Analysis Summary: Hypothyroidism

Phenotype Description

Cases come from three sources:

- A positive report of a hypothyroidism diagnosis:
  - Your Medical History:
    - "Have you ever been diagnosed with hypothyroidism (underactive thyroid)?" (Yes, No, I'm not sure)
  - Research Snippet:
    - "Have you ever been diagnosed by a doctor with any of the following thyroid conditions?"/ "Hypothyroidism" (Yes, No, I don't know)
  - Baldness survey:
    - "Have you been diagnosed with any of the following? Please check all that apply: Hypothyroidism (underactive thyroid)" (Yes, No)
  - Health Intake survey
    - "Have you ever been diagnosed with or treated for any of the following conditions? (Any type of thyroid disease, not cancer)"
    - "What type of thyroid disease were you diagnosed with?" (Hashimoto's thyroiditis)
- Report of thyroid hormone replacement medication on either of two Research Snippets:
  - "Do you currently take medication for hypothyroidism (low thyroid hormone levels)?" (Yes, No, I'm not sure)
  - "Do you take any thyroid hormone replacement medications (such as Levothroid, Levoxyl, or Synthroid)?"
- Reported elevated TSH levels, from one Research Snippet:
  - "Have you ever been told by a doctor that your thyroid stimulating hormone (TSH) levels were elevated, indicating hypothyroidism?" (Yes, No, I'm not sure)

Controls answered none of these questions affirmatively and at least one negatively.

Exclusions:

- Hyperthyroidism (general health or baldness surveys)
  - "Have you ever been diagnosed by a doctor with any of the following thyroid conditions? Hyperthyroidism (Yes, No, I don't know)"
- thyroid cancer (general health or cancer surveys or iqb.thyroid_cancer)
  - "Have you ever been diagnosed by a doctor with any of the follwing common cancers? Thyroid Cancer (Yes, No, I don't know)"
  - "What type(s) of cancer were you diagnosed with? Please check all that apply: Thyroid cancer (Yes, No)"
- radioactive iodine treatment (iqb.iodine_treatment_ever)
  - "Have you ever received radioactive iodine treatment for goiter or hyperthyroidism (overactive thyroid)?" (Yes, No, I'm not sure)
- thyroid removal (iqb.thyroid_removed)
  - "Have you ever had all or part of your thyroid surgically removed?" (Yes, No, I'm not sure)

Phenotype Statistics

The following table shows demographics of unrelated, European individuals included in the GWAS.

Phenotype	Group	Total	M	F	(0,30]	(30,45]	(45,60]	(60,Inf]
hypothyroidism	case	17558	3903	13655	804	3135	5453	8166
	control	117083	67264	49819	16231	36526	31197	33129

The following table shows the phenotypic distribution across 23andMe genotyping platforms for individuals included in the GWAS.

Phenotype	Group	Total	v1/v2	v3	v4
hypothyroidism	case	17558	1651	14058	1849
	control	117083	14079	93136	9868

Null Model with Covariates

The following table shows results of fitting a model for the trait based on just the covariates. Principal coordinates have been standardized, so these effect sizes are in units of standard deviations.

	Estimate	Std. Error	z value	Pr(>|z|)	LRT	Pr(>Chi)
age	0.03350	0.000563	59.5	0.0	3770.6	0.0
sexF	1.56816	0.019390	80.9	0.0	7786.6	0.0
pc.0	−0.01679	0.008434	−2.0	0.047	3.9	0.048
pc.1	−0.01530	0.008977	−1.7	0.088	2.9	0.087
pc.2	−0.02803	0.009003	−3.1	0.0018	9.8	0.0018
pc.3	−0.00722	0.008729	−0.8	0.41	0.7	0.41
pc.4	0.04648	0.009549	4.9	1.1×10^{-6}	24.9	6.2×10^{-7}

SNP-level QC information

The following table shows results for QC filters on the genotyped data:

	failed	passed
no filters	0	1030430
not V1-only, chrM, chrY	4790	1025640
parent-offspring test	2129	1023511
MAF > 0%	3203	1020494
HWE > 1e-20	48225	972832
gt.rate > 90%	30775	952826
batch effects	28267	945446

The following table shows results for QC filters on the imputed dosage data:

	failed	passed
no filters	0	13733809
MAF > 0%	0	13733809
imputation quality	0	13733809
batch effects	2168	13731641

The following table shows results for QC filters on the merged association test results:

	passed	total
imputed only	12833621	12833621
both passed	898002	13731623
genotyped only	47444	13779067
no test result	−10030	13769037
failed to converge	−92626	13676411

Genetic Association Tests

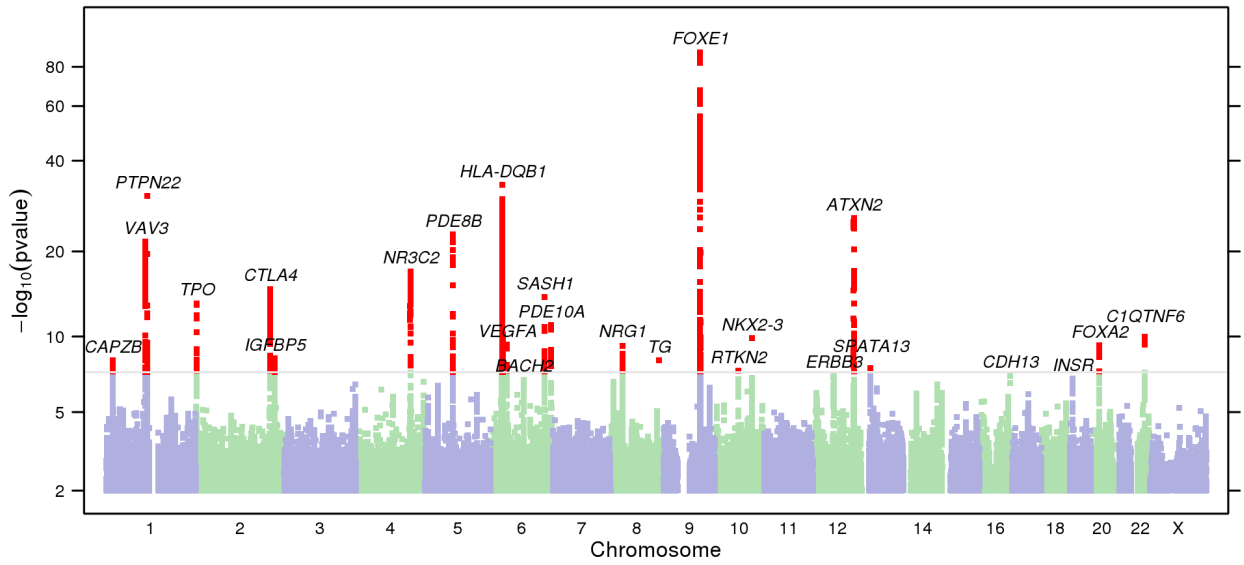
We performed logistic regression assuming an additive model for allelic effects, using the model:

hypothyroidism ~ age + sex + pc.0 + pc.1 + pc.2 + pc.3 + pc.4 + genotype

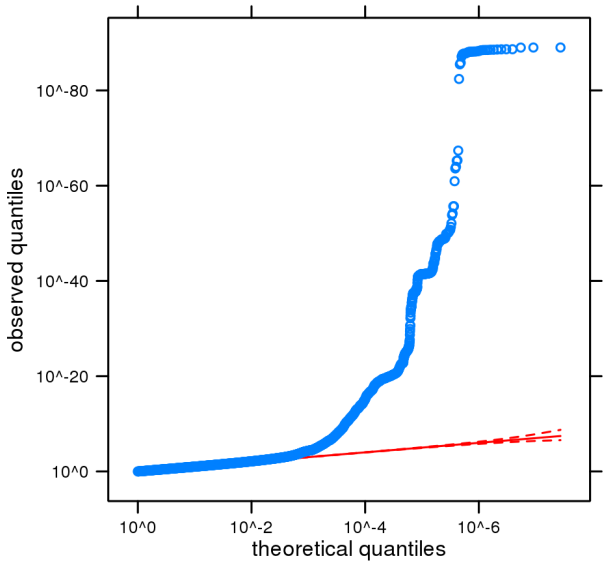
This genome-wide association analysis includes data from 17558 cases and 117083 controls of European ancestry, filtered to remove close relatives.

The results in this report have been adjusted for a genomic control inflation factor λ=1.074. The equivalent inflation factor for 1000 cases and 1000 controls λ_{1000}= 1.002 , and for 10000, λ_{10000}= 1.024 .

Manhattan Plot



Q-Q Plot of GWAS Results



Index SNPs for Strongest Associations

cytoband	assay.name	scaffold	position	alleles	src	pvalue	OR	95% CI	gene.context
9q22.33	rs10759927	chr9	100542176	A/G	I	9.7×10^{-90}	1.313	[1.278,1.349]	XPA--[]--FOXE1
6p21.32	rs9273370	chr6	32626492	A/G	I	4.5×10^{-34}	0.852	[0.830,0.874]	HLA-DQA1--[]HLA-DQB1
1p13.2	rs2476601	chr1	114377568	A/G	I	2.1×10^{-31}	0.786	[0.755,0.818]	[PTPN22]
12q24.12	rs10774625	chr12	111910219	A/G	I	1.4×10^{-26}	0.875	[0.854,0.897]	[ATXN2]
5q13.3	rs1479567	chr5	76528022	A/G	I	1.4×10^{-23}	0.880	[0.859,0.902]	[PDE8B]
1p13.3	rs17020055	chr1	108336533	A/C	I	2.7×10^{-22}	1.225	[1.177,1.276]	[VAV3]
4q31.23	rs76342258	chr4	149631793	G/T	I	8.1×10^{-18}	0.870	[0.843,0.899]	NR3C2---[]
2q33.2	rs3087243	chr2	204738919	A/G	I	1.4×10^{-15}	1.105	[1.079,1.133]	CTLA4[]--ICOS
6q24.3	rs6914622	chr6	148514301	G/T	I	1.2×10^{-14}	1.109	[1.081,1.139]	SAMD5---[]---SASH1
2p25.3	rs11675342	chr2	1407628	C/T	I	6.4×10^{-14}	1.099	[1.072,1.126]	SNTG2--[]-TPO

6q27	rs1079418	chr6	166047034	A/G	I	9.3×10^{-12}	0.912	[0.888,0.937]	[PDE10A]
22q12.3	22:37583733:C_CG	chr22	37583733	D/I	I	1.0×10^{-10}	1.085	[1.059,1.113]	[C1QTNF6]
10q24.2	rs10748781	chr10	101283330	A/C	I	1.4×10^{-10}	1.088	[1.060,1.116]	GOT1--[]-NKX2-3
6p21.1	rs10223666	chr6	43805502	C/G	I	4.6×10^{-10}	0.917	[0.893,0.943]	VEGFA--[]---C6orf223
20p11.21	rs201295667	chr20	22630515	D/I	I	5.4×10^{-10}	0.902	[0.873,0.932]	FOXA2--[]---SSTR4
8p12	rs2466075	chr8	32432949	A/G	I	5.9×10^{-10}	1.084	[1.057,1.112]	[NRG1]
2q35	rs1861628	chr2	217628430	A/G	I	5.6×10^{-9}	1.087	[1.057,1.118]	IGFBP5--[]--TNP1
8q24.22	rs121912648	chr8	133894854	C/T	G	7.3×10^{-9}	3.657	[2.432,5.497]	[TG]
1p36.13	rs12138950	chr1	19839115	A/C	I	7.5×10^{-9}	0.903	[0.872,0.935]	CAPZB--[]--MINOS1
13q12.12	rs9511143	chr13	24774647	C/T	I	2.6×10^{-8}	0.920	[0.894,0.948]	[SPATA13]
10q21.2	rs10821973	chr10	64052337	A/G	I	4.1×10^{-8}	1.073	[1.046,1.100]	RTKN2--[]--ZNF365
12q13.2	rs7312770	chr12	56467587	C/T	I	8.0×10^{-8}	0.932	[0.908,0.956]	RPS26--[]-ERBB3
16q23.3	rs7193703	chr16	83658143	A/G	I	8.4×10^{-8}	0.049	[0.010,0.252]	[CDH13]
19p13.2	rs7508679	chr19	7222832	C/T	I	1.3×10^{-7}	0.935	[0.912,0.959]	[INSR]
6q15	rs661713	chr6	90975999	A/G	I	1.5×10^{-7}	0.935	[0.912,0.959]	[BACH2]

Quality Statistics for Index SNPs

assay.name	is.v2	is.v3	is.v4	gt.rate	hw.p.value	p.date	freq.b	avg.rsqr	min.rsqr	p.batch	dose.b	qc.mask
rs10759927	FALSE	FALSE	FALSE					0.9923	0.9861	0.040	0.6669	v2v3v4
rs9273370	FALSE	FALSE	FALSE					0.9472	0.9091	0.022	0.3988	v2v3v4
rs2476601	TRUE	TRUE	TRUE	0.9999	0.0080	0.82	0.9067	0.9996	0.9990	0.069	0.9081	v2v3v4
rs10774625	FALSE	TRUE	FALSE	0.9997	0.00029	0.013	0.4893	0.9970	0.9702	0.28	0.4912	v2v3v4
rs1479567	FALSE	FALSE	FALSE					0.9958	0.9945	0.60	0.6067	v2v3v4
rs17020055	TRUE	TRUE	TRUE	0.9990	0.59	0.035	0.0901	1.0000	0.9996	0.22	0.0898	v2v3v4
rs76342258	FALSE	FALSE	FALSE					0.9958	0.9928	0.69	0.1896	v2v3v4
rs3087243	TRUE	TRUE	TRUE	1.0000	0.00042	0.30	0.5501	1.0000	0.9998	0.040	0.5483	v2v3v4
rs6914622	FALSE	FALSE	FALSE					0.9739	0.9599	0.079	0.3153	v2v3v4
rs11675342	FALSE	TRUE	FALSE	0.9672	4.9×10^{-12}	1.6×10^{-12}	0.4435	0.9972	0.9851	0.0022	0.4327	v2v3v4
rs1079418	FALSE	FALSE	FALSE					0.9979	0.9960	0.0030	0.3197	v2v3v4
22:37583733:C_CG	FALSE	FALSE	FALSE					0.9857	0.9840	0.58	0.4297	v2v3v4
rs10748781	FALSE	FALSE	FALSE					0.9178	0.8617	0.019	0.4196	v2v3v4
rs10223666	FALSE	FALSE	FALSE					0.9875	0.8875	0.67	0.2984	v2v3v4
rs201295667	FALSE	FALSE	FALSE					0.6496	0.6287	0.0018	0.3315	v2v3v4
rs2466075	FALSE	FALSE	FALSE					0.9177	0.9115	0.042	0.4960	v2v3v4
rs1861628	TRUE	TRUE	TRUE	0.9981	0.0014	0.96	0.7409	0.9981	0.9958	0.16	0.7379	v2v3v4
rs121912648	FALSE	TRUE	TRUE	0.9999	1.0	0.21	0.0006					
rs12138950	TRUE	TRUE	TRUE	0.9828	2.0×10^{-10}	0.00013	0.1522	0.9979	0.9969	0.85	0.1538	v2v3v4
rs9511143	FALSE	FALSE	FALSE					0.8052	0.7718	0.84	0.6947	v2v3v4
rs10821973	FALSE	FALSE	FALSE					0.9655	0.9507	0.00080	0.4094	v2v3v4
rs7312770	FALSE	FALSE	FALSE					0.8993	0.8810	0.0022	0.5288	v2v3v4
rs7193703	FALSE	FALSE	FALSE					0.6404	0.3270	0.11	0.0006	v2v3v4
rs7508679	TRUE	TRUE	TRUE	0.9926	0.78	0.074	0.4218	1.0000	0.9998	0.77	0.4209	v2v3v4
rs661713	TRUE	TRUE	TRUE	0.9990	0.070	0.36	0.3952	0.9981	0.9973	0.19	0.3945	v2v3v4

SNP Statistics in the GWAS Sample

assay.name	AA.0	AB.0	BB.0	im.num.0	dose.b.0	AA.1	AB.1	BB.1	im.num.1	dose.b.1
rs10759927				117083	0.6606				17558	0.7135
rs9273370				117083	0.4060				17558	0.3732
rs2476601	965	19243	96872	117083	0.9095	223	3407	13928	17558	0.8902
rs10774625	24071	46186	22862	117083	0.4934	4033	6958	3063	17558	0.4643
rs1479567				117083	0.6126				17558	0.5839
rs17020055	97343	18674	920	117083	0.0878	14042	3295	201	17558	0.1054
rs76342258				117083	0.1934				17558	0.1751
rs3087243	24029	57734	35318	117083	0.5482	3259	8565	5733	17558	0.5704
rs6914622				117083	0.3127				17558	0.3344
rs11675342	28147	44731	17343	117083	0.4304	3892	6889	2856	17558	0.4533
rs1079418				117083	0.3182				17558	0.3005
22:37583733:C_CG				117083	0.4241				17558	0.4418
rs10748781				117083	0.4164				17558	0.4332
rs10223666				117083	0.2998				17558	0.2837
rs201295667				117083	0.3322				17558	0.3190
rs2466075				117083	0.4927				17558	0.5103
rs1861628	8001	45089	63752	117083	0.7351	1086	6502	9935	17558	0.7490
rs121912648	102896	99	0			15862	43	0		
rs12138950	82698	29545	2755	117083	0.1541	12767	4150	359	17558	0.1418
rs9511143				117083	0.6961				17558	0.6828
rs10821973				117083	0.4062				17558	0.4212
rs7312770				117083	0.5290				17558	0.5140
rs7193703				117083	0.0007				17558	0.0001
rs7508679	38933	57085	20736	117083	0.4217	6133	8469	2893	17558	0.4068
rs661713	42670	56245	18085	117083	0.3958	6718	8214	2615	17558	0.3837

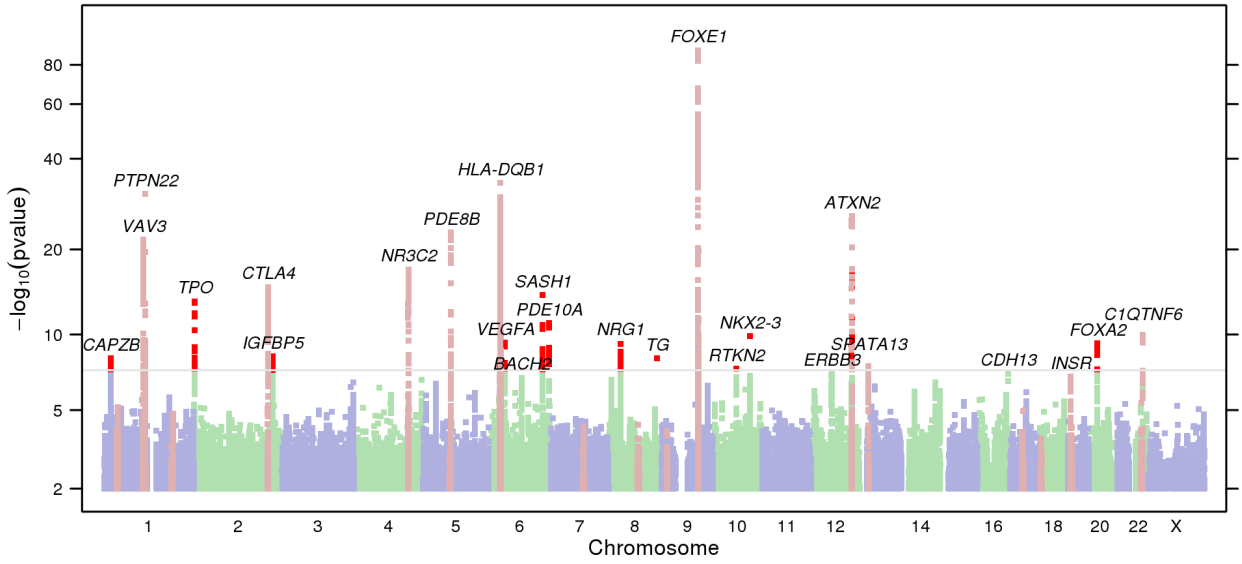
Annotations from NHGRI GWAS Catalog

The following table shows, for each index SNP, all entries in the NHGRI GWAS Catalog that are within 500kb and in at least moderate linkage disequilibrium ($r^2 > 0.5$).

region	position	our.name	our.pval	dist	rsqr	assay.name	pvalue	pubmed.id	trait	genes
9q22.33	100542176	rs10759927	9.7×10^{-90}	4424	1.000	rs925489	2.0×10^{-19}	22493691	Hypothyroidism	KRT18P13, FOXE1, C9orf156
9q22.33	100542176	rs10759927	9.7×10^{-90}	6837	0.994	rs7850258	4.0×10^{-9}	21981779	Hypothyroidism	FOXE1
9q22.33	100542176	rs10759927	9.7×10^{-90}	7852	0.994	rs1443438	1.0×10^{-9}	23251661	Obesity-related traits	XPA, FOXE1
9q22.33	100542176	rs10759927	9.7×10^{-90}	13933	0.988	rs965513	3.0×10^{-10}	23894154	Thyroid cancer	FOXE1
9q22.33	100542176	rs10759927	9.7×10^{-90}	13933	0.988	rs965513	5.0×10^{-12}	20350937	Thyroid cancer (Papillary, radiation-related)	FOXE1, TMOD1, …
9q22.33	100542176	rs10759927	9.7×10^{-90}	13933	0.988	rs965513	2.0×10^{-27}	19198613	Thyroid cancer	FOXE1
6p21.32	32626492	rs9273370	4.5×10^{-34}	−50014	0.508	rs9271100	1.0×10^{-12}	19838193	Systemic lupus erythematosus	HLA-DRB1
6p21.32	32626492	rs9273370	4.5×10^{-34}	−22120	0.671	rs9272346	2.0×10^{-8}	23181788	Asthma	HLA-DQA1
6p21.32	32626492	rs9273370	4.5×10^{-34}	−22120	0.671	rs9272346	6.0×10^{-129}	18978792	Type 1 diabetes	HLA
6p21.32	32626492	rs9273370	4.5×10^{-34}	−22120	0.671	rs9272346	5.0×10^{-134}	17554300	Type 1 diabetes	MHC
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	2.0×10^{-15}	23128233	Crohn's disease	PTPN22,DCLRE1B
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	3.0×10^{-13}	22493691	Hypothyroidism	PHTF1, RSBN1, PTPN22
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	1.0×10^{-40}	18978792	Type 1 diabetes	PTPN22
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	6.0×10^{-42}	18794853	Rheumatoid arthritis	PTPN22
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	5.0×10^{-26}	17554300	Type 1 diabetes	PTPN22
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	6.0×10^{-25}	17554300	Rheumatoid arthritis	PTPN22
1p13.2	114377568	rs2476601	2.1×10^{-31}	−73760	0.985	rs6679677	8.0×10^{-24}	17554260	Type 1 diabetes	PHTF1, PTPN22
12q24.12	111910219	rs10774625	1.4×10^{-26}	−201761	0.533	rs1265564	1.0×10^{-16}	22293688	Type 1 diabetes	CUX2
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	5.0×10^{-11}	24026423	Platelet counts	SH2B3, ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	3.0×10^{-8}	23417110	Beta-2 microglubulin plasma levels	SH2B3, ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	4.0×10^{-19}	23222517	Red blood cell traits	SH2B3, ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	3.0×10^{-12}	22493691	Hypothyroidism	SH2B3, ATXN2, …
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	1.0×10^{-26}	22139419	Platelet counts	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	4.0×10^{-25}	21909115	Diastolic blood pressure	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	2.0×10^{-38}	21829393	Type 1 diabetes autoantibodies	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	6.0×10^{-6}	21378990	Coronary heart disease	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	6.0×10^{-6}	20453842	Rheumatoid arthritis	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	3.0×10^{-27}	19430480	Type 1 diabetes	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	5.0×10^{-9}	19430479	Systolic blood pressure	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	3.0×10^{-14}	19430479	Diastolic blood pressure	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	7.0×10^{-19}	19198610	Eosinophil counts	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	−5848	0.989	rs4766578	4.0×10^{-18}	22561518	Vitiligo	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	0	1.000	rs10774625	2.0×10^{-13}	21060863	Retinal vascular caliber	ATXN2,PTPN11,SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	7.0×10^{-12}	23263486	Urate levels	ATXN2, PTPN11
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	7.0×10^{-20}	21909110	Blood pressure	ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	3.0×10^{-19}	21383967	Celiac disease and Rheumatoid arthritis	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	4.0×10^{-11}	20383146	Chronic kidney disease	ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	7.0×10^{-21}	20190752	Celiac disease	SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	3.0×10^{-18}	19430483	Diastolic blood pressure	ATXN2, SH2B3
12q24.12	111910219	rs10774625	1.4×10^{-26}	97537	0.933	rs653178	8.0×10^{-8}	18311140	Celiac disease	SH2B3, ATXN2
12q24.12	111910219	rs10774625	1.4×10^{-26}	162205	0.762	rs11065987	8.0×10^{-11}	23297363	Tetralogy of Fallot	PTPN11
12q24.12	111910219	rs10774625	1.4×10^{-26}	162205	0.762	rs11065987	2.0×10^{-9}	20686565	LDL cholesterol	BRAP
12q24.12	111910219	rs10774625	1.4×10^{-26}	162205	0.762	rs11065987	7.0×10^{-12}	20686565	Cholesterol, total	BRAP
12q24.12	111910219	rs10774625	1.4×10^{-26}	162205	0.762	rs11065987	1.0×10^{-11}	19862010	Hemoglobin	TRAFD1
12q24.12	111910219	rs10774625	1.4×10^{-26}	162205	0.762	rs11065987	1.0×10^{-12}	19862010	Hematocrit	SH2B3, ATXN2
5q13.3	76528022	rs1479567	1.4×10^{-23}	−9580	0.962	rs4704397	2.0×10^{-6}	22493691	Hypothyroidism	PDE8B
5q13.3	76528022	rs1479567	1.4×10^{-23}	−9580	0.962	rs4704397	2.0×10^{-20}	18514160	Thyroid stimulating hormone	PDE8B
									Thyroid hormone	

5q13.3	76528022	rs1479567	1.4×10^{-23}	2327	0.984	rs6885099	6.0×10^{-24}	23408906	levels	PDE8B
5q13.3	76528022	rs1479567	1.4×10^{-23}	7789	0.984	rs2046045	3.0×10^{-27}	22494929	Thyroid function	PDE8B
1p13.3	108336533	rs17020055	2.7×10^{-22}	29483	0.862	rs4915077	8.0×10^{-10}	22493691	Hypothyroidism	VAV3
4q31.23	149631793	rs76342258	8.1×10^{-18}	3232	1.000	rs10519980	7.0×10^{-6}	22493691	Hypothyroidism	ATP5LP4, LOC285423
4q31.23	149631793	rs76342258	8.1×10^{-18}	20817	1.000	rs10028213	3.0×10^{-10}	22494929	Thyroid function	NR3C2
4q31.23	149631793	rs76342258	8.1×10^{-18}	37713	0.967	rs10032216	9.0×10^{-16}	23408906	Thyroid hormone levels	NR3C2
2q33.2	204738919	rs3087243	1.4×10^{-15}	−45043	0.673	rs231735	6.0×10^{-9}	19503088	Rheumatoid arthritis	CTLA4
2q33.2	204738919	rs3087243	1.4×10^{-15}	0	1.000	rs3087243	2.0×10^{-17}	21829393	Type 1 diabetes autoantibodies	CTLA4
2q33.2	204738919	rs3087243	1.4×10^{-15}	0	1.000	rs3087243	1.0×10^{-8}	20453842	Rheumatoid arthritis	CTLA4
2q33.2	204738919	rs3087243	1.4×10^{-15}	0	1.000	rs3087243	1.0×10^{-15}	19430480	Type 1 diabetes	CTLA4
2q33.2	204738919	rs3087243	1.4×10^{-15}	0	1.000	rs3087243	8.0×10^{-11}	18978792	Type 1 diabetes	CTLA4
6q24.3	148514301	rs6914622	1.2×10^{-14}	6991	0.690	rs9497965	3.0×10^{-8}	23408906	Thyroid hormone levels	SASH1
6q27	166047034	rs1079418	9.3×10^{-12}	−551	1.000	rs753760	6.0×10^{-20}	23408906	Thyroid hormone levels	PDE10A
10q24.2	101283330	rs10748781	1.4×10^{-10}	907	0.768	rs4409764	1.0×10^{-54}	23128233	Inflammatory bowel disease	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	907	0.768	rs4409764	2.0×10^{-20}	21102463	Crohn’s disease	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	4434	0.760	rs10883365	6.0×10^{-8}	17554300	Crohn’s disease	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	4434	0.760	rs10883365	4.0×10^{-10}	17554261	Crohn’s disease	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	6971	0.702	rs6584283	8.0×10^{-21}	21297633	Ulcerative colitis	Intergenic
10q24.2	101283330	rs10748781	1.4×10^{-10}	6971	0.702	rs6584283	2.0×10^{-6}	20228798	Ulcerative colitis	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	6971	0.702	rs6584283	2.0×10^{-7}	19915572	Ulcerative colitis	NKX2, NKX3
10q24.2	101283330	rs10748781	1.4×10^{-10}	8263	0.748	rs11190140	1.0×10^{-8}	20228799	Ulcerative colitis	NKX2-3
10q24.2	101283330	rs10748781	1.4×10^{-10}	8263	0.748	rs11190140	3.0×10^{-16}	18587394	Crohn’s disease	NKX2-3
6p21.1	43805502	rs10223666	4.6×10^{-10}	−931	0.799	rs729761	8.0×10^{-16}	23263486	Urate levels	VEGFA
6p21.1	43805502	rs10223666	4.6×10^{-10}	1107	0.981	rs881858	9.0×10^{-14}	20383146	Chronic kidney disease	VEGFA
6p21.1	43805502	rs10223666	4.6×10^{-10}	6260	0.870	rs9472138	7.0×10^{-16}	23408906	Thyroid hormone levels	VEGFA
6p21.1	43805502	rs10223666	4.6×10^{-10}	6260	0.870	rs9472138	4.0×10^{-6}	18372903	Type 2 diabetes	VEGFA
2q35	217628430	rs1861628	5.6×10^{-9}	−2907	0.987	rs13015993	8.0×10^{-11}	23408906	Thyroid hormone levels	IGFBP5
1p36.13	19839115	rs12138950	7.5×10^{-9}	0	1.000	rs12138950	3.0×10^{-18}	21565293	Thyroid volume	CAPZB
1p36.13	19839115	rs12138950	7.5×10^{-9}	2059	0.876	rs10799824	4.0×10^{-21}	23408906	Thyroid hormone levels	CAPZB
12q13.2	56467587	rs7312770	8.0×10^{-8}	−76951	0.512	rs705702	9.0×10^{-26}	22885925	Polycystic ovary syndrome	RAB5B, SUOX
12q13.2	56467587	rs7312770	8.0×10^{-8}	−66502	0.768	rs10876864	8.0×10^{-12}	22951725	Vitiligo	PMEL, DGKA, …
12q13.2	56467587	rs7312770	8.0×10^{-8}	−55100	0.574	rs1701704	2.0×10^{-13}	21804548	Asthma	IKZF4
12q13.2	56467587	rs7312770	8.0×10^{-8}	−55100	0.574	rs1701704	3.0×10^{-8}	20596022	Alopecia areata	IKZF4
12q13.2	56467587	rs7312770	8.0×10^{-8}	−55100	0.574	rs1701704	9.0×10^{-10}	18198356	Type 1 diabetes	RAB5B, SUOX, …
12q13.2	56467587	rs7312770	8.0×10^{-8}	−50659	0.574	rs2456973	3.0×10^{-14}	22561518	Vitiligo	IKZF4
12q13.2	56467587	rs7312770	8.0×10^{-8}	3038	0.788	rs11171739	1.0×10^{-11}	17554300	Type 1 diabetes	ERBB3
12q13.2	56467587	rs7312770	8.0×10^{-8}	14593	0.578	rs2292239	3.0×10^{-27}	21829393	Type 1 diabetes autoantibodies	ERBB3
12q13.2	56467587	rs7312770	8.0×10^{-8}	14593	0.578	rs2292239	2.0×10^{-25}	19430480	Type 1 diabetes	ERBB3
12q13.2	56467587	rs7312770	8.0×10^{-8}	14593	0.578	rs2292239	3.0×10^{-16}	18978792	Type 1 diabetes	ERBB3
12q13.2	56467587	rs7312770	8.0×10^{-8}	14593	0.578	rs2292239	2.0×10^{-20}	17554260	Type 1 diabetes	ERBB3
19p13.2	7222832	rs7508679	1.3×10^{-7}	1016	0.528	rs4804416	3.0×10^{-10}	23408906	Thyroid hormone levels	INSR
19p13.2	7222832	rs7508679	1.3×10^{-7}	1016	0.528	rs4804416	5.0×10^{-6}	22493691	Hypothyroidism	INSR
6q15	90975999	rs661713	1.5×10^{-7}	−54259	0.698	rs370409	2.0×10^{-6}	21841780	Graves' disease	BACH2, MAP3K7
6q15	90975999	rs661713	1.5×10^{-7}	−18536	0.526	rs3757247	3.0×10^{-8}	22561518	Vitiligo	BACH2
6q15	90975999	rs661713	1.5×10^{-7}	−18536	0.526	rs3757247	1.0×10^{-6}	18840781	Type 1 diabetes	BACH2
6q15	90975999	rs661713	1.5×10^{-7}	−17768	0.581	rs11755527	3.0×10^{-8}	21829393	Type 1 diabetes autoantibodies	BACH2
6q15	90975999	rs661713	1.5×10^{-7}	−17768	0.581	rs11755527	5.0×10^{-8}	19430480	Type 1 diabetes	BACH2
6q15	90975999	rs661713	1.5×10^{-7}	−17768	0.581	rs11755527	5.0×10^{-12}	18978792	Type 1 diabetes	BACH2
6q15	90975999	rs661713	1.5×10^{-7}	20770	0.544	rs12212193	4.0×10^{-8}	21833088	Multiple sclerosis	BACH2

Replication of GWAS Catalog Results



The following table shows, for each GWAS Catalog result for similar traits, our association test result for our best available proxy (distance < 100kb, $r^2 > 0.8$).

region	position	our.name	our.pval	dist	rsqr	assay.name	pvalue	pubmed.id	trait	genes
1p34.3	38279987	rs3748682	6.9×10^{-6}	0	1.000	rs3748682	9.0×10^{-6}	22493691	Hypothyroidism	MTF1
1p13.3	108366016	rs4915077	9.5×10^{-21}	0	1.000	rs4915077	8.0×10^{-10}	22493691	Hypothyroidism	VAV3
1p13.2	114303808	rs6679677	2.2×10^{-31}	0	1.000	rs6679677	3.0×10^{-13}	22493691	Hypothyroidism	PHTF1, RSBN1, PTPN22
1q31.1	187902981	rs655167	0.0057	0	1.000	rs655167	7.0×10^{-6}	22493691	Hypothyroidism	LOC100129274
2q33.2	204734487	rs231779	8.6×10^{-14}	0	1.000	rs231779	7.0×10^{-6}	22493691	Hypothyroidism	CTLA4
4q31.23	149635025	rs10519980	1.6×10^{-17}	0	1.000	rs10519980	7.0×10^{-6}	22493691	Hypothyroidism	ATP5LP4, LOC285423
5q13.3	76518442	rs4704397	7.2×10^{-23}	0	1.000	rs4704397	2.0×10^{-6}	22493691	Hypothyroidism	PDE8B
6p21.33	31018407	rs2517532	1.8×10^{-23}	0	1.000	rs2517532	1.0×10^{-8}	22493691	Hypothyroidism	LOC729792, HCG22, C6orf15, HLA-C, HLA-B, DHFRP2, HCP5 HLA-DRB9, HLA-DRB5, HLA-DRB1, HLA-DQA1, HLA-DQB1,
6p21.32	32663631	rs3129720	2.5×10^{-23}	0	1.000	rs3129720	5.0×10^{-7}	22493691	Hypothyroidism	HLA-DQA2
7q21.13	88481442	rs10248351	0.080	0	1.000	rs10248351	7.0×10^{-6}	22493691	Hypothyroidism	C7orf62, ZNF804B
8q21.13	81438420	rs1051920	0.011	0	1.000	rs1051920	4.0×10^{-6}	22493691	Hypothyroidism	ZBTB10, RPSAP47
9p22.3	14470833	rs10961534	0.00011	0	1.000	rs10961534	7.0×10^{-6}	22493691	Hypothyroidism	TRNAH, GUG, ZDHHC21
9q22.33	100546600	rs925489	2.2×10^{-89}	0	1.000	rs925489	2.0×10^{-19}	22493691	Hypothyroidism	KRT18P13, FOXE1, C9orf156
9q22.33	100549013	rs7850258	3.3×10^{-89}	0	1.000	rs7850258	4.0×10^{-9}	21981779	Hypothyroidism	FOXE1
12q24.12	111884608	rs3184504	6.7×10^{-26}	0	1.000	rs3184504	3.0×10^{-12}	22493691	Hypothyroidism	SH2B3, ATXN2, LOC100101246, BRAP, NAA25, C12orf51, PTPN11
13q12.12	24042510	rs10162002	0.21	0	1.000	rs10162002	5.0×10^{-6}	22493691	Hypothyroidism	SACS, TNFRSF19
17q12	32464154	rs9901756	0.61	0	1.000	rs9901756	7.0×10^{-6}	22493691	Hypothyroidism	LOC100131744, CCL2
18p11.31	6567182	rs948426	0.037	0	1.000	rs948426	1.0×10^{-6}	22493691	Hypothyroidism	LOC100130480
19p13.2	7223848	rs4804416	1.0×10^{-6}	0	1.000	rs4804416	5.0×10^{-6}	22493691	Hypothyroidism	INSR
22q12.3	37581422	rs229526	3.1×10^{-7}	0	1.000	rs229526	9.0×10^{-6}	22493691	Hypothyroidism	C1QTNF6

Nearby Nonsynonymous SNPs

region	position	our.name	our.pval	dist	rsqr	assay.name	gene	aa.chg
6p21.32	32626492	rs9273370	4.5×10^{-34}	−21235	0.598	rs1047989	HLA-DQA1	L8M
6p21.32	32626492	rs9273370	4.5×10^{-34}	−17387	0.613	rs1129740	HLA-DQA1	C34Y
6p21.32	32626492	rs9273370	4.5×10^{-34}	−17366	0.757	rs1071630	HLA-DQA1	F41S
1p13.2	114377568	rs2476601	2.1×10^{-31}	0	1.000	rs2476601	PTPN22	R620W
12q24.12	111910219	rs10774625	1.4×10^{-26}	−25611	0.934	rs3184504	SH2B3	W262R
8q24.22	133894854	rs121912648	7.3×10^{-9}	0	1.000	rs121912648	TG	R296*

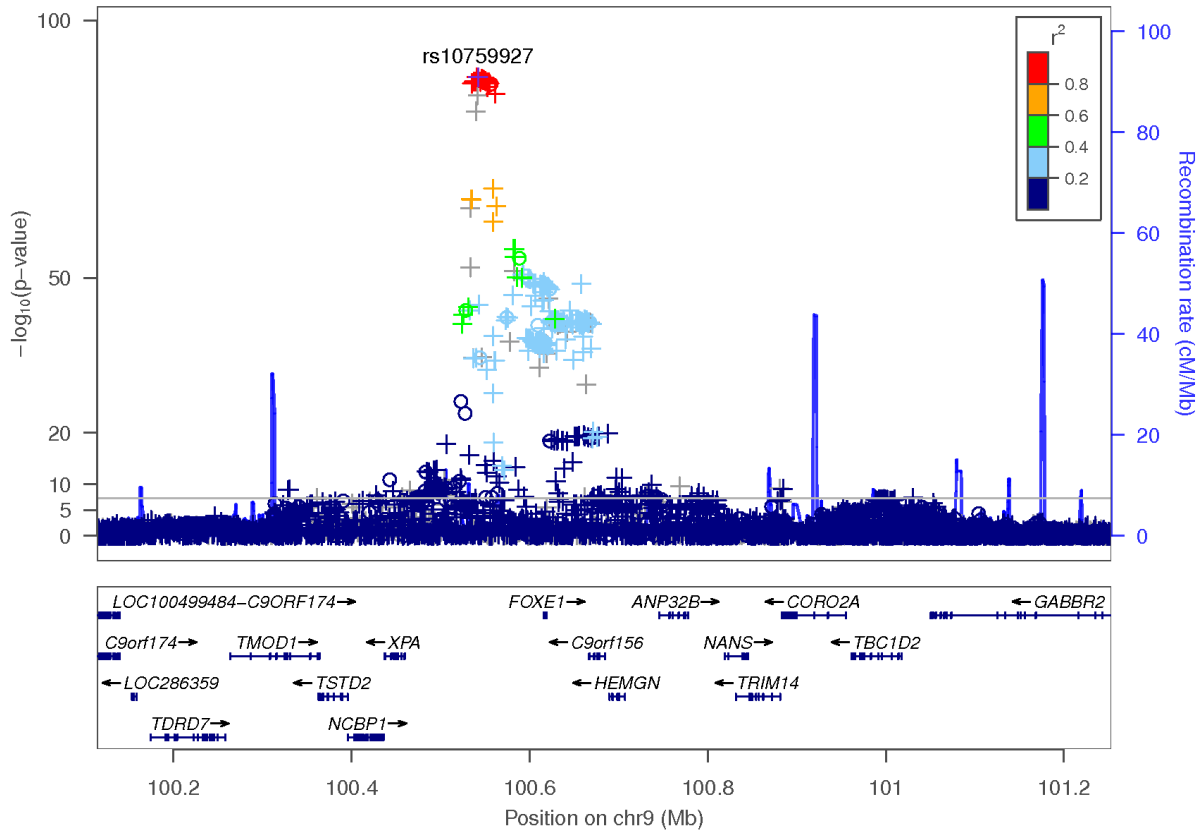
Nearby Expression QTLs

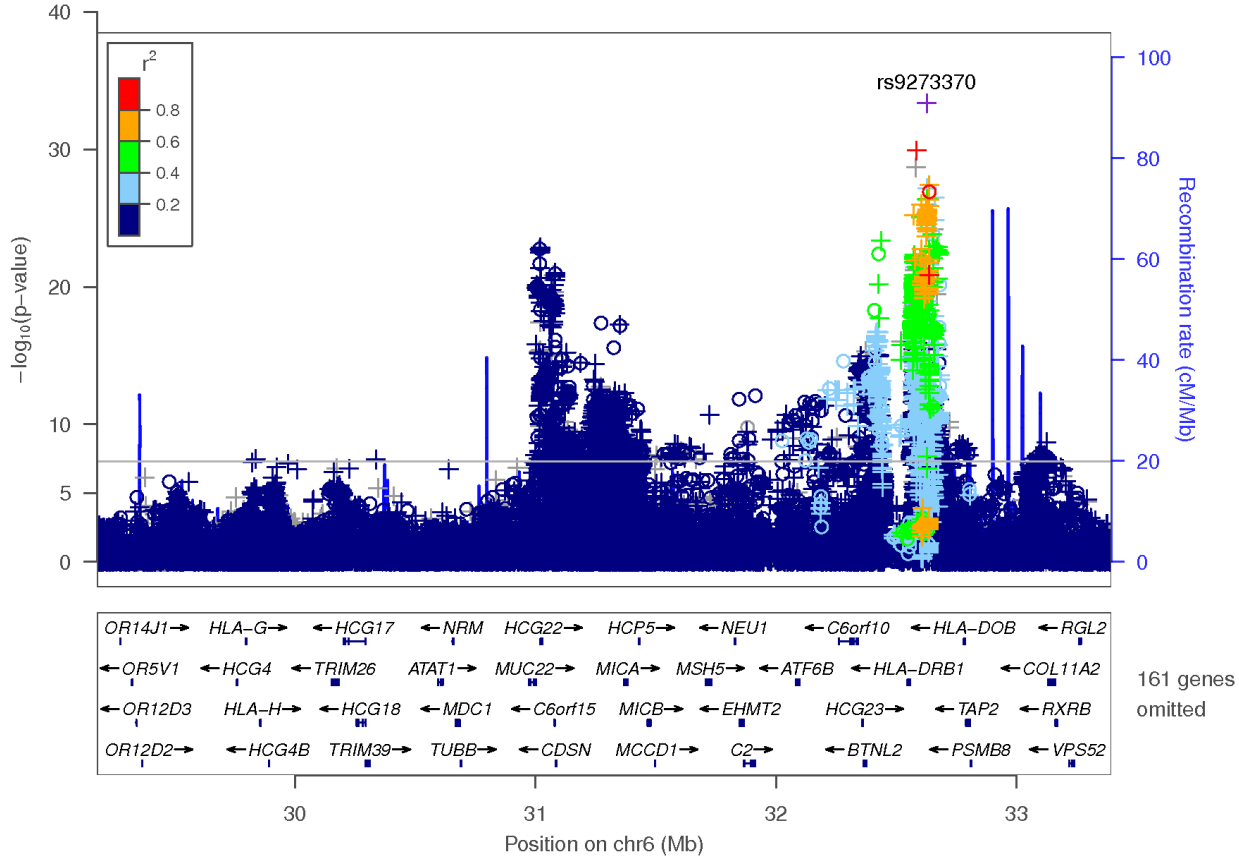
no eQTLs were found

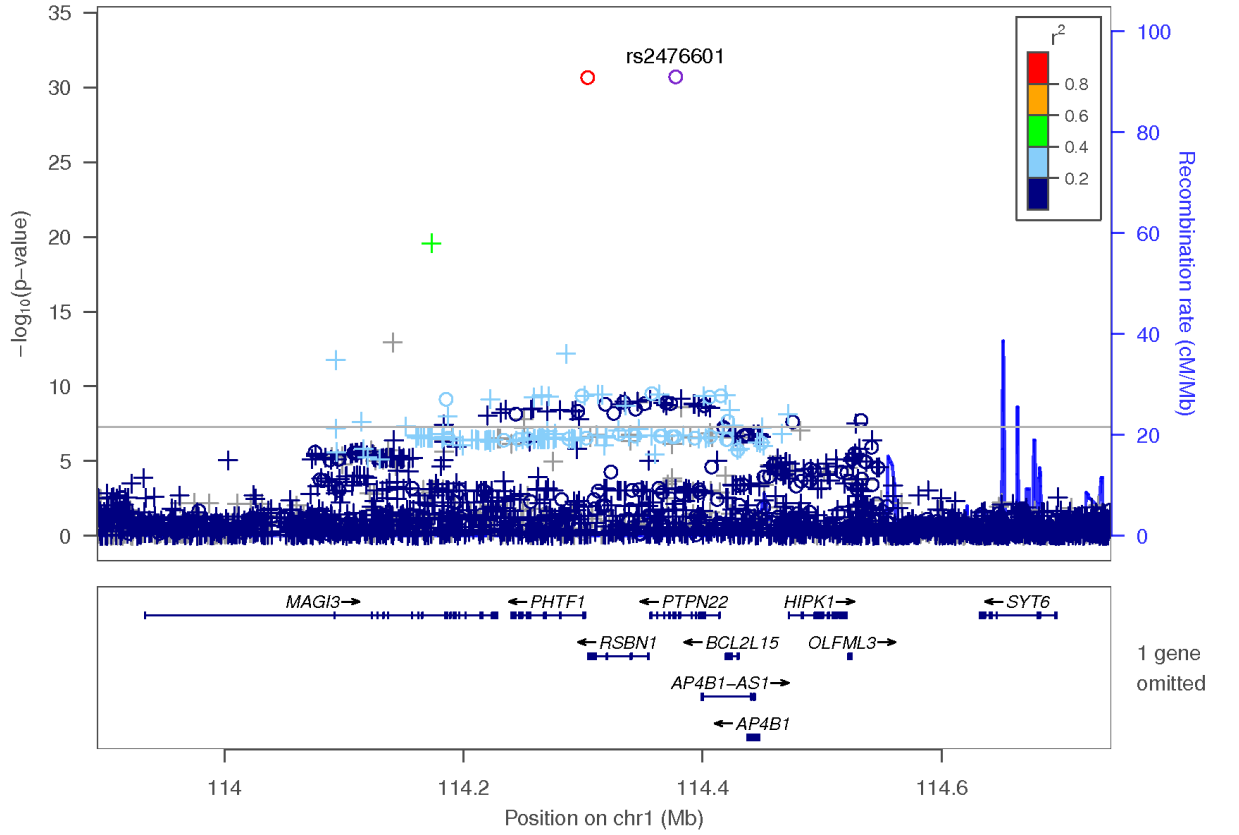
Nearby Clinical Variants

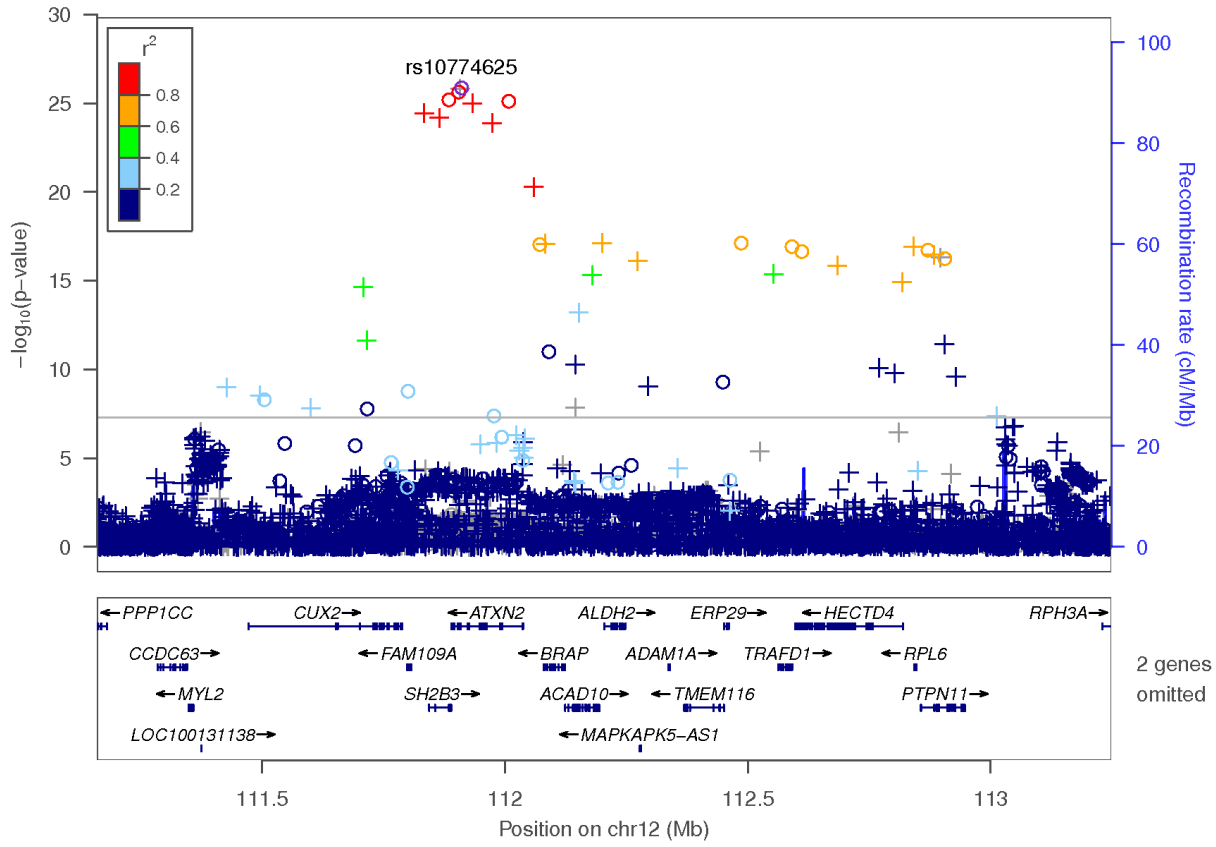
source	region	our.name	our.pval	dist	rsqr	assay.name	gene	phenotype	accession
clinvar	1p13.2	rs2476601	2.1×10^{-31}	0	1.000	rs2476601	PTPN22	Diabetes mellitus type 1	SNOMED CT46635009
clinvar	1p13.2	rs2476601	2.1×10^{-31}	0	1.000	rs2476601	PTPN22	Rheumatoid arthritis	SNOMED CT69896004
clinvar	1p13.2	rs2476601	2.1×10^{-31}	0	1.000	rs2476601	PTPN22	Systemic lupus erythematosus	SNOMED CT55464009
clinvar	8q24.22	rs121912648	7.3×10^{-9}	0	1.000	rs121912648	TG	Iodotyrosyl coupling defect	SNOMED CT23536000
clinvar	8q24.22	rs121912648	7.3×10^{-9}	0	1.000	rs121912648	TG	Autoimmune thyroid disease 3	NCBI curation

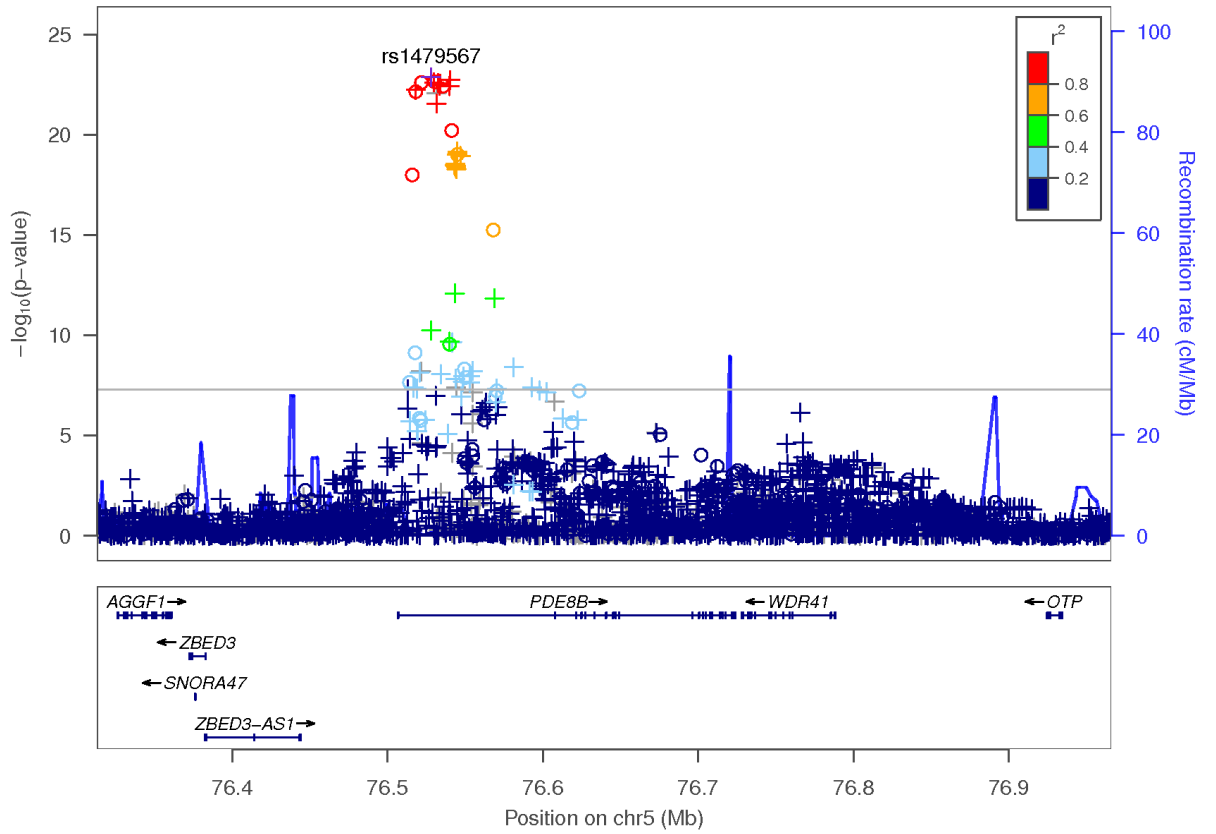
Regional Association Plots

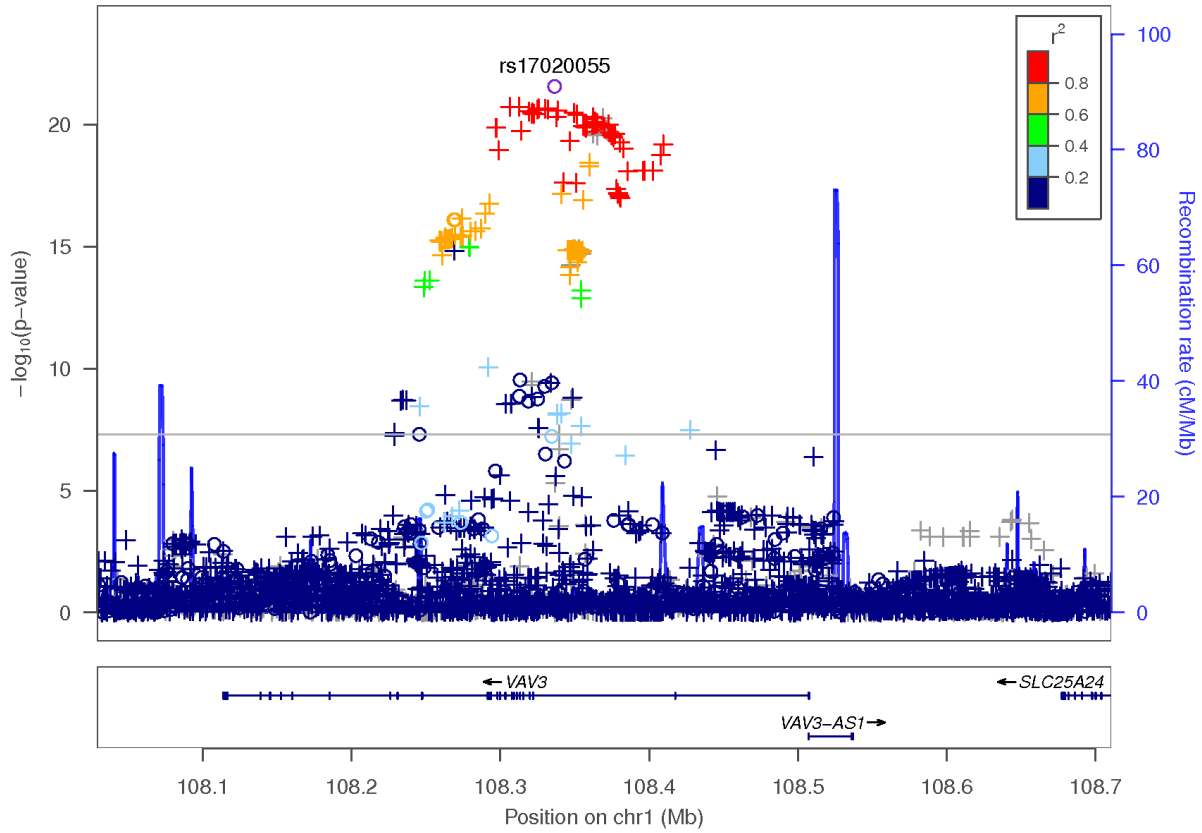


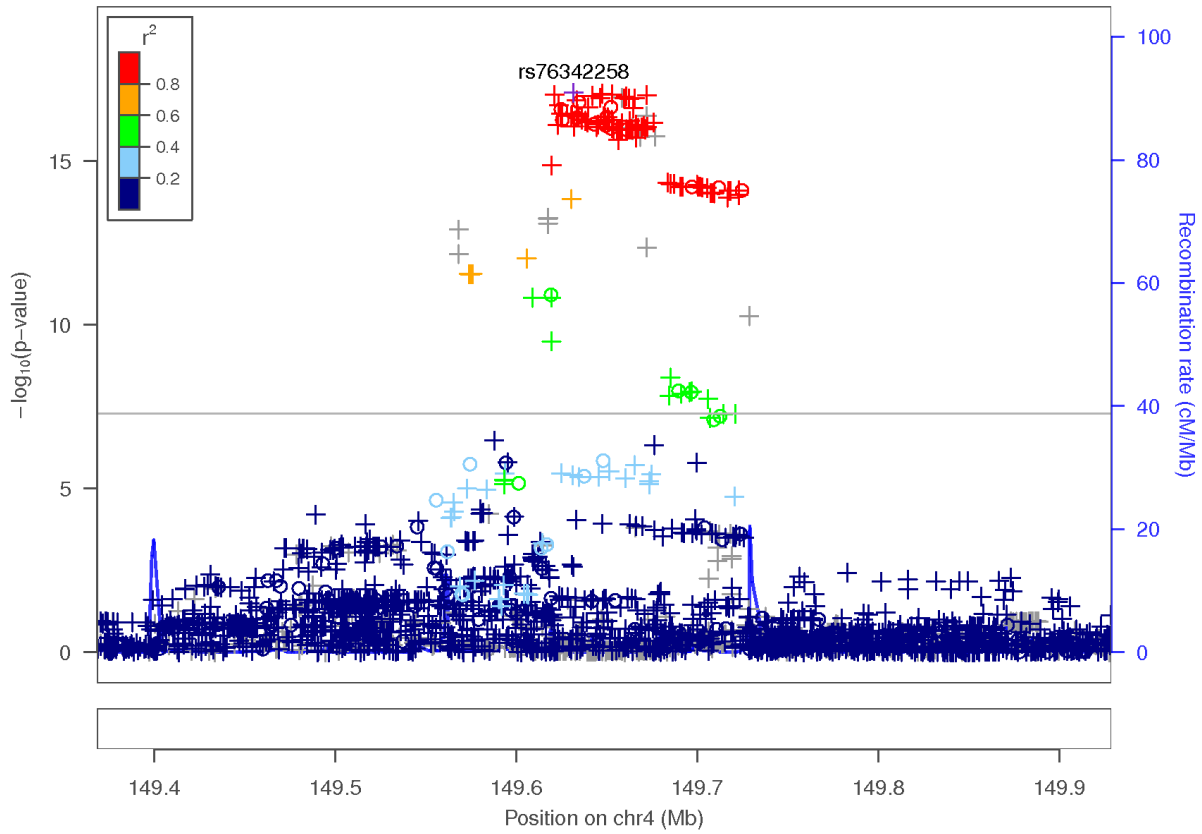

rs9273370
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
OR14J1 HLA−G HCG17 NRM HCG22 HCP5 NEU1 C6orf10 HLA−DOB RGL2
OR5V1 HCG4 TRIM26 ATAT1 MUC22 MICA MSH5 ATF6B HLA−DRB1 COL11A2
OR12D3 HLA−H HCG18 MDC1 C6orf15 MICB EHMT2 HCG23 TAP2 RXRB
OR12D2 HCG4B TRIM39 TUBB CDSN MCCD1 C2 BTNL2 PSMB8 VPS52
161 genes omitted
Position on chr6 (Mb)

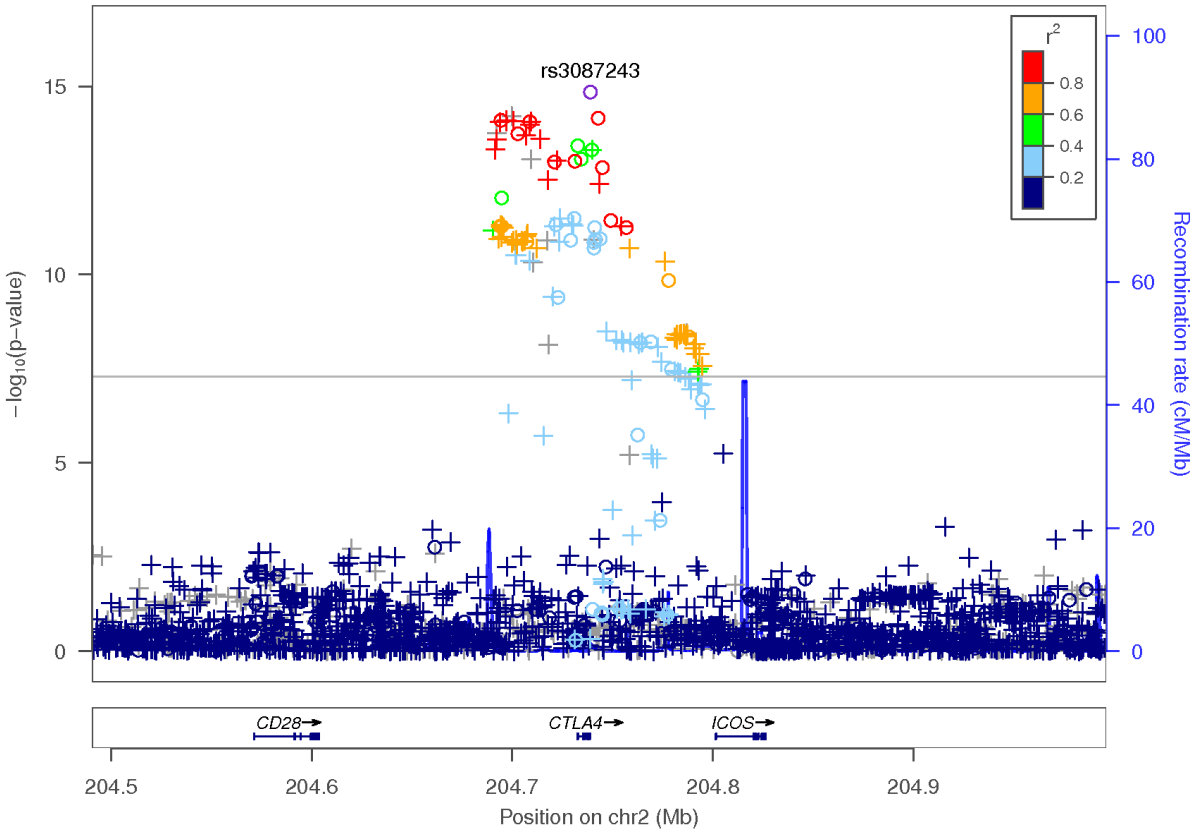

rs2476601
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
MAGI3 PHTF1 PTPN22 HIPK1 SYT6
RSBN1 BCL2L15 OLFML3
AP4B1−AS1
AP4B1
1 gene omitted
Position on chr1 (Mb)

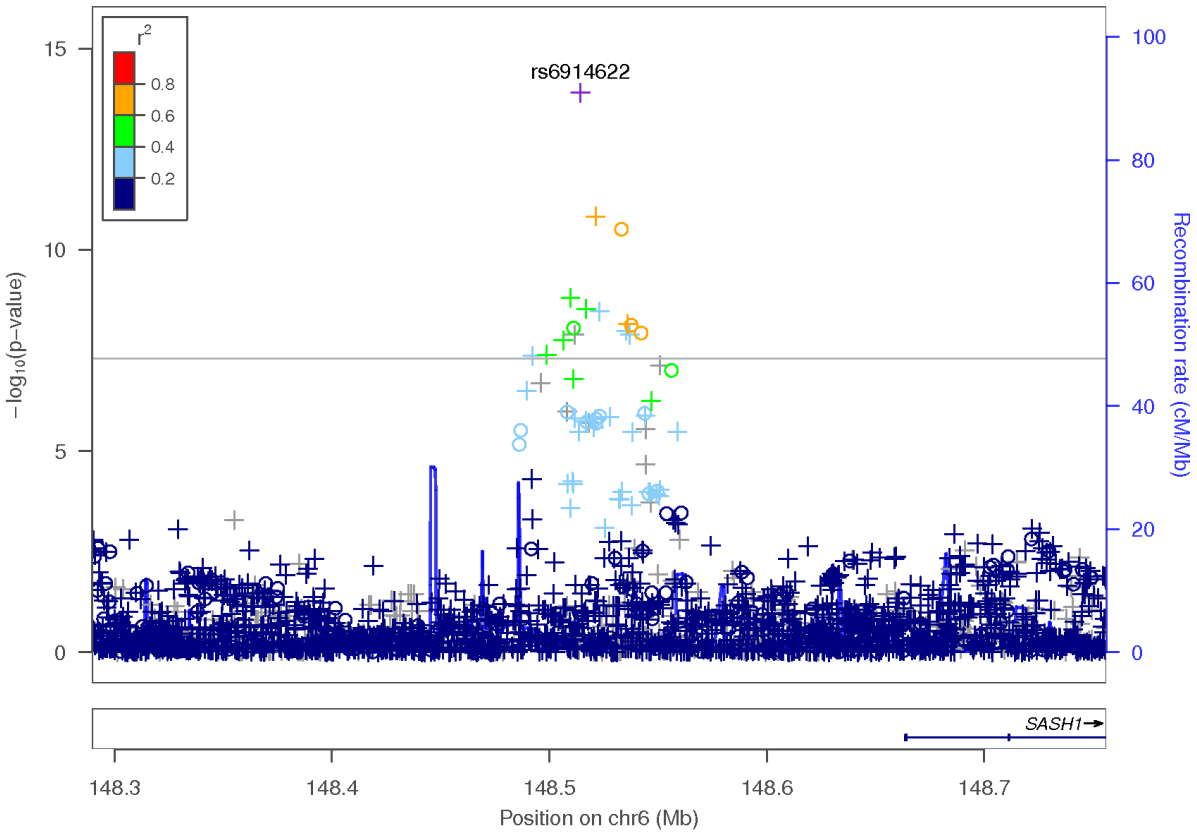

rs10774625
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
PPP1CC
CUX2
ATXN2
ALDH2
ERP29
HECTD4
RPH3A
CCDC63
FAM109A
BRAP
ADAM1A
TRAFD1
RPL6
MYL2
SH2B3
ACAD10
TMEM116
PTPN11
LOC100131138
MAPKAPK5−AS1
2 genes omitted
Position on chr12 (Mb)

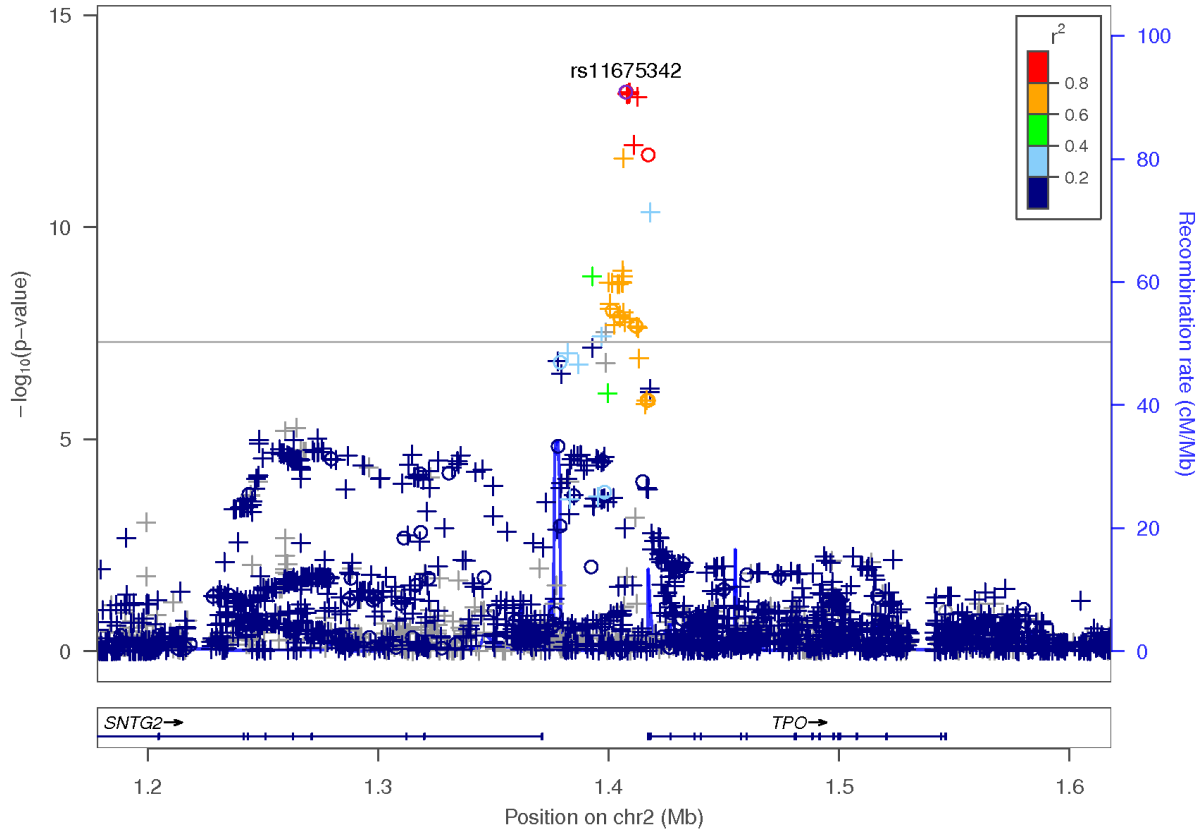

rs1479567
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
AGGF1
PDE8B
WDR41
OTP
ZBED3
SNORA47
ZBED3−AS1
Position on chr5 (Mb)

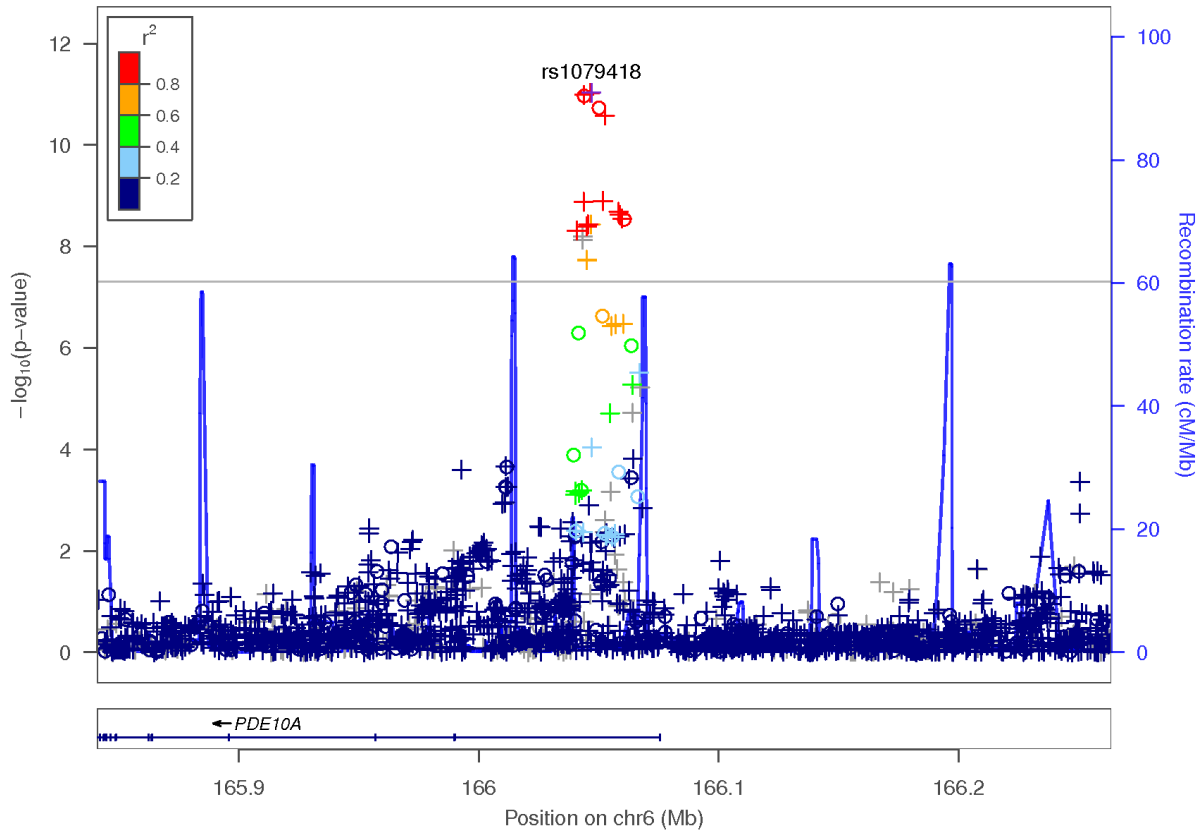

rs17020055
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
VAV3
SLC25A24
VAV3−AS1
Position on chr1 (Mb)


rs76342258
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
Position on chr4 (Mb)

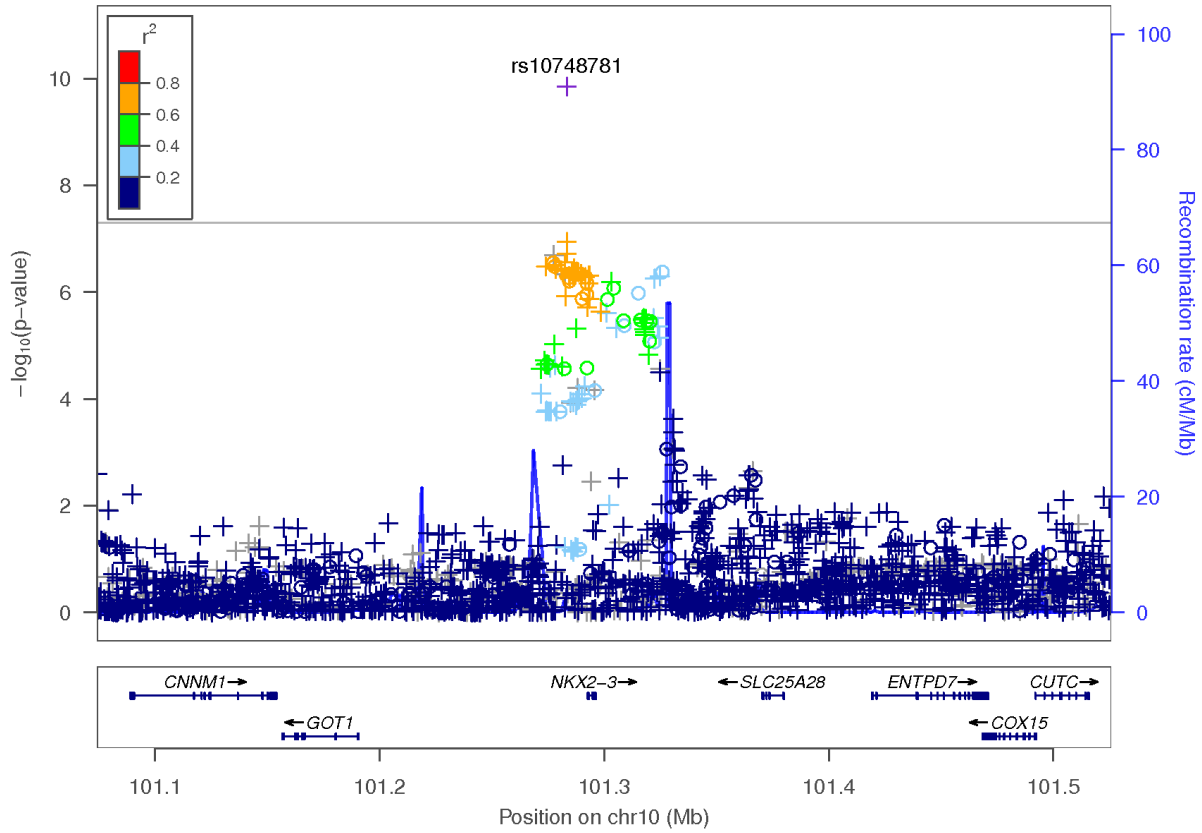

rs3087243
r²
0.8
0.6
0.4
0.2
15
10
5
0
100
80
60
40
20
0
−log₁₀(p−value)
Recombination rate (cM/Mb)
CD28
CTLA4
ICOS
204.5
204.6
204.7
204.8
204.9
Position on chr2 (Mb)

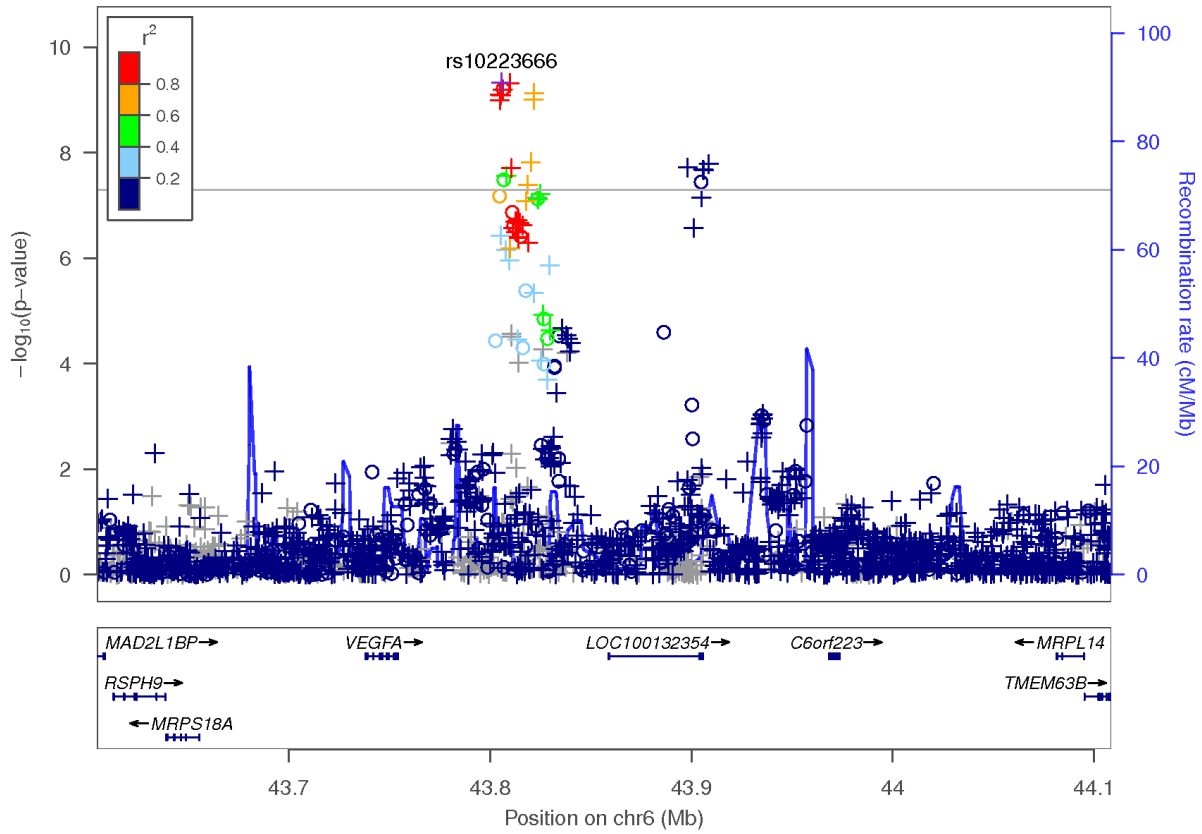

rs6914622
r²
0.8
0.6
0.4
0.2
15
10
5
0
100
80
60
40
20
0
−log₁₀(p−value)
Recombination rate (cM/Mb)
SASH1
148.3
148.4
148.5
148.6
148.7
Position on chr6 (Mb)

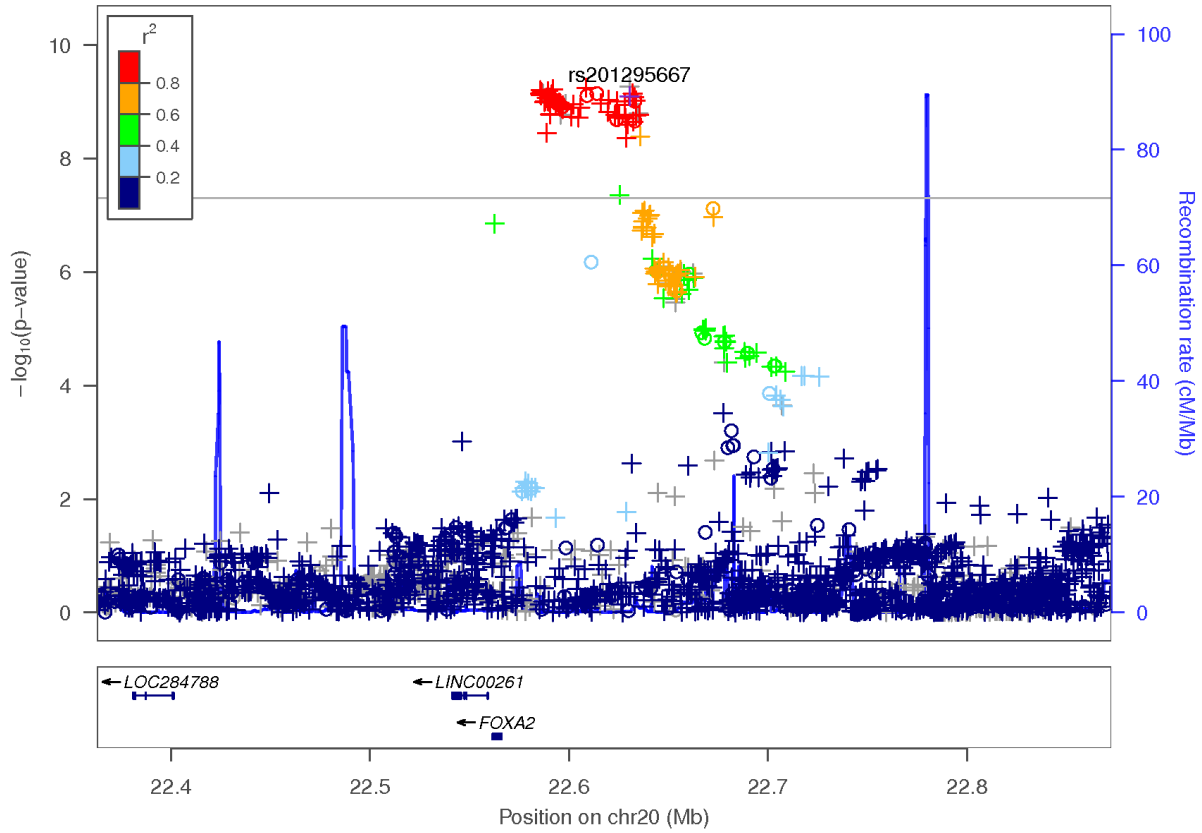


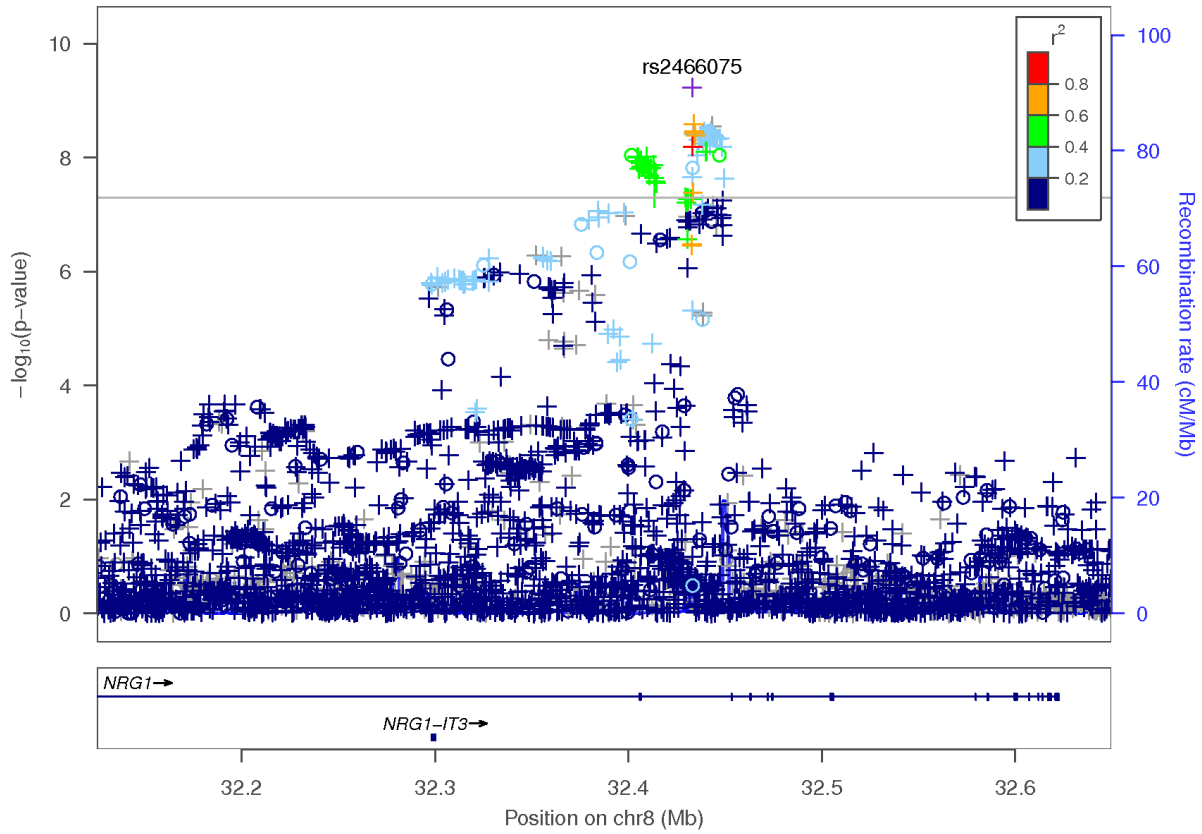


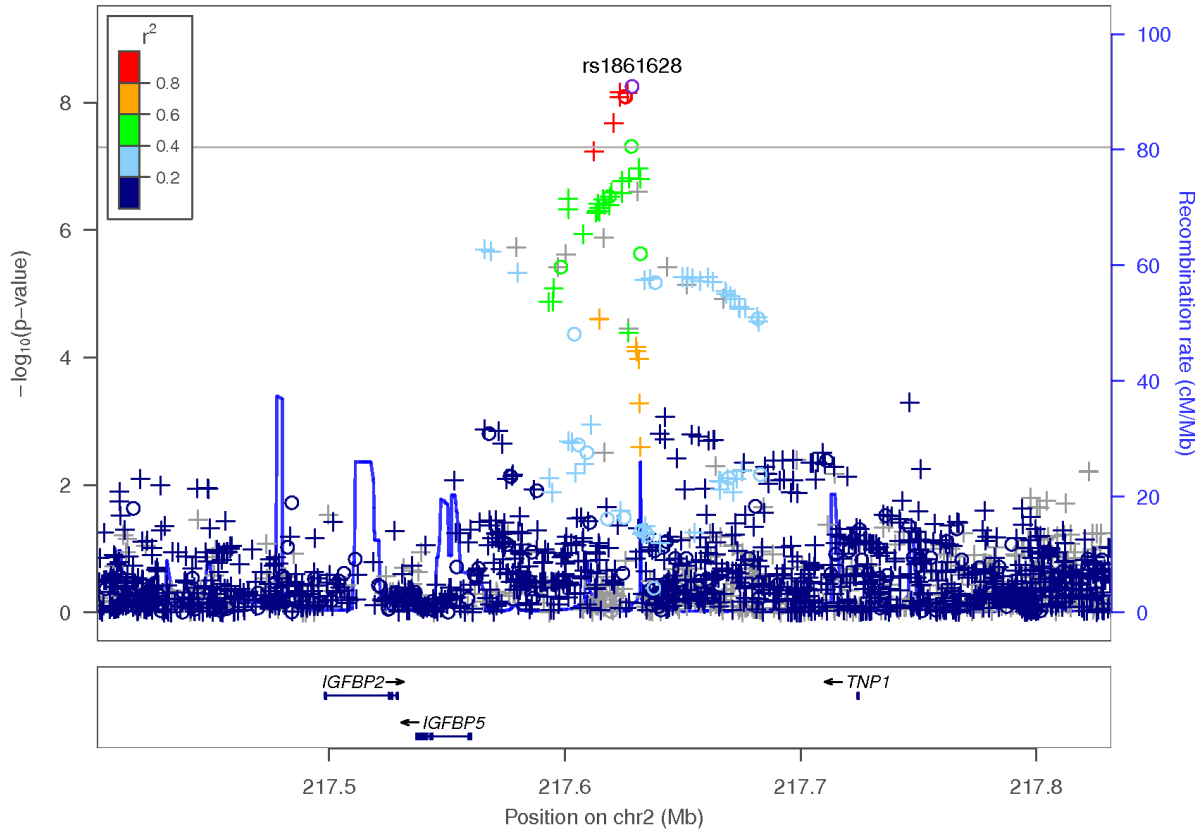
locuszoom plot for 22:37583733:C_CG failed

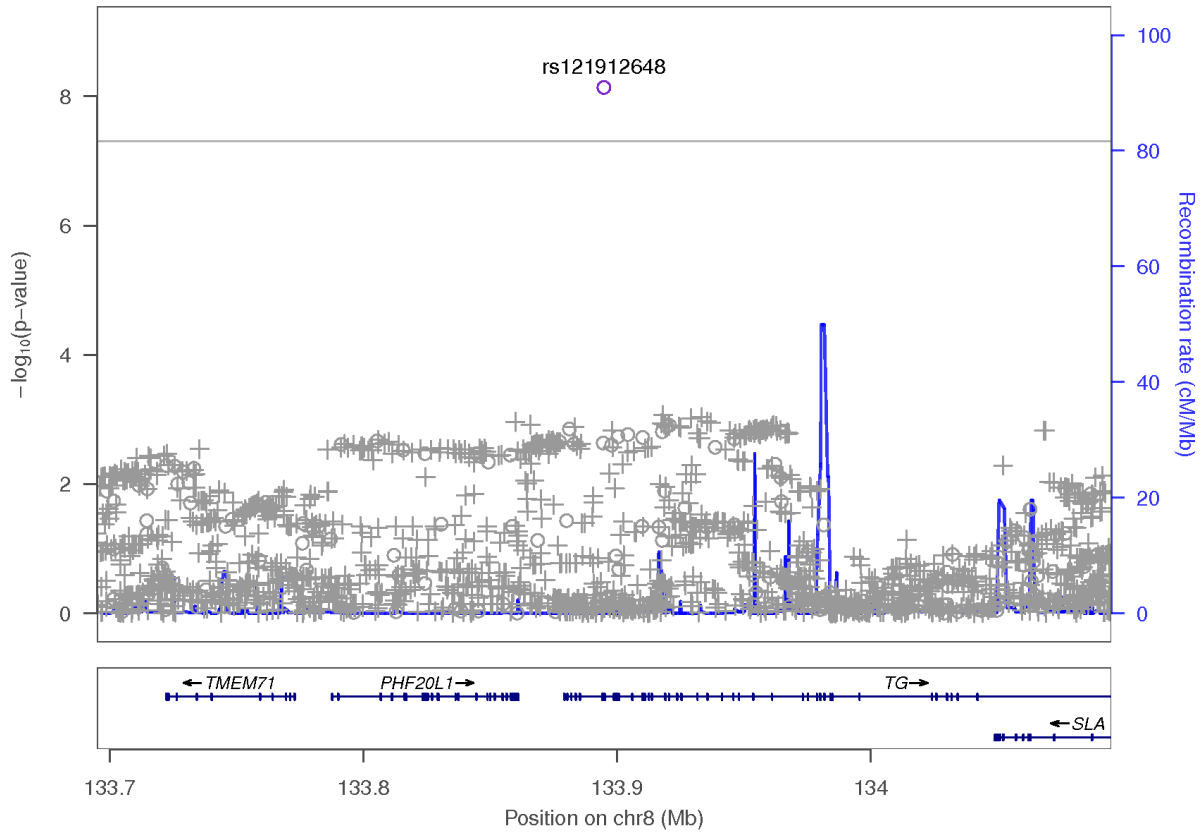

rs10748781
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
CNNM1
GOT1
NKX2−3
SLC25A28
ENTPD7
CUTC
COX15
101.1
101.2
101.3
101.4
101.5
Position on chr10 (Mb)

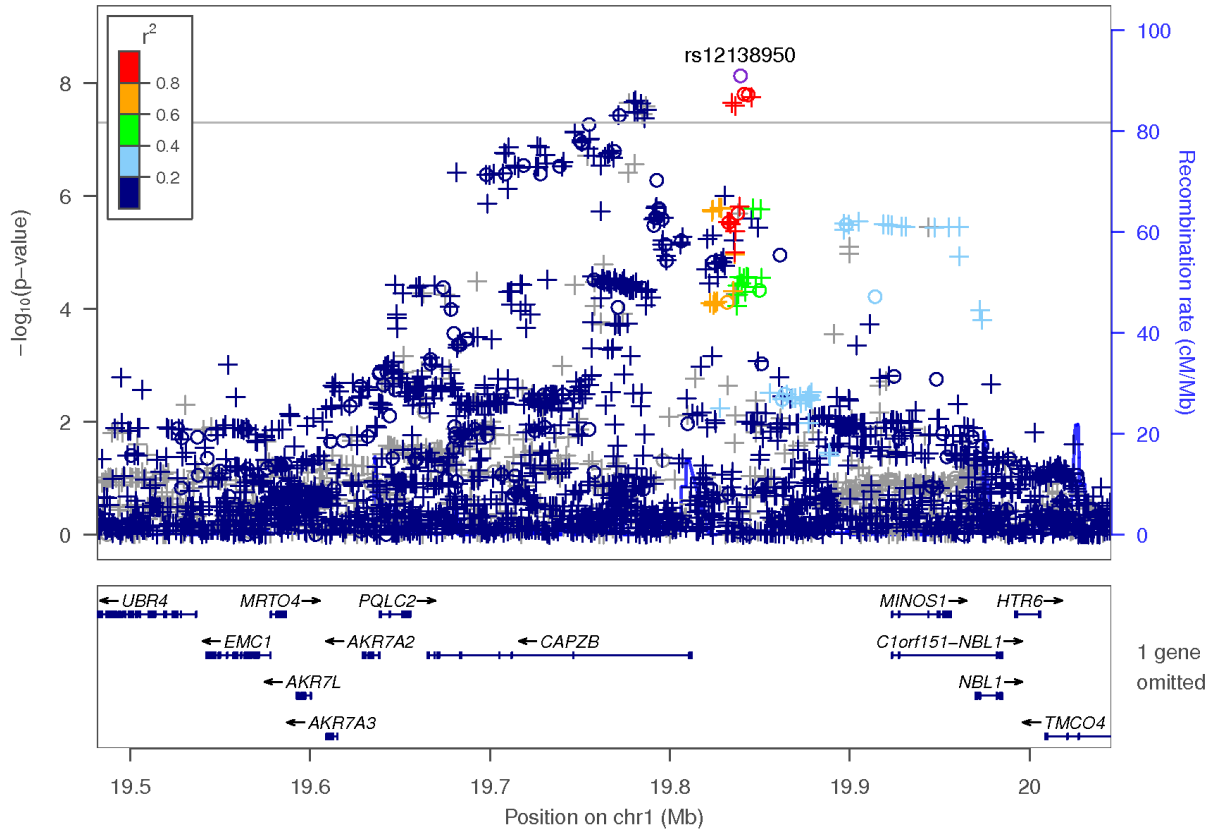

rs10223666
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
MAD2L1BP
RSPH9
MRPS18A
VEGFA
LOC100132354
C6orf223
MRPL14
TMEM63B
43.7
43.8
43.9
44
44.1
Position on chr6 (Mb)

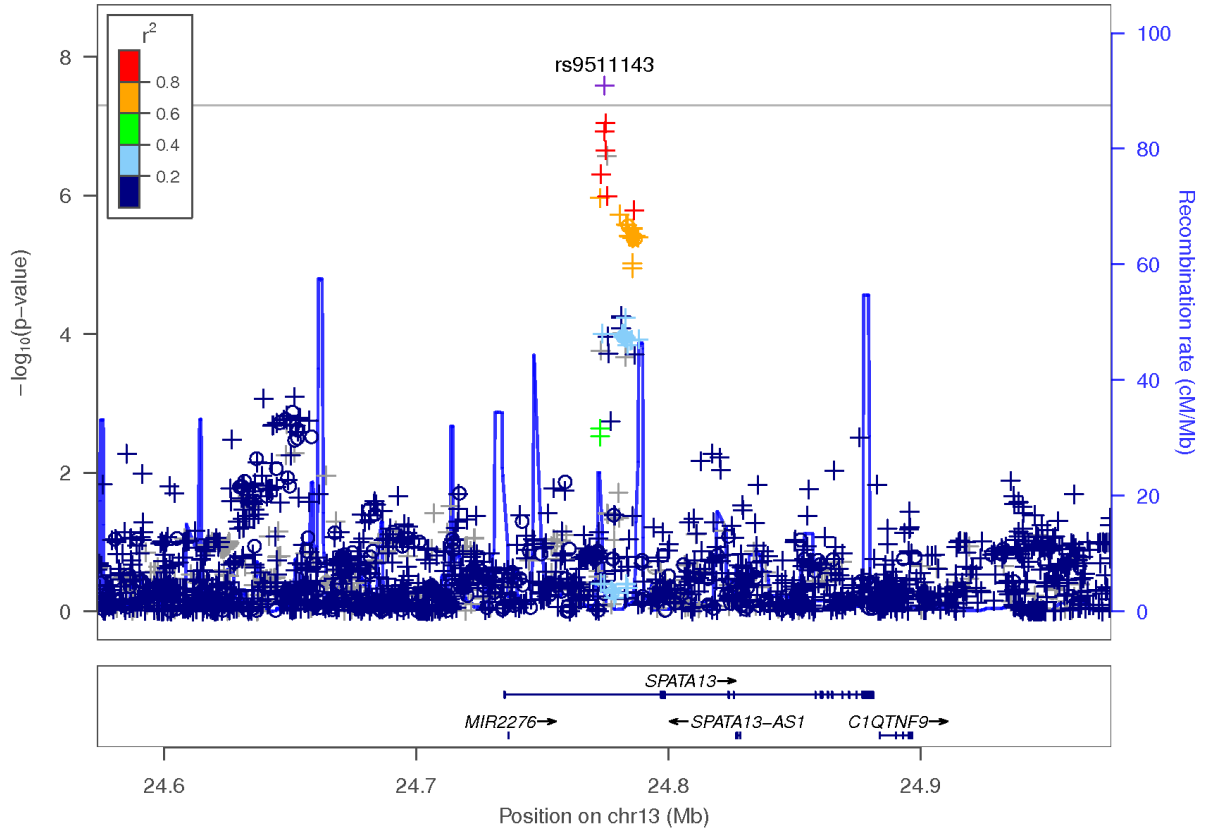

r²
0.8
0.6
0.4
0.2
rs201295667
−log10(p−value)
Recombination rate (cM/Mb)
LOC284788
LINC00261
FOXA2
22.4
22.5
22.6
22.7
22.8
Position on chr20 (Mb)

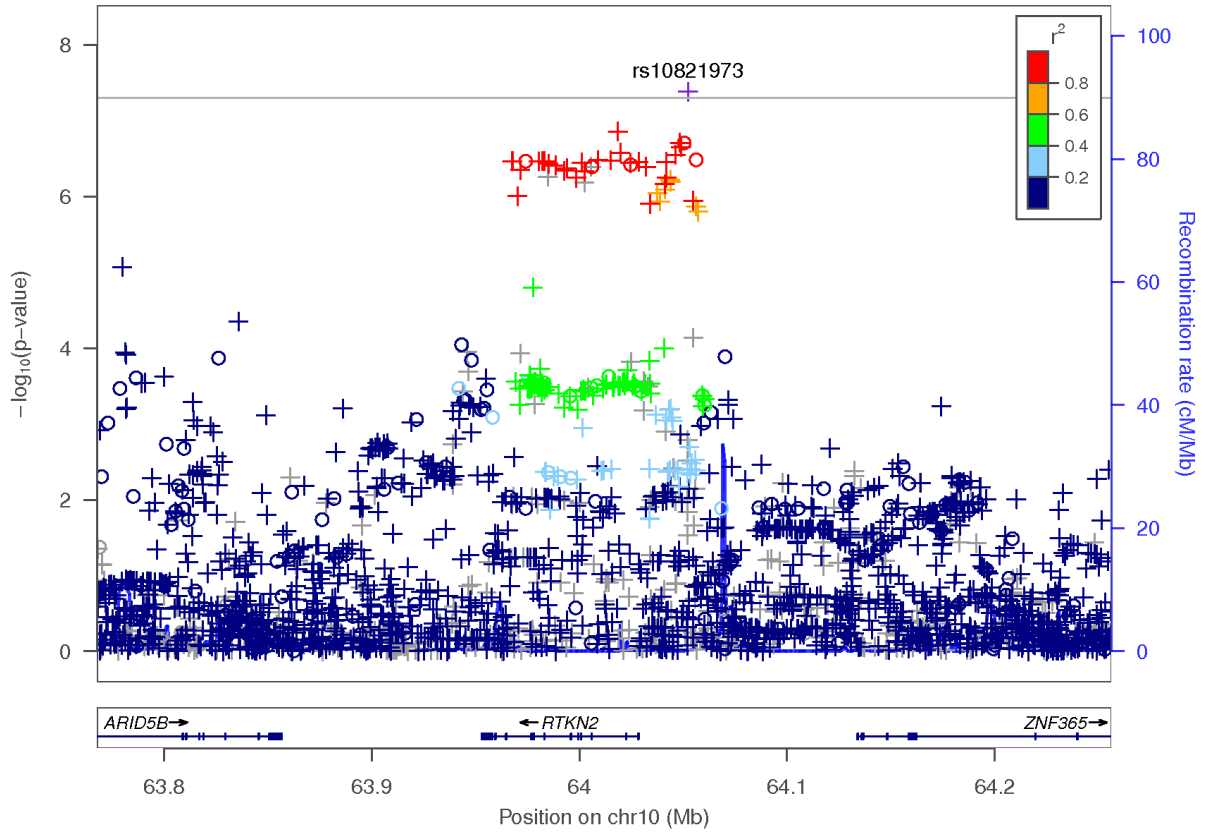

r²
0.8
0.6
0.4
0.2
rs2466075
−log10(p−value)
Recombination rate (cM/Mb)
NRG1
NRG1−IT3
32.2
32.3
32.4
32.5
32.6
Position on chr8 (Mb)

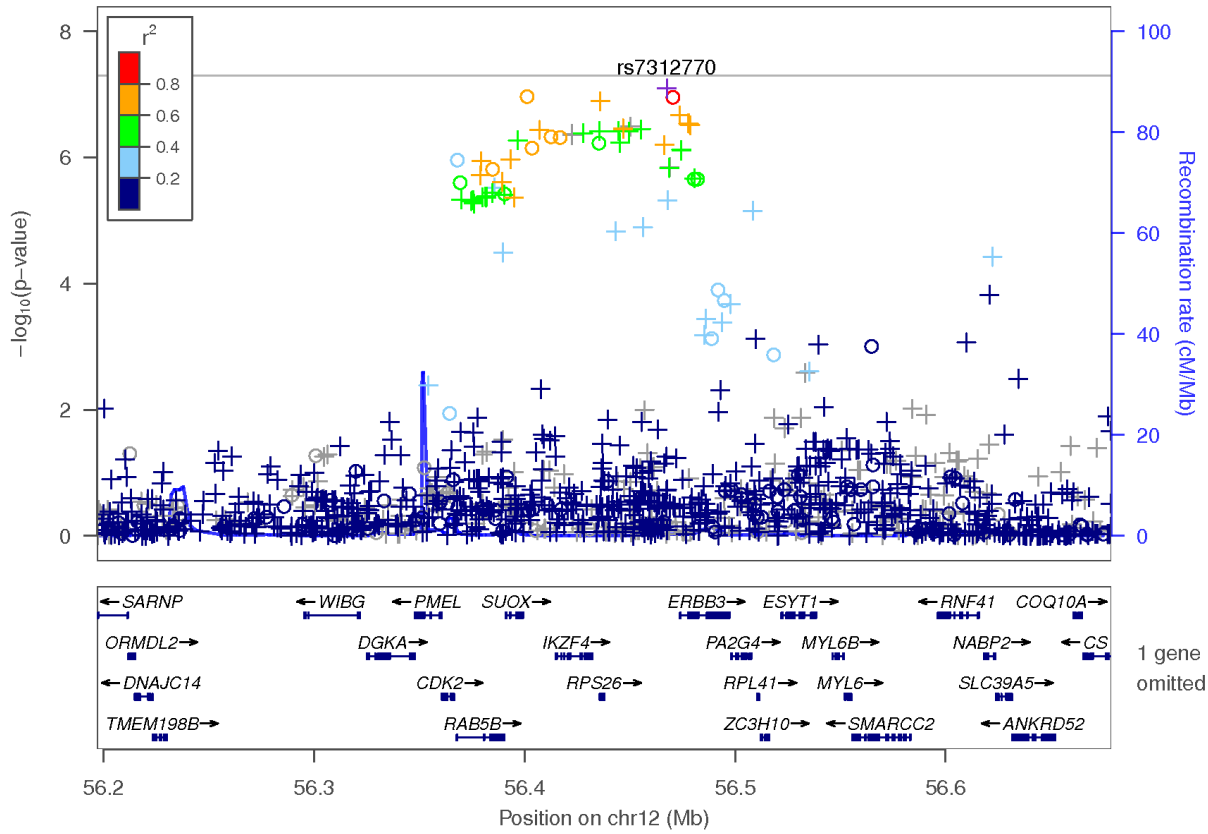

r²
0.8
0.6
0.4
0.2
rs1861628
−log10(p−value)
Recombination rate (cM/Mb)
IGFBP2
IGFBP5
TNP1
217.5
217.6
217.7
217.8
Position on chr2 (Mb)

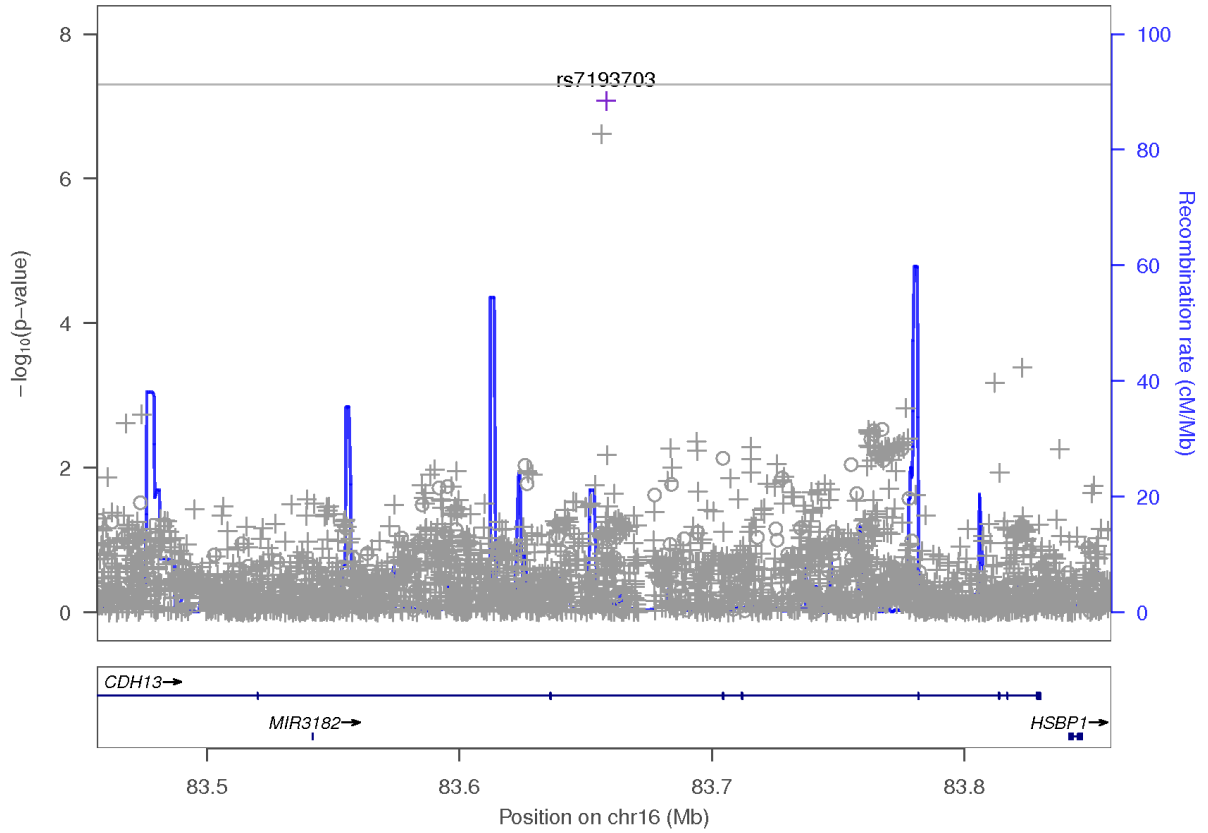

rs121912648
−log10(p−value)
Recombination rate (cM/Mb)
TMEM71
PHF20L1
TG
SLA
133.7
133.8
133.9
134
Position on chr8 (Mb)

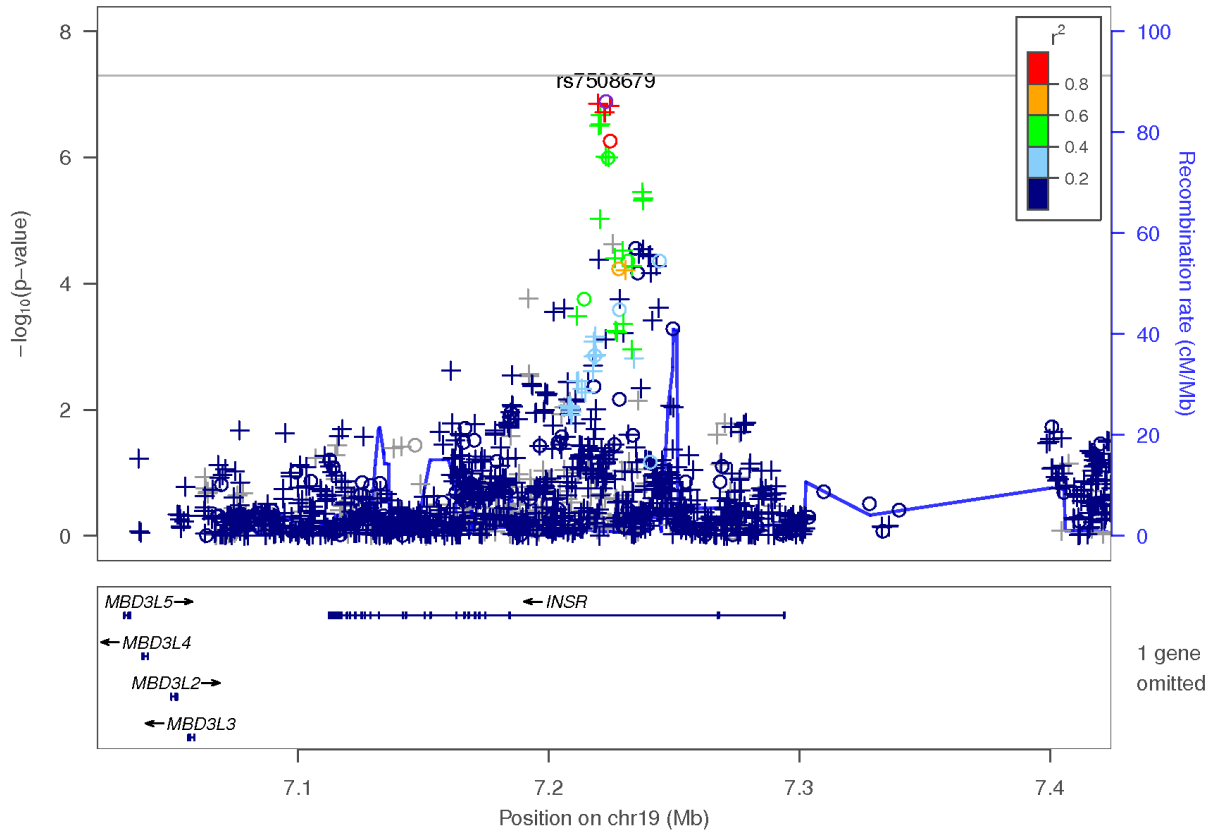

rs12138950
r²
0.8
0.6
0.4
0.2
−log₁₀(p−value)
Recombination rate (cM/Mb)
UBR4
MRTO4
PQLC2
MINOS1
HTR6
EMC1
AKR7A2
CAPZB
C1orf151−NBL1
AKR7L
NBL1
AKR7A3
TMCO4
1 gene
omitted
Position on chr1 (Mb)

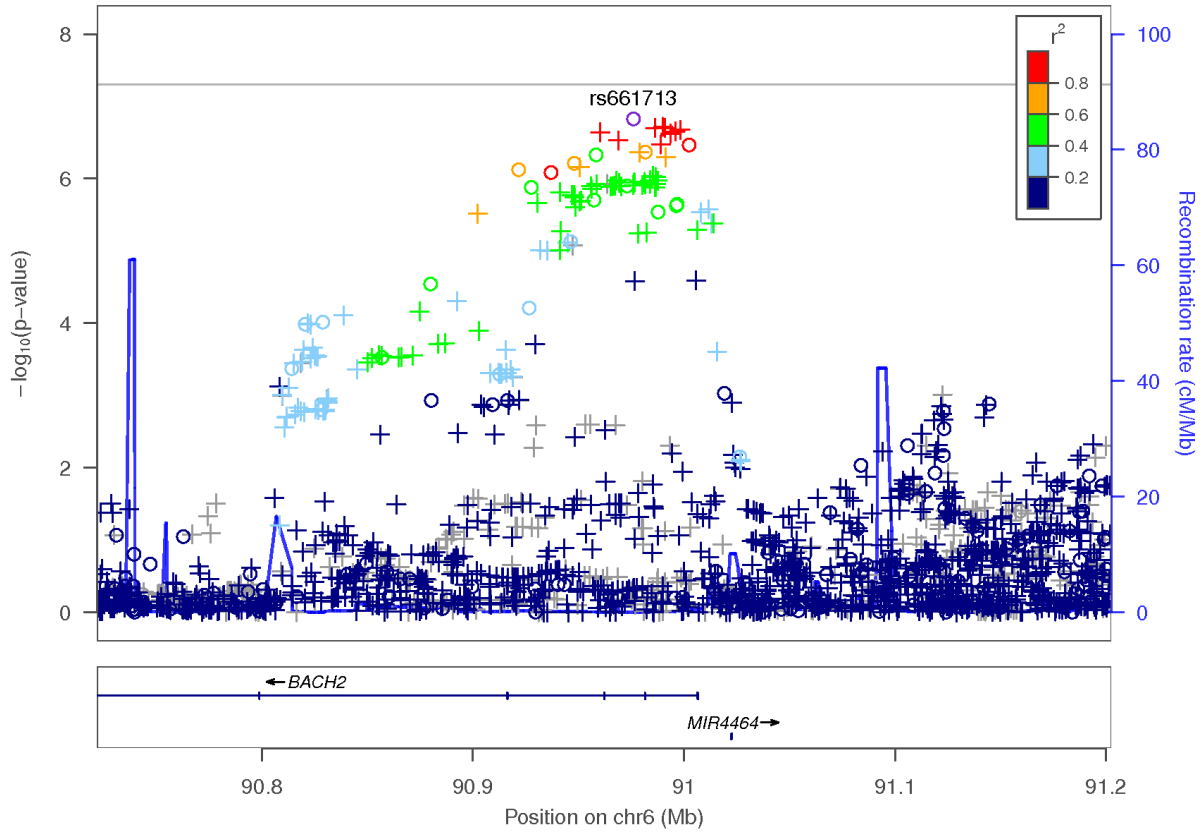

rs9511143
r²
0.8
0.6
0.4
0.2
−log₁₀(p−value)
Recombination rate (cM/Mb)
SPATA13
MIR2276
SPATA13−AS1
C1QTNF9
Position on chr13 (Mb)


rs10821973
r²
0.8
0.6
0.4
0.2
−log₁₀(p−value)
Recombination rate (cM/Mb)
ARID5B
RTKN2
ZNF365
63.8
63.9
64
64.1
64.2
Position on chr10 (Mb)


rs7312770
r²
0.8
0.6
0.4
0.2
−log₁₀(p−value)
Recombination rate (cM/Mb)
SARNP
WIBG
PMEL
SUOX
ERBB3
ESYT1
RNF41
COQ10A
ORMDL2
DGKA
IKZF4
PA2G4
MYL6B
NABP2
CS
DNAJC14
CDK2
RPS26
RPL41
MYL6
SLC39A5
TMEM198B
RAB5B
ZC3H10
SMARCC2
ANKRD52
1 gene
omitted
56.2
56.3
56.4
56.5
56.6
Position on chr12 (Mb)


rs7193703
−log10(p−value)
Recombination rate (cM/Mb)
CDH13
MIR3182
HSBP1
Position on chr16 (Mb)


rs7508679
r2
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
MBD3L5
INSR
MBD3L4
MBD3L2
MBD3L3
1 gene
omitted
Position on chr19 (Mb)


rs661713
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
BACH2
MIR4464
Position on chr6 (Mb)