

**Meta-analysis of genome scans and replication identify *CD6*, *IRF8*, and *TNFRSF1A*
as novel multiple sclerosis susceptibility loci**

Supplementary Materials

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I. Supplementary Tables

Supplementary Table 1a. Demographic profile of the MS subjects used in the meta-analysis

Subject Source	IMSGC	IMSGC	BWH	Gene MSA	Gene MSA	Gene MSA
Analysis stratum	UK	US	US	CH	NL	US
Number of Cases	453	342	860	230	253	486
Female:Male ratio	3.0:1.0	3.2:1.0	3.2:1.0	2.8:1.0	2.9:1.0	3.1:1.0
Mean Disease Duration, years (range)	11 (0-40)	16 (<1-36)	14 (2-53)	12 (<1-58)	13 (<1-39)	15 (1-59)
Mean age at onset, years (range)	27 (10-48)	29 (11-50)	33 (9-60)	33 (8-59)	33 (13-71)	33 (1-70)
Disease course, n (%)						
“Bout onset”	421 (93%)	324 (95%)	824 (96%)	183 (77%)	133 (84%)	470 (78%)
Relapse Remitting	269 (59%)	255 (75%)	641 (75%)	142 (60%)	111 (70%)	362 (60%)
Secondary Progressive	152 (34%)	69 (20%)	183 (21%)	41 (17%)	22 (14%)	108 (18%)
Primary Progressive	32 (7%)	17 (5%)	5 (1%)	22 (9%)	19 (12)	36 (6%)
Clinically Isolated Syndrome	0	0	26 (3%)	26 (11%)	7 (4)	76 (13%)
Unknown	0	1 (<1%)	5 (1%)	7 (3%)	0	23 (4%)

Glossary: BWH = Brigham & Women’s Hospital, Boston; CH = Switzerland; NA = not available; NL = Netherlands; UK = United kingdom; US = United States. “Bout onset MS” is used here to describe subjects whose disease course started with discrete attacks of inflammatory demyelination. Each subject with MS is used only once in our analyses.

Supplementary Table 1b. Demographic profile of subjects with MS used in the replication study

Analysis stratum	US					UK	
	BWH	WU	ACP	UCSF	RUSH	UC	1958 BC
Number of controls	407 ¹	13	35	142	489	-	1030
Number of Cases	227	152	597	407	-	831	-
Female:Male ratio	2.8:1.0	3.1:1.0	3.1:1.0	5.6:1.0	-	2.28:1.0	-
Mean Disease Duration, years (range)	12 (<1-58)	13 (<1-39)	15 (1-56)	12(<1-47)	-	14 (<1-54)	-
Mean age at onset, years (range)	33 (8-59)	33 (13-71)	33 (1-70)	42 (3-60)	-	32 (10-67)	-
Disease course, n (%)					-		-
“Bout onset”	178 (78%)	128 (84%)	463 (78%)	345 (85%)	-	732 (88%)	-
Relapse Remitting	136 (60%)	106 (70%)	358 (60%)	237 (58%)	-	NA ²	-
Secondary Progressive	42 (19%)	22 (14%)	105 (18%)	111 (27%)	-	NA ²	-
Primary Progressive	17 (8%)	17 (11%)	36 (6%)	23 (6%)	-	84 (10%)	-
Clinically Isolated Syndrome	25 (11%)	7 (4%)	75 (13%)	10 (2%)	-	0 (0%)	-
Unknown	7 (3%)	0	23 (4%)	26 (6%)	-	15 (2%)	-

¹ BWH controls – these subjects of European ancestry recruited in the Boston area include (1) unaffected spouses from our MS Genetics collections (n=14), (2) The BWH PhenoGenetic Project subjects (n=292), and healthy subjects from the HPCGG collection (n=101) (see methods for details). These subjects do not overlap with BWH control subjects used in the meta-analysis.

² NA – the breakdown of remitting relapsing and secondary progressive subjects is not available in this cohort.

Glossary: 1958 BC – 1958 birth cohort; ACP – Accelerated Cure Project; BWH – Brigham & Women’s Hospital; RUSH – RUSH University; UC – University of Cambridge, UK; UCSF – University California, San Francisco; UK – United Kingdom; US – United States; WU – Washington University, St. Louis

Supplementary Table 1c. Demographic features of MS and CIS subjects involved in the analysis of RNA expression in PBMCs.

	GA Treated subjects	IFNβ treated subjects	Untreated subjects
Female:Male ratio (n)	51:13	69:25	73:9
Self-declared European ancestry	100%	100%	100%
Mean disease duration at time of sampling (range)	6 (0-30)	8 (0-43)	8 (0-38)
Mean age at onset, years (range)	36 (17-57)	35 (17-56)	36 (17-63)
Disease course, n			
Relapse Remitting	63	93	74
Clinically Isolated Syndrome	1	1	8

Supplementary Table 2. SNPs included in the replication panel.

SNP	CHR	BP	MAF _{CEU}	P_{meta}	Genes	Selection criterion
rs12025416	1	116750329	0.18	4.74×10^{-8}	<i>CD58</i>	Top 100 loci
rs1800693	12	6310270	0.48	7.52×10^{-8}	<i>PLEKHG6, TNFRSF1A, SCNN1A, LTBR</i>	Top 100 loci
rs9596270	13	49740441	0.04	8.26×10^{-8}	NA	Top 100 loci
rs6896969	5	40460183	0.42	1.44×10^{-7}	<i>PTGER4</i>	Top 100 loci
rs17824933	11	60517188	0.19	2.32×10^{-7}	<i>TMEM132A, SLC15A3, CD6</i>	Top 100 loci
rs1790100	12	122181605	0.20	2.74×10^{-7}	<i>MPHOSPH9</i>	Top 100 loci
rs10244467	7	22584456	0.05	3.37×10^{-7}	<i>IL6, TOMM7</i>	Top 100 loci
rs1356122	3	155666264	0.12	3.78×10^{-7}	<i>GPR149</i>	Top 100 loci
rs17086658	4	57010834	0.06	8.13×10^{-7}	<i>KIAA1211, AASDH</i>	Top 100 loci
rs11870121	17	71370533	0.23	8.55×10^{-7}	NA	Top 100 loci
rs2104286	10	6139051	0.23	1.52×10^{-6}	<i>IL2RA, RBM17</i>	Top 100 loci
rs11230555	11	60519710	0.13	1.64×10^{-6}	<i>TMEM132A, SLC15A3, CD6</i>	Top 100 loci
rs426921	18	63402133	0.16	1.71×10^{-6}	NA	Top 100 loci
rs10802786	1	232026264	0.02	1.91×10^{-6}	NA	Top 100 loci
rs10815231	9	547015	0.17	2.53×10^{-6}	<i>KANK1</i>	Top 100 loci
rs931555	5	35839334	0.23	2.73×10^{-6}	<i>SPEF2, IL7R</i>	Top 100 loci
rs9901869	17	42930205	0.49	2.85×10^{-6}	<i>C17orf57, NPEPPS</i>	Top 100 loci
rs2853694	5	158681666	0.46	3.35×10^{-6}	<i>UBLCP1, IL12B</i>	Top 100 loci
rs2839578	21	43025706	0.39	3.49×10^{-6}	<i>PDE9A</i>	Top 100 loci
rs1017429	4	42954446	0.29	3.90×10^{-6}	NA	Top 100 loci
rs4668993	2	15902899	0.36	5.13×10^{-6}	NA	Top 100 loci
rs11772925	7	149865757	0.22	5.32×10^{-6}	<i>GIMAP2, GIMAP1, GIMAP5</i>	Top 100 loci
rs11860603	16	11072518	0.21	5.62×10^{-6}	<i>CLEC16A</i>	Top 100 loci
rs11736632	4	57013263	0.04	5.67×10^{-6}	<i>KIAA1211, AASDH</i>	Top 100 loci
rs8023613	15	30739485	0.25	6.60×10^{-6}	<i>ARHGAP11A, SCG5, GREM1</i>	Top 100 loci
rs1376041	16	56247384	0.28	7.25×10^{-6}	<i>GPR56, GPR97, CCDC135</i>	Top 100 loci
rs1182580	1	104158803	0.48	7.62×10^{-6}	NA	Top 100 loci
rs479505	10	97350709	0.11	8.25×10^{-6}	<i>SORBS1, ALDH18A1</i>	Top 100 loci

rs201763	13	49917022	0.21	8.32x10 ⁻⁶	NA	Top 100 loci
rs7814564	8	26835382	0.03	8.55x10 ⁻⁶	ADRA1A	Top 100 loci
rs7517186	1	41573114	0.43	8.83x10 ⁻⁶	EDN2	Top 100 loci
rs11667601	19	16531660	0.11	9.13x10 ⁻⁶	C19orf44,CHERP,SLC35E1,MED26	Top 100 loci
rs1250540	10	80706013	0.40	9.89x10 ⁻⁶	ZMIZ1	Top 100 loci
rs11604291	11	72680764	0.02	1.02x10 ⁻⁵	P2RY2,P2RY6,ARHGEF17	Top 100 loci
rs10203141	2	179015804	0.43	1.04x10 ⁻⁵	OSBPL6	Top 100 loci
rs6699421	1	143483220	0.13	1.06x10 ⁻⁵	NA	Top 100 loci
rs10191601	2	204280876	0.37	1.08x10 ⁻⁵	RAPH1	Top 100 loci
rs9924445	16	85304319	0.03	1.09x10 ⁻⁵	NA	Top 100 loci
rs2293152	17	37735055	0.40	1.13x10 ⁻⁵	STAT5B,STAT5A,STAT3	Top 100 loci
rs1000361	3	27785323	0.38	1.26x10 ⁻⁵	EOMES	Top 100 loci
rs2726453	4	106677440	0.45	1.28x10 ⁻⁵	PPA2	Top 100 loci
rs1611927	8	4586651	0.19	1.36x10 ⁻⁵	CSMD1	Top 100 loci
rs1035946	16	24881927	0.18	1.38x10 ⁻⁵	SLC5A11,ARHGAP17	Top 100 loci
rs17581498	17	71305642	0.12	1.45x10 ⁻⁵	ITGB4,GALK1,H3F3B,UNK,UNC13D,WBP2	Top 100 loci
rs4737206	8	66292544	0.31	1.53x10 ⁻⁵	NA	Top 100 loci
rs11023151	11	14202675	0.15	1.54x10 ⁻⁵	SPON1,RRAS2	Top 100 loci
rs11256497	10	6127800	0.37	1.60x10 ⁻⁵	IL2RA,RBM17	Top 100 loci
rs711663	3	4437774	0.02	1.63x10 ⁻⁵	SUMF1	Top 100 loci
rs1658957	9	6662097	0.50	1.68x10 ⁻⁵	GLDC	Top 100 loci
rs12300846	12	9634751	0.35	1.85x10 ⁻⁵	KLRB1	Top 100 loci
rs254837	5	158615778	0.07	1.96x10 ⁻⁵	RNF145,UBLCP1,IL12B	Top 100 loci
rs13073434	3	155593744	0.04	2.02x10 ⁻⁵	GPR149	Top 100 loci
rs6479810	10	63870066	0.15	2.26x10 ⁻⁵	NA	Top 100 loci
rs16971851	15	31599801	0.27	2.32x10 ⁻⁵	RYR3	Top 100 loci
rs17760402	18	53915666	0.03	2.38x10 ⁻⁵	NEDD4L	Top 100 loci
rs11164814	1	92973394	0.23	2.44x10 ⁻⁵	EVI5,RPL5,FAM69A	Top 100 loci
rs2357954	2	54274088	0.42	2.54x10 ⁻⁵	ACYP2	Top 100 loci
rs7184083	16	11135415	0.40	2.64x10 ⁻⁵	CLEC16A	Top 100 loci
rs7814314	8	136905069	0.25	2.79x10 ⁻⁵	NA	Top 100 loci

rs1193335	7	127210755	0.35	3.04x10 ⁻⁵	<i>C7orf54,LRRRC4,SND1</i>	Top 100 loci
rs17445836	16	84575164	0.27	3.05x10 ⁻⁵	<i>IRF8</i>	Top 100 loci
rs10892613	11	120063294	0.14	3.06x10 ⁻⁵	<i>GRIK4</i>	Top 100 loci
rs10148925	14	59157663	0.06	3.07x10 ⁻⁵	<i>RTN1</i>	Top 100 loci
rs11811702	1	33019276	0.28	3.07x10 ⁻⁵	<i>S100PBP,FNDC5,HPCA,TMEM54,RNF19B</i>	Top 100 loci
rs7089861	10	6150332	0.37	3.11x10 ⁻⁵	<i>IL2RA,RBM17</i>	Top 100 loci
rs1420810	14	86572905	0.10	3.47x10 ⁻⁵	NA	Top 100 loci
rs10503052	18	57050613	0.32	3.50x10 ⁻⁵	NA	Top 100 loci
rs1193345	1	17659020	0.07	3.56x10 ⁻⁵	<i>ARHGEF10L</i>	Top 100 loci
rs10775336	16	56103237	0.06	3.60x10 ⁻⁵	<i>COQ9,POLR2C,DOK4,CCDC102A,GPR114</i>	Top 100 loci
rs4821818	22	37490539	0.12	3.61x10 ⁻⁵	<i>GTPBP1,UNC84B,DNAL4,NPTXR</i>	Top 100 loci
rs1862511	19	6537268	0.33	3.69x10 ⁻⁵	<i>TNFSF9,CD70</i>	Top 100 loci
rs17179734	14	71670843	0.04	3.69x10 ⁻⁵	<i>RGS6</i>	Top 100 loci
rs135382	22	47118481	0.16	3.73x10 ⁻⁵	NA	Top 100 loci
rs2214935	7	22068600	0.29	3.78x10 ⁻⁵	<i>RAPGEF5</i>	Top 100 loci
rs1404773	2	215964838	0.18	3.81x10 ⁻⁵	<i>ATIC</i>	Top 100 loci
rs11643026	16	62173482	0.03	3.88x10 ⁻⁵	NA	Top 100 loci
rs6583176	3	198013888	0.21	3.89x10 ⁻⁵	<i>PAK2</i>	Top 100 loci
rs154929	18	56968545	0.33	3.91x10 ⁻⁵	NA	Top 100 loci
rs2492853	9	88061478	0.27	3.95x10 ⁻⁵	NA	Top 100 loci
rs11658169	17	19812514	0.40	3.99x10 ⁻⁵	<i>AKAP10</i>	Top 100 loci
rs1519529	2	136807989	0.24	4.06x10 ⁻⁵	NA	Top 100 loci
rs4468527	14	51394881	0.07	4.09x10 ⁻⁵	<i>GNG2</i>	Top 100 loci
rs7314705	12	30090640	0.08	4.10x10 ⁻⁵	NA	Top 100 loci
rs11580092	1	58546047	0.31	4.13x10 ⁻⁵	NA	Top 100 loci
rs4606981	2	133161908	0.25	4.14x10 ⁻⁵	<i>GPR39</i>	Top 100 loci
rs17782451	16	87006977	0.03	4.16x10 ⁻⁵	<i>ZFPM1</i>	Top 100 loci
rs158968	5	57977726	0.16	4.18x10 ⁻⁵	<i>RAB3C</i>	Top 100 loci
rs395561	5	106889874	0.44	4.22x10 ⁻⁵	<i>EFNA5</i>	Top 100 loci
rs16967121	15	36710299	0.08	4.26x10 ⁻⁵	NA	Top 100 loci
rs17280766	7	13410609	0.11	4.27x10 ⁻⁵	NA	Top 100 loci

rs7622984	3	30183339	0.03	4.30x10 ⁻⁵	NA	Top 100 loci
rs4976682	5	176658608	0.08	4.39x10 ⁻⁵	<i>NSD1,RAB24,PRELID1,MXD3,LMAN2,RGS14</i>	Top 100 loci
rs6131888	20	16925054	0.38	4.43x10 ⁻⁵	NA	Top 100 loci
rs741195	22	19318320	0.30	4.45x10 ⁻⁵	<i>MED15</i>	Top 100 loci
rs12260682	10	126644390	0.05	4.54x10 ⁻⁵	<i>ZRANB1,CTBP2</i>	Top 100 loci
rs11704699	22	16144735	0.13	4.67x10 ⁻⁵	NA	Top 100 loci
rs536858	1	66485047	0.37	4.67x10 ⁻⁵	<i>PDE4B</i>	Top 100 loci
rs9940149	16	240642	0.19	4.88x10 ⁻⁵	<i>LUC7L,ITFG3,RGS11,ARHGDIG,PDIA2,AXIN1</i>	Top 100 loci
rs2022771	14	85999679	0.42	4.89x10 ⁻⁵	NA	Top 100 loci
rs9380353	6	4.9358023	0.01	7.98x10 ⁻⁷	<i>SYNGAP1</i>	candidate gene
rs892999	6	4.53196386	0.10	5.84x10 ⁻⁶	<i>TNFAIP3</i>	candidate gene
rs4149576	12	-4.53201476	0.50	5.84x10 ⁻⁶	<i>PLEKHG6,TNFRSF1A,SCNN1A,LTBR</i>	candidate gene
rs4239162	17	4.46025727	0.49	8.19x10 ⁻⁶	<i>TBX21</i>	candidate gene
rs12490899	3	-4.02659066	0.05	5.66x10 ⁻⁵	<i>TGFBR2</i>	candidate gene
rs4680534	3	3.9832558	0.26	6.80x10 ⁻⁵	<i>IL12A</i>	candidate gene
rs9621545	22	3.91774763	0.16	8.94x10 ⁻⁵	<i>SYN3</i>	candidate gene
rs6910219	6	-3.89874907	0.13	9.67x10 ⁻⁵	<i>SYNGAP1</i>	candidate gene
rs2760524	1	-3.8745058	0.19	0.000107	<i>RGS1</i>	candidate gene
rs1401884	16	3.85832945	0.25	0.000114	<i>IRF8</i>	candidate gene
rs187084	3	-3.84741066	0.31	0.000119	<i>TLR9</i>	candidate gene
rs3806680	3	-3.83709057	0.26	0.000125	<i>IL5RA</i>	candidate gene
rs6926566	6	-3.80337239	0.49	0.000143	<i>FYN</i>	candidate gene
rs13022141	2	3.7757472	0.22	0.000160	<i>CXCR4</i>	candidate gene
rs6732091	2	-3.75454028	0.39	0.000174	<i>CD28</i>	candidate gene
rs11165441	1	-3.68849054	0.17	0.000226	<i>TGFBR3</i>	candidate gene
rs12042693	1	3.65037616	0.07	0.000262	<i>CD247</i>	candidate gene
rs352074	6	3.62046123	0.19	0.000294	<i>MARCKS</i>	candidate gene
rs4678000	3	-3.59664401	0.35	0.000322	<i>CD86</i>	candidate gene
rs7232625	18	-3.56942573	0.23	0.000358	<i>BCL2</i>	candidate gene
rs17066096	6	-3.54356096	0.16	0.000395	<i>IL22RA2</i>	candidate gene
rs1699105	11	3.53205875	0.47	0.000412	<i>SORL1</i>	candidate gene

rs7132171	12	-3.51655461	0.43	0.000437	<i>LRRK2</i>	candidate gene
rs17239559	19	3.51637621	0.36	0.000437	<i>LILRB3,LILRA6,LILRB5</i>	candidate gene
rs2832359	21	3.42082542	0.11	0.000624	<i>GRIK1</i>	candidate gene
rs10758669	9	3.41947965	0.31	0.000627	<i>JAK2</i>	candidate gene
rs9347662	6	3.39209523	0.18	0.000694	<i>PARK2</i>	candidate gene
rs12913890	15	-3.32848956	0.50	0.000873	<i>RORA</i>	candidate gene
rs11088251	21	3.32481796	0.19	0.000885	<i>IFNAR1,IFNGR2</i>	candidate gene
rs12669882	7	3.31232375	0.04	0.000925	<i>DNAJB6</i>	candidate gene
rs9321619	6	-3.30980717	0.40	0.000934	<i>OLIG3</i>	candidate gene
rs2834044	21	-3.30486051	0.26	0.000950	<i>OLIG2</i>	candidate gene
rs2083914	8	6289562	0.18	0.00266	<i>ANGPT2,MCPH1</i>	nscSNP
rs2303759	19	54560863	0.31	0.00273	<i>SLC6A16,CD37,TEAD2,DKKL1,FLJ32658,PTH2</i>	nscSNP
rs11640138	16	11270230	0.34	0.00423	<i>SOCS1,TNP2,PRM3,PRM2,PRM1</i>	nscSNP
rs2236293	9	35831783	0.38	0.00513	<i>NPR2,SPAG8,HINT2,C9orf128,C9orf127,OR13J1</i>	nscSNP
rs6571751	14	20840570	0.43	0.00572	<i>HNRNPC,RPGRI1,SUPT16H</i>	nscSNP
rs3816800	15	23476187	0.41	0.00684	<i>ATP10A</i>	nscSNP
rs3814281	15	81296820	0.15	0.00801	<i>FSD2,WHDC1,HOMER2</i>	nscSNP
rs4792311	17	12855734	0.33	0.00867	<i>RICH2,ELAC2</i>	nscSNP
rs3135388	6	32521029	0.25	7.44x10 ⁻¹⁶⁴	<i>HLA DRB1*1501</i>	Known locus
rs2743951	6	29817213	0.50	7.38x10 ⁻¹¹	<i>HLA B*4402</i>	Known locus
rs2300747	1	116905738	0.13	2.44x10 ⁻⁷	<i>CD58</i>	Known locus
rs6897932	5	35910332	0.24	7.71x10 ⁻⁶	<i>IL7R</i>	Known locus
rs12708716	16	11087374	0.29	0.000170	<i>CLEC16A</i>	Known locus
rs10735781	1	92893695	0.33	0.00192	<i>EVI5</i>	Known locus
rs763361	18	65682622	0.48	0.157	<i>CD226</i>	Known locus
rs2049114	12	122182218	0.21	1.30x10 ⁻⁷	<i>MPHOSPH9</i>	Secondary Analysis
rs17765606	16	64540948	0.04	5.20x10 ⁻⁷	NA	Secondary Analysis
rs4368946	8	98497864	0.06	2.90x10 ⁻⁶	NA	Secondary Analysis
rs882300	2	136809987	0.48	8.30x10 ⁻⁶	<i>CXCR4</i>	Secondary Analysis
rs918434	19	52452069	0.38	1.10x10 ⁻⁵	<i>SAE1,BBC3,CCDC9,C5AR1</i>	Secondary Analysis
rs7217180	17	54979905	0.18	1.10x10 ⁻⁵	<i>DHX40</i>	Secondary Analysis

rs13251655	8	119829740	0.21	1.10x10 ⁻⁵	NA	Secondary Analysis
rs4668486	2	16193790	0.22	1.20x10 ⁻⁵	NA	Secondary Analysis
rs750780	11	33874170	0.17	1.20x10 ⁻⁵	LMO2	Secondary Analysis
rs11865121	16	11074189	0.22	1.30x10 ⁻⁵	CLEC16A	Secondary Analysis
rs6691787	1	68118647	0.23	1.30x10 ⁻⁵	NA	Secondary Analysis
rs2304494	17	37216477	0.09	1.60x10 ⁻⁵	JUP,SC65,FKBP10,NT5C3L,KLHL10,KLHL11	Secondary Analysis
rs7137953	12	119357405	0.13	1.60x10 ⁻⁵	COX6A1,TRIAP1,GATC,SFRS9,DYNLL1,COQ5	Secondary Analysis
rs12999011	2	190330293	0.16	1.60x10 ⁻⁵	SLC40A1,ASNSD1,ANKAR	Secondary Analysis
rs10454951	5	6305863	0.05	1.70x10 ⁻⁵	FLJ33360	Secondary Analysis
rs2325566	13	73281941	0.25	1.70x10 ⁻⁵	KLF12	Secondary Analysis
rs12419184	11	125561518	0.13	1.70x10 ⁻⁵	RPUSD4,FAM118B	Secondary Analysis
rs10507622	13	58443686	0.03	1.80x10 ⁻⁵	NA	Secondary Analysis
rs10885868	10	117912102	0.33	1.80x10 ⁻⁵	GFRA1	Secondary Analysis
rs6973638	7	15170510	0.40	1.90x10 ⁻⁵	TMEM195	Secondary Analysis
rs820240	17	71094622	0.15	1.90x10 ⁻⁵	LLGL2,RECQL5	Secondary Analysis
rs17304143	15	60364343	0.10	2.10x10 ⁻⁵	NA	Secondary Analysis
rs1294012	1	9219447	0.03	2.20x10 ⁻⁵	H6PD	Secondary Analysis
rs7349811	5	96513963	0.48	2.20x10 ⁻⁵	NA	Secondary Analysis
rs2277136	8	6322616	0.16	2.40x10 ⁻⁵	ANGPT2,MCPH1	Secondary Analysis
rs251921	16	13110329	0.45	2.40x10 ⁻⁵	NA	Secondary Analysis
rs1582844	2	153592544	0.02	2.40x10 ⁻⁵	NA	Secondary Analysis
rs2760524	1	189262205	0.19	2.40x10 ⁻⁵	RGS1	Secondary Analysis
rs927544	13	46354052	0.24	2.50x10 ⁻⁵	HTR2A	Secondary Analysis
rs17346755	5	58000989	0.13	2.50x10 ⁻⁵	RAB3C	Secondary Analysis
rs7311897	12	8911595	0.08	2.80x10 ⁻⁵	A2ML1,PHC1	Secondary Analysis
rs1880719	4	83974614	0.38	2.90x10 ⁻⁵	SCD5	Secondary Analysis
rs4740392	9	130894500	0.18	3.00x10 ⁻⁵	FIBCD1,LAMC3	Secondary Analysis
rs10822550	10	66863143	0.49	3.10x10 ⁻⁵	NA	Secondary Analysis
rs3794716	17	78152456	0.09	3.10x10 ⁻⁵	FOXK2,WDR45L,RAB40B	Secondary Analysis
rs4150894	8	86292120	0.03	3.20x10 ⁻⁵	LRRCC1,E2F5,C8orf59,CA13	Secondary Analysis
rs1838724	5	53277764	0.23	3.30x10 ⁻⁵	ARL15	Secondary Analysis

rs655763	11	108682027	0.23	3.30x10 ⁻⁵	NA	Secondary Analysis
rs10803554	2	137719928	0.47	3.30x10 ⁻⁵	<i>THSD7B</i>	Secondary Analysis
rs9586741	13	104537871	0.35	3.40x10 ⁻⁵	NA	Secondary Analysis
rs616582	2	111658226	0.38	3.40x10 ⁻⁵	<i>BCL2L11</i>	Secondary Analysis

Genes: All genes found within a segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP.

NA: not available - there is no gene found within the segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP

N.B. Within each SNP category, SNPs are ranked by P value. The P values reported for the “secondary analysis” SNPs are the P values derived from the analysis that includes a term for gender (see supplementary methods). The *IL2RA* locus SNP rs2104286 is a known association but was included into the replication panel as one of the top 100 loci SNPs.

Supplementary Table 3. Comprehensive results of the replication and joint analyses with the meta-analysis results.

CHR	SNP	A1	A2	BP	CHISQ	OR	L95	U95	MAF_USA	MAF_UK	$P_{\text{replication}}$	P_{meta}	P_{Joint}	Genes of interest
6	rs3135388	A	G	32521029	335.10	2.75	2.46	3.07	0.22	0.21	7.35×10^{-75}	7.44×10^{-164}	3.80×10^{-225}	<i>BTNL2,HLA-DRA</i>
6	rs2523393	G	A	29813638	30.55	0.78	0.72	0.85	0.41	0.41	3.26×10^{-8}	3.36×10^{-11}	1.04×10^{-17}	<i>ZFP57,HLA-F</i>
12	rs1800693	C	T	6310270	17.57	1.20	1.10	1.31	0.45	0.42	2.77×10^{-5}	7.52×10^{-8}	1.59×10^{-11}	<i>TNFRSF1A</i>
16	rs17445836	A	G	84575164	17.40	0.80	0.72	0.89	0.19	0.22	3.03×10^{-5}	3.05×10^{-5}	3.73×10^{-9}	<i>IRF8</i>
1	rs2300747	G	A	116905738	14.31	0.77	0.68	0.88	0.12	0.11	0.000155	2.44×10^{-7}	3.10×10^{-10}	<i>CD58,IGSF3</i>
12	rs4149576	T	C	6319376	12.94	1.17	1.07	1.27	0.46	0.43	0.000322	5.84×10^{-6}	1.03×10^{-8}	<i>PLEKHG6,TNFRSF1A,SCNN1A,LTBR</i>
2	rs882300	T	C	136692725	15.75	0.84	0.77	0.92	0.39	0.46	0.000517	7.23×10^{-5}	1.37×10^{-7}	<i>CXCR4</i>
1	rs10735781	G	C	92893695	10.43	1.16	1.06	1.26	0.38	0.37	0.0012	0.00192	7.55×10^{-6}	<i>EVI5</i>
11	rs17824933	G	C	60517188	10.39	1.18	1.07	1.30	0.25	0.23	0.0013	4.74×10^{-8}	3.79×10^{-9}	<i>TMEM132A,SLC15A3,CD6</i>
1	rs12025416	C	T	116839810	10.34	0.81	0.71	0.92	0.13	0.11	0.0013	2.32×10^{-7}	1.16×10^{-9}	<i>CD58</i>
16	rs1401884	C	G	84571052	10.16	0.84	0.75	0.93	0.17	0.19	0.0014	0.000114	6.83×10^{-7}	<i>IRF8</i>
10	rs7089861	G	C	6150332	9.51	0.86	0.78	0.95	0.26	0.24	0.0020	3.11×10^{-5}	3.38×10^{-7}	<i>IL2RA,RBM17</i>
16	rs12708716	G	A	11087374	9.43	0.87	0.79	0.95	0.35	0.33	0.0021	0.00017	1.49×10^{-6}	<i>CLEC16A</i>
16	rs11640138	G	A	11270230	8.99	0.88	0.81	0.96	0.45	0.44	0.0027	0.00423	3.41×10^{-5}	<i>SOCS1,TNP2,PRM3,PRM2,PRM1</i>
16	rs11865121	A	C	11074189	8.42	0.87	0.80	0.96	0.31	0.29	0.0037	1.30×10^{-5}	1.77×10^{-7}	<i>CLEC16A</i>
16	rs7184083	A	G	11135415	8.41	1.14	1.04	1.24	0.37	0.36	0.0037	2.64×10^{-5}	5.94×10^{-7}	<i>CLEC16A</i>
10	rs2104286	C	T	6139051	7.87	0.87	0.79	0.96	0.24	0.25	0.0050	1.52×10^{-6}	9.33×10^{-8}	<i>IL2RA,RBM17</i>
6	rs9321619	G	A	137916101	7.78	0.89	0.81	0.96	0.47	0.46	0.0053	0.000934	1.71×10^{-5}	<i>OLIG3</i>
16	rs11860603	C	T	11072518	7.60	0.88	0.80	0.96	0.32	0.29	0.0058	5.62×10^{-6}	3.04×10^{-7}	<i>CLEC16A</i>
13	rs9586741	C	A	104537871	6.71	0.89	0.81	0.97	0.30	0.32	0.0096	3.40×10^{-5}	1.27×10^{-4}	NA
7	rs2214935	G	A	22261885	6.46	1.12	1.03	1.23	0.34	0.34	0.0110	3.78×10^{-5}	2.93×10^{-6}	<i>RAPGEF5</i>
3	rs4680534	C	T	161181639	6.18	1.12	1.02	1.22	0.37	0.36	0.0129	6.80×10^{-5}	5.58×10^{-6}	<i>IL12A</i>
12	rs7137953	T	C	119379068	5.96	1.15	1.03	1.28	0.19	0.18	0.0147	1.60×10^{-5}	2.19×10^{-5}	<i>COX6A1,TRIAP1,GATC,SFRS9,DYNLL1,COQ5</i>
10	rs1250540	G	A	80706013	5.91	1.12	1.02	1.22	0.35	0.40	0.0151	9.89×10^{-6}	1.59×10^{-6}	<i>ZMIZ1</i>
1	rs2760524	A	G	190797171	5.88	0.87	0.77	0.97	0.16	0.17	0.0153	0.000107	9.77×10^{-6}	<i>RGS1</i>
16	rs1376041	T	C	56247384	5.87	0.89	0.81	0.98	0.30	0.30	0.0154	7.25×10^{-6}	0.1886	<i>GPR56,GPR97,CCDC135</i>
3	rs7622984	A	T	30183339	5.61	0.81	0.68	0.96	0.06	0.06	0.0179	4.30×10^{-5}	0.2786	NA
5	rs6897932	T	C	35910332	5.60	0.89	0.81	0.98	0.25	0.27	0.0180	7.71×10^{-6}	1.67×10^{-6}	<i>SPEF2,IL7R,CAPSL</i>

6	rs17066096	G	A	137494601	5.58	1.13	1.02	1.24	0.26	0.24	0.0182	0.000395	3.33x 10 ⁻⁵	<i>IL22RA2</i>
12	rs7311897	C	T	8911595	5.42	0.83	0.71	0.97	0.08	0.08	0.0200	2.80x10 ⁻⁵	5.67x 10 ⁻⁵	<i>A2ML1,PHC1</i>
10	rs10822550	G	A	66863143	5.36	1.11	1.02	1.20	0.48	0.46	0.0207	3.10x10 ⁻⁵	1.71x 10 ⁻⁵	NA
1	rs11811702	G	A	33122770	5.29	0.89	0.81	0.98	0.27	0.24	0.0215	3.07x10 ⁻⁵	5.82 x 10 ⁻⁶	<i>S100PBP,FNDC5,HPCA,TMEM54,RNF19B</i>
15	rs16971851	A	G	31599801	5.10	0.89	0.81	0.98	0.23	0.24	0.0239	2.32x10 ⁻⁵	0.2080	<i>RYR3</i>
1	rs11165441	A	G	91996935	5.10	0.87	0.78	0.98	0.15	0.16	0.0240	0.000226	3.01x 10 ⁻⁵	<i>TGFBR3</i>
5	rs6896969	A	C	40460183	4.58	0.91	0.83	0.99	0.38	0.40	0.0324	1.44x10 ⁻⁷	2.40x 10 ⁻⁷	<i>PTGER4</i>
6	rs892999	A	G	138180398	4.56	1.18	1.01	1.37	0.09	0.09	0.0327	5.84x10 ⁻⁶	3.12 x 10 ⁻⁶	<i>TNFAIP3</i>
22	rs11704699	G	T	16150181	4.33	0.86	0.75	0.99	0.11	0.10	0.0375	4.67x10 ⁻⁵	0.2009	NA
7	rs17280766	G	A	13603894	4.26	0.83	0.69	0.99	0.06	0.05	0.0389	4.27x10 ⁻⁵	1.63x 10 ⁻⁵	NA
2	rs4606981	C	T	133044646	3.95	0.91	0.82	1.00	0.26	0.27	0.0468	4.14x10 ⁻⁵	0.1720	<i>GPR39</i>
17	rs4239162	A	G	43110809	3.90	0.92	0.84	1.00	0.49	0.49	0.0484	8.19x10 ⁻⁶	6.93 x 10 ⁻⁶	<i>NPEPPS,KPNB1,TBKBP1,TBX21</i>
12	rs1790100	G	T	122222678	3.86	1.11	1.00	1.22	0.24	0.22	0.0495	2.74x10 ⁻⁷	7.21x 10 ⁻⁷	<i>MPHOSPH9</i>
5	rs4976682	T	C	176658608	3.74	0.88	0.77	1.00	0.11	0.11	0.0532	4.39x10 ⁻⁵	2.56x 10 ⁻⁵	<i>NSD1,RAB24,PRELID1,MXD3,LMAN2,RGS14</i>
22	rs9621545	G	C	31451988	3.68	1.11	1.00	1.23	0.20	0.20	0.0551	8.94x10 ⁻⁵	4.44x 10 ⁻⁵	<i>SYN3</i>
10	rs11256497	A	G	6127800	3.68	1.09	1.00	1.19	0.40	0.38	0.0552	1.60x10 ⁻⁵	1.33x 10 ⁻⁵	<i>IL2RA,RBM17</i>
2	rs10191601	C	T	204163615	3.67	1.09	1.00	1.19	0.43	0.40	0.0555	1.08x10 ⁻⁵	1.02x 10 ⁻⁵	<i>RAPH1</i>
11	rs655763	C	T	108682027	3.59	1.09	1.00	1.19	0.34	0.33	0.0582	3.30x10 ⁻⁵	4.91x 10 ⁻⁵	NA
1	rs11164814	G	A	93033961	3.55	1.10	1.00	1.21	0.28	0.27	0.0596	2.44x10 ⁻⁵	1.99x 10 ⁻⁵	<i>EVI5,RPL5,FAM69A</i>
2	rs4668486	A	C	16160643	3.46	0.91	0.82	1.01	0.24	0.23	0.0630	1.20x10 ⁻⁵	4.33x 10 ⁻⁵	NA
12	rs2049114	T	C	122223291	3.38	1.10	0.99	1.22	0.24	0.22	0.0659	1.30x10 ⁻⁷	1.15 x 10 ⁻⁶	<i>MPHOSPH9</i>
2	rs10803554	C	T	137602666	3.11	1.08	0.99	1.18	0.42	0.39	0.0777	3.30x10 ⁻⁵	0.0015	<i>THSD7B</i>
8	rs4150894	A	G	86292120	3.06	1.29	0.97	1.72	0.02	0.02	0.0802	3.20x10 ⁻⁵	2.16x 10 ⁻⁴	<i>LRRCC1,E2F5,C8orf59,CA13</i>
16	rs17765606	G	A	64540948	3.00	1.24	0.97	1.59	0.04	0.02	0.0832	5.20x10 ⁻⁷	9.35x 10 ⁻⁵	NA
17	rs3794716	A	G	78152456	2.91	1.16	0.98	1.36	0.07	0.07	0.0883	3.10x10 ⁻⁵	4.19x 10 ⁻⁴	<i>FO XK2,WDR45L,RAB40B</i>
17	rs9901869	G	A	42930205	2.88	1.08	0.99	1.17	0.49	0.49	0.0895	2.85x10 ⁻⁶	8.72 x 10 ⁻⁶	<i>C17orf57,NPEPPS</i>
15	rs12913890	C	G	58944903	2.80	1.08	0.99	1.17	0.47	0.48	0.0942	0.000873	4.63x 10 ⁻⁴	<i>RORA</i>
16	rs9924445	A	G	85304319	2.72	1.19	0.97	1.46	0.05	0.04	0.0989	1.09x10 ⁻⁵	2.46x 10 ⁻⁵	NA
2	rs6732091	A	G	204220071	2.72	1.08	0.99	1.17	0.40	0.37	0.0994	0.000174	1.60x 10 ⁻⁴	<i>CD28</i>
9	rs2492853	C	T	90021744	2.70	0.92	0.83	1.02	0.23	0.24	0.100	3.95x10 ⁻⁵	0.1044	NA
6	rs6926566	T	C	112190592	2.69	0.93	0.85	1.01	0.42	0.41	0.101	0.000143	1.44x 10 ⁻⁴	<i>FYN</i>

2	rs1404773	A	T	215847577	2.64	1.09	0.98	1.21	0.22	0.20	0.105	3.81x10 ⁻⁵	0.1001	AT1C
4	rs1880719	T	C	83836459	2.63	0.93	0.86	1.02	0.43	0.46	0.105	2.90x10 ⁻⁵	2.21x 10 ⁻⁴	SCD5
1	rs1182580	T	C	104248305	2.53	0.93	0.86	1.02	0.44	0.48	0.112	7.62x10 ⁻⁶	2.37x 10 ⁻⁵	NA
20	rs6131888	G	A	16925054	2.44	0.93	0.85	1.02	0.38	0.36	0.118	4.43x10 ⁻⁵	0.0961	NA
22	rs741195	G	C	19323766	2.43	0.92	0.84	1.02	0.23	0.25	0.119	4.45x10 ⁻⁵	0.0957	MED15
17	rs7217180	A	G	54979905	2.40	1.08	0.98	1.20	0.24	0.22	0.121	1.10x10 ⁻⁵	2.31x 10 ⁻⁴	DHX40
1	rs7517186	A	C	41676608	2.28	1.07	0.98	1.17	0.40	0.39	0.131	8.83x10 ⁻⁶	0.0512	EDN2
9	rs2236293	A	G	35831783	2.23	1.07	0.98	1.16	0.43	0.42	0.135	0.00513	0.4051	NPR2,SPAG8,HINT2,C9orf128,C9orf127,OR13J1
14	rs4468527	A	G	51394881	2.19	1.10	0.97	1.25	0.13	0.12	0.139	4.09x10 ⁻⁵	9.97x 10 ⁻⁵	GGN2
19	rs2303759	G	T	54560863	2.16	1.07	0.98	1.18	0.28	0.27	0.142	0.00273	0.0018	SLC6A16,CD37,TEAD2,DKKL1,FLJ32658,PTH2
5	rs931555	T	C	35839334	2.13	0.93	0.85	1.02	0.30	0.33	0.144	2.73x10 ⁻⁶	1.87x 10 ⁻⁵	SPEF2,IL7R
18	rs763361	T	C	65682622	2.10	1.07	0.98	1.16	0.48	0.47	0.148	0.157	0.0429	DOK6,CD226
16	rs1035946	G	A	24881927	1.94	0.93	0.83	1.03	0.19	0.18	0.163	1.38x10 ⁻⁵	6.43x 10 ⁻⁵	SLC5A11,ARHGAP17
5	rs1838724	T	C	53277764	1.91	1.07	0.97	1.19	0.24	0.22	0.167	3.30x10 ⁻⁵	6.89x 10 ⁻⁴	ARL15
21	rs2839578	C	G	43025706	1.89	1.07	0.97	1.17	0.32	0.31	0.170	3.49x10 ⁻⁶	0.0290	PDE9A
11	rs10892613	A	G	120063294	1.84	1.09	0.96	1.24	0.13	0.12	0.175	3.06x10 ⁻⁵	1.20x 10 ⁻⁴	GRIK4
17	rs4792311	A	G	12855734	1.79	0.94	0.86	1.03	0.31	0.28	0.181	0.00867	0.4081	RICH2,ELAC2
4	rs11736632	A	G	56867092	1.75	1.12	0.95	1.32	0.07	0.07	0.186	5.67x10 ⁻⁶	4.59x 10 ⁻⁵	KIAA1211,AASDH
2	rs616582	T	C	111658466	1.60	1.06	0.97	1.15	0.45	0.42	0.206	3.40x10 ⁻⁵	0.0018	BCL2L11
15	rs17304143	T	G	60364343	1.57	1.08	0.96	1.22	0.15	0.13	0.210	2.10x10 ⁻⁵	3.57x 10 ⁻⁴	NA
5	rs395561	C	A	106889874	1.56	1.06	0.97	1.15	0.43	0.39	0.211	4.22x10 ⁻⁵	2.00x 10 ⁻⁴	EFNA5
17	rs17581498	G	T	71305642	1.50	1.08	0.95	1.22	0.14	0.13	0.221	1.45x10 ⁻⁵	1.11x 10 ⁻⁴	ITGB4,GALK1,H3F3B,UNK,UNC13D,WBP2
18	rs7232625	C	A	59106929	1.48	0.93	0.82	1.05	0.14	0.15	0.224	0.000358	8.57x 10 ⁻⁴	BCL2,FVT1
7	rs10244467	C	T	22777741	1.45	0.91	0.78	1.06	0.08	0.08	0.228	3.37x10 ⁻⁷	0.0087	IL6,TOMM7
17	rs2304494	T	C	37216477	1.45	1.10	0.94	1.29	0.07	0.09	0.228	1.70x10 ⁻⁵	0.0720	JUP,SC65,FKBP10,NT5C3L,KLHL10,KLHL11
5	rs10454951	A	G	6305863	1.45	1.09	0.95	1.26	0.09	0.11	0.228	1.60x10 ⁻⁵	0.0644	FLJ33360
15	rs16967121	A	G	36710299	1.42	1.10	0.94	1.30	0.08	0.07	0.234	4.26x10 ⁻⁵	2.39x 10 ⁻⁴	NA
7	rs11772925	T	C	150059042	1.28	0.93	0.83	1.05	0.15	0.15	0.259	5.32x10 ⁻⁶	8.01x 10 ⁻⁵	GIMAP2,GIMAP1,GIMAP5
8	rs7814314	G	A	136905069	1.25	0.94	0.85	1.05	0.21	0.24	0.263	2.79x10 ⁻⁵	2.25x 10 ⁻⁴	NA
16	rs9940149	A	G	240642	1.11	0.94	0.85	1.05	0.20	0.17	0.292	4.88x10 ⁻⁵	3.82x 10 ⁻⁴	LUC7L,ITFG3,RGS11,ARHGDI5,PDIA2,AXIN1
19	rs918434	G	C	52452069	1.08	1.05	0.96	1.14	0.44	0.42	0.298	1.10x10 ⁻⁵	7.54x 10 ⁻⁴	SAE1,BBC3,CCDC9,C5AR1

10	rs1914184	G	T	63870389	1.08	1.05	0.96	1.14	0.41	0.39	0.299	0.000963	0.1315	ZNF365
6	rs352074	G	T	114323639	1.07	0.95	0.85	1.05	0.21	0.17	0.301	0.000294	0.0012	MARCKS,HDAC2
15	rs3816800	G	C	23476187	1.04	0.96	0.88	1.04	0.47	0.48	0.309	0.00684	0.2649	ATP10A
2	rs12999011	C	T	190213032	0.97	1.07	0.94	1.21	0.13	0.13	0.324	1.60x10 ⁻⁵	0.0615	SLC40A1,ASNSD1,ANKAR
11	rs1699105	G	A	120947829	0.97	0.96	0.88	1.04	0.40	0.40	0.324	0.000412	0.0882	SORL1
13	rs201763	G	T	49917022	0.95	0.96	0.87	1.05	0.30	0.31	0.329	8.32x10 ⁻⁶	1.65x 10 ⁻⁴	NA
2	rs7574456	C	T	136606529	0.85	1.05	0.95	1.16	0.24	0.27	0.356	2.50x10 ⁻⁵	0.0011	CXCR4
5	rs17346755	G	T	58000989	0.85	0.95	0.85	1.06	0.19	0.18	0.356		6.71x 10 ⁻⁴	RAB3C
17	rs11658169	C	T	19812514	0.85	0.96	0.88	1.05	0.39	0.38	0.357	3.99x10 ⁻⁵	4.85x 10 ⁻⁴	AKAP10
22	rs135382	T	C	47176626	0.79	0.95	0.83	1.07	0.13	0.14	0.374	3.73x10 ⁻⁵	5.09x 10 ⁻⁴	NA
1	rs6691787	T	C	68179214	0.79	1.05	0.95	1.16	0.23	0.21	0.374	1.30x10 ⁻⁵	0.0028	NA
16	rs251921	G	C	13110329	0.75	1.04	0.95	1.13	0.48	0.48	0.386	2.40x10 ⁻⁵	7.65x 10 ⁻⁴	NA
2	rs4668993	T	C	15869752	0.73	0.96	0.88	1.05	0.41	0.40	0.394	5.13x10 ⁻⁶	0.0122	NA
3	rs711663	G	A	4437774	0.72	1.16	0.82	1.63	0.01	0.02	0.395	1.63x10 ⁻⁵	3.49x 10 ⁻⁴	SUMF1
10	rs12260682	G	C	126644390	0.72	0.92	0.75	1.12	0.05	0.04	0.398	4.54x10 ⁻⁵	0.0291	ZRANB1,CTBP2
6	rs6910219	T	A	33570006	0.71	1.06	0.93	1.20	0.12	0.12	0.401	9.67x10 ⁻⁵	0.0010	SYNGAP1,ZBTB9
4	rs17086658	T	C	56864663	0.62	1.06	0.92	1.22	0.10	0.10	0.431	8.13x10 ⁻⁷	0.0049	KIAA1211,AASDH
5	rs158968	C	A	57977726	0.60	0.96	0.87	1.06	0.23	0.21	0.438	4.18x10 ⁻⁵	7.38x 10 ⁻⁴	RAB3C
6	rs9347662	C	G	162896005	0.57	0.96	0.86	1.07	0.17	0.17	0.452	0.000694	0.0041	PARK2
1	rs1294012	T	C	9207768	0.53	1.10	0.85	1.43	0.03	0.02	0.466	2.20x10 ⁻⁵	0.0132	H6PD
4	rs2726453	G	T	106539285	0.53	1.03	0.95	1.12	0.45	0.46	0.468	3.78x10 ⁻⁷	4.28x 10 ⁻⁴	PPA2
3	rs1356122	C	G	155666256	0.53	1.04	0.93	1.16	0.18	0.18	0.468	1.28x10 ⁻⁵	0.0031	GPR149
1	rs11580092	A	G	58606614	0.52	0.97	0.88	1.06	0.33	0.33	0.470	4.13x10 ⁻⁵	0.0222	NA
18	rs426921	T	C	63402133	0.52	0.96	0.85	1.08	0.15	0.16	0.471	2.54x10 ⁻⁵	1.41x 10 ⁻⁴	NA
2	rs2357954	C	T	54215941	0.52	1.03	0.95	1.13	0.38	0.39	0.471	1.71x10 ⁻⁶	0.0180	ACYP2
16	rs10775336	G	C	56103237	0.51	0.94	0.80	1.11	0.08	0.07	0.477	3.60x10 ⁻⁵	0.0205	COQ9,POLR2C,DOK4,CCDC102A,GPR114
17	rs820240	A	G	71094622	0.50	0.96	0.86	1.07	0.19	0.16	0.478	1.90x10 ⁻⁵	0.0435	LLGL2,RECQL5
11	rs11023151	G	A	14202675	0.49	0.96	0.84	1.08	0.13	0.14	0.482	1.54x10 ⁻⁵	0.0141	SPON1,RRAS2
5	rs254837	G	C	158615778	0.49	0.95	0.83	1.09	0.11	0.10	0.483	1.96x10 ⁻⁵	5.83x 10 ⁻⁴	RNF145,UBLCP1,IL12B
8	rs2277136	C	T	6322616	0.39	1.04	0.92	1.18	0.14	0.13	0.533	2.40x10 ⁻⁵	0.0054	ANGPT2,MCPH1
9	rs1658957	G	A	6662097	0.37	1.03	0.94	1.12	0.49	0.49	0.544	1.68x10 ⁻⁵	0.0120	GLDC

18	rs17760402	G	C	53915666	0.33	1.07	0.86	1.33	0.04	0.04	0.567	2.38x10 ⁻⁵	9.15x 10 ⁻⁴	<i>NEDD4L</i>
18	rs154929	A	G	56968545	0.32	0.97	0.88	1.08	0.21	0.24	0.569	3.91x10 ⁻⁵	0.0161	NA
5	rs2853694	T	G	158681666	0.32	0.98	0.90	1.06	0.50	0.49	0.570	3.35x10 ⁻⁶	3.16x 10 ⁻⁴	<i>UBLCP1,IL12B</i>
8	rs2083914	T	G	6289562	0.32	1.03	0.92	1.16	0.17	0.15	0.574	0.00266	0.0135	<i>ANGPT2,MCPH1</i>
2	rs1519529	G	C	136690727	0.30	1.03	0.93	1.13	0.26	0.28	0.584	4.06x10 ⁻⁵	0.0013	NA
8	rs7814564	T	A	26835382	0.30	0.93	0.73	1.19	0.03	0.03	0.585	8.55x10 ⁻⁶	5.59x 10 ⁻⁴	<i>ADRA1A</i>
8	rs1611927	T	A	4586651	0.28	1.03	0.93	1.14	0.21	0.22	0.599	1.36x10 ⁻⁵	0.0093	<i>CSMD1</i>
13	rs9596270	C	T	49740441	0.27	0.96	0.81	1.13	0.07	0.07	0.606	8.26x10 ⁻⁸	5.06x 10 ⁻⁵	NA
3	rs187084	G	A	52236071	0.26	1.02	0.94	1.12	0.40	0.37	0.611	0.000119	0.0232	<i>ALAS1,TLR9,TWF2,PPM1M,WDR82</i>
10	rs479505	A	G	97350709	0.25	0.97	0.86	1.09	0.15	0.16	0.617	8.25x10 ⁻⁶	6.21x 10 ⁻⁴	<i>SORBS1,ALDH18A1</i>
19	rs1862511	A	G	6537268	0.23	0.98	0.89	1.07	0.29	0.29	0.629	3.69x10 ⁻⁵	0.0132	<i>TNFSF9,CD70</i>
2	rs10203141	G	C	178898543	0.22	1.02	0.94	1.11	0.41	0.40	0.638	1.04x10 ⁻⁵	7.61x 10 ⁻⁴	<i>OSBPL6</i>
19	rs17239559	C	T	59398234	0.21	0.98	0.90	1.07	0.38	0.41	0.645	0.000437	0.0060	<i>LILRB3,LILRA6,LILRB5</i>
15	rs3814281	A	G	81296820	0.20	1.03	0.91	1.17	0.13	0.14	0.655	0.00801	0.1352	<i>FSD2,WHDC1,HOMER2</i>
11	rs11604291	G	A	72680764	0.18	0.95	0.74	1.21	0.03	0.03	0.671	1.02x10 ⁻⁵	0.0066	<i>P2RY2,P2RY6,ARHGEP17</i>
1	rs536858	G	C	66545614	0.18	0.98	0.90	1.07	0.40	0.40	0.675	4.67x10 ⁻⁵	0.0129	<i>PDE4B</i>
3	rs6583176	A	G	198009975	0.17	1.02	0.92	1.14	0.20	0.19	0.682	3.89x10 ⁻⁵	0.0116	<i>PAK2</i>
14	rs1420810	A	G	86572905	0.16	0.97	0.84	1.13	0.09	0.09	0.687	3.47x10 ⁻⁵	0.0109	NA
8	rs13251655	C	T	119829740	0.16	1.02	0.93	1.12	0.32	0.30	0.689	3.88x10 ⁻⁵	0.0037	NA
16	rs11643026	A	T	62173482	0.16	0.95	0.74	1.22	0.03	0.03	0.689	1.10x10 ⁻⁵	0.0114	NA
16	rs17782451	G	C	87006977	0.15	0.95	0.74	1.22	0.03	0.03	0.694	4.16x10 ⁻⁵	0.0116	<i>ZFPM1</i>
13	rs10507622	T	C	58443686	0.14	0.97	0.81	1.15	0.07	0.06	0.707	1.80x10 ⁻⁵	0.0137	NA
1	rs12042693	A	G	165780347	0.14	0.97	0.84	1.12	0.10	0.09	0.713	0.000262	0.0253	<i>CD247,CREG1</i>
8	rs4368946	C	T	98497864	0.11	1.03	0.87	1.21	0.08	0.06	0.746	2.90x10 ⁻⁶	0.0041	NA
14	rs6571751	G	A	20840570	0.10	1.01	0.93	1.10	0.50	0.49	0.748	0.00572	0.0966	<i>HNRNPC,RPGRIP1,SUPT16H</i>
2	rs1582844	A	G	153475282	0.10	0.95	0.67	1.34	0.01	0.02	0.754	2.40x10 ⁻⁵	0.0198	NA
13	rs927544	G	A	46354052	0.10	1.02	0.92	1.12	0.26	0.31	0.757	4.89x10 ⁻⁵	0.0137	<i>HTR2A</i>
14	rs2022771	C	T	85999679	0.10	0.99	0.91	1.07	0.45	0.45	0.757	2.50x10 ⁻⁵	0.0026	NA
12	rs12300846	A	T	9634751	0.09	1.01	0.93	1.11	0.37	0.36	0.763	1.85x10 ⁻⁵	0.0016	<i>KLRB1</i>
7	rs6973638	C	T	15363795	0.09	0.99	0.91	1.08	0.46	0.46	0.764	1.70x10 ⁻⁵	0.0031	<i>TMEM195</i>
11	rs12419184	T	C	125561518	0.09	1.02	0.88	1.20	0.09	0.08	0.764	1.90x10 ⁻⁵	0.0053	<i>RPUSD4,FAM118B</i>

22	rs4821818	C	T	37495985	0.09	1.02	0.89	1.17	0.12	0.12	0.766	3.61x10 ⁻⁵	0.0089	<i>GTPBP1,UNC84B,DNAL4,NPTXR</i>
3	rs4678000	A	G	123373425	0.08	1.01	0.93	1.10	0.39	0.40	0.782	0.000322	0.0076	<i>CD86,CASR</i>
18	rs10503052	A	G	57050613	0.08	1.01	0.93	1.11	0.33	0.33	0.783	3.50x10 ⁻⁵	0.0083	NA
3	rs1000361	G	A	27785323	0.07	1.01	0.93	1.11	0.34	0.35	0.792	1.26x10 ⁻⁵	0.0014	<i>EOMES</i>
21	rs2834044	T	C	33277432	0.06	1.01	0.92	1.11	0.29	0.26	0.800	0.00095	0.0142	<i>OLIG2</i>
11	rs11230555	A	C	60519710	0.06	0.99	0.89	1.10	0.21	0.22	0.804	1.64x10 ⁻⁶	5.23x 10 ⁻⁴	<i>TMEM132A,SLC15A3,CD6</i>
13	rs2325566	G	T	73281941	0.06	0.99	0.90	1.09	0.30	0.27	0.810	1.70x10 ⁻⁵	0.0036	<i>KLF12</i>
21	rs11088251	C	A	33692680	0.06	1.02	0.90	1.15	0.14	0.14	0.811	0.000885	0.0141	<i>IFNAR1,IFNGR2,TMEM50B</i>
11	rs750780	A	G	33874170	0.05	0.99	0.89	1.10	0.21	0.19	0.818	1.20x10 ⁻⁵	0.0111	<i>LMO2</i>
3	rs13073434	G	C	155593736	0.04	1.02	0.82	1.27	0.03	0.05	0.834	2.02x10 ⁻⁵	0.0056	<i>GPR149</i>
3	rs12490899	T	C	30649258	0.04	1.02	0.82	1.27	0.04	0.04	0.848	5.66x10 ⁻⁵	0.0087	<i>TGFBR2</i>
1	rs4970891	C	T	144721950	0.03	0.99	0.89	1.10	0.21	0.20	0.852	0.000199	0.0157	NA
9	rs4740392	A	G	132854767	0.03	0.99	0.89	1.11	0.18	0.20	0.863	3.00x10 ⁻⁵	0.0253	<i>FIBCD1,LAMC3</i>
7	rs1193335	T	G	127404040	0.02	0.99	0.91	1.09	0.35	0.36	0.888	3.04x10 ⁻⁵	0.0058	<i>C7orf54,LRRC4,SND1</i>
19	rs11667601	A	G	16531660	0.02	1.01	0.90	1.13	0.16	0.15	0.894	9.13x10 ⁻⁶	0.0017	<i>C19orf44,CHERP,SLC35E1,MED26</i>
14	rs17179734	G	A	71670843	0.02	0.99	0.82	1.19	0.05	0.06	0.895	3.69x10 ⁻⁵	0.0034	<i>RGS6</i>
3	rs3806680	G	A	3127384	0.01	0.99	0.90	1.10	0.24	0.27	0.911	0.000125	0.0067	<i>CNTN4,IL5RA,TRNT1,CRBN</i>
12	rs7132171	G	C	38936016	0.01	1.00	0.91	1.08	0.43	0.41	0.911	0.000437	0.0127	<i>LRRK2</i>
4	rs1017429	A	T	42808275	0.01	1.00	0.91	1.09	0.40	0.41	0.939	3.90x10 ⁻⁶	0.0019	NA
15	rs8023613	T	G	30739485	0.01	1.00	0.91	1.11	0.23	0.22	0.943	6.60x10 ⁻⁶	0.0017	<i>ARHGAP11A,SCG5,GREM1</i>
10	rs10885868	T	C	117912102	0.00	1.00	0.91	1.09	0.38	0.38	0.950	1.80x10 ⁻⁵	0.0053	<i>GFRA1</i>
9	rs10815231	G	T	547015	0.00	1.00	0.89	1.11	0.18	0.18	0.958	2.53x10 ⁻⁶	0.0011	<i>KANK1</i>
14	rs10148925	G	A	59157663	0.00	1.01	0.81	1.24	0.04	0.05	0.962	3.07x10 ⁻⁵	0.0047	<i>RTN1</i>
1	rs1193345	G	A	17786301	0.00	1.00	0.84	1.20	0.06	0.07	0.968	3.56x10 ⁻⁵	0.0050	<i>ARHGEF10L</i>
17	rs2293152	G	C	37735055	0.00	1.00	0.92	1.09	0.39	0.39	0.972	1.13x10 ⁻⁵	0.0028	<i>STAT5B,STAT5A,STAT3</i>
12	rs7314705	C	T	30090640	0.00	1.00	0.85	1.17	0.08	0.07	0.980	4.10x10 ⁻⁵	0.0052	NA
21	rs2832359	A	T	29790149	0.00	1.00	0.86	1.16	0.09	0.09	0.992	0.000624	0.0193	<i>GRIK1</i>

Genes: All genes found within a segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP.

NA: not available - there is no gene found within the segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP

N.B. SNPs are ranked by their P value in the replication analysis ($P_{\text{replication}}$). The meta analysis P values (P_{meta}) and the P values in the joint analysis (P_{joint} : meta-analysis + replication analysis) are also shown.

Success of selection strategies: Success in this endeavor can be defined in different ways. Here, we define success as exceeding a threshold of nominal significance ($P < 0.05$) in the replication analysis. Further, out of the 41 SNPs meeting this threshold, we only consider those 28 SNPs that are not found in a known MS susceptibility locus. Of the 28 remaining SNPs, 12 were in the “Top 100 loci” category. Since 100 loci were tested, the replication success rate is 12% for this category of SNPs. 8 of the 32 “candidate gene” SNPs or 25% replicate, and 5 of the 41 “secondary analysis” SNPs or 12% met our threshold of success. Also, 1 of the 8 nscSNPs (13%) met the threshold of success. Thus, all strategies were relatively equivalent in terms of success rate at the replication stage, with perhaps a slight excess in our “candidate gene” group. However, the numbers are too small to provide a definitive recommendation in terms of a SNP selection strategy; all strategies appear to be appropriate. Notably, all three novel SNPs (rs1800693, rs17445836, and rs17824933) meeting a threshold of genome-wide significance are found in the “Top 100 loci”.

Supplementary Table 4. Logistic regression analyses to identify independent effects in susceptibility loci using the replication data.

Chrom	Locus	SNP	rank order in locus	P _{replication}	P _{residual}
1	CD58	rs2300747	1	0.0002	-
		rs12025416	2	0.001	0.81
5	IL7R	rs6897932	1	0.018	-
		rs931555	2	0.1628	0.34
6	MHC	rs3135388	1	1.7x10 ⁻⁷⁷	-
		rs2523393	2	4.2x10 ⁻⁸	<0.0001
10	IL2RA	rs7089861	1	0.0013	-
		rs2104286	2	0.0029	0.062
		rs11256497	3	0.079	0.51
12	TNFRSF1	rs1800693	1	0.000005	-
		rs4149576	2	0.0001	0.45
		rs4149584	3	0.004	0.035
16	IRF8	rs17445836	1	0.0001	-
		rs1401884	2	0.0032	0.26
16	CLEC16A	rs12708716	1	0.0014	-
		rs11865121	2	0.0024	0.74
		rs11860603	3	0.0042	0.92

In the replication data analyzed here, it appears that only the MHC has evidence of independent associations. Nonetheless, the evidence suggests that there may be an independent risk allele within the *IL2RA* locus: rs7089861 and rs2104286 (the original MS associated SNP) are not in LD ($r^2=0.17$ in HapMap CEU samples) and may represent distinct effects on MS susceptibility which need larger sample sizes to be fully defined. Of note, the second type I diabetes mellitus risk allele in the *IL2RA* locus (rs11594656) has been shown to have an independent effect on MS risk (Maier *et al.*, *PLOS Genetics* 2009, e1000322) but is not in LD with rs7089861 ($r^2=0.23$ in HapMap CEU samples). Thus, further studies in larger sample collections may be able to establish independent roles for at least 3 *IL2RA* alleles in MS susceptibility.

Supplementary Table 5a. Putative shared susceptibility loci between MS and other inflammatory diseases at *IL12A*, *OLIG3/TNFAIP3*, *PTGER4*, and *RGS1* loci

MS locus	MS associated SNP	MS Meta-Analysis P-value	Inflammatory Disease	Inflammatory disease SNP	MS Meta-Analysis P-value	r^2
<i>IL12A</i>	rs4680534	6.8×10^{-5}	Celiac disease	rs9811792	0.0031	0.47
<i>PTGER4</i>	rs6896969	1.4×10^{-7}	Crohn's disease	rs9292777	2.2×10^{-7}	0.97
<i>RGS1</i>	rs2760524	0.00011	Celiac disease	rs2816316	0.00049	0.86
<i>OLIG3/TNFAIP3</i>	rs892999	4.27×10^{-5}	Psoriasis	rs610604	0.71	<0.01
			Rheumatoid arthritis	rs13192841	0.18	
				rs10499194	0.18	
			Systemic Lupus Erythematosus	rs6920220	0.06	
				rs5029939	0.84	
				rs6922466	0.58	

r^2 values are calculated using HapMap CEU data for each pair of MS and other inflammatory disease SNPs within each locus.

We present P values from our meta-analysis of MS whole genome scans for both the best SNP in the MS meta-analysis (third column) and the best SNP reported for another disease (sixth column) at each locus.

Supplementary Table 5b. Overlap of the MS and Crohn's disease replication studies following meta-analysis

Gene of Interest	Chrom	MS			Crohn's disease			Distance (bp)	r^2
		SNP	bp	P_{joint}	SNP	bp	P_{joint}		
<i>PPA2</i>	4	rs2726453	106463957	0.00036	rs10010325	106463957	5.0×10^{-5}	213483	0.0012
<i>PTGER4</i>	5	rs6896969	40460183	1.5×10^{-7}	rs4613763	40428485	3.1×10^{-27}	31698	0.092
<i>IL12B</i>	5	rs2853694	158681666	0.00025	rs10045431	158747111	1.9×10^{-13}	65445	0.03
<i>IRF8</i>	16	rs17445836	84575164	7.6×10^{-9}	rs10863202	84545499	1.4×10^{-5}	29665	0.14
<i>STAT3</i>	17	rs2293152	37735055	0.0036	rs744166	37767727	3.4×10^{-12}	32672	0.45
<i>NEDD4L</i>	18	rs17760402	53915666	0.0011	rs158865	54054001	2.0×10^{-5}	138335	0.02
<i>BCL2,FVT1</i>	18	rs7232625	59106929	0.00090	rs7227145	59311578	0.00095	204649	0.000071

Distance: distance between the MS-associated and Crohn's disease-associated SNPs.

$P_{\text{joint}} = P$ value in the joint analysis of the replication and meta-analysis data. Results for the Crohn's disease analysis are taken the work of Barrett and colleagues²⁶. MS results are taken from Supplemental Table 4.

Supplementary Table 6a. Detailed results of Gene set Enrichment Analysis of the quantitative trait analyses.

Gene Set associated with rs17445836 ^G	Size	NES	FDR q-val
<i>Untreated Subjects</i>			
TAKEDA_NUP8_HOXA9_10D_UP*	27	2.81	<10 ⁻⁴
VERHAAK_AML_NPM1_MUT_VS_WT_UP	37	2.80	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_16D_UP*	19	2.71	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_3D_UP*	29	2.70	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_8D_UP*	24	2.70	<10 ⁻⁴
HOHENKIRK_MONOCYTE_DEND_DN	21	2.39	<10 ⁻⁴
CARIES_PULP_UP	35	2.38	<10 ⁻⁴
CMV-UV_HCMV_6HRS_UP	17	2.28	<10 ⁻⁴
BRCA_ER_NEG*	62	2.28	<10 ⁻⁴
IFNA_HCMV_6HRS_UP*	21	2.25	<10 ⁻⁴
BOQUEST_CD31PLUS_VS_CD31MINUS_UP*	43	2.25	<10 ⁻⁴
SANA_TNFA_ENDOTHELIAL_UP	19	2.23	<10 ⁻⁴
RADAEVA_IFNA_UP*	16	2.22	<10 ⁻⁴
DAC_PANC_UP*	21	2.20	1.40 x 10 ⁻⁴
DER_IFNB_UP*	17	2.15	5.49 x 10 ⁻⁴
REOVIRUS_HEK293_UP*	23	2.12	7.69 x 10 ⁻⁴
RUTELLA_HEMATOGFSNDCS_DIFF*	63	2.10	9.07 x 10 ⁻⁴
JISON_SICKLECELL_DIFF*	36	2.08	9.74 x 10 ⁻⁴
RAS_ONCOGENIC_SIGNATURE*	26	2.05	0.00130
SANA_IFNG_ENDOTHELIAL_UP	15	2.00	0.00191
ICHIBA_GVHD*	21	1.99	0.00203
DIAB_NEPH_DN*	33	1.95	0.00323
TAKEDA_NUP8_HOXA9_8D_DN	15	1.94	0.00342
CMV_HCMV_TIMECOURSE_ALL_UP	31	1.92	0.00380
UVB_NHEK3_ALL	34	1.87	0.00706
LEI_MYB_REGULATED_GENES	16	1.85	0.00784
PASSERINI_SIGNAL	21	1.83	0.00933
TARTE_MATURE_PC	29	1.82	0.00978
WIELAND_HEPATITIS_B_INDUCED	20	1.80	0.0128
HSC_MATURE_ADULT	24	1.79	0.0133
HSC_MATURE_SHARED	16	1.77	0.0159
FLECHNER_KIDNEY_TRANSPLANT_REJECTION_UP	18	1.76	0.0161
AGEING_KIDNEY_UP	32	1.76	0.0164
MATSUDA_VALPHAINKT_DIFF	18	1.74	0.0190
HSC_MATURE_FETAL	18	1.71	0.0238
CMV_ALL_UP	17	1.70	0.0256
LEE_TCELLS2_UP	84	1.68	0.0305

PROLIFERATION_GENES	23	1.66	0.0344
UVC_HIGH_ALL_DN	16	1.65	0.0377
STEMCELL_HEMATOPOIETIC_UP	69	1.63	0.0410
CHIARETTI_T_ALL_DIFF	30	1.64	0.0415
BROCKE_IL6	19	1.63	0.0417
KRETZSCHMAR_IL6_DIFF	19	1.62	0.0440
<i>Interferon b Treated Subjects</i>			
TAKEDA_NUP8_HOXA9_3D_UP*	30	3.04	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_10D_UP*	20	3.02	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_8D_UP*	18	2.76	<10 ⁻⁴
TAKEDA_NUP8_HOXA9_16D_UP*	15	2.76	<10 ⁻⁴
RADAEVA_IFNA_UP*	17	2.75	<10 ⁻⁴
REOVIRUS_HEK293_UP*	29	2.66	<10 ⁻⁴
IFNA_HCMV_6HRS_UP*	15	2.47	<10 ⁻⁴
DER_IFNA_UP*	16	2.39	<10 ⁻⁴
DER_IFNB_UP*	20	2.39	1.28 x 10 ⁻⁴
RAS_ONCOGENIC_SIGNATURE*	25	2.30	3.61 x 10 ⁻⁴
KUMAR_HOXA_DIFF	26	2.28	6.38 x 10 ⁻⁴
CMV_HCMV_TIMECOURSE_ALL_UP	46	2.25	8.76 x 10 ⁻⁴
HSA04620_TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	16	2.21	0.00108
IFN_BETA_UP	16	2.17	0.00151
IFN_ANY_UP	18	2.16	0.00154
BRCA1_OVEREXP_UP	26	2.14	0.00157
WIELAND_HEPATITIS_B_INDUCED	16	2.15	0.00158
HSC_MATURE_ADULT	29	2.16	0.00164
KNUDSEN_PMNS_DN	30	2.12	0.00180
CHEN_HOXA5_TARGETS_UP	30	2.06	0.00362
JISON_SICKLECELL_DIFF*	51	2.00	0.00733
CHIARETTI_T_ALL_DIFF	26	1.97	0.009571
BOQUEST_CD31PLUS_VS_CD31MINUS_UP*	46	1.96	0.0102
POD1_KO_DN	67	1.93	0.0127
RUTELLA_HEMATOGFSNDCS_DIFF*	68	1.89	0.0177
ICHIBA_GVHD*	27	1.86	0.0219
UVC_HIGH_ALL_DN	38	1.86	0.0226
UVC_XPCS_4HR_DN	23	1.84	0.0256
BRENTANI_SIGNALING	18	1.83	0.0278
FLECHNER_KIDNEY_TRANSPLANT_WELL_UP	63	1.82	0.0280
CMV_ALL_UP	19	1.82	0.0282
UVC_XPCS_ALL_DN	48	1.81	0.0293
BRCA_ER_NEG*	66	1.79	0.0338
AGEING_KIDNEY_UP	35	1.77	0.0360

TARTE_MATURE_PC	26	1.77	0.0367
LEE_TCELLS2_UP	108	1.77	0.0370
DIAB_NEPH_DN*	39	1.77	0.0373
DAC_PANC_UP*	25	1.73	0.0474

GA Treated Subjects

LEE_TCELLS4_UP	24	2.62	<10 ⁻⁴
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* Gene sets that have an FDR q-value in both the untreated and IFN β -treated subjects

Here, we use gene set enrichment analysis to assess more modest but coordinated and widespread increase in gene expression that correlate with rs17445836^G (see Supplementary Methods for details). In short, we assessed each treatment group separately: 94 subjects treated with IFN β , 82 subjects that are untreated, and 64 subjects treated with GA. In each group, a QTL analysis using an additive model was performed to assess the correlation of rs17445836^G to each Affymetrix U133 2.0 that met our quality criteria and had an expression level >3. Then, within each of the three patient subgroups, we extracted those probes with a nominal $P < 0.05$ and promoted these probes to the gene set enrichment analysis (GSEA). The β value of each probe was used as the input parameter for GSEA analysis. For each patient subgroup, a gene set was considered in the analysis only if between 15-200 of its genes had an input β value. Thus, 147 gene sets were considered in the interferon β analysis, 93 gene sets in the untreated analysis, and 223 gene sets in the GA analysis. Supplementary Table 10 lists those genes whose expression correlates with rs17445836^G in the gene sets that are shared between the untreated and IFN β treated subjects

Supplementary Table 6b. List of genes whose RNA expression correlates with rs17445836^G in those gene sets which are found to be significant in the analyses of both the untreated and IFN β treated subjects.

Genes contributing to the assessment of each gene set with an FDR q-value < 0.05 in untreated subjects and in IFN β -treated subjects – data from untreated subjects															
TAKEDA_NUP8_HOXA9_10D_UP	TAKEDA_NUP8_HOXA9_16D_UP	TAKEDA_NUP8_HOXA9_3D_UP	TAKEDA_NUP8_HOXA9_8D_UP	BRCA_E_R_NEG	IFNA_HCMV_6HRS_UP	BOQUE_ST_CD31PLUS_VS_CD31MINUS_UP	RADADEV_A_IFNA_UP	DAC_PANC_UP	DER_IFNB_UP	REOVIRUS_HEK293_UP	RUTELL_A_HEMATOXINS_DCS_DIFF	JISON_SICKLECELL_DIFF	RAS_ONCOGENIC_SIGNATURE	ICHIBA_GVHD	DIAB_NEPH_DN
BIRC4BP	BIRC4BP	BIRC4BP	BIRC4BP	ADM	BAZ1A	AP2S1	BST2	AP4S1	BST2	ADM	AIF1	ADM	ABCA1	ACSL1	ADM
BTLA	BTLA	BST2	EPST11	AIF1	BIRC4BP	ATF3	EIF2AK2	BST2	CEBPD	ATF3	AOAH	AKR1A1	CASP1	AIF1	AIF1
CDKN1C	EPST11	CDKN1C	GCH1	ARHGAP21	BST2	BIRC4BP	HLA-E	CD55	EIF2AK2	BST2	ASAH1	ASCC3L1	CD55	ATP1B3	ALDH3B1
EIF2AK2	EREG	EIF2AK2	GZMB	ATF3	C1ORF38	BST2	IFI44	CDKN1A	GMFB	CD55	ATP13A3	ATF3	CSNK1D	CASP1	ATP13A3
EPST11	IFI44	EPST11	HERC5	ATP1B3	CASP1	CDKN1C	IFI44L	CDKN1C	HLA-E	CEBPG	ATP1B3	BLVRA	CXCL5	CTSS	BST2
HBS1L	IFI44L	FLJ11286	IFI44	C1ORF112	ECGF1	CTSS	IFI6	DUSP5	IFI44	DUSP1	B4GALT5	BST2	DLL1	CYBB	CASP1
HERC5	IFI6	HERC5	IFI44L	C1ORF38	GCH1	DUSP1	IFIT2	IER3	IFI6	GADD45A	C11ORF32	CALCOCO2	DUSP1	FGL2	CD55
IFI44	IFIT1	IFI44	IFI6	CASP1	IFI44L	FGL2	IFITM2	IFI6	IFIT2	IFI44L	C5AR1	CDKN1A	DUSP5	GRN	CDC14A
IFI44L	IFIT2	IFI44L	IFIH1	CCDC93	IFIT3	FLJ22662	IFITM3	IFIH1	IFIT3	IFIT3	CASP1	CTSL	EREG	IFIT1	CDKN1C
IFI6	ISG15	IFI6	IFIT1	CD300A	IFIT5	GAS7	IRF7	IFIT5	IFIT5	IFIT5	CD300A	DYNLT1	FBXO9	IFIT3	CEBPD
IFIH1	LILRB1/LILRA1	IFIH1	IFIT2	CD86	IRF7	HLA-DRB1	ISG15	IRF7	ISG15	IFITM3	CD55	ECGF1	FOS	IL18BP	CTNNA1
IFIT1	LOC129607	IFIT1	IFIT3	CDK2AP1	ISG15	ICA1	MX1	MX1	MX1	IRF7	CD84	GADD45A	GTPBP2	IRF7	DPP6
IFIT2	LY6E	IFIT2	IFIT5	CEBPG	MX1	IER5	MX2	OAS1	MX2	ISG15	CD86	HIST2H2A	IER3	ISG15	DUSP1
IFIT3	MX1	IFIT3	IRF7	CORO1C	MX2	IFI44	OAS1	OAS2	OAS1	MX2	CDKN1A	IFI30	LYN	ITPK1	GAB2
IRF7	MX2	IFIT5	ISG15	CSTA	MYD88	IFI44L	PLSCR1	PLAUR	OAS2	OAS1	CDKN1C	IFI44	MFSD2	NFKBIZ	GADD45A
ISG15	OAS2	IGHM	ISYNA1	CYBB	OAS1	IFIH1	UBE2L6	RAB31	PLAUR	OAS2	CEBPD	IFIT1	MXD1	RPAP1	GLUL
LILRA2	OAS3	IRF7	LY6E	DAPK1	OAS2	IGLC1		SERPINA1	RBBP4	PLSCR1	CTSB	IFIT2	MYD88	S100A8	GMFB
LILRA5	SMPDL3A	ISG15	MTSS1	DNAJC15	PLSCR1	IL3RA		SLC7A7		RAB3GAP1	CTSL	IFIT3	NFKBIZ	S100A9	IGFBP7
LOC129607	SOX4	LOC129607	MX1	DRAM	STX11	ING1		SOD2		UBE2L6	CXCL5	JAK2	NOLC1	TSPAN4	ING1
LY6E		LY6E	MX2	ECGF1	UBE2L6	KLF4		SPON1		USP9X	CYBB	KYNU	PLAUR	TYROBP	ISG15
MX1		MX1	OAS1	EXT1	WARS	LMO2		SVIL		ZFHX1B	DUSP5	LAMP2	SAT1	WARS	LASS6
MX2		MX2	OAS2	FAM46A		MAFB				ZFX	ELL3	LILRA2	SERPINA1		MTSS1
NEXN		OAS1	OAS3	FGL2		MAP3K8				ZNF264	EREG	LY6E	SLC16A3		NAB1
OAS1		OAS2	SOX4	FNDC3B		MTSS1					FCN1	MX1	SLC25A37		OAS1
OAS2		OAS3		FUT4		MX1					FLJ2027	NAB1	TCF7L2		OAS2

OAS3	PARP9	GALNT3	MX2	3	FTH1	NUCB1	TIMP1	PLSCR1
SOX4	PLSCR1	GCH1	PECAM1		HDAC9	PLEK		PTGER4
	PRIC285	GSTP1	PFKFB3		HLA-E	RPL19		RBBP4
	SOX4	GZMB	PRG1		IER5	SNN		SCRN1
		IFI30	PRG4		IFI6	ST3GAL5		TOP2B
		IFI44	PTGER4		IFITM2	TCF3		UBE2L6
		KYNU	RHOB		IGFBP7	TIMP1		USP9X
		LAMP2	SEC14L1		ITPK1	TOP2B		WARS
		LAP3	SH2B3		KYNU	TRAF5		
		LGALS9	SLC16A3		LAMP2	UBE2L6		
		LYN	SLC7A1		LASS6	USP9X		
		MARCKS	SMAD1		LGALS3			
		MX2	SOD2		/GALIG			
		OAS2	SOX4		LILRA2			
		PARVB	SPTBN1		LILRB2			
		PITRM1	SSH1		LMO2			
		PLAUR	STX11		MAFB			
		PLEK	WARS		MARCKS			
		PLSCR1			MX2			
		PRG1			MYD88			
		PRIM2A			PECAM1			
		S100A8			PKNOX1			
		S100A9			PLSCR1			
		SACS			RAB20			
		SLC15A3			RAB3GA			
		SLC16A3			P1			
		SLC25A3			RAMP1			
		7			S100A9			
		SLC7A1			SCARB2			
		SLC7A7			SCO2			
		SNN			SLC16A5			
		SOD2			SLC30A1			
		SSR1			SLC7A7			
		TGFBI			SOD2			
		TMEM140			STK17A			
		TNFSF13B			TCF3			
		TYROBP			TCF7L2			
		WARS			TRAF3			
					TRAF5			

Genes contributing to the assessment of each gene set with an FDR q-value < 0.05 in untreated subjects and in IFN β -treated subjects – data from IFN β -treated subjects															
TAKEDA_NUP8_HOXA9_10D_UP	TAKED_A_NUP8_HOXA9_16D_UP	TAKED_A_NUP8_HOXA9_3D_UP	TAKED_A_NUP8_HOXA9_8D_UP	BRCA_E_R_NEG	BOQUEST_CD31PLUS_VS_CD31MINUS_UP	IFNA_H_CMV_6H_RS_UP	RADAE_VA_IFNA_UP	DAC_PA_NC_UP	DER_IF_NB_UP	REOVIR_US_HEK293_UP	RUTELL_A_HEM_ATOGF_SNDCS_DIFF	JISON_SICKLE_CELL_D_1FF	RAS_O_NCOGE_NIC_SIG_NATURE	ICHIBA_GVHD	DIAB_N_EPH_DN
APOL6	BIRC4B_P	BIRC4B_P	ABCB1	AIM1	ALCAM	BIRC4B_P	ADAR	ADRBK1	ADAR	AKAP10	AKR1B1	ANP32B	ARHGAP27	AIM1	ABI1
BIRC4BP	FN1	C17ORF27	BIRC4B_P	AKR1B1	BIRC4B_P	IFIT5	BCL2	BARD1	BTG1	CDC27	ASAH1	ARHGEF7	CCNL1	AKAP9	ACBD3
EIF2AK2	IFI44	CUGBP2	C17ORF27	AMD1	BTG2	IRF7	E2F2	CD74	CASP8	DUSP1	ASMTL	BTF3	DUSP1	APBB1P	ADD3
FAM55C	IFI6	EIF2AK2	HERC5	BIRC2	CCNL1	MX2	EIF2AK2	ENOSF1	CD164	FUS	BTG1	BTG1	EDG4	BTG2	AKAP10
FN1	IFIT1	FLJ11286	IFI44	CARHP1	CD44	PLSCR1	HLA-B	FOXO3A	EIF2AK2	IFIT5	C12ORF4	COX11	EHD1	CASP6	ARL1
HERC5	LILRB1 /// LILRA1	HERC5	IFI6	CD44	CD74	PML	IFI44	FSCN1	GMFB	IFITM3	CCNI	CUL1	FBXO9	CD74	BIRC2
IFI44	LOC129607	IFI44	IFIH1	CD74	CUGBP2	PSCD1	IFI6	HERC3	HLA-B	IRF7	CCNL1	DGKA	FLJ43663	ELAC2	CAPN2
IFI6	MCOLN2	IFI6	IFIT1	CDKN2C	DUSP1	RABGAP1L	IFITM2	HLA-G	IFI44	ISGF3G	CD47	DYNLT1	FN1	FAS	CD164
IFIH1	MPP7	IFIH1	IFIT5	CMPK	EDNRB	RSAD2	IFITM3	IFI6	IFI6	KIAA0256	CRIM1	EDG4	GTPBP2	FLOT1	CD47
IFIT1	MX2	IFIT1	IRF7	CNIH4	ENG	SAMHD1	IRF7	IFIH1	IFIT5	LOC56902	CUGBP2	EEF1A1	HNRPH1	IFIT1	CDC14A
IRF7	NEGR1	IFIT5	MAP7	CUGBP2	FLJ43663	STAT1	MX2	IFIT5	MX2	LSM5	EIF2S1	EEF2	LGALS8	IRF7	CITED2
LOC129607	OAS3	IRF7	MX2	DNM1L	FLT1	TDRD7	PLSCR1	IRF7	PML	MAP4K5	EPB41L3	EIF3S12	LRRFIP1	LAPTM5	CRI1
MCOLN2	RSAD2	ISGF3G	MYCN	EML4	FN1	TREX1	RSAD2	LAPTM5	PPP3CA	MX2	FLJ20273	EIF4A2	MCL1	LCP2	CRIM1
MX2	SAMHD1	LOC129607	NEGR1	FBL	GFOD1	TRIM21	SOCS1	LGP2	PTPN11	PFDN4	FSCN1	FBL	MFSD2	LPHN1	DNAJA1
NEGR1	SOX4	MAP7	OAS3	FSCN1	GLS	TRIM22	STAT1	NCOR2	PYHIN1	PLSCR1	GLS	FN1	PIAS1	MARVELD1	DNM1L
OAS3		MX2	RSAD2	FUS	HLA-B		UBE2D3	PAEP	STAT1	PML	GPD2	GLS	PIK3CD	NCOA3	DUSP1
RSAD2		MYCN	SOX4	GALNT3	HLA-C		VAT1	PAK2	TMEM1	RAB3GAP1	GTF3A	HLCS	PRSS1	OSBP5	EXOC7
SOX4		NCOA7	STAT1	GFOD1	HLA-DRB1			PML	TRIM21	RAB5A	HADHA	HNRPH1	RAPH1	RPAP1	GLUL
SP110		NEGR1		GLS	HLA-F			PSAT1	TRIM22	RSAD2	IFI6	IFI44	RUNX1	RPL22	GMFB
STAT1		OAS3		GMPS	HSPA6			RCN3	XRCC6	SAMHD1	IFITM2	IFIT1	SAT1	SAMHD1	LASS6
		PARP12		GOLT1B	IFI44			SLC16A4		STAT1	IL18	IFNAR2	SOCS1	SOCS1	MRCL3

PARP14	HLA-F	IFIH1	SPON1	TDRD7	IL1R2	IMPDH2	TBX3	SPTLC2	NPTN
PARP9	HMGA1	ITGA4	SVIL	TLK1	ITGA4	JAK1	TCF7L2	STAT1	PCID1
PLSCR1	IFI44	KLF4	TAP2	TRIM21	JAK1	NAP1L1	TIA1	TAP2	PLSCR1
RAD50	IFNAR2	LAPTM5	ULK2	TRIM22	KIAA0922	NPM1	TRIM22	TAPBP	PTPN11
RSAD2	IL1R2	LCP2		WEE1	LASS6	OGT		UBAP2L	RABGA P1L
SOX4	IRF5	LRMP		ZF	LOC93349	PSMB2		UBE1L	SET
SP110	KIAA0922	MARS		ZFX	LRMP	PTPRM			SMARC C1
STAT1	LAP3	MX2		ZNF264	MCL1	RASGR P2			STAT1
TRIM22	LAPTM5	PGS1			METTL9	RBBP6			TAPBP
	LCP2	PSAT1			MX2	RPL21			TLK1
	LOC56902	PSCD1			NCOA3	RPL22			TMED5
	MRPL37	PTPRM			NFATC2 IP	RPL37			TRIM22
	MX2	RABGA P1L			NKTR	RPL4			UBR2
	NCK1	SAMHD 1			NOTCH2	RPL5			ULK2
	NMB	SCARF1			PACSIN 2	RPL7			UNG
	PHACTR 2	SEC14L 1			PGS1	RPL9			YWHAZ
	PLSCR1	SH2B3			PIGP	RPS27A			
	PSAT1	SHMT2			PKNOX1	RPS7			
	PSCD1	SLC43A 1			PLOD3	RSAD2			
	PSCD4	SOX4			PLSCR1	RSU1			
	PSMB2	SPTLC2			PRKCB1	SET			
	PTPLB	SSH1			PSCD1	SFRS5			
	RASGR P2	TMEM70			RAB3GA P1	SMC5			
	RIOK3	ZBTB16			RAB8B	SNN			
	RP6- 213H19. 1				RASGR P2	SPTLC2			
	RSAD2				RNASSET 2	STAT1			

				RSU1						RPL22	TDRD7			
				SAMD4A						RPL5	UNG			
				SAMHD1						RSAD2	VRK2			
				SNN						RUNX1	YWHAH			
				SSR1						SCARB2				
				STAT1						SEPHS1				
				STEAP3						SMARCC1				
				SYNCRIP						SP110				
				TANK						SPTLC2				
				TFDP1						STAT1				
				TIA1						TCF7L2				
				TRIM22						TEGT				
				UCL3						TIA1				
				USP13						TLR1				
				VRK2						TM9SF4				
				WDR43						TMEM97				
				XRN1						TNFAIP8				
				ZNF313						UBAP2L				
				ZNF777						VAT1				
										VDR				

Supplementary Table 7. Analysis of the replication data using logistic regression with an additive model for genotype effect and with gender and country of origin (US or UK) included as covariates.

Chr	SNP	Position (bp)	P _{gender}	P _{replication}	Genes
6	rs3135388	32521029	2.0 x 10 ⁻⁵⁶	7.35 x 10 ⁻⁷⁵	<i>HLA DRB1</i>
6	rs2523393	29813638	7.7 x 10 ⁻⁷	3.26 x 10 ⁻⁸	<i>HLA B</i>
12	rs1800693	6310270	1.0 x 10 ⁻⁵	2.77 x 10 ⁻⁵	<i>TNFRSF1A</i>
16	rs17445836	84575164	0.0002	3.03 x 10 ⁻⁵	<i>IRF8</i>
2	rs882300	136692725	0.0002	7.23 x 10 ⁻⁵	<i>CXCR4</i>
1	rs2300747	116905738	2.1 x 10 ⁻⁵	1.55 x 10 ⁻⁴	<i>CD58,IGSF3</i>
12	rs4149576	6319376	0.0001	3.22 x 10 ⁻⁴	<i>TNFRSF1A</i>
1	rs10735781	92893695	0.0028	0.0012	<i>EVI5</i>
11	rs17824933	60517188	0.0126	0.0013	<i>TMEM132A,SLC15A3,CD6</i>
1	rs12025416	116839810	0.0001	0.0013	<i>CD58</i>
16	rs1401884	84571052	0.009	0.0014	<i>IRF8</i>
10	rs7089861	6150332	0.0019	0.0020	<i>IL2RA,RBM17</i>
16	rs12708716	11087374	0.0016	0.0021	<i>CLEC16A</i>
16	rs11640138	11270230	0.0041	0.0027	<i>SOCS1,TNP2,PRM3,PRM2,PRM1</i>
16	rs11865121	11074189	0.004	0.0037	<i>CLEC16A</i>
16	rs7184083	11135415	0.0247	0.0037	<i>CLEC16A</i>
10	rs2104286	6139051	0.0084	0.0050	<i>IL2RA,RBM17</i>
6	rs9321619	137916101	0.0096	0.0053	<i>OLIG3</i>
16	rs11860603	11072518	0.0061	0.0058	<i>CLEC16A</i>
13	rs9586741	104537871	0.015	0.0096	NA
7	rs2214935	22261885	0.0106	0.0110	<i>RAPGEF5</i>
3	rs4680534	161181639	0.0268	0.0129	<i>IL12A</i>
12	rs7137953	119379068	0.0079	0.0147	<i>COX6A1,TRIAP1,GATC,SFRS9,DYNLL1,COQ5</i>
10	rs1250540	80706013	0.0508	0.0151	<i>ZMIZ1</i>
1	rs2760524	190797171	0.014	0.0153	<i>RGS1</i>
16	rs1376041	56247384	0.0168	0.0154	<i>GPR56,GPR97,CCDC135</i>
3	rs7622984	30183339	0.0674	0.0179	NA
5	rs6897932	35910332	0.0115	0.0180	<i>SPEF2,IL7R,CAPSL</i>
6	rs17066096	137494601	0.0355	0.0182	<i>IL22RA2</i>
12	rs7311897	8911595	0.0106	0.0200	<i>A2ML1,PHC1</i>
10	rs10822550	66863143	0.0157	0.0207	NA
1	rs11811702	33122770	0.0222	0.0215	<i>S100PBP,FNDC5,HPCA,TMEM54,RNF19B</i>
15	rs16971851	31599801	0.047	0.0239	<i>RYR3</i>
1	rs11165441	91996935	0.0246	0.0240	<i>TGFBR3</i>
5	rs6896969	40460183	0.0264	0.0324	<i>PTGER4</i>
6	rs892999	138180398	0.0091	0.0327	<i>TNFAIP3</i>
22	rs11704699	16150181	0.185	0.0375	NA
7	rs17280766	13603894	0.0243	0.0389	NA
2	rs4606981	133044646	0.0564	0.0468	<i>GPR39</i>
17	rs4239162	43110809	0.0802	0.0484	<i>NPEPPS,KPNB1,TBKBP1,TBX21</i>
12	rs1790100	122222678	0.0801	0.0495	<i>MPHOSPH9</i>
5	rs4976682	176658608	0.1159	0.0532	<i>NSD1,RAB24,PRELID1,MXD3,LMAN2,RGS14</i>
22	rs9621545	31451988	0.0791	0.0551	<i>SYN3</i>
10	rs11256497	6127800	0.0641	0.0552	<i>IL2RA,RBM17</i>
2	rs10191601	204163615	0.0381	0.0555	<i>RAPH1</i>
11	rs655763	108682027	0.0534	0.0582	NA
1	rs11164814	93033961	0.1111	0.0596	<i>EVI5,RPL5,FAM69A</i>
2	rs4668486	16160643	0.1668	0.0630	NA
12	rs2049114	122223291	0.1102	0.0659	<i>MPHOSPH9</i>
2	rs10803554	137602666	0.1289	0.0777	<i>THSD7B</i>

8	rs4150894	86292120	0.1046	0.0802	<i>LRRCC1,E2F5,C8orf59,CA13</i>
16	rs17765606	64540948	0.0791	0.0832	NA
17	rs3794716	78152456	0.0704	0.0883	<i>FOXK2,WDR45L,RAB40B</i>
17	rs9901869	42930205	0.2112	0.0895	<i>C17orf57,NPEPPS</i>
15	rs12913890	58944903	0.3529	0.0942	<i>RORA</i>
16	rs9924445	85304319	0.2685	0.0989	NA
2	rs6732091	204220071	0.0609	0.0994	<i>CD28</i>
9	rs2492853	90021744	0.1954	0.1003	NA
6	rs6926566	112190592	0.1838	0.1012	<i>FYN</i>
2	rs1404773	215847577	0.8808	0.1045	<i>ATIC</i>
4	rs1880719	83836459	0.1447	0.1050	<i>SCD5</i>
1	rs1182580	104248305	0.3191	0.1119	NA
20	rs6131888	16925054	0.1793	0.1179	NA
22	rs741195	19323766	0.1901	0.1188	<i>MED15</i>
17	rs7217180	54979905	0.1666	0.1212	<i>DHX40</i>
1	rs7517186	41676608	0.2801	0.1309	<i>EDN2</i>
9	rs2236293	35831783	0.1175	0.1350	<i>NPR2,SPAG8,HINT2,C9orf128,C9orf127,OR13J1</i>
21	rs876498	42714896	0.1571	0.1362	<i>TFF1,TMPRSS3,UBASH3A,RSPH1</i>
14	rs4468527	51394881	0.0961	0.1387	<i>GNG2</i>
19	rs2303759	54560863	0.2207	0.1420	<i>SLC6A16,CD37,TEAD2,DKKL1,FLJ32658,PTH2</i>
5	rs931555	35839334	0.1074	0.1440	<i>SPEF2,IL7R</i>
18	rs763361	65682622	0.2864	0.1475	<i>DOK6,CD226</i>
16	rs1035946	24881927	0.156	0.1633	<i>SLC5A11,ARHGAP17</i>
5	rs1838724	53277764	0.0918	0.1667	<i>ARL15</i>
21	rs2839578	43025706	0.323	0.1696	<i>PDE9A</i>
11	rs10892613	120063294	0.4397	0.1751	<i>GRIK4</i>
17	rs4792311	12855734	0.2075	0.1810	<i>RICH2,ELAC2</i>
4	rs11736632	56867092	0.3308	0.1860	<i>KIAA1211,AASDH</i>
2	rs616582	111658466	0.5956	0.2064	<i>BCL2L11</i>
1	rs8192284	152693594	0.1964	0.2095	<i>IL6R,SHE,TDRD10</i>
15	rs17304143	60364343	0.3947	0.2097	NA
5	rs395561	106889874	0.4554	0.2114	<i>EFNA5</i>
17	rs17581498	71305642	0.3105	0.2206	<i>ITGB4,GALK1,H3F3B,UNK,UNC13D,WBP2</i>
18	rs7232625	59106929	0.2248	0.2238	<i>BCL2,FVT1</i>
7	rs10244467	22777741	0.116	0.2282	<i>IL6,TOMM7</i>
17	rs2304494	37216477	0.1968	0.2282	<i>JUP,SC65,FKBP10,NT5C3L,KLHL10,KLHL11</i>
5	rs10454951	6305863	0.2637	0.2284	<i>FLJ33360</i>
15	rs16967121	36710299	0.0799	0.2342	NA
7	rs11772925	150059042	0.4273	0.2588	<i>GIMAP2,GIMAP1,GIMAP5</i>
8	rs7814314	136905069	0.345	0.2628	NA
16	rs9940149	240642	0.3543	0.2923	<i>LUC7L,ITFG3,RGS11,ARHGDIG,PDIA2,AXIN1</i>
19	rs918434	52452069	0.2339	0.2977	<i>SAE1,BBC3,CCDC9,C5AR1</i>
10	rs1914184	63870389	0.7591	0.2987	<i>ZNF365</i>
6	rs352074	114323639	0.558	0.3014	<i>MARCKS,HDAC2</i>
15	rs3816800	23476187	0.3403	0.3088	<i>ATP10A</i>
11	rs1699105	120947829	0.3065	0.3237	<i>SORL1</i>
2	rs12999011	190213032	0.6717	0.3237	<i>SLC40A1,ASNSD1,ANKAR</i>
13	rs201763	49917022	0.2395	0.3293	NA
2	rs7574456	136606529	0.365	0.3558	<i>CXCR4</i>
5	rs17346755	58000989	0.1984	0.3560	<i>RAB3C</i>
17	rs11658169	19812514	0.3877	0.3567	<i>AKAP10</i>
19	rs34536443	10324118	0.1616	0.3608	
22	rs135382	47176626	0.374	0.3739	NA
1	rs6691787	68179214	0.741	0.3743	NA

16	rs251921	13110329	0.2696	0.3861	NA
2	rs4668993	15869752	0.8993	0.3935	NA
3	rs711663	4437774	0.6205	0.3951	SUMF1
10	rs12260682	126644390	0.6035	0.3977	ZRANB1,CTBP2
6	rs6910219	33570006	0.7558	0.4006	SYNGAP1,ZBTB9
5	rs432482	96513963	0.2999	0.4236	
4	rs17086658	56864663	0.7799	0.4311	KIAA1211,AASDH
13	rs9516129	92191496	0.2214	0.4346	GPC5
5	rs158968	57977726	0.574	0.4382	RAB3C
6	rs9347662	162896005	0.5577	0.4522	PARK2
1	rs1294012	9207768	0.23	0.4658	H6PD
4	rs2726453	106539285	0.3854	0.4678	PPA2
3	rs1356122	155666256	0.257	0.4680	GPR149
1	rs11580092	58606614	0.6505	0.4702	NA
18	rs426921	63402133	0.4009	0.4712	NA
2	rs2357954	54215941	0.6477	0.4712	ACYP2
16	rs10775336	56103237	0.5748	0.4772	COQ9,POLR2C,DOK4,CCDC102A,GPR114
17	rs820240	71094622	0.6909	0.4775	LLGL2,RECQL5
11	rs11023151	14202675	0.5659	0.4823	SPON1,RRAS2
5	rs254837	158615778	0.7926	0.4828	RNF145,UBLCP1,IL12B
13	rs9523776	92143920	0.4338	0.4899	GPC5
13	rs9523762	92129887	0.6348	0.5113	GPC5
8	rs2277136	6322616	0.7451	0.5334	ANGPT2,MCPH1
9	rs1658957	6662097	0.2447	0.5444	GLDC
18	rs17760402	53915666	0.3727	0.5672	NEDD4L
18	rs154929	56968545	0.7566	0.5691	NA
5	rs2853694	158681666	0.7797	0.5703	UBLCP1,IL12B
8	rs2083914	6289562	0.6271	0.5741	ANGPT2,MCPH1
2	rs1519529	136690727	0.4878	0.5836	NA
8	rs7814564	26835382	0.7402	0.5849	ADRA1A
8	rs1611927	4586651	0.8085	0.5989	CSMD1
13	rs9596270	49740441	0.3668	0.6064	NA
3	rs187084	52236071	0.5981	0.6111	ALAS1,TLR9,TWF2,PPM1M,WDR82
10	rs479505	97350709	0.7631	0.6171	SORBS1,ALDH18A1
19	rs1862511	6537268	0.8995	0.6290	TNFSF9,CD70
2	rs10203141	178898543	0.7819	0.6378	OSBPL6
19	rs17239559	59398234	0.6502	0.6445	LILRB3,LILRA6,LILRB5
15	rs3814281	81296820	0.6503	0.6551	FSD2,WHDC1,HOMER2
11	rs11604291	72680764	0.9006	0.6714	P2RY2,P2RY6,ARHGEF17
1	rs536858	66545614	0.8023	0.6745	PDE4B
3	rs6583176	198009975	0.831	0.6816	PAK2
14	rs1420810	86572905	0.982	0.6868	NA
8	rs13251655	119829740	0.624	0.6886	NA
16	rs11643026	62173482	0.6211	0.6888	NA
16	rs17782451	87006977	0.4313	0.6940	ZFFM1
13	rs10507622	58443686	0.8582	0.7066	NA
1	rs12042693	165780347	0.8765	0.7131	CD247,CREG1
8	rs4368946	98497864	0.8552	0.7457	NA
14	rs6571751	20840570	0.7951	0.7478	HNRNPC,RPGRIP1,SUPT16H
2	rs1582844	153475282	0.8056	0.7538	NA
13	rs927544	46354052	0.8573	0.7565	HTR2A
14	rs2022771	85999679	0.4218	0.7569	NA
12	rs12300846	9634751	0.661	0.7626	KLRB1
7	rs6973638	15363795	0.8043	0.7641	TMEM195

11	rs12419184	125561518	0.6582	0.7644	<i>RPUSD4,FAM118B</i>
22	rs4821818	37495985	0.7286	0.7660	<i>GTPBP1,UNC84B,DNAL4,NPTXR</i>
3	rs4678000	123373425	0.7136	0.7818	<i>CD86,CASR</i>
18	rs10503052	57050613	0.5091	0.7828	NA
3	rs1000361	27785323	0.9998	0.7921	<i>EOMES</i>
21	rs2834044	33277432	0.6204	0.7998	<i>OLIG2</i>
11	rs11230555	60519710	0.9445	0.8040	<i>TMEM132A,SLC15A3,CD6</i>
13	rs2325566	73281941	0.2852	0.8097	<i>KLF12</i>
21	rs11088251	33692680	0.8975	0.8105	<i>IFNAR1,IFNGR2,TMEM50B</i>
11	rs750780	33874170	0.717	0.8181	<i>LMO2</i>
3	rs13073434	155593736	0.2617	0.8336	<i>GPR149</i>
3	rs12490899	30649258	0.7625	0.8482	<i>TGFBR2</i>
1	rs4970891	144721950	0.9826	0.8518	NA
9	rs4740392	132854767	0.7091	0.8626	<i>FIBCD1,LAMC3</i>
7	rs1193335	127404040	0.9802	0.8880	<i>C7orf54,LRRC4,SND1</i>
19	rs11667601	16531660	0.4983	0.8940	<i>C19orf44,CHERP,SLC35E1,MED26</i>
14	rs17179734	71670843	0.9322	0.8953	<i>RGS6</i>
3	rs3806680	3127384	0.925	0.9107	<i>CNTN4,IL5RA,TRNT1,CRBN</i>
12	rs7132171	38936016	0.9954	0.9113	<i>LRRK2</i>
4	rs1017429	42808275	0.919	0.9387	NA
15	rs8023613	30739485	0.9218	0.9430	<i>ARHGAP11A,SCG5,GREM1</i>
10	rs10885868	117912102	0.9129	0.9498	<i>GFRA1</i>
9	rs10815231	547015	0.6038	0.9578	<i>KANK1</i>
14	rs10148925	59157663	0.8761	0.9616	<i>RTN1</i>
1	rs1193345	17786301	0.7223	0.9681	<i>ARHGEF10L</i>
17	rs2293152	37735055	0.7299	0.9721	<i>STAT5B,STAT5A,STAT3</i>
12	rs7314705	30090640	0.779	0.9800	NA
21	rs2832359	29790149	0.9807	0.9920	<i>GRIK1</i>

Genes: All genes found within a segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP.

NA: not available - there is no gene found within the segment defined by all SNPs with an $r^2 > 0.5$ with the reference SNP

N.B. SNPs are ranked by their P value in the logistic regression model with the gender and country covariates (P_{gender}). The CMH P values ($P_{\text{replication}}$) from Supplementary Table 4 are included for reference.

II. Supplementary Figure

Supplementary Figure 1. LD maps of the three novel MS susceptibility loci. (a) *TNFRSF1A*, (b) *IRF8*, and (c) *CD6*. Data from HapMap CEU samples were used to prepare each panel. In each panel, the chromosomal segment of interest is outlined at the top of the panel. The physical positions are based on human genome build 36. The genes found within the chromosomal are outlined below the chromosomal segment. The SNPs found in HapMap at a minor allele frequency > 0.05 in CEU samples were used to prepare these plots. The SNP with the most extreme association with MS susceptibility is highlighted with a red arrowhead. Finally, pairwise LD relationships are portrayed using a white (low) to red (high) scale: $D' < 1$, $LOD < 2$ = white; $D' = 1$, $LOD < 2$ = blue; $D' < 1$, $LOD \geq 2$ = shades of pink/red; $D' = 1$, $LOD \geq 2$ = bright red.



