

Analysis Summary: Childhood Ear Infections

Phenotype Description

Data on childhood ear infections comes from one source:

- Research snippet:
 - “Did you have several ear infections as a child (under the age of 18)?” (Yes, No, I’m not_sure)

Cases gave a positive response to this question, and controls gave a negative response to this question.

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]
iqb.childhood_ear_infections	case	46936	22914	24022	7829	14299	12580	12228
	control	74874	38359	36515	9778	20720	21043	23333

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

Phenotype	Group	Total	v1/v2	v3	v4
iqb.childhood_ear_infections	case	46936	2652	36693	7591
	control	74874	4190	58650	12034

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	-0.0103	0.000374	-27.5	4.4×10^{-166}	760.5	2.1×10^{-167}
sexF	0.1093	0.011859	9.2	3.0×10^{-20}	85.1	2.9×10^{-20}
pc.0	0.0543	0.006068	8.9	3.8×10^{-19}	81.2	2.0×10^{-19}
pc.1	-0.0451	0.006011	-7.5	5.9×10^{-14}	56.9	4.5×10^{-14}
pc.2	-0.0417	0.006058	-6.9	5.8×10^{-12}	47.7	5.1×10^{-12}
pc.3	0.0297	0.005925	5.0	5.5×10^{-7}	25.1	5.4×10^{-7}
pc.4	0.0107	0.005907	1.8	0.069	3.3	0.069

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	-8685	13770382
failed to converge	-15718	13754664

Genetic Association Tests

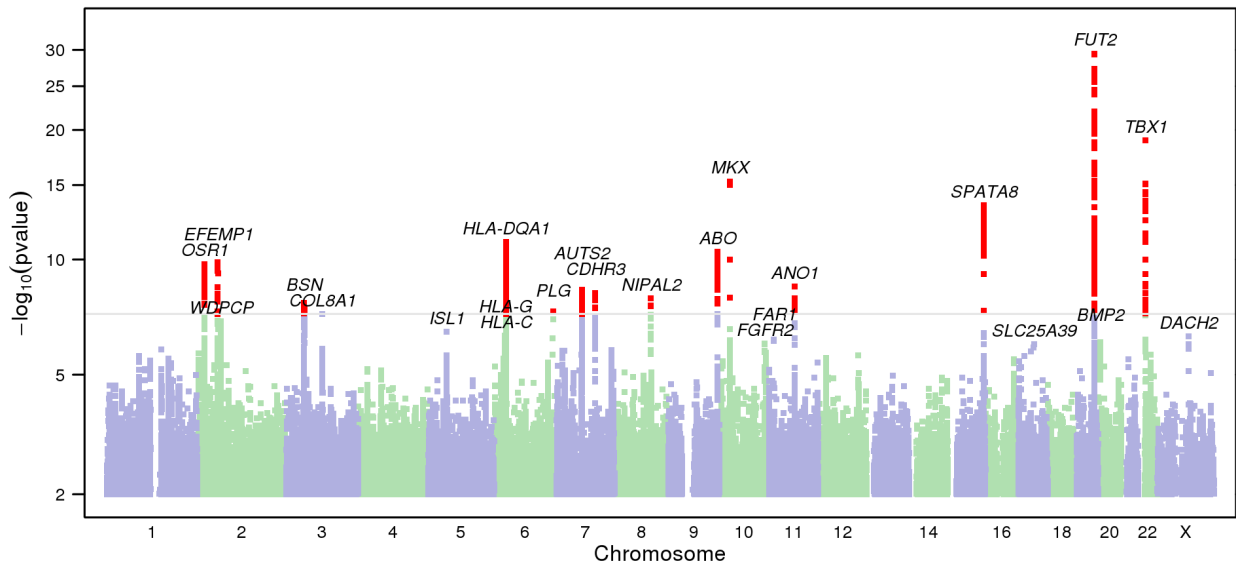
We performed logistic regression assuming an additive model for allelic effects, using the model:

$$iqb.childhood_ear_infections \sim age + sex + pc.0 + pc.1 + pc.2 + pc.3 + pc.4 + genotype$$

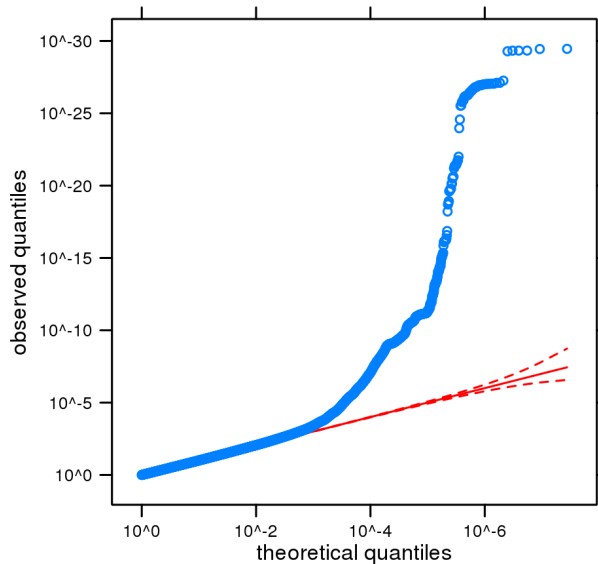
This genome-wide association analysis includes data from 46936 cases and 74874 controls of European ancestry, filtered to remove close relatives.

The results in this report have been adjusted for a genomic control inflation factor $\lambda=1.087$. The equivalent inflation factor for 1000 cases and 1000 controls $\lambda_{1000}= 1.002$, and for 10000, $\lambda_{10000}= 1.015$.

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
19q13.33	rs681343	chr19	49206462	C/T	I	3.5×10 ⁻³⁰	0.905	[0.889,0.920]	[FUT2]
22q11.21	rs1978060	chr22	19749525	A/G	I	1.2×10 ⁻¹⁹	1.089	[1.069,1.109]	[TBX1]
10p12.1	rs2808290	chr10	27900882	C/T	I	5.1×10 ⁻¹⁶	0.930	[0.914,0.947]	RAB18--[]--MKX
15q26.2	rs7174062	chr15	97452829	A/G	I	3.5×10 ⁻¹⁴	1.077	[1.057,1.098]	SPATA8---[]---LINC00923
6p21.32	rs4329147	chr6	32566577	C/T	I	9.5×10 ⁻¹²	1.111	[1.078,1.146]	HLA-DRB5--[]--HLA-DQA1
9q34.2	9:136149095:CA_C	chr9	136149095	D/I	I	3.7×10 ⁻¹¹	0.942	[0.925,0.959]	[ABO]
2p16.1	rs1802575	chr2	56093204	C/G	I	1.5×10 ⁻¹⁰	1.088	[1.061,1.117]	[EFEMP1]
2p24.1	rs5829676	chr2	19274784	D/I	I	1.8×10 ⁻¹⁰	0.945	[0.929,0.961]	NT5C1B-RDH14---[]---OSR1
11q13.3	rs72931768	chr11	69829717	C/G	I	2.6×10 ⁻⁹	1.086	[1.057,1.116]	FGF3---[]--ANO1
7q11.22	rs35213789	chr7	69268012	C/T	I	3.7×10 ⁻⁹	0.943	[0.925,0.962]	[AUTS2]
7q22.3	rs114947103	chr7	105658927	C/T	I	5.4×10 ⁻⁹	0.935	[0.914,0.956]	[CDHR3]
8q22.2	rs13281988	chr8	99372329	C/G	I	9.8×10 ⁻⁹	0.947	[0.930,0.965]	NIPAL2--[]--KCNS2
3p21.31	rs67035515	chr3	49656530	D/I	I	1.6×10 ⁻⁸	1.067	[1.043,1.091]	[BSN]
6q26	rs73015965	chr6	161127501	A/G	I	3.8×10 ⁻⁸	1.434	[1.262,1.630]	[PLG]
3q12.1	rs151208372	chr3	99171868	A/T	I	5.0×10 ⁻⁸	1.094	[1.059,1.130]	DCBLD2---[]---COL8A1
2p15	rs11405769	chr2	63658293	D/I	I	1.1×10 ⁻⁷	0.950	[0.932,0.968]	[WDPCP]
5q11.1	rs62366894	chr5	50631991	C/T	I	2.8×10 ⁻⁷	0.943	[0.922,0.964]	PARP8---[]--ISL1
6p22.1	rs34590927	chr6	29809784	D/I	I	4.0×10 ⁻⁷	0.940	[0.918,0.963]	HLA-G--[]--HLA-H
6p21.33	rs3130436	chr6	31220783	A/G	I	4.2×10 ⁻⁷	0.949	[0.930,0.968]	HCG27--[]--HLA-C
Xq21.2	rs183992155	chrX	85858185	A/T	I	4.2×10 ⁻⁷	0.268	[0.143,0.503]	[DACH2]
11p15.2	rs187558225	chr11	13656956	C/G	I	5.6×10 ⁻⁷	0.520	[0.398,0.678]	PTH---[]--FAR1
20p12.3	rs6085792	chr20	6960528	C/T	I	7.3×10 ⁻⁷	0.956	[0.939,0.973]	BMP2---[]---HAO1
10q26.13	rs41258305	chr10	123357482	C/T	I	7.9×10 ⁻⁷	1.096	[1.057,1.137]	[FGFR2]
17q21.31	rs76477327	chr17	42398997	C/T	I	8.6×10 ⁻⁷	1.177	[1.104,1.256]	[SLC25A39]

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
rs681343	FALSE	TRUE	FALSE	0.9986	0.26	0.64	0.4816	0.9997	0.9976	0.42	0.4821	v2v3v4
rs1978060	FALSE	FALSE	FALSE					0.9081	0.8821	0.0052	0.5998	v2v3v4
rs2808290	FALSE	FALSE	FALSE					0.9617	0.9538	0.36	0.4946	v2v3v4
rs7174062	FALSE	FALSE	FALSE					0.9975	0.9944	0.23	0.7297	v2v3v4
rs4329147	FALSE	FALSE	FALSE					0.7160	0.5594	4.4×10 ⁻¹³	0.8301	v3
9:136149095:CA_C	FALSE	FALSE	FALSE					0.9931	0.9848	0.031	0.6363	v2v3v4
rs1802575	FALSE	FALSE	FALSE					0.9915	0.9870	0.0084	0.8729	v2v3v4
rs5829676	FALSE	FALSE	FALSE					0.9986	0.9979	0.66	0.6039	v2v3v4
rs72931768	FALSE	FALSE	FALSE					0.9395	0.8109	1.4×10 ⁻¹⁷	0.8791	v2v3v4
rs35213789	FALSE	FALSE	FALSE					0.9941	0.9847	0.0096	0.2612	v2v3v4
rs114947103	FALSE	FALSE	FALSE					0.9682	0.8696	1.9×10 ⁻⁸	0.8219	v2v3v4
rs13281988	FALSE	FALSE	FALSE					0.9917	0.9895	0.26	0.6920	v2v3v4
rs67035515	FALSE	FALSE	FALSE					0.9732	0.9290	9.8×10 ⁻²⁸	0.1807	v2v3v4
rs73015965	FALSE	TRUE	TRUE	0.9997	4.1×10 ⁻⁵	0.15	0.0052	0.9874	0.9756	0.27	0.0051	v3
rs151208372	FALSE	FALSE	FALSE					0.9669	0.9440	0.10	0.9207	v2v3v4
rs11405769	FALSE	FALSE	FALSE					0.9646	0.9464	0.0015	0.7097	v2v3v4
rs62366894	FALSE	FALSE	FALSE					0.9174	0.9015	0.027	0.1965	v2v3v4
rs34590927	FALSE	FALSE	FALSE					0.8677	0.8398	0.0068	0.1789	v2v3v4
rs3130436	FALSE	FALSE	FALSE					0.9728	0.9577	0.00017	0.2375	v2v3v4
rs183992155	FALSE	FALSE	FALSE					0.7172	0.4937	0.084	0.0004	v2v3v4
rs187558225	FALSE	FALSE	FALSE					0.6653	0.5410	0.0030	0.0019	v2v3v4
rs6085792	FALSE	FALSE	FALSE					0.9657	0.9567	0.26	0.3858	v2v3v4
rs41258305	FALSE	FALSE	FALSE					0.9341	0.7914	0.084	0.9356	v2v3v4
rs76477327	FALSE	FALSE	FALSE					0.6369	0.5847	0.19	0.0272	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
rs681343	15419	28787	14366	74874	0.4922	10192	18573	7875	46936	0.4691
rs1978060				74874	0.5980				46936	0.6185
rs2808290				74874	0.5017				46936	0.4847
rs7174062				74874	0.7245				46936	0.7381
rs4329147				58210	0.8250				36390	0.8350
9:136149095:CA_C				74874	0.6418				46936	0.6296
rs1802575				74874	0.8693				46936	0.8788
rs5829676				74874	0.6067				46936	0.5926
rs72931768				74874	0.8766				46936	0.8856
rs35213789				74874	0.2643				46936	0.2523
rs114947103				74874	0.8261				46936	0.8169
rs13281988				74874	0.6974				46936	0.6868
rs67035515				74874	0.1787				46936	0.1886
rs73015965	69988	678	0	58210	0.0047	43670	594	0	36390	0.0069
rs151208372				74874	0.9188				46936	0.9254
rs11405769				74874	0.7122				46936	0.7011
rs62366894				74874	0.1992				46936	0.1906
rs34590927				74874	0.1811				46936	0.1738
rs3130436				74874	0.2404				46936	0.2310
rs183992155				74874	0.0006				46936	0.0002
rs187558225				74874	0.0021				46936	0.0014

rs6085792	74874	0.3892	46936	0.3783
rs41258305	74874	0.9347	46936	0.9403
rs76477327	74874	0.0260	46936	0.0287

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
19q13.33	49206462	rs681343	3.5×10^{-30}	-290	1.000	rs516246	2.0×10^{-6}	23251661	Obesity-related traits	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	-290	1.000	rs516246	1.0×10^{-15}	23128233	Crohn's disease	DBP,SPHK2,IZUMO1,FUT2
									Liver enzyme levels (gamma-glutamyl transferase)	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	-290	1.000	rs516246	8.0×10^{-10}	22001757	Cholesterol, total	FUT2,FLJ36070
19q13.33	49206462	rs681343	3.5×10^{-30}	-45	0.995	rs492602	2.0×10^{-10}	20686565	Vitamin B12 levels	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	-45	0.995	rs492602	5.0×10^{-17}	18776911	Liver enzyme levels (alkaline phosphatase)	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	141	0.697	rs281377	1.0×10^{-15}	22001757	Folate pathway vitamin levels	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	523	0.884	rs602662	2.0×10^{-15}	19744961	Folate pathway vitamin levels	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	523	0.884	rs602662	3.0×10^{-20}	19303062	Crohn's disease	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	2403	0.879	rs504963	2.0×10^{-8}	20570966	Metabolic traits	FUT2
19q13.33	49206462	rs681343	3.5×10^{-30}	2548	0.884	rs503279	4.0×10^{-20}	21886157	Pubertal anthropometrics	MAMSTR
19q13.33	49206462	rs681343	3.5×10^{-30}	7812	0.821	rs281379	5.0×10^{-8}	23449627	Crohn's disease	FUT2,RASIP1
19q13.33	49206462	rs681343	3.5×10^{-30}	7812	0.821	rs281379	7.0×10^{-12}	21102463	Bipolar disorder	SPHK2, SEC1, ...
19q13.33	49206462	rs681343	3.5×10^{-30}	21810	0.653	rs2287921	3.0×10^{-6}	21926972	Retinal vascular caliber	RASIP1,IZUMO1,FUT1,FUT2,CA11,FGF21,FLJ36070
19q13.33	49206462	rs681343	3.5×10^{-30}	21810	0.653	rs2287921	2.0×10^{-25}	21060863	Dietary macronutrient intake	FGF21
19q13.33	49206462	rs681343	3.5×10^{-30}	42268	0.639	rs838145	4.0×10^{-10}	23636237	Interstitial lung disease	
6p21.32	32566577	rs4329147	9.5×10^{-12}	-376549	0.577	rs3132946	8.0×10^{-6}	23583980	Lumiracoxib-related liver injury	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	-260598	0.608	rs3129900	7.0×10^{-25}	20639878	Multiple sclerosis	C6orf10
6p21.32	32566577	rs4329147	9.5×10^{-12}	-230390	0.608	rs3129934	7.0×10^{-16}	22457343	Multiple sclerosis	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	-230390	0.608	rs3129934	9.0×10^{-11}	18941528	Hepatitis C induced liver cirrhosis	Intergenic
6p21.32	32566577	rs4329147	9.5×10^{-12}	-165498	0.839	rs3129860	1.0×10^{-9}	23321320	Multiple sclerosis	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	-153526	0.819	rs3135388	4.0×10^{-225}	19525953	Multiple sclerosis	HLA-DRA
6p21.32	32566577	rs4329147	9.5×10^{-12}	-153526	0.819	rs3135388	9.0×10^{-81}	17660530	Multiple sclerosis	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	-153032	0.819	rs3129889	1.0×10^{-206}	22190364	Crohn's disease	HLA-DRB5,HLA-DQA1,HLA-DRB1,HLA-DRA,BTNL2
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	5.0×10^{-12}	23850713	Ulcerative colitis	HLA-DRB1, HLA-DQA1
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	1.0×10^{-18}	23511034	Inflammatory bowel disease	MHC
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	8.0×10^{-11}	21699788	Immunoglobulin A	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	3.0×10^{-33}	20694011	Multiple sclerosis	DQA1
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	4.0×10^{-17}	20598377	Multiple sclerosis	HLA-DRB1
6p21.32	32566577	rs4329147	9.5×10^{-12}	20277	0.828	rs9271366	7.0×10^{-184}	19525955	Multiple sclerosis (OCB status)	HLA-DQA1
6p21.32	32566577	rs4329147	9.5×10^{-12}	25623	0.556	rs9271640	2.0×10^{-20}	23472185	Menarche (age at onset)	KLHDC8B
3p21.31	49656530	rs67035515	1.6×10^{-8}	-445798	0.512	rs7617480	3.0×10^{-8}	21102462		

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, $r^2 > 0.8$).

no relevant GWAS catalog terms were available

Nearby Nonsynonymous SNPs

region	position	our.name	our.pval	dist	rsqr	assay.name	gene	aa.chg
19q13.33	49206462	rs681343	3.5×10^{-30}	212	1.000	rs601338	FUT2	W154*
19q13.33	49206462	rs681343	3.5×10^{-30}	523	0.884	rs602662	FUT2	G258S
19q13.33	49206462	rs681343	3.5×10^{-30}	25764	0.652	rs2287922	RASIP1	R601C

6p21.32	32566577	rs4329147	9.5×10^{-12}	43884	0.617	rs9260	HLA-DQA1	M230V
7q22.3	105658927	rs114947103	5.4×10^{-9}	-476	0.968	rs6967330	CDHR3	C529Y
6q26	161127501	rs73015965	3.8×10^{-8}	0	1.000	rs73015965	PLG	K38E
6p22.1	29809784	rs34590927	4.0×10^{-7}	-116773	0.694	rs1736924	HLA-F	P272S

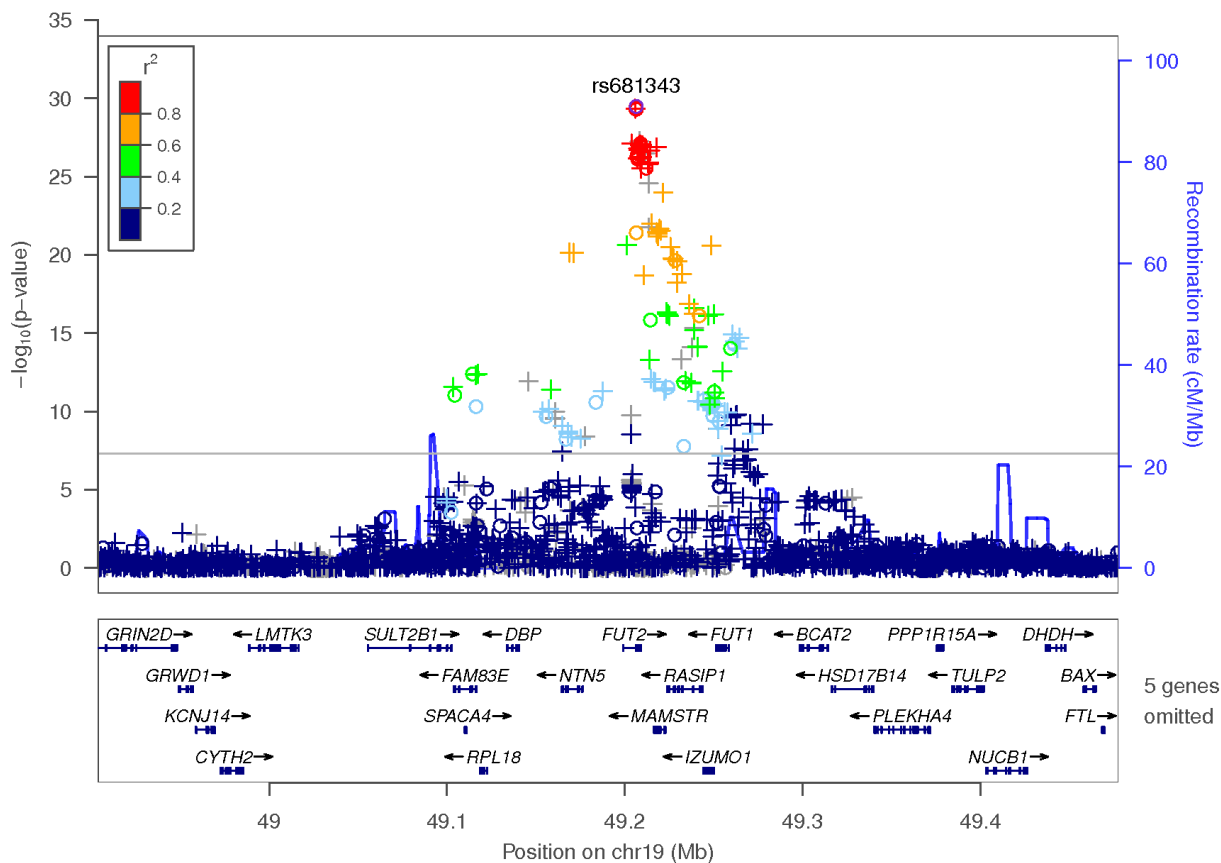
Nearby Expression QTLs

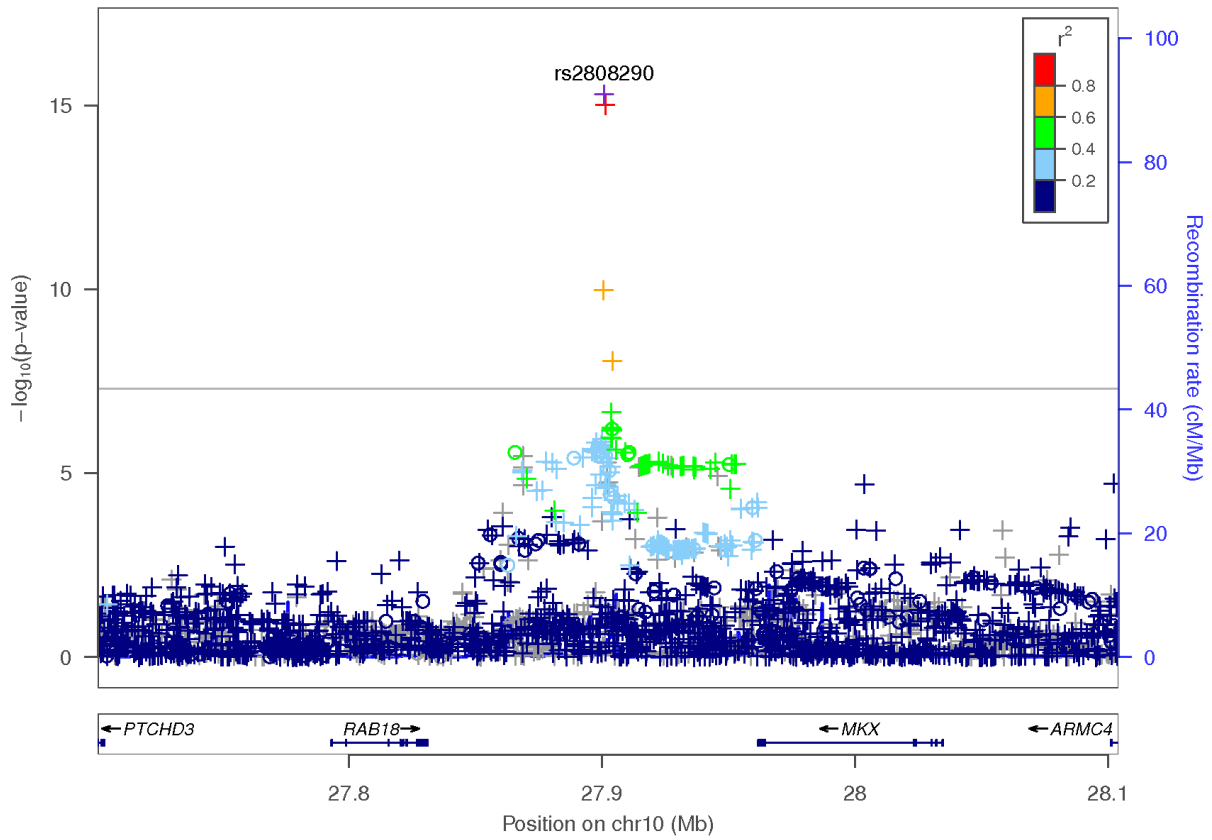
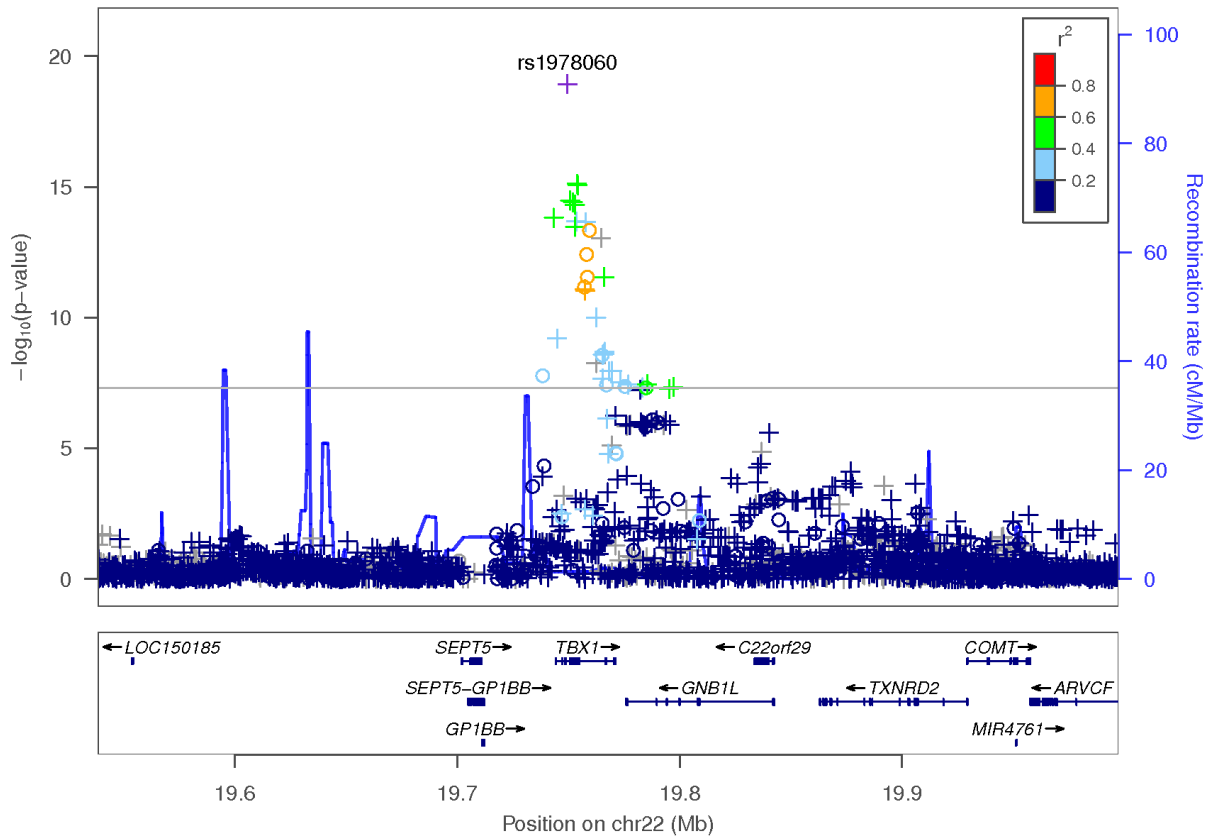
region	position	our.name	our.pval	dist	rsqr	assay.name	eqtl.dist	eqtl.gene	eqtl.pval	eqtl.rsqr	tissue	pubmed.id
3p21.31	49656530	rs67035515	1.6×10^{-8}	-470794	0.512	rs7617480	-169201	P4HTM	7.6×10^{-5}		Lymphoblastoid	20220756
3p21.31	49656530	rs67035515	1.6×10^{-8}	-470794	0.512	rs7617480	-722595	ATRIP	0.00065		Lymphoblastoid	20220756
3p21.31	49656530	rs67035515	1.6×10^{-8}	-442893	0.512	rs9586	900845	RBM6	0.00061	0.041	B-Cell	22446964
3p21.31	49656530	rs67035515	1.6×10^{-8}	-65902	0.841	rs11130208	-209763	RHOA	2.0×10^{-5}		Lymphoblastoid	20220756
3p21.31	49656530	rs67035515	1.6×10^{-8}	-14503	0.831	rs4241405	181841	AMT	5.9×10^{-8}	0.076	Lymphoblastoid	24037378
3p21.31	49656530	rs67035515	1.6×10^{-8}	80793	0.981	rs11130217	-282976	AMT	0.00025	0.047	B-Cell	22446964
3p21.31	49656530	rs67035515	1.6×10^{-8}	221734	0.971	rs1996663	116880	GMPPB	2.7×10^{-6}	0.017	Monocyte	20502693
2p15	63658293	rs11405769	1.1×10^{-7}	-228118	0.720	rs12151606	178939	C2ORF86	0.00010	0.053	Monocyte	22446964
2p15	63658293	rs11405769	1.1×10^{-7}	75728	0.890	rs262487	-64395	MDH1	5.4×10^{-11}		Liver	18462017
6p22.1	29809784	rs34590927	4.0×10^{-7}	-184783	0.675	rs3130250	409485	PPP1R11	1.5×10^{-8}	0.022	Monocyte	20502693
6p22.1	29809784	rs34590927	4.0×10^{-7}	-76409	0.729	rs1737058	887751	DHX16	0.00029	0.047	B-Cell	22446964
6p22.1	29809784	rs34590927	4.0×10^{-7}	-76409	0.729	rs1737058	-162815	GABBR1	1.2×10^{-5}	0.068	Monocyte	22446964
6p22.1	29809784	rs34590927	4.0×10^{-7}	-76409	0.729	rs1737058	-861252	TRIM27	3.8×10^{-5}	0.060	Monocyte	22446964
6p22.1	29809784	rs34590927	4.0×10^{-7}	22548	0.564	rs2524035	628390	HLA-E	0.00012	0.052	B-Cell	22446964
6p22.1	29809784	rs34590927	4.0×10^{-7}	107362	0.796	rs1655904	622024	ABCF1	6.0×10^{-9}	0.025	Monocyte	20502693
6p22.1	29809784	rs34590927	4.0×10^{-7}	107362	0.796	rs1655904	750439	MDC1	2.8×10^{-6}	0.017	Monocyte	20502693
6p21.33	31220783	rs3130436	4.2×10^{-7}	11328	0.633	rs3130542	-2000400	LOC646317	0.00064	0.041	Monocyte	22446964

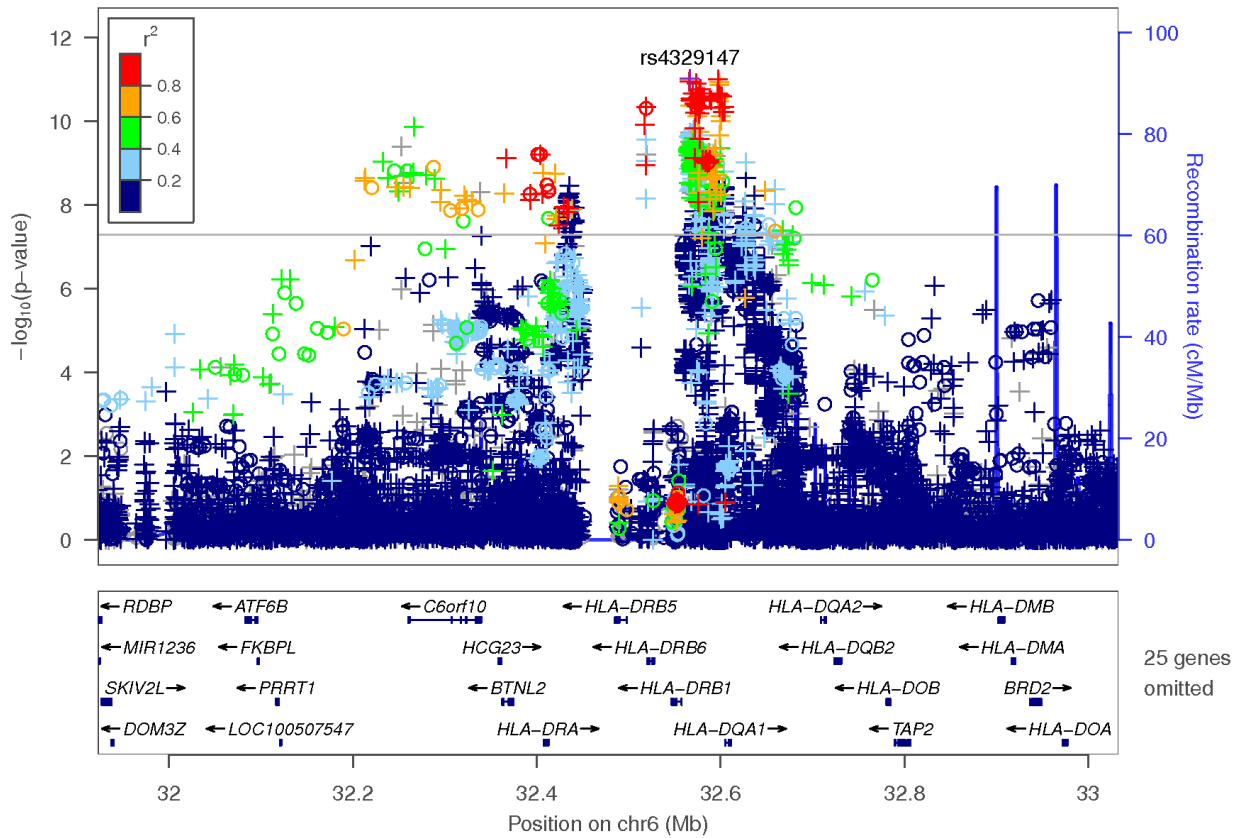
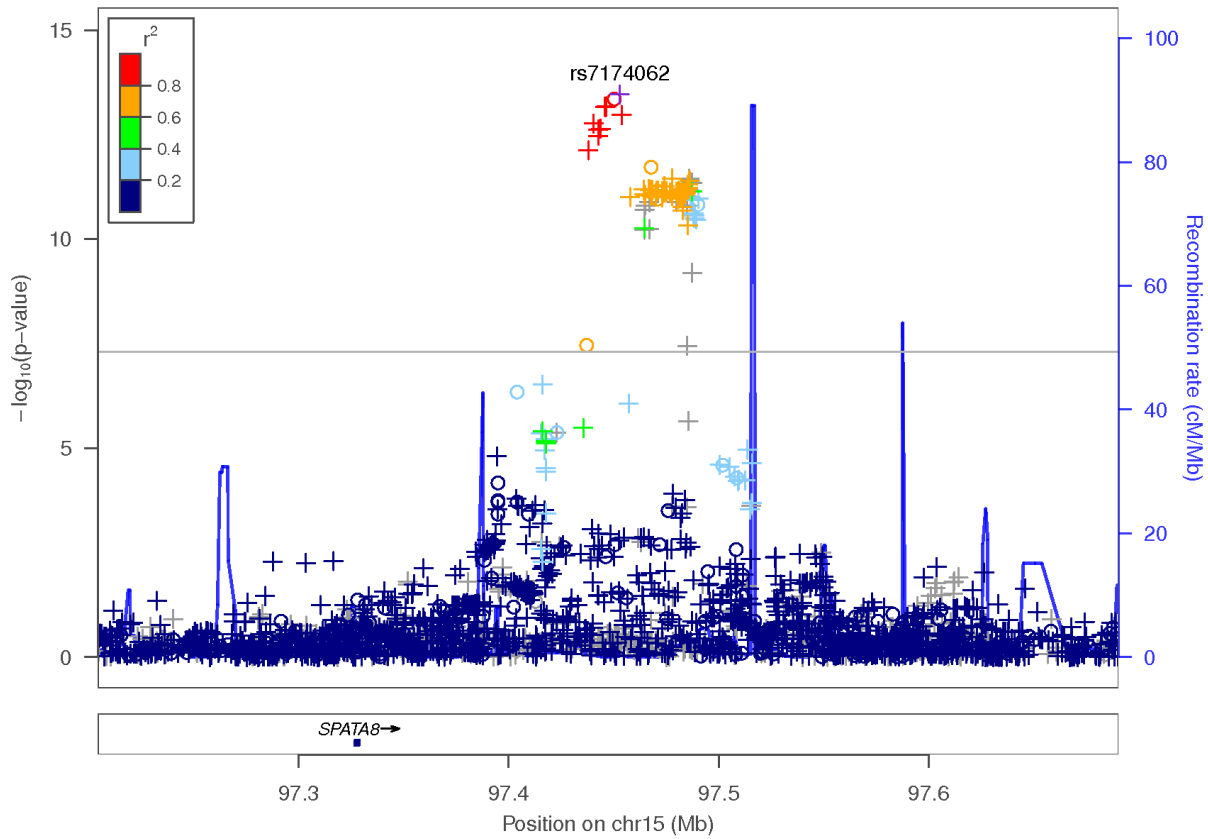
Nearby Clinical Variants

source	region	our.name	our.pval	dist	rsqr	assay.name	gene	phenotype	accession
clinvar	19q13.33	rs681343	3.5×10^{-30}	212	1.000	rs601338	FUT2	Vitamin b12 plasma level quantitative trait locus 1	NCBI curation

Regional Association Plots







locuszoom plot for 9:136149095:CA_C failed

