Supplementary Information for

Genome-wide association analysis identifies new susceptibility loci for Behçet's disease and epistasis between *HLA-B*51* and *ERAP1*

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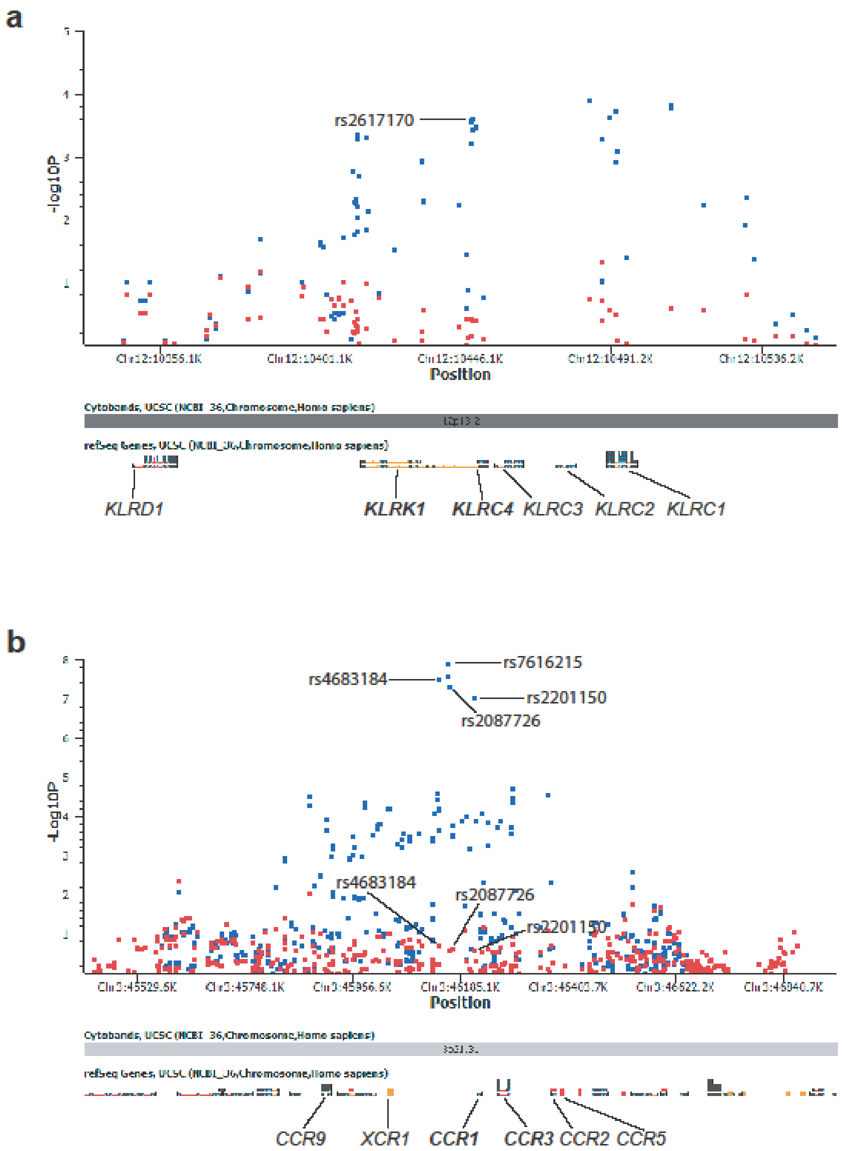
Supplementary Figure 1.

Conditional regression analysis of the *KLRK1-KLRC1* and the *CCR1-CCR3* loci.



Conditional regression analysis with covariates (**a**) rs2617170 in the *KLRK1-KLRC1* locus, and (**b**) rs7616215 in the *CCR1-CCR3* locus. $-\log_{10}P$ values are shown. Blue and red dots represent values before and after the conditioning, respectively.

Supplementary Table 1. SNP associations with $p<3x10^{-5}$ determined from the imputed genotype data in Turkish GWAS samples.

Marker	Chromosome	Position	Chi-Squared P	Original GWAS Chi-Squared P	Gene	Odds Ratio
rs6660226	1	67517189	1.08E-05		*IL23R-IL12RB2*	0.771
rs924080	1	67532728	5.36E-06	5.35E-06	*IL23R-IL12RB2*	0.764
rs3024490	1	205011934	3.02E-07	2.22E-07	*IL10*	1.357
rs1800871	1	205013257	3.02E-07		*IL10*	1.357
rs7572482	2	191723317	2.92E-05	3.18E-05	*STAT4*	1.269
rs10177805	2	235090172	2.49E-05		*ARL4C*	0.642
rs4678929	3	33388267	1.73E-05		*FBXL2*	0.719
rs2291897	3	33394426	1.47E-05	1.82E-05	*FBXL2*	0.717
rs4045539	3	33396182	1.56E-05		*UBP1*	0.718
rs1807844	3	33447941	2.13E-05	5.56E-05	*UBP1*	0.722
rs1357540	3	33454986	2.13E-05	2.69E-05	*UBP1*	0.722
rs6781484	3	33520789	4.66E-06		*CLASP2*	0.728
rs12487660	3	33567576	2.90E-05	2.70E-05	*CLASP2*	0.755
rs10510749	3	46155420	2.63E-05	4.22E-05	*CCR1-CCR3*	0.694
rs7616215	3	46180690	1.29E-08		*CCR1-CCR3*	0.702
rs9990343	3	46314816	1.87E-05	2.76E-05	*CCR1-CCR3*	0.770
rs11706279	3	71600333	9.30E-06		*FOXP1*	1.291
rs9819066	3	71605800	7.07E-06	4.55E-06	*FOXP1*	1.300
rs6549391	3	71612605	1.32E-05		*FOXP1*	1.302
rs9828629	3	71613036	1.42E-05	8.89E-06	*FOXP1*	1.289
rs6789751	3	71629434	1.15E-05		*FOXP1*	1.304
rs11720121	3	71677948	2.76E-05	1.28E-05	*FOXP1*	1.285
rs6549400	3	71689156	1.85E-05	8.46E-06	*FOXP1*	1.292
rs10049211	3	72597366	5.11E-06	5.35E-06	*RYBP*	0.768
rs17809756	3	161112778	1.20E-05		*IL12A*	1.637
rs17810546	3	161147744	1.20E-05	1.49E-05	*IL12A*	1.637
rs7634425	3	184503286	2.63E-05	2.97E-05	*MCF2L2*	0.760
rs1010769	3	184507213	2.26E-05		*MCF2L2*	0.759
rs936551	4	811490	1.11E-07	5.29E-08	*CPLX1*	0.739
rs2018601	4	136913913	2.36E-05		*none*	0.786
rs1869947	4	154862953	2.41E-06		*RNF175*	1.623
rs1495714	4	177074783	1.78E-05	1.93E-05	*GPM6A*	1.287
rs4690647	4	177109914	1.10E-05	1.13E-05	*GPM6A*	1.288
rs7731137	5	153985847	1.73E-05	9.50E-05	*LARP1*	1.291
rs10486156	7	7315158	2.15E-06	3.69E-06	*COL28A1-C1GALT1*	0.709
rs13247109	7	111565661	1.75E-05		*DOCK4*	0.638

rs13232973	7	111565822	2.26E-05		*DOCK4*	0.642
rs7004739	8	126397565	2.49E-05	2.14E-05	*NSMCE2*	1.271
rs17303101	9	118221615	1.04E-05		*ASTN2*	1.320
rs17220352	9	118287880	6.61E-06		*ASTN2*	1.389
rs488709	9	137699712	2.80E-05		*LCN9*	0.648
rs10898549	11	86281138	1.65E-05		*FZD4-PRSS23*	0.709
rs2617150*	12	10423701	1.20E-05		*KLRK1*	0.630
rs7295696	12	116915710	2.21E-05	1.77E-05	*KSR2-RFC5*	0.782
rs3764147	13	43355925	8.55E-06	7.36E-06	*LACC1*	0.748
rs1373904	13	43373398	7.78E-06		*LACC1*	0.749
rs1041167	13	45518136	2.55E-05		*ZC3H13*	0.750
rs8040564	15	51915197	2.92E-05		*WDR72*	1.271
rs7165549	15	51916365	1.14E-05		*WDR72*	1.287
rs9952236	18	48489851	2.39E-05		*DCC*	1.336

*SNP association data from the Japanese BD GWAS.

Supplementary Table 2. Association of 22 selected variants in Turkish replication samples (838 cases and 630 controls).

Marker	Chromosome	Position	Chi-Squared P	Loci*	Odds Ratio
rs7574070†	**2**	**191718733**	**1.2E-05**	***STAT4***	**1.337**
rs2291897	3	33394426	0.287	*FBXL2-CLASP2*	0.904
rs6781484	3	33520789	0.321	*FBXL2-CLASP2*	0.940
rs7616215	**3**	**46180690**	**1.1E-05**	***CCR1-CCR3***	**0.70**
rs9819066	3	71605800	0.621	*FOXP1*	1.040
rs10049211	3	72597366	0.414	*RYBP*	1.064
rs17809756	3	161112778	0.019	*IL12A*	1.424
rs17810546	**3**	**161147744**	**0.020**	***IL12A***	**1.414**
rs1010769	3	184507213	0.636	*MCF2L2*	1.044
rs936551	4	811490	0.316	*CPLX1*	0.927
rs1869947	4	154862953	0.039	*RNF175*	1.304
rs4690647	4	177109914	0.351	*GPM6A*	1.074
rs7731137	5	153985847	0.646	*LARP1*	1.036
rs10486156	7	7315158	0.274	*COL28A1-C1GALT1*	0.902
rs13247109	7	111565661	0.866	*DOCK4*	0.980
rs17220352	9	118287880	0.819	*ASTN2*	1.022
rs10898549	11	86281138	0.520	*FZD4-PRSS23*	1.068
rs2617170‡	**12**	**10452224**	**7.6E-04**	***KLRC4***	**0.767**
rs7295696	12	116915710	0.847	*KSR2-RFC5*	0.986
rs1373904	13	43373398	0.240	*LACC1*	0.904
rs7165549	15	51916365	0.673	*WDR72*	1.033
rs9952236	18	48489851	0.312	*DCC*	1.095

*Loci highlighted in **bold** were selected for validation and fine-map analysis.

†Surrogate marker for imputed *STAT4* SNP rs7572482.

‡Surrogate marker for Japanese BD GWAS *KLRK1* SNP rs2617150.

Supplementary Table 3. Cochran-Mantel-Haenszel meta-analysis of BD associated loci with Japanese cases restricted to those fulfilling the International Study Group diagnostic criteria for Behçet's disease.

	Series*	**Method**	**Diagnosis**	**Subject *n***	**C**	**T**	**MAF(%)**	**OR (95% CI)**	***P* value**
CCR1-CCR3 **rs7616215**	Turkish Discovery	TOF-MS	BD	1180	630	1730	27	0.71 (0.63-0.80)	2.17x10^{-8}
			Control	1258	855	1661	34		
	Japanese replication	Affy 500K	BD	494	126	862	12.8	0.79 (0.66-1.01)	0.057
			Control	692	215	1169	15.5		
	Turkish replication	TOF-MS	BD	816	441	1191	27	0.70 (0.60-0.82)	1.09x10^{-5}
			Control	630	436	824	34.6		
	Combined		**BD**	**2490**				**0.72 (0.66-0.78)**	**2.38x10^{-13}**
			Control	**2580**					
	Series	**Method**	**Diagnosis**	**Subject *n***	**A**	**C**	**MAF(%)**	**OR (95% CI)**	***P* value**
STAT4 **rs7574070**	Turkish Discovery	TOF-MS	BD	1166	1128	1204	48.4	1.28 (1.14-1.43)	1.92x10^{-5}
			Control	1250	1059	1441	42.4		
	Japanese replication	Affy 500K	BD	433	454	412	52.4	1.23 (1.01-1.37)	0.015
			Control	716	676	756	47.2		
	Turkish replication	TOF-MS	BD	815	803	827	49.3	1.34 (1.15-1.55)	1.12x10^{-4}
			Control	630	530	730	42.1		
	Combined		**BD**	**2414**				**1.28 (1.18-1.39)**	**4.07x10^{-10}**
			Control	**2596**					
	Series	**Method**	**Diagnosis**	**Subject *n***	**T**	**C**	**MAF(%)**	**OR (95% CI)**	***P* value**
KLRC4 **rs2617170 (KLCR4 p.Asn104Ser)**	Turkish Discovery	TOF-MS	BD	1144	734	1554	32.1	0.80 (0.71-0.90)	2.54x10^{-4}
			Control	1257	933	1581	37.1		
	Japanese replication	Affy 500K	BD	470	302	638	32.1	0.79 (0.66-0.94)	8.26x10^{-3}
			Control	657	493	821	37.5		
	Turkish replication	TaqMan	BD	821	510	1132	31.1	0.77 (0.66-0.89)	7.61x10^{-4}
			Control	628	465	791	37		
	Combined		**BD**	**2435**				**0.79 (0.72-0.85)**	**1.03x10^{-8}**
			Control	**2542**					

*TOF-MS, time-of-flight mass-spectrometry; MAF, minor allele frequency, OR, odds ratio; 95%CI, 95% confidence interval.

Meta-analysis results are denoted in **bold**.

Supplementary Table 4. Cochran-Mantel-Haenszel meta-analysis of *ERAP1* non-synonymous coding variant rs17482078 in BD (cases with and without uveitis combined).

	Series*	**Method**	**Diagnosis**	**Subject *n***	**TT**	**CC+CT**	**TT(%)**	**OR (95% CI)**	***P* value**
ERAP1 **rs17482078 (ERAP1 p.Arg725Gln)**	Turkish Discovery	TOF-MS	BD	1180	60	1120	5.08	2.73 (2.45-7.23)	2.14×10^{-5}
			Control	1245	24	1221	1.93		
	Turkish replication	TOF-MS	BD	837	37	800	4.42	4.12 (2.46-11.7)	2.35×10^{-4}
			Control	630	7	623	1.11		
	Combined		**BD**	**2017**				**3.08 (2.04-4.65)**	$\mathbf{4.35\times10^{-8}}$
			Control	**1875**					

*Meta-analysis result is denoted in **bold**.

Supplementary Table 5. SNP associations in *IL12A* and *ERAP1* loci in Japanese GWAS samples.

Marker	Chromosome	Position	Chi-Squared P	MAF	Gene	Odds Ratio
rs17753629	3	161130149	7.50E-01	0.113	*IL12A*	1.04
rs6441282	3	161181771	1.69E-01	0.219	*IL12A*	1.15
rs2133310	3	161199046	5.93E-01	0.147	*IL12A*	1.06
rs545232	3	161214725	1.03E-01	0.197	*IL12A*	1.18
rs2290674	5	96110187	5.39E-01	0.060	*ERAP1*	1.11
rs17401719	5	96114802	5.63E-01	0.084	*ERAP1*	1.09
rs27038	5	96138710	6.19E-01	0.229	*ERAP1*	1.05
rs28050	5	96171180	2.22E-01	0.286	*ERAP1*	0.89
rs34735	5	96191820	9.01E-01	0.368	*ERAP1*	1.01
rs2042382	5	96214448	3.33E-01	0.139	*ERAP1*	1.12
rs2927615	5	96223958	7.91E-01	0.020	*ERAP1*	1.08
rs1230358	5	96237497	2.14E-01	0.311	*ERAP1*	0.89
rs3733904	5	96241929	2.46E-01	0.132	*ERAP1*	0.87
rs2549779	5	96242143	8.02E-01	0.440	*ERAP1*	0.98
rs2549780	5	96242540	5.01E-01	0.491	*ERAP1*	0.95
rs11135484	5	96247645	1.91E-02	0.489	*ERAP1*	0.82
rs7733301	5	96289346	9.92E-02	0.124	*ERAP1*	0.81

Supplementary Table 6. Quality scores for the Turkish GWAS imputation.

Chromosome	Median Quality	Median Rsq	% Quality>0.9	% Rsq>0.3	Median dose R2
1	0.976	0.916	80.5	95.3	0.99988
2	0.973	0.911	79.9	95.9	0.99973
3	0.975	0.916	80.4	96.1	0.99978
4	0.974	0.911	78.6	95.3	0.99987
5	0.973	0.906	78.6	95.5	0.99982
6	0.988	0.957	85.5	96.9	0.99988
7	0.972	0.907	78.3	95.3	0.99980
8	0.977	0.925	82.7	96.9	0.99970
9	0.978	0.924	81.6	95.8	0.99962
10	0.971	0.901	78.6	95.5	0.99982
11	0.973	0.907	78.4	95.5	0.99982
12	0.974	0.912	78.6	95.0	0.99986
13	0.972	0.905	78.5	95.4	0.99989
14	0.971	0.899	77.9	95.0	0.99986
15	0.967	0.880	74.5	93.0	0.99969
16	0.960	0.860	72.5	93.0	0.99963
17	0.969	0.894	75.1	93.1	0.99985
18	0.976	0.919	79.3	95.3	0.99984
19	0.970	0.886	73.6	91.1	0.99989
20	0.967	0.884	74.5	93.3	0.99982
21	0.980	0.937	82.9	95.7	0.99978
22	0.972	0.905	78.5	95.4	0.99982

Quality indicates the average posterior probability for the most likely genotype.

Rsq indicates the squared correlation between imputed and true genotypes.