	Sample QC							
	Start	<99% Call frequency	Fail Autosomal Heterozygosity	Fail IBD	Fail PCA	Remaining	ACPA-POS	ACPA-NEG
UK cases	4,269	243	5	126	25	3,870	2,406	1,000
UK controls	8,926	145	5	285	61	8,430	-	-
Swedish EIRA cases	2,968	62	14	41	89	2,762	1,762	987
Swedish EIRA controls	2,106	76	6	22	62	1,940	-	-
US cases	3,621	487	19	488	91	2,536	1,803	593
US controls	3,887	480	41	98	1,134	2,134	-	-
Dutch cases	704	12	3	16	25	648	330	301
Dutch controls	2,085	23	1	33	24	2,004	-	-
Swedish Umea cases	1,085	139	2	85	7	852	524	242
Swedish Umea controls	1,021	3	3	44	8	963	-	-
Spanish cases	914	53	10	13	31	807	397	216
Spanish controls	447	14	2	29	3	399	-	-
Total cases	13,561	996	53	769	268	11,475	7,222	3,339
Total controls	18,472	741	58	511	1,292	15,870		

Supplementary Table 1: Quality control measures implemented on the Immunochip array data illustrating numbers of samples failing in each collection.

Start	196,524
Chromosome Y	1,735
Mitochondrial	1
Non-polymorphic (all samples)	12,715
Low cluster separation (< 0.4)	12,510
Low call frequency(< 0.98)	2,243
Illumina default exclusions	936
Duplicate SNPs	835
Remaining for analysis	165,549

Group	SNP loss			Final	
	Call Frequency (<0.99)	HWE	MAF		
UK	2,468	680	36,543	125,858	
US	10,484	299	34,769	119,997	
SE-E	3,851	248	36,788	124,662	
SE-U	3,229	156	38,037	124,127	
NL	3,321	233	37,070	124,925	
ES	4,491	51	36,169	124,838	
Included in Study (passed QC in at least 2 studies)					129,464

Supplementary Table 2: Summary of SNPs failing Immunochip quality control metrics.

Chr	SNP	POSITION*	GENE	Allele	STUDY P	STUDY OR	ACPA + P	ACPA+ OR	ACPA - P	ACPA - OR	Autoimmune disease associations
a) previously known associated loci											
6	rs660895	32,577,380	HLA	**G**	**<1E-300**	2.265	**<1E-300**	3.0299	**1.54E-08**	1.2083	Multiple
1	rs2476601	114,377,568	PTPN22	A	**9.01E-62**	1.5935	**7.53E-77**	1.7845	1.75E-04	1.1828	RA, T1D, SLE, CD
5	rs71624119	55,440,730	ANKRD55	**A**	**5.59E-20**	0.8134	**1.20E-11**	0.8378	**5.18E-12**	0.7843	RA, T2D
6	rs6920220	138,006,504	TNFAIP3	A	**1.84E-10**	1.1509	**2.27E-13**	1.2026	3.79E-02	1.0732	CeD, RA, SLE, Ps, T1D, MS, PBC
4	rs12506688	26,104,113	RBPJ	A	**3.73E-10**	1.1337	**2.51E-10**	1.1571	4.16E-02	1.0652	RA, T1D
6	rs59466457	167,537,754	CCR6	A	**3.47E-06**	1.0903	**2.74E-10**	1.1455	6.44E-01	0.9869	CD,RA, AITD
2	rs13426947	191,933,254	STAT4	**A**	**7.19E-10**	1.1533	**7.50E-09**	1.1663	2.67E-03	1.1116	SLE,RA, CeD, PBC
9	rs2812378	34,710,260	CCL21	G	**1.31E-08**	1.1167	**7.23E-10**	1.1473	1.40E-02	1.0756	RA
20	rs6032662	44,734,310	CD40	G	1.72E-05	0.9104	**1.37E-09**	0.8564	7.10E-01	1.0123	RA, MS
1	rs2843401	2,528,133	MMEL1	A	6.87E-07	0.9055	**6.58E-09**	0.8738	6.02E-01	0.9842	CeD,RA, UC, MS, AITD, PBC
2	rs10209110	100,672,692	AFF3	**A**	**1.13E-08**	0.8996	**6.79E-08**	0.891	0.01231	0.9317	RA, T1D
2	rs34695944	61,124,850	REL	G	4.14E-06	1.0918	**2.58E-08**	1.13	2.90E-01	1.0314	Ps,RA , CeD, CD, UC
2	rs11571302	204,742,934	CTLA4	A	4.73E-07	0.9104	**4.49E-08**	0.8886	1.22E-01	0.9569	RA, AITD, T1D,CeD
5	rs39984	102,597,292	GIN1	**A**	**9.29E-08**	0.8792	3.04E-06	0.8756	1.32E-04	0.8674	RA, SLE
3	rs35677470	58,183,636	DNASE1L3	**A**	1.74E-07	1.1946	1.09E-06	1.2095	1.41E-02	1.1382	RA, SLE
7	rs3807306	128,580,680	IRF5	C	2.48E-07	0.9093	1.90E-07	0.8947	2.22E-02	0.9374	SLE,RA, UC, PBC
22	rs3218251	37,545,505	IL2RB	A	5.82E-06	1.0987	1.91E-07	1.1325	2.15E-01	1.0402	RA,T1D
2	rs1980422	204,610,396	CD28	G	4.62E-06	1.1051	2.57E-07	1.1376	0.4738	1.0244	RA, AITD, T1D,CeD

11	rs4938573	118,741,842	DDX6	G	3.97E-05	0.9072	5.31E-07	0.8703	6.31E-01	0.983	RA, SLE, MS, PBC, CeD
2	rs6546146	65,556,324	SPRED2	A	1.91E-05	0.9205	7.98E-07	0.8952	5.05E-01	0.9805	RA
6	rs629326	159,496,713	TAGAP	C	5.61E-03	0.9492	1.13E-06	0.8993	5.19E-01	1.0187	CeD, RA, CD, T1D, MS
9	rs10739580	123,695,282	TRAF1	G	4.56E-05	1.0846	1.68E-06	1.1152	9.53E-02	1.0527	RA, SLE
10	rs10795791	6,108,340	IL2RA	**G**	3.01E-06	1.0921	4.71E-06	1.1047	6.30E-02	1.0551	RA, MS,T1D, CD
8	rs4840565	11,345,545	BLK	**G**	3.88E-06	1.0987	3.46E-04	1.0877	1.01E-04	1.1275	SLE, RA
1	rs798000	117,280,696	CD2	G	8.92E-05	1.0802	6.19E-06	1.1081	4.43E-01	1.0234	RA, MS
12	rs10683701	58,092,089	KIF5A	-	4.39E-05	0.9221	2.31E-05	0.9072	4.03E-01	0.9751	RA,MS
1	rs16843807	198,745,722	PTPRC	C	1.10E-04	0.8905	2.48E-05	0.863	6.38E-01	0.9787	RA
10	rs947474	6,390,450	PRKCQ	**G**	2.51E-05	0.9038	3.98E-05	0.8872	0.1236	0.94	RA, T1D, CeD
1	rs11810143	161,480,649	FCGR2A	**G**	9.34E-05	1.1153	1.74E-04	1.1339	0.1453	1.0709	RA, CD, SLE, UC
6	rs6911690	106,470,963	PRDM1	G	5.17E-04	0.9004	1.69E-04	0.8692	0.4235	0.9605	CD, RA, SLE
4	rs78560100	123,041,471	IL2-21	**C**	4.48E-04	1.131	1.18E-03	1.1425	0.00334	1.1802	CeD, T1D, RA, UC
11	rs570676	36,492,191	TRAF6	A	4.81E-03	0.94	1.10E-03	0.93	0.46	0.97	RA
b) newly associated loci on Immunochip											
19	rs34536443	10,463,118	TYK2	G	**2.70E-13**	0.6885	**2.25E-14**	0.6208	1.16E-02	0.8246	MS, CD, Ps, T1D, SLE
23	rs13397	153,248,248	IRAK1	A	**2.52E-12**	1.2342	**1.23E-12**	1.2747	3.12E-05	1.206	SLE, T1D, CeD
15	rs8026898	69,991,417	TLE3	A	**2.22E-09**	1.1327	**1.37E-10**	1.1662	3.70E-03	1.0969	BD
15	rs8043085	38,828,140	RASGRP1	A	1.63E-07	1.1193	**1.40E-10**	1.1713	3.72E-01	1.0303	T1D
1	rs2240336	17,674,402	PADI4	A	**3.64E-08**	0.9003	**5.91E-09**	0.8794	2.83E-02	0.9381	RA
1	rs8192284	154,426,970	IL6R	**C**	**1.32E-08**	0.897	1.57E-07	0.8903	2.44E-02	1	Asthma, CHD
16	rs13330176	86,019,087	IRF8	A	9.31E-07	1.1131	**4.03E-08**	1.1475	7.72E-01	1.0099	SLE, UC, MS, PBC
c) suggestive associated loci on Immunochip											

7	rs75351767	37,427,351	ELMO1	**G**	2.94E-07	1.1604	3.85E-05	1.1473	5.95E-05	1.1917	
17	rs12936409	38,043,649	IKZF3	**A**	3.72E-07	1.1029	6.90E-07	1.1158	1.13E-01	1.0483	CD, UC T1D
6	rs72928038	90,976,768	BACH2	**A**	8.23E-07	1.1282	1.12E-04	1.1156	2.16E-03	1.1207	T1D, CD
3	rs1875463	143,165,502	SLC9A9	**A**	1.51E-06	0.8996	2.88E-04	0.9119	4.75E-05	0.8709	
10	rs12764378	63,800,004	ARID5B	A	1.81E-05	1.0994	1.64E-06	1.1292	6.96E-01	1.0135	
5	rs6579837	150,434,894	TNIP1	A	4.04E-05	1.1498	1.71E-06	1.2062	2.48E-02	1.1239	SLE, Ps
14	rs911263	68,753,593	ACTN1	G	4.59E-04	0.9302	2.28E-06	0.8924	8.33E-01	0.9934	T1D
10	rs3802604	8,102,272	GATA3	G	5.07E-05	1.0813	3.68E-06	1.1085	2.17E-01	1.0372	
18	rs62097857	12,857,758	PTPN2	**A**	4.46E-06	1.2224	8.80E-05	1.2171	1.14E-04	1.2825	CD, CeD, T1D
13	rs7993214	40,350,912	COG6	A	1.02E-04	0.9263	4.55E-06	0.9005	4.32E-01	0.9768	
1	rs61828284	173,299,743	TNFSF18 / TNFSF4	A	5.68E-05	0.8659	5.47E-06	0.8256	8.26E-01	0.9885	CD, SLE
13	rs17230016	82,338,338	SPRY2	**G**	9.61E-06	0.8838	1.78E-04	0.886	1.44E-03	0.8709	

Supplementary Table 3: Summary of lead SNPs for RA associated loci on Immunochip. Results are from 11,475 RA cases versus 15,870 controls (STUDY) or for a subset of 7,222 ACPA positive cases (ACPA +) or 3,297 ACPA negative cases (ACPA -) versus the 15,870 controls. Associations reaching genome wide significance **emboldened** and underlined .*co-ordinates based on GRCh37 assembly

	Locus	Chr	All Immunochip +GWAS			ACPA + Immunochip +GWAS		
			bp**	SNP	P	bp**	SNP	P
known	MMEL1	1	2,528,133	rs2843401	**3.62E-08**	2,528,133	rs2843401	**7.24E-10**
	REL	2	61,136,129	rs13031237	**1.40E-09**	61,136,129	rs13031237	**1.26E-11**
	SPRED2	2	65,597,671	rs11673987	**3.49E-08**	65,598,241	rs1858036	**7.48E-10**
	AFF3	2	100,806,514	rs6712515	**2.82E-11**	100,806,514	rs6712515	**2.00E-11**
	STAT4	2	191,969,879	rs10181656	**2.34E-13**	191,921,874	rs11893432	**1.53E-11**
	CD28|CTLA4	2	204,738,919	rs3087243	**7.48E-11**	204,738,919	rs3087243	**3.88E-11**
	RBPJ	4	26,086,569	rs17630466	**5.67E-13**	26,104,113	rs12506688	**6.00E-13**
	ANKRD55	5	55,440,730	rs71624119*	**5.68E-20**	55,440,730	rs71624119*	**1.20E-11**
	GIN1	5	102,608,924	rs2561477	**6.52E-10**	102,608,924	rs2561477	8.56E-08
	TNFAIP3	6	138,006,504	rs6920220	**4.24E-15**	138,006,504	rs6920220	**3.55E-18**
	TAGAP	6	159,489,791	rs212389	2.99E-05	159,489,791	rs212389	**9.11E-09**
	CCR6	6	167,540,842	rs1571878	**2.29E-08**	167,540,842	rs1571878	**1.23E-12**
	IRF5	7	128,580,680	rs3807306	**7.12E-10**	128,580,680	rs3807306	**4.75E-10**
	CCL21	9	34,710,260	rs2812378	**8.50E-09**	34,710,260	rs2812378	**1.26E-09**
	TRAF1	9	123,683,569	rs2269060	3.71E-07	123,683,569	rs2269060	**1.73E-08**
	IL2RA	10	6,108,340	rs10795791	**1.11E-09**	6,108,340	rs10795791	**1.19E-09**
	DDX6	11	118,611,781	rs10892279	**2.95E-08**	118,611,781	rs10892279	**1.34E-10**
	CD40	20	44,747,947	rs4810485	2.20E-07	44,747,947	rs4810485	**8.86E-11**
new	PADI4	1	17,674,108	rs2240339	**2.57E-10**	17,674,108	rs2240339	**1.46E-10**
	POU3F1	1	38,616,871	rs883220	1.19E-07	38,616,871	rs883220	**2.09E-08**
	IL6R	1	154,426,970	rs2228145*	**1.30E-08**	154,426,970	rs2228145*	1.58E-07
	GATA3	10	8,095,340	rs2275806	7.38E-08	8,095,340	rs2275806	**4.58E-08**
	ARID5B	10	63,800,004	rs12764378	**1.00E-08**	63,800,004	rs12764378	**4.45E-10**
	CD5	11	60,909,581	rs595158	**3.35E-08**	60,909,581	rs595158	5.56E-06
	RASGRP1	15	38,828,140	rs8043085	**1.76E-08**	38,828,140	rs8043085	**4.82E-11**
	TLE3	15	69,991,417	rs8026898	**6.03E-11**	69,991,417	rs8026898	**6.52E-12**
	IRF8	16	86,019,087	rs13330176	1.68E-07	86,019,087	rs13330176	**5.30E-09**
	IKZF3	17	38,062,196	rs2305480	**4.20E-09**	38,040,763	rs2872507	**2.79E-09**
	TYK2	19	10,463,118	rs34536443*	**2.69E-13**	10,463,118	rs34536443*	**2.24E-14**
	RCAN1	21	35,911,599	rs2834512	4.31E-07	35,911,599	rs2834512	**3.06E-08**
	RUNX1	21	36715,761	rs9979383	**5.03E-10**	36,715,761	rs9979383	**3.69E-08**

Supplementary Table 4. Combined analysis of Immunochip results and imputed GWAS data from non-overlapping samples.

Results from the full Immunochip analysis (11,475 RA cases versus 15,870 controls) were added to non-overlapping , ACPA positive samples (2,363) from the latest GWAS meta analysis (All Immunochip +GWAS). In addition the ACPA positive GWAS samples were added to the ACPA positive Immunochip analysis (7,222 cases versus 15,870 controls) (ACPA+Immunochip +GWAS). Associations reaching genome wide significance **emboldened** and underlined**.***SNP not on GWAS.**co-ordinates based on GRCh37 assembly

CHR	SNP	POS	GENE	META ACPA+ (P value)	META ACPA + (OR)	META ACPA- (P value)	META ACPA- (OR)	META OR of OR (P value)	META OR of OR (OR)
	a) Loci more significant in ACPA positive at p< 0.05 level								
1	rs2476601	114,179,091	PTPN22	9.23E-78	1.79	2.60E-04	1.18	2.44E-19	1.49
6	rs59466457	167,457,744	CCR6	4.77E-10	1.14	6.84E-01	0.99	1.00E-06	1.16
20	rs6032662	44,167,717	CD40	4.22E-09	0.86	8.31E-01	1.01	5.96E-06	0.85
15	rs8043085	36,615,432	RASGRP1	3.45E-10	1.17	3.63E-01	1.03	2.13E-04	1.14
6	rs629326	159,416,701	TAGAP	2.59E-06	0.90	7.17E-01	1.01	2.36E-04	0.89
11	rs4938573	118,247,052	DDX6	4.84E-07	0.87	5.96E-01	0.98	1.46E-03	0.89
15	rs77397211	36,757,788	RASGRP1	1.10E-03	1.15	5.24E-01	0.96	1.53E-03	1.21
2	rs34695944	60,978,354	REL	1.76E-08	1.13	3.59E-01	1.03	1.81E-03	1.10
1	rs2843401	2,517,993	MMEL1	8.00E-09	0.87	5.41E-01	0.98	1.88E-03	0.90
6	rs58721818	138,285,432	TNFAIP3	5.94E-12	1.46	8.99E-02	1.14	2.15E-03	1.27
2	rs6546146	65,409,828	SPRED2	6.03E-07	0.89	5.08E-01	0.98	2.20E-03	0.91
19	rs34536443	10,324,118	TYK2	3.03E-14	0.62	7.50E-03	0.82	2.95E-03	0.77
16	rs13330176	84,576,588	IRF8	8.72E-08	1.14	7.26E-01	1.01	3.40E-03	1.11
10	rs12722508	6,128,749	IL2RA	2.01E-05	0.85	8.91E-01	1.01	3.67E-03	0.86
1	rs798000	117,082,219	CD2	4.31E-06	1.11	4.69E-01	1.02	7.27E-03	1.09
10	rs12764378	63,470,010	ARID5B	9.00E-07	1.13	6.56E-01	1.02	8.81E-03	1.10
2	rs11571302	204,451,179	CTLA4/CD28	4.56E-08	0.89	1.05E-01	0.96	8.90E-03	0.92
6	rs6920220	138,048,197	TNFAIP3	3.09E-13	1.20	2.20E-02	1.08	9.86E-03	1.10
4	rs932036	25,699,960	RBPJ	3.55E-10	1.16	1.76E-02	1.08	1.78E-02	1.08
17	rs2872507	35,294,289	GSDML	1.31E-06	1.11	2.39E-01	1.03	2.76E-02	1.07
9	rs2812378	34,700,260	CCL21	5.18E-10	1.15	1.17E-02	1.08	3.56E-02	1.07
21	rs2834512	34,833,469	RCAN1	2.93E-04	0.88	5.07E-01	0.97	4.41E-02	0.91
17	rs12936409	35,297,175	GSDML	7.71E-07	1.11	1.13E-01	1.05	4.52E-02	1.06
	b) Significant in both ACPA positive and negative and no significant difference at p< 0.05 level								
5	rs71624119	55,476,487	ANKRD55	1.71E-11	0.84	6.23E-12	0.79	8.25E-02	1.07

8	rs4840565	11,382,954	BLK	3.43E-04	1.09	8.53E-05	1.13	3.32E-01	0.97
21	rs9979383	35,637,631	RUNX1	3.15E-05	0.91	9.90E-05	0.89	5.54E-01	1.02
5	rs39984	102,625,191	GIN1	3.83E-06	0.88	1.65E-04	0.87	7.61E-01	1.01
1	rs2014863	197,076,224	PTPRC	8.74E-04	1.08	8.35E-04	1.10	3.69E-01	0.97
2	rs932169	191,637,523	STAT4	2.39E-02	1.09	1.16E-03	1.18	1.20E-01	0.92
19	rs3176767	10,310,751	ICAM3	2.71E-05	1.11	1.91E-03	1.11	8.59E-01	1.01
4	rs78560100	123,260,921	IL2_21	1.17E-03	1.14	2.14E-03	1.18	6.41E-01	0.97
2	rs13426947	191,641,499	STAT4	4.94E-09	1.17	2.62E-03	1.11	1.70E-01	1.05
11	rs595158	60,666,157	CD5	1.76E-05	1.10	5.97E-03	1.08	6.42E-01	1.01
3	rs35677470	58,158,676	DNASE1L3	1.50E-06	1.21	9.28E-03	1.15	5.16E-01	1.04

Supplementary Table 5. Comparison of the known and newly discovered confirmed RA susceptibility loci in ACPA positive (7,222 cases versus 15,870 controls) and ACPA negative disease (3,297 cases versus 15,870 controls) on Immunochip. OR of OR is a formal test to assess, the difference in association between the two serological forms of disease.

Chromosome name	REGION Position on Chromosome (bp)	Lead SNP	GRAIL p-value	CANDIDATE GENE
1	2,528,133	rs2843401	7.09E-06	TNFRSF14
1	17,674,537	rs2240335	4.04E-02	PADI4
1	38,616,871	rs883220	9.67E-01	POU3F1
1	114,377,568	rs2476601	2.87E-05	PTPN22
1	117,263,138	rs11586238	3.69E-10	CD2
1	154,426,970	rs2228145	3.05E-05	IL6R
1	161,467,042	rs12746613	4.33E-06	FCGR2B
1	167,411,384	rs864537	2.20E-11	CD247
1	198,700,442	rs10919563	1.25E-10	PTPRC
2	61,136,129	rs13031237	2.18E-06	REL
2	65,595,586	rs934734	1.44E-01	SPRED2
2	100,806,940	rs11676922	5.37E-01	AFF3
2	191,935,804	rs10168266	9.61E-09	STAT4
2	204,610,396	rs1980422	2.77E-12	CD28
2	204,738,919	rs3087243	1.42E-11	ICOS
3	58,556,841	rs13315591	8.95E-01	DNASE1L3
4	26,104,113	rs12506688	7.39E-01	RBPJ
4	123,509,421	rs6822844	4.32E-09	IL2
5	55,438,580	rs6859219	1.00E+00	ANKRD55
5	102,608,924	rs2561477	9.36E-01	GIN1
6	106,568,034	rs548234	1.80E-04	PRDM1
6	138,002,637	rs10499194	2.12E-04	TNFAIP3
6	159,482,521	rs394581	1.62E-05	TAGAP
6	167,540,842	rs1571878	4.26E-07	CCR6
7	128,594,183	rs10488631	3.26E-04	IRF5
8	11,343,973	rs2736340	2.59E-02	BLK
9	34,743,681	rs951005	9.60E-06	CCL21
9	123,640,500	rs1953126	2.08E-06	TRAF1
10	6,099,045	rs2104286	4.41E-10	IL2RA
10	6,393,260	rs4750316	4.22E-08	PRKCQ
10	8,095,340	rs2275806	7.26E-05	GATA3
10	63,800,004	rs12764378	8.84E-01	ARID5B
11	36,525,293	rs540386	6.71E-11	RAG1
11	60,909,581	rs595158	3.99E-11	CD5
11	118,611,781	rs10892279	9.19E-01	DDX6
12	57,968,715	rs1678542	6.58E-01	B4GALNT1
15	38,828,140	rs8043085	6.82E-08	RASGRP1
15	69,991,417	rs8026898	9.43E-01	KIF23
16	86,019,087	rs13330176	3.00E-07	IRF8
17	38,040,763	rs2872507	2.47E-05	IKZF3
19	10,295,433	rs4804493	7.51E-01	DNMT1

20	44,734,310	rs6032662	4.38E-10	CD40
21	35,911,599	rs2834512	1.97E-01	RCAN1
21	36,715,761	rs9979383	9.14E-02	RUNX1
21	43,836,186	rs11203203	1.06E-01	UBASH3A
22	21,982,892	rs2298428	9.64E-01	YDJC
22	37,544,810	rs3218253	1.00E-08	IL2RB

Supplementary Table 6. Results from a GRAIL analysis indicating the most likely RA susceptibility gene in regions associated at genome wide association levels.

Locus	Gene	Index					Secondary effect					LD with index	1-SNP model	Haplotypic risk		
		SNP	alleles (M/m)	MAF	p	OR	SNP	alleles (M/m)	MAF	p	OR	(r2/D´)	Vs. 2-SNP	haplotype	Freq.	OR
2q33	CD28	rs1980422	A/G	0.23	3.37E-09	1.15	rs55686954	G/A	0.04	4.27-E05	0.8	0.015/1.00	3.27E-05	AA	0.04	base
														AG	0.72	1.26
														GG	0.23	1.43
														GA	0.0002	-
15q14	RASGRP1	rs8043085	C/A	0.23	4.78E-12	1.18	rs77397211	A/G	0.07	1.13E-04	1.17	0.001/0.18	1.25E-04	CA	0.70	base
														CG	0.06	1.17
														AA	0.23	1.18
														AG	0.01	1.39
2p16-p15	REL	rs34695944	A/G	0.37	8.54E-11	1.15	rs78404002	G/A	0.05	9.12E-05	0.78	0.023/0.93	7.39E-05	AA	0.04	base
														AG	0.58	1.2
														GG	0.38	1.36
														GA	0.005	-
2q32	STAT4	rs7574865	C/A	0.22	9.61E-09	1.15	rs3024921	T/A	0.06	6.66E-06	1.18	0.021/1.00	5.27E-06	CT	0.71	base
														AT	0.24	1.15
														CA	0.06	1.20
														AA	0	-
6q23	TNFAIP3	rs6920220	G/A	0.22	1.24E-14	1.20	rs58721818	G/A	0.03	4.36E-08	1.34	0.030/0.47	5.80E-08	GG	0.76	base
														AG	0.21	1.18
														GA	0.02	1.37
														AA	0.02	1.55
19p13	TYK2	rs34536443	C/G	0.05	1.57E-14	0.63	rs12720356	A/C	0.10	1.22E-05	0.85	0.004/1.00	1.02E-05	CA	0.88	base
														CC	0.09	0.85
														GA	0.04	0.62
														GC	0	-

Supplementary Table 7: Haplotype analysis of six loci with additional independent effects on Immunochip.

Chr	POS	Gene region	Lead SNP	Low MAF SNP	MAF UNAFF	MAF AFF	P	OR	r^2 to lead	Location	REG POT7X	CONS 17WAY
2	61,320,107	REL	rs78404002[a]	rs78404002	0.05	**0.04**	3.42E-05	0.83	lead	INTRONIC	0.00	0.00
2	61,391,558	REL		rs17008218	0.05	**0.04**	4.39E-05	0.83	1	INTRONIC	0.00	0.08
2	61,581,489	REL		rs17009924	0.05	**0.04**	9.47E-05	0.84	0.92	INTRONIC	0.00	0.00
2	61,629,635	REL		rs78534076	0.05	**0.04**	4.91E-05	0.83	0.93	INTERGENIC	0.00	0.03
2	204,294,760	CTLA4	rs55686954[a]	rs55686954	**0.04**	**0.03**	1.20E-07	0.77	lead	INTRONIC	0.15	0.00
6	138,178,293	TNFAIP3	rs58721818[a]	rs117267050	**0.03**	**0.04**	6.31E-08	1.31	0.92	INTERGENIC	0.00	0.00
6	138,239,199	TNFAIP3		rs5029949	**0.03**	**0.04**	3.51E-08	1.31	0.91	INTRONIC	0.00	0.01
6	138,269,057	TNFAIP3		rs7752903	**0.03**	**0.04**	3.15E-08	1.32	0.95	INTERGENIC	0.00	0.006
6	138,272,082	TNFAIP3		rs7749323	**0.03**	**0.04**	2.87E-08	1.32	0.95	INTERGENIC	0.00	0.00
6	138,284,130	TNFAIP3		rs6932056	**0.03**	**0.04**	3.93E-06	1.30	0.95	INTERGENIC	0.00	0.003
6	138,285,393	TNFAIP3		rs61117627	**0.03**	**0.04**	1.25E-08	1.34	1	INTERGENIC	0.006	0.00
6	138,285,432	TNFAIP3		rs58721818	**0.03**	**0.04**	4.07E-09	1.34	lead	INTERGENIC	0.11	0.035
19	10,288,721	TYK2	rs34536443	rs74956615	0.06	**0.04**	5.21E-11	0.74	1	3’ UTR	0.00	0.998
19	10,324,118	TYK2		rs34536443	**0.05**	**0.03**	2.70E-13	0.69	lead	Non Synonymous	0.39	0.19

Supplementary Table 8: Low MAF (<5%) SNPs (in either cases or controls) in strong LD (r^2>0.9) with a lead SNP from Immunochip analysis.
[a]=Lead SNP reported for these regions is an independent affect in region after conditioning on most associated SNP

GWAS						IMMUNOCHIP							
Index SNP	GENE	CHR	MAF	P	OR	Index SNP	MAF	P	OR	GWAS index SNP		r^2	D'
										P	OR		
*rs13315591[a]	PXK	3	0.09	$4.6x10^{-8}$	1.29	rs35677470	0.08	$1.7 X 10^{-07}$	1.19	0.28	1.03	0.27	0.58
rs10488631	IRF5	7	0.11	$4.2x10^{-11}$	1.19	rs3807306	0.49	$1.9 X 10^{-07}$	0.89	$1.8 X 10^{-05}$	1.1	0.2	1
rs934734	SPRED2	2	0.49	$5.3x10^{-10}$	1.13	rs6546146	0.38	$8.0 X 10^{-07}$	0.9	$3.0 X 10^{-04}$#	1.07	0.53	0.95
rs3761847	*TRAF1*	*9*	*0.43*	*$2.1x10^{-7}$*	*1.13*	*rs10739580*	*0.33*	*$1.7 X 10^{-06}$*	*1.12*	*$1.7 X 10^{-04}$*	*1.07*	*0.74*	*1*
rs2104286	IL2RA	10	0.27	$2x10^{-3}$	0.92	rs10795791	0.4	$3.0 X 10^{-06}$	1.09	$1.0 X 10^{-04}$#	0.91	0.25	1
rs11586238	CD2	1	0.24	$1x10^{-5}$	1.13	rs798000	0.34	$6.2 X 10^{-06}$	1.11	*$3.0 X 10^{-03}$*#	1.07	0.33	0.72
rs10919563	PTPRC	1	0.13	$2x10^{-4}$	0.88	rs2014863	0.36	$2.1 X 10^{-05}$	1.09	$7.7 X 10^{-04}$	0.91	0.07	1
rs1678542	KIF5A	12	0.38	$2x10^{-4}$	0.91	rs10683701	0.33	$2.3 X 10^{-05}$	0.9	*$1.0 X 10^{-03}$*#	0.93	0.27	0.58
rs548234	PRDM1	6	0.33	$9.7x10^{-5}$	1.1	rs6911690	0.12	$1.2 X 10^{-04}$	0.87	0.02	1.04	0.1	1
rs6822844	IL2-IL21	4	0.18	$7x10^{-4}$	0.9	rs78560100	0.07	$5.8 X 10^{-04}$	1.13	0.01	0.94	0.02	1
*rs540386[b]	TRAF6	11	0.14	$3x10^{-4}$	0.88	rs570676	0.38	$2.1 X 10^{-03}$	0.93	0.07	0.95	0.18	1

Supplementary Table 9: Comparison of lead SNPs for previously confirmed RA loci indentified by GWAS and Immunochip analysis where the focus of association has moved (r^2<0.8).*Actual SNP not found on Immunochip. Perfect proxy (r^2 and D' = 1) used for Immunochip comparison [a] = rs9813011 [b]= rs5030437. #= Result from ACPA positive analysis

Gene	Chr	Before Immunochip		Results from Immunochip					
		0.1cM localisation	Region size	SNP	LD region r^2>0.9*	Region size	All SNPS (ns) in r^2>0.9 region	LD SNPS (ns) r^2>0.9	Localization of LD region (r2>0.9) relative to nearest genes
a) Known loci on Immunochip									
PTPN22	1p13	113,863,087-114,527,968	665kb	**rs2476601**[b]	114,303,808-114,377,568	73.76kb	682 (27)	2 (1)	Complete RSBN1; Exon 14 to 52.62kb 3' of PTPN22
ANKRD55	5q11	55,414,956-55,447,909	33kb	**rs71624119**[a]	55,440,730-55,442,249	1.52kb	19 (0)	2 (0)	Intron 6 of ANKRD55
TNFAIP3	6q23	137,896,596-138,125,335	229kb	**rs6920220**[b]	137,959,235-138,006,504	47.27kb	761 (0)	9 (0)	181.85kb 5' of TNFAIP3
TNFAIP3	**6q23**	137,896,596-138,125,335	229kb	**rs58721818**[g]	**138,178,293-138,243,739**	**65.45kb**	**835 (38)**	**7 (0)**	**TNFAIP3**
RBPJ	4p15	26,028,805-26,134,465	106kb	**rs932036**[a]	26,085,480-26,128,710	43.23kb	486 (0)	25 (0)	36.37kb 5' of RBPJ
CCR6	6q27	167,355,854-167,547,954	192kb	**rs59466457**[b]	167,526,096-167,540,842	14.75kb	234 (0)	6 (0)	Intron 1 of CCR6
STAT4	2q32	191,873,553-192,007,734	134kb	**rs13426947**[a]	191,900,449-191,935,804	35.36kb	398 (11)	10 (0)	Intron 5 to 18 of STAT4
STAT4	**2q32**	191,873,553-	134kb	**rs932169**[e]	**191,929,278-191,929,278**	**1bp**	**1 (0)**	**1 (0)**	**Intron 8 of STAT4**

		192,007,734							
CCL21	9p13	34,649,442-34,974,974	325kb	**rs2812378**[b]	34,707,373-34,710,338	2.97kb	41 (4)	3 (0)	CCL21
CD40	20q13	44,594,228-44,784,336	190kb	**rs6032662**[b]	44,730,245-44,747,947	17.70kb	239 (1)	10 (0)	16.67kb 5' to intron 1 of CD40
MMEL1	1p36	2,406,888-2,785,671	378kb	**rs2843401**[b]	2,516,781-2,709,164	192.38kb	4571 (73)	85 (1)	Complete MMEL1, C1ORF93; TTC34
AFF3	2q11	100,544,954-101,038,647	493kb	**rs10209110**[a]	100,640,432-100,730,111	89.68kb	990 (2)	18 (0)	5' region to intron 2 of AFF3
REL	2p16	60,914,729-61,864,047	949kb	**rs34695944**[b]	61,072,664-61,164,331	91.67kb	876 (18)	14 (0)	Complete REL
REL	**2p16**	60,914,729-61,8640,47	949kb	**rs78404002**[g]	61,466,603-61,776,131	309.53kb	3579 (24)	5 (0)	**78.23kb 5' to intron 53 of USP34; SNORA70B; XPO1; 315.96kb 3' of REL**
CTLA4	2q33	204,678,417-204,816,382	138kb	**rs11571302**[b]	204,738,919-204,745,003	6.08kb	83 (0)	4 (0)	236bp 3' of CTLA4; 56.47kb 5' of ICOS;
GIN1	5q21	102,098,582-102,711,659	613kb	**rs39984**[a]	102,595,778-102,625,335	29.56kb	385 (7)	40 (0)	Intron 1 to 10.97kb 3' of C5orf30; 139.92kb 5'of GIN1
PXK	3p14	58,154,177-58,549,297	395kb	**rs35677470**[a]	58,181,499-58,183,636	2.14kb	37 (2)	2 (1)	Exon 8 to intron 9 of DNASE1L3; 134.97kb 5' of PXK
IRF5	7q32	128,549,568-	228kb	**rs3807306**[b]	128,580,680-128,580,680	1bp	1 (0)	1 (0)	Intron 1 of IRF5

		128,777,520							
IL2RB	22q12	37,537,514-37,562,111	24kb	**rs3218251**[b]	37,544,245-37,545,505	1.26kb	24 (0)	5 (0)	Intron 1 of IL2RB
DDX6	11q23	118,341,921-118,765,600	423kb	**rs4938573**[b]	118,662,993-118,745,884	82.89kb	1169 (0)	48 (0)	Complete SETP16; 1.14kb 5' of DDX6
SPRED2	2p14	65,397,595-65,717,094	319kb	**rs6546146**[b]	65,556,324-65,598,300	41.98kb	585 (7)	13 (0)	Intron 1 to intron 4 of SPRED2
TAGAP	6q25	159,340,939-159,541,830	201kb	**rs629326**[b]	159,489,791-159,496,713	6.92kb	90 (0)	3 (0)	23.61kb 5' of TAGAP
TRAF1	9q33	123,351,121-124,131,512	780kb	**rs10739580**[b]	123,640,500-123,708,286	67.79kb	920 (21)	75 (0)	Complete TRAF1
IL2RA	10p15	6,030,243-6,161,781	131kb	**rs10795791**[a]	6,106,266-6,108,340	2.08kb	29 (0)	4 (0)	1.93kb 5' of IL2RA
BLK	8p23	11,285,384-11,414,013	128kb	**rs4840565**[a]	11,338,383-11,352,485	14.10kb	267 (0)	5 (0)	13.13kb 5' to intron 1 of BLK
CD2	1p13	117,231,902-117,299,420	67kb	**rs798000**[b]	117,280,696-117,280,696	1bp	2 (0)	1 (0)	16.31kb 5' of CD2
CD28	2q33	204,446,380-204,690,355	244kb	**rs1980422**[f]	204,610,004-204,634,569	24.57kb	314 (0)	7 (0)	7.45kb 3' of CD28; 97.94kb 5' of CTLA4
CD28	**2q33**	204,446,380-204,690,355	244kb	**rs55686954**	204,586,515-204,586,515	1bp	1(0)	1(0)	Intron 1 of CD28; 145.99kb 5' of CTLA4

PTPRC	1q31	197,311,228-197,938,330	627kb	**rs2014863**[a]	198,791,907-198,810,008	18.10kb	175 (0)	6 (0)	65.36kb 3' of PTPRC
KIF5A	12q13	57,626,582-58,124,534	497kb	**rs10683701**[b]	58,034,835-58,105,094	70.26kb	945 (8)	104 (0)	snoU13;52.90kb 5' to intron 5 of OS9; 54.42kb 3' of KIF5A
PRKCQ	10p15	6,388,071-6,545,104	157kb	**rs947474**[a]	6,390,450-6,390,450	1bp	1 (0)	1 (0)	78.66kb 3' of PRKCQ
FCGR2A	1q23	161,282,384-161,679,644	397kb	**rs10494360**[b]	161,463,876-161,480,649	16.77kb	230 (13)	17 (0)	11.34kb 5' to exon 5 of FCGR2A
PRDM1	6q21	106,532,756-106,627,910	95kb	**rs6911690**[b]	106,435,981-106,508,640	72.66kb	831 (0)	59 (0)	25.55kb 5' of PRDM1
IL2-IL21	4q27	122,982,314-123,565,302	583kb	**rs78560100**[a]	123,030,583-123,503,591	473.01kb	5420 (73)	119 (0)	KIAA1109;ADAD1;IL2; 30.19kb 3' of IL21
TRAF6	11p12			**rs570676**[b]	36,486,064-36,519,624	33.56kb	434 (14)	11 (0)	Intron 3 to 22.51kb 3' of TRAF6
b) Novel loci on Immunochip									
TYK2	19p13	10,396,336-10,628,468	232kb	**rs34536443**[b]	10,427,721-10,492,274	64.55kb	973 (124)	3 (1)	47.96kb 5' to exon 13 of RAVER1; complete ICAM3; complete TYK2
TYK2	**19p13**	10,396,336-10,628,468	232kb	**rs3176767**[g]	**10,446,897-10,449,778**	**2.88kb**	**58 (8)**	**16 (1)**	**Intron 1 to intron 2 of ICAM3; 11.43kb 3' of TYK2**
IRAK1	Xq28	153,170,618-154,445,759	1,275kb	**rs13397**[b]	153,196,345-153,248,248	51.9kp	406 (52)	3 (0)	5' to exon 2 of TMEM187; HCFC1; 25kb 3' of IRAK1

TLE3[#]	15q23			**rs8026898**[b]	69,984,462-70,010,647	26.19kb	376 (0)	6 (0)	329.48kb 3' of TLE3
RASGRP1	15q14	38,814,377-38,972,177	157kb	**rs8043085**[b]	38,828,140-38,844,106	15.97kb	192 (0)	4 (0)	Intron 2 of RASGRP1;
RASGRP1	**15q14**	38,814,377-38,972,177	157kb	**rs77397211**[f]	**38,970,496-38,970,496**	**1bp**	**1 (0)**	**1 (0)**	**112.72kb 5' of RASGRP1**
PADI4	1p36	17,597,181-17,679,598	82kb	**rs2240336**[b]	17,673,102-17,674,402	1.30kb	19 (0)	3 (0)	Intron 9 PADI4
IL6R	1q21	155,019,710-156,045,183	1,025kb	**rs8192284**[a] (rs2228145)	154,418,749-154,428,283	9.54kb	132 (4)	10 (1)	Intron 6 to intron 9 of IL6R
IRF8	16q24	85,993,580-86,024,104	30kb	**rs13330176**[b]	86,016,026-86,019,087	3.06kb	56 (0)	4 (0)	59.83kb 3' of IRF8
(c) Novel loci adding GWAS data									
ARID5B[#]	10q21			**rs12764378**[d]	63,786,554-63,800,004	13.45kb	164 (0)	4 (0)	Intron 4 of ARID5B
RUNX1[#]	21q22			**rs9979383**[c]	36,712,588-36,715,761	3.17kb	62 (0)	3 (0)	5' region of RUNX1
IKZF3	17q12	37,382,674-38,240,216	857kb	**rs12936409/ rs2872507**[c]	37,912,377-38,080,912	168.54kb	1935 (70)	49 (1)	IKZF3;GSDMB; Intron 1 to 164.92kb 3' of ORMDL3
POU3F1[#]	1p34			**rs883220**[d]	38,614,867-38,644,861	30.00kb	427 (0)	9 (0)	102.42kb 5' of POU3F1
RCAN1[#]	21q22			**rs2834512**[d]	35,909,625-35,930,915	21.29kb	370 (0)	13 (0)	Intron 1 of RCAN1
CD5	11q12	60,723,898-	112kb	**rs595158**[c]	60,888,001-	34.63kb	475 (35)	30 (1)	Intron 5 to 27.31kb 3'

		60,836,519		60,922,634				of CD5; Intron 1
GATA3[#]	10p14		**rs2275806**[d]	8,095,340-8,097,368	2.03kb	36 (0)	2 (0)	to 9.73kb 3'of VPS37C 227bp 5' to exon 2 of GATA3

Supplementary Table 10. Localisation of association signals from GWAS and Immunochip for non-HLA RA loci. Previously indentified loci are shown with the most significantly associated SNP on Immunochip (2a). Novel loci are shown with either the best SNP on Immunochip (Table 2b), if $<5x10^{-8}$, or from the most associated SNP from the combined analysis of GWAS and Immunochip data (2c). [a] indicates the data is from all RA samples on Immunochip, [b] is data from Immunochip for ACPA positive individuals, [c] is data from adding GWAS samples and RA Immunochip data and [d] is from ACPA positive Immunochip and GWAS data. SNPs in **bold** represent secondary effects at loci. Secondary effects are defined as $p<5x10^{-4}$, with low evidence of LD between SNPs ($r^2<0.05$), MAF>1%, and a p value that didn't vary substantially on conditioning. [e], [f] and [g] indicate secondary effects where the effect was seen in Immunochip data from all samples, ACPA positive samples or both respectively.*co-ordinates based on GRCh37 assembly. [#]region not included for dense mapping on Immunochip

REGION	SNP	CHR	POS	r^2 with index SNP	Location	REGPOT7X	CONS 17WAY	MAF
Intergenic SNPs with the strongest evidence for regulatory potential								
rs10739580 TRAF1	rs1930786	9	122,731,290	1.00	UPSTREAM	0.798	0.000	0.44
rs4840565 BLK	rs922483	8	11,389,321	0.97	5’ UTR	0.511	0.005	0.33
rs6032662 CD40	rs1883832	20	44,180,389	1.00	5’ UTR	0.486	0.000	0.26
rs10739580 TRAF1	rs881375	9	122,692,719	0.97	INTERGENIC	0.407	0.800	0.43
rs39984 GIN1	rs2288787	5	102,628,605	1.00	INTRONIC	0.399	0.024	0.34
Intergenic SNPs with the strongest evidence for conservation								
rs6911690 PRDM1	rs9320143	6	106,542,674	0.96	INTERGENIC	0.342	1.000	0.13
rs12936409 IKZF3	rs12946510	17	35,165,903	0.90	DOWNSTREAM	0.341	1.000	0.49
rs6911690 PRDM1	rs9399967	6	106,606,016	1.00	INTERGENIC	0.264	1.000	0.13
rs10683701 KIF5A	rs774891	12	56,354,838	0.95	NON-CODING GENE	0.209	1.000	0.33
rs78560100 IL2-IL21	rs62323937	4	123,337,405	0.96	INTRONIC	0.000	1.000	0.08
rs12764378 ARID5B	rs12764378	10	63,470,010	Index	INTRONIC	0.000	1.000	0.18
rs6911690 PRDM1	rs9373828	6	106,594,709	1.00	INTERGENIC	0.148	0.998	0.12
rs6911690 PRDM1	rs7756056	6	106,594,631	1.00	INTERGENIC	0.082	0.998	0.12
rs34536443 TYK2	rs74956615	19	10,288,721	1.00	3’ UTR	0.000	0.998	0.02
Intergenic snps with evidence for both conservation (>0.5) and regulatory potential (>0.1)								
rs6911690 PRDM1	rs9320143	6	106,542,674	0.96	INTERGENIC	0.342	1.000	0.13
rs12936409 IKZF3	rs12946510	17	35,165,903	0.90	DOWNSTREAM	0.341	1.000	0.49
rs6911690 PRDM1	rs9399967	6	106,606,016	1.00	INTERGENIC	0.264	1.000	0.13
rs10683701 KIF5A	rs774891	12	56,354,838	0.95	NON-CODING GENE	0.209	1.000	0.33
rs6911690 PRDM1	rs9373828	6	106,594,709	1.00	INTERGENIC	0.148	0.998	0.12

rs12936409 IKZF3	rs10445308	17	35,191,573	0.94	INTRONIC	0.169	0.989	0.48
rs34695944 REL	rs13017599	2	61,017,835	1.00	DOWNSTREAM	0.231	0.978	0.37
rs34695944 REL	rs67574266	2	60,962,333	1.00	5’ UTR	0.345	0.975	0.37
rs78560100 IL2|IL21	rs62321698	4	123,500,153	0.95	INTRONIC	0.221	0.973	0.07
rs6920220 TNFAIP3	rs6927172	6	138,043,868	1.00	INTERGENIC	0.229	0.965	0.16
rs78560100 IL2|IL21	rs79212788	4	123,648,588	0.93	INTERGENIC	0.108	0.933	0.08
rs39984 GIN1	rs556560	5	102,651,823	0.91	INTERGENIC	0.175	0.818	0.36
rs10739580 TRAF1	rs881375	9	122,692,719	0.97	INTERGENIC	0.407	0.800	0.43
rs12936409 IKZF3	rs9891174	17	35,285,328	1.00	INTRONIC	0.101	0.531	0.47

Supplementary Table 11. Intergenic potential causal SNPs. Intergenic SNPs in strong LD (r2>0.9) with a lead SNP on Immunochip with evidence for either strong regulatory potential (regpot7x >0.35) or conservation (cons17way >0.998), or evidence for both (regpot7x >0.1, cons17way >0.5).

Gene1	SNP1	Gene2	SNP 2	p-value	Z-score
MMEL	rs2843401	FCGR2A	rs11810143	1.73E-05	4.297
PRKCQ	rs947474	GATA3	rs2275806	8.33E-05	3.935
PTPN22	rs2476601	RBPJ	rs12506688	1.44E-04	3.802
PADI4	rs2240336	TAGAP	rs629326	3.26E-04	3.594
ANKRD55	rs71624119	TRAF6	rs570676	4.76E-04	3.494
CTLA4	rs11571302	RASGRP1	rs8043085	4.89E-04	3.487

Supplementary Table 12. Pairwise interactions remaining statistically significant after Bonferroni correction.

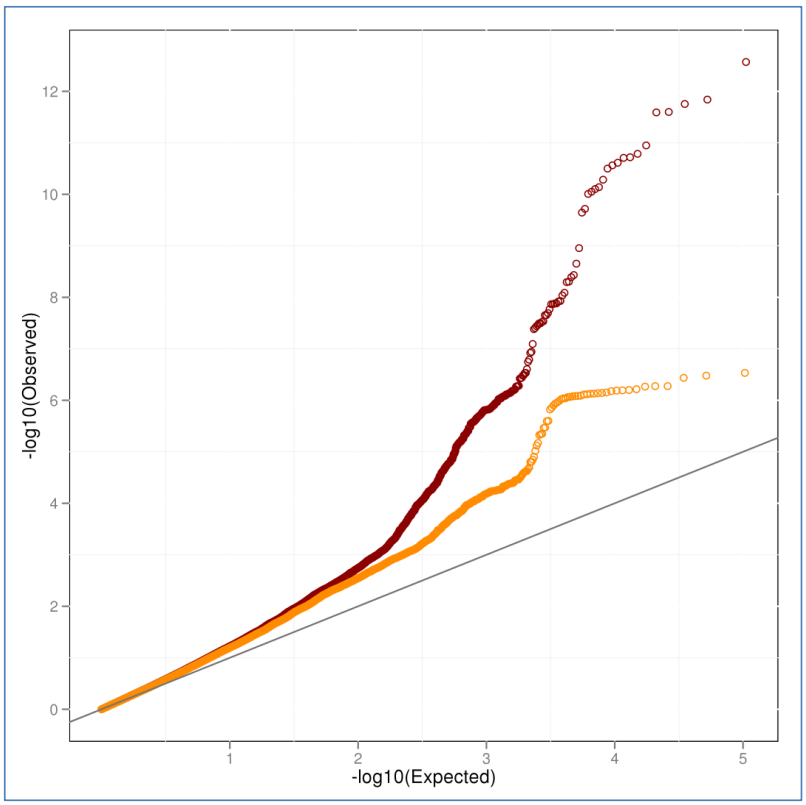
Gene	Top variant(s) Celiac disease	MAF*	*P* Celiac	OR Celiac	Top Variant(s) RA	*MAF**	P RA	OR RA	P for Celiac SNP in RA iChip	OR for Celiac SNP in RA iChip	r^2	*D'*
MMEL1[a]	**rs4445406**	0.34	5.4×10^{-12}	0.87	**rs2843401**	0.33	*$6.6x10^{-9}$*	*0.87*	$1.6x10^{-5}$	*0.92*	0.88	0.96
REL/PUS10[a]	**rs13003464**	0.39	$4.3x10^{-16}$	1.17	**rs34695944**	0.37	*$2.6x10^{-8}$*	*1.13*	0.5	*0.99*	0.02	0.16
					rs78404002	0.05	$3.4x10^{-5}$	0.85			0.06	1
STAT4[a]	**rs6715106**	0.06	8.4×10^{-9}	0.79	**rs13426947a**	0.19	$7.2x10^{-10}$	1.15	$3.5x10^{-4}$	0.86	0.02	1
					rs932169b	0.09	$6.6x10^{-6}$	1.16			0.004	1
STAT4	**Signal 2 rs6752770**	0.29	1.3×10^{-6}	1.10	**rs13426947a**	0.19	$7.2x10^{-10}$	1.15	$1.3x10^{-3}$	1.07	0.15	0.45
					rs932169b	0.09	$6.6x10^{-6}$	1.16			0.01	0.34
STAT4	**Signal 3 rs12998748**	0.12	2.6×10^{-4}	0.90	**rs13426947a**	0.19	$7.2x10^{-10}$	1.15	$5x10^{-3}$	0.92	0.03	1
					rs932169b	0.09	$6.6x10^{-6}$	1.16			0.005	1
CD28[a]	**rs1980422**	0.23	$1`.4 \times 10^{-15}$	1.19	**rs11571302a**	0.48	$4.5x10^{-8}$	0.89	$8.7x10^{-6}$	1.11	0.006	0.14
					rs1980422b	0.23	$8.7x10^{-6}$	1.12			1	1
CTLA4	**Signal 2 rs34037980**	0.22	1.6×10^{-5}	0.91	**rs11571302a**	0.48	$4.5x10^{-8}$	0.89	$1.6x10^{-3}$	0.93	0.21	1
					rs1980422b	0.23	$8.7x10^{-6}$	1.12			0	0.02
CD28	**Signal 3 rs10207814**	0.04	1.3×10^{-4}	1.20	**rs11571302a**	0.48	$4.5x10^{-8}$	0.89	0.8	1.01	0.05	1
					rs1980422b	0.23	$8.7x10^{-6}$	1.12			0.01	1
IL2 _IL21[a]	**rs13132308**	0.16	1.9×10^{-38}	0.71	**rs78560100**	0.07	$5.8x10^{-4}$	1.13	0.01	0.94	0.02	0.99
IL2 _IL21	**Signal 2 rs62323881**	0.07	8.6×10^{-5}	1.15	**rs78560100**	0.07	$5.8x10^{-4}$	1.13	$9x10^{-4}$	1.12	1	1
BACH2[b]	**rs7753008**	0.38	2.7×10^{-7}	1.10	**rs72928038**	0.18	$8.2x10^{-7}$	1.13	$7.8x10^{-3}$	1.05	0.2	0.86
TNFAIP3[a]	**rs17264332**	0.21	5.0×10^{-30}	1.29	**rs6920220a**	0.2	$2.3x10^{-13}$	1.2	$2.4x10^{-10}$	1.15	1	1
					rs58721818b	0.03	$1.2x10^{-8}$	1.38			0.03	0.47
TNFAIP3	**Signal 2 [imm_6_ 138043754]**	0.19	2.1×10^{-7}	0.88	**rs6920220a**	0.2	$2.3x10^{-13}$	1.2	$2.4x10^{-4}$	0.91	0.05	1
	rs77027760				**rs58721818b**	0.03	$1.2x10^{-8}$	1.38			0.007	1
TAGAP[a]	**rs182429**	0.43	8.5×10^{-16}	1.16	**rs629326**	0.41	$1.1x10^{-6}$	0.9	0.02	0.97	0.44	0.69
TAGAP	**Signal 2 rs1107943**	0.07	2.8×10^{-6}	1.18	**rs629326**	0.41	$1.1x10^{-6}$	0.9	0.3	0.97	0.06	1

ELMO1[b]	**[1kg_7_ 37384979]** **rs79758729**	0.10	2.1×10^{-8}	1.18	**rs75351767**	0.10	$2.9x10^{-7}$	1.16	$9.1x10^{-7}$	1.15	0.98	0.99
PVT1[b]	**rs10808568**	0.26	2.2×10^{-5}	0.91	**rs6651252**	0.13	$2.0x10^{-5}$	0.88	0.05	0.96	0.02	0.19
PRKCQ[a]	**rs2387397**	0.23	1.9×10^{-8}	0.88	**rs947474a** **rs569158b**	0.17 0.18	$2.5x10^{-5}$ $3.2x10^{-4}$	0.9 1.1	$4.7x10^{-4}$	0.92	0.75 0.008	1 0.36
DDX6[a]	**rs10892258**	0.24	1.7×10^{-11}	0.86	**rs4938573**	0.18	$5.3x10^{-7}$	0.87	$1.5x10^{-4}$	0.91	0.62	0.88
PTPN2[b]	**rs11875687**	0.15	1.9×10^{-10}	1.17	**rs62097857**	0.04	$4.46x10^{-6}$	1.22	$1x10^{-4}$	1.1	0.008	1
PTPN2	**Signal 2 rs62097857**	0.04	5.2×10^{-5}	1.20	**rs62097857**	0.04	$4.46x10^{-6}$	1.22	$4.5x10^{-6}$	1.22	1	1
IRAK1[a]	**rs13397**	0.13	2.7×10^{-8}	1.18	**rs13397**	0.12	2.7×10^{-8}	1.18	$2.5x10^{-12}$	1.23	1	1

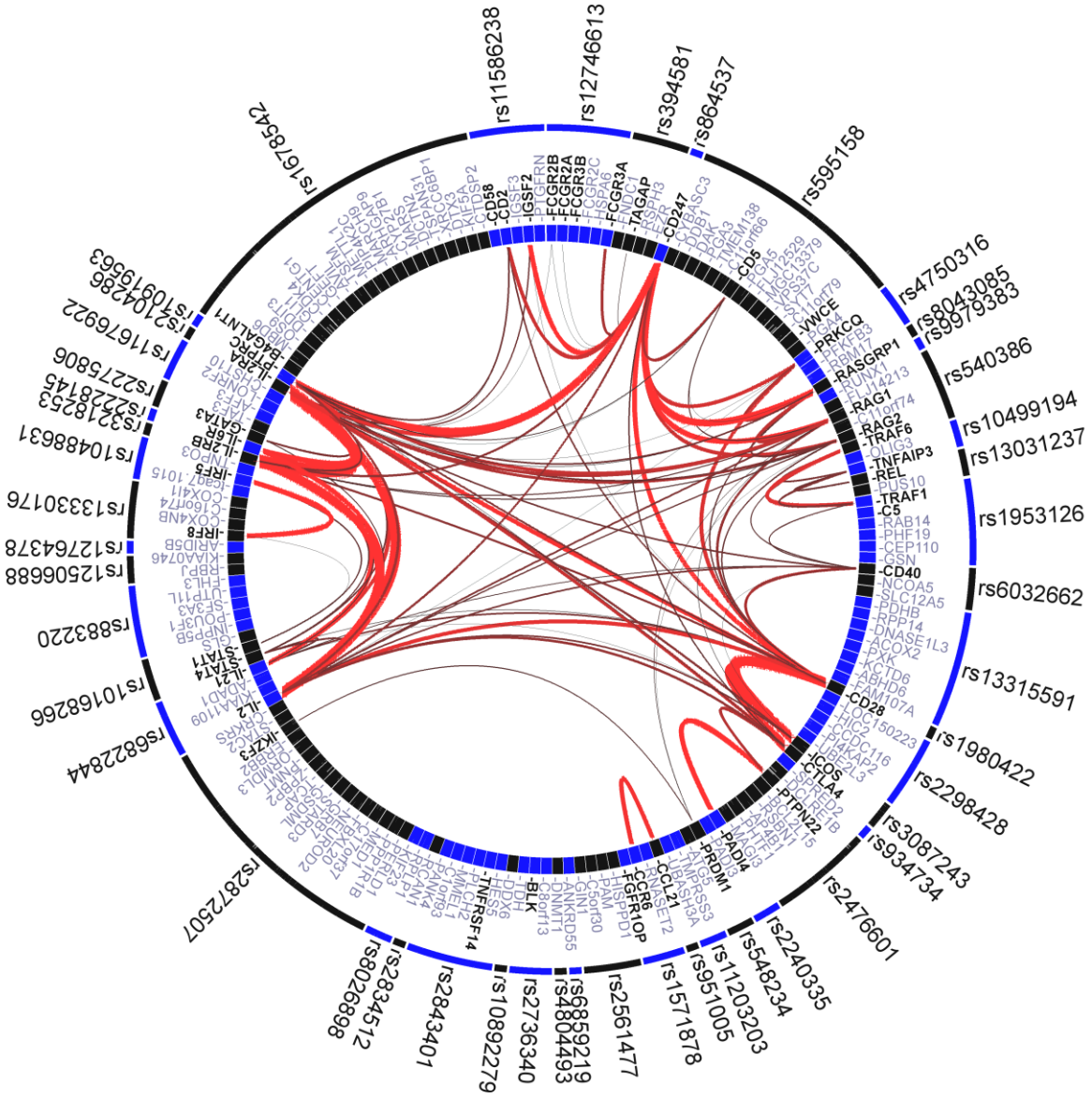
Supplementary Table 14: Comparison of Immunochip dense mapping data in celiac disease and RA, for loci that are either confirmed at genome-wide significance in both diseases ($p<5x10^{-8}$) [a], or are confirmed in celiac disease and highly suggestive ($p<2 \times 10^{-5}$) in RA [b].*All MAF in controls

SNP	Study P-value	λGC corrected (1.23)	Gender_covariate
rs34536443	2.30E-14	2.76E-14	9.00E-15
rs13397	1.20E-12	1.48E-10	1.20E-12
rs8026898	1.40E-10	1.69E-10	4.30E-11
rs8043085	1.40E-10	1.72E-10	1.10E-10
rs2240336	5.90E-09	7.27E-09	2.17E-08
rs8192284	1.30E-08	1.62E-08	7.20E-08
rs13330176	4.00E-08	4.95E-08	4.05E-08

Supplementary Table 15. Results for novel loci on Immunochip after λGC and gender correction



Supplementary Figure 1: QQ plot of observed versus expected results for the meta-analysis of the six sample collections. Red – excluding the MHC region and all other previously identified susceptibility loci, Orange – excluding the MHC region and all other previously identified and newly discovered loci.



Supplementary Figure 2. GRAIL-VIZ plots for the confirmed rheumatoid arthritis genes. Associated genomic regions are along the outer circle, with the inner circle showing the individual genes. The thickness of lines connecting genes shows the strength of the GRAIL signal.

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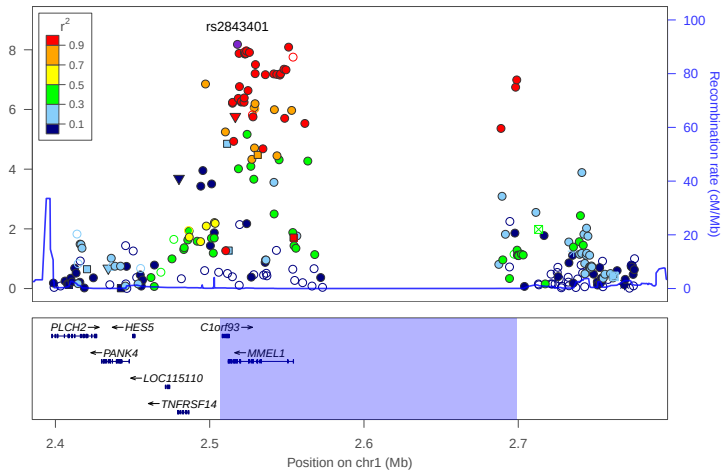

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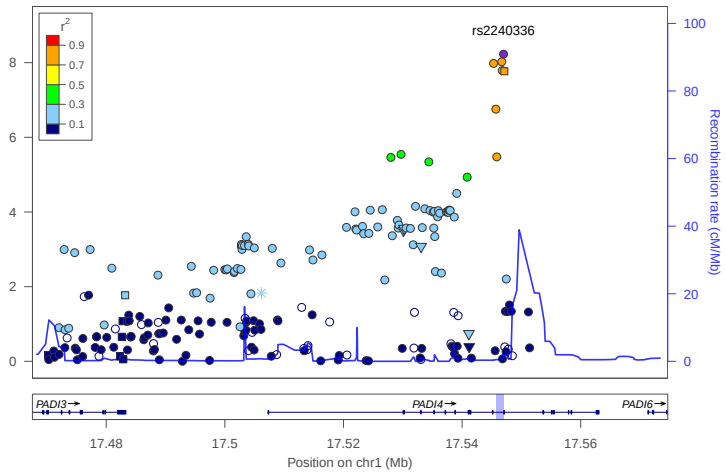

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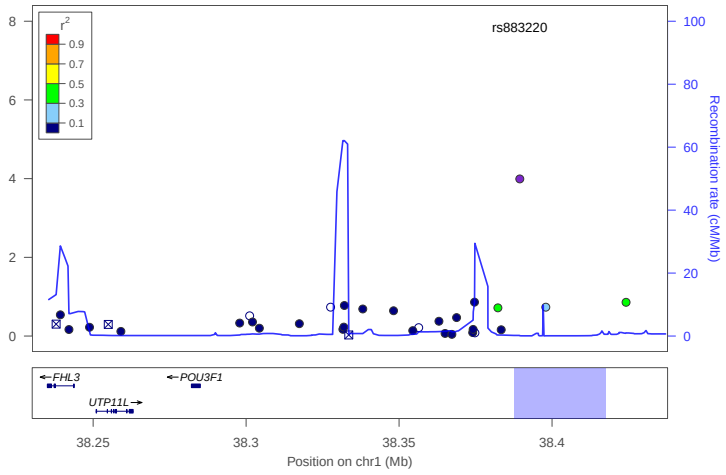

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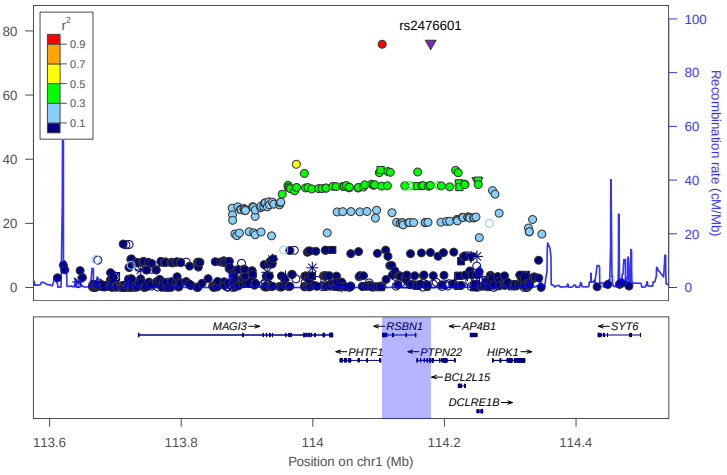

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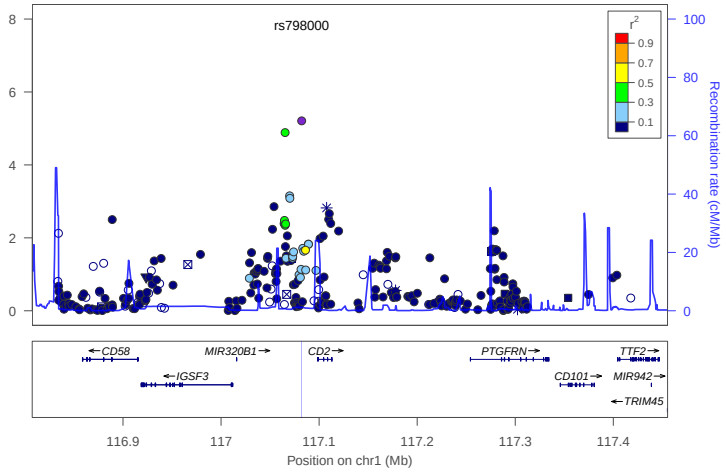

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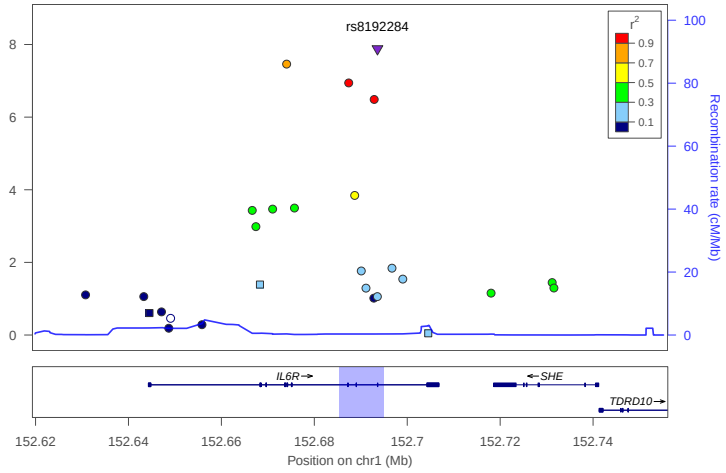

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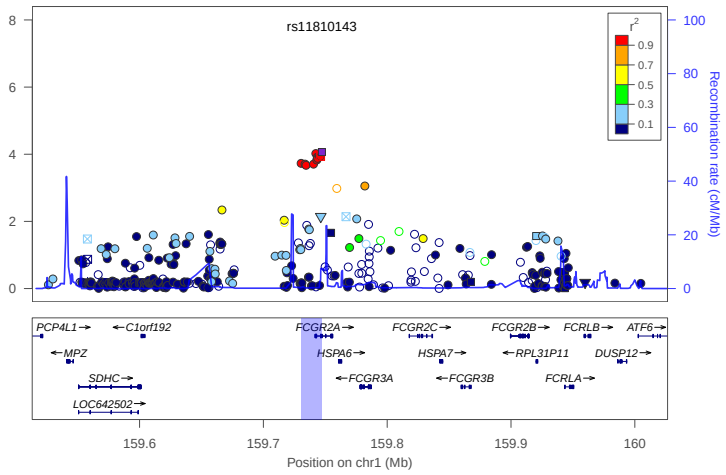

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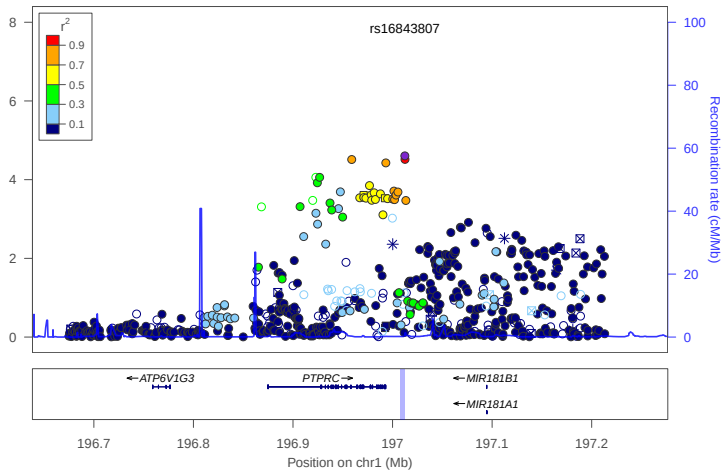

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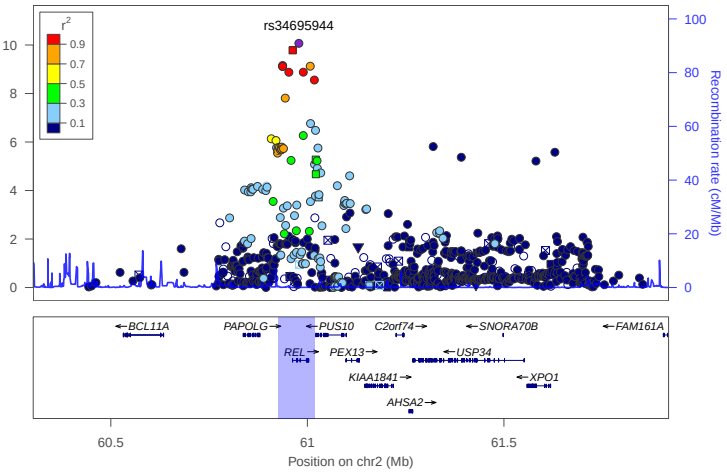

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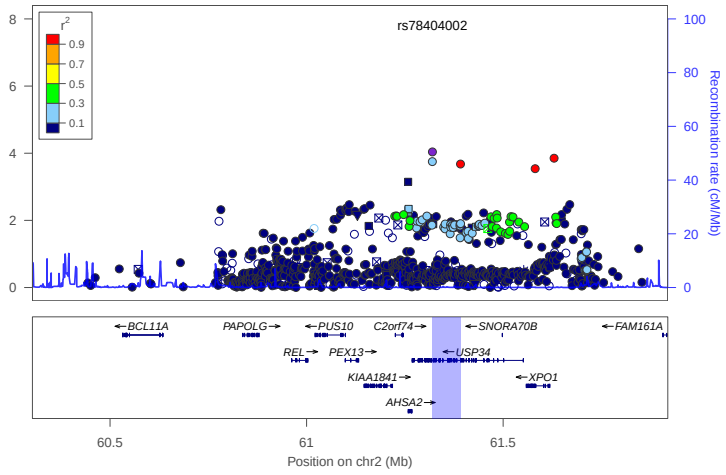

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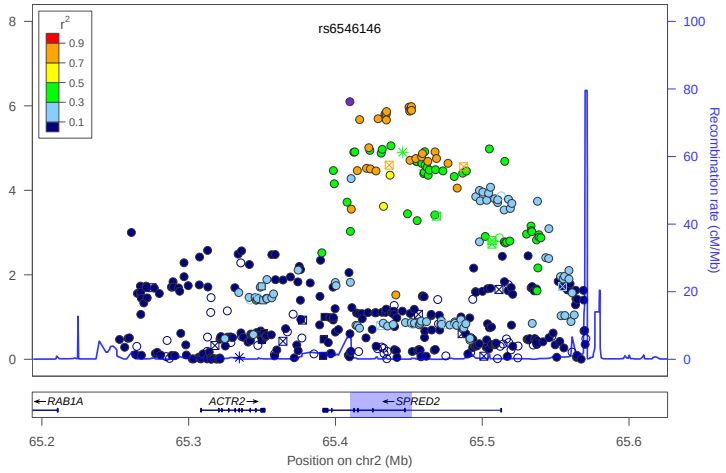

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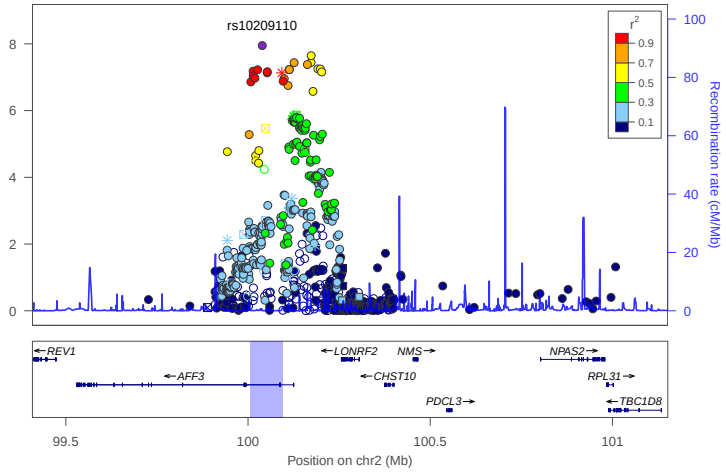

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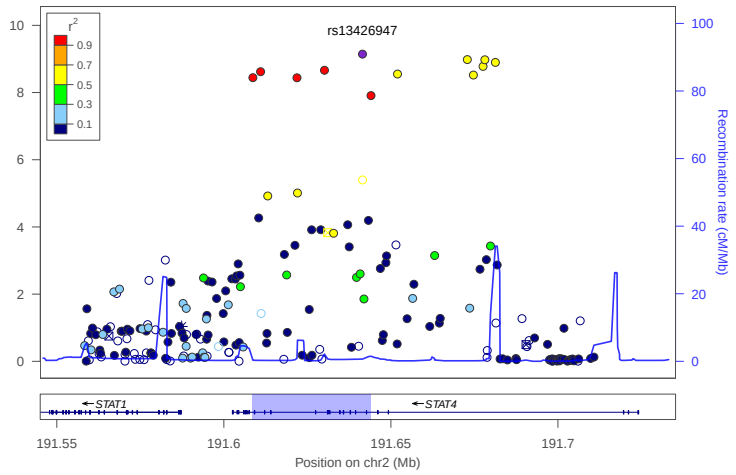

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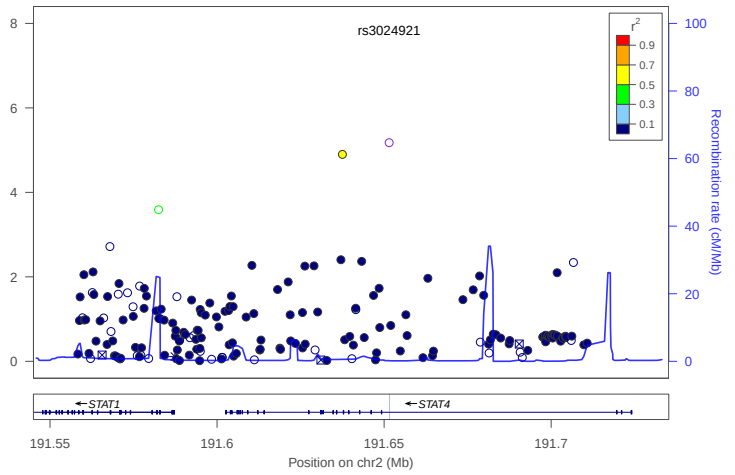

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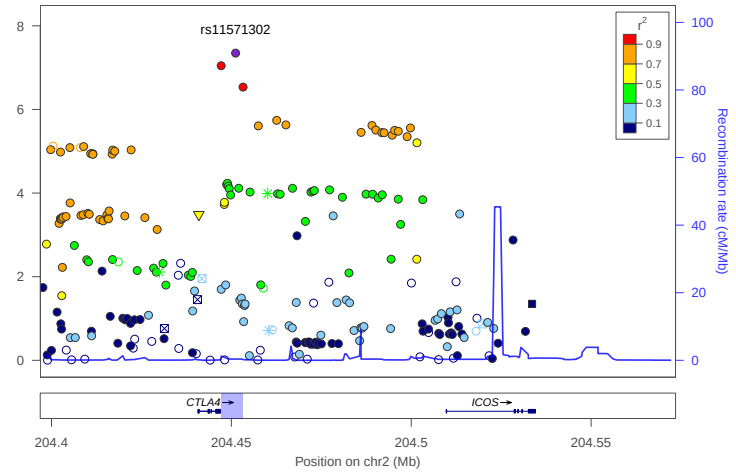

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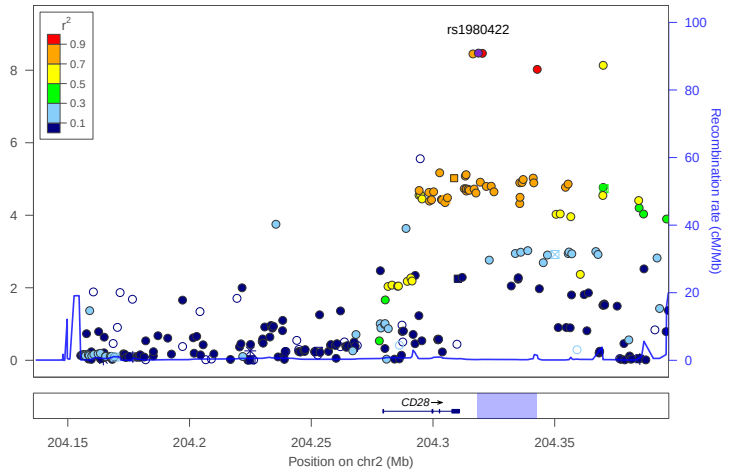

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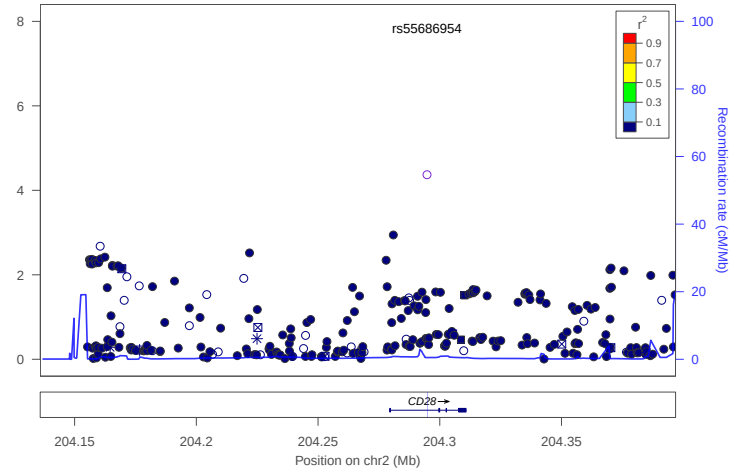

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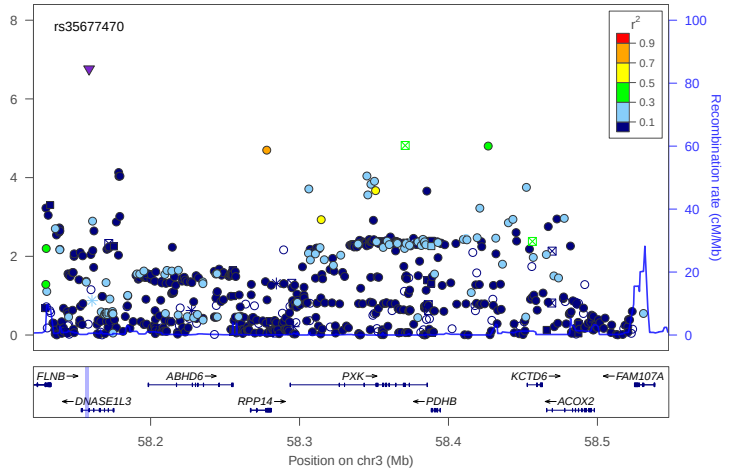

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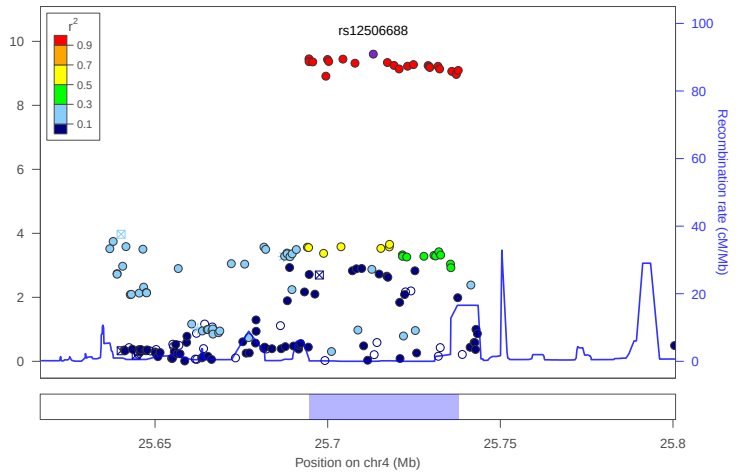

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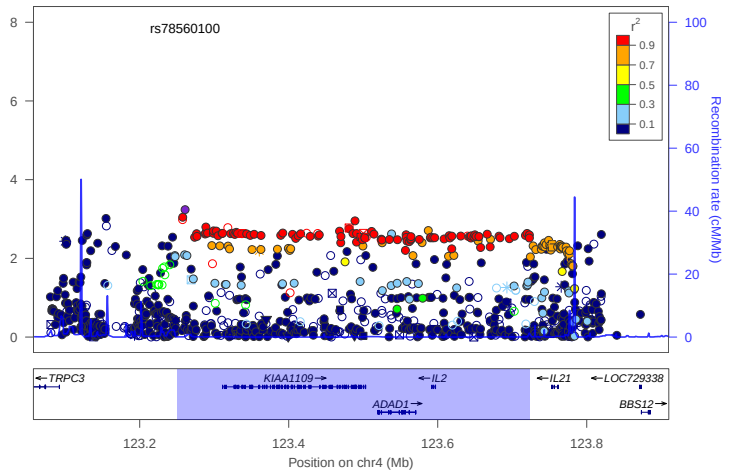

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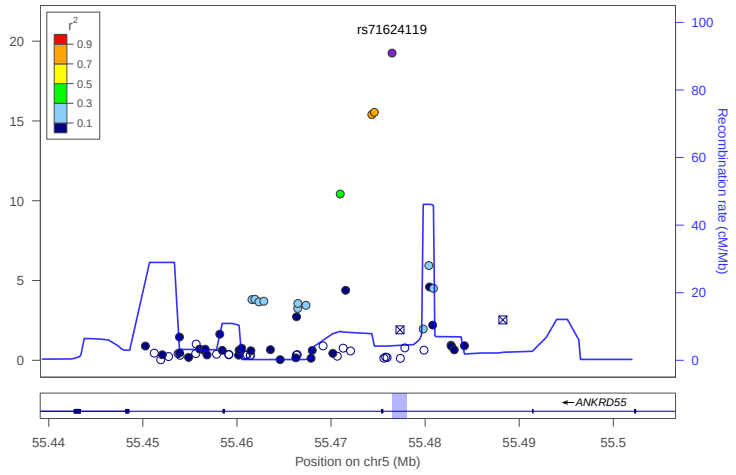

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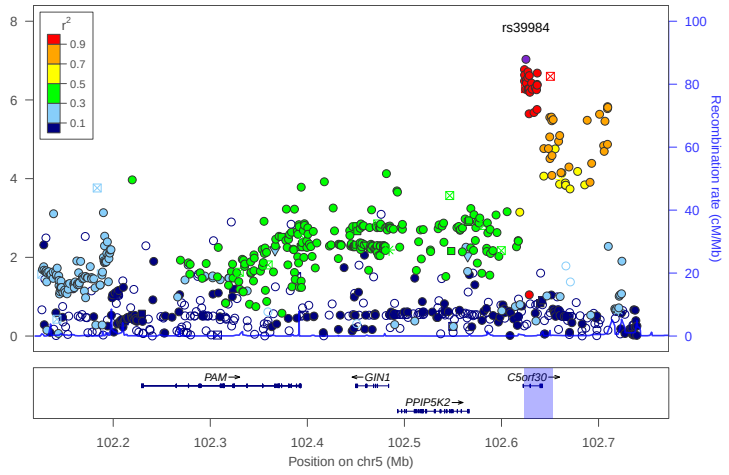

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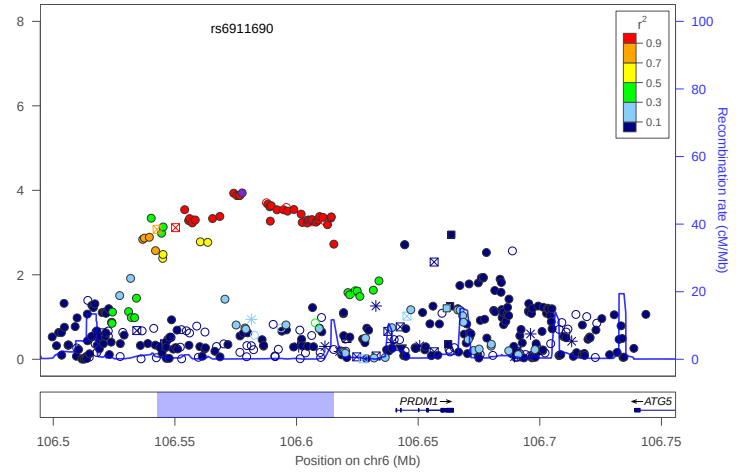

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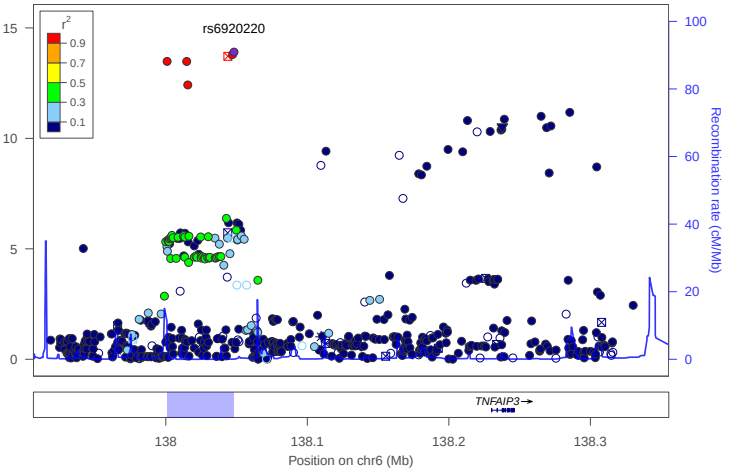

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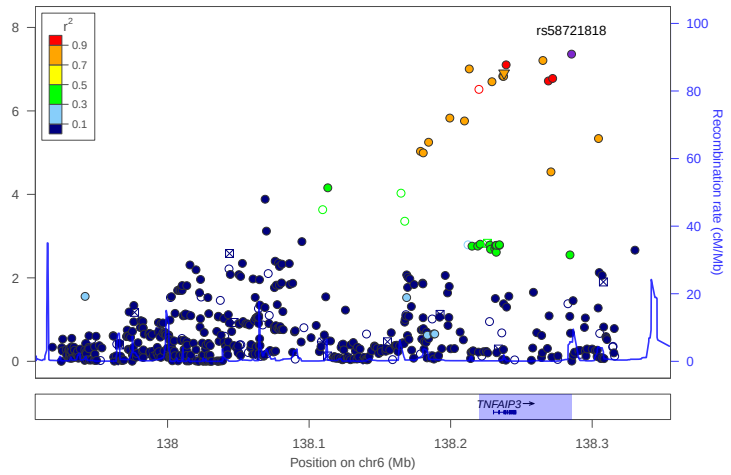

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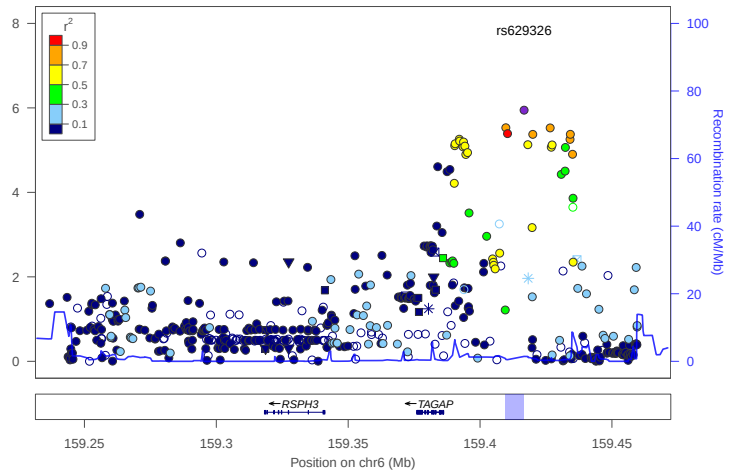

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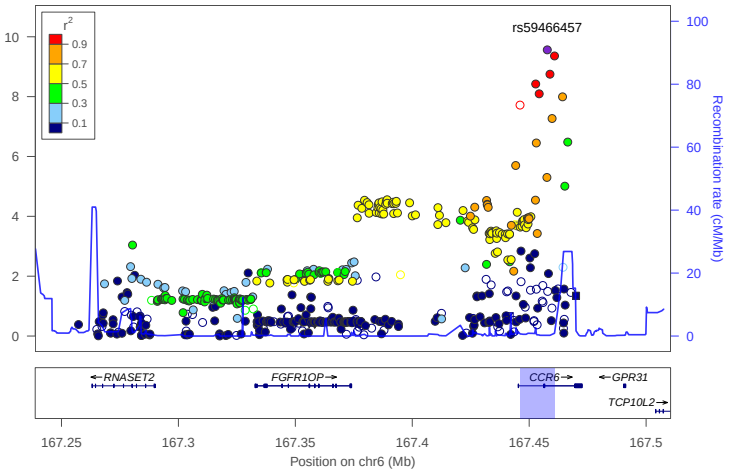

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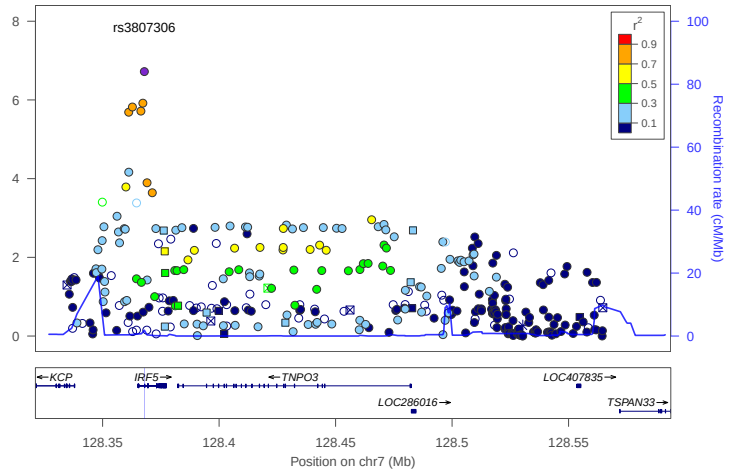

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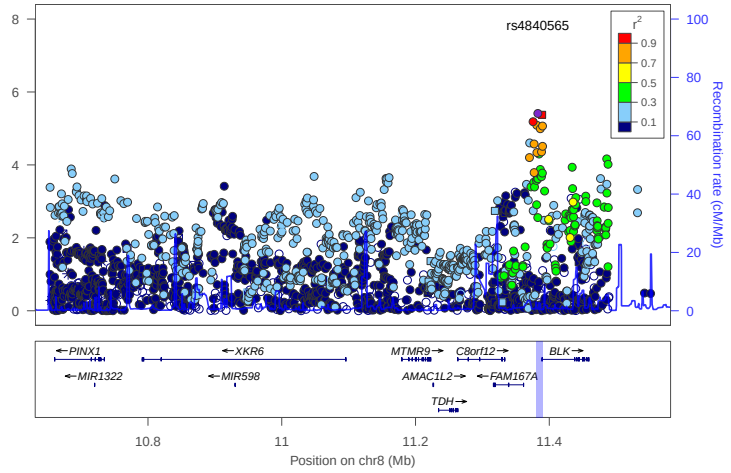

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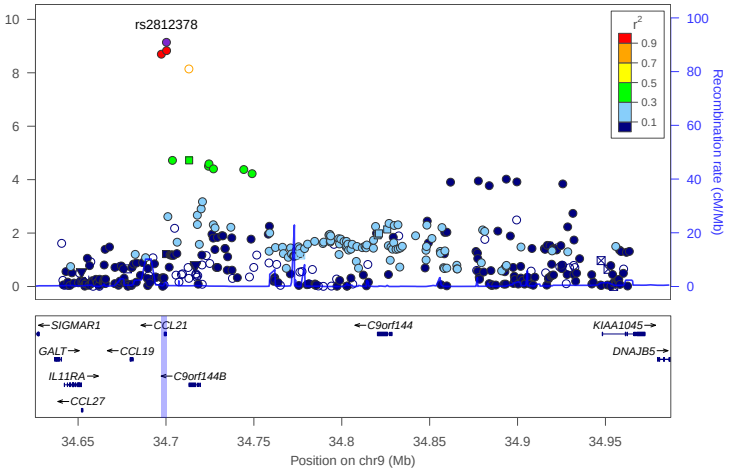

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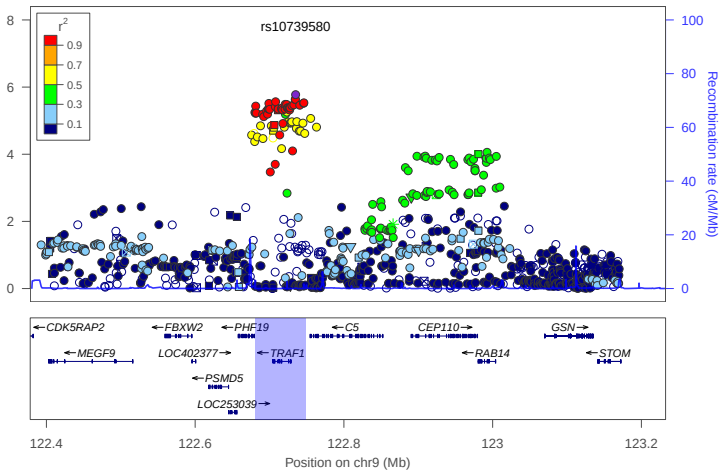

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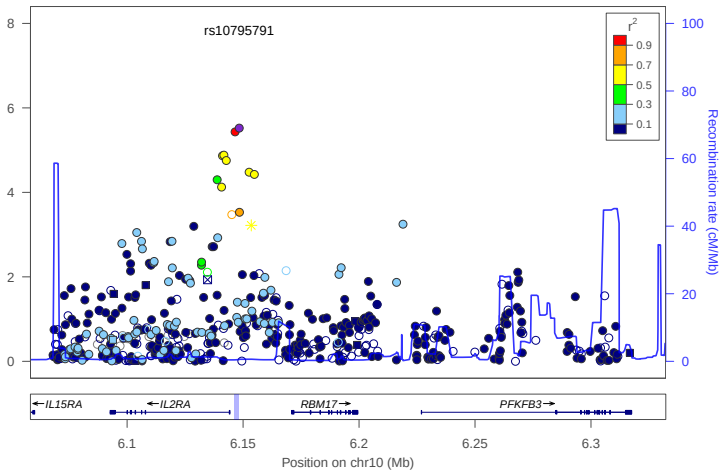

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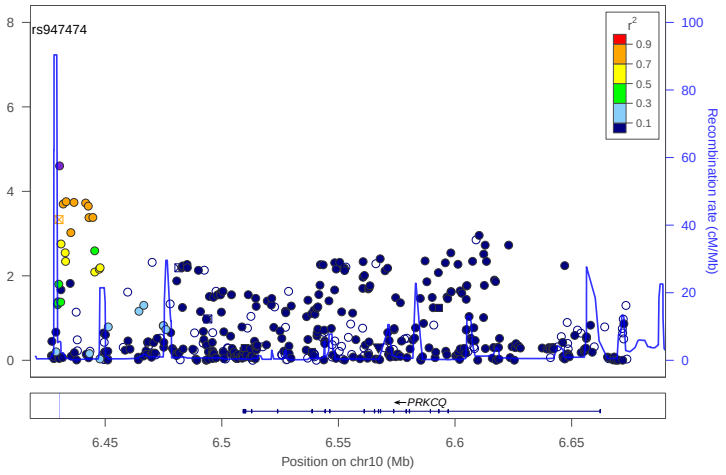

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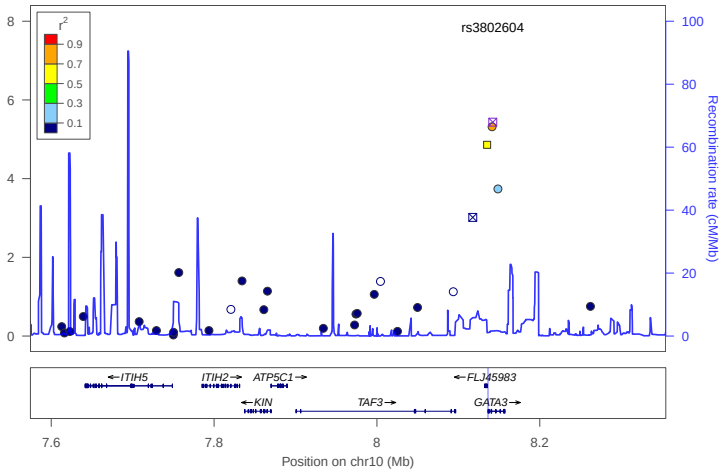

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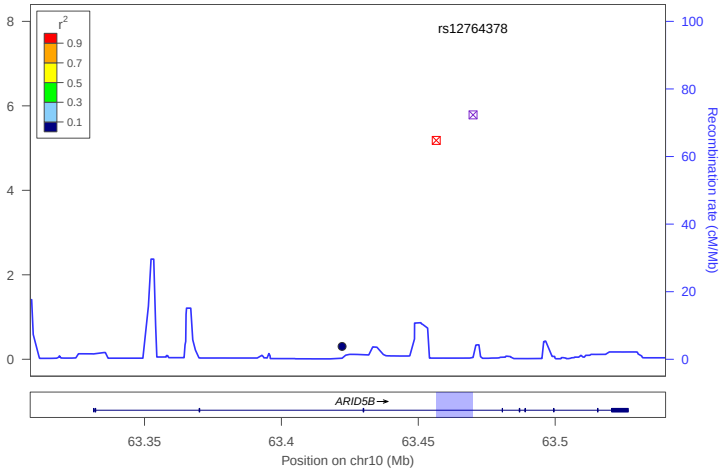

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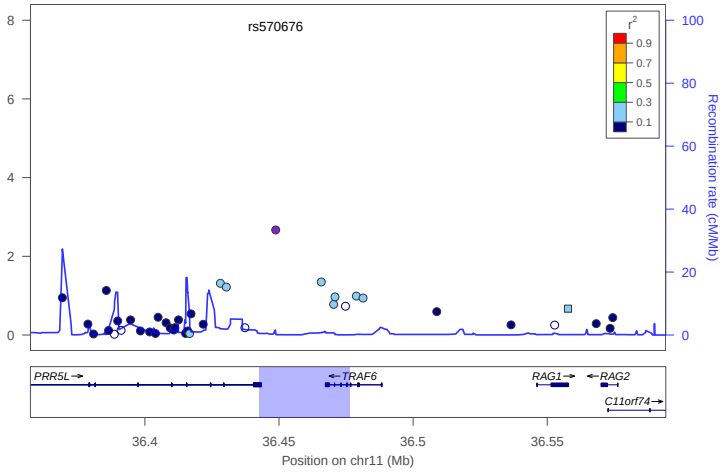

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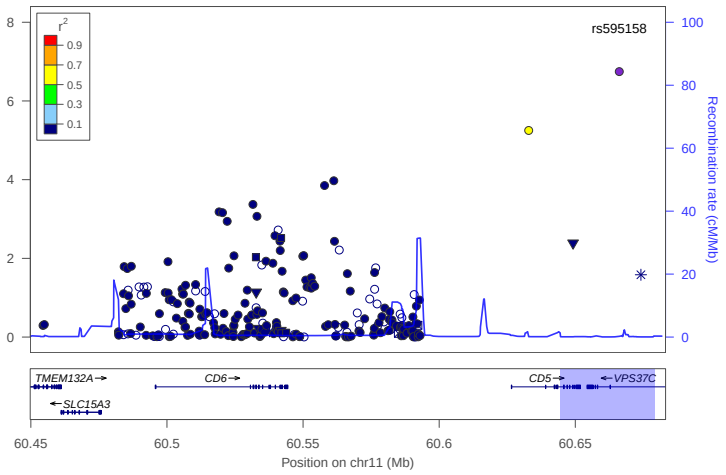

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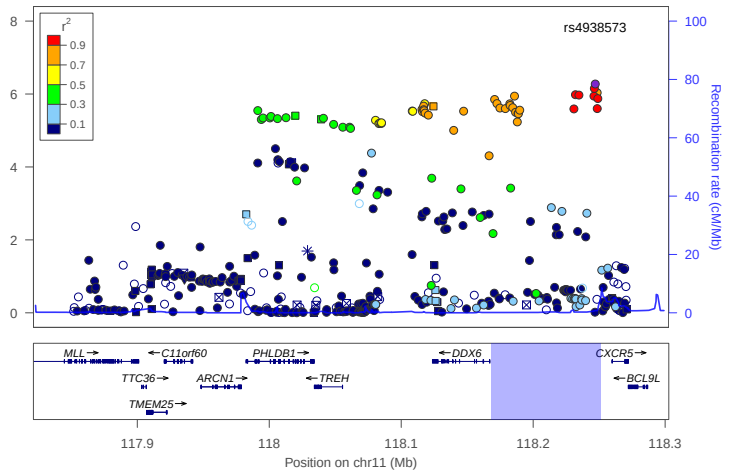

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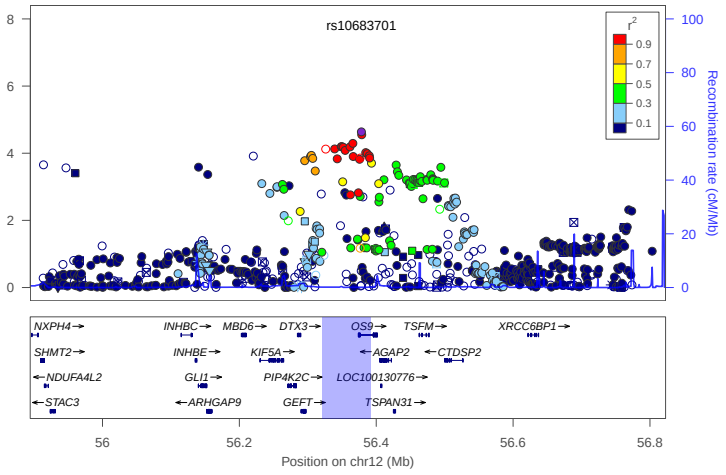

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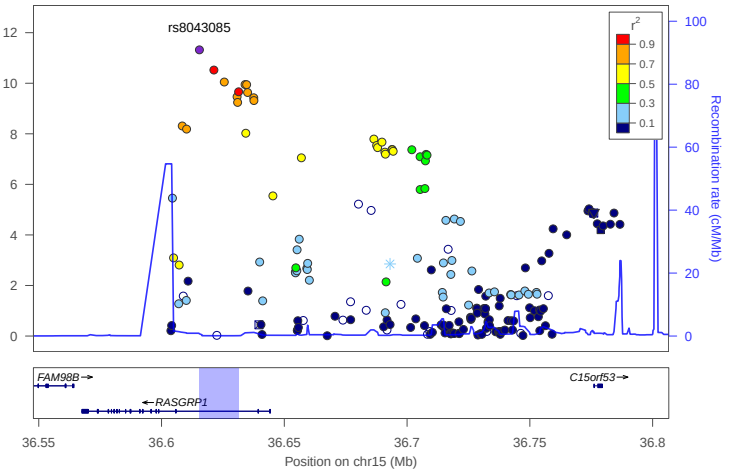

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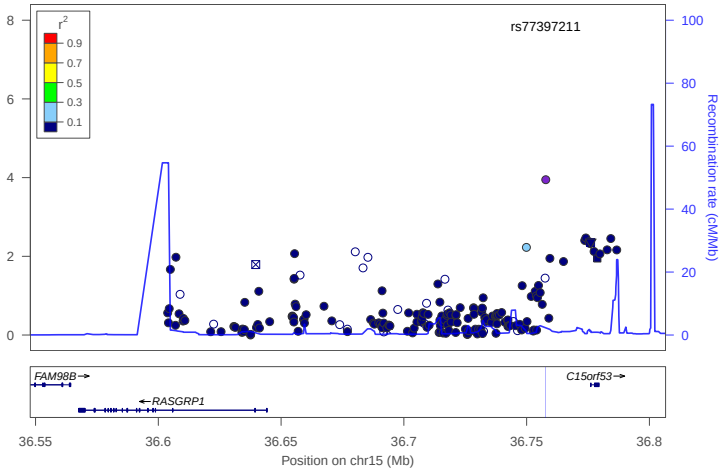

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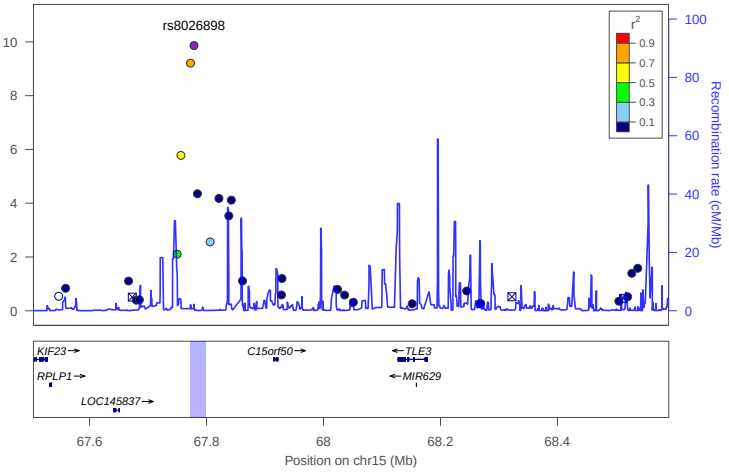

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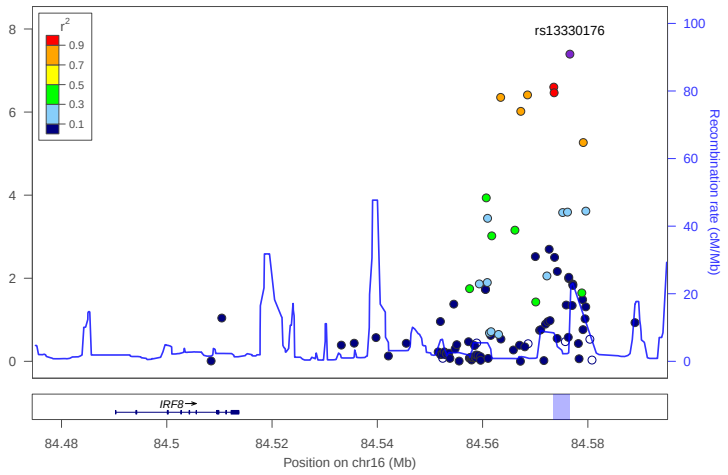

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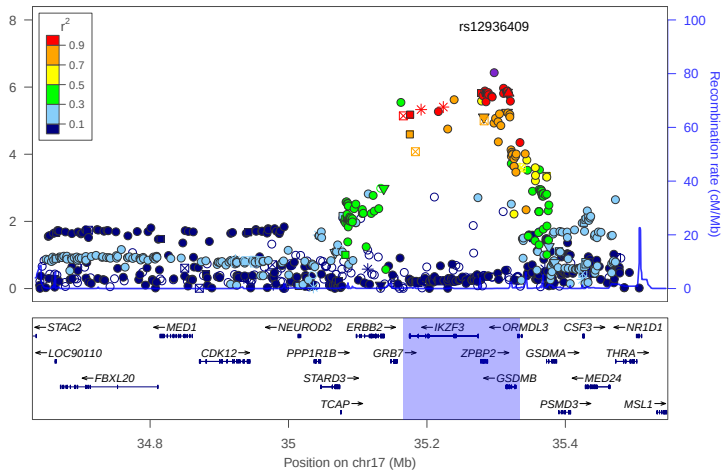

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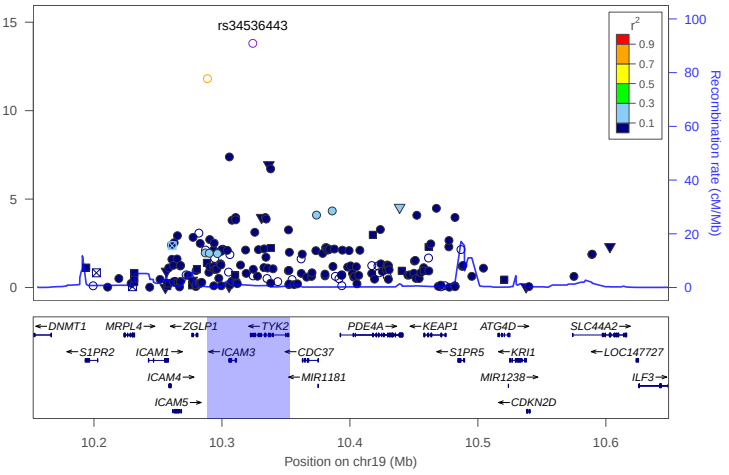

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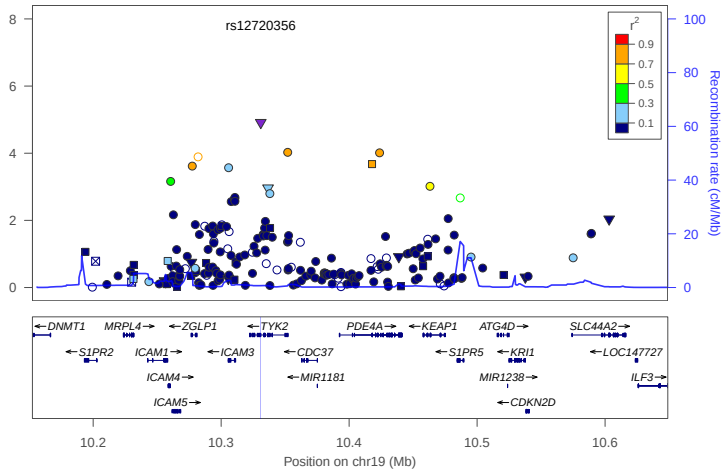

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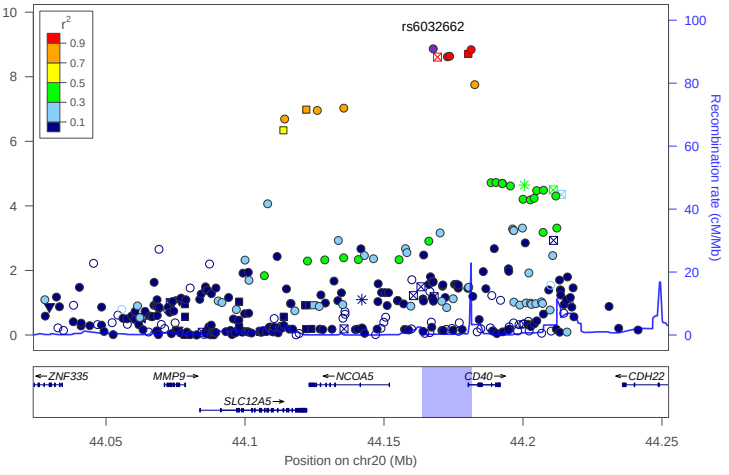

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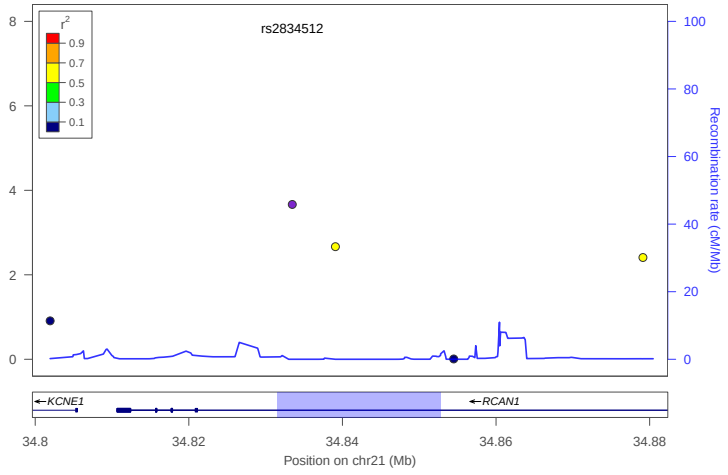
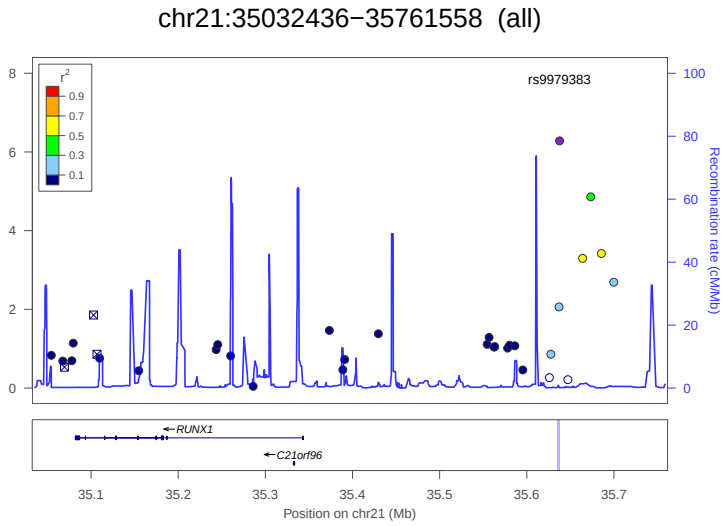
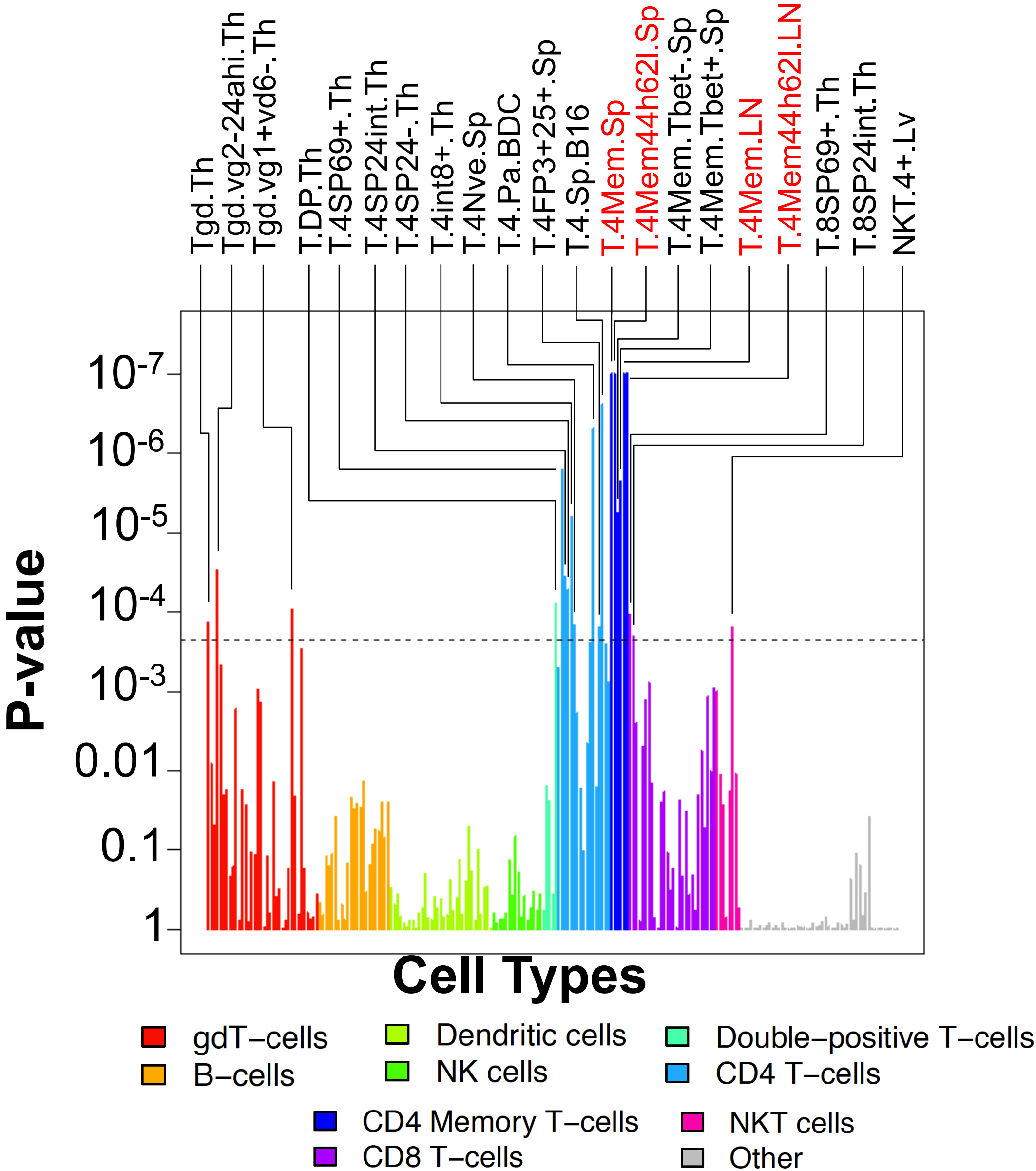
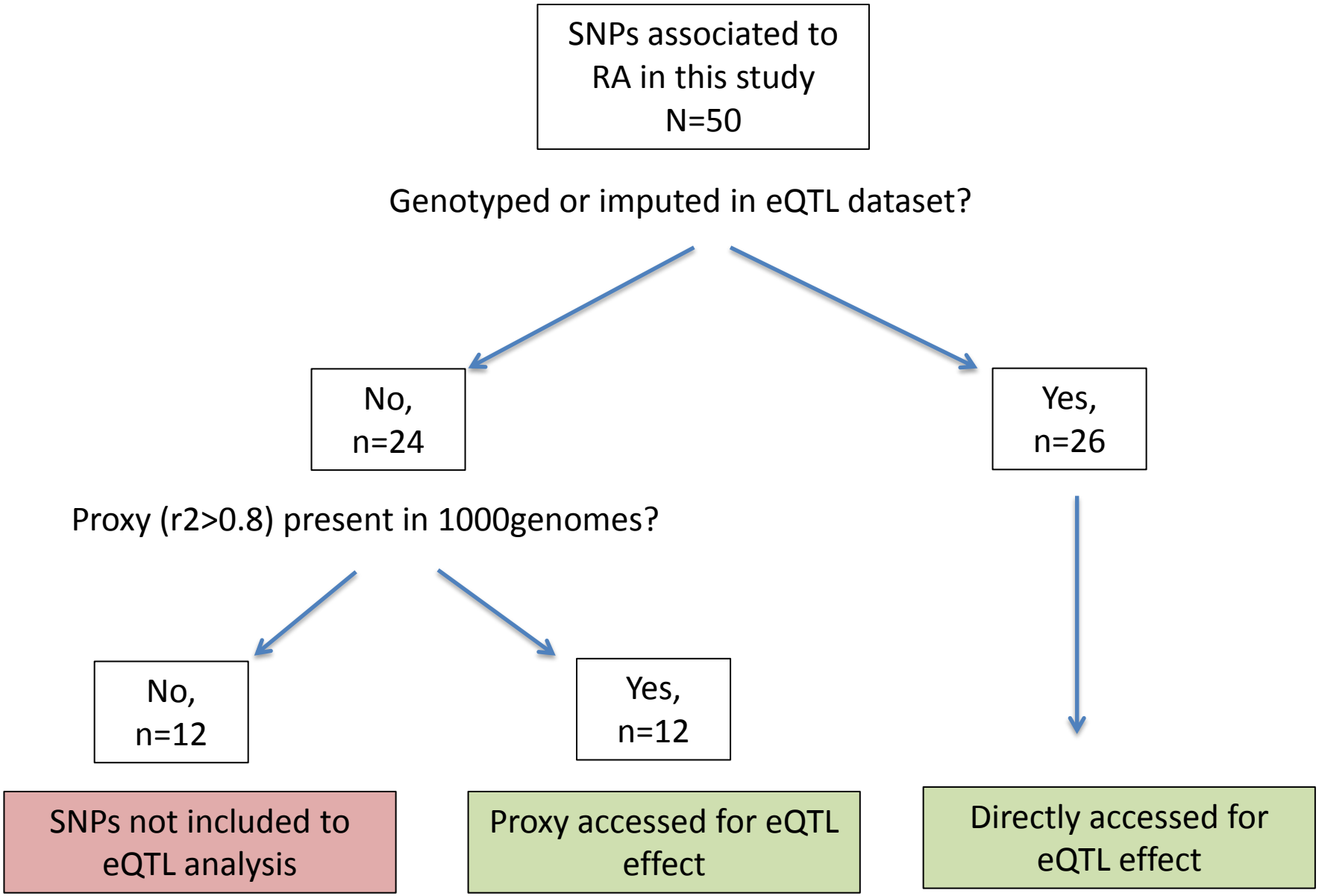



chr21:35032436−35761558 (all)
rs9979383
r2
0.9
0.7
0.5
0.3
0.1
Recombination rate (cM/Mb)
RUNX1
C21orf96
Position on chr21 (Mb)

Supplementary Figure 3: Regional association plots of immunochip data for all previously known and novel regions. The linkage disequilibrium based localisation (r^2 >= 0.9 with index SNP) of the association signal is indicated in the gene track by a light blue box. SNP annotation provided by LocusZoom databases (triangle - framestop/splice site, inverted triangle - nonsynonymous, box - synonymous/UTR, star - transcription factor binding site, crossed-box - multi-species conserved site).


Tgd.Th
Tgd.vg2-24ahi.Th
Tgd.vg1+vd6-.Th
T.DP.Th
T.4SP69+.Th
T.4SP24int.Th
T.4SP24-.Th
T.4int8+.Th
T.4Nve.Sp
T.4.Pa.BDC
T.4FP3+25+.Sp
T.4.Sp.B16
T.4Mem.Sp
T.4Mem44h62l.Sp
T.4Mem.Tbet-.Sp
T.4Mem.Tbet+.Sp
T.4Mem.LN
T.4Mem44h62l.LN
T.8SP69+.Th
T.8SP24int.Th
NKT.4+.Lv
P-value
10-7
10-6
10-5
10-4
10-3
0.01
0.1
1
Cell Types
gdT−cells
B−cells
Dendritic cells
NK cells
Double−positive T−cells
CD4 T−cells
CD4 Memory T−cells
CD8 T−cells
NKT cells
Other

Supplementary Figure 4: We evaluated the cell-specific expression of genes contained in 47 RA loci in 223 murine immune-cell types. To do this we compared specific expression of genes within RA loci to genes within randomly selected loci matched for gene number. We show the Bonferroni-corrected p-value ($0.05/223 = 2.24 \times 10^{-4}$) with a dotted line. We labeled all cell types that are significant after adjusting for multiple hypothesis at the top of the plot. The four most significant cell types ($p<10^{-7}$, CD4 memory T-cells in subcutaneous lymph node and spleen, and $CD44^{high}CD62^{low}$ CD4 memory T-cells in subcutaneous lymph node and spleen) are labeled in red.



Supplementary Figure 5. Scheme of SNP selection for eQTL analysis

Supplementary Note

Sample collections

United Kingdom (UK): The UK Manchester cohort of patients with rheumatoid arthritis (n =4752) were recruited from across the UK. All cases were European ancestry of Northern European descent and all fulfilled the 1987 American College of Rheumatology classification criteria modified for genetic studies. All participants were recruited after providing informed consent and the study was approved by the North West Research Ethics Committee (MREC 99/8/84). Serum RF and ACPA antibody titre were measured using commercially available kits [RF-PAIA Immunoturbidimetric Assay for rheumatoid factor, DiastatTM ACPA Kit (Axis-Shield Diagnostics Limited, UK)]. Patients with titres _40 units/ml and _5 units/ml were defined as positive for RF and ACPA antibodies, respectively.

United States (US): Cases from the U.S. have been studied and reported on previously and include three major datasets, totalling 2740 rheumatoid arthritis cases submitted for genotyping on the Immunochip. The NARAC cases (n=1312, 69% ACPA+) are largely derived from families with rheumatoid arthritis affected sibling pairs supplemented with singleton subjects whose siblings did not meet criteria for study entry, US singleton rheumatoid arthritis subjects and subjects from trio families[18, 19]. A second selected group of all ACPA+ rheumatoid arthritis subjects (n=660) included patients recruited by Dr. Frederick Wolfe in his practice as well as rheumatoid arthritis subjects enrolled in a published inception cohort as well as subjects followed in the National Database for Rheumatic Diseases, directed by Dr. Wolfe[20, 21]. A third cohort of subjects (N=768, 44% ACPA+) were derived from an inception cohort study, SONORA, as described previously[22].

Sweden EIRA (SE-E): Swedish cohort consisting of 2955 incidence rheumatoid arthritis cases and 2086 matched controls from Swedish epidemiological and genetic study of rheumatoid arthritis (EIRA) study, which is described elsewhere[23] All rheumatoid arthritis patients met the American College for Rheumatology 1987 (ACR-87) revised criteria for rheumatoid arthritis and blood samples were collected at 19 rheumatology units across Sweden (mainly middle and south of country). Controls were matched by date of birth, sex and residence area, were invited by mail and were asked to leave a blood sample in local ward. Ethics permit was received and informed consent was registered according to the current Swedish law.

Sweden Umea (SE-U): The Swedish Umea cohort is an inception cohort of patients fulfilling the American College of Rheumatology (ACR) 1987 criteria for classical rheumatoid arthritis (Arnett et al 1988) from the four most northern counties of Sweden. The controls are randomly selected, matched for age and sex, donors to the population based Medical Biobank of Northern Sweden. The patients and controls have the same ethnic background. Detection of Anti-Cyclic citrullinated peptide antibodies was analysed using enzyme-linked immunoassays (Euro-Diagnostica, Malmö, Sweden) according to manufacturer's instructions. Cut-off for positivity was 25 AU/ml. The regional

Ethics Committee at the University Hospital of Umeå approved this study and all participants gave their written informed consent.

The Netherlands (NL): Patients visiting the out-patient clinic with arthritis in at least one joints and symptom duration of less than two year were included in the Leiden-Early Arthritis Clinic (Leiden-EAC). Patients that were diagnosed with rheumatoid arthritis according to the 1987 ACR criteria within one year after inclusion in the Leiden-EAC were included in the current study (n=648).The study was approved by the local ethical committee and all patients gave their informed consent. Controls were obtained from the blood donors and have been described[3].

Spain (ES): The Spanish cohort of rheumatoid arthritis patients (n=914) were recruited across Spain fulfilling the American College of Rheumatology 1987 classification criteria. The controls (n=447) were obtained from the Spanish DNA Bank, matched by age and sex. Both patients and controls were white of Southern European descent. All participants were recruited after providing informed consent.

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Wilson, Dr Kimme Hyrich.

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Coronary Artery Disease

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Type 2 Diabetes

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Tuberculosis

Melanie Newport[47], Giorgio Sirugo, (Gambia)[47], Emily Lyons[3], Fredrik Vannberg[3] & Adrian V. S. Hill, (Oxford)[3]

Ankylosing Spondylitis

Linda A. Bradbury[48], Claire Farrar[49], Jennifer J. Pointon[48], Paul Wordsworth[49] & Matthew A. Brown[48,49]

Autoimmune Thyroid Disease

Jayne A. Franklyn[50], Joanne M. Heward[50], Matthew J. Simmonds[50] & Stephen C. L. Gough[50]

Breast Cancer

Sheila Seal[51], Breast Cancer Susceptibility Collaboration (UK)[55], Michael R. Stratton[51,52] & Nazneen Rahman[51]

Multiple Sclerosis

Maria Ban[53], An Goris[53], Stephen J. Sawcer[53] & Alastair Compston[53]

Gambian Controls

David Conway[47], Muminatou Jallow[47], Melanie Newport[47], Giorgio Sirugo, (Gambia)[47], Kirk A. Rockett[3] & Dominic P. Kwiatkowski, (Oxford)[3,5]

DNA, Genotyping, Data QC and Informatics

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