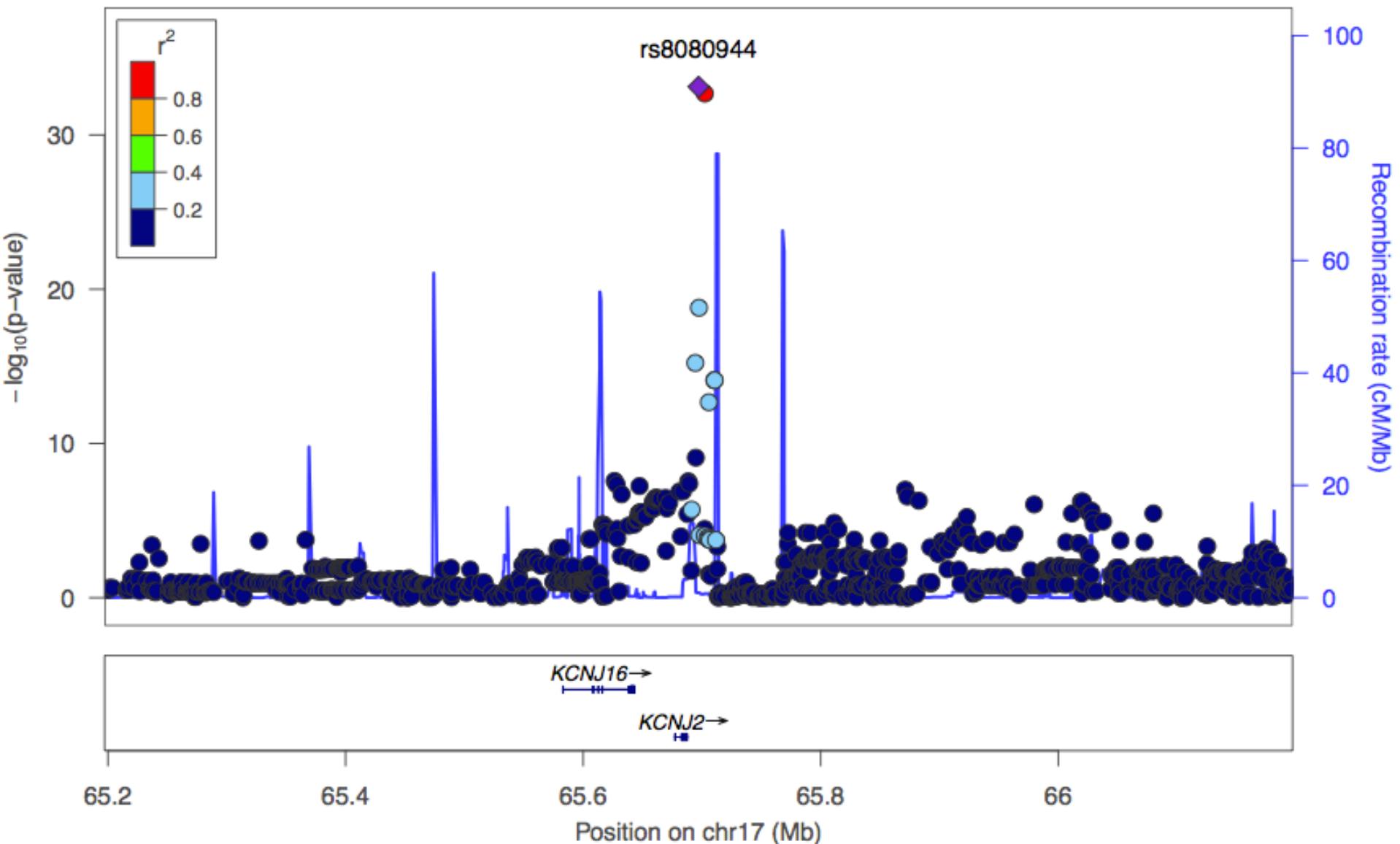
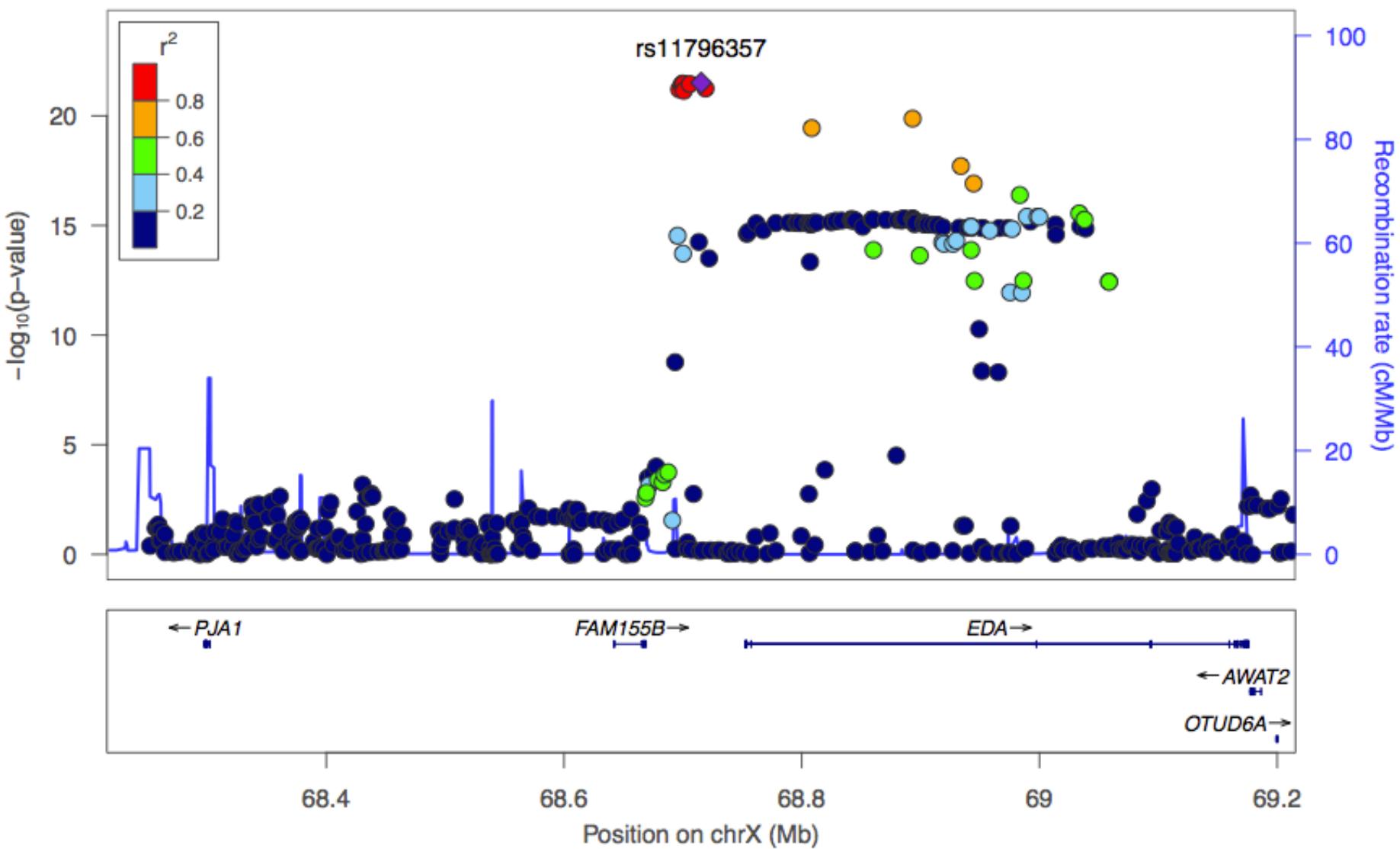


Supplementary Figure 1: QQ plot for the combined meta-analysis of (a) ‘Age at first tooth’ and (b) ‘number of teeth’ respectively. Both QQ plots show substantial deviation from the line of expectation for low p values only, suggesting the existence of common genetic variants influencing primary tooth eruption, but not substantial population stratification. The genomic inflation factors were $\lambda = 1.07$ for ‘age at first tooth’, and $\lambda = 1.06$ for ‘number of teeth’.

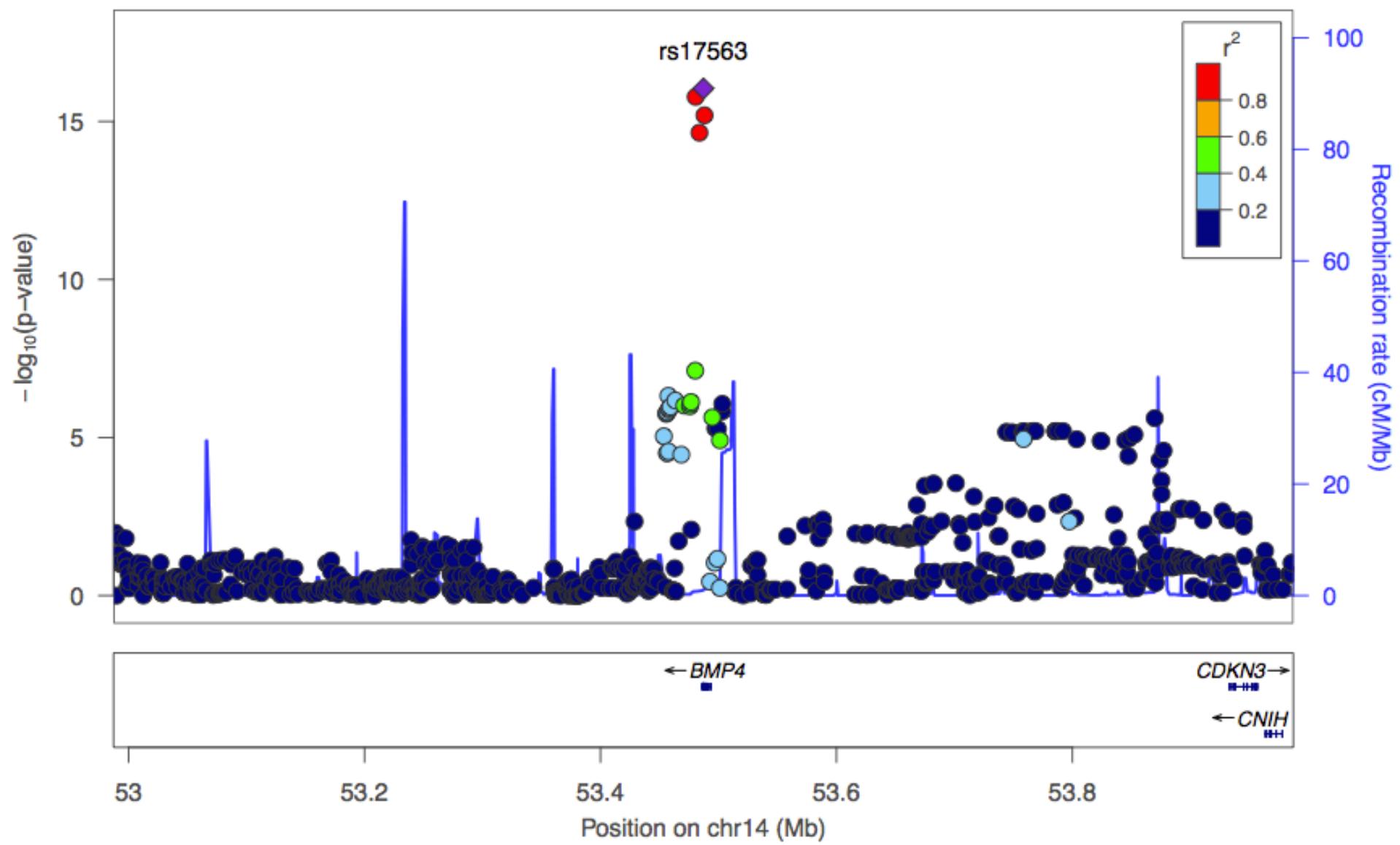
(A)



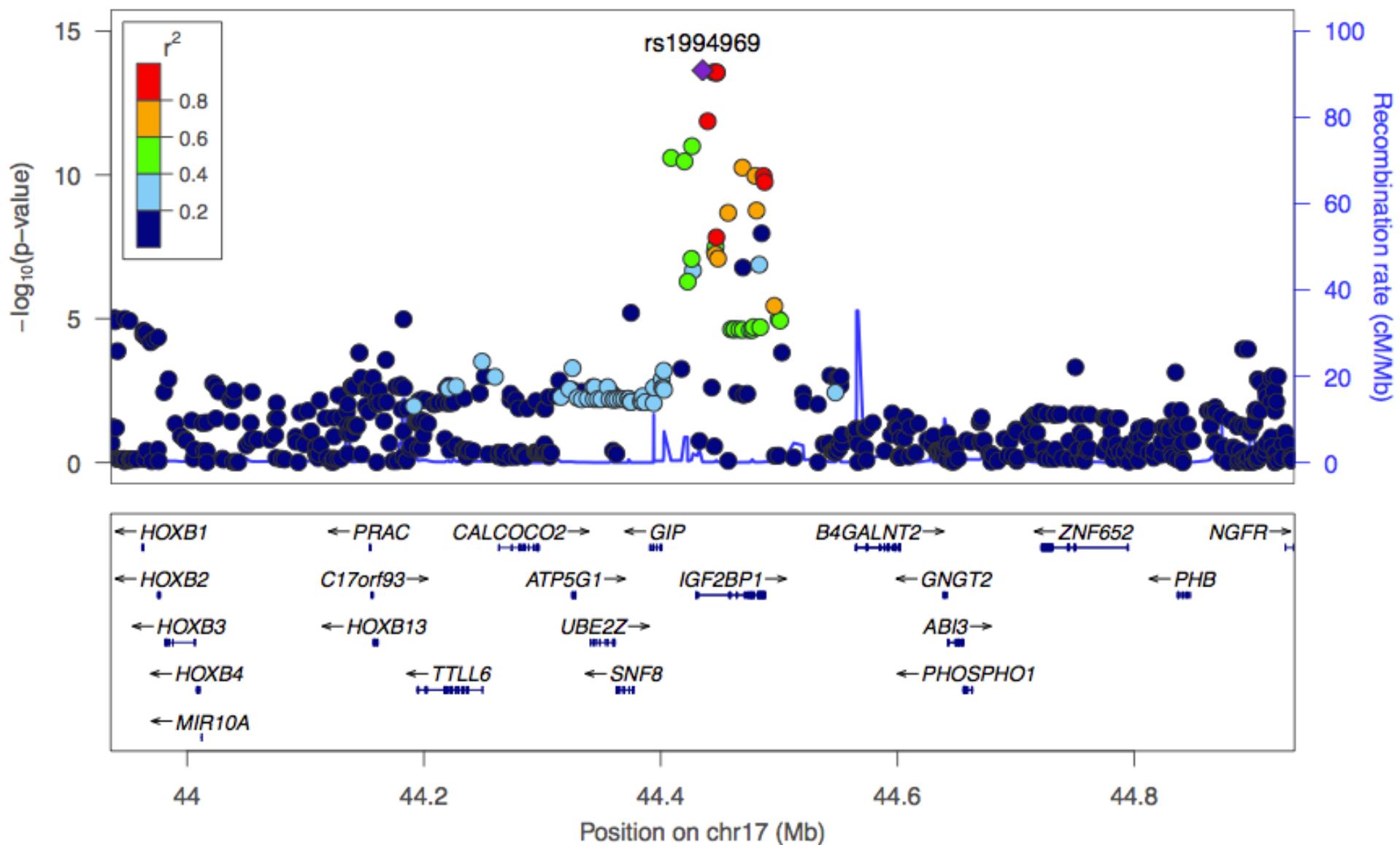
(B)



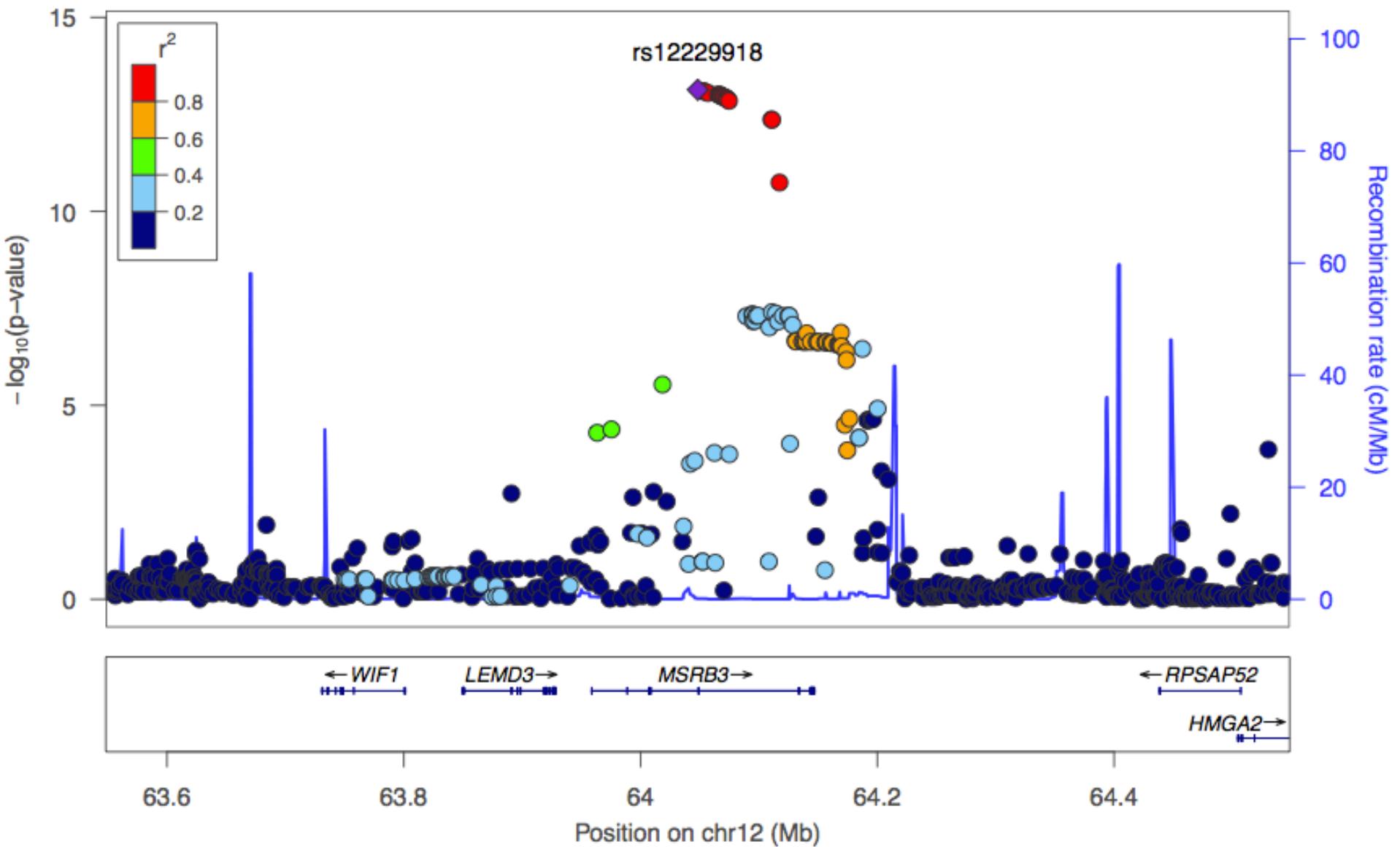
(C)



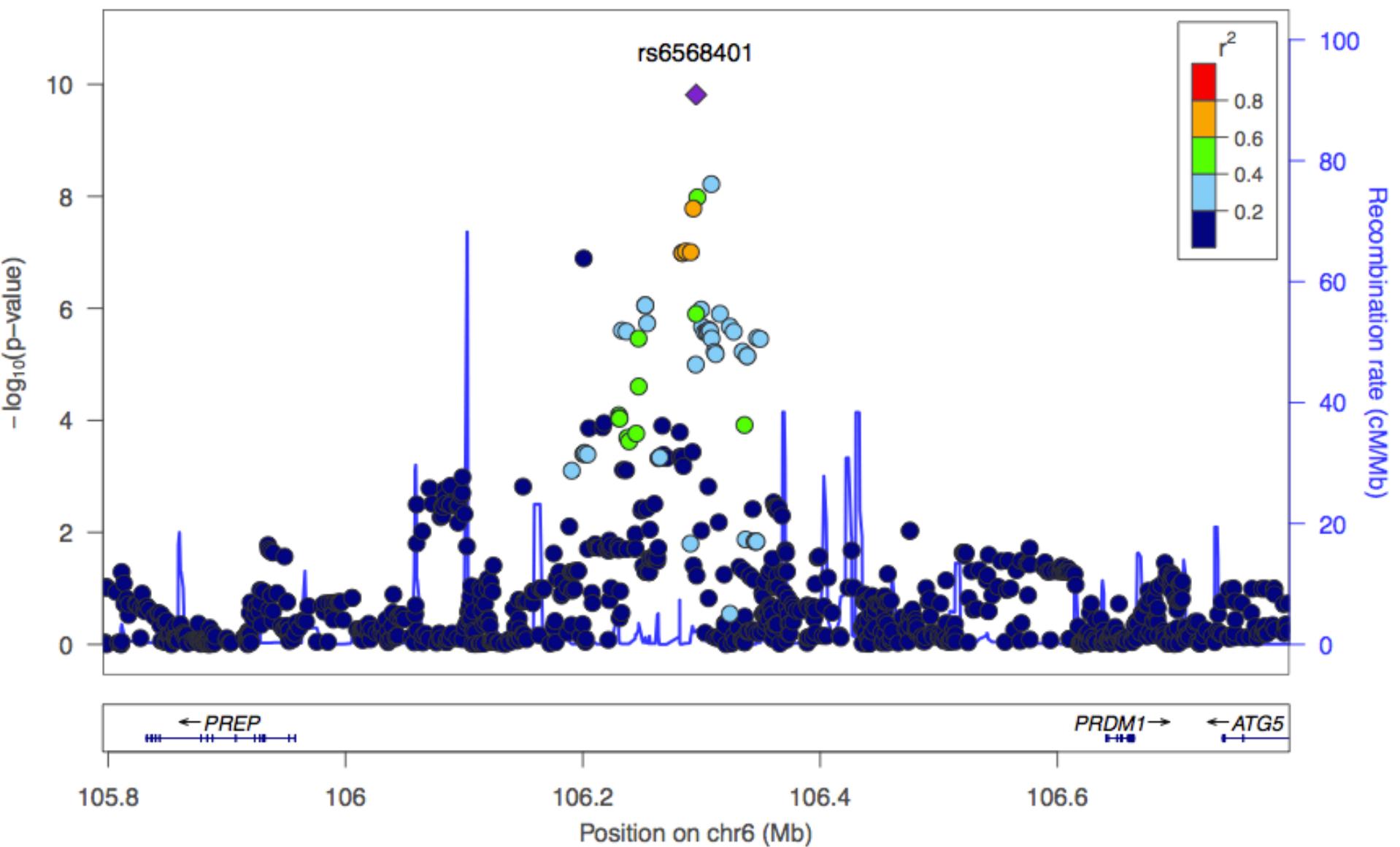
(D)



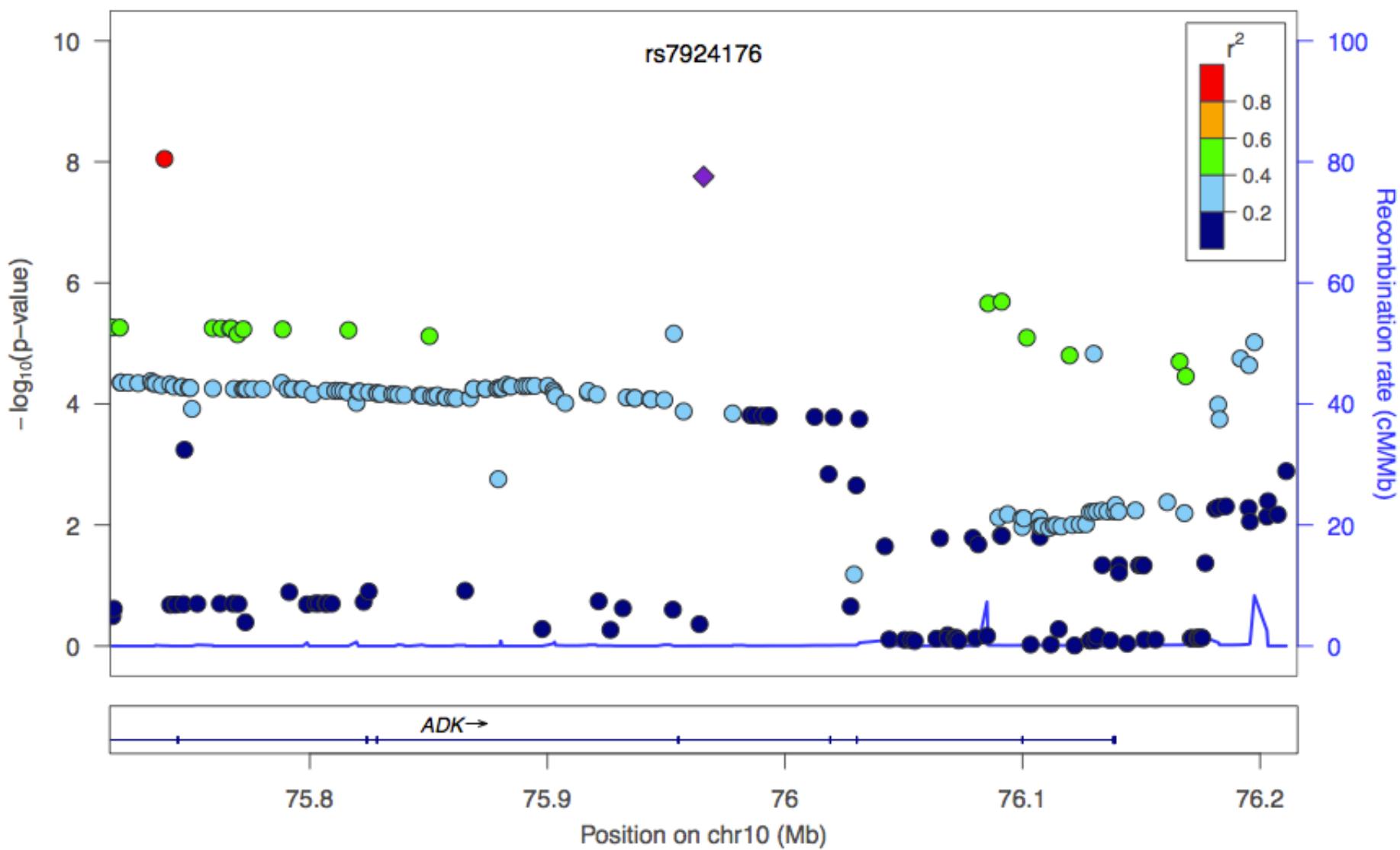
(E)



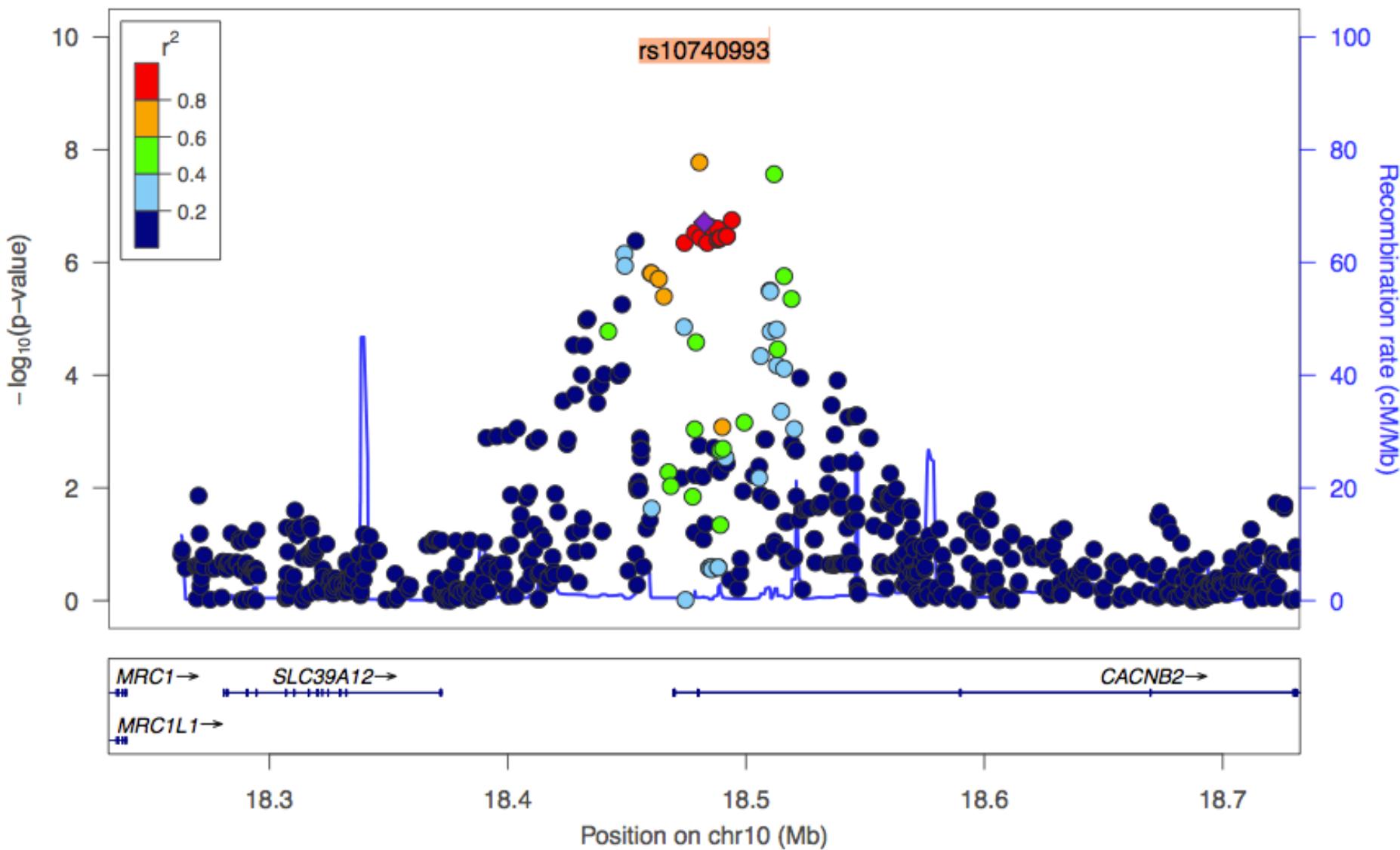
(F)

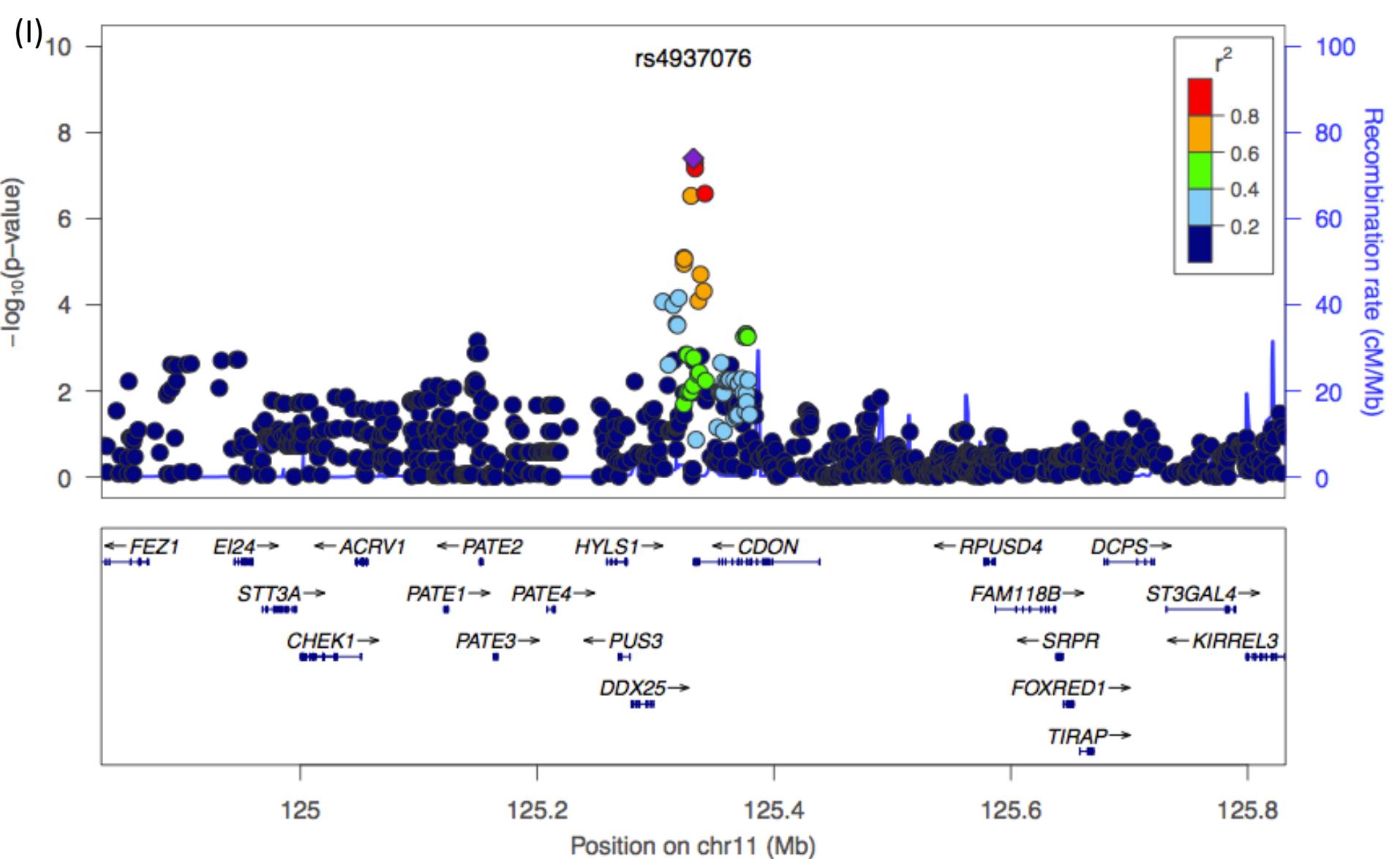


(G)

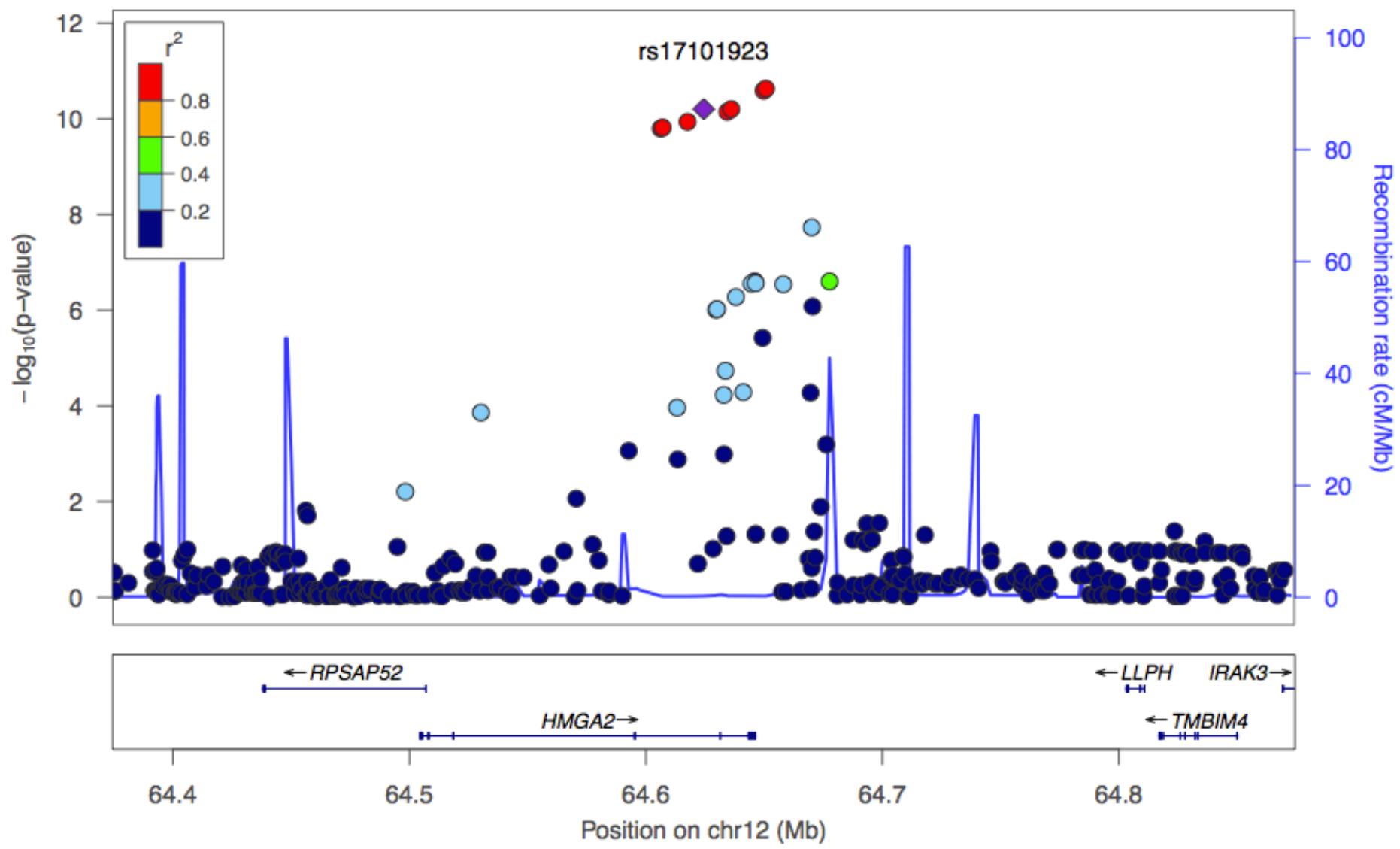


(H)

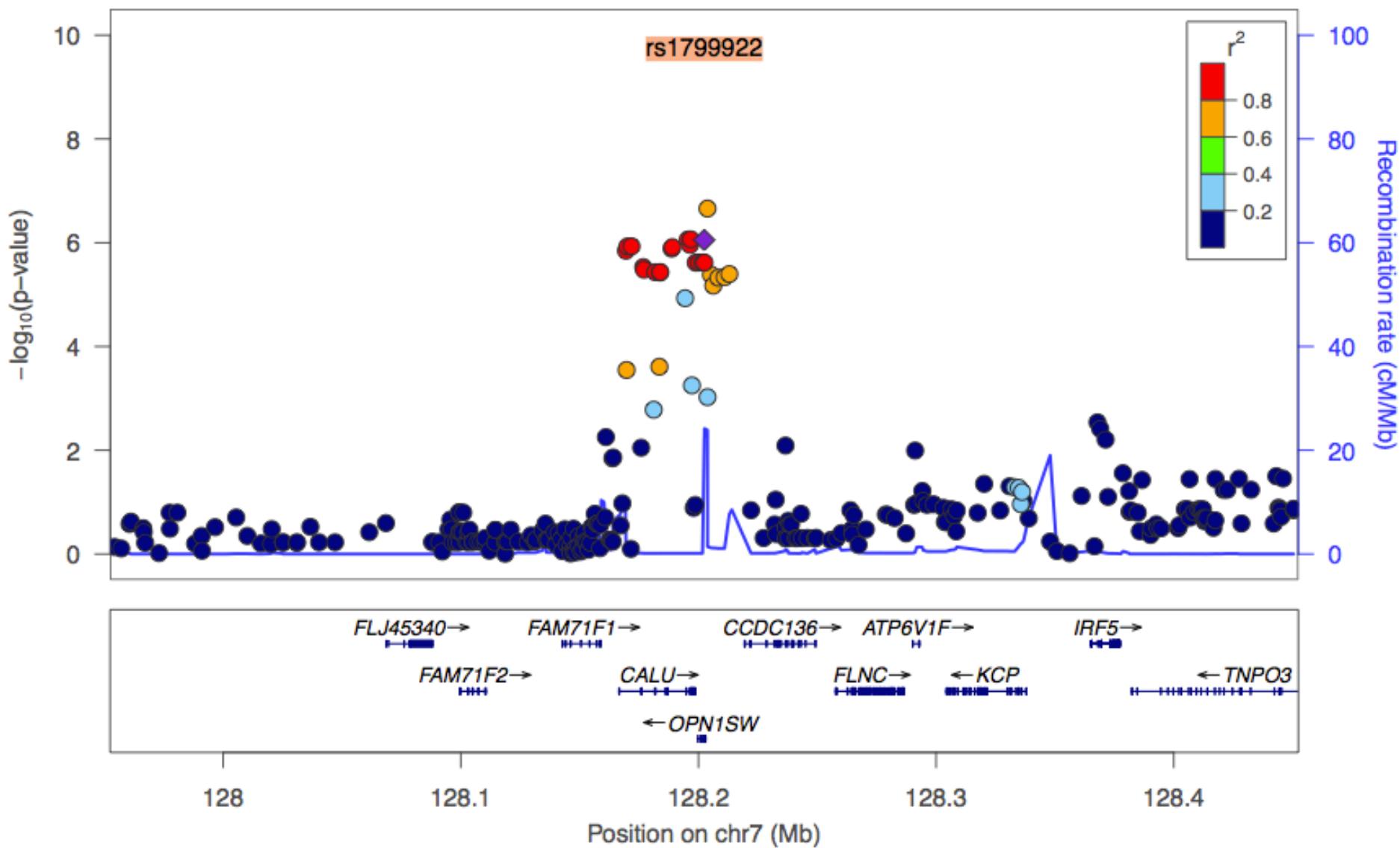




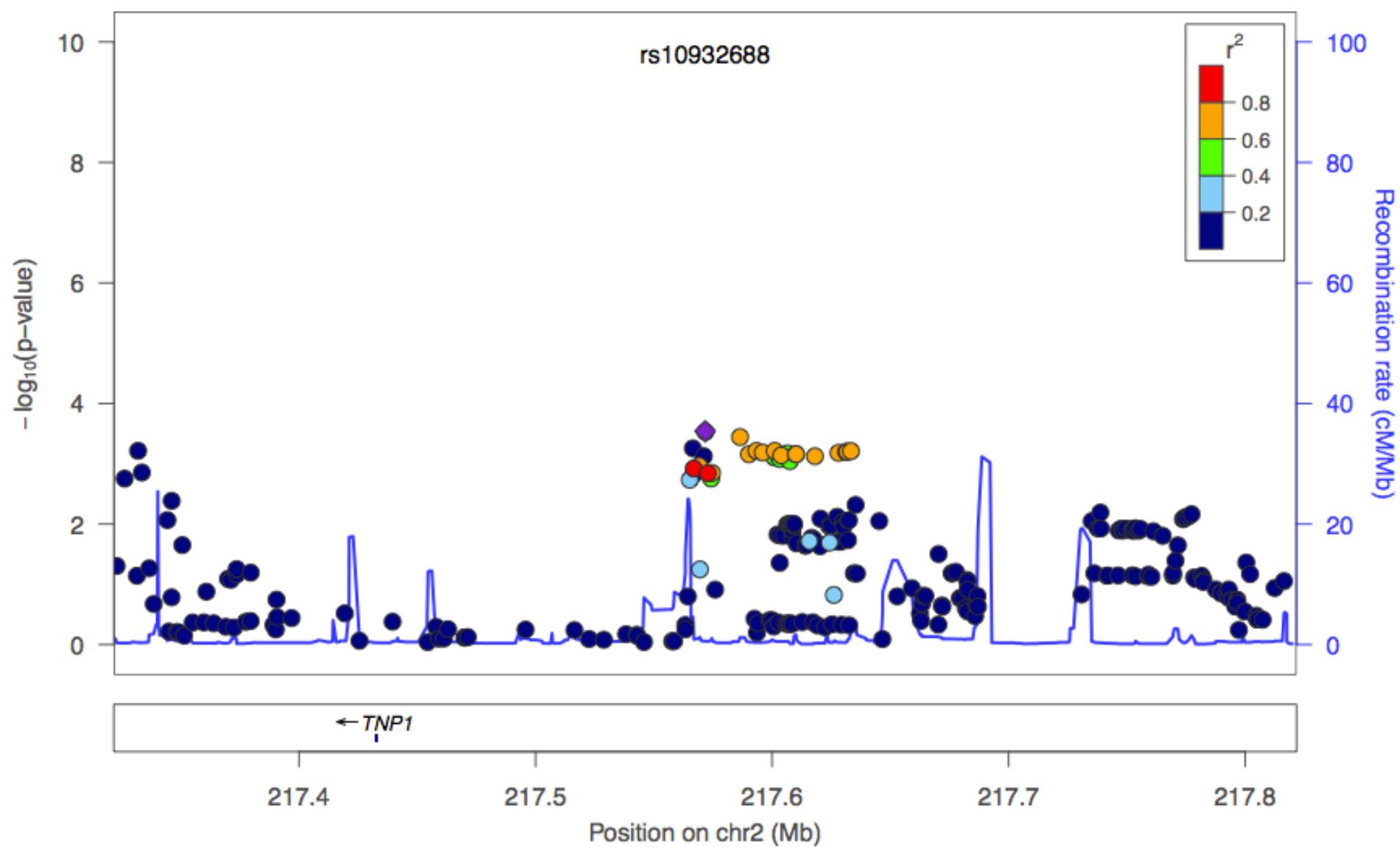
(J)



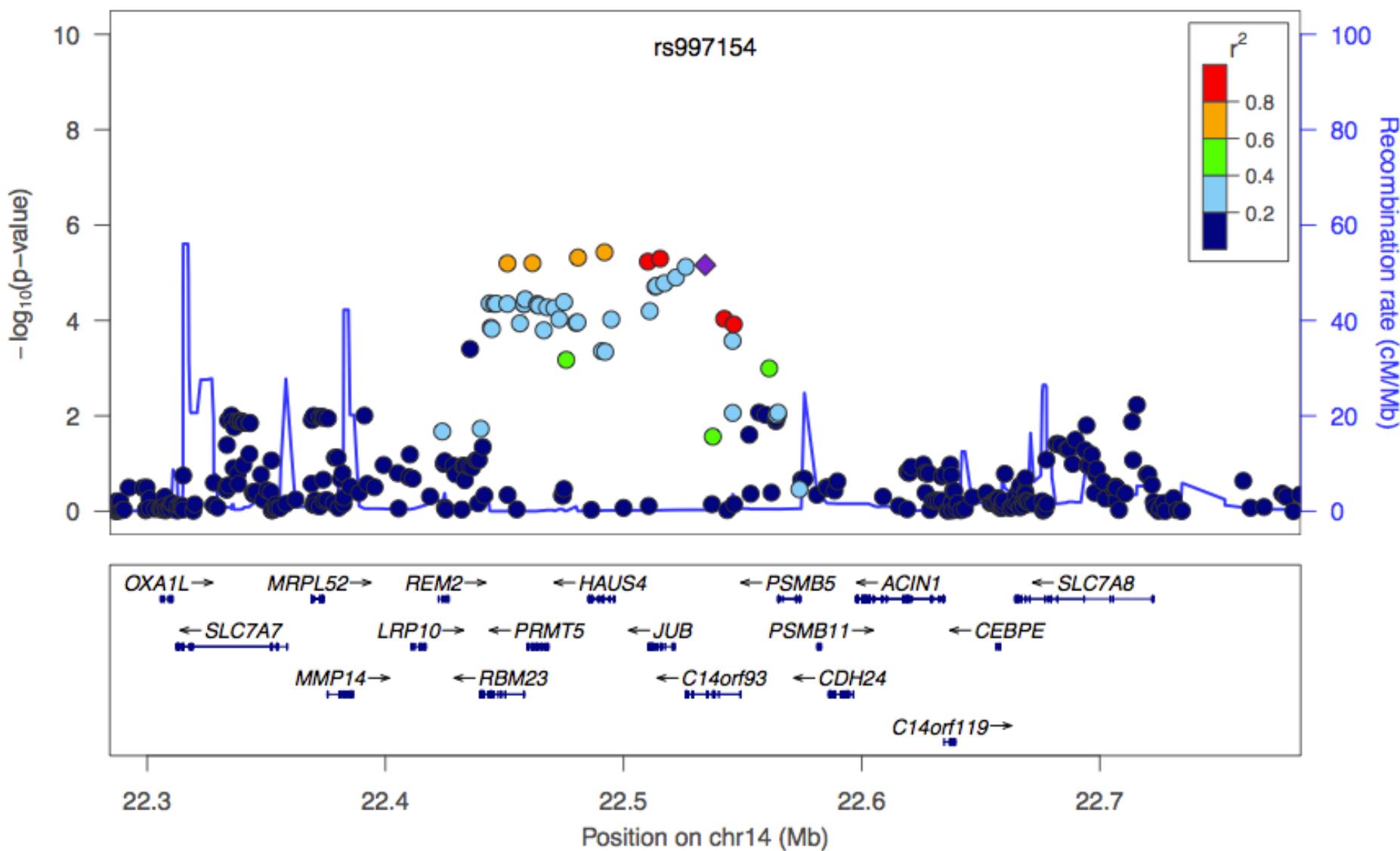
(K)



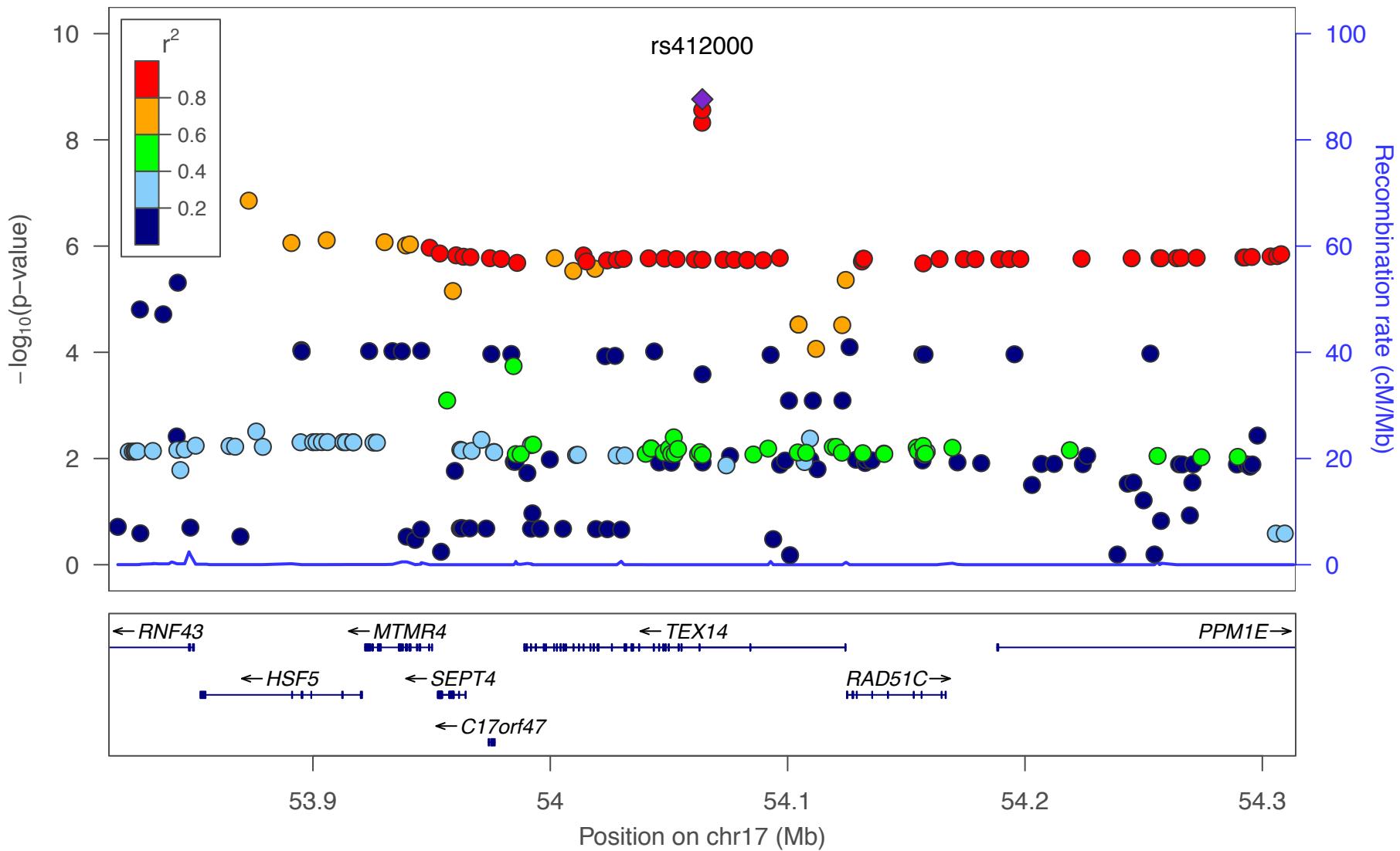
(L)

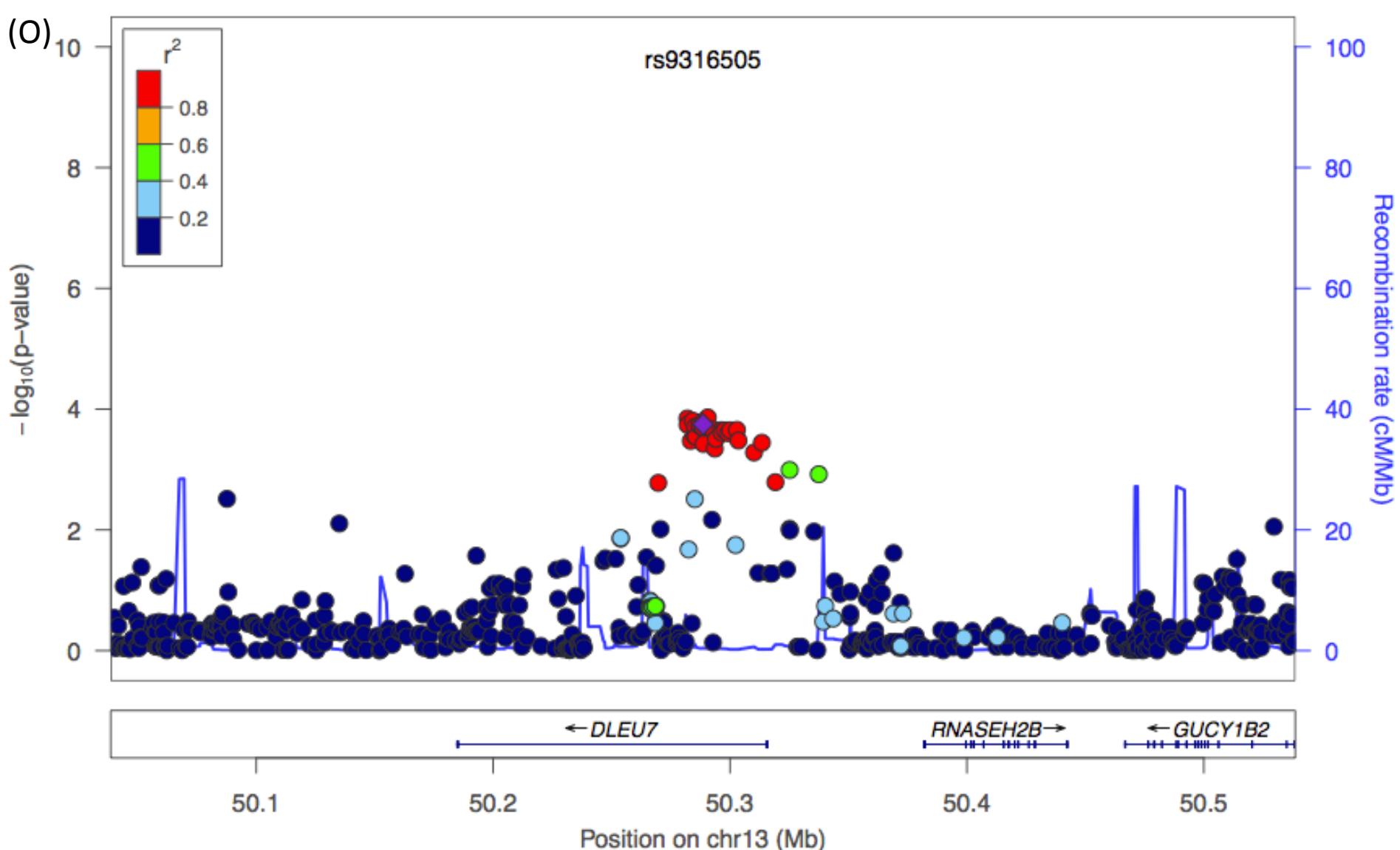


(M)



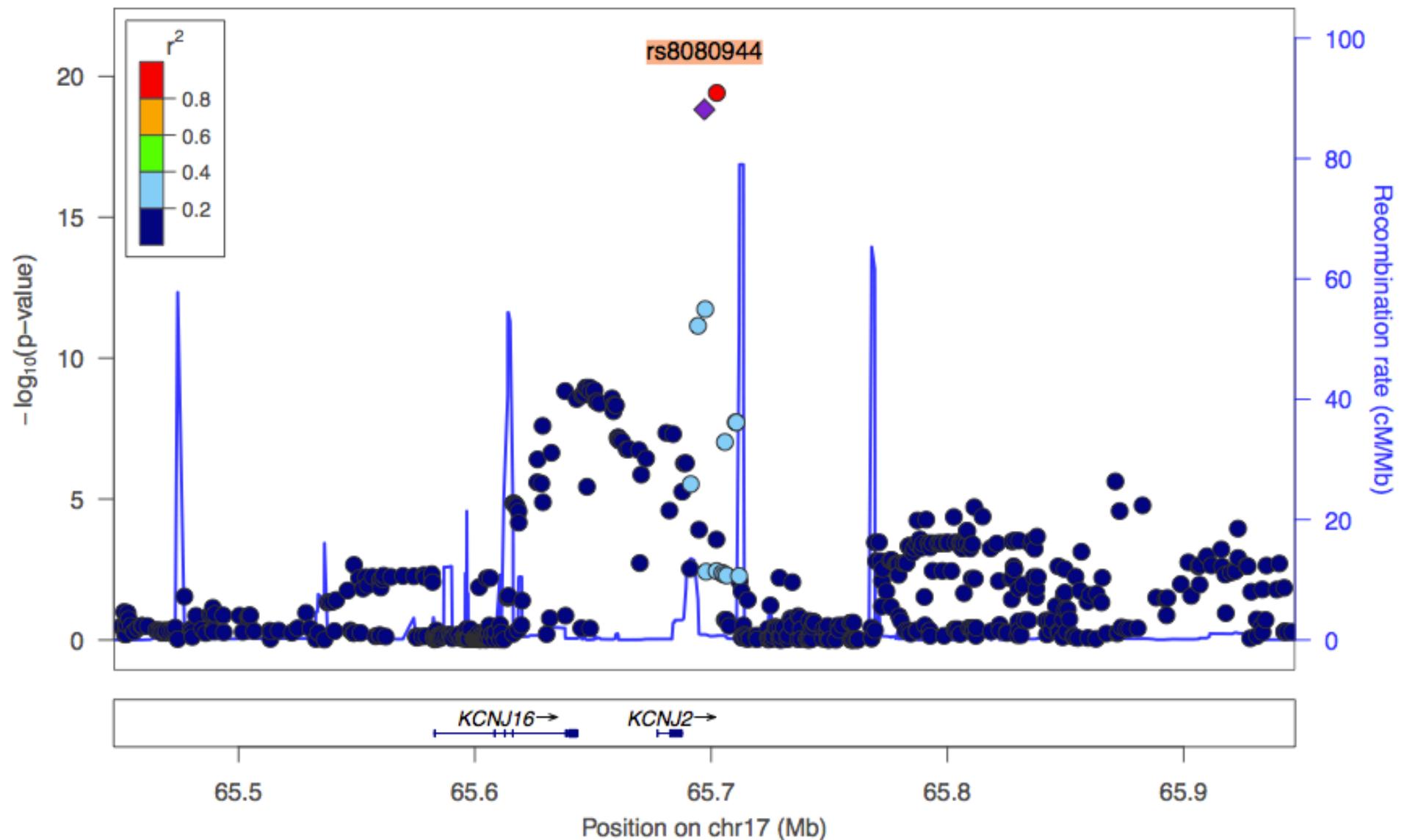
(N)



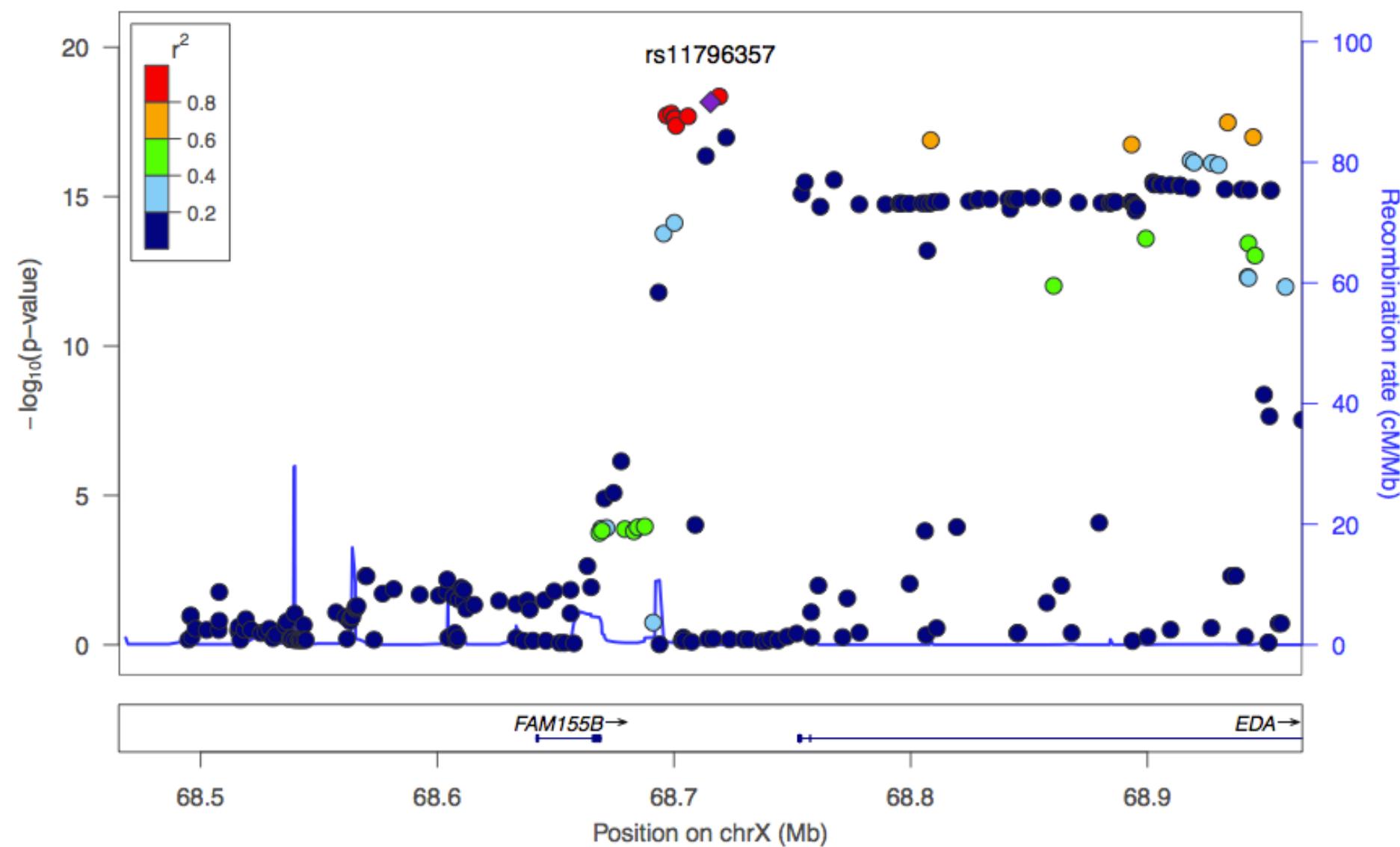


Supplementary Figure 2: Linkage disequilibrium and Association plot of loci reaching genome-wide significance for 'age at first tooth' in meta-analysis of ALSPAC and NFBC (A) rs8080944 *KCNJ16-KCNJ2* region (B) rs11796357 *FAM155-EDA* gene region (C) rs17563 *BMP4* gene region (D) rs1994969 *IGF2BP1* gene region (E) rs12229918 gene *MSRB3* (F) rs6568401 (G) rs7924176 *ADK* gene region (H) rs10740993 *CACNB2* gene region (I) rs4937076 *CDON* gene region. (J) rs17101923 *HMGA2* gene region (K) rs1799922 *CALU* (L) rs10932688 2q35 region (M) rs997154 *AJUBA* gene region (N) rs412000 *TEX14/RAD51C* region (O) rs9316505 gene region. The most significant SNPs in each region plotted in purple. Genes are based on Genome browser (RefSeq Genes). Arrows on genes give direction of transcription.

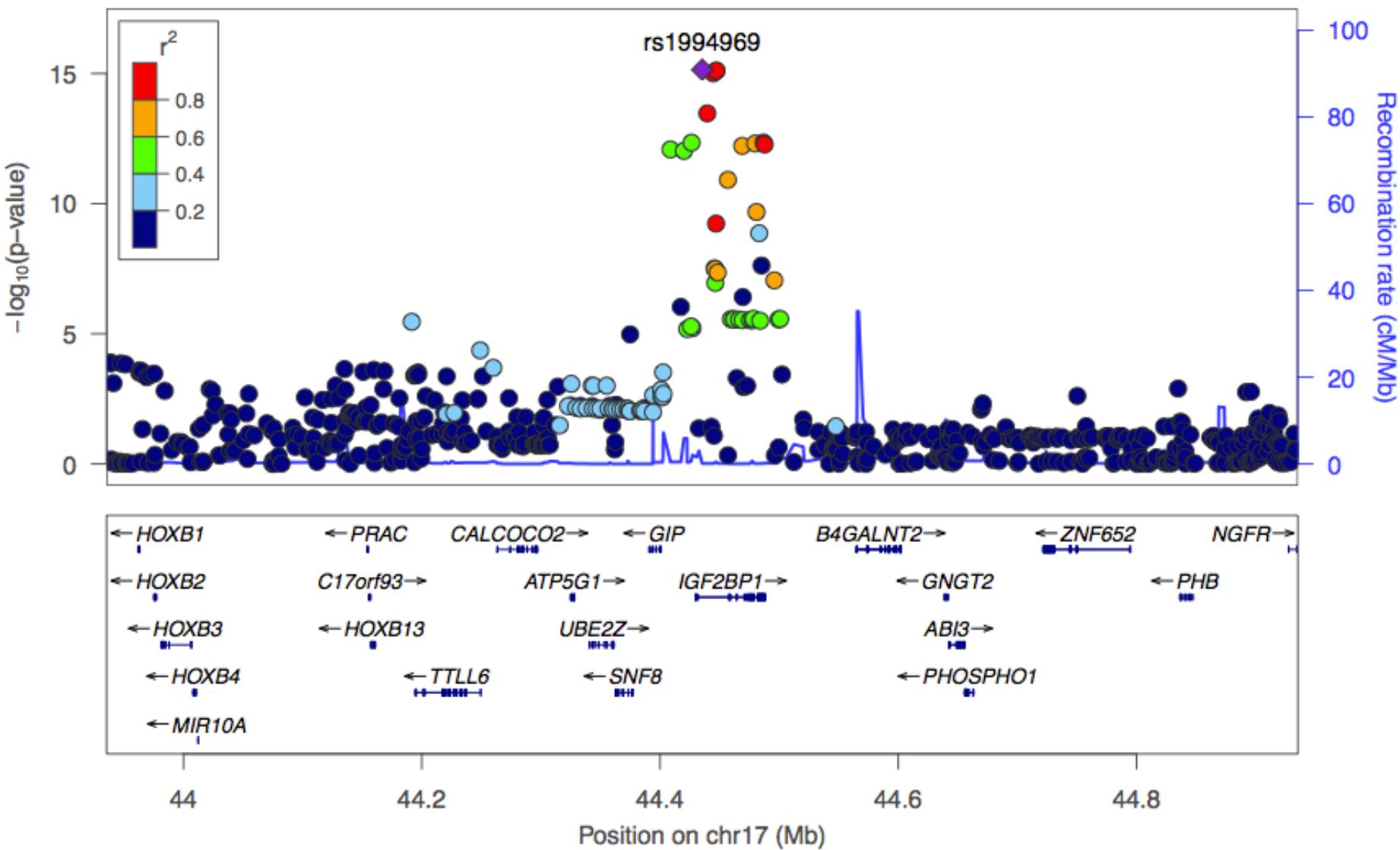
(A)



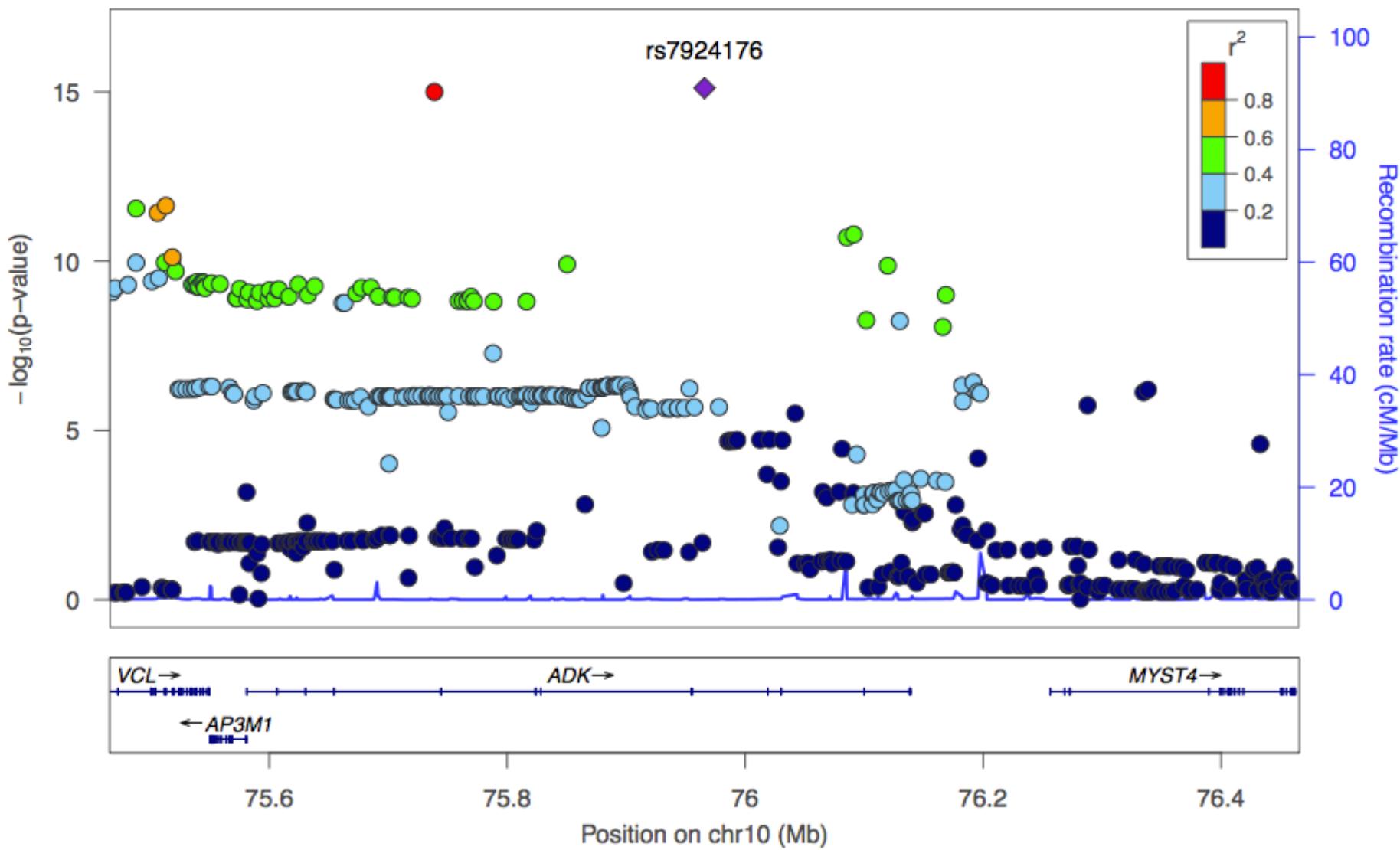
(B)



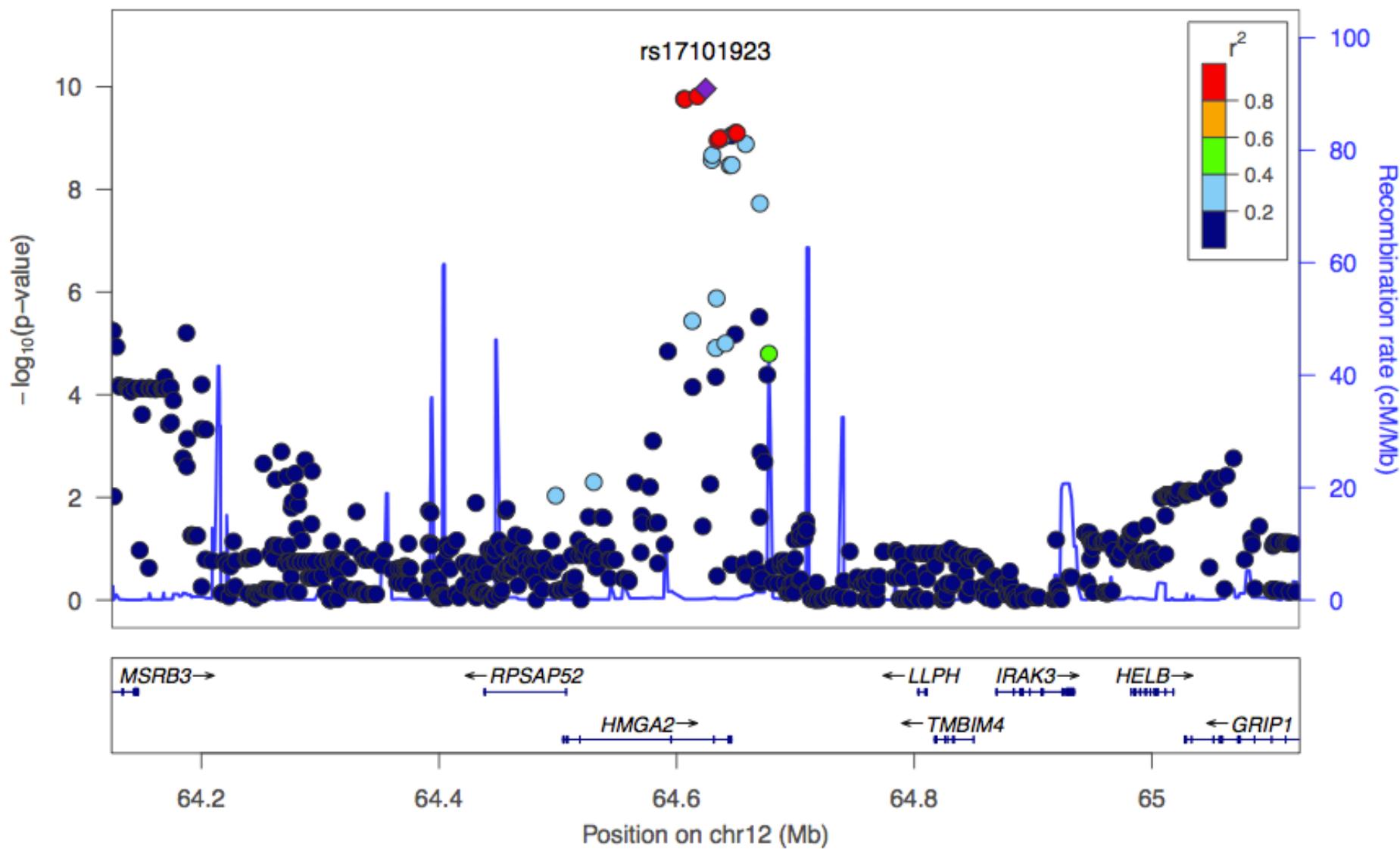
(C)



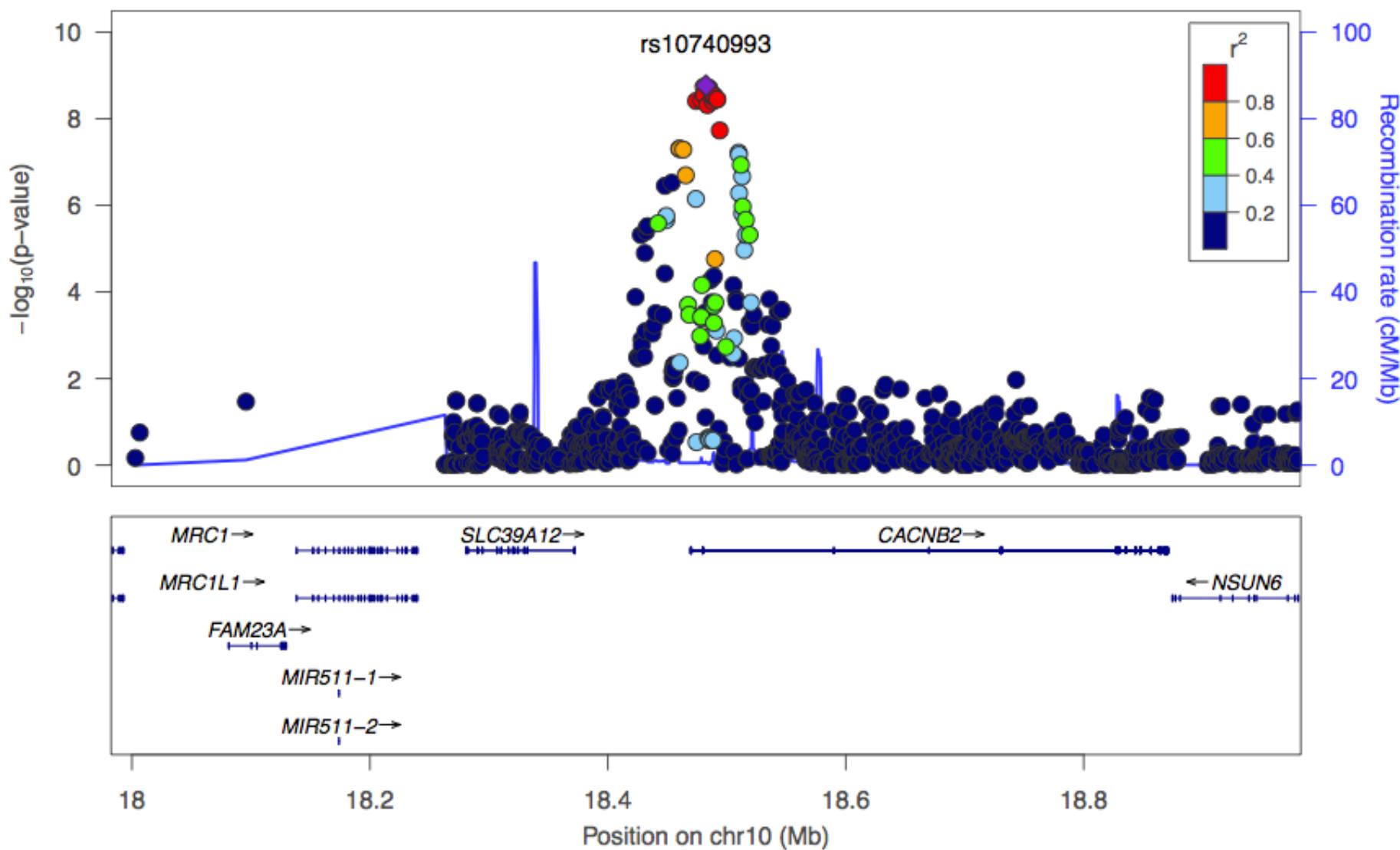
(D)



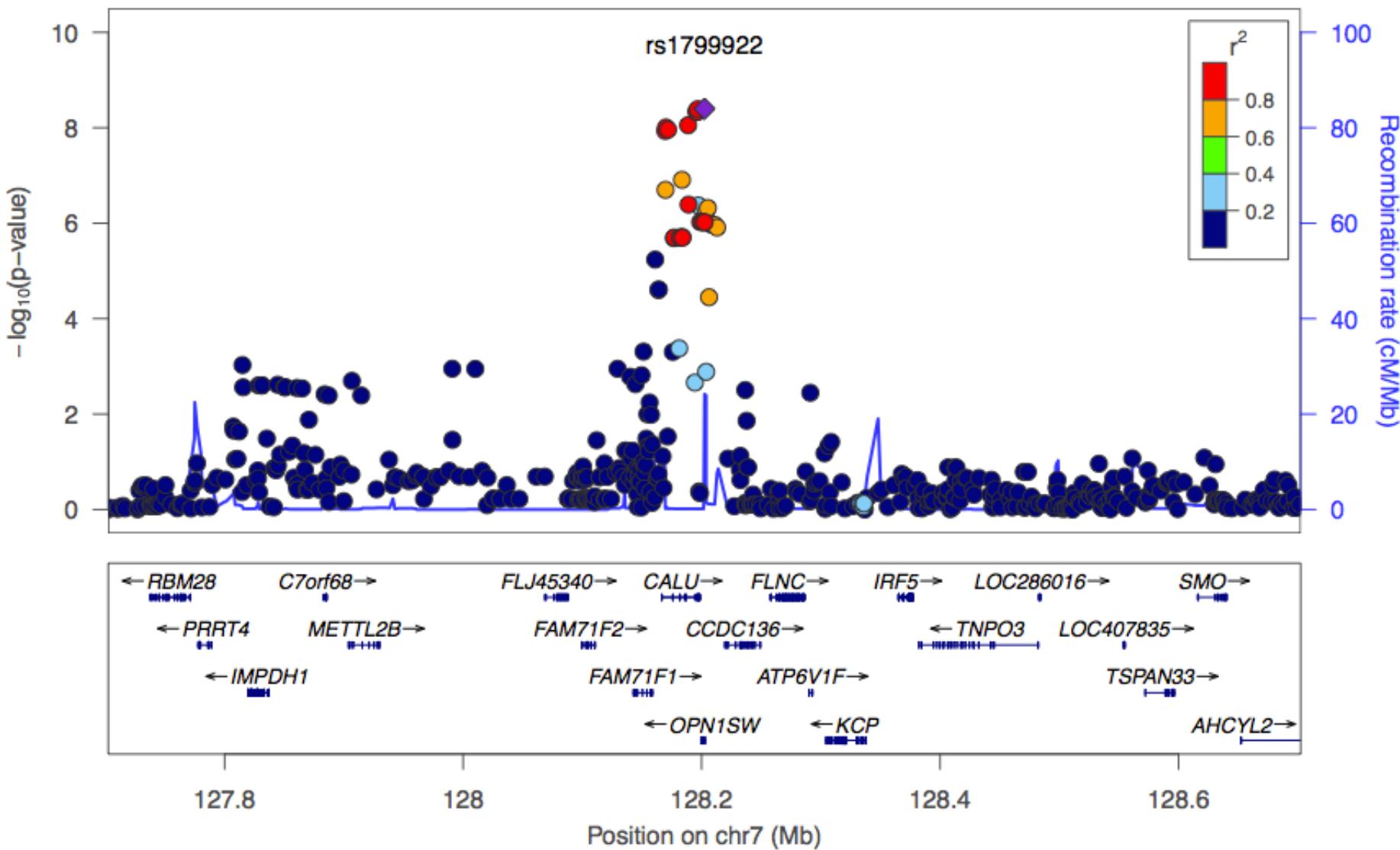
(E)



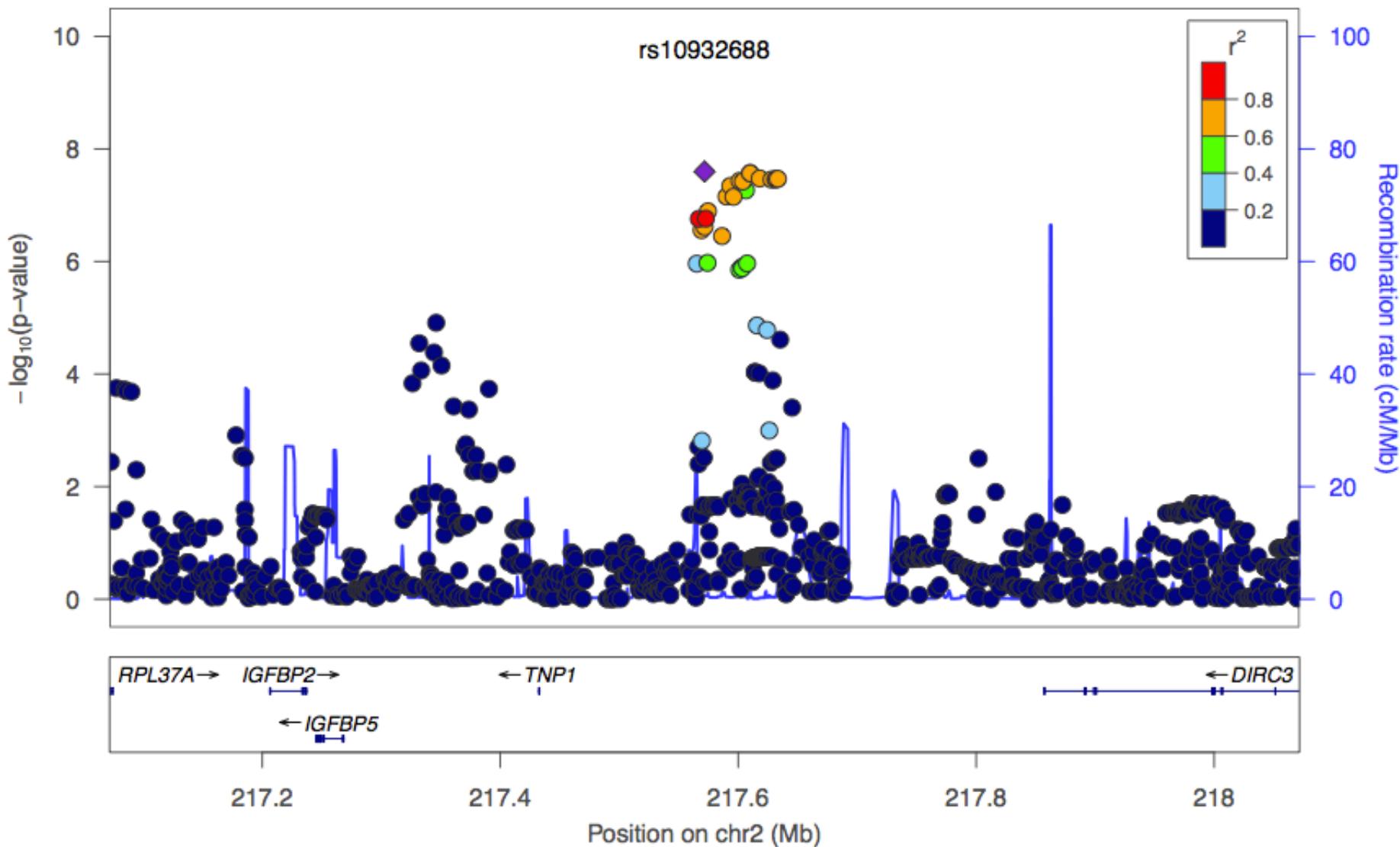
(F)



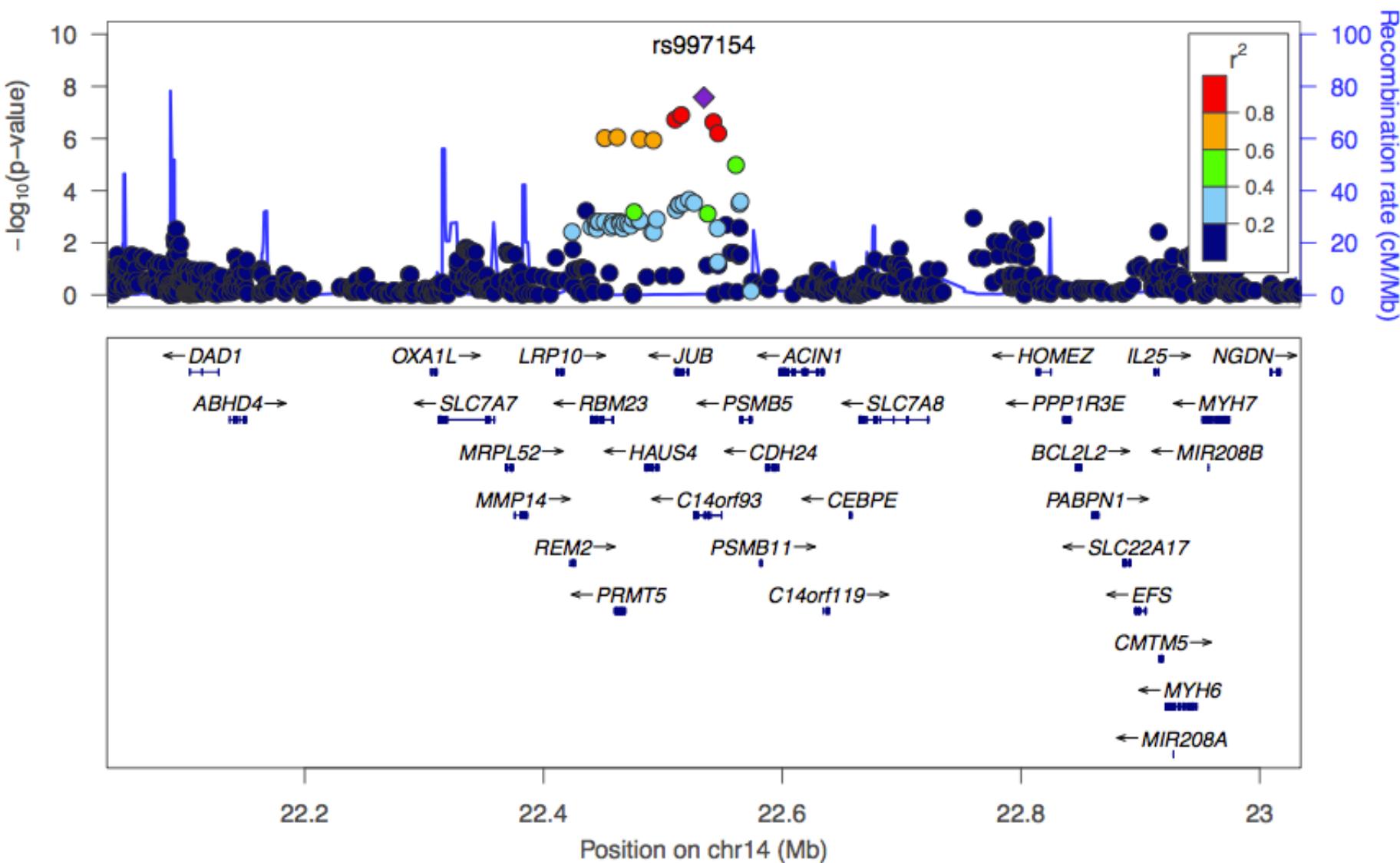
(G)



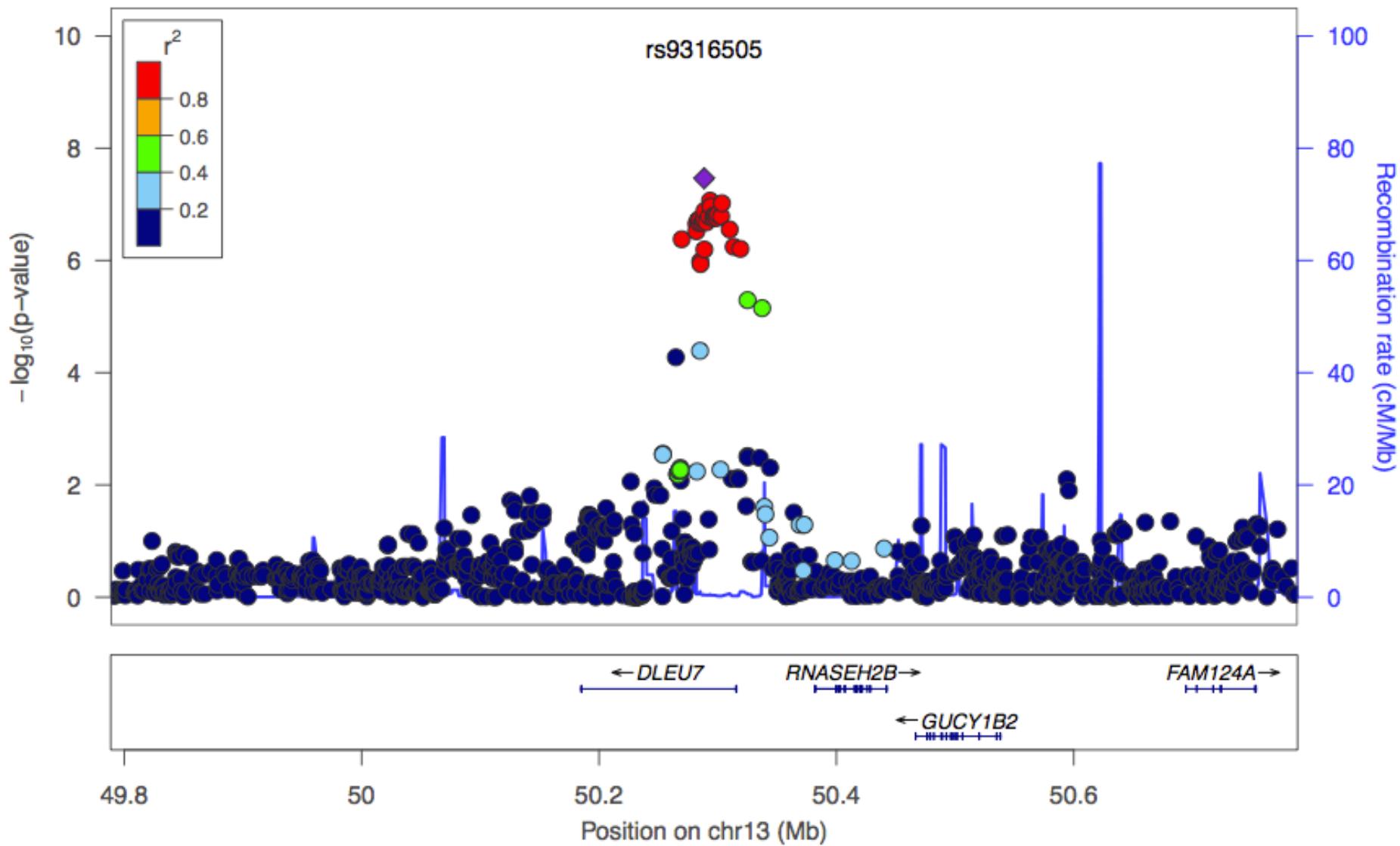
(H)



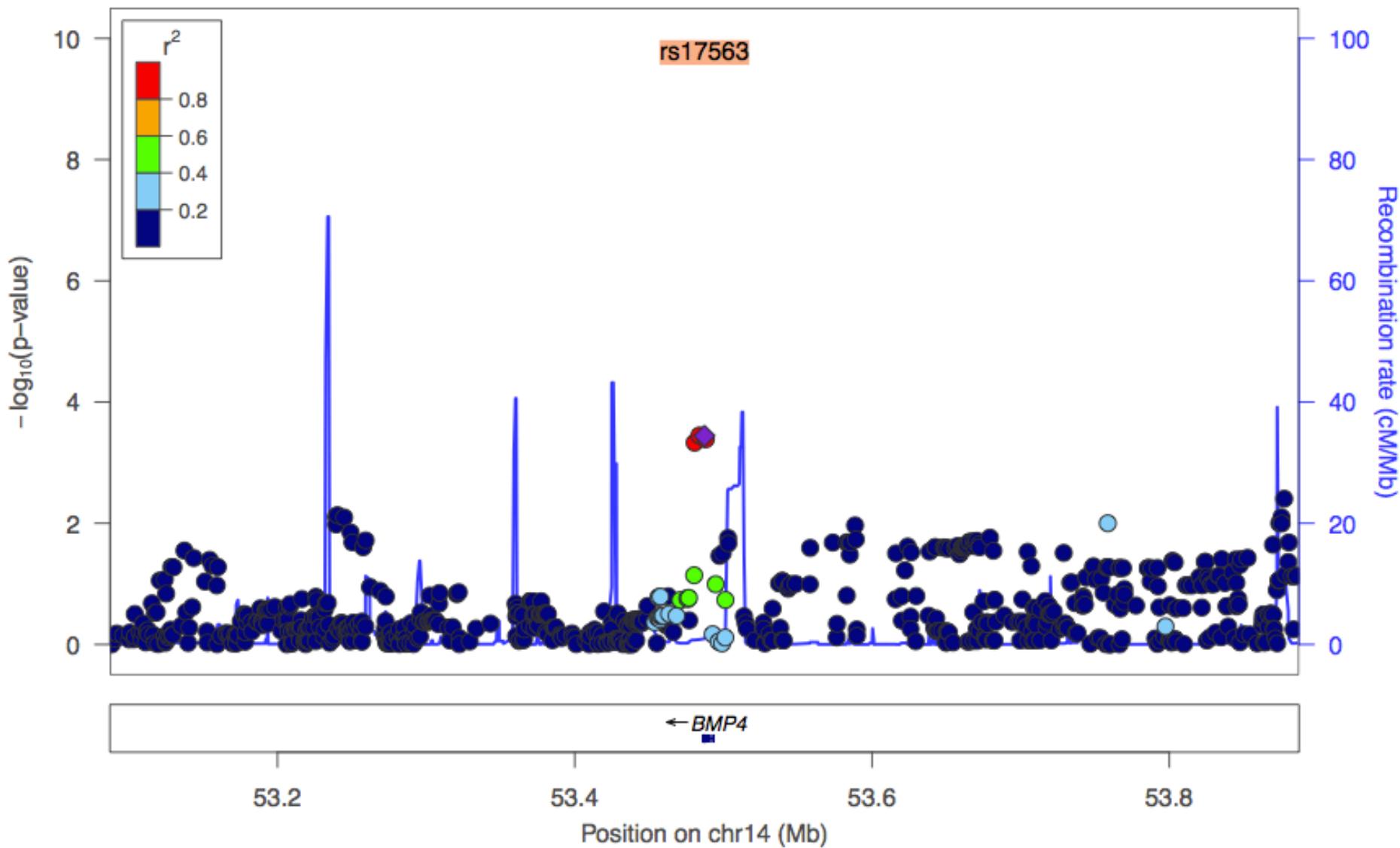
(I)



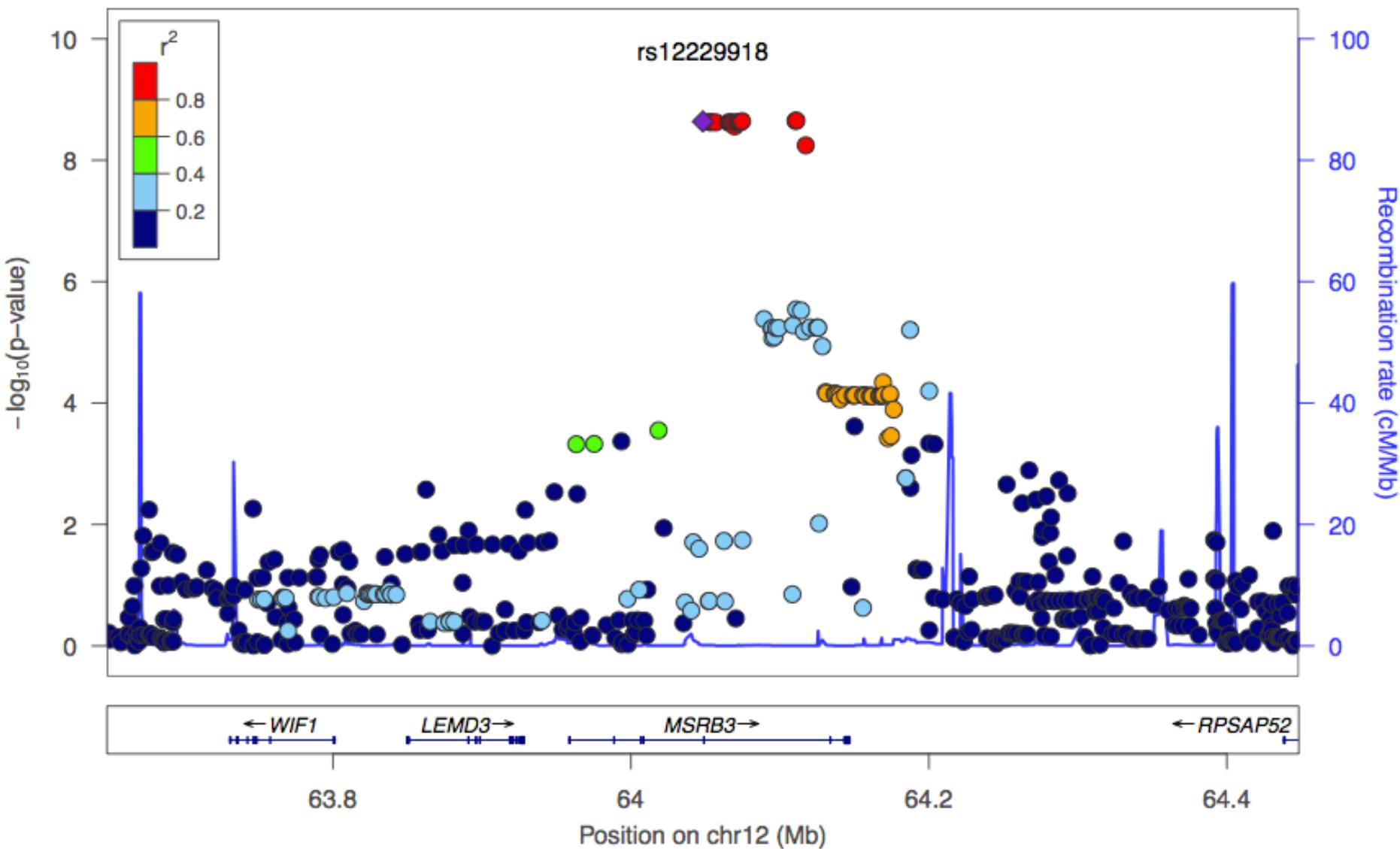
(J)



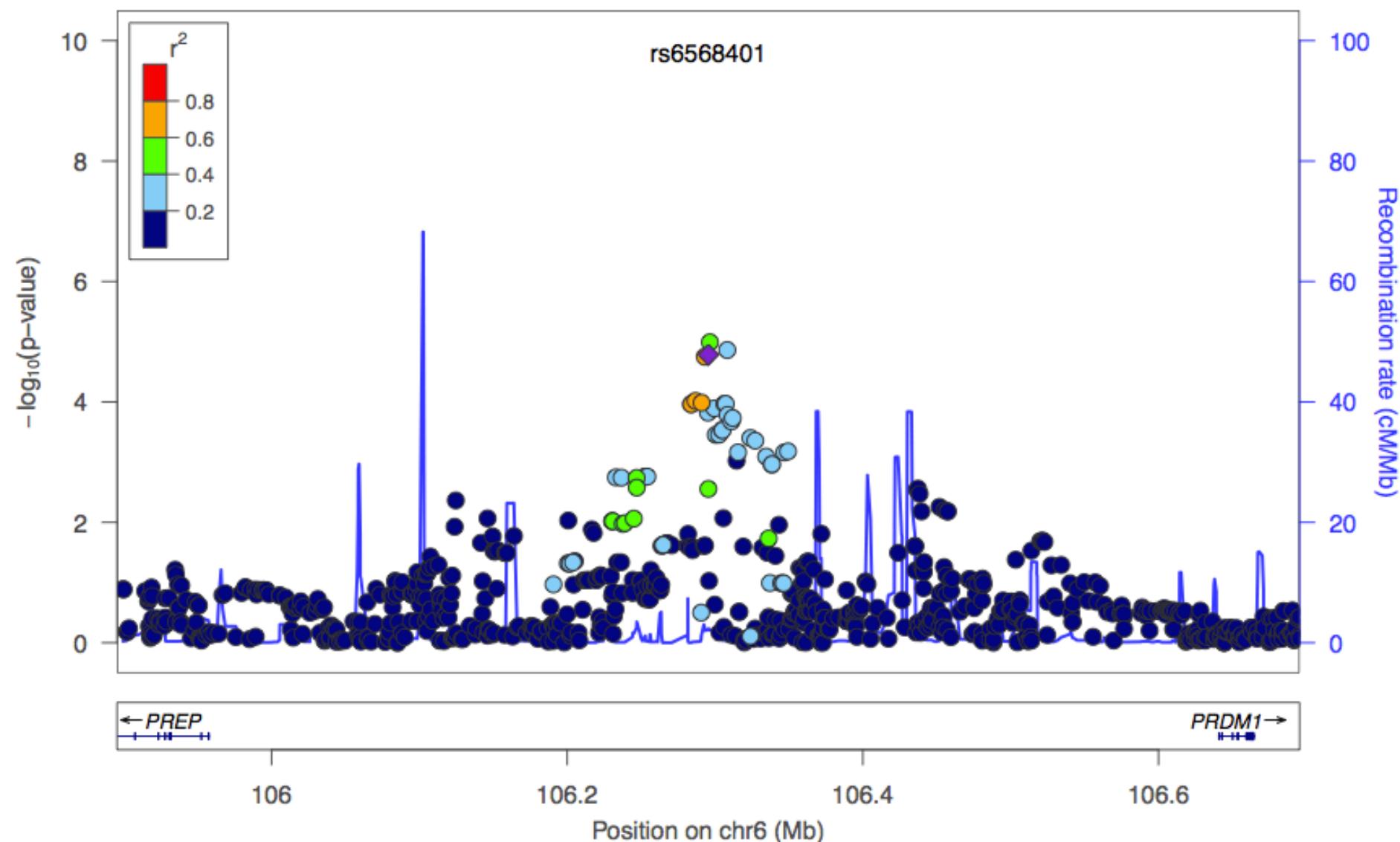
(K)



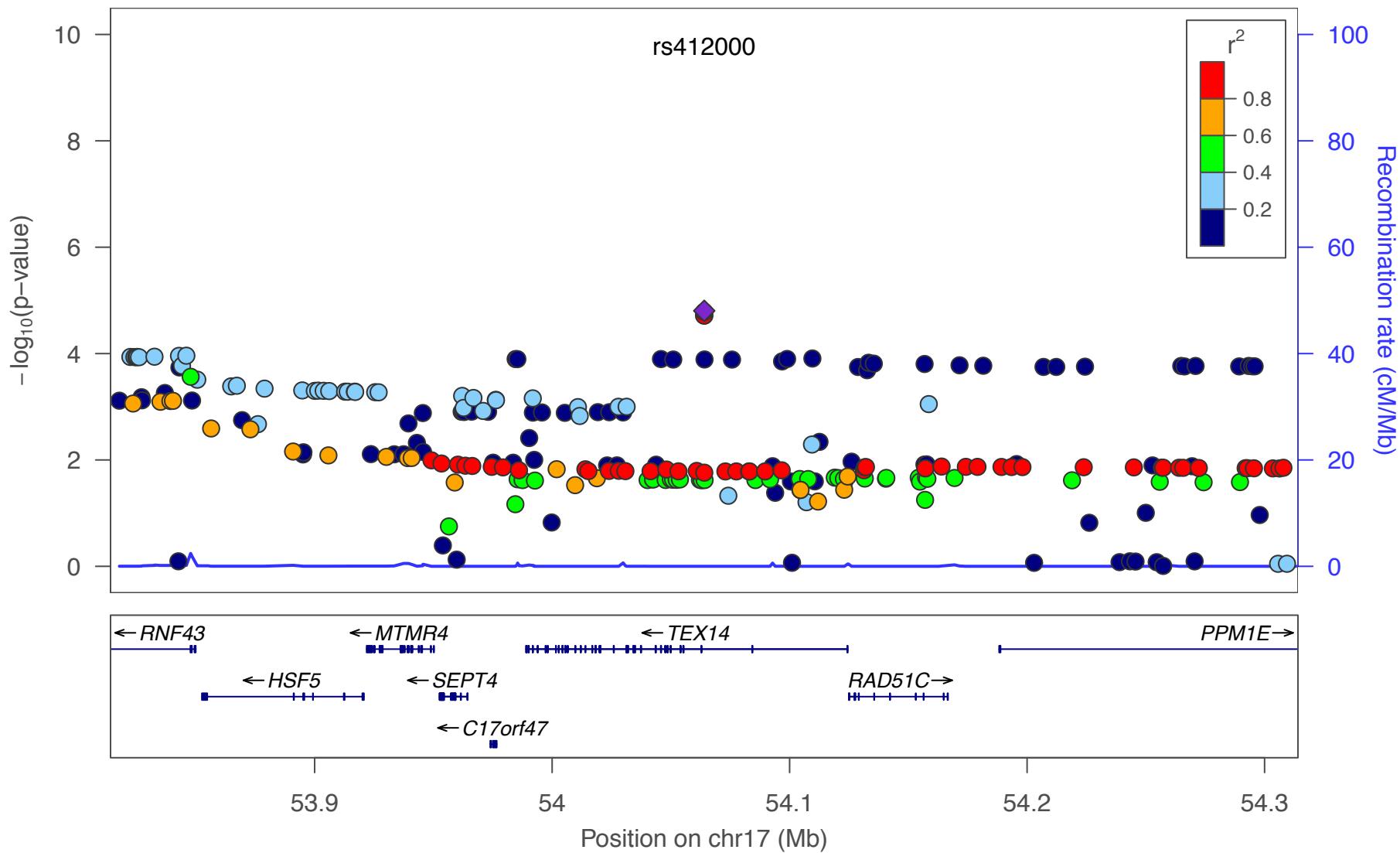
(L)

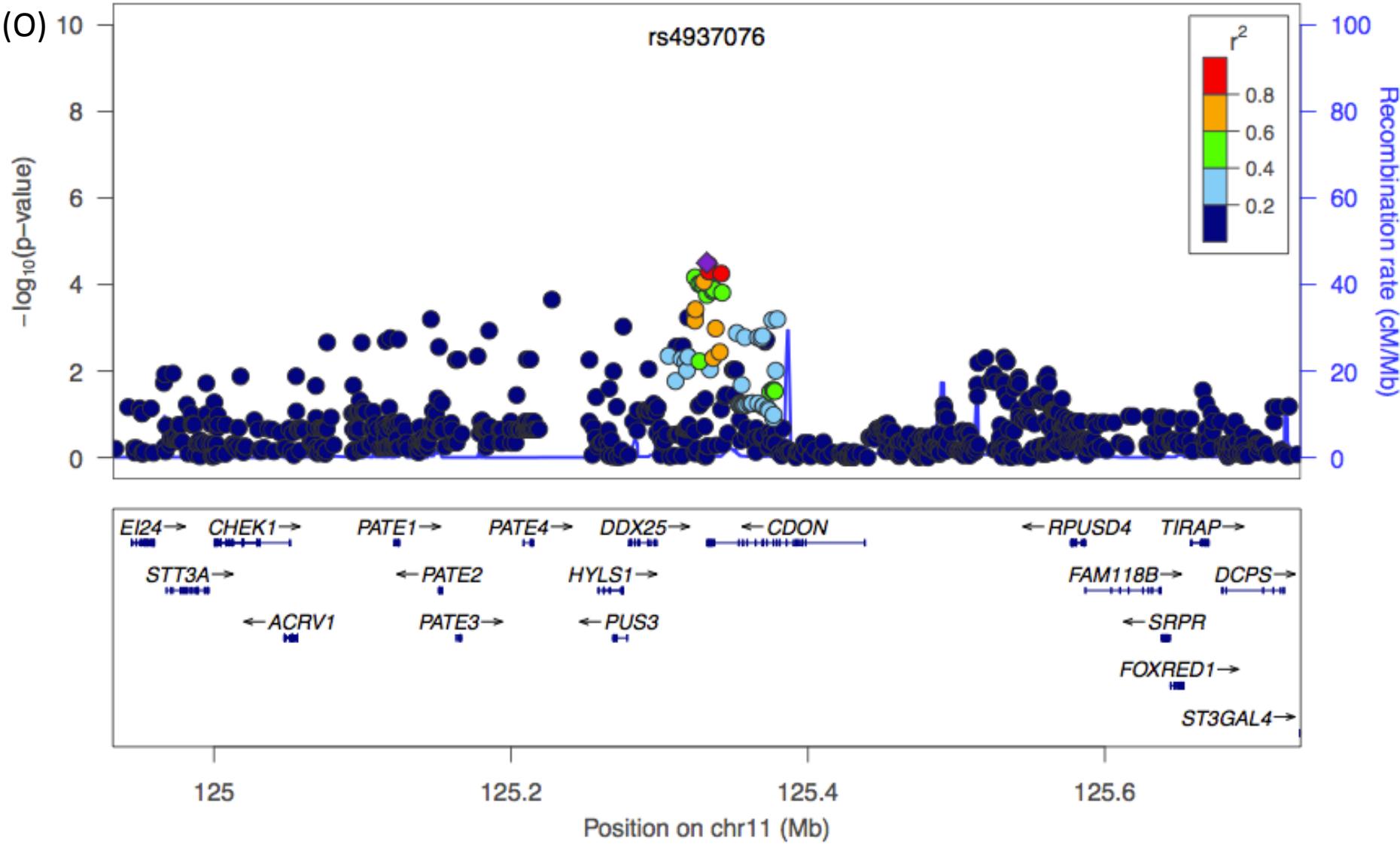


(M)

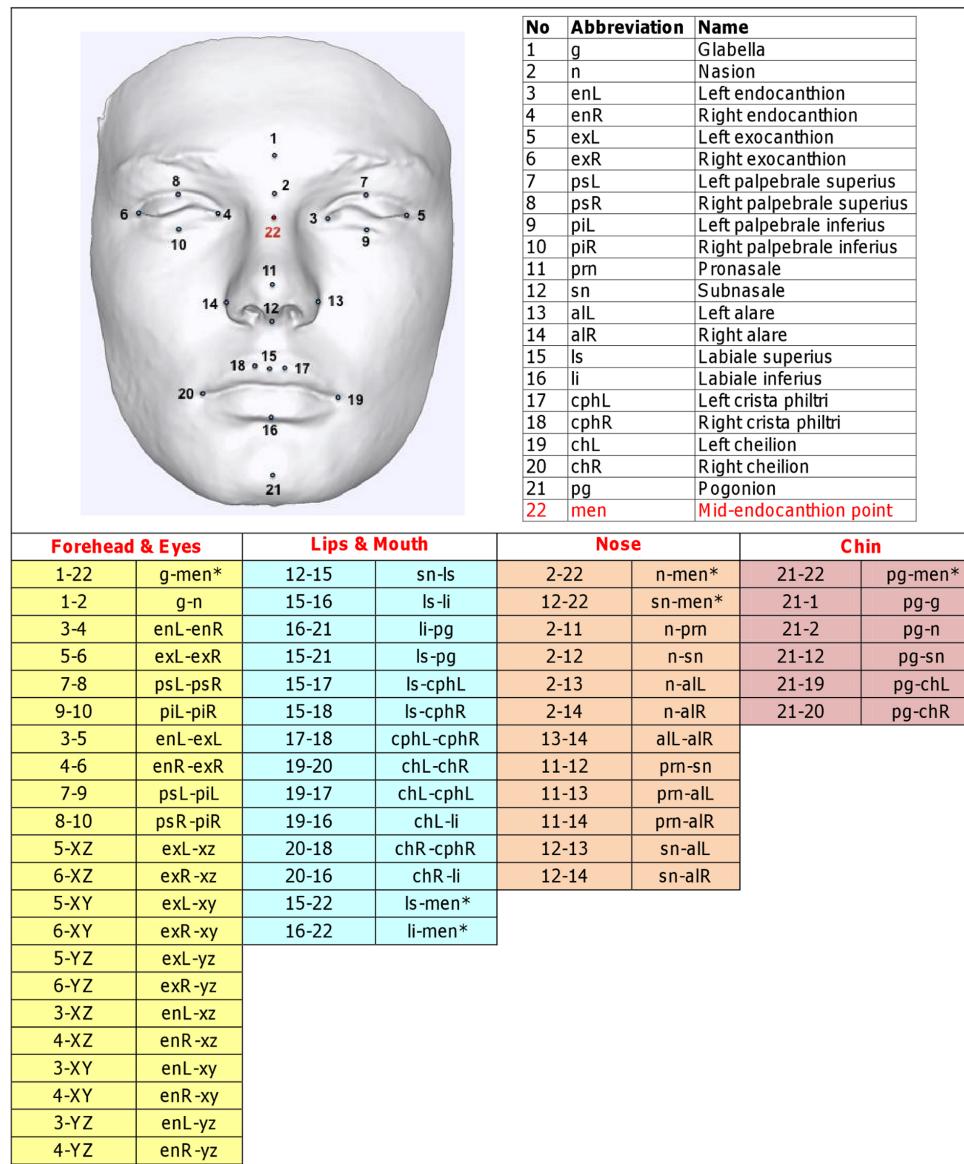


(N)





Supplementary Figure 3: Linkage disequilibrium and Association plot of loci reaching genome-wide significance for ‘number of teeth’ at one year in meta-analysis of ALSPAC and NFBC. (A) rs8080944 *KCNJ16-KCNJ2* region (B) rs11796357 *FAM155-EDA* gene region (C) rs1994969 *IGF3BP1* gene region (D) rs7924176 *ADK* gene region (E) rs17101923 *HMGA2* gene region (F) rs10740993 *CACNB2* gene region (G) rs1799922 *CALU* (H) rs10932688 2q35 (I) rs997154 *AJUBA* gene region (J) rs9316505 *DLEU7* gene region (K) rs17563 *BMP4* gene region (L) rs12229918 *MSRB3* gene region (M) rs6568401 region(N) rs412000 *TEX14/RAD51C* region (O) rs4937076 *CDON* gene region. The most significant SNPs in each region plotted in purple. Genes are based on Genome browser (RefSeq Genes). Arrows on genes give direction of transcription.



Supplementary Figure 4: Position and Definition of the 22 Landmarks and the 54 parameters analysed in Paternoster et al. (2012): Parameters with pairs of numbers denote the direct 3D distance between pairs of landmarks. Those with “xz”, “xy” or “yz” denote the prominence of the landmark from the xz, xy, or yz planes. *“men” (point 22) denotes the midendocanthion or midintercanthal point (the midpoint between left and right endocanths); this point does not lie on the facial surface

MARKER	GENE REGION/LOCUS	CHR	BP	A1	A2	EFFECT ALSPAC	SE ALSPAC	PVALUE ALSPAC	EFFECT NFBC	SE NFBC	PVALUE NFBC	EFFECT META	SE META	PVALUE META
rs2057579	TMEM9	1	199365898	T	C	-0.067	0.045	1.4x10-01	-0.176	0.036	1.3x10-06	-0.133	0.028	2.6x10-06
rs11956881	PP187	5	127951662	C	T	-0.26	0.091	4.4x10-03	-0.324	0.078	3.4x10-05	-0.297	0.059	5.7x10-07
rs9388501	AK127472	6	126944704	C	T	-0.236	0.043	2.7x10-08	-0.085	0.035	1.3x10-02	-0.145	0.027	5.9x10-08
rs10225279	CR623750	7	19099597	T	G	-0.19	0.043	1.0x10-05	-0.117	0.036	9.5x10-04	-0.147	0.027	8.5x10-08
rs339039	OPN1SW	7	128203797	A	G	-0.176	0.045	9.4x10-05	-0.149	0.043	6.0x10-04	-0.162	0.031	2.2x10-07
rs1157136	CR600271,CR593328	8	129971092	T	C	-0.181	0.043	2.4x10-05	-0.131	0.038	5.0x10-04	-0.153	0.028	6.5x10-08
rs10824218	ADK	10	76091222	A	T	-0.195	0.043	6.0x10-06	-0.086	0.036	1.6x10-02	-0.131	0.028	2.0x10-06
rs7103884	FGF3	11	69372742	T	C	-0.195	0.043	7.4x10-06	-0.09	0.035	1.1x10-02	-0.132	0.027	1.5x10-06
rs421007	KRT6B	12	51137112	G	T	-0.115	0.043	7.5x10-03	-0.132	0.035	1.5x10-04	-0.125	0.027	3.7x10-06
rs10877809	FAM19A2	12	60873839	A	G	-0.134	0.048	5.5x10-03	-0.177	0.046	1.3x10-04	-0.156	0.033	2.7x10-06
rs17105278	RAD51L1	14	67798232	C	T	-0.122	0.049	1.3x10-02	-0.157	0.039	4.4x10-05	-0.144	0.03	2.1x10-06
rs12708948	IRX5	16	53635746	T	C	-0.183	0.046	8.0x10-05	-0.128	0.044	3.5x10-03	-0.154	0.032	1.4x10-06
rs11860308	CES8,UNQ440/PRO873	16	65593020	C	T	-0.238	0.082	3.8x10-03	-0.206	0.055	1.7x10-04	-0.216	0.046	2.2x10-06
rs2429369	HSF5	17	53856419	G	A	-0.196	0.045	1.1x10-05	-0.118	0.037	1.3x10-03	-0.15	0.028	1.4x10-07
rs7502947	FAM33A	17	54584498	A	G	-0.182	0.045	4.4x10-05	-0.128	0.036	4.3x10-04	-0.15	0.028	1.1x10-07
rs1993104	FPR1	19	56932061	C	T	-0.107	0.049	2.8x10-02	-0.184	0.043	1.7x10-05	-0.151	0.032	2.8x10-06

Supplementary Table 1: SNPs showing suggestive association in the meta-analysis for ‘age at first tooth’ ($5 \times 10^{-6} > p > 5 \times 10^{-8}$). Variants reported are ≥ 500 kb apart. The P-value for each cohort is corrected for gestational age and sex. ALSPAC was also corrected for age at measurement. P-values were calculated using a fixed effects inverse variance meta-analysis. All alleles refer to the forward strand. Positions of SNPs reported correspond to HapMap release II build 36. The effect allele (A1) is defined as the allele associated with earlier tooth eruption

SNP	GENE REGION/LOCUS	CHR	BP	A1	A2	EFFECT ALSPAC	SE ALSPAC	PVALUE ALSPAC	EFFECT NFBC	SE NFBC	PVALUE NFBC	EFFECT META	SE META	PVALUE META
rs6704363	TMEM9	1	199363006	A	G	0.08	0.032	1.2x10-02	0.156	0.037	2.9x10-05	0.111	0.024	3.8x10-06
rs183780	EDAR	2	108961614	T	C	0.115	0.036	1.5x10-03	0.174	0.044	7.1x10-05	0.139	0.028	6.3x10-07
rs6967145	IGF2BP3	7	23483993	G	C	0.081	0.031	9.9x10-03	0.179	0.038	2.3x10-06	0.121	0.024	5.8x10-07
rs2390854	STK31	7	23984902	C	T	0.064	0.035	6.5x10-02	0.234	0.043	4.7x10-08	0.132	0.027	1.1x10-06
rs11768140	MPP6	7	24518518	A	G	0.119	0.038	1.7x10-03	0.148	0.042	4.8x10-04	0.132	0.028	3.1x10-06
rs1445570	PAG1	8	82002247	A	G	0.134	0.031	1.2x10-05	0.078	0.037	3.7x10-02	0.111	0.024	2.6x10-06
rs12379293	ZCCHC6	9	88264170	A	C	0.152	0.036	1.9x10-05	0.103	0.042	1.4x10-02	0.132	0.027	1.2x10-06
rs451722	BC093087	9	89011338	G	A	0.092	0.035	7.5x10-03	0.159	0.04	8.7x10-05	0.121	0.026	4.6x10-06
rs7103884	FGF3	11	69372742	T	C	0.178	0.031	1.0x10-08	0.058	0.037	1.1x10-01	0.128	0.024	6.8x10-08
rs11173690	FAM19A2	12	59671837	C	G	0.142	0.039	2.4x10-04	0.132	0.051	1.0x10-02	0.138	0.031	7.5x10-06
rs17732182	PPM1H	12	61312398	T	C	0.165	0.04	3.9x10-05	0.202	0.058	5.6x10-04	0.177	0.033	9.0x10-08
rs7146941	PAX9	14	36180966	A	C	0.1	0.032	1.9x10-03	0.129	0.037	4.9x10-04	0.112	0.024	3.7x10-06
rs1956529	RAD51L1	14	67858677	C	T	0.079	0.032	1.3x10-02	0.176	0.037	2.0x10-06	0.12	0.024	6.4x10-07
rs4131946	AF275804	16	53419975	A	T	0.114	0.034	8.7x10-04	0.127	0.039	1.1x10-03	0.12	0.026	3.1x10-06
rs400688	SLC25A11	17	4780674	G	A	0.137	0.04	6.3x10-04	0.139	0.042	9.3x10-04	0.138	0.029	2.0x10-06
rs4130668	DNAH2	17	7680389	T	C	0.128	0.037	6.1x10-04	0.133	0.038	4.1x10-04	0.13	0.027	8.6x10-07
rs2680700	RNF43	17	53795541	T	G	0.122	0.032	1.1x10-04	0.138	0.036	1.3x10-04	0.129	0.024	5.6x10-08
rs2240899	FLJ35776,DLGAPI	18	3585011	C	G	0.147	0.031	2.9x10-06	0.066	0.044	1.4x10-01	0.12	0.026	2.8x10-06

Supplementary Table 2: SNPs showing suggestive association in the meta-analysis for ‘number of teeth’ ($5 \times 10^{-6} > p > 5 \times 10^{-8}$) . Variants reported are ≥ 500 kb apart. The P-value for each cohort is corrected for gestational age and sex. ALSPAC was also corrected for age at measurement. P-values were calculated using a fixed effects inverse variance meta-analysis. All alleles refer to the forward strand. Positions of SNPs reported correspond to HapMap release II build 36. The effect allele (A1) is defined as the allele associated with an increase in the number of teeth.

PRIMARY SNP	LOCUS	SIGNIFICANCE THRESHOLD CONDITIONAL ANALYSES	AGE AT FIRST TOOTH			NUMBER OF TEETH		
			MOST STRONGLY ASSOCIATED SNP AFTER CONDITIONING ON PRIMARY SNP	P VALUE OF SNP BEFORE CONDITIONAL ANALYSIS	P VALUE OF SNP AFTER CONDITIONAL ANALYSIS	MOST STRONGLY ASSOCIATED SNP AFTER CONDITIONING ON PRIMARY SNP	P VALUE OF SNP BEFORE CONDITIONAL ANALYSIS	P VALUE OF SNP AFTER CONDITIONAL ANALYSIS
rs8080944	<i>KCNJ2 KCNJ16</i>	4.5x10 ⁻⁴	rs11077486	6.201x10 ⁻⁰⁵	2.024x10 ⁻⁰⁵	rs9788982	3.413x10 ⁻⁰⁹	8.103x10 ⁻⁰⁷
rs11796357	<i>FAM155E – EDA</i>	1.0x10 ⁻³	rs2520397	4.800x10 ⁻¹⁶	8.449x10 ⁻⁰⁶	rs2804391	1.254x10 ⁻⁰⁶	9.654x10 ⁻⁰⁷
rs17563	<i>BMP4</i>	2.5x10 ⁻⁴	rs1951867	8.000x10 ⁻⁰³	8.000x10 ⁻⁰⁵	rs1458991	7.854x10 ⁻⁰³	4.813x10 ⁻⁰⁷
rs1994969	<i>IGF2BP1</i>	6.5x10 ⁻⁴	rs8069452	3.588x10 ⁻⁰⁶	8.221x10 ⁻⁰⁶	rs9894411	9.298x10 ⁻⁰⁷	1.770x10 ⁻⁰⁵
rs12229918	<i>MSRB3</i>	4.3x10 ⁻⁴	rs1870566	6.000x10 ⁻⁰³	4.000x10 ⁻⁰³	rs1976274	2.348x10 ⁻⁰⁹	1.892x10 ⁻⁰⁵
rs6568401	<i>6q21</i>	3.8x10 ⁻⁴	rs6913299	9.000x10 ⁻⁰³	4.000x10 ⁻⁰³	rs3935361	2.751x10 ⁻⁰³	3.478x10 ⁻⁰³
rs4937076	<i>CDON</i>	3.5x10 ⁻⁴	rs533239	1.400x10 ⁻⁰²	1.100x10 ⁻⁰²	rs600281	4.994x10 ⁻⁰³	1.917x10 ⁻⁰³
rs7924176	<i>ADK VCL AP3MI</i>	1.6x10 ⁻³	rs11597376	1.000x10 ⁻⁰³	6.000x10 ⁻⁰³	rs7075347	9.271x10 ⁻⁰³	7.457x10 ⁻⁰²
rs17101923	<i>HMG A2</i>	4.5x10 ⁻⁴	rs1472259	1.222x10 ⁻⁰⁵	3.454x10 ⁻⁰⁶	rs1472259	6.322x10 ⁻⁰⁵	2.228x10 ⁻⁰⁵
rs10740993	<i>CACNB2</i>	4.9x10 ⁻⁴	rs12359352	4.159x10 ⁻⁰⁷	6.377x10 ⁻⁰⁴	rs7901587	3.536x10 ⁻⁰⁷	1.000x10 ⁻⁰³
rs1799922	<i>CALU/OPN1SW</i>	7.7x10 ⁻⁴	rs3807306	8.848x10 ⁻⁰⁷	1.337x10 ⁻⁰²	rs339072	4.90x10 ⁻⁰⁴	1.600x10 ⁻⁰²
rs10932688	<i>2q35</i>	2.7x10 ⁻⁴	rs12474719	6.092x10 ⁻⁰³	3.627x10 ⁻⁰³	rs12474719	2.839x10 ⁻⁰⁵	1.000x10 ⁻⁰³
rs997154	<i>AJUBA/C14orf93</i>	2.5x10 ⁻⁴	rs1263663	6.064x10 ⁻⁰³	5.274x10 ⁻⁰³	rs178752	1.000x10 ⁻⁰³	1.000x10 ⁻⁰³
rs9316505	<i>DLEU7</i>	1.1x10 ⁻⁴	rs2050936	3.062x10 ⁻⁰³	8.437x10 ⁻⁰³	rs2812245	2.603x10 ⁻⁰²	4.135x10 ⁻⁰²
rs412000	<i>TEX15/RAD51C</i>	7.2x10 ⁻⁴	rs3785492	4.891x10 ⁻⁰⁶	1.955x10 ⁻⁰²	rs7215531	7.626x10 ⁻⁰³	1.238x10 ⁻⁰³

Supplementary Table 3: Results for the conditional analysis in each genome-wide significant region.

MARKER	GENE/LOCUS	ALLELES	FREQ1	EFFECT	STDERR	PVALUE
rs17101923	<i>HMG A2</i>	G/T	0.19	0.1281	0.0206	4.7x10 ⁻¹⁰
rs7924176	<i>ADK VCL AP3M1</i>	A/G	0.58	0.0937	0.0157	2.5x10 ⁻⁹
rs10932688	2q35	G/C	0.72	0.0802	0.0179	7.7x10 ⁻⁶
rs10740993	<i>CACNB2</i>	C/T	0.43	0.0619	0.0155	6.6x10 ⁻⁵
rs17563	<i>BMP4</i>	G/A	0.39	0.0528	0.0162	0.0011
rs6568401	6q21	C/T	0.74	0.0586	0.0187	0.0017
rs12229918	<i>MSRB3</i>	C/G	0.36	0.0405	0.0162	0.0126

Supplementary Table 4: Results for pleotropic analysis of genome wide significance P<5x10⁻⁸ in meta-analysis for secondary dentition (Geller et al). All alleles refer to the forward strand. Positions of SNPs reported correspond to HapMap release II build 36. The Increaser allele is defined in bold.

		Pathway P value thresholds					
P-value criterion for SNPs	Number of genes	P<0.05		P<0.01		P<0.001	
		Number of pathways	P value	Number of pathways	P value	Number of pathways	P value
0.0001	118	70	0.017	19	0.049	4	0.053
0.0005	262	49	0.174	16	0.089	2	0.159
0.001	410	73	0.063	16	0.110	3	0.086
0.005	1358	157	0.004	50	0.002	11	0.004

(A) Number of significantly over-represented pathways in the ‘age at first tooth’ GWAS.

		Pathway P value thresholds					
P-value criterion for SNPs	Number of genes	P<0.05		P<0.01		P<0.001	
		Number of pathways	P value	Number of pathways	P value	Number of pathways	P value
0.0001	90	25	0.196	6	0.258	1	0.255
0.0005	254	26	0.546	5	0.542	1	0.355
0.001	408	56	0.146	13	0.167	0	1.000
0.005	1272	60	0.273	17	0.130	0	1.000

(B) Number of significantly over-represented pathways in the ‘number of teeth’ GWAS.

Supplementary Table 6: Summary statistics from ALIGATOR analyses for (a) the ‘time to first tooth’ GWAS and (b) the ‘number of teeth’ GWAS . The first column gives the P-value criteria (left-most column) GWAS threshold. The second column displays the number of genes with one or more SNPs with a p-value less than the labelled threshold. Third column displays number of pathways with a p-value less than the labelled threshold, the adjacent P value indicates whether this number is significantly greater than that expected by chance, similarly for the subsequent columns.