: 100,909.4K
2: 100,969.4K
Chromosome 2
LONC01104
LONRF2

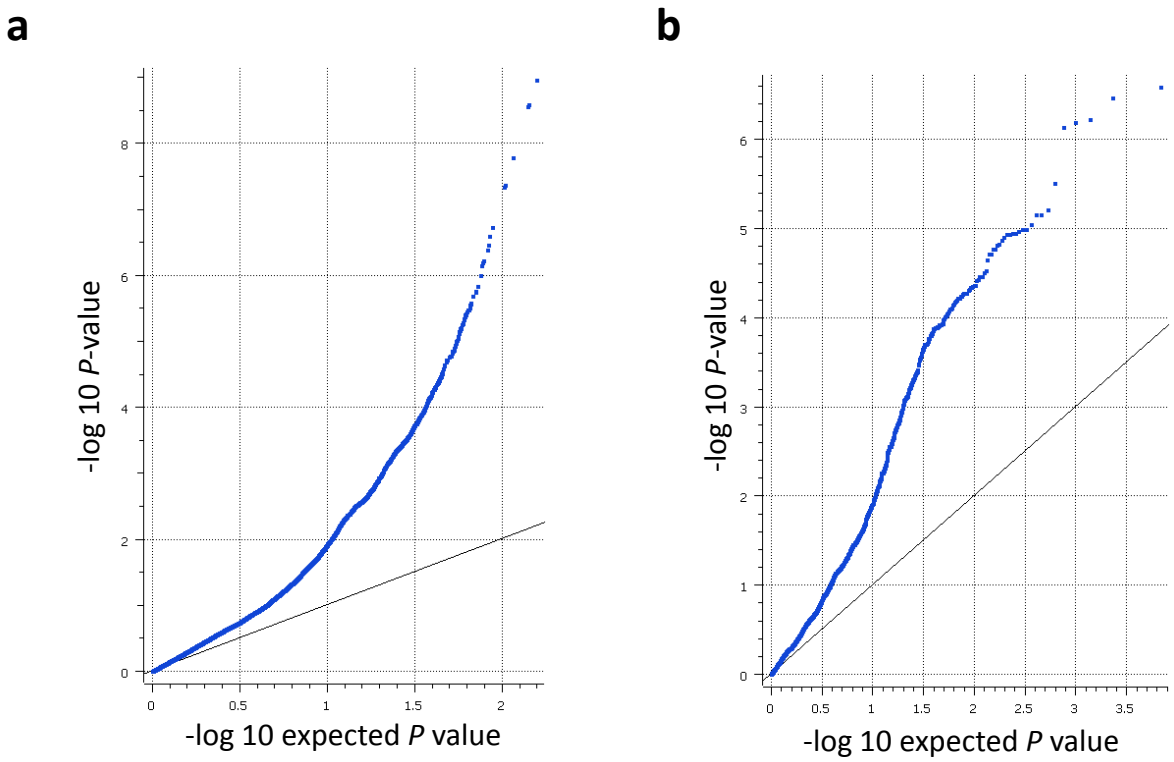

g
-log10 P
Immunochip
Imputed
rs116379815
3: 49,970.0K
3: 50,030.0K
3: 50,090.0K
3: 50,150.0K
Chromosome 3
MON1A
RBM6
RBM5
h
-log10 P
Immunochip
Imputed
rs9819066
3: 71,050.0K
3: 71,250.0K
3: 71,450.0K
3: 71,650.0K
Chromosome 3
MIR1284
GPR27
FOXP1
EIF4E3 PROK2
i
-log10 P
Immunochip
Imputed
rs11248047
4: 727.6K
4: 777.6K
4: 827.6K
4: 877.6K
4: 927.6K
Chromosome 4
PCGF3
CPLX1
GAK
TMEM175 DGKQ
j
-log10 P
Immunochip
Imputed
rs13190001
5: 131,653.3K
5: 131,713.3K
5: 131,773.3K
Chromosome 5
LOC553103
SLC22A4
MIR3936
SLC22A5
C5orf56
IRF1
k
-log10 P
Immunochip
Imputed
rs17705333
rs62443371
7: 41,543.0K
7: 41,643.0K
7: 41,743.0K
7: 41,843.0K
Chromosome 7
INHBA
INHBA-AS1
l
-log10 P
Immunochip
Imputed
rs9656588
7: 50,193.0K
7: 50,293.0K
7: 50,393.0K
Chromosome 7
C7orf72
IKZF1


m
-log10 P
Immunochip
Imputed
rs2230801
rs12155807
rs11785163
8: 90,804.3K
8: 90,854.3K
8: 90,904.3K
8: 90,954.3K
Chromosome 8
RIPK2
OSGIN2
NBN
n
-log10 P
Immunochip
Imputed
rs911603
9: 117,620.3K
9: 117,660.3K
9: 117,700.3K
9: 117,740.3K
Chromosome 9
TNFSF8
o
-log10 P
Immunochip
Imputed
rs1698386
rs28734985
10: 59,826.9K
10: 59,926.9K
10: 60,026.9K
10: 60,126.9K
Chromosome 10
IPMK
CISD1
UBE2D1
TFAM
p
-log10 P
Immunochip
Imputed
rs58950470
rs10896027
11: 65,392.1K
11: 65,432.1K
11: 65,472.1K
Chromosome 11
MIR4690
MIR4489
RNASEH2C
MAP3K11
PCNXL3
SIPA1
RELA
KAT5
q
-log10 P
Immunochip
Imputed
rs2121033
13: 44,433.7K
13: 44,533.7K
13: 44,633.7K
Chromosome 13
CCDC122
LACC1
LINC00284
r
-log10 P
Immunochip
Imputed
rs4906762
rs61998597
15: 25,934.3K
15: 25,994.3K
15: 26,054.3K
Chromosome 15
ATP10A



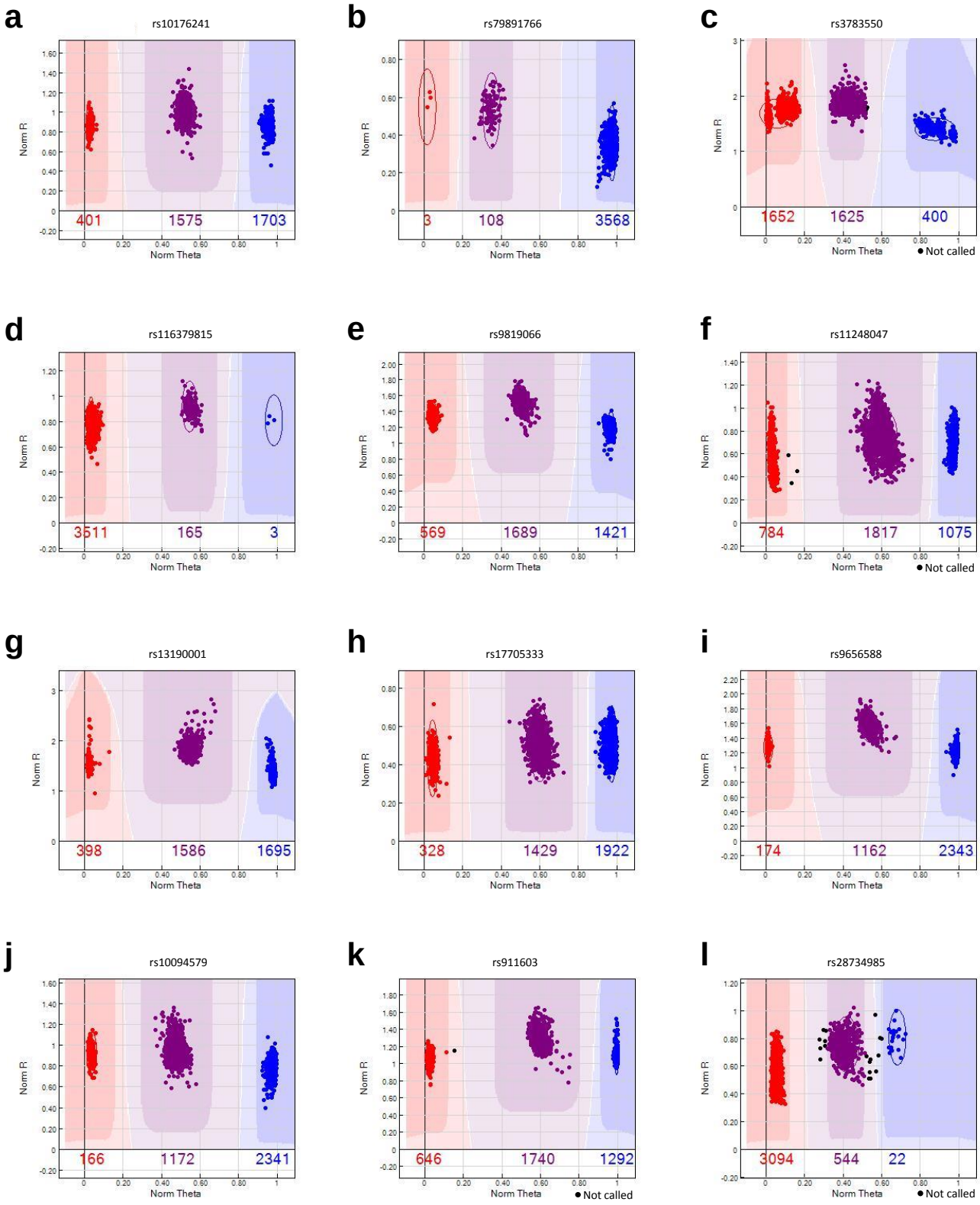
Supplementary Figure 3: Novel loci with suggestive associations ($P<5\times10^{-5}$) in the basic allele test in the Turkish population by direct genotyping or imputation.

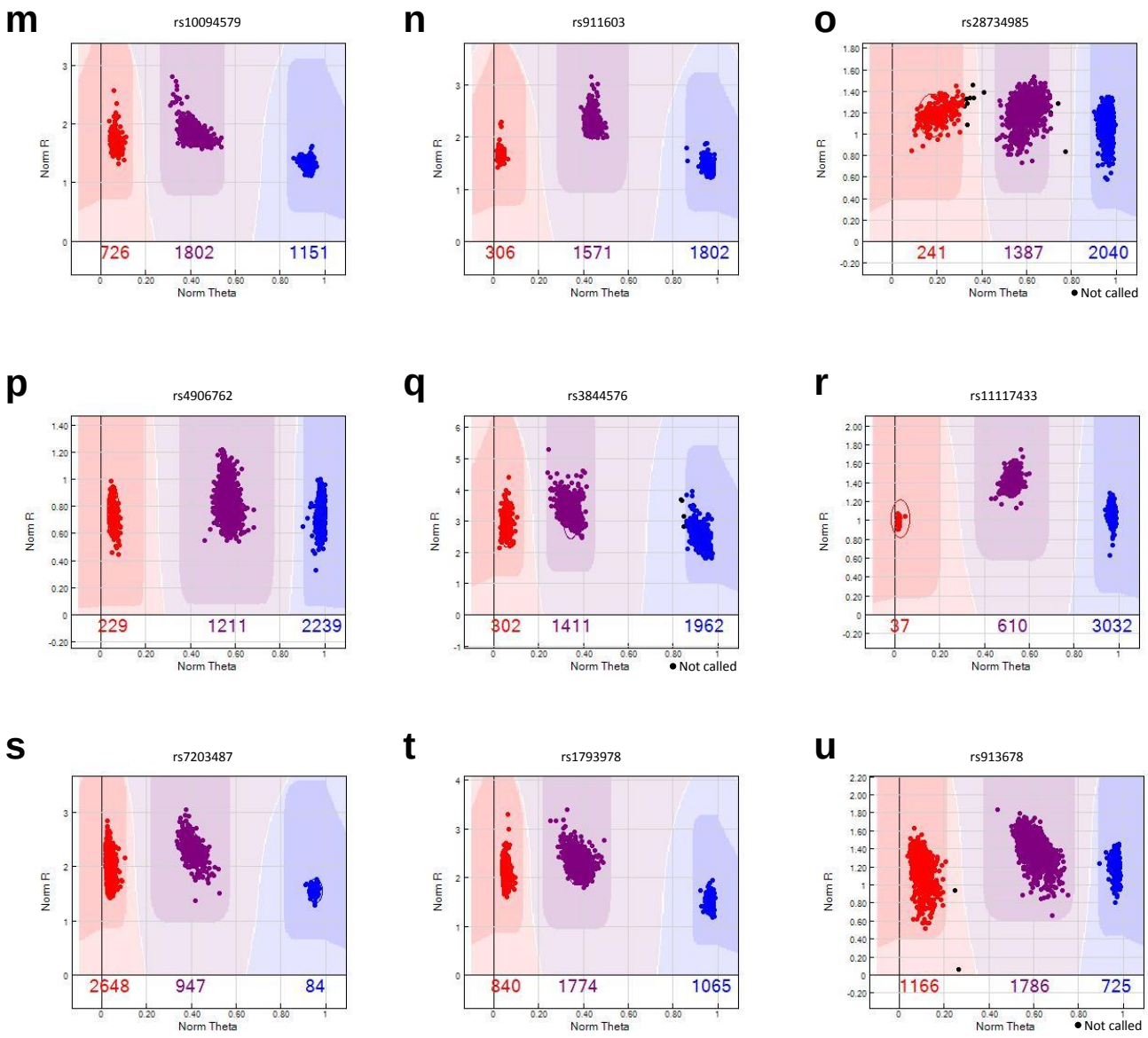
Solid line indicates genome-wide significance ($P<5\times10^{-8}$). Build 37/hg19 was applied for marker maps. (a) The *IL1A-IL1B* locus. (b) The *ADO-EGR2* locus. (c) The *IRF8* locus. (d) The *CEBPB-PTPN1* locus. (e) The *THADA* locus. (f) The *LONRF2* locus. (g) The *RBM6* locus. (h) The *FOXP1* locus. (i) The *CPLX1* locus. (j) The *C5orf56* locus. (k) The *INHBA* locus. (l) The *IKZF1* locus. (m) The *RIPK2* locus. (n) The *TNFSF8* locus. (o) The *IPMK-UBE2D1* locus. (p) The *MAP3K11-KAT5* locus. (q) The *LACC1* locus. (r) The *ATP10A* locus. (s) The *SOCS1-TNP2* locus. (t) The *CKM-KLC3* locus. Four loci (a-d) reached genome-wide significance.



Supplementary Figure 4: P-P plots of the association test for markers located within the reported susceptibility loci for other diseases in the current study.

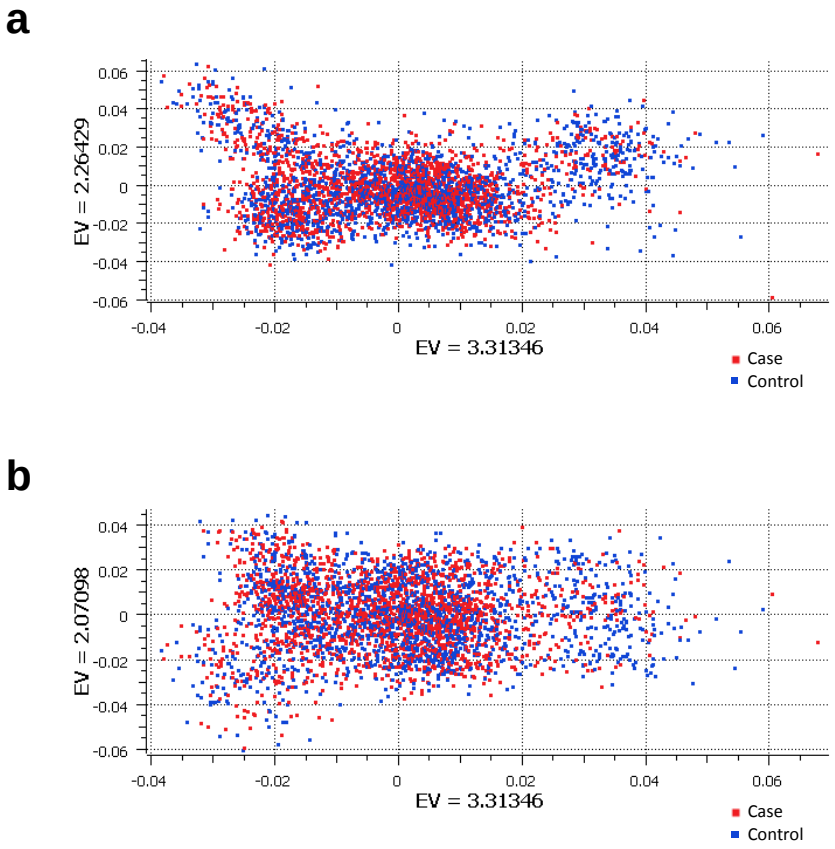
Markers located within the reported susceptibility loci for IBD (a), and leprosy (b). Markers located within the MHC region were excluded in this analysis.


a
rs10176241
401
1575
1703
b
rs79891766
3
108
3568
c
rs3783550
1652
1625
400
Not called
d
rs116379815
3511
165
3
e
rs9819066
569
1689
1421
f
rs11248047
784
1817
1075
Not called
g
rs13190001
398
1586
1695
h
rs17705333
328
1429
1922
i
rs9656588
174
1162
2343
j
rs10094579
166
1172
2341
k
rs911603
646
1740
1292
Not called
l
rs28734985
3094
544
22
Not called
Norm R
Norm Theta



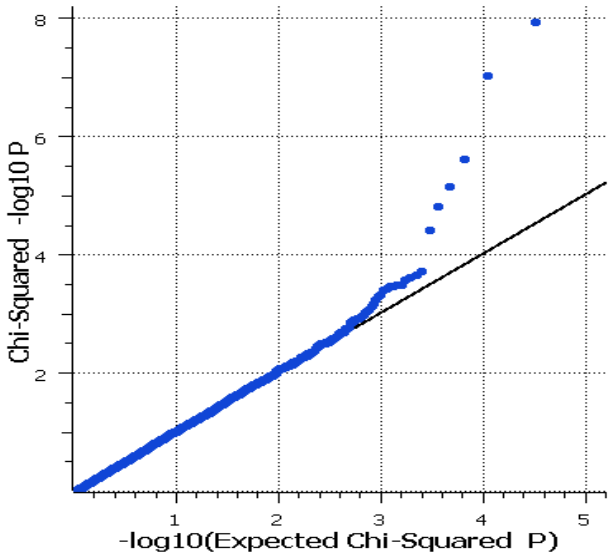
Supplementary Figure 5: The genotype clusters of the lead SNP in each novel suggestive susceptibility locus.

(a) The *THADA* locus. (b) The *LONRF2* locus. (c) The *IL1A-IL1B* locus. (d) The *RBM6* locus. (e) The *FOXP1* locus. (f) The *CPLX1* locus. (g) The *C5orf56* locus. (h) The *INHBA* locus. (i) The *IKZF1* locus. (j) The *RIPK2* locus. (k) The *TNFSF8* locus. (l) The *IPMK-UBE2D1* locus. (m) The *ADO-EGR2* locus. (n) The *MAP3K11-KAT5* locus. (o) The *LACC1* locus. (p) The *ATP10A* locus. (q) The *SOCS1-TNP2* locus. (r) The *IRF8* locus. (s) The *IRF8* locus (independent marker). (t) The *CKM-KLC3* locus. (u) The *CEBPB-PTPN1* locus.



Supplementary Figure 6: Analysis of genetic matching of cases and controls.

(a) Principal components analysis (PCA)-first versus second component. (b) PCA-first versus third component (LD-pruned data with marker pairwise $r^2 < 0.5$).



Supplementary Figure 7: P-P plot demonstrating minimal genomic inflation.

LD-pruned data after removing long LD regions including the MHC region were used to calculate genomic inflation (λ_{GC} is 1.031 and λ_{1000} is 1.017).

Supplementary Table 1: Numeric association testing of imputed HLA class I and II types in 1900 Behçet's disease cases and 1779 controls from Turkey.

HLA type	Allele Frequency		*P*- value	OR	95% CI
	Cases	Controls			
*HLA-B*51*	0.380	0.168	5.67E-90	3.26	2.89 - 3.68
*HLA-Cw*15*	0.139	0.068	4.24E-22	2.16	1.84 - 2.53
*HLA-Cw*16*	0.100	0.049	2.24E-15	2.06	1.72 - 2.48
*HLA-Cw*14*	0.092	0.044	1.50E-15	2.16	1.78 - 2.63
*HLA-A*02*	0.308	0.242	5.75E-10	1.38	1.25 - 1.53
*HLA-A*03*	0.081	0.125	1.36E-09	0.63	0.54 - 0.73
*HLA-Cw*12*	0.091	0.135	1.75E-09	0.64	0.55 - 0.74
*HLA-B*18*	0.033	0.063	2.18E-09	0.51	0.40 - 0.64
*HLA-DQB1*03*	0.496	0.435	3.65E-07	1.27	1.16 - 1.39
*HLA-B*49*	0.019	0.038	1.69E-06	0.50	0.37 - 0.67
*HLA-Cw*07*	0.155	0.196	4.35E-06	0.75	0.67 - 0.85
*HLA-B*35*	0.116	0.154	7.49E-06	0.73	0.64 - 0.84
*HLA-A*33*	0.013	0.028	9.32E-06	0.48	0.34 - 0.67
*HLA-DQB1*02*	0.116	0.151	1.61E-05	0.75	0.65 - 0.85

Supplementary Table 2: Numeric association testing and conditional analysis of imputed two-digit MHC Class I and II alleles in the additive model in 1900 Behçet's disease cases and 1779 controls from Turkey.

HLA Allele	Covariates	*P*- Value	OR	95% CI
*HLA-B*51*	None	5.67E-90	3.26	2.89 - 3.68
*HLA-A*03*	*HLA-B*51*	3.73E-09	0.62	0.52 - 0.72
*HLA-B*15*	*HLA-B*51, HLA-A*03*	2.53E-06	1.76	1.39 - 2.23

P- value < 5×10^{-5} was considered independent association in conditional regression analysis.

Supplementary Table 3: Association results in 1900 Behçet's disease cases and 1779 controls from Turkey for the markers reported with genome-wide significant association in previous studies.

Variant	Nearest gene(s)	Chr.	Position hg19	Type	Risk/Protective Allele[a]	RAF cases	RAF controls	OR	95% CI	*P* -value[b]	Reported OR	Reported 95% CI	Reported *P*- value	Reference
rs1495965	*IL23R-IL12RB2*	1	67753508	Genotyped	C/T	0.571	0.519	1.23	1.13 - 1.35	6.98E-06	1.35	1.24 - 1.47	1.9E-11	[1]
rs924080	*IL23R-IL12RB2*	1	67760140	Genotyped	T/C	0.669	0.612	1.28	1.16 - 1.41	3.44E-07	1.28	1.18 - 1.39	6.69E-09	[2]
rs1518111	*IL10*	1	206944645	Genotyped	T/C	0.367	0.302	1.34	1.22 - 1.48	2.74E-09	1.45	1.34 - 1.58	3.54E-18	[2]
rs1800871	*IL10*	1	206946634	Genotyped	A/G	0.374	0.313	1.31	1.19 - 1.44	4.36E-08	1.45	1.32 - 1.60	1.0E-14	[1]
rs7574070[c]	*STAT4*	2	192010488	-	A/C						1.27	1.17 - 1.37	1.29E-09	[5]
rs897200[c]	*STAT4*	2	192017771	-	A/G						1.45	1.30 - 1.60	6.20E-09	[4]
rs7616215	*CCR1*	3	46205686	Genotyped	T/C	0.730	0.660	1.40	1.26 - 1.54	4.94E-11	1.39	1.27 - 1.52	4.30E-13	[5]
rs13092160	*CCR1*	3	46254791	Genotyped	T/C	0.899	0.857	1.49	1.29 - 1.72	2.79E-08	3.57	2.5 - 5.0	4.33E-09	[3]
rs17810546	*IL12A*	3	159665050	Genotyped	G/A	0.088	0.056	1.63	1.36 - 1.96	1.01E-07	1.66	1.42 - 1.93	1.12E-10	[9]
rs1874886	*IL12A*	3	159729655	Genotyped	A/G	0.349	0.319	1.14	1.04 - 1.26	0.0067	1.61	1.36 - 1.89	1.62E-08	[10]
rs17482078	*ERAP1*	5	96118866	Genotyped	TT/TC+CC[e]	0.167	0.143	2.46	1.65 - 3.68	5.80E-06	4.56	2.88 - 7.22	4.73E-11	[5]
rs7753873[d]	*TNFAIP3*	6	138173422	Genotyped	A/C	0.903	0.899	1.04	0.90 - 1.22	0.59	1.81	1.51 - 2.18	8.35E-11	[7]
rs2848479	*JRKL-CNTN5*	11	98087599	Genotyped	A/G	0.442	0.442	1.00	0.91 - 1.09	0.94	1.66	1.42 - 1.94	3.29E-10	[10]
rs2617170	*KLRC4*	12	10560957	Genotyped	C/T	0.683	0.629	1.27	1.16 - 1.40	8.77E-07	1.28	1.18 - 1.39	1.34E-09	[5]
M694V[c]	*MEFV*	16	3293407	-	A/G						2.65		1.79E-12	[6]
rs681343	*FUT2*	19	49206462	Imputed	T/C	0.562	0.510	1.23	1.12 - 1.35	8.58E-06	1.30	1.19 - 1.41	4.78E-09	[8]

[a]Risk and protective alleles are based on original studies[1-10].

[b]*P* -value < 0.0045 was considered significantly confirmed (see methods).

[c]Markers were not genotyped or imputed in the current study.

[d]Because no data were available for rs9494885, the result of rs7753873 (r^2=1) is shown in the table.

[e]The recessive model was applied for rs17482078 as the original study reported.

Supplementary Table 4: Comparison of statistical power between this study and the previous GWAS for loci with newly identified genome-wide significant associations in the Turkish population.

Immunochip Lead SNP	Nearest gene(s)	Statisitical Power		SNP in high LD on GWAS chip	P_{GWAS}
		1900 cases/1779 controls (Immunochip)	1215 cases/1278 controls (GWAS)		
rs3783550	*IL1A-IL1B*	0.62	0.24	rs10496444 (r^2=0.98)	0.0021
rs17753641	*IL12A* [a]	0.79	0.36	No	-
rs11117433	*IRF8*	0.61	0.24	No	-
rs913678	*CEBPB-PTPN1*	0.74	0.36	rs913678	3.10E-05

[a]*IL12A* had a marker (rs17810546) with suggestive evidence for association in the GWAS collection that did not reach statistical significance with the Turkish replication collection[3].

Supplementary Table 5: Association with Behçet's disease in Turkish discovery collection (1900 cases and 1779 controls) of lead SNPs genotyped by the Immunochip for novel suggestive loci with $P<5\times10^{-5}$.

Marker	Nearest gene(s)	Chr.	Position hg19	Minor/Major allele	MAF cases	MAF controls	OR	95% CI	*P*
rs10176241	*THADA*	2	43648176	A/G	0.301	0.347	0.81	0.74 - 0.90	3.05E-05
rs79891766	*LONRF2*	2	100869755	T/C	0.010	0.022	0.44	0.30 - 0.66	3.60E-05
rs116379815	*RBM6*	3	50055358	G/A	0.032	0.014	2.31	1.65 - 3.22	4.17E-07
rs9819066	*FOXP1*	3	71523110	T/C	0.407	0.360	1.22	1.11 - 1.34	4.56E-05
rs11248047	*CPLX1*	4	821553	A/G	0.431	0.492	0.78	0.71 - 0.86	1.27E-07
rs13190001	*C5orf56*	5	131744482	T/C	0.347	0.299	1.24	1.13 - 1.37	1.19E-05
rs17705333	*INHBA*	7	41718754	A/G	0.262	0.307	0.80	0.72 - 0.89	1.82E-05
rs9656588	*IKZF1*	7	50306780	T/C	0.184	0.227	0.77	0.69 - 0.86	5.28E-06
rs10094579	*RIPK2*	8	90849305	A/C	0.227	0.180	1.34	1.19 - 1.50	6.03E-07
rs911603	*TNFSF8*	9	117697584	A/C	0.388	0.438	0.81	0.74 - 0.89	1.17E-05
rs28734985	*IPMK-UBE2D1*	10	60084051	G/A	0.068	0.094	0.70	0.59 - 0.83	4.10E-05
rs1509966	*ADO-EGR2*	10	64552607	A/G	0.415	0.471	0.80	0.73 - 0.87	1.47E-06
rs10896027	*MAP3K11-RELA*	11	65420760	G/C	0.275	0.320	0.81	0.73 - 0.89	2.58E-05
rs9316059	*LACC1*	13	44486789	T/A	0.233	0.278	0.79	0.71 - 0.88	1.16E-05
rs4906762	*ATP10A*	15	25986565	T/C	0.207	0.248	0.79	0.71 - 0.89	3.81E-05
rs3844576	*SOCS1-TNP2*	16	11357616	A/C	0.298	0.249	1.28	1.15 - 1.42	3.09E-06
rs1793978	*CKM-KLC3*	19	45837269	A/G	0.446	0.495	0.82	0.75 - 0.90	2.70E-05

Supplementary Table 6: Association analysis after imputation of loci with stronger associations than markers on the Immunochip (1900 Behçet's disease cases and 1779 controls from Turkey).

Marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	A1 Allele Frequency		OR	95% CI	*P*	P_{GC}	Lead SNP Immunochip	r^2	D'
						cases	controls							
rs6761913	*THADA*	2	43665245	G	C	0.370	0.421	0.81	0.73 - 0.89	1.59×10^{-5}	2.14×10^{-5}	rs10176241	0.39	0.72
rs79891766	*LONRF2*	2	100869755	T	C	0.008	0.020	0.41	0.27 - 0.63	2.25×10^{-5}	2.99×10^{-5}	rs79891766	1	1
rs4402765	*IL1A-IL1B*	2	113568847	C	G	0.345	0.278	1.40	1.20 - 1.50	2.22×10^{-9}	3.85×10^{-9} [a]	rs3783550	0.97	0.99
rs13190001	*C5orf56*	5	131744482	T	C	0.330	0.279	1.27	1.15 - 1.41	2.74×10^{-6}	3.87×10^{-6}	rs13190001	1	1
rs62443371	*INHBA*	7	41722498	A	G	0.238	0.286	0.78	0.70 - 0.87	6.59×10^{-6}	9.07×10^{-6}	rs17705333	1	1
rs11785163	*RIPK2*	8	90869409	A	C	0.250	0.195	1.37	1.21 - 1.55	3.55×10^{-7}	5.32×10^{-7}	rs10094579	1	1
rs1698386	*IPMK-UBE2D1*	10	59928968	C	A	0.056	0.082	0.67	0.55 - 0.80	1.36×10^{-5}	1.83×10^{-5}	rs28734985	0.0044	0.83
rs7075773	*ADO-EGR2*	10	64598621	T	C	0.275	0.343	0.73	0.66 - 0.81	1.69×10^{-9}	2.96×10^{-9} [a]	rs1509966	0.30	0.77
rs58950470	*MAP3K11-RELA*	11	65383755	T	G	0.258	0.315	0.76	0.68 - 0.84	6.25×10^{-7}	9.21×10^{-7}	rs10896027	0.90	0.99
rs2121033	*LACC1*	13	44475052	G	C	0.235	0.281	0.79	0.71 - 0.87	8.88×10^{-6}	1.21×10^{-5}	rs9316059	0.99	1
rs61998597	*ATP10A*	15	25987459	G	A	0.194	0.237	0.77	0.69 - 0.87	9.54×10^{-6}	9.54×10^{-6}	rs4906762	1	1
rs123187	*CKM-KLC3*	19	45830947	G	A	0.458	0.513	0.80	0.73 - 0.88	4.60×10^{-6}	6.40×10^{-6}	rs1793978	0.97	1

[a] Exceeds genome-wide significance.

Supplementary Table 7: Regression analysis in 1900 cases and 1779 controls from Turkey conditioning on the lead genotyped or imputed SNP from each region to test for independent secondary associations.

Best secondary marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	Covariates	$P_{condition}$	OR	95% CI
rs4347211	*IL10*	1	206978340	G	A	rs1518110	1.11×10^{-4}	0.80	0.71 - 0.89
rs4591347	*IL1A-IL1B*	2	113658705	T	C	rs4402765[a]	0.0033	1.23	1.07 - 1.40
rs2097285	*CCR1*	3	46441176	G	T	rs7616215	5.37×10^{-4}	0.73	0.61 - 0.87
rs2647935	*IL12A*	3	159684522	T	C	rs17753641	0.0057	1.21	1.06 - 1.38
rs224070	*ADO-EGR2*	10	64508418	A	G	rs7075773[a]	0.008	1.17	1.04 - 1.31
rs7203487	***IRF8***	**16**	**86016694**	**C**	**T**	**rs11117433**	$\mathbf{2.99\times10^{-5}}$	**1.32**	**1.16 - 1.50**
rs11860004	*IRF8*	16	86001879	A	T	rs11117433, rs7203487	0.036	0.90	0.81 - 0.99
rs13038695	*CEBPB-PTPN1*	20	49048440	G	A	rs913678	0.33	1.05	0.95 - 1.15

Bold indicates the significant *P*- value ($P < 5 \times 10^{-5}$).

[a] Imputed marker.

Supplementary Table 8: Replication study in the Iranian population (genotypes determined in 969 cases and 826 controls) for the peak markers from the novel loci identified by Turkish Immunochip data

Marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	A1 Allele Freq.		*P* -value	OR	95% CI	Statistical Power[a]
						Case	Control				
rs10176241	*THADA*	2	43648176	A	G	0.268	0.303	0.022	0.84	0.73 - 0.98	0.34
rs79891766	*LONRF2*	2	100869755	T	C	0.019	0.016	0.45	1.22	0.73 - 2.02	0.22
rs3783550	*IL1A-IL1B*	2	113532885	G	T	0.327	0.301	0.098	1.13	0.98 - 1.31	0.80
rs116379815	*RBM6*	3	50055358	G	A	0.028	0.026	0.76	1.07	0.71 - 1.60	0.95
rs9819066	*FOXP1*	3	71523110	T	C	0.396	0.366	0.072	1.13	0.99 - 1.30	0.39
rs11248047	*CPLX1*	4	821553	A	G	0.435	0.456	0.21	0.92	0.80 - 1.05	0.68
rs13190001	*C5orf56*	5	131744482	T	C	0.287	0.281	0.69	1.03	0.89 - 1.19	0.41
rs17705333	*INHBA*	7	41718754	A	G	0.285	0.271	0.36	1.07	0.92 - 1.24	0.38
rs9656588	*IKZF1*	7	50306780	T	C	0.186	0.218	0.019	0.82	0.70 - 0.97	0.47
rs10094579	*RIPK2*	8	90849305	A	C	0.168	0.136	0.0090	1.28	1.06 - 1.54	0.49
rs911603	*TNFSF8*	9	117697584	A	C	0.402	0.444	0.013	0.84	0.74 - 0.96	0.45
rs28734985[b]	*IPMK-UBE2D1*	10	60084051	G	A	-	-	-	-		
rs1509966	*ADO-EGR2*	10	64552607	A	G	0.434	0.493	5.09E-04[C]	0.79	0.69 - 0.90	0.56
rs10896027	*MAP3K11-RELA*	11	65420760	G	C	0.303	0.292	0.49	1.05	0.91 - 1.22	0.37
rs2121033[b]	*LACC1*	13	44475052	G	C	0.256	0.307	0.0012[c]	0.78	0.67 - 0.91	0.51
rs4906762	*ATP10A*	15	25986565	T	C	0.210	0.223	0.33	0.92	0.79 - 1.08	0.34
rs3844576	*SOCS1*	16	11357616	A	C	0.324	0.301	0.14	1.11	0.96 - 1.28	0.61
rs7203487	*IRF8*	16	86016694	C	T	0.158	0.117	4.13E-04[C]	1.42	1.17 - 1.72	0.54
rs11117433	*IRF8*	16	86019516	C	G	0.067	0.088	0.023	0.75	0.58 - 0.96	0.62
rs1793978	*CKM*	19	45837269	T	C	0.436	0.443	0.68	0.97	0.85 - 1.11	0.40
rs913678	*CEBPB-PTPN1*	20	48955424	C	T	0.483	0.420	1.59E-04[C]	1.29	1.13 - 1.48	0.86

[a] Statistical power was estimated from effect size in the Turkish population, allele frequency and sample size in the Iranian population.

[b] rs28734985 for *UBE2D1* and rs9316059 for *LACC1* failed in genotyping by TOF-MS. rs2121033, the lead SNP for *LACC1* after imputation, was genotyped instead of rs9316059 (r^2 = 0.99 in Turks).

[c] Significantly replicated (*P* < 0.0014, see method).

Supplementary Table 9: Replication study in the Japanese population GWAS imputed data (608 cases and 737 controls) for the peak markers from the novel loci identified by Turkish Immunochip data.

Marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	A1 Allele Freq.		*P* -value	OR	95% CI	Statistical Power[a]
						Case	Control				
rs10176241	*THADA*	2	43648176	A	G	0.645	0.669	0.21	0.90	0.76 - 1.06	0.26
rs79891766[b]	*LONRF2*	2	100869755	T	C	-	-	-	-		-
rs3783550	*IL1A-IL1B*	2	113532885	G	T	0.767	0.748	0.24	1.11	0.93 - 1.33	0.46
rs116379815[b]	*RBM6*	3	50055358	G	A	-	-	-	-		-
rs9819066[b]	*FOXP1*	3	71523110	T	C	-	-	-	-		-
rs11248047[b]	*CPLX1*	4	821553	A	G	-	-	-	-		-
rs13190001	*C5orf56*	5	131744482	T	C	0.281	0.248	0.062	1.18	0.99 - 1.42	0.23
rs17705333[b]	*INHBA*	7	41718754	A	G	-	-	-	-		-
rs9656588	*IKZF1*	7	50306780	T	C	0.460	0.443	0.39	1.07	0.92 - 1.25	0.56
rs10094579	*RIPK2*	8	90849305	A	C	0.087	0.063	0.038	1.43	1.02 - 2.00	0.11
rs911603	*TNFSF8*	9	117697584	A	C	0.587	0.588	0.95	0.99	0.85 - 1.17	0.30
rs28734985[b]	*IPMK-UBE2D1*	10	60084051	G	A	-	-	-	-		-
rs1509966	*ADO-EGR2*	10	64552607	A	G	0.339	0.361	0.24	0.91	0.77 - 1.07	0.32
rs10896027	*MAP3K11-RELA*	11	65420760	G	C	0.704	0.694	0.60	1.05	0.88 - 1.26	0.28
rs9316059	*LACC1*	13	44486789	T	A	0.225	0.301	5.41E-05[c]	0.67	0.56 - 0.82	0.34
rs4906762	*ATP10A*	15	25986565	T	C	0.248	0.217	0.083	1.19	0.98 - 1.45	0.21
rs3844576	*SOCS1*	16	11357616	A	C	0.777	0.767	0.57	1.06	0.87 - 1.28	0.28
rs7203487[b]	*IRF8*	16	86016694	C	T	-	-	-	-		-
rs11117433[b]	*IRF8*	16	86019516	C	G	-	-	-	-		-
rs1793978[b]	*CKM*	19	45837269	T	C	-	-	-	-		-
rs913678[b]	*CEBPB-PTPN1*	20	48955424	C	T	-	-	-	-		-

[a] Statistical power was estimated from effect size in the Turkish population, allele frequency and sample size in the Japanese population.

[b] SNPs not genotyped or imputed in the Japanese population.

[c] Significantly replicated ($P < 0.0014$, see method).

Supplementary Table 10: Meta-analysis of Turkish and Japanese cohorts for the directly genotyped markers from the Turkish collection that replicated in the Japanese cohort.

Marker	Nearest gene	A1	A2	Turkish			Japanese			Combined					
				OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	P_{GC}	I^2	P_{het}
rs9316059	*LACC1*	T	A	0.79	0.71-0.88	1.16×10^{-5}	0.67	0.56-0.82	5.41×10^{-5}[a]	0.76	0.69-0.84	**7.17×10^{-9}**	**1.37×10^{-8}**	0.49	0.16

Bold indicates genome-wide significance in meta-analysis.

[a] Determined with imputed genotypes.

Supplementary Table 11: Meta-analysis between Turkish and Japanese for markers from novel loci with suggestive associations (P <5×10^{-5}) available in imputed data of both Turkish Immunochip genotyping and Japanese previous GWAS.

Marker	Nearest gene(s)	Chr.	Position hg19	A1/A2	Turkish							Japanese					Combined					
					Lead SNP Immunochip	r^2	D'	A1 Freq. Case	A1 Freq. Control	OR	95% CI	P	A1 Freq. Case	A1 Freq. Control	OR	95% CI	P	OR	95% CI	P	P_{GC}	I^2	P_{het}
rs2230801	*RIPK2*	8	90784979	C/T	rs10094579	0.38	0.98	0.108	0.079	1.43	1.22-1.68	9.60×10^{-6}	0.030	0.009	3.41	1.80-6.47	6.39×10^{-5}	1.52	1.30-1.77	**4.89×10^{-9}**	**6.57×10^{-9}**	0.25	0.25
rs224127	*ADO-EGR2*	10	64461273	A/G	rs1509966	0.48	0.85	0.475	0.418	1.26	1.15-1.39	1.56×10^{-6}	0.587	0.621	1.30	1.11-1.51	0.0011	1.27	1.17-1.38	**6.62×10^{-9}**	**9.46×10^{-9}**	0	0.81
rs2121033	*LACC1*	13	44475052	G/C	rs9316059	0.99	1	0.235	0.281	0.79	0.71-0.87	8.88×10^{-6}	0.275	0.353	0.69	0.58-0.83	4.68×10^{-5}	0.76	0.69-0.83	**4.09×10^{-9}**	**5.51×10^{-9}**	0.42	0.19
rs142105922	*IRF8*	16	86002593	AAT/-	rs11117433	0.62	0.95	0.050	0.077	0.63	0.52-0.77	5.58×10^{-6}	0.053	0.087	0.59	0.43-0.82	0.0013	0.62	0.53-0.74	**3.01×10^{-8}**	**4.14×10^{-8}**	0	0.65

Bold indicates genome-wide significance.

Supplementary Table 12: Regression analysis of the lead/independent markers genotyped by the Immunochip for the locus identified in meta-analysis of the Turkish and Japanese cohorts conditioning on the lead markers .

Marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	Lead/independent marker	$P_{condition}$	OR	95% CI
rs2230801	*RIPK2*	8	90784979	C	T	rs10094579	0.094	1.19	0.97 - 1.45
rs224127	*ADO-EGR2*	10	64461273	A	G	rs1509966	0.095	1.11	0.98 - 1.26
rs2121033	*LACC1*	13	44475052	G	C	rs9316059	0.27	0.47	0.12 - 1.89
rs142105922	*IRF8*	16	86002593	AAT	-	rs11117433	0.50	0.90	0.66 - 1.23
rs142105922	*IRF8*	16	86002593	AAT	-	rs7203487 [a]	5.67E-05	0.67	0.55 - 0.81

[a] rs7203487 is the disease susceptible SNP with independent association from rs11117433.

Supplementary Table 13: Results of the basic association test in the Iranian population for markers identified in the meta-analysis for Turkish and Japanese populations.

Marker	Nearest gene(s)	Chr.	Position hg19	A1	A2	Iranian					
						A1 Freq. Case	A1 Freq. Control	OR	95% CI	*P*	Statistical Power[a]
rs2230801	*RIPK2*	8	90784979	C	T	0.064	0.058	1.11	0.84 - 1.46	0.47	0.32
rs224127	*ADO-EGR2*	10	64461273	A	G	0.426	0.387	1.18	1.03 - 1.35	0.017	0.59
rs2121033	***LACC1***	**13**	**44475052**	**G**	**C**	**0.256**	**0.307**	**0.78**	**0.67 - 0.91**	**0.0012**	**0.51**
rs1401884[b]	*IRF8*	16	86013551	C	G	0.048	0.069	0.68	0.51 - 0.91	0.0088	0.47

[a] Statistical power was estimated from effect size in the Turkish population, allele frequency and sample size in the Iranian population.

[b] rs142105922 for *IRF8* failed in genotyping by TOF-MS. rs1401884 in high LD with rs142105922 was genotyped ($r^2 = 0.84$).

Bold indicates significant association in the replication study.

Supplementary Table 14: Description of susceptibility markers for Behcet's disease in the current study.

SNP	Locus	Annotation	Regulatory Features	Functional effects of disease risk allele	Gene Function
rs3783550	*IL1A-IL1B*	Intronic	Promotor histone marks, DNAse, Motifs changed	*IL1A* : Decreased gene exprssion (Skin, Lymphoblastoid cell)	*IL1A* : IL-1α is highly expressed in the epidermis and plays an important role in skin barrier functions against pathogens[11]. *IL1B* : IL-1β is processed to its active form by caspase-1, a component of the activated inflammasome, and is an important mediator of the inflammatory response[12].
rs4402765		Intergenic	Enhancer histone marks, Motifs changed	*IL1A* : Decreased gene expression (Skin, Lymphoblastoid cell)	
rs2230801	*RIPK2*	Missense (p.Ile259Thr)	Evolutionarily conserved regions, Enhancer histone marks	*RIPK2* : Possibly damaging (p.Ile259Thr)	*RIPK2* : *RIPK2* encodes receptor-interacting serine-threonine kinase 2, which acts in the NOD2 response to the lipoprotein Pam¬3Cys and muramyl dipeptide (MDP), a component of peptidoglycan from bacteria[13].
rs1509966	*ADO-EGR2*	Intergenic	Enhancer histone marks, DNAse, Motifs changed	*ADO* : Increased gene expression (Muscle) *ADO* : Decreased gene expression (Testis)	*ADO* : ADO encodes cysteamine (2-aminoethanethiol) dioxygenase, which exhibits cysteamine dioxygenase activity[14]. *EGR2* : EGR2 is an important transcription factor involved in T cell anergy and regulation of IL-2 and IFN γ, and involved in the differentiation of LAG3+ regulatory T cells, which highly express IL-10[15,16].
rs7075773		Intergenic	Motifs changed	*ADO* : Increased gene expression (Lung)	
rs224127		Intergenic	Motifs changed	*ADO* : Increased gene expression (whole blood, Muscle) *ADO* : Decreased gene expression (Testis)	
rs2121033	*LACC1*	Intergenic[a]	Motifs changed	*LACC1* : Increased gene expression (Heart, Muscle) *LACC1* : Decreased gene expression (Esophagus mucosa, Artery) *CCDC122* : Increased gene expression (Heart, Muscle, Adipose)	*LACC1* : *LACC1* encodes laccase (multicopper oxidoreductase) domain containing 1, which is highly expressed in macrophages and involved in immunometabolic function through increasing fatty-acid oxidation and promoting glycolysis[17]. *CCDC122* : *CCDC122* encodes coiled-coil domain containing 122.
rs11117433	*IRF8*	Intergenic	Promotor histone marks, Enhancer histone marks, DNAse, Motifs changed		*IRF8* : IRF8 is a transcription factor that plays roles in innate immune responses and adaptive immune cell development[18].
rs7203487		Intergenic	Promotor histone marks, Enhancer histone marks, DNAse		
rs142105922		Intergenic	Enhancer histone marks, Motifs changed		
rs913678	*CEBPB-PTPN1*	Intergenic	Evolutionarily conserved regions, Promotor histone marks, Enhancer histone marks, Protein bound, DNAse, Motifs changed	*CEBPB* : Decreased gene expression (Whole blood)	*CEBPB* : C/EBPβ is known to play a fundamental role in the antibacterial activity of macrophages[19]. *PTPN1* : PTPN1 is an enzyme that dephosphorylates JAK2 and TYK2, members of Janus kinase (JAK) family, which interact with the IL-12 receptor and the IL-23 receptor[20].

Features of susceptibility markers in the current study were investigated using Haploreg v4.1. Functional effects of nonsynonymous coding variants were predicted by Polyphen-2. eQTL data were extracted from Genevar, Blood eQTL browser and GTEx.

[a]The missense variant of *LACC1* , rs3764147 (p.Ile254Val), which is predicted benign, is in high LD with rs2121033 (r^2=0.93).

Supplementary Table 15: Disease association for homozygous *FUT2* non-secretor alleles of two ancestry-specific single nucleotide polymorphisms.

Population	Marker	Non-secretor Allele	*FUT2* Mutation	Homozygote Freq.		OR	95% CI	*P*
				Case	Control			
Turkish	rs601338[a]	A	p.Trp143Ter	0.354	0.264	1.52	1.32 - 1.76	6.51×10^{-9}
Iranian	rs601338	A	p.Trp143Ter	0.312	0.220	1.61	1.30 - 2.00	1.65×10^{-5}
Japanese	rs1047781	T	p.Ile129Phe	0.214	0.141	1.66	1.24 - 2.22	6.50×10^{-4}
Combined [b]						**1.56**	**1.40 - 1.75**	**5.89×10^{-15}**

[a] Imputed data.

[b] *P* -value for heterogeneity is 0.83 and I^2 is 0.

Supplementary Table 16: Overlap of susceptibility genes for Behçet's disease with inflammatory bowel disease (Crohn's disease and ulcerative colitis) and leprosy.

Disease	Number of Genes		Enrichment (fold)	*P*
	Total	Shared		
IBD	146	11	98.5	$< 1.0 \times 10^{-6}$
Crohn's disease	120	10	109.1	$< 1.0 \times 10^{-6}$
Ulcerative colitis	99	5	66.3	$< 1.0 \times 10^{-6}$
Leprosy	18	4	290.5	$< 1.0 \times 10^{-6}$

Supplementary Table 17: Association of susceptibility genes for Behçet's disease in other immune-related diseases and leprosy.

Locus	Marker	IBD	Pso	CeD	MS	AS	PBC	SLE	RA	T1D	SSc	SJO	JIA	CD[a]	UC[a]	Leprosy
MHC Class I	*HLA-B*51*															
IL1A-IL1B [b]	rs4402765															
MEFV	p.Met694Val															
KLRC4	rs2617170															
CEBPB-PTPN1	rs913678	**rs913678**													**rs913678**	
CCR1	rs7616215															
RIPK2	rs2230801															
LACC1 [c]	rs2121033	**rs3764147**												**rs3764147**		**rs3764147**
FUT2	rs601338	**rs516246**								**rs516246**				**rs516246**		
ADO-EGR2	rs7075773	rs10761659*												rs10761659*	rs10761659*	
ERAP1	rs17482078	rs1363907*	rs27432*			rs30187*								rs1363907*		
IL10	rs1518111															
IRF8	rs11117433						**rs11117433**									
IL12A	rs17810546			**rs17810546**												
IL23R-IL12RB2	rs1495965															
TNFAIP3 [b]	rs9494885															
STAT4	rs7574070															

Susceptibility loci with $P < 5\times10^{-8}$ for Behçet's disease and the corresponding effect of these markers in other immune related diseases are shown in the table[1-10,21-45]. Comparisons of the effect directions between disease-associated markers are shown by color, where pink indicates concordance of risk alleles between diseases and blue indicates discordance of risk alleles. Grey boxes mark diseases that share risk loci with Behçet's disease, but for which no commonality between markers associated with the two diseases could be identified. In cases where disease-associated markers were different, the alleles used for concordance analyses were defined by MAF for markers with high LD ($r^2>0.8$) or by eQTL directional concordance (increasing or decreasing gene expression) of the disease risk alleles for markers identified as eQTLs (bold markers mark alleles identified by MAF; asterisks mark alleles identified by eQTL directional concordance).

[a]The subgroups of inflammatory bowel disease, Crohn's disease and ulcerative colitis, are separately displayed.

[b]*IL1A-IL1B* and *TNFAIP3* showed genome-wide significance in a single population and has not been replicated in independent cohorts.

[c]*LACC1* was identified in Mendelian systemic JIA[44] and CD families[45]

IBD, inflammatory bowel disease; Pso, psoriasis; CeD, celiac disease; MS, multiple sclerosis; AS, ankylosing spondylitis; PBC, primary biliary cirrhosis; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; T1D, type 1 diabetes; SSc, systemic sclerosis; SJO, Sjögren's syndrome; JIA, juvenile idiopathic arthritis; CD, Crohn's disease; UC, ulcerative colitis

Supplementary Table 18: Pathway analysis for 21 genes associated with Behçet's disease.

Rank	Pathway	Count	Genes	$P_{corrected}$
1	defense response	11	*KLRC4, CEBPB, IL23R, MEFV, CCR1, IL12A, IL1B, RIPK2, HLA-B, IL10, IL1A*	1.50E-06
2	inflammatory response	8	*CEBPB, IL23R, MEFV, CCR1, IL1B, RIPK2, IL10, IL1A*	3.70E-05
3	immune response	10	*CEBPB, IL23R, CCR1, IRF8, IL12A, ERAP1, IL1B, HLA-B, IL10, IL1A*	4.20E-05
4	response to bacterium	6	*IL12RB2, IL12A, ERAP1, IL1B, RIPK2, IL10*	4.50E-04
5	response to wounding	8	*CEBPB, IL23R, MEFV, CCR1, IL1B, RIPK2, IL10, IL1A*	4.90E-04
6	response to molecule of bacterial origin	5	*IL12RB2, IL12A, IL1B, RIPK2, IL10*	5.10E-04
7	regulation of cytokine production	6	*CEBPB, IL12A, IL1B, RIPK2, IL10, IL1A*	5.30E-04
8	anti-apoptosis	6	*CEBPB, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	5.50E-04
9	response to lipopolysaccharide	5	*IL12RB2, IL12A, IL1B, RIPK2, IL10*	5.70E-04
10	regulation of interleukin-6 production	4	*CEBPB, IL1B, RIPK2, IL10*	0.00110
11	regulation of T cell proliferation	4	*IL12A, IL1B, RIPK2, IL10*	0.0050
12	negative regulation of cell death	6	*CEBPB, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.0051
13	cytokine-mediated signaling pathway	4	*STAT4, CCR1, IL1B, IL1A*	0.0052
14	negative regulation of programmed cell death	6	*CEBPB, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.0055
15	negative regulation of apoptosis	6	*CEBPB, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.0055
16	regulation of cytokine biosynthetic process	4	*CEBPB, IL1B, IL10, IL1A*	0.0058
17	regulation of mononuclear cell proliferation	4	*IL12A, IL1B, RIPK2, IL10*	0.0075
18	regulation of leukocyte proliferation	4	*IL12A, IL1B, RIPK2, IL10*	0.0075
19	regulation of lymphocyte proliferation	4	*IL12A, IL1B, RIPK2, IL10*	0.0077
20	positive regulation of cytokine production	4	*IL12A, IL1B, RIPK2, IL1A*	0.0087
21	response to organic substance	7	*IL12RB2, EGR2, IL12A, IL1B, RIPK2, PTPN1, IL10*	0.0110
22	positive regulation of angiogenesis	3	*ERAP1, IL1B, IL1A*	0.017
23	regulation of T cell activation	4	*IL12A, IL1B, RIPK2, IL10*	0.017
24	regulation of cell death	7	*CEBPB, IL12A, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.017
25	regulation of apoptosis	7	*CEBPB, IL12A, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.017
26	regulation of programmed cell death	7	*CEBPB, IL12A, IL1B, RIPK2, TNFAIP3, IL10, IL1A*	0.017
27	regulation of interleukin-2 production	3	*IL1B, RIPK2, IL1A*	0.020
28	regulation of lymphocyte activation	4	*IL12A, IL1B, RIPK2, IL10*	0.026
29	positive regulation of T cell proliferation	3	*IL12A, IL1B, RIPK2*	0.031
30	acute-phase response	3	*CEBPB, IL1B, IL1A*	0.031
31	regulation of leukocyte activation	4	*IL12A, IL1B, RIPK2, IL10*	0.032
32	regulation of cell activation	4	*IL12A, IL1B, RIPK2, IL10*	0.036

Supplementary Table 19: International Criteria for Behçet's disease

Sign/symptom	Points
Ocular lesions	2
Genital aphthous	2
Oral aphthous	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test[a]	1

Scoring ≥ 4 indicates Behçet's disease

[a]Pathergy test is optional.

Supplementary Table 20: Japanese Behçet's disease criteria

Major symptom
Recurrent aphthous ulcerlations of the oral mucous membrane
Skin lesions
Ocular symptoms
Genital ulcers
Minor symptom
Arthritis
Epididymitis
Gastrointestinal lesions
Vascular lesions
Central nervous system symptoms

(1) three major symptoms or two major and two minor symptoms; or (2) typical ocular symptoms and another major symptom or two minor symptoms that appear during the clinical course.

Supplementary Table 21: Characteristics of Turkish, Iranian and Japanese populations.

Characteristics	Discovery	Replication			
	Turkish	Iranian		Japanese	
N (cases / controls)	1900 / 1779	982 / 826		608 / 737	
Male / Female (%)	53.4 / 46.6	52.2 / 47.8	*NS*	59.7 / 40.3	*NS*
Onset age, mean ± SD	38.7 ± 11.6	32.1 ± 9.1	*	33.7 ± 10.4	*
Recurrent oral aphthous ulcers (%)	99.8	98.9	*	98.1	*
Uveitis (%)	39.4	56.3	*	86.9	*
Genital ulcers (%)	77.8	62.8	*	60.6	*
Skin lesions (%)	87.2	52.4	*	86.6	*NS*
Pathergy reaction (%)	67.6	45.5	*	55.9	*NS*
Arthritis (%)	45.3	19.1	*	40.7	*NS*
Vascular involvement (%)	23.2	5.2	*	4.5	*
Neurologic involvement (%)	7.4	6.2	*NS*	6.3	*NS*
Intestinal involvement (%)	1.3	4.1	*	14.9	*
Positive family history (%)	19.2	8.6	*	3.2	*

*P < 0.05 in comparison between Turkish and replication collections.

NS , No significance

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