

Supplementary Table 1: GWAS loci with functional outside variants

Lead SNP	Gene Target	Regulatory Circuitry
rs10201872	SP100	PreSTIGE
rs10488631	IRF5	Hi-C
rs1077667	C3	Super
rs1077667	GPR108	Super
rs10892279	TRAPPC4	Hi-C
rs10892279	UPK2	Hi-C
rs10995271	ADO	Hi-C
rs11150589	SEPHS2	Super
rs11175593	LRRK2	PreSTIGE
rs11203203	RSPH1	Hi-C, Super
rs11203203	TMPRSS3	Hi-C, Super
rs11755724	RREB1	Hi-C
rs11860650	ITGAD	PreSTIGE
rs12025416	ATP1A1OS	PreSTIGE
rs12456021	ALPK2	Super
rs12531711	IRF5	Hi-C
rs12711490	IRF8	Super
rs12928822	RMI2	Super
rs13239597	IRF5	Hi-C
rs13277113	FAM167A	Super
rs13333054	IRF8	Super
rs1335532	ATP1A1OS	PreSTIGE
rs13428812	DNMT3A	Super
rs16940202	IRF8	PreSTIGE
rs1738074	RSPH3	Hi-C
rs17445836	IRF8	Super
rs17810546	IL12A	Hi-C
rs2176082	PXK	Super
rs2283792	YPEL1	Super
rs2284553	IL10RB	Hi-C
rs2297441	C20orf195	Super
rs2300747	ATP1A1OS	PreSTIGE
rs2413583	PDGFB	Super
rs2413583	SYNGR1	Super
rs2425752	NCOA5	Hi-C, Super
rs2431697	C5orf54	Super
rs2762051	DLEU1	Hi-C
rs290986	SYK	PreSTIGE, Hi-C, Super
rs3024493	DYRK3	Hi-C
rs3024493	FAIM3	Hi-C
rs3024493	IL19	PreSTIGE, Hi-C, Super
rs3024505	DYRK3	Hi-C
rs3024505	IL19	PreSTIGE, Hi-C, Super
rs354033	ZNF767	Super

(Continued)

Lead SNP	Gene Target	Regulatory Circuitry
rs4308217	ILDR1	Super
rs4656940	CD244	PreSTIGE, Hi-C
rs4656940	CD48	Super
rs4656940	LY9	PreSTIGE, Hi-C, Super
rs4656940	SLAMF7	PreSTIGE, Super
rs4680534	IL12A	Hi-C
rs4780355	RMI2	Super
rs4781011	CLEC16A	Hi-C
rs4781011	DEXI	Super
rs4781011	FAM18A	PreSTIGE
rs4810485	CD40	Super
rs4810485	NCOA5	Hi-C
rs4953911	MGAT5	Super
rs6074022	CD40	Super
rs6074022	NCOA5	Hi-C
rs615672	HLA-DQA1	Super
rs615672	HLA-DQB1	Super
rs615672	HLA-DRB1	Super
rs630923	TRAPPC4	Hi-C
rs630923	UPK2	Hi-C
rs6445975	PXK	Super
rs6498169	CIITA	Super
rs6498169	DEXI	Super
rs660895	HLA-DQA1	PreSTIGE, Super
rs660895	HLA-DQB1	Super
rs660895	HLA-DRB5	PreSTIGE, Super
rs660895	HLA-DRB6	PreSTIGE, Super
rs6716753	SP100	PreSTIGE
rs7155603	FLVCR2	Super
rs7172677	C15orf39	Super
rs7200786	SOCS1	Super
rs7238078	ALPK2	Super
rs7238078	MALT1	PreSTIGE, Hi-C, Super
rs7253363	ELOF1	Super
rs7423615	SP100	PreSTIGE
rs7923837	KIF11	Super
rs806321	DLEU1	Hi-C
rs874040	C4orf52	Hi-C
rs907611	SYT8	Super
rs9596270	DLEU1	Hi-C
rs960709	ANXA6	Hi-C, Super
rs960709	GM2A	Hi-C
rs9888739	ITGAD	PreSTIGE

Supplementary Table 2: Outside variant loci evaluated in luciferase reporter assays

Enhancer region (hg18)	Gene Target(s)	Functional Outside Variants	Primer sequences	
chr9:92,597,336-92,599,537	SYK	rs10993693, rs290997	FWD	GGAGACAUGATCTTGGTATGAGAAAACCATCT
			REV	GGGAAAGUGCGCAGATTTAGATCTTCATTCA
chr16:84,546,145-84,547,502	IRF8	rs7199472	FWD	GGAGACAUGGAGGTGACTTCTGCATTGA
			REV	GGGAAAGUCGGTACAAAGGCCTGAGGT
chr1:159,025,419-159,027,509	SLAMF7, LY9	rs1333065, rs12405457	FWD	GGAGACAUCAGAACCTGTCCCCTCATCA
			REV	GGGAAAGUGCTGAACTGAACTTAAGGCTGA
chr18:54,380,385-54,381,923	MALT1	rs8090585	FWD	GGAGACAUGGAGGTGACTTCTGCATTGA
			REV	GGGAAAGUCGGTACAAAGGCCTGAGGT
chr2:230,891,662-230,892,865	SP100	rs11679076	FWD	GGAGACAUCAGGATTCGATACCATCACTCA
			REV	GGGAAAGUGAAAACCTCATCCATCTCATCTGC
chr6:32,683,356-32,684,808	HLA-DQA1	rs646984	FWD	GGAGACAUCCCATCGTCTAAAACATGCAC
			REV	GGGAAAGUCCAAAACCTTGCCCTTTTTAATG
chr12:38,848,086-38,849,374	LRRK2	rs728624, rs728623, rs2708489, rs1948380	FWD	GGAGACAUTTGTGTCAGTAATCATTTATCTGCAT
			REV	GGGAAAGUTGAGATATGAAAAATAGTTTCAGCAA

Supplementary Table 3: Summary of candidate “third SNPs” evaluated

			"3rd" SNPs with effects: Independent effect on expression, no additional variance explained by GWAS or outside variant			"3rd" SNP with effects that are imputed on GWAS panel		
Gene	Candidate "3rd" SNPs per gene	Number tests per gene	P<7.5E-8 (uncorrected)	P<0.05 (corrected)	P<5E-3 (uncorrected)	P<7.5E-8 (uncorrected)	P<0.05 (corrected)	P<5E-3 (uncorrected)
ADO	3094	5638	16	61	116	8	20	50
ALPK2	3489	7275	0	0	15	NA	NA	15
ATP1A1OS	2396	3806	0	1	1	NA	1	1
C20orf195	4680	8976	0	0	14	NA	NA	6
C3	4823	9289	0	0	47	NA	NA	5
C4orf52	3064	5928	15	15	15	15	15	15
CD244	3359	6147	11	11	11	11	11	11
CD40	3292	6160	0	0	20	NA	NA	3
CD48	2897	5245	0	3	29	NA	3	29
CIITA	3827	7729	0	0	11	NA	NA	10
CLEC16A	4115	8417	0	0	55	NA	NA	49
DEXI	4101	8387	2	30	121	2	30	121
DLEU1	3113	5821	0	80	89	NA	80	89
DNMT3A	2859	5307	0	0	26	NA	NA	5
DYRK3	1771	3143	0	0	15	NA	NA	14
ELOF1	3546	6010	0	0	49	NA	NA	21
FAIM3	2352	4416	0	0	3	NA	NA	1
FAM18A	3829	7553	0	0	36	NA	NA	5
FLVCR2	2783	5221	0	0	3	NA	NA	*
GPR108	4875	9459	12	15	116	12	15	111
HLA-DQA1	22081	53643	30	30	30	30	30	30
HLA-DQB1	22346	54378	0	0	0	NA	NA	NA
HLA-DRB1	21533	52289	0	0	0	NA	NA	NA
HLA-DRB5	20633	49967	237	390	1377	111	214	668
HLA-DRB6	20865	50545	10	10	10	10	10	10
IL10RB	2735	5805	0	1	51	NA	1	45
IL12A	2703	4451	32	33	33	32	33	33
IL19	2286	4304	0	0	0	NA	NA	NA
ILDR1	2951	5931	0	0	13	NA	NA	3
IRF5	3305	6393	13	18	20	13	18	20
IRF8	4764	9180	0	0	13	NA	NA	8
KIF11	2579	4495	0	0	144	NA	NA	11
LRRK2	3431	6717	0	1	60	NA	1	54
LY9	3060	5556	0	10	11	NA	10	11
MALT1	3473	7217	0	0	6	NA	NA	5
MGAT5	3212	6454	0	0	41	NA	NA	2
NCOA5	3230	5904	0	0	12	NA	NA	7
PDGFB	3300	6724	10	32	32	10	32	32
RMI2	4124	8710	0	0	0	NA	NA	NA

Supplementary Table 3: Summary of candidate “third SNPs” evaluated (continued)

Gene	Candidate "3rd" SNPs per gene	Number tests per gene	"3rd" SNPs with effects: Independent effect on expression, no additional variance explained by GWAS or outside variant			"3rd" SNP with effects that are imputed on GWAS panel		
			P<7.5E-8 (uncorrected)	P<0.05 (corrected)	P<5E-3 (uncorrected)	P<7.5E-8 (uncorrected)	P<0.05 (corrected)	P<5E-3 (uncorrected)
RREB1	4184	8352	0	0	9	NA	NA	2
RSPH1	4852	9082	0	0	0	NA	NA	NA
RSPH3	3806	7802	143	171	204	125	150	166
SEPHS2	1291	2363	0	6	8	NA	6	8
SLAMF7	3053	5595	4	8	8	4	8	8
SOCS1	3990	8212	0	0	31	NA	NA	31
SP100	3425	7299	0	0	6	NA	NA	3
SYK	3953	7381	0	0	0	NA	NA	NA
SYNGR1	3172	6404	0	0	0	NA	NA	NA
SYT8	4991	10399	0	0	15	NA	NA	14
TMPRSS3	4898	9394	0	0	25	NA	NA	15
TRAPPC4	2488	5352	36	36	36	36	36	36
UPK2	2415	5133	0	0	0	NA	NA	NA
YPEL1	2986	5942	0	0	78	NA	NA	6
ZNF767	3676	7272	0	14	15	NA	7	7
ANXA6	3595	7191	0	0	0	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
C15orf39	2018	3906	0	43	61	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
C5orf54	3451	6671	0	0	24	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
FAM167A	4904	10348	59	59	59	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
GM2A	3627	7237	8	8	8	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
ITGAD	2129	4297	2	6	11	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac
PXK	2847	5551	0	1	140	Lupus or Celiac	Lupus or Celiac	Lupus or Celiac

* gene excluded from percentage calculations

NOTE: only loci associated with RA, MS, UC and CD were evaluated for impact on clinical risk