

SUPPLEMENTARY INFORMATION

Multiple common variants for celiac disease influencing immune gene expression

Patrick CA Dubois, Gosia Trynka, Lude Franke, Karen A Hunt, Jihane Romanos, Alessandra Curtotti, Alexandra Zhernakova, Graham AR Heap, Róza Ádány, Arpo Aromaa, Maria Teresa Bardella, Leonard H van den Berg, Nicholas A Bockett, Emilio G. de la Concha, Bárbara Dema, Rudolf SN Fehrmann, Miguel Fernández-Arquero, Szilvia Fialat, Elvira Grandone, Peter M Green, Harry JM Groen, Rhian Gwilliam, Roderick HJ Houwen, Sarah E Hunt, Katri Kaukinen, Dermot Kelleher, Ilma Korponay-Szabo, Kalle Kurppa, Pádraic MacMathuna, Markku Mäki, Maria Cristina Mazzilli, Owen T McCann, M Luisa Mearin, Charles A Mein, Muddassar M Mirza, Vanisha Mistry, Barbara Mora, Katherine I Morley, Chris J Mulder, Joseph A Murray, Concepción Núñez, Elvira Oosterom, Roel A Ophoff, Isabel Polanco, Leena Peltonen, Mathieu Platteel, Anna Rybak, Veikko Salomaa, Joachim J Schweizer, Maria Pia Sperandeo, Greetje J Tack, Graham Turner, Wieke HM Verbeek, Rinse K Weersma, Victorien M Wolters, Elena Urcelay, Bozena Cukrowska, Luigi Greco, Susan L. Neuhausen, Ross McManus, Donatella Barisani, Panos Deloukas, Jeffrey C Barrett, Paivi Saavalainen, Cisca Wijmenga, David A van Heel

Contents:

Page 2 - 3 : **Supplementary Note** Detailed description of case and control subjects; genotype calling; expression probe re-mapping.

Page 3: **References for Supplementary Information**

Page 4: **Supplementary Table 1** Subjects used in eQTL mapping analysis.

Page 5: **Supplementary Table 2** Conditional logistic regression to test for multiple independent associations.

Pages 6,7: **Supplementary Table 3** Details of Illumina expression probes corresponding to Table 3 findings.

Pages 8-15: **Supplementary Figure 1** LD structure, genes and association results for 39 non-HLA coeliac disease associated regions.

Pages 16-21: **Supplementary Figure 2** Detailed eQTL genotype - expression correlation analyses.

Pages 22-42: **Supplementary Figure 3** Co-localisation of case/control association and genotype-expression correlation (eQTL) signals.

Supplementary Note

Detailed description of case and control subjects:

GWAS: UK(1) celiac cases were previously described¹, with removal of additional individuals showing genetic relatedness to UK(2) individuals, and were matched to 1958 Birth Cohort population controls genotyped by the Type 1 Diabetes Genetics Consortium². Details of Dutch and Italian cohorts were previously described^{3,4}. UK(2) celiac cases were partly previously described⁵, with additional individuals recruited through Celiac UK membership. UK(2) controls comprised 2434 population controls from the 1958 Birth Cohort and 2502 National Service population controls. Finnish affected individuals (sporadic cases, or unrelateds from affected families across Finland) were partly previously described⁶. Finnish population controls comprised 904 samples from Finrisk (Corogene, excluding coronary heart disease) and 925 samples from Health 2000 (excluding metabolic syndrome and positive celiac disease serology).

Follow-up: USA comprised 525 celiac cases and 340 controls from the Mayo Clinic (Minnesota), and 448 celiac cases and 215 controls from the University of California Irvine⁷. Polish celiac cases were diagnosed in hospital clinics, and controls from donors at the Children's Memorial Health Institute (Warsaw), excluding celiac serology positive samples. Italian samples comprised 377 celiac cases and 94 controls from Rome, and 637 celiac cases and 711 celiac serology negative controls from Naples⁸. Irish celiac cases and controls were as described, with additional samples⁹. 259 Finnish celiac cases were recruited similarly to GWAS samples, and controls were an additional 653 population controls from the Finrisk study. 965 Hungarian celiac cases were collected from Budapest and Debrecen children clinic, and 1067 controls representative of the Hungarian population were selected from an epidemiological study. Part of the Hungarian cohorts have been described earlier⁶. Spanish celiac cases were recruited in Madrid hospitals, controls were donors and hospital employees¹⁰.

Detailed description of genotype calling:

To minimize calling biases arising from batch effects and the use of different genotyping platforms, we attempted to call cases and controls together from the same collections if possible, and maximized samples size to reduce problems when clustering rare variants. Genotypes were called separately in the following five pools from normalized R, theta data: pool A (n=2199: 778 UK1 cases together with 1421 1958 birth cohort controls genotyped on the Illumina Hap550v1-1 platform as described in our previous study¹. Genotype data from the 1421 controls was then discarded and UK1 case data subsequently merged with UK1 controls for analysis. UK1 controls were called separately in pool B (2596 1958 birth cohort individuals genotyped for the Type 1 Diabetes Genetics Consortium on the Illumina Hap550-2v3 platform)². Separate calling of UK1 case and UK1 control individuals was required due to differences in genotype cluster intensity characteristics observed for UK1 case data (Hap300v1-1) and controls (Hap550-2v3). Pool C comprised UK3 cases and controls (n=6963, 1894 cases on Human 670-QuadCustom_v1 and 5069 controls on 1.2M-DuoCustom_v1). Pool D comprised Dutch and Italian cases and controls (n=2917 on 670-QuadCustom_v1). Pool E comprised Health2000 and Finrisk cohorts and Finnish cases (n=6760, 674 cases on Human 670-QuadCustom_v1, 912 Finrisk

controls, 927 Health2000 controls, 4247 additional Finrisk and H2000 cases and internal controls- Human 610-Quad). The 4247 additional samples were then discarded.

Detailed description of expression probe re-mapping:

We used Ensembl52 to obtain, for each annotated gene, the transcript with the largest number of exons and included this main spliced transcript in our reference set. Second, we added one sequence per intron, extending intron boundaries 40 bp on each side to allow mapping of the 50 bp probe sequences, overlapping exon-intron junctions. Last, a version of the reference DNA genome with masked annotated transcripts was included. Probe sequences were mapped versus the composite reference using novoalign v2.05.12 (www.novocraft.com) permitting alignment against all possible sequences originating from the same transcript (parameters -t 150 -v 20 20 200 [>]([^_]*_)). For each probe we determined whether it mapped uniquely to one particular genomic locus, or, if multiple hits were present (e.g. across exons) that these resided < 250kb from the probe.

References for Supplementary Information

1. van Heel, D.A. et al. A genome-wide association study for celiac disease identifies risk variants in the region harboring IL2 and IL21. *Nat Genet* **39**, 827-9 (2007).
2. Barrett, J.C. et al. Genome-wide association study and meta-analysis find that over 40 loci affect risk of type 1 diabetes. *Nat Genet* (2009).
3. Coenen, M.J. et al. Common and different genetic background for rheumatoid arthritis and coeliac disease. *Hum Mol Genet* (2009).
4. Romanos, J. et al. Six new coeliac disease loci replicated in an Italian population confirm association with coeliac disease. *J Med Genet* **46**, 60-3 (2009).
5. Hunt, K.A. et al. Newly identified genetic risk variants for celiac disease related to the immune response. *Nat Genet* **40**, 395-402 (2008).
6. Koskinen, L.L. et al. Fine mapping of the CELIAC2 locus on chromosome 5q31-q33 in the Finnish and Hungarian populations. *Tissue Antigens* **74**, 408-16 (2009).
7. Garner, C.P. et al. Replication of celiac disease UK genome-wide association study results in a US population. *Hum Mol Genet* **18**, 4219-25 (2009).
8. Megiorni, F. et al. HLA-DQ and susceptibility to celiac disease: evidence for gender differences and parent-of-origin effects. *Am J Gastroenterol* **103**, 997-1003 (2008).
9. Hunt, K.A. et al. Large scale replication of a genome-wide association study in celiac disease. *American Society of Human Genetics Meeting*, platform talk 26 (2007).
10. Dema, B. et al. Association of IL18RAP and CCR3 with coeliac disease in the Spanish population. *J Med Genet* **46**, 617-9 (2009).

Supplementary Table 1 Subjects used in eQTL mapping analysis.

Numbers are shown after quality control steps.

Case/Control	Population	Number of individuals	Genotype platform	Expression platform
Controls	Dutch	324	Hap370	HT-12
Amyotrophic Lateral Sclerosis	Dutch	414	Hap370	HT-12
Ulcerative Colitis	Dutch	49	610-Quad	HT-12
Chronic Obstructive Pulmonary Disease	Dutch	453	610-Quad	HT-12
Celiac disease	UK	111	Hap300	Ref-8 v2
Amyotrophic Lateral Sclerosis	Dutch	59	Hap300	Ref-8 v2
Controls	Dutch	59	Hap300	Ref-8 v2

Supplementary Table 2 Conditional logistic regression to test for multiple independent associations.

Locus	Chr	Position (bp, B36)	LD block (Mb)	SNP	Pairwise SNP ^a r ²	Pairwise SNP ^a D'	P _{combined} (CMH analysis)	P _{combined} ^b (logistic regression)	P _{combined} conditioned on alternate SNP ^c (logistic regression)
Residual evidence of multiple independent SNPs at a locus (p<10⁻³, both before and after conditioning on alternate SNP)									
<i>REL</i>	2	60972975	60.78-61.74	rs842647	0.247	0.906	2.88x10 ⁻⁸	2.40x10 ⁻¹²	6.82 x10 ⁻⁴
		61040333		rs13003464			3.71x10 ⁻¹³	1.03x10 ⁻¹⁶	3.00x10 ⁻⁸
CCR1/CCR3	3	46210205	45.90-46.57	rs13098911	0.135	0.781	3.26x10 ⁻¹⁷	1.49x10 ⁻¹⁶	7.77 x10 ⁻⁸
		46327388		rs6441961			2.93x10 ⁻¹⁵	3.87x10 ⁻¹⁸	1.39x10 ⁻⁹
<i>IL12A^d</i>	3	161147744	161.07-161.23	rs17810546	0.160	0.957	4.56x10 ⁻¹⁸	2.34x10 ⁻¹⁵	5.66 x10 ⁻⁹
		161179692		rs9811792			1.03x10 ⁻¹¹	1.66x10 ⁻¹⁰	2.83x10 ⁻⁴
<i>IRF4</i>	6	328546	0.32-0.40	rs1033180	0.079	0.880	5.58x10 ⁻⁰⁸	1.60x10 ⁻⁸	1.02x10 ⁻⁴
		356064		rs872071			8.22x10 ⁻⁰⁷	9.12x10 ⁻¹³	4.26x10 ⁻⁹
<i>THEMIS / PTPRK</i>	6	128320491	127.99-128.32	rs802734	0.077	0.993	2.62x10 ⁻¹⁴	2.43x10 ⁻¹²	9.00x10 ⁻⁸
		128337195		rs7738609			2.88x10 ⁻¹⁰	1.63x10 ⁻¹²	4.07x10 ⁻⁸
<i>ETSI</i>	11	127886184	127.84-127.89	rs11221332	0.196	0.934	5.28x10 ⁻¹⁶	2.04x10 ⁻¹⁶	4.98x10 ⁻⁹
		127926136		rs4245079			5.34x10 ⁻¹⁰	2.46x10 ⁻¹¹	6.83x10 ⁻⁴

^apairwise LD estimated for 6785 individuals from UK 2 GWAS

^blogistic regression performed with sample collections as binary dummy covariates

^clogistic regression performed as for b, conditioned on alternate SNP at locus

^dno follow-up data for rs9811792, all SNP analyses confined to GWAS collections

Supplementary Table 3 Details of Illumina expression probes corresponding to Table 3 findings.

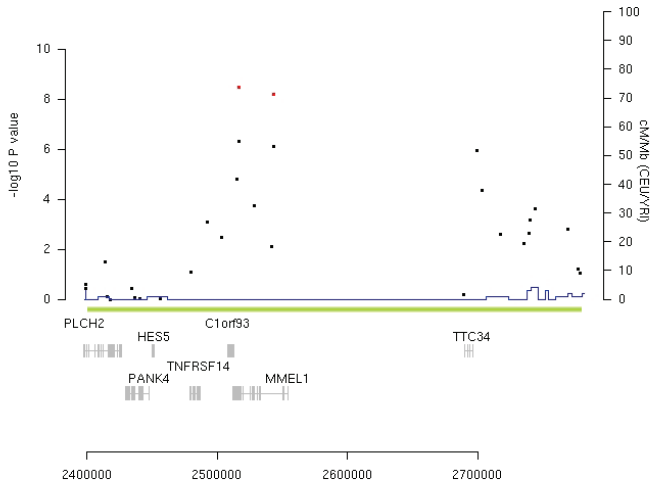
Unique Identifier	HGNC Name	Platform	ILMN Code	Array Address ID	Probe Sequence
650452	PLCH2	HumanHT12	ILMN_2061565	650452	CTTCGAGGCTGGCCCTGCCAGGCAGTTTTCCCGCGTTTTAGGATCTGTA
6520725	TNFRSF14	HumanHT12	ILMN_1697409	6520725	AGCCAAGGCTGGACTGGGTTGGCTGCAGTGTGGTGTAGTGGATAACCAC
2070246	MMEL1	HumanHT12	ILMN_1718488	2070246	TTCTTCATCAACTATGCCAGGTGTGGTGCGGGTCTACCGGCCCGAGTT
Human_RefSeq-8_v2-6250338	C1orf93	Human_RefSeq-8_v2	ILMN_12752	6250338	GTGGGTGGGTGTGACAGCAGGAGCATTGCCATCTTGGACAAACATGGCCA
610193	PARK7	HumanHT12	ILMN_1744713	610193	AATTGTTGAAGCCCTGAATGGCAAGGAGGTGGCGGCTCAAGTGAAGGCTC
6290400	CD247	HumanHT12	ILMN_1676924	6290400	AAACCCGTCAATGTACTAGGATACTGCTGCGTCATTACAGGGCACAGGCC
3890689	CD247	HumanHT12	ILMN_2377669	3890689	ACTGTGCGTCATTACAGGGCACAGGCCATGGATGGAAAACGCTCTCTGC
1300279	DDX59	HumanHT12	ILMN_1748077	1300279	CTGGGATATTGCAAAACGAGTAAAGCCCACAGGATCCATTCTCCCCCTC
1170220	AHSA2	HumanHT12	ILMN_1798308	1170220	GGGAAC TGCCAGAAGAACACTATGCCATGGTTGCACTGAATTTGTGCC
4810020	PLEK	HumanHT12	ILMN_1795762	4810020	GCCCTCCCTCAATTCCTGTAAACATTCCTGAAGCTGTTCCCACTCCAG
6520180	IL18RAP	HumanHT12	ILMN_1721762	6520180	GGGTACTTTAGTACACAACCCCCTAAGATTTCCAGTGGTCCGAGCAG
1780433	UBE2E3	HumanHT12	ILMN_1733142	1780433	GGGTGTCCTTGTCTCTCCTAGTACCACCTGTGCAACAGCGAAAGTTT
6550333	CXCR6	HumanHT12	ILMN_1674640	6550333	TGCTGGCACCACCAGGCACCTCACAGAAATGAGATCAGGCTCTGCCTCAC
2190671	CCR3	HumanHT12	ILMN_1763322	2190671	GCCTTCCACTCACCTCTAAAACAGTCCCTTCAAACCTCCAGTGCAACAC
Human_RefSeq-8_v2-7570670	CCR3	Human_RefSeq-8_v2	ILMN_2506	7570670	CCATCCACAGCAGAGCCGGAACCTCTCTATTGTGTTTTAGGTCAGATGCAG
3850161	KTELC1	HumanHT12	ILMN_1774800	3850161	TGATGGCTTCATGATCCAGCACAGTGCCTCACACAAAGAACTATTGGGTG
6550288	KTELC1	HumanHT12	ILMN_1811104	6550288	GGATTTCAAGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTC
3520349	BACH2	HumanHT12	ILMN_1777792	3520349	AGCTGTCTGCTTCAGAAAAGTGAGGGCTCCAGGAATGAGGAGAATCTTCAA
4860242	TAGAP	HumanHT12	ILMN_1676408	4860242	ATAAGCTCCCCCGGCCAACCTCCTGCTACTCAAGCACTTGGTCTATGTG
5890739	TAGAP	HumanHT12	ILMN_1739985	5890739	ATGAGAAATCCCCAACTATGATCTCACCATCTGTTTGCCAAGTCCAGGC
5360364	TAGAP	HumanHT12	ILMN_2333774	5360364	TGGCCATCTGCATTGGACCCAACATGCTCACCTGGAGAATGACCAGAGC
2750154	ELMO1	HumanHT12	ILMN_1784320	2750154	AGCGTTTGGTGTACCTTCTCCTGGGAGGTCCTGCTGCAACTCAAGTTCC
2450131	ZMIZ1	HumanHT12	ILMN_1771627	2450131	CGTACACACATAAACACACCACCAGTGCAGCCTGAAGTAACTCCACAG
6560301	SH2B3///ATXN2	HumanHT12	ILMN_1752046	6560301	AAGGCCTTGGACTCTTCCCTGAGGGTTGCCTGAAATTCCTTCATGCTTTC
Human_RefSeq-8_v2-3190129	TMEM116	Human_RefSeq-8_v2	ILMN_23612	3190129	CCACCAACTAAAGCAGGAGGCTCGGCGTGATGCAGATACCAGACACCAT
2070736	TMEM116	HumanHT12	ILMN_2052871	2070736	GCAGGGGCTTAAATTCCTGGAATCCACCCTGACTTTTCTGCCAGTACT
840253	ALDH2	HumanHT12	ILMN_1793859	840253	GCAAGCTTCTCCCTCAGCCATTGATGGAAAAGTTCAGCAAGATCAGCAAC
4540072	AC009121.6	HumanHT12	ILMN_1790537	4540072	CGGCCCTGAAAGACAACAGCTCCCTTCTGCTTCGGACACCACTCAAAC

4070615	WNT3	HumanHT12	ILMN_1803593	4070615	ACGCGTGGTAAATGACCCAGACCCAACCTCGCCTGTGGACGGGGAGGCTCT
3520672	ARL17///LRRC37A ///LRRC37A2	HumanHT12	ILMN_1783673	3520672	AACAGCCCCACACACAGCAGGGGCCTGAGAAGTTAGCGGGAAACGCCGTC
4880037	LOC388397	HumanHT12	ILMN_1678312	4880037	CCCCACCTCCAAAAGGGCTGGGGACAGCAGGTGTATCCTTGTTAGTTC
5260138	NSF	HumanHT12	ILMN_1680353	5260138	CCTGTGATTCTGGTGGCCAGTATCCTGGATTCCTCTAAGATCTGCCTC
1410484	NSF	HumanHT12	ILMN_1680687	1410484	TCAGCACCACCATCCACGTGCCAACATTGCCACAGGAGAGCAGCTGTTG
Human_RefSeq-8_v2-7200373	RRP1///AP001053.1	Human_RefSeq-8_v2	ILMN_15485	7200373	GTGGCGGGGAGACAGAGGGGCGATGGCCAGTTTCTTTGGGCTGAAAAT
1230242	UBE2L3	HumanHT12	ILMN_1677877	1230242	TTCACACCCGCCTGGTTTCTTGAAGTGTGCTGGGTCCTTCCCTCTGCTCC
6480360	TLR8	HumanHT12	ILMN_1657892	6480360	CAGTTGGTCATCAACTATTTCCCTTGACTGCTGCTGGGATGGCCTGC
3390612	TLR8	HumanHT12	ILMN_1705047	3390612	GCTCCATCCTCCAGTGGCCTGACAACCCGAAGGCAGAAGGCTGTTTTGG

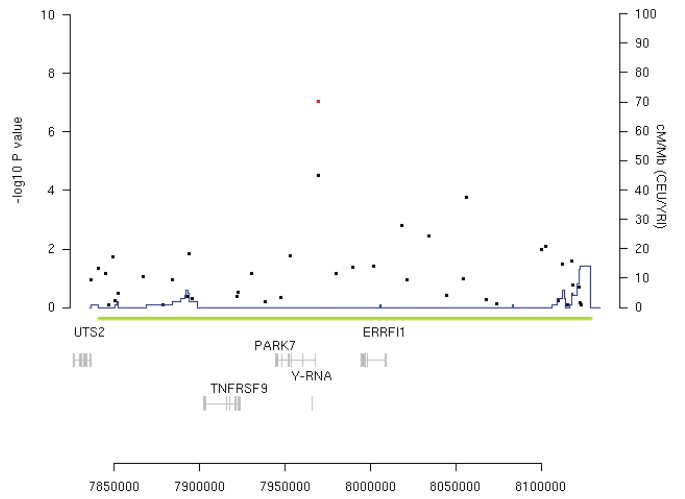
Supplementary Figure 1 LD structure, genes and association results for 39 non-HLA coeliac disease associated regions.

Chromosomal positions based on NCBI Build 36 co-ordinates. P_{GWAS} values (left Y axis and black points) are from 4,533 cases and 10,750 controls. P_{combined} values (left Y axis and red points) are from 9,451 cases and 16,434 controls. Recombination rate (HapMap) shown in blue (right Y axis). The green bar indicates the narrow linkage disequilibrium block as reported in **Table 2**, the complete X axis shows an additional 0.05% of base positions for clarity. All genes with HUGO identifiers are displayed (as annotated in Ensembl v54), for multiple transcripts only the largest is shown.

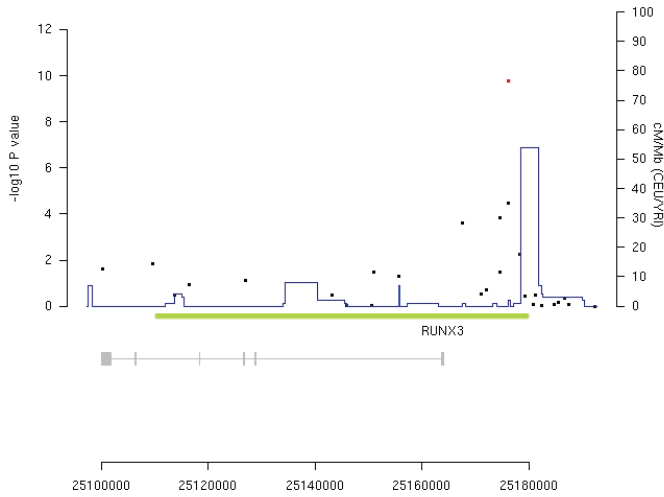
Chromosome 1



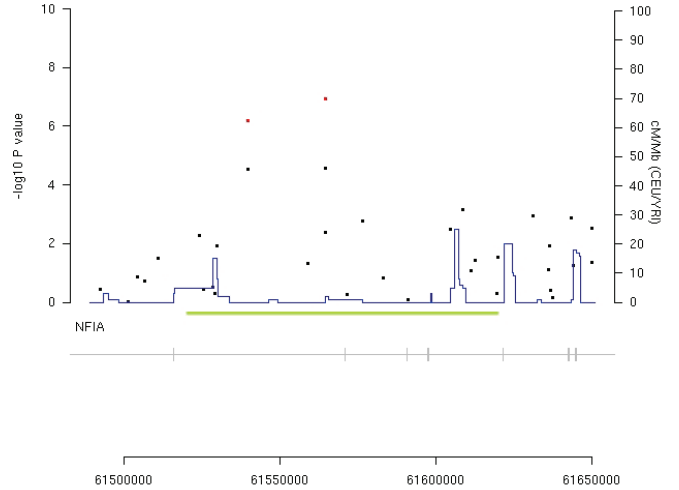
Chromosome 1



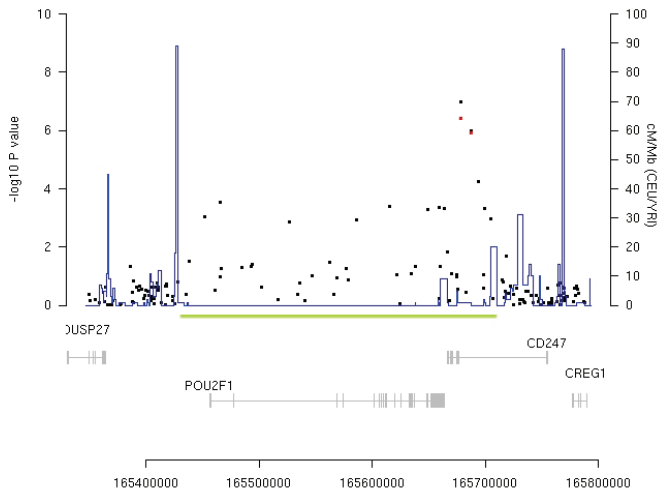
Chromosome 1



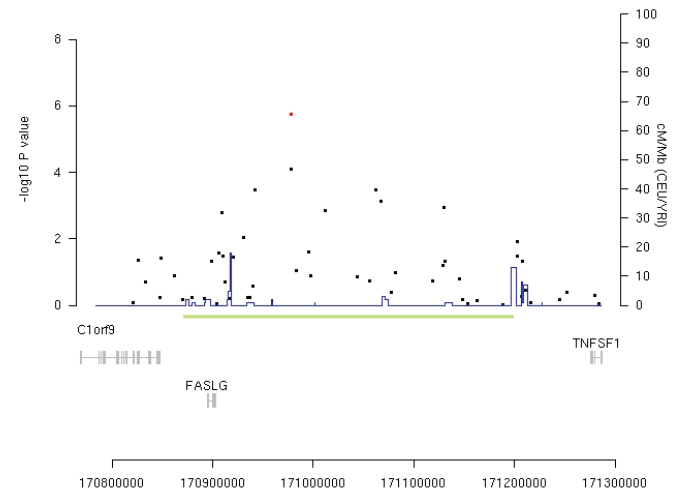
Chromosome 1



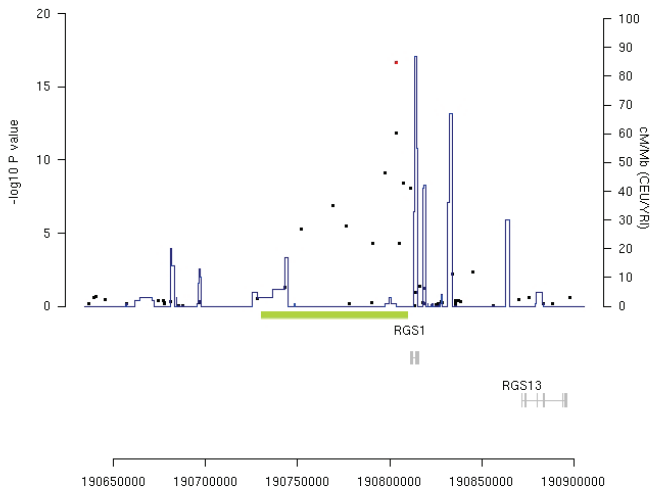
Chromosome 1



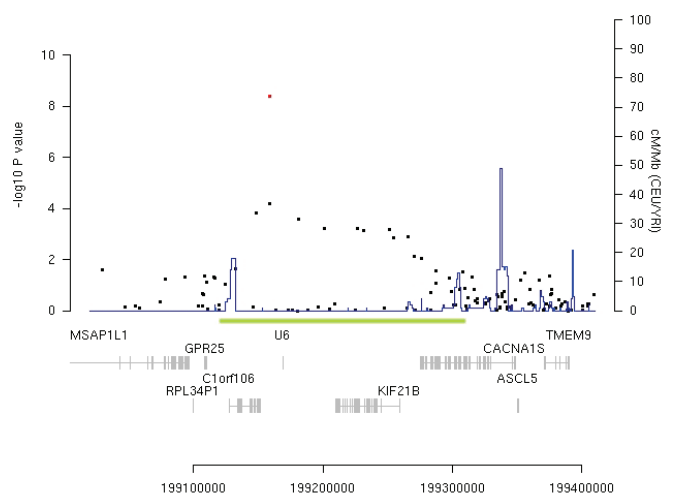
Chromosome 1



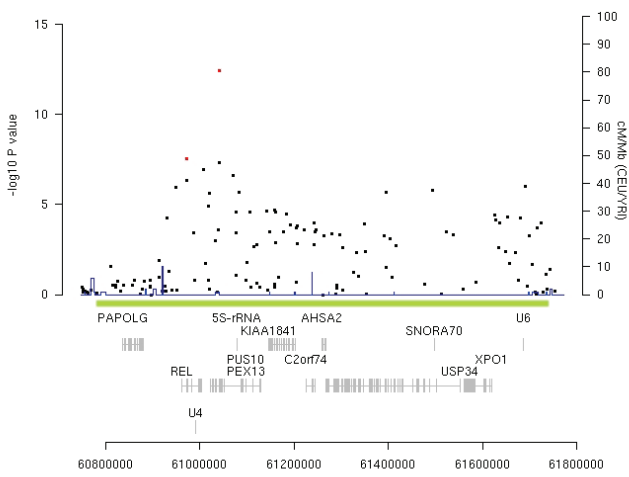
Chromosome 1



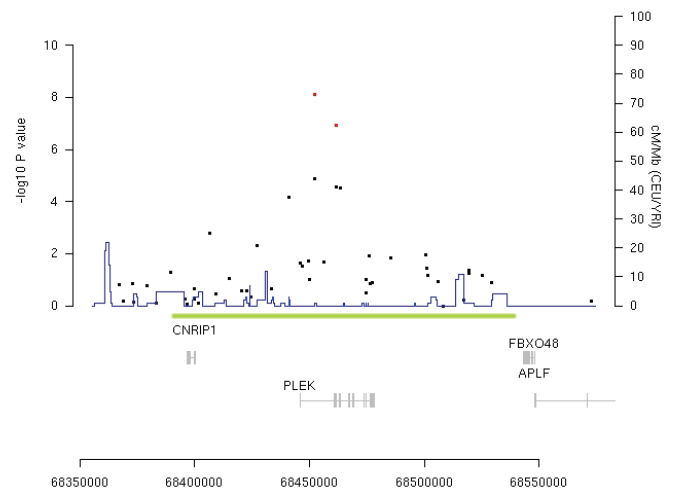
Chromosome 1



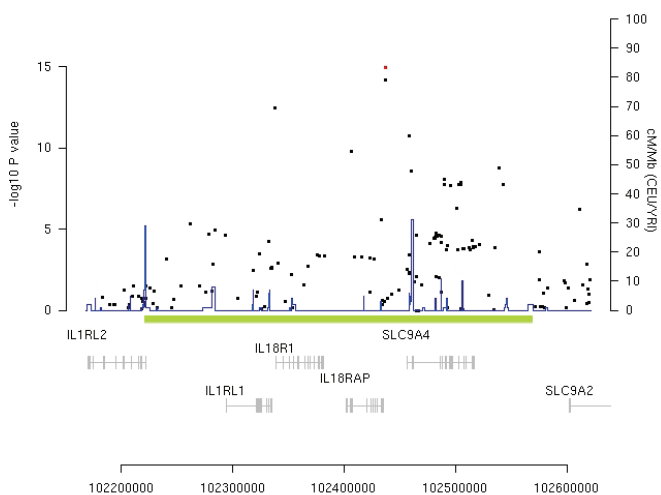
Chromosome 2



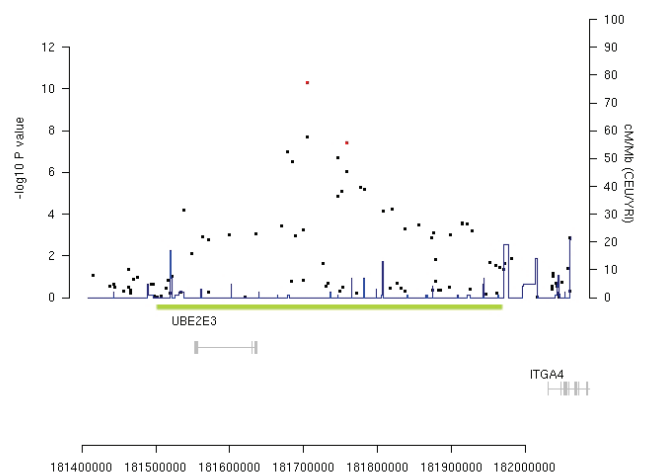
Chromosome 2



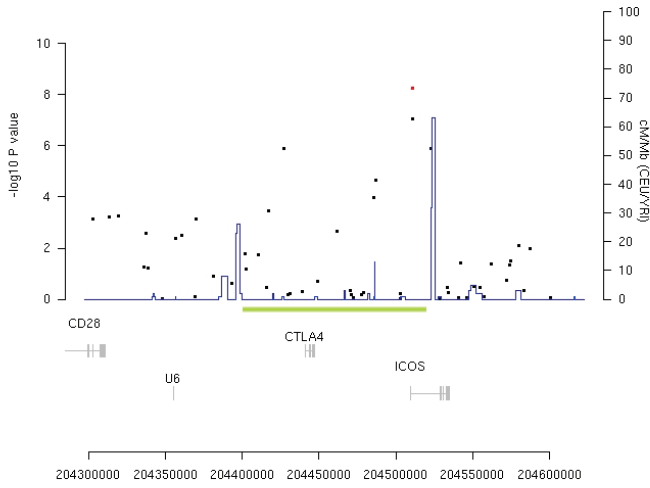
Chromosome 2



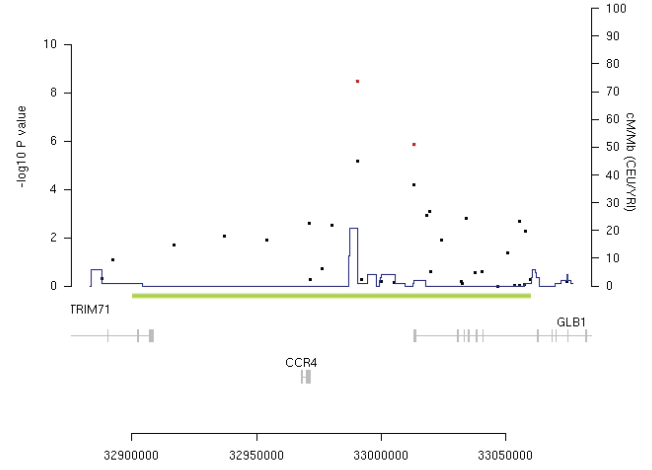
Chromosome 2



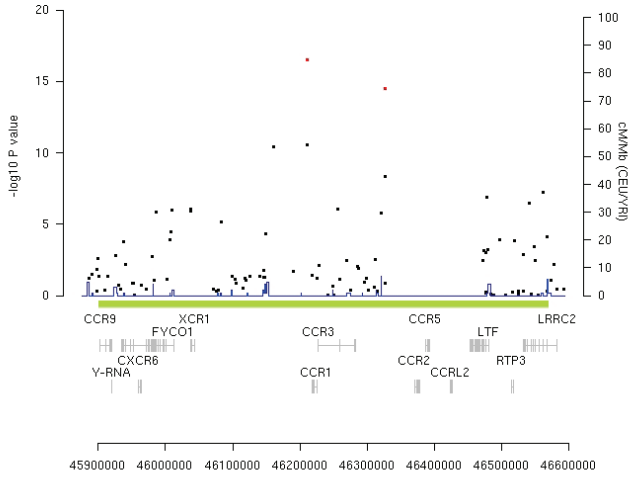
Chromosome 2



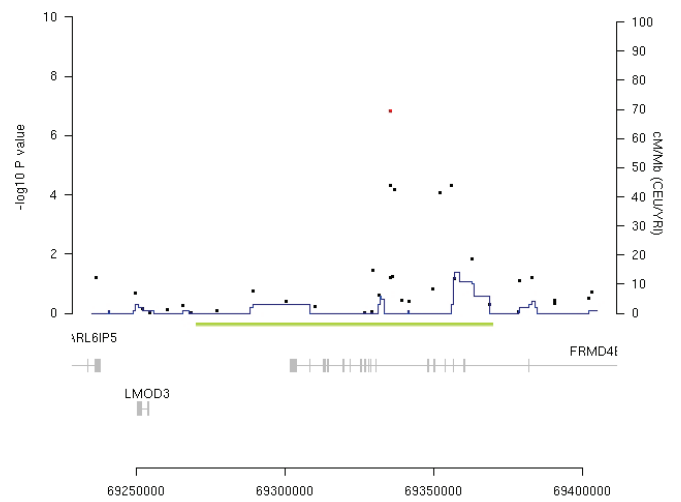
Chromosome 3



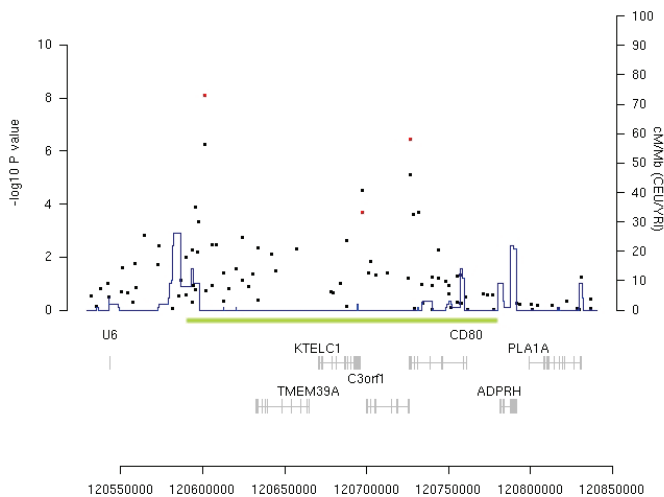
Chromosome 3



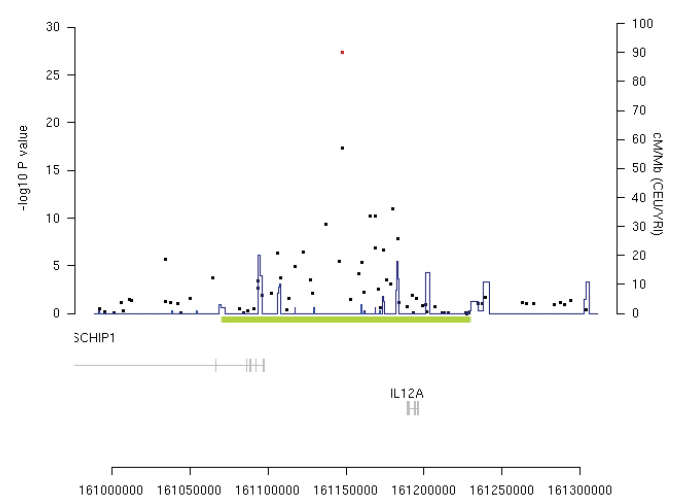
Chromosome 3



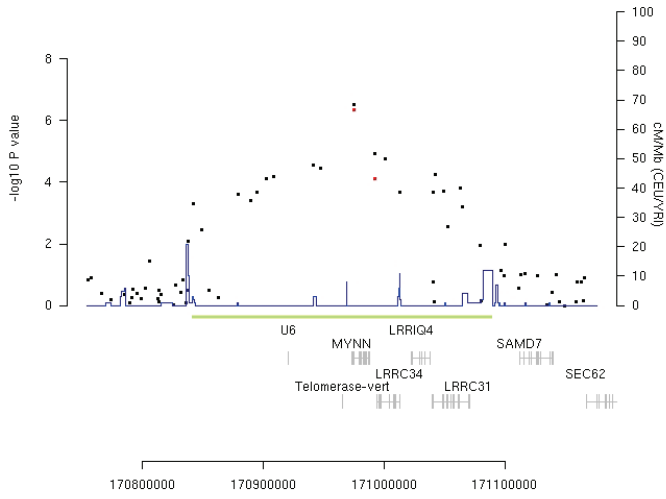
Chromosome 3



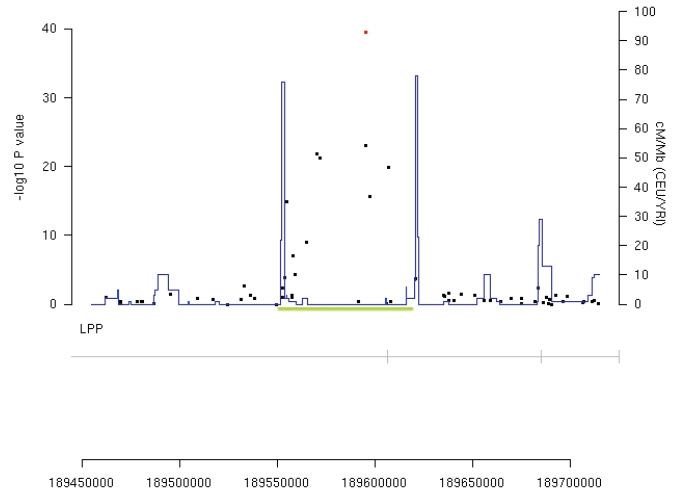
Chromosome 3



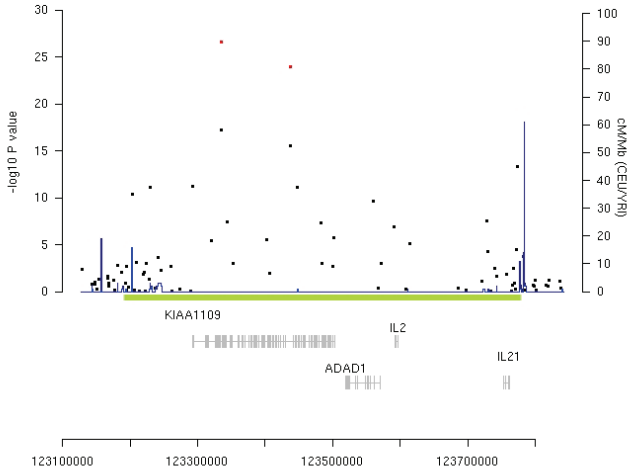
Chromosome 3



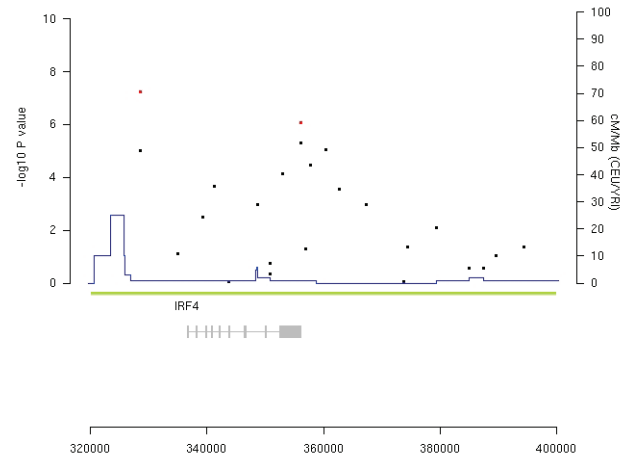
Chromosome 3



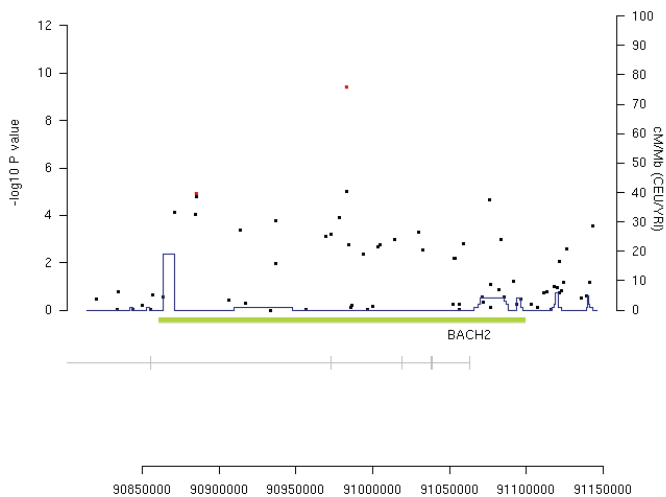
Chromosome 4



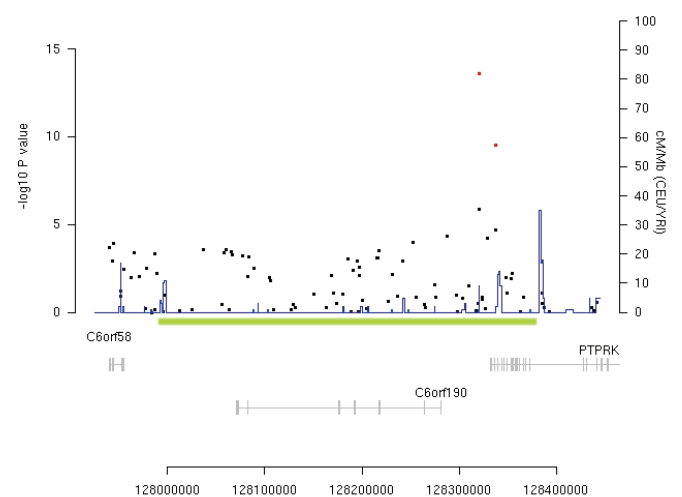
Chromosome 6

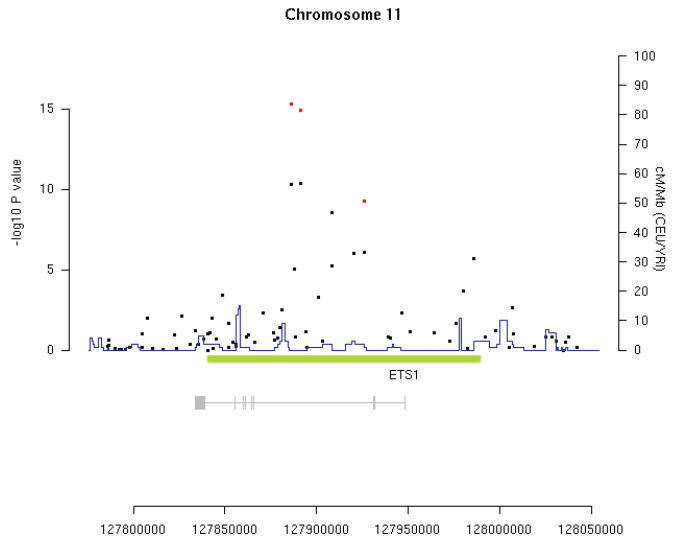
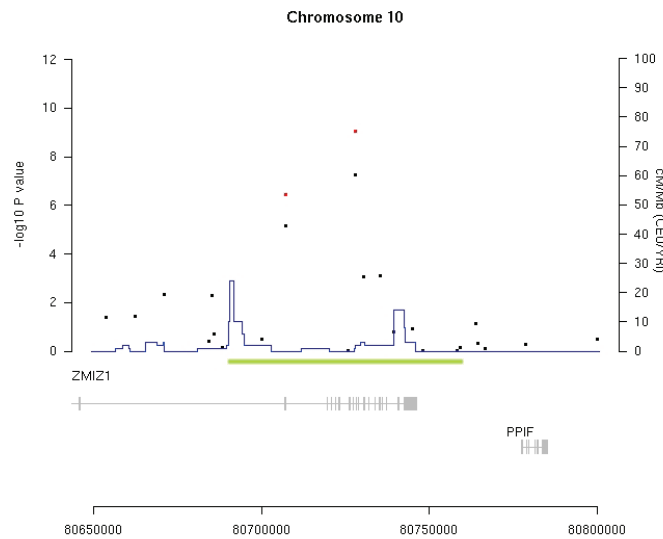
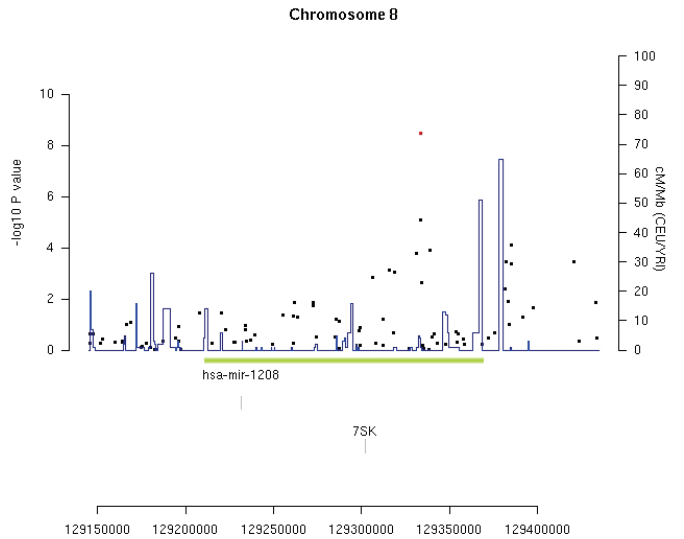
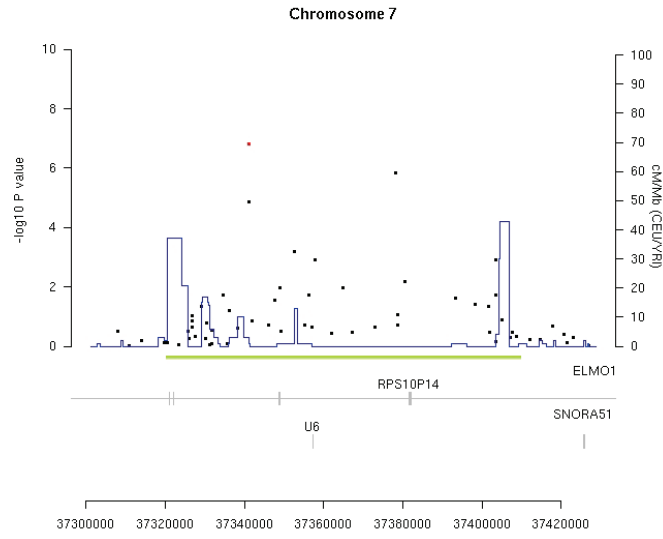
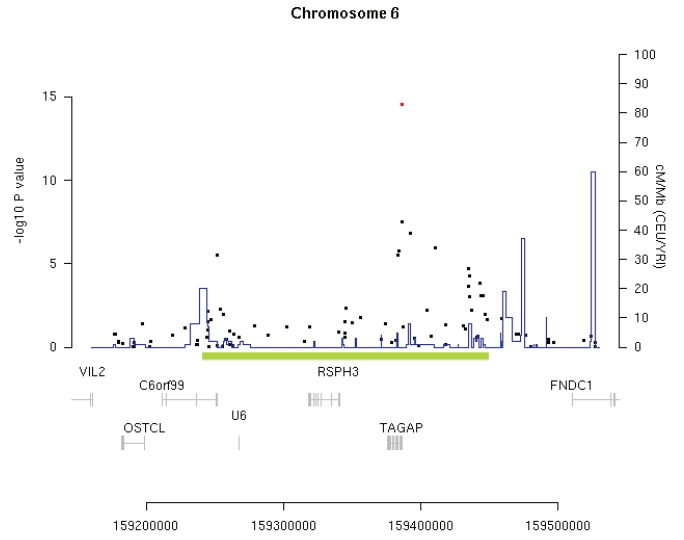
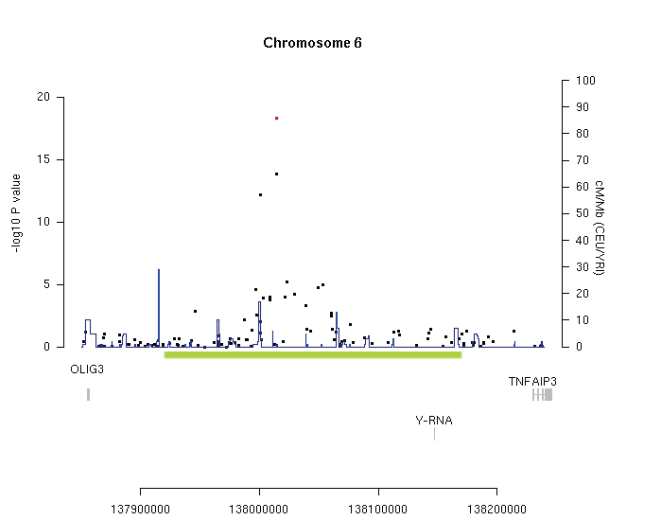


Chromosome 6

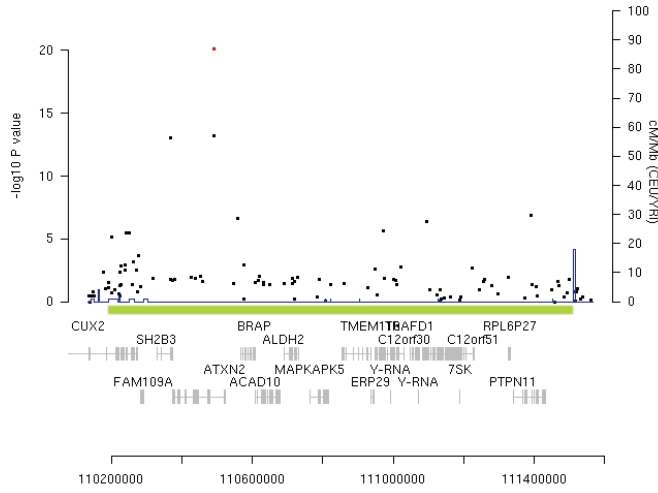


Chromosome 6

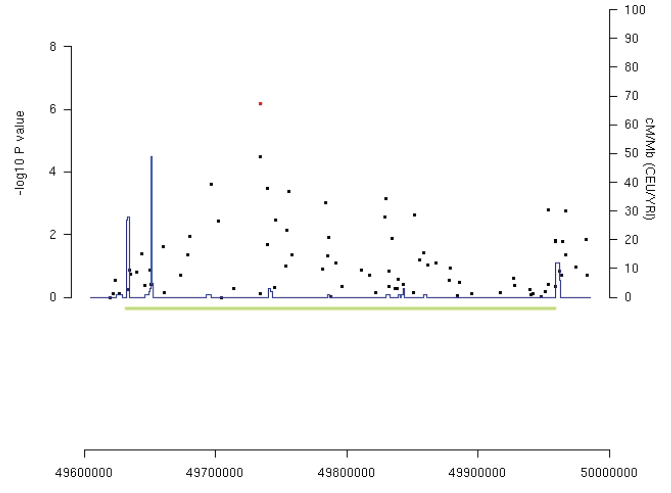




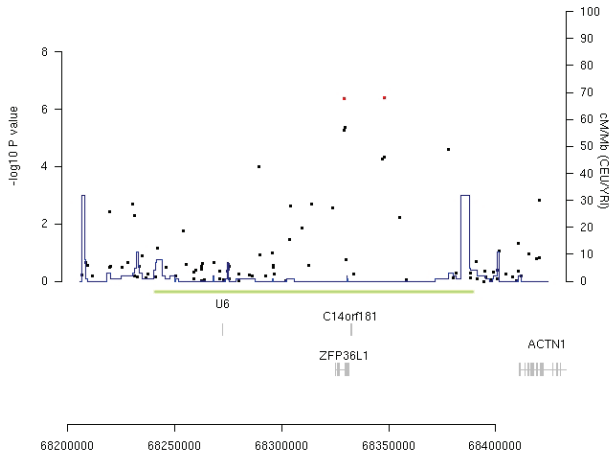
Chromosome 12



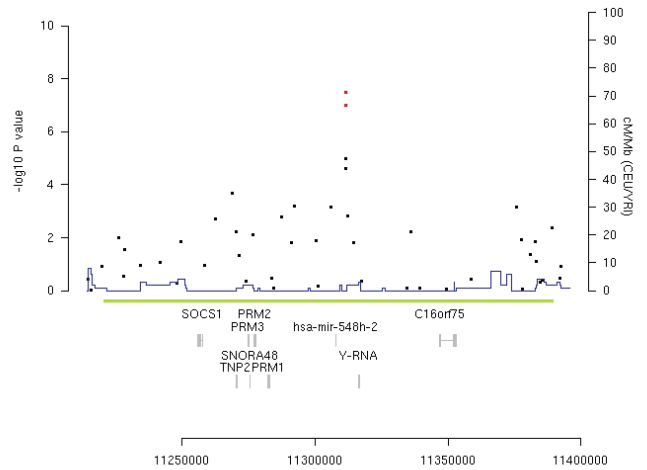
Chromosome 13



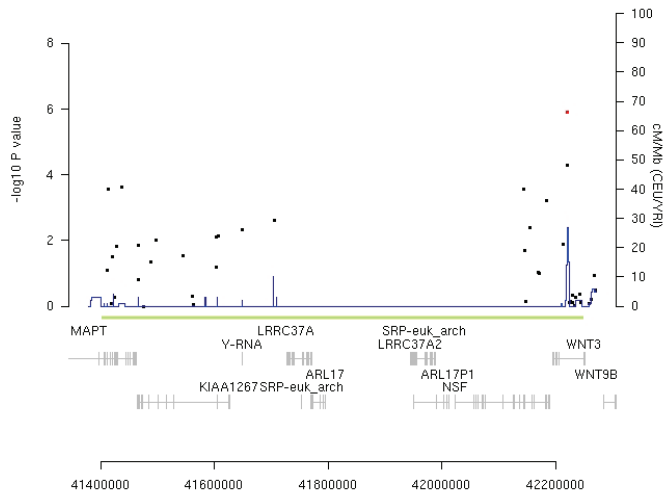
Chromosome 14



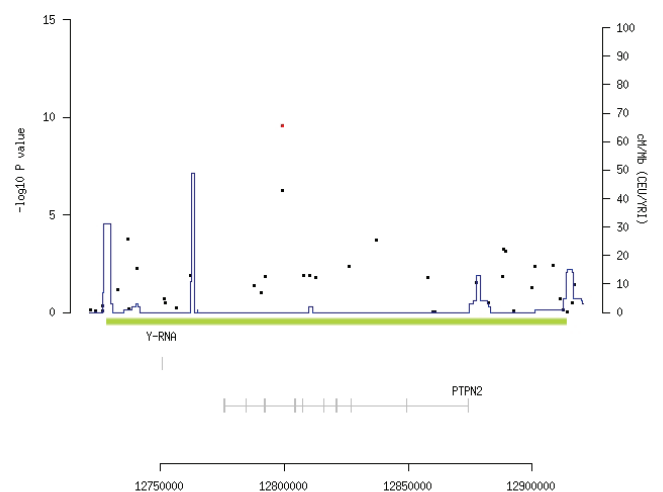
Chromosome 16



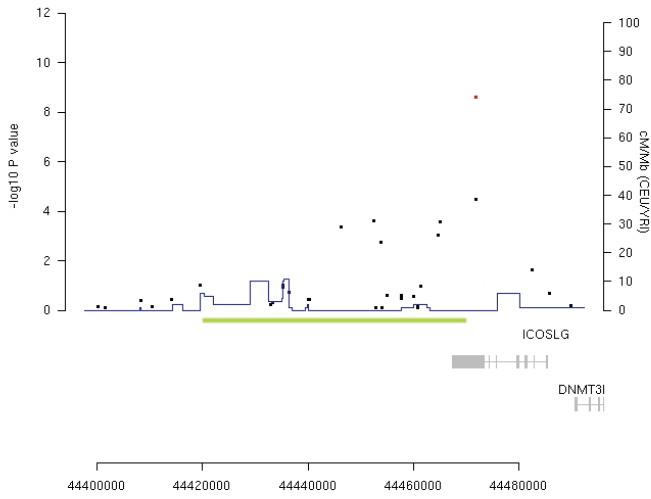
Chromosome 17



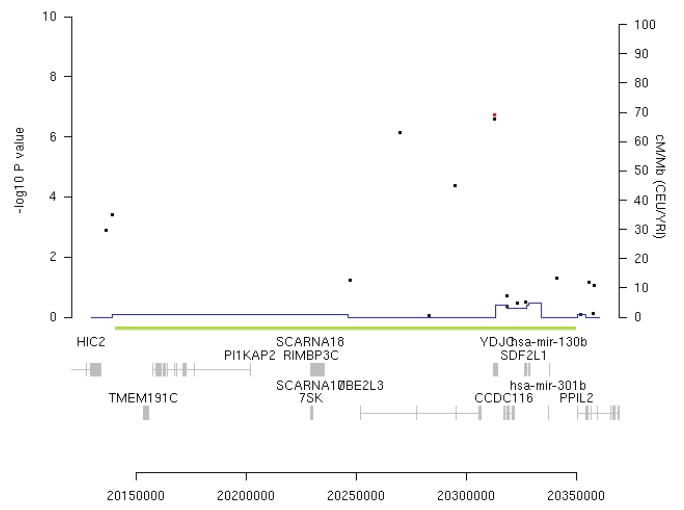
Chromosome 18



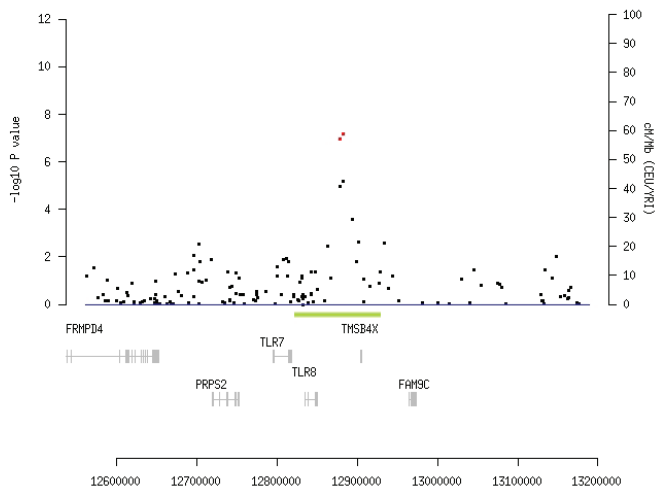
Chromosome 21



Chromosome 22



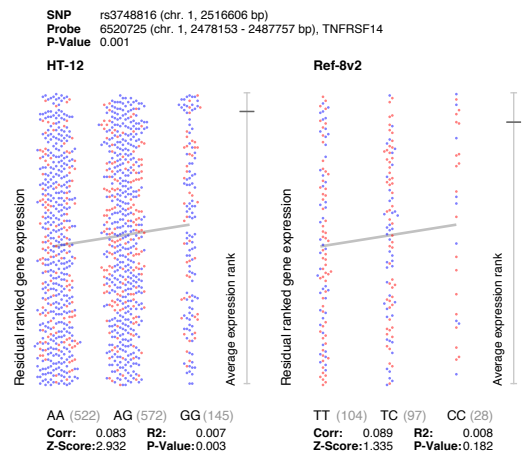
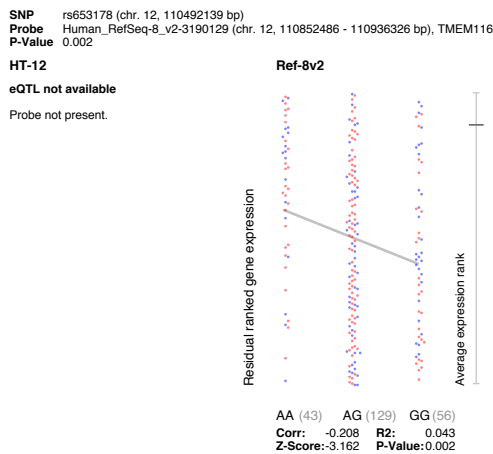
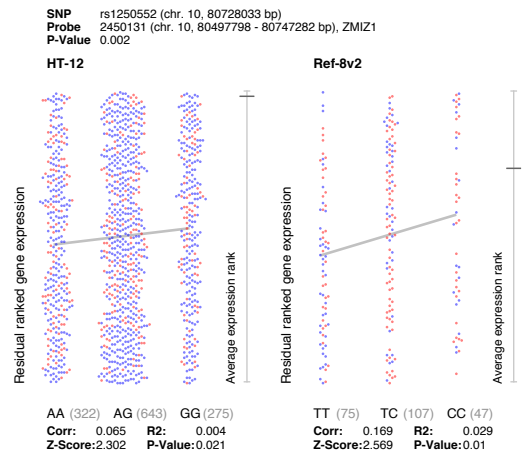
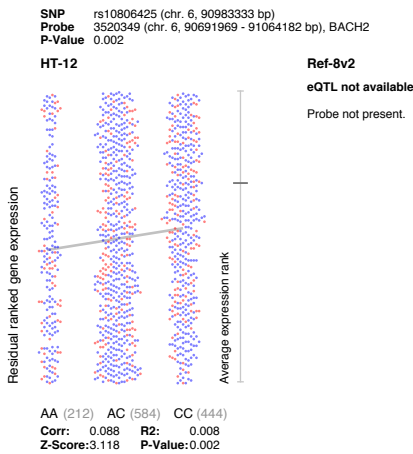
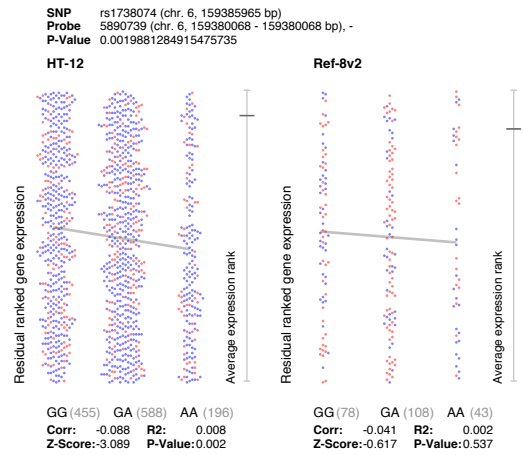
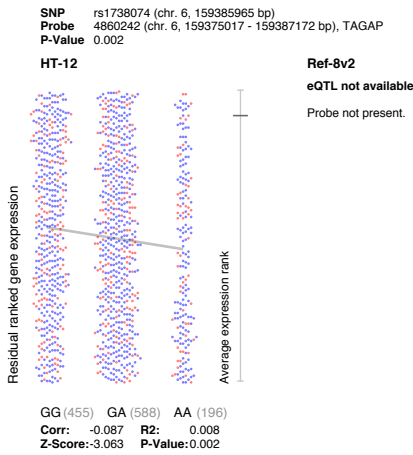
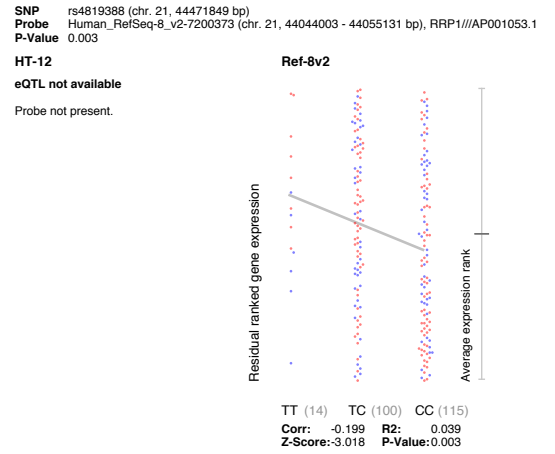
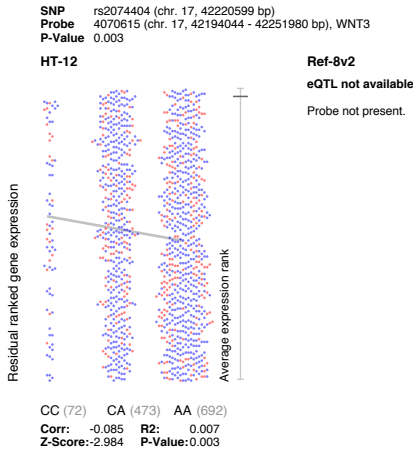
Chromosome X



Supplementary Figure 2 Detailed eQTL genotype - expression correlation analyses.

Individual level gene expression data (residual variance after Transcriptional Components removed) from 1469 PAXgene samples. Spearman Rank Correlation coefficients and *P* values shown for HT-12 and Ref8 data, and meta-analysis results. Right Y axis, average expression rank, is a measure of how strongly the tested probe is expressed amongst all probes in the dataset. eQTL plots are presented in descending *P* value order.

● Females
● Males



● Females

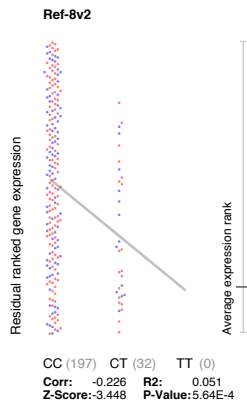
● Males

SNP rs13098911 (chr. 3, 46210205 bp)
Probe Human_RefSeq-8_v2-7570670 (chr. 3, 46226186 - 46284166 bp), CCR3
P-Value 5.69E-4

HT-12

eQTL not available

Probe not present.

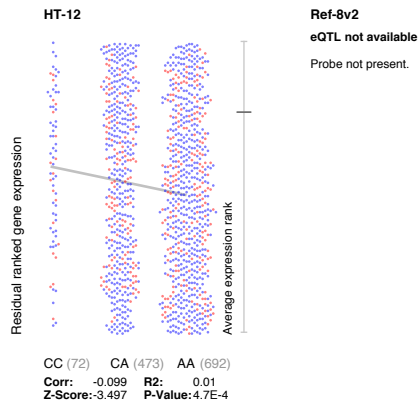


SNP rs2074404 (chr. 17, 42220599 bp)
Probe 1410484 (chr. 17, 42022391 - 42191000 bp), NSF
P-Value 4.28E-4

HT-12

eQTL not available

Probe not present.

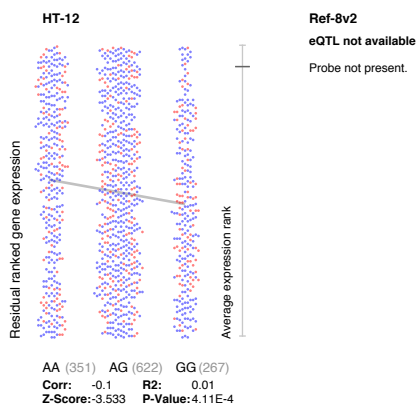


SNP rs653178 (chr. 12, 110492139 bp)
Probe 2070736 (chr. 12, 110852486 - 110933626 bp), TMEM116
P-Value 3.68E-4

HT-12

eQTL not available

Probe not present.

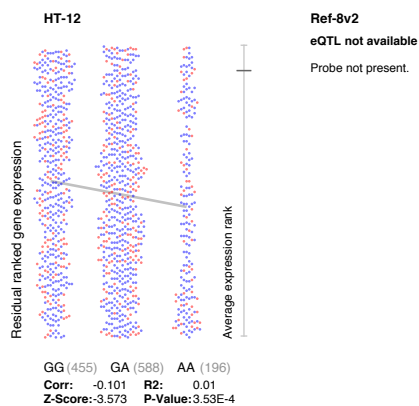


SNP rs1738074 (chr. 6, 159385965 bp)
Probe 5360364 (chr. 6, 159375017 - 159387172 bp), TAGAP
P-Value 3.23E-4

HT-12

eQTL not available

Probe not present.

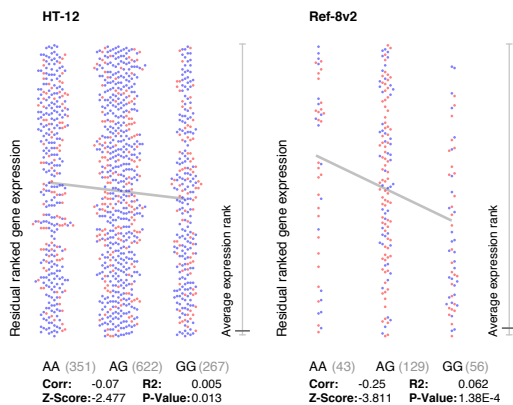


SNP rs653178 (chr. 12, 110492139 bp)
Probe 840253 (chr. 12, 110687729 - 110733165 bp), ALDH2
P-Value 1.44E-4

HT-12

eQTL not available

Probe not present.

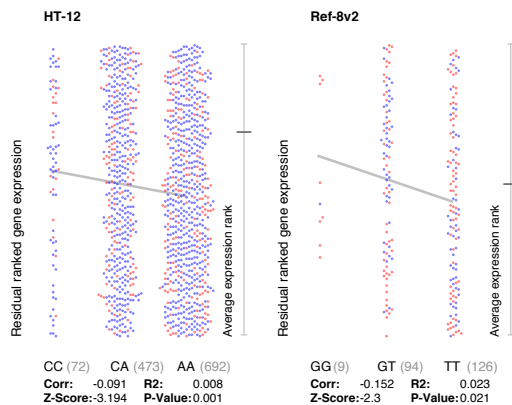


SNP rs2074404 (chr. 17, 42220599 bp)
Probe 3520572 (chr. 17, 41796319 - 41852371 bp), ARL17//LRRC37A//LRRC37A2
P-Value 1.17E-4

HT-12

eQTL not available

Probe not present.

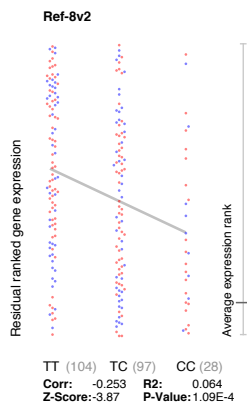


SNP rs3748816 (chr. 1, 2516606 bp)
Probe Human_RefSeq-8_v2-6250338 (chr. 1, 2507097 - 2513762 bp), C1orf93
P-Value 1.16E-4

HT-12

eQTL not available

Probe not present.

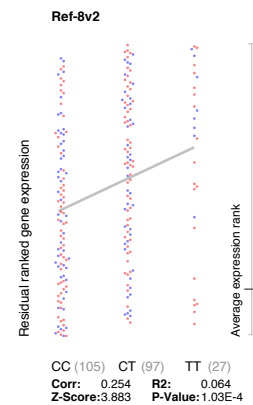


SNP rs6441961 (chr. 3, 46327388 bp)
Probe Human_RefSeq-8_v2-7570670 (chr. 3, 46226186 - 46284166 bp), CCR3
P-Value 1.02E-4

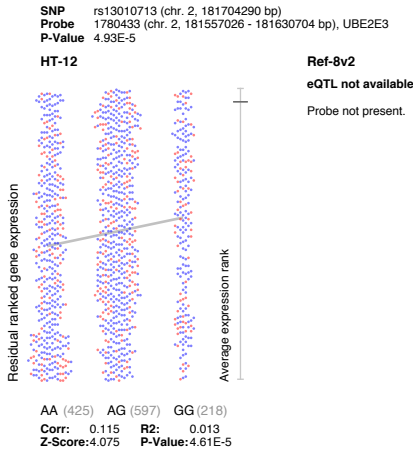
HT-12

eQTL not available

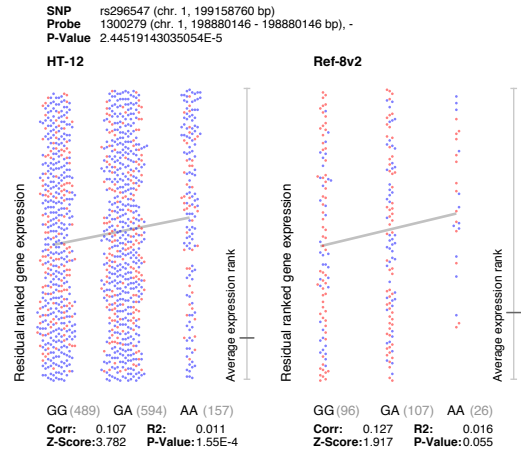
Probe not present.



● Females
● Males



Ref-8v2
eQTL not available
Probe not present.

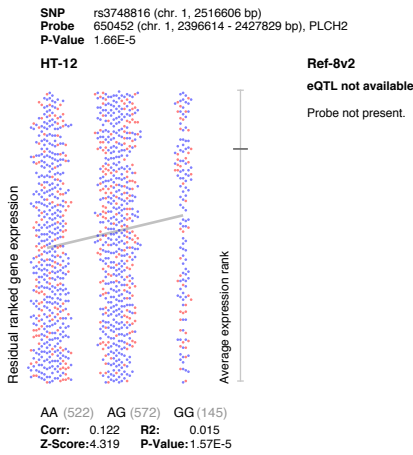


Ref-8v2

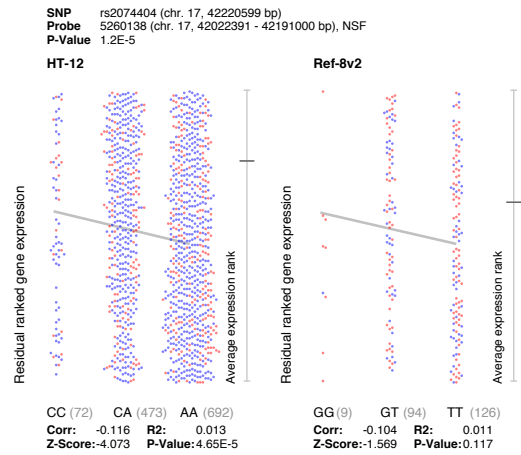
Residual ranked gene expression

Average expression rank

GG (96) GA (107) AA (26)
Corr: 0.127 R2: 0.016
Z-Score:1.917 P-Value:0.055



Ref-8v2
eQTL not available
Probe not present.

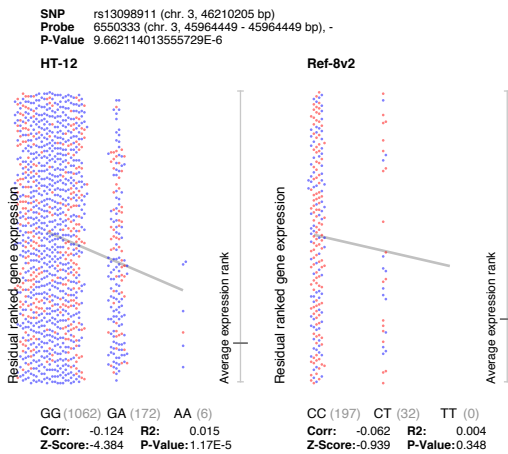


Ref-8v2

Residual ranked gene expression

Average expression rank

GG (9) GT (94) TT (126)
Corr: -0.104 R2: 0.011
Z-Score:-1.569 P-Value:0.117

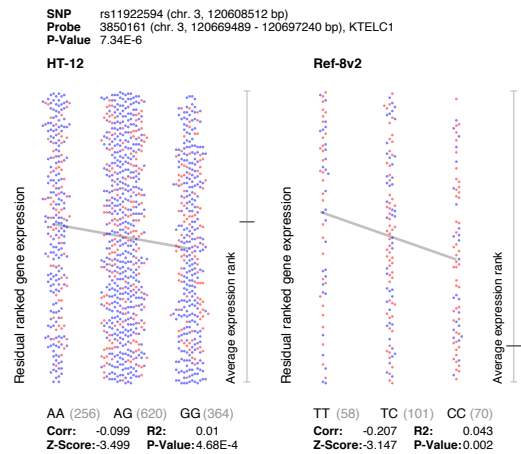


Ref-8v2

Residual ranked gene expression

Average expression rank

CC (197) CT (32) TT (0)
Corr: -0.062 R2: 0.004
Z-Score:-0.939 P-Value:0.348

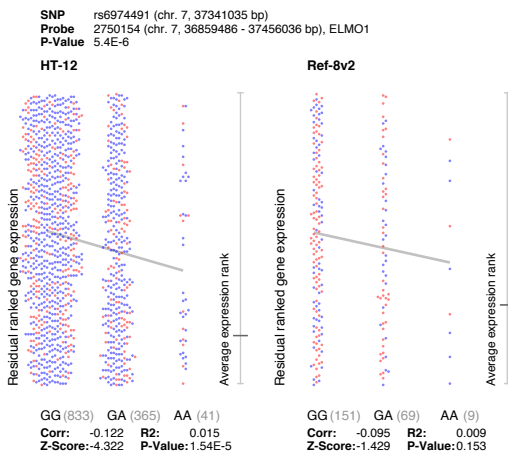


Ref-8v2

Residual ranked gene expression

Average expression rank

TT (58) TC (101) CC (70)
Corr: -0.207 R2: 0.043
Z-Score:-3.147 P-Value:0.002

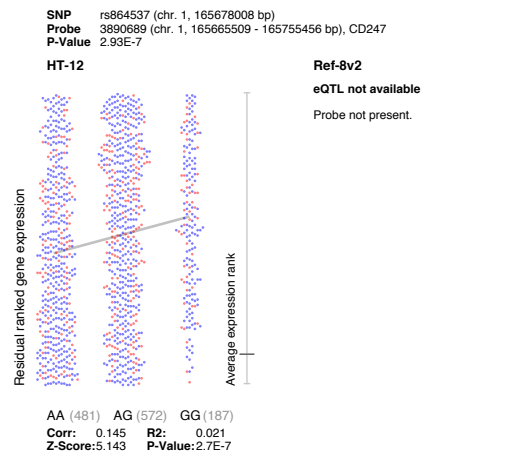


Ref-8v2

Residual ranked gene expression

Average expression rank

GG (151) GA (69) AA (9)
Corr: -0.095 R2: 0.009
Z-Score:-1.429 P-Value:0.153



Ref-8v2
eQTL not available
Probe not present.

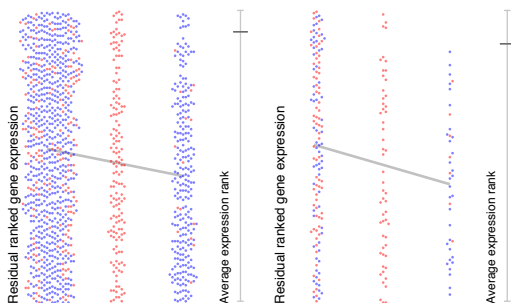
● Females

● Males

SNP rs5979785 (chr. 23, 12881445 bp)
 Probe 3390612 (chr. 23, 12833679 - 12852209 bp), TLR8
 P-Value 1.07E-7

HT-12

Ref-8v2



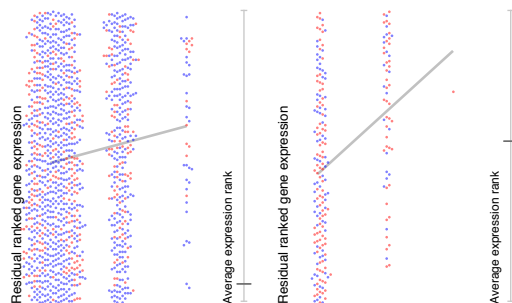
AA (826) AG (155) GG (259)
 Corr: -0.132 R2: 0.017
 Z-Score:-4.663 P-Value:3.12E-6

TT (136) TC (55) CC (38)
 Corr: -0.173 R2: 0.03
 Z-Score:-2.617 P-Value:0.009

SNP rs12928822 (chr. 16, 11311394 bp)
 Probe 4540072 (chr. 16, 11317137 - 11354118 bp), AC009121.6
 P-Value 1.02E-8

HT-12

Ref-8v2



GG (865) GA (334) AA (41)
 Corr: 0.115 R2: 0.013
 Z-Score:4.063 P-Value:4.85E-5

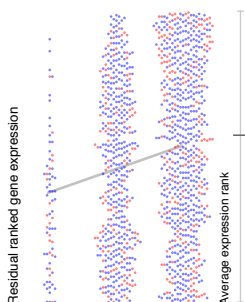
CC (167) CT (61) TT (1)
 Corr: 0.327 R2: 0.107
 Z-Score:5.065 P-Value:4.09E-7

SNP rs2074404 (chr. 17, 42220599 bp)
 Probe 4880037 (chr. 17, 42485154 - 42485154 bp), -
 P-Value 1.7789864987600641E-9

HT-12

Ref-8v2

eQTL not available
 Probe not present.



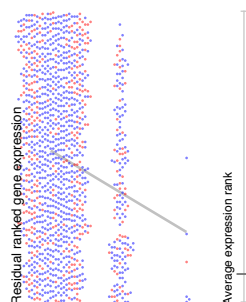
CC (72) CA (473) AA (692)
 Corr: 0.17 R2: 0.029
 Z-Score:6.034 P-Value:1.6E-9

SNP rs13098911 (chr. 3, 46210205 bp)
 Probe 2190671 (chr. 3, 46226186 - 46284166 bp), CCR3
 P-Value 5.5E-10

HT-12

Ref-8v2

eQTL not available
 Probe not present.

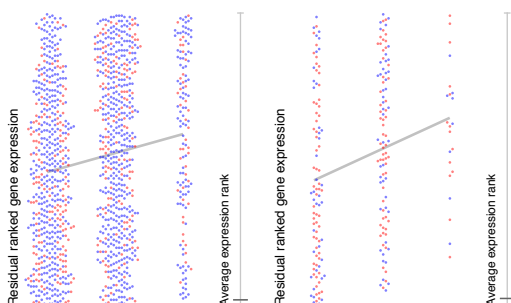


GG (1062) GA (172) AA (6)
 Corr: -0.174 R2: 0.03
 Z-Score:-6.18 P-Value:6.4E-10

SNP rs842647 (chr. 2, 60972975 bp)
 Probe 1170220 (chr. 2, 61257057 - 61270564 bp), AHS2
 P-Value 3.3E-10

HT-12

Ref-8v2



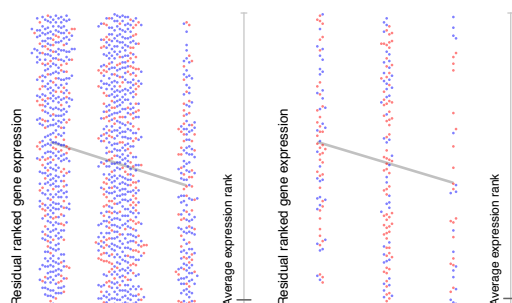
AA (542) AG (557) GG (140)
 Corr: 0.151 R2: 0.023
 Z-Score:5.328 P-Value:9.91E-8

AA (101) AG (106) GG (22)
 Corr: 0.235 R2: 0.055
 Z-Score:3.582 P-Value:3.41E-4

SNP rs13003464 (chr. 2, 61040333 bp)
 Probe 1170220 (chr. 2, 61257057 - 61270564 bp), AHS2
 P-Value 6.39E-11

HT-12

Ref-8v2



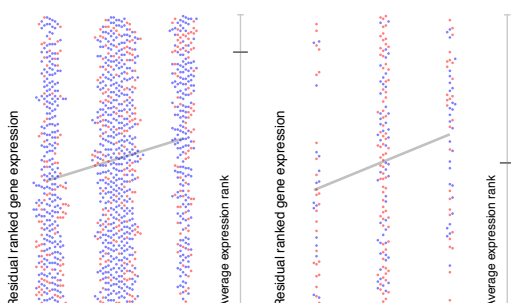
AA (452) AG (611) GG (176)
 Corr: -0.17 R2: 0.029
 Z-Score:-6.026 P-Value:1.68E-9

AA (75) AG (118) GG (36)
 Corr: -0.162 R2: 0.026
 Z-Score:-2.458 P-Value:0.014

SNP rs653178 (chr. 12, 110492139 bp)
 Probe 6560301 (chr. 12, 110350268 - 110448836 bp), SH2B3//ATXN2
 P-Value 9.24E-12

HT-12

Ref-8v2



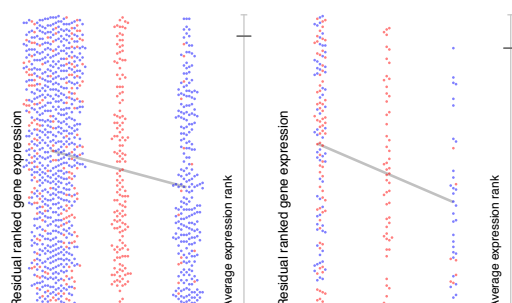
AA (351) AG (622) GG (267)
 Corr: 0.171 R2: 0.029
 Z-Score:6.057 P-Value:1.38E-9

AA (43) AG (129) GG (56)
 Corr: 0.215 R2: 0.046
 Z-Score:3.268 P-Value:0.001

SNP rs5979785 (chr. 23, 12881445 bp)
 Probe 6480360 (chr. 23, 12833679 - 12852209 bp), TLR8
 P-Value 3.88E-13

HT-12

Ref-8v2

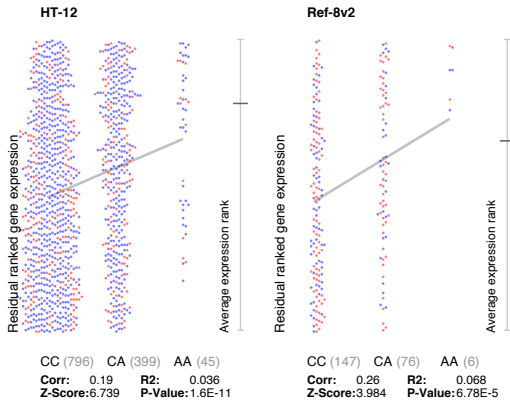


AA (826) AG (155) GG (259)
 Corr: -0.174 R2: 0.03
 Z-Score:-6.171 P-Value:6.79E-10

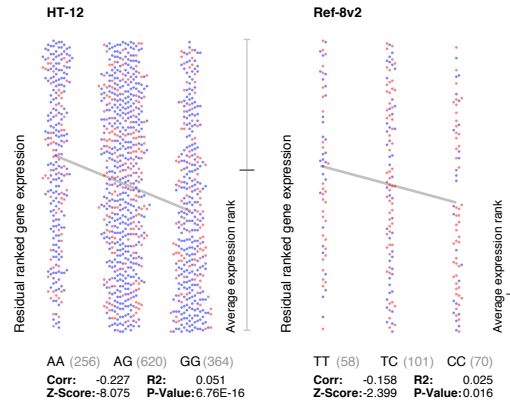
TT (136) TC (55) CC (38)
 Corr: -0.259 R2: 0.067
 Z-Score:-3.958 P-Value:7.55E-5

● Females
● Males

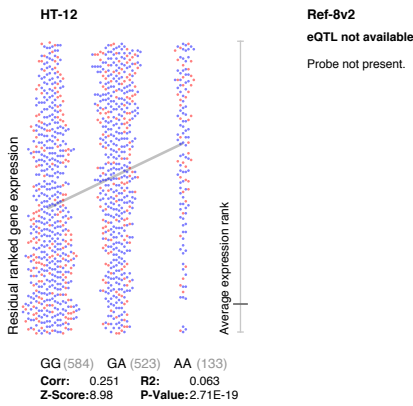
SNP rs12727642 (chr. 1, 7969259 bp)
Probe 610193 (chr. 1, 7943348 - 7968928 bp), PARK7
P-Value 9.76E-15



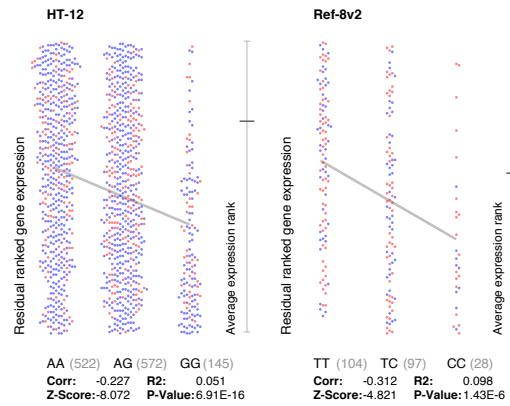
SNP rs11922594 (chr. 3, 120608512 bp)
Probe 6550288 (chr. 3, 120669489 - 120697240 bp), KTELC1
P-Value 5.09E-17



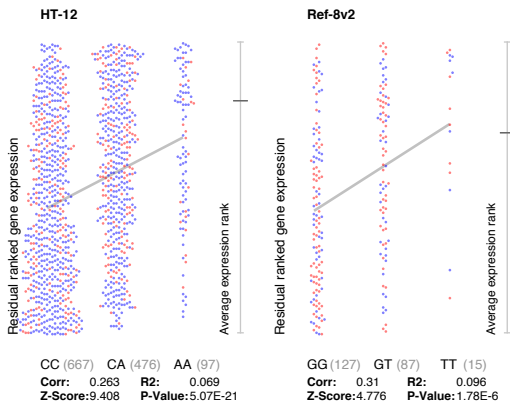
SNP rs6441961 (chr. 3, 46327388 bp)
Probe 2190671 (chr. 3, 46226186 - 46284166 bp), CCR3
P-Value 2.87E-19



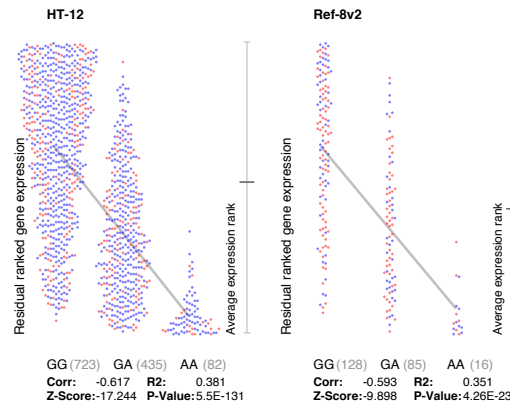
SNP rs3748816 (chr. 1, 2516606 bp)
Probe 2070246 (chr. 1, 2510941 - 2555289 bp), MMEL1
P-Value 1.03E-20



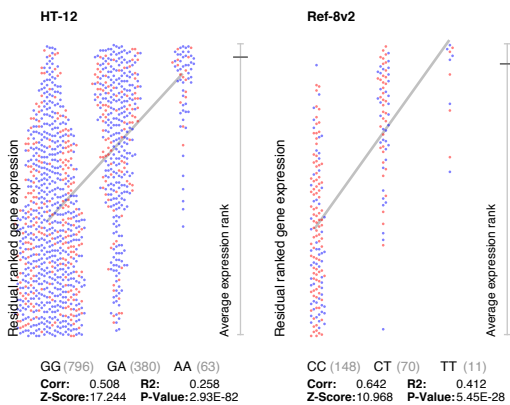
SNP rs3816281 (chr. 2, 68461451 bp)
Probe 4810020 (chr. 2, 68444826 - 68479088 bp), PLEK
P-Value 7.97E-26



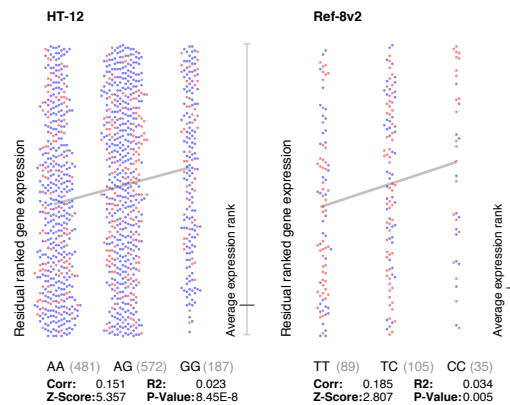
SNP rs917997 (chr. 2, 102437000 bp)
Probe 6520180 (chr. 2, 102400686 - 102436457 bp), IL18RAP
P-Value 7.35E-87



SNP rs2298428 (chr. 22, 20312892 bp)
Probe 1230242 (chr. 22, 20308188 - 20308188 bp), -
P-Value 1.955586158829425E-90



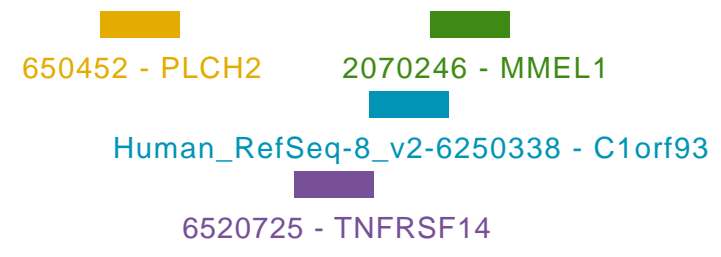
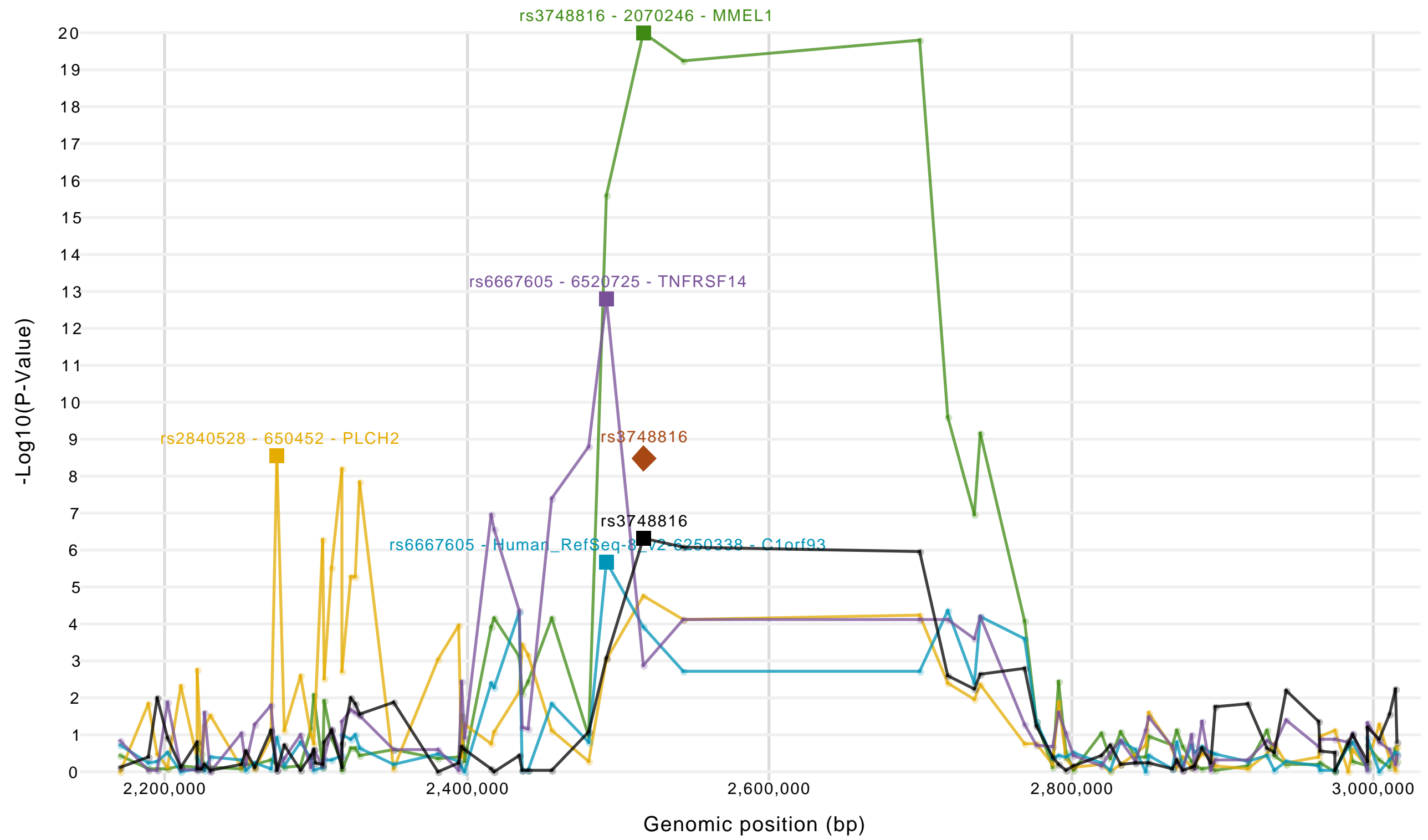
SNP rs864537 (chr. 1, 165678008 bp)
Probe 6290400 (chr. 1, 165665509 - 165755456 bp), CD247
P-Value 1.77E-9



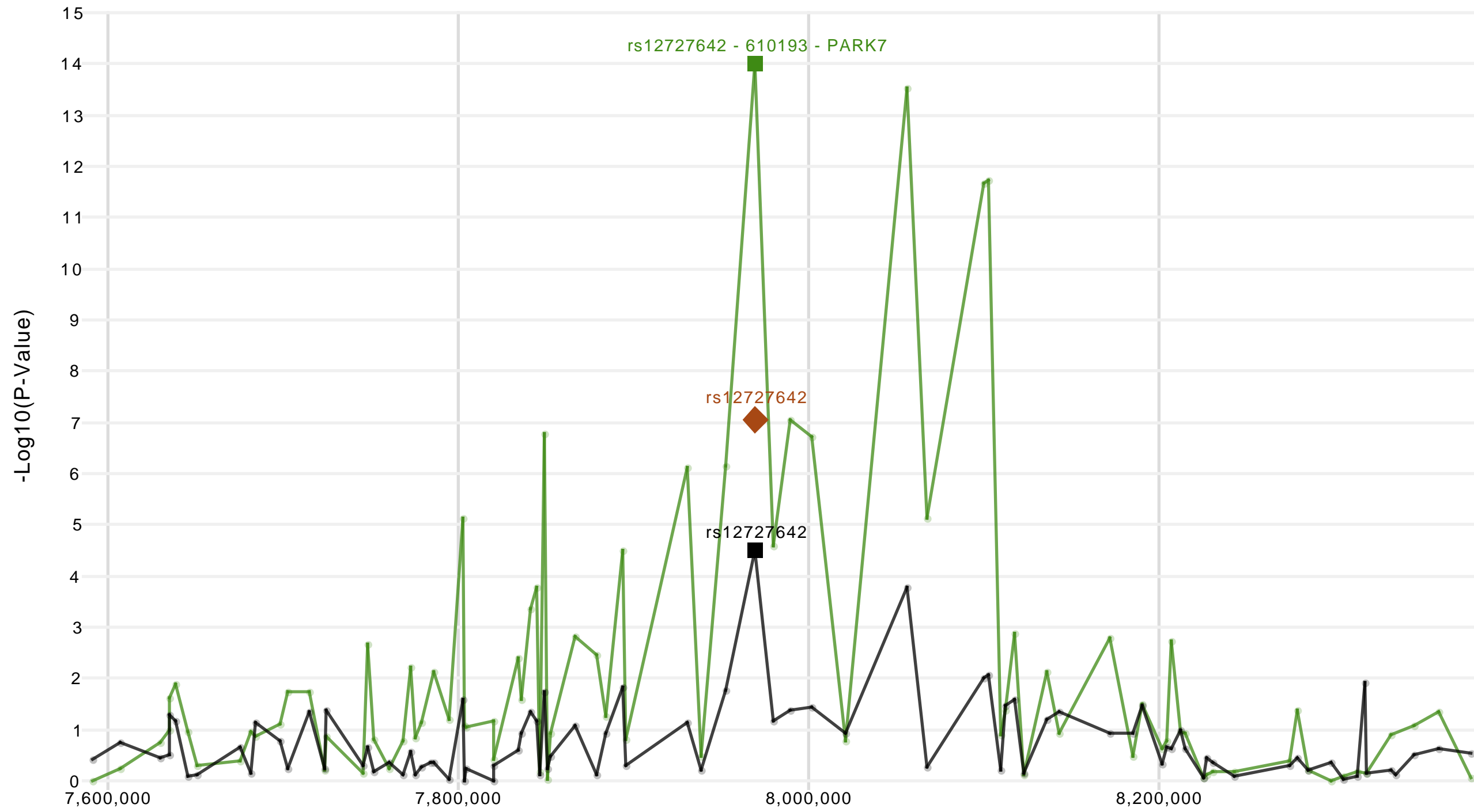
Supplementary Figure 3 Co-localisation of case/control association and genotype-expression correlation (eQTL) signals.

Plots shown for regions described in Table 3. Chromosomal positions based on NCBI Build 36 co-ordinates. P_{GWAS} values (black points and black line) are from 4,533 cases and 10,750 controls. P_{combined} values (red points) are from 9,451 cases and 16,434 controls. Genotype-expression correlation P values for SNP positions across the genome at each tested eQTL are shown in a different colour for each probe (annotated with Illumina ArrayAddressID and gene name).

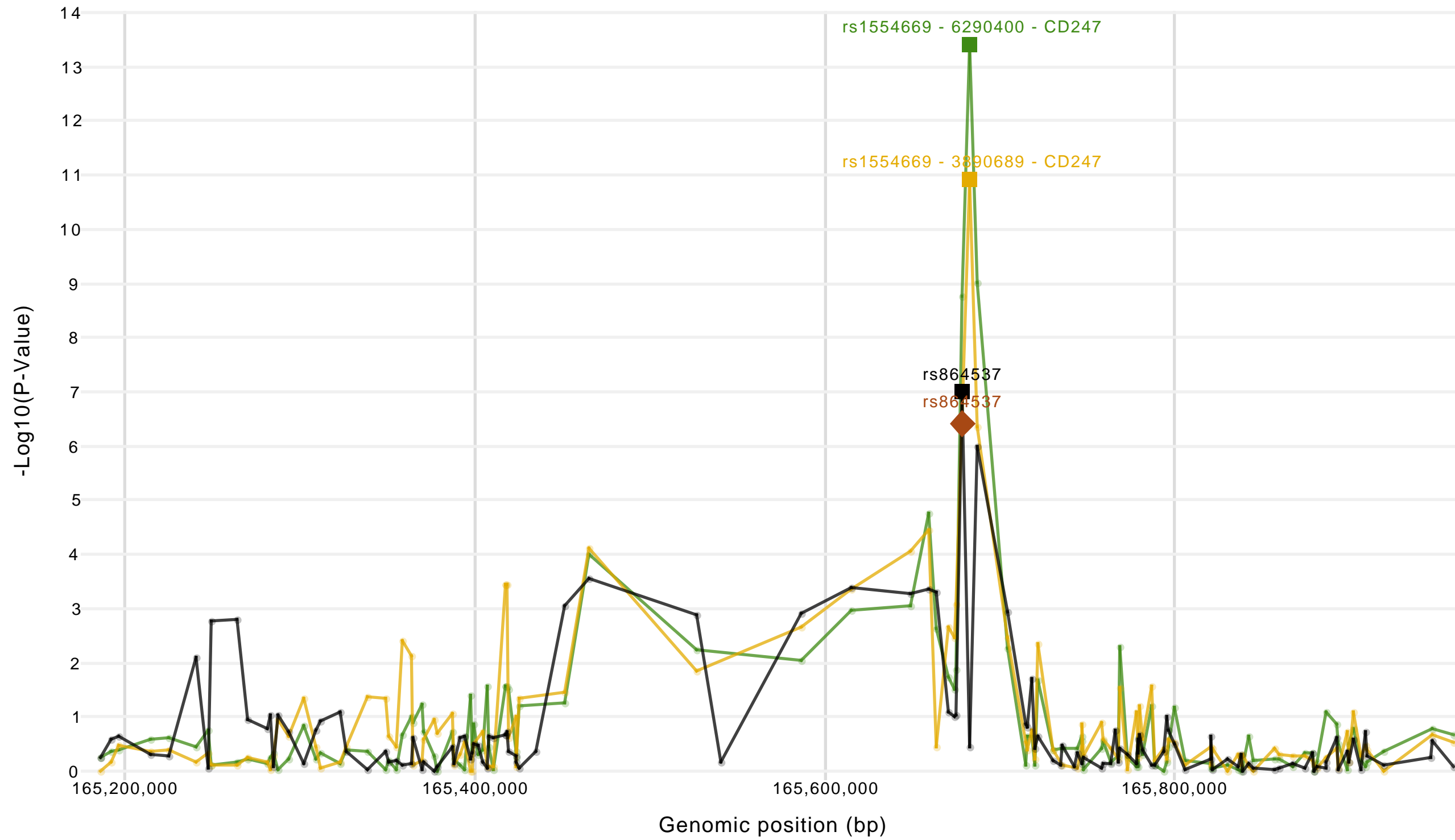
Chromosome 1



Chromosome 1

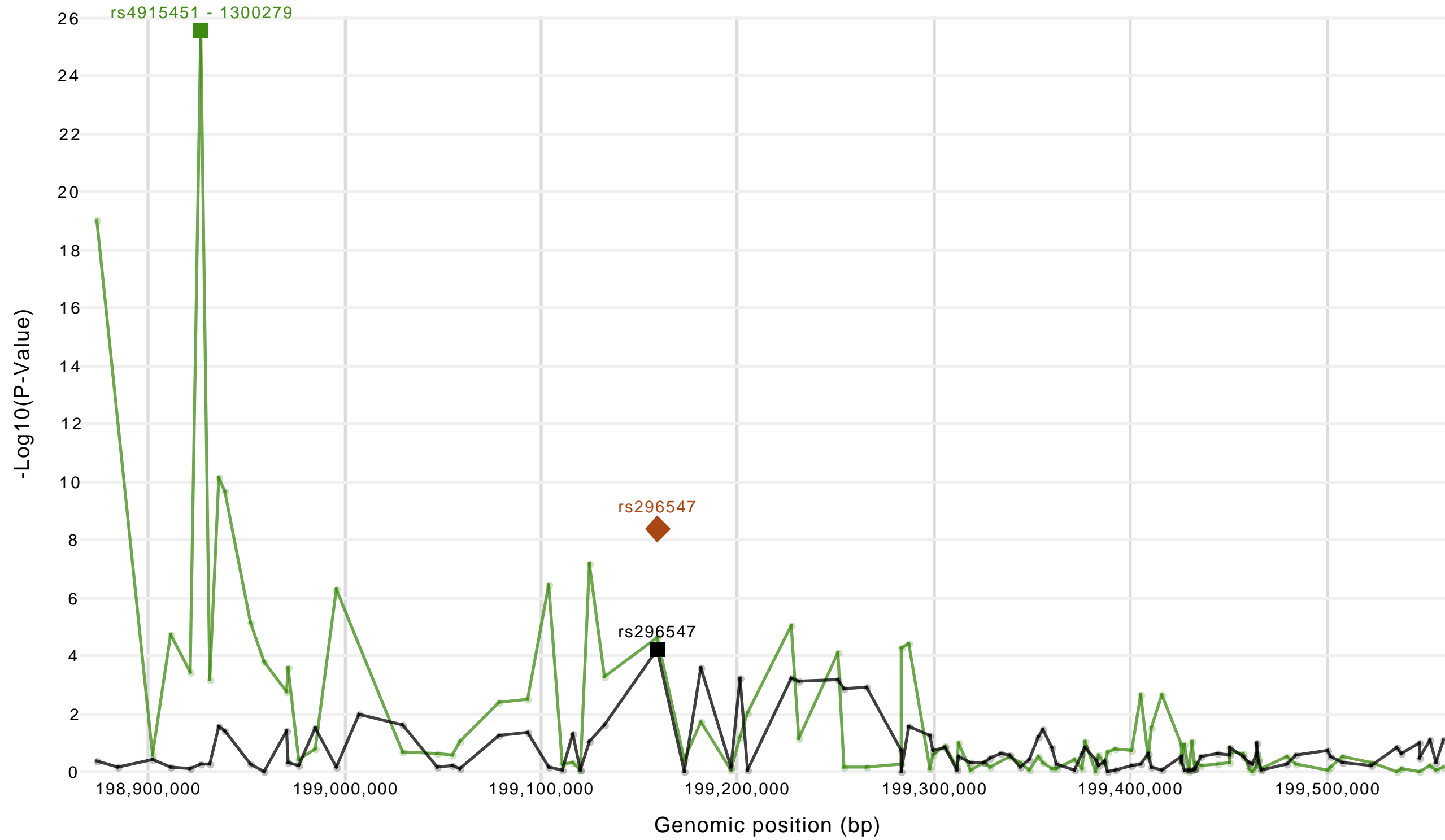


Chromosome 1



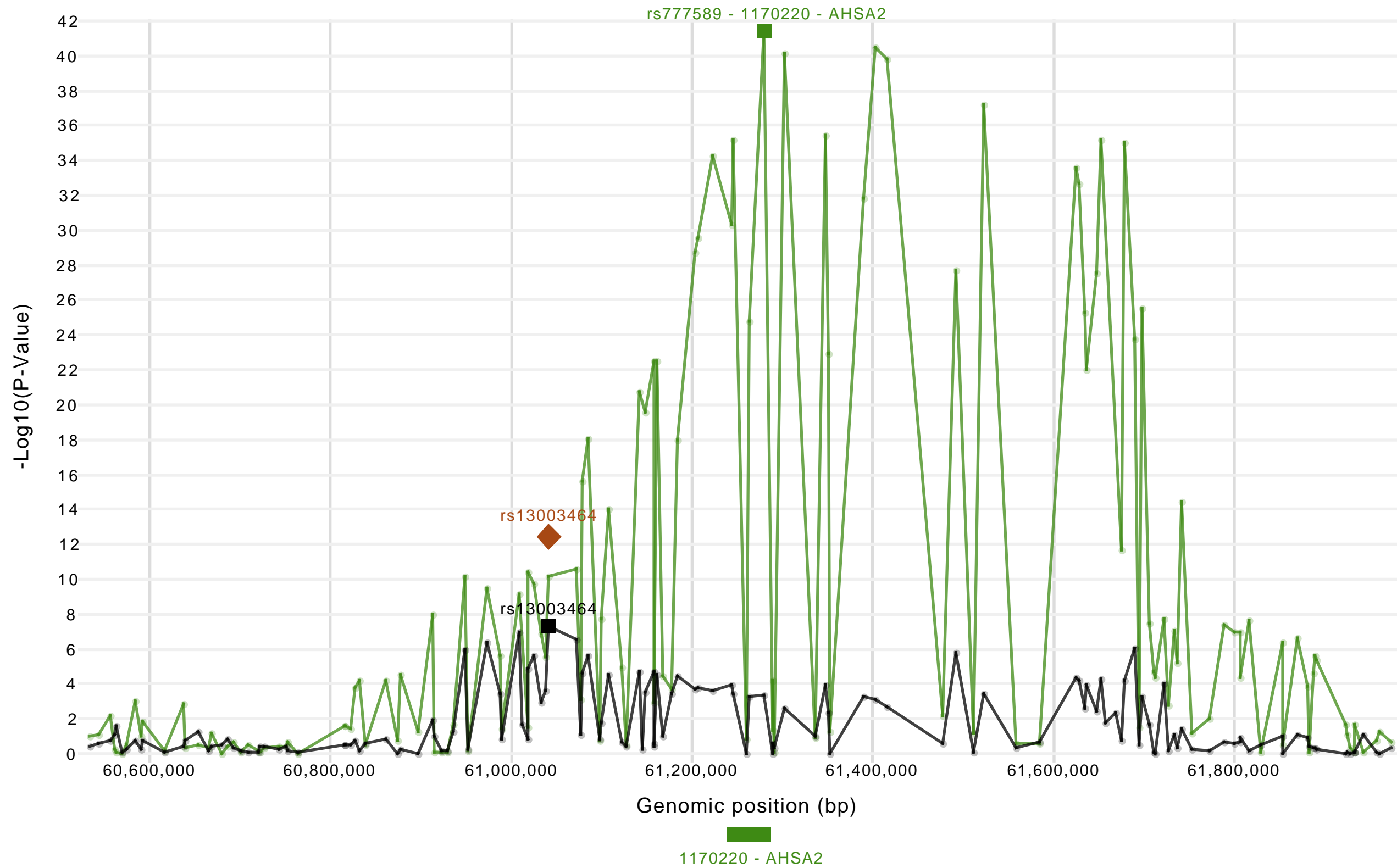
6290400 - CD247
3890689 - CD247

Chromosome 1

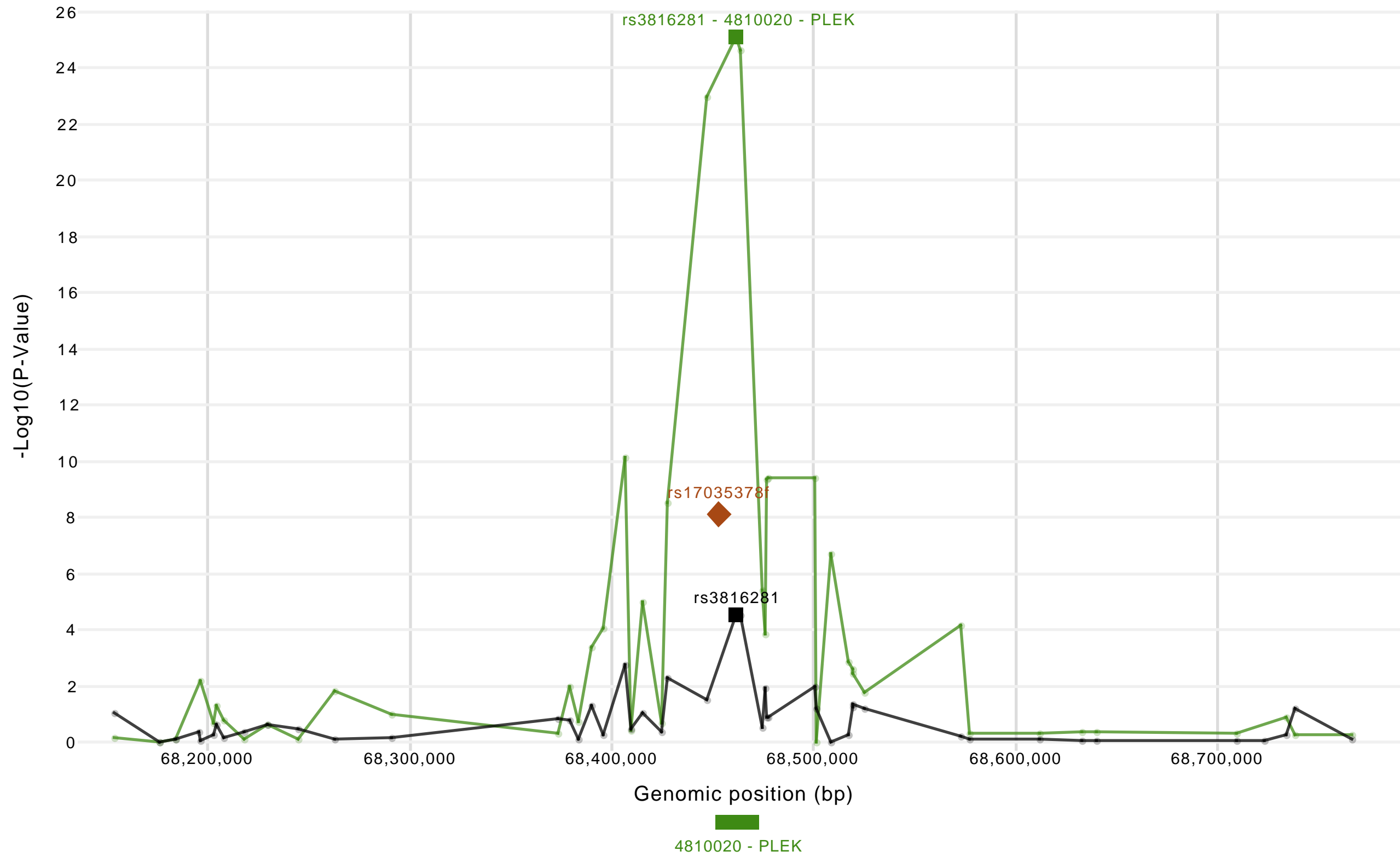


1300279

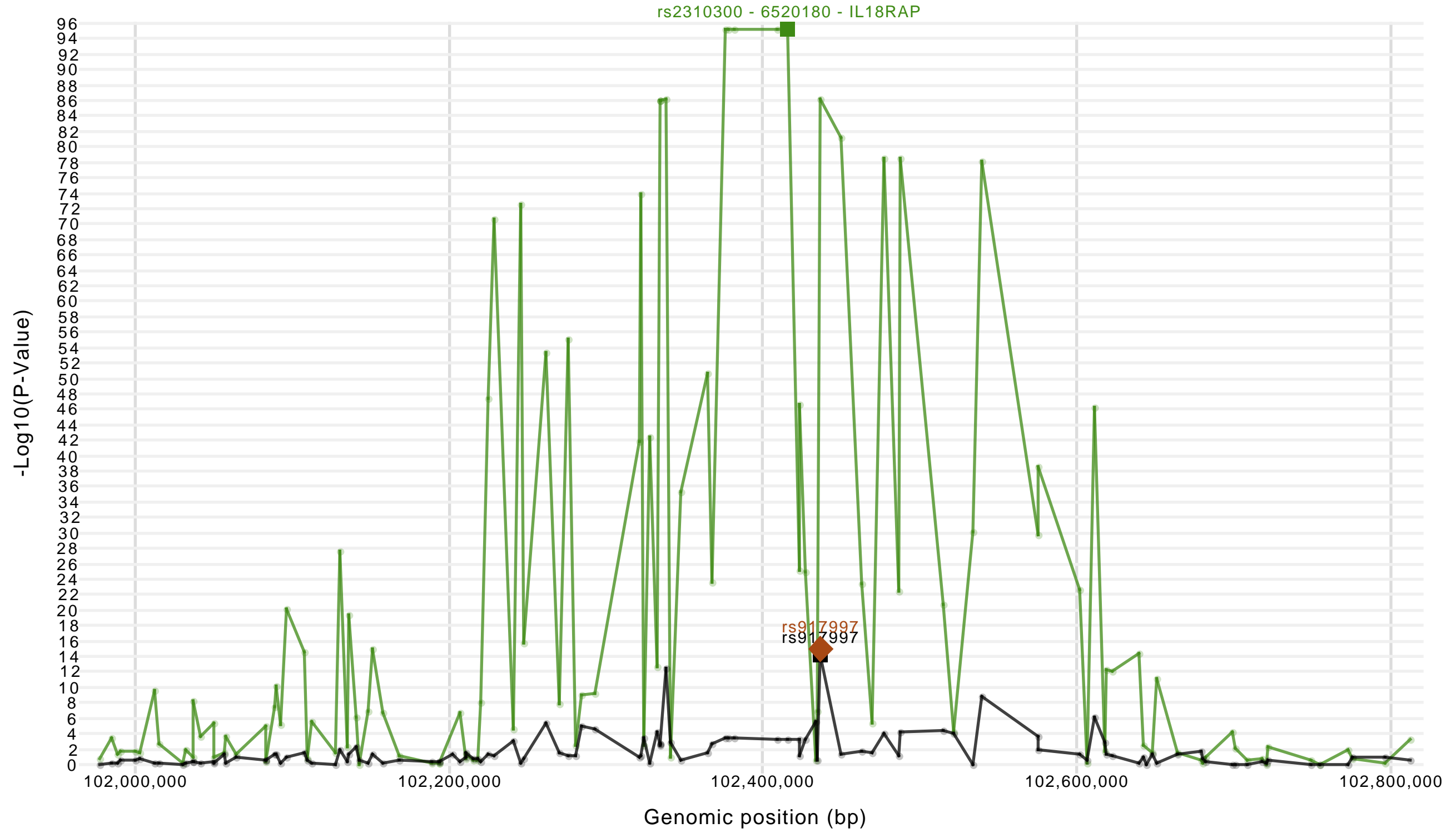
Chromosome 2



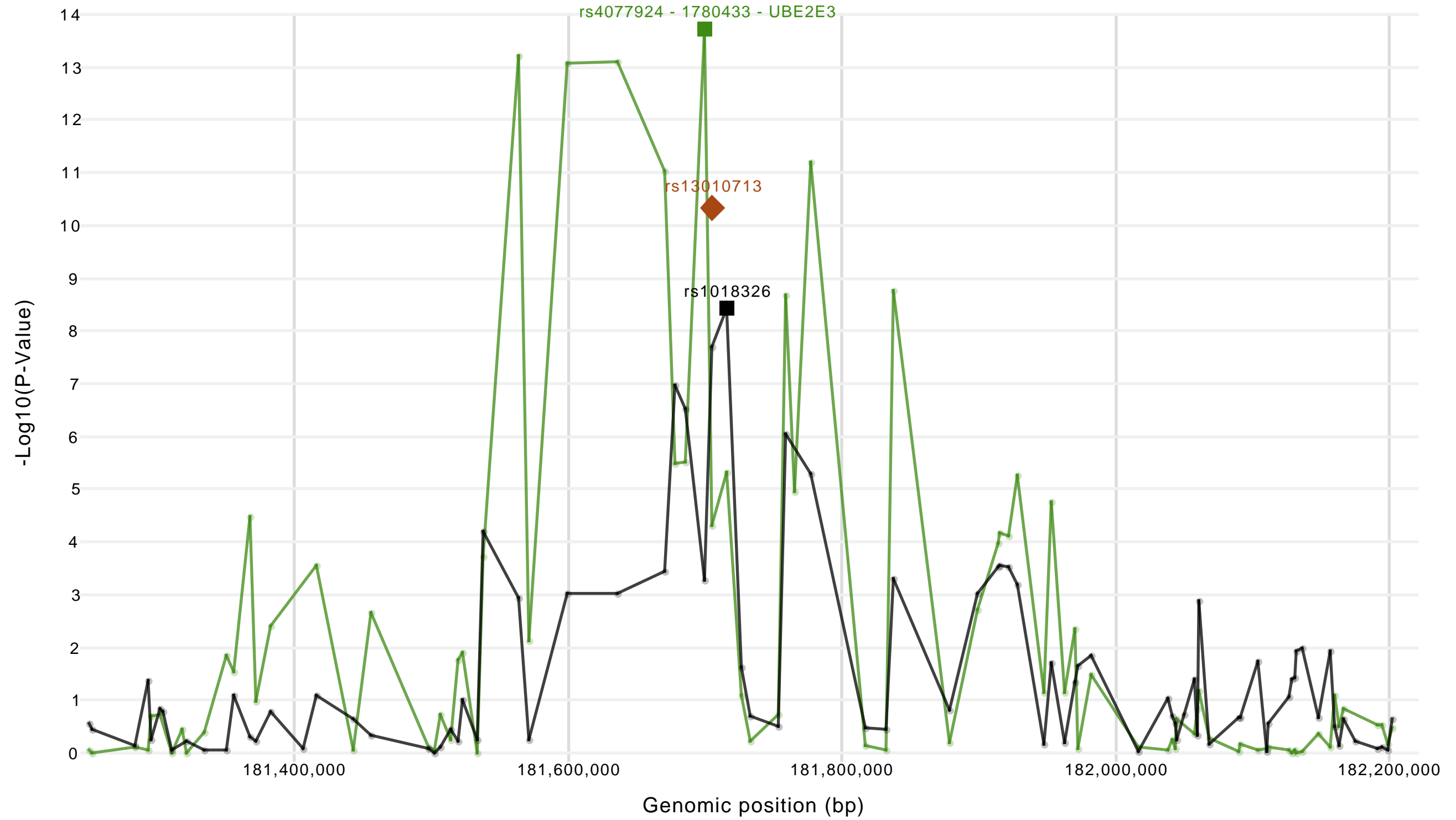
Chromosome 2



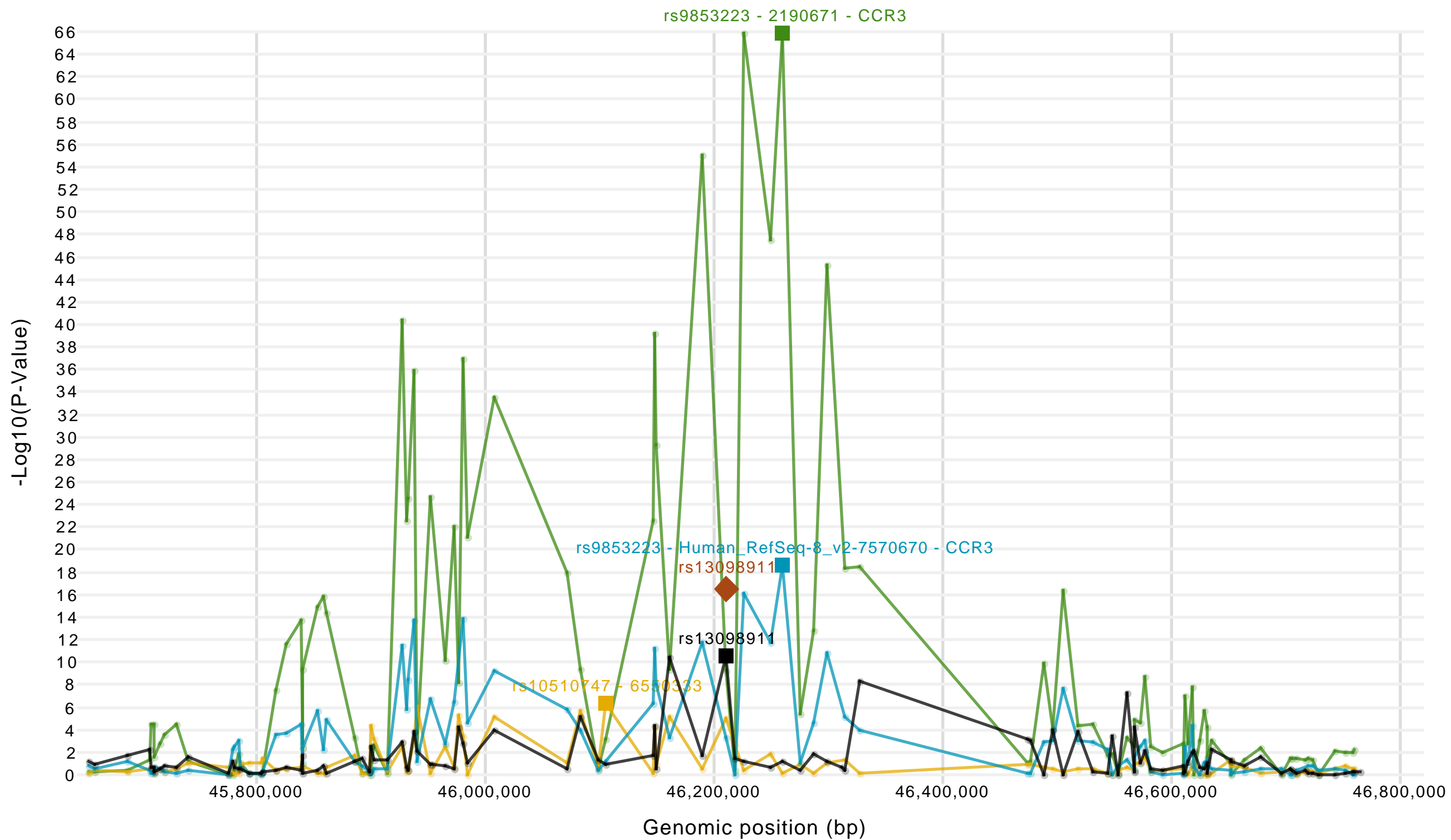
Chromosome 2



Chromosome 2



Chromosome 3

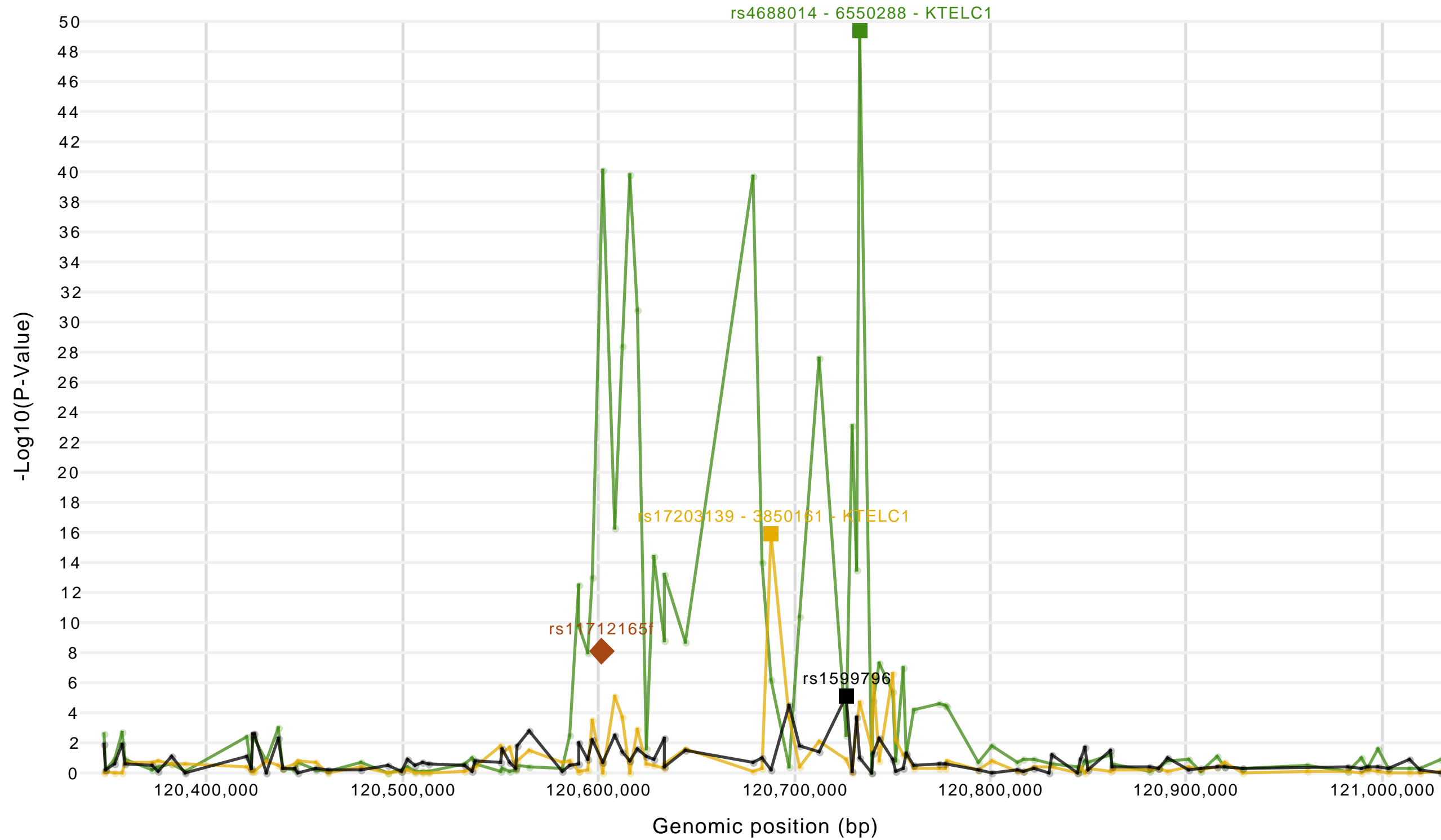


6550333

2190671 - CCR3

Human_RefSeq-8_v2-7570670 - CCR3

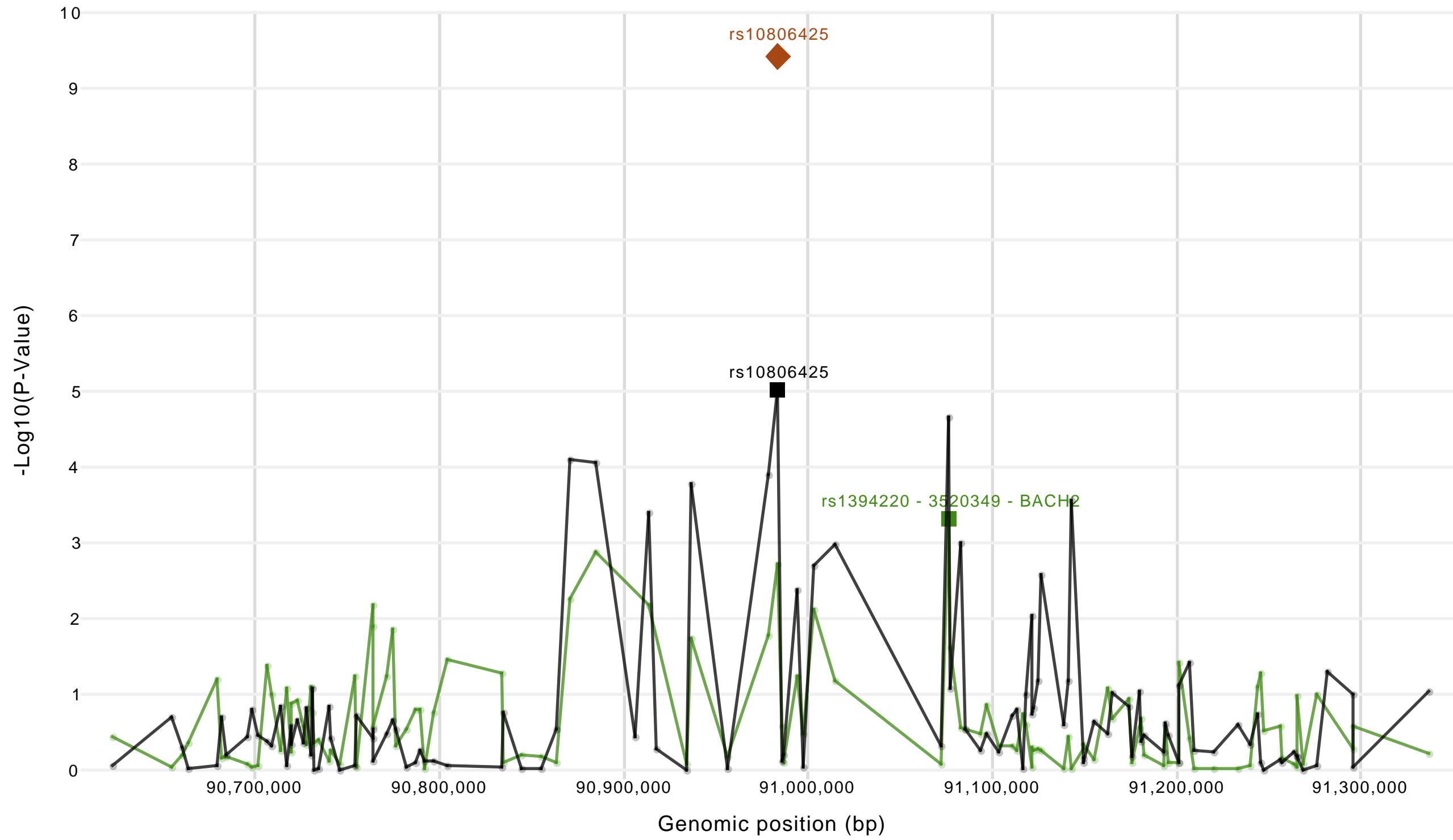
Chromosome 3



Genomic position (bp)

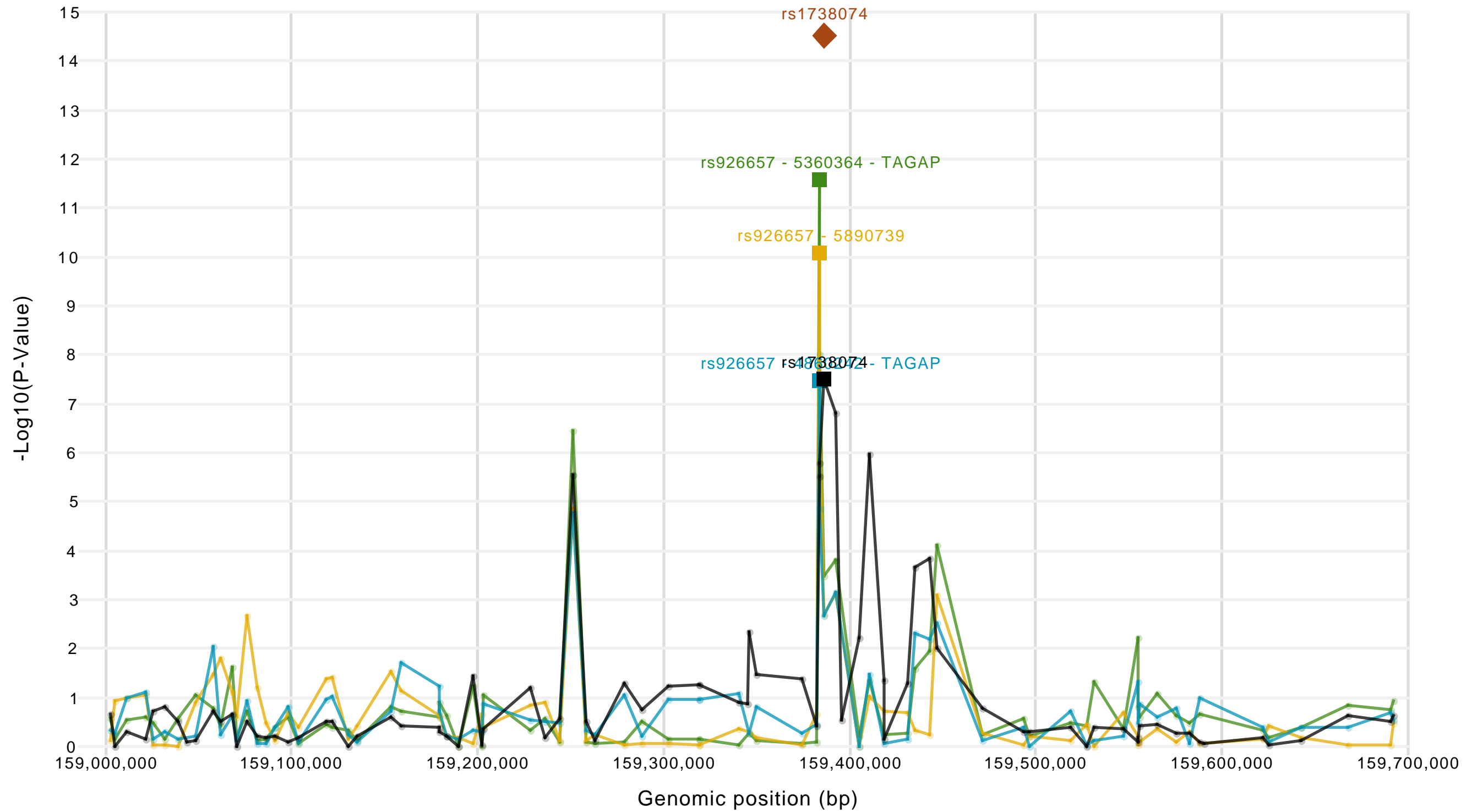
6550288 - KTELC1
3850161 - KTELC1

Chromosome 6



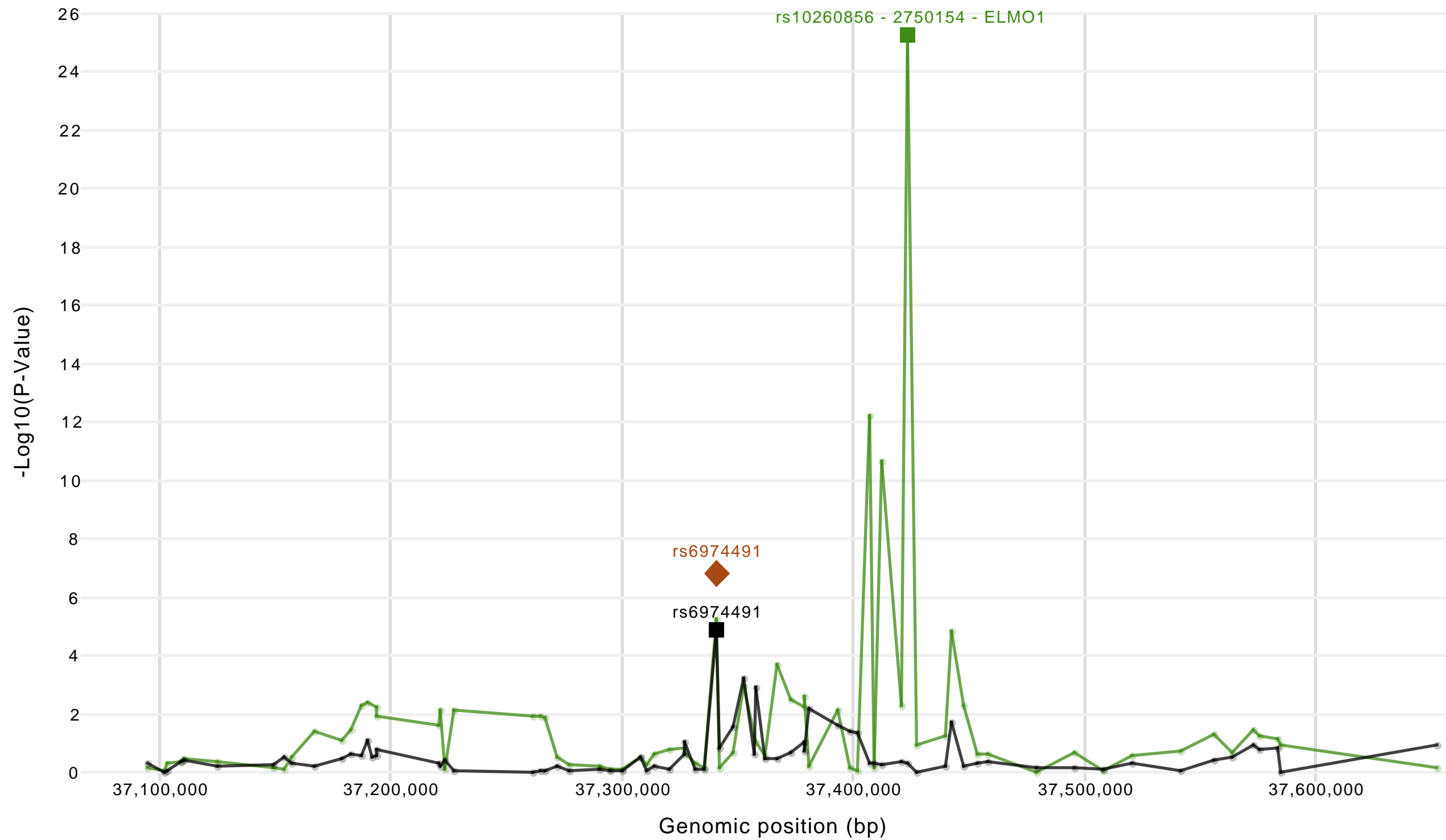
3520349 - BACH2

Chromosome 6



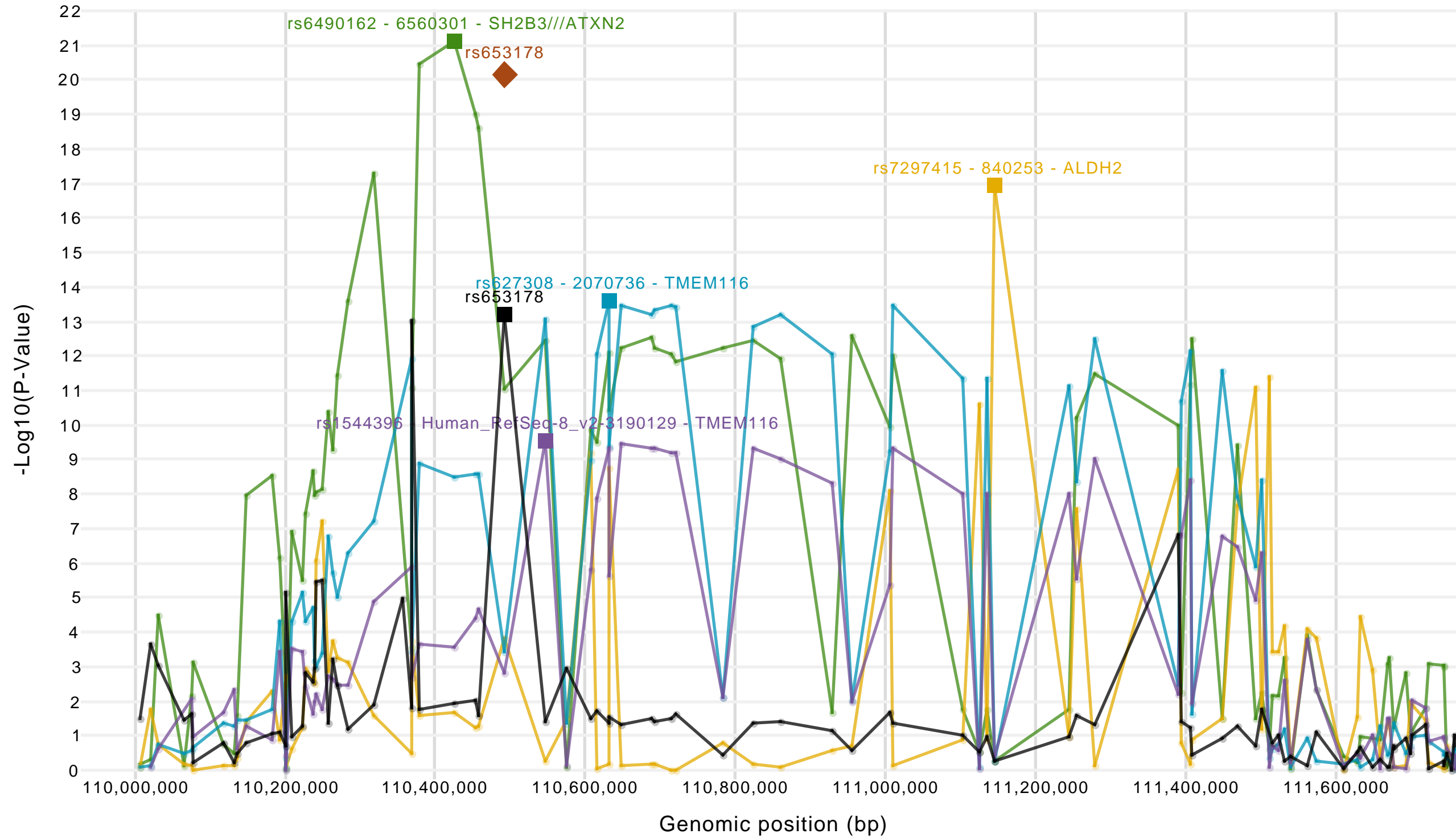
■
5360364 - TAGAP
■
5890739
■
4860242 - TAGAP

Chromosome 7



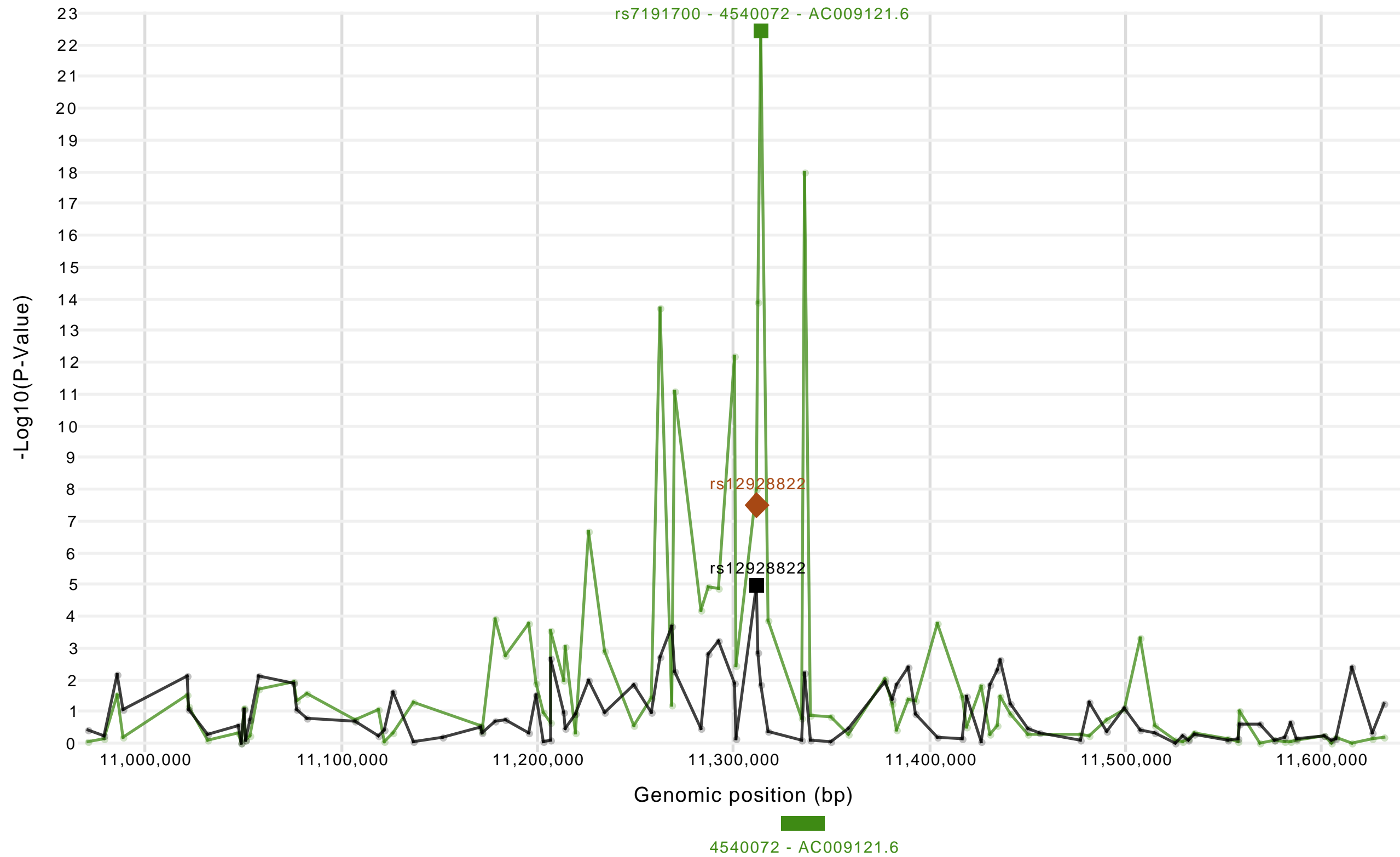
2750154 - ELMO1

Chromosome 12

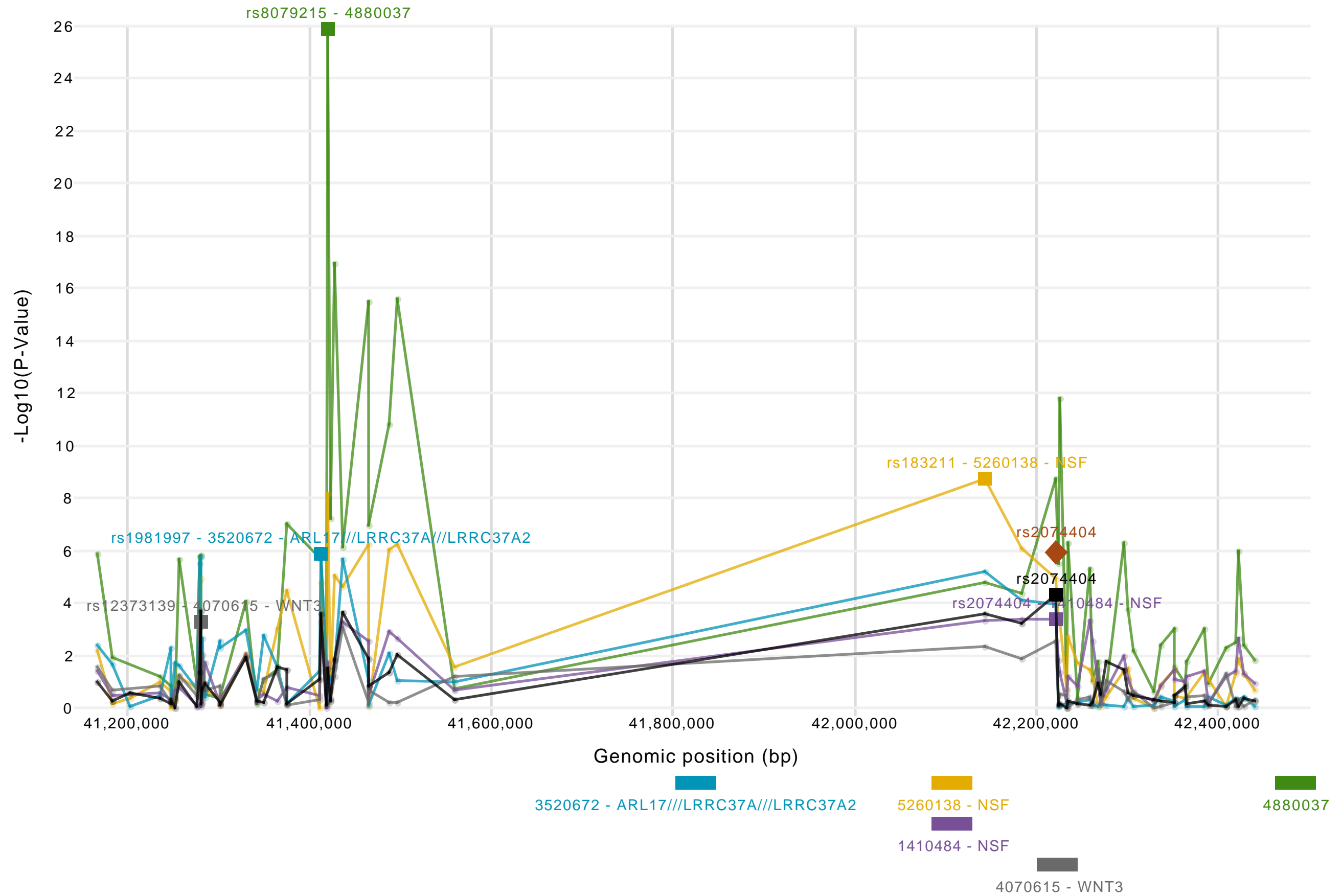


6560301 - SH2B3///ATXN2 840253 - ALDH2 2070736 - TMEM116
Human_RefSeq-8_v2-3190129 - TMEM116

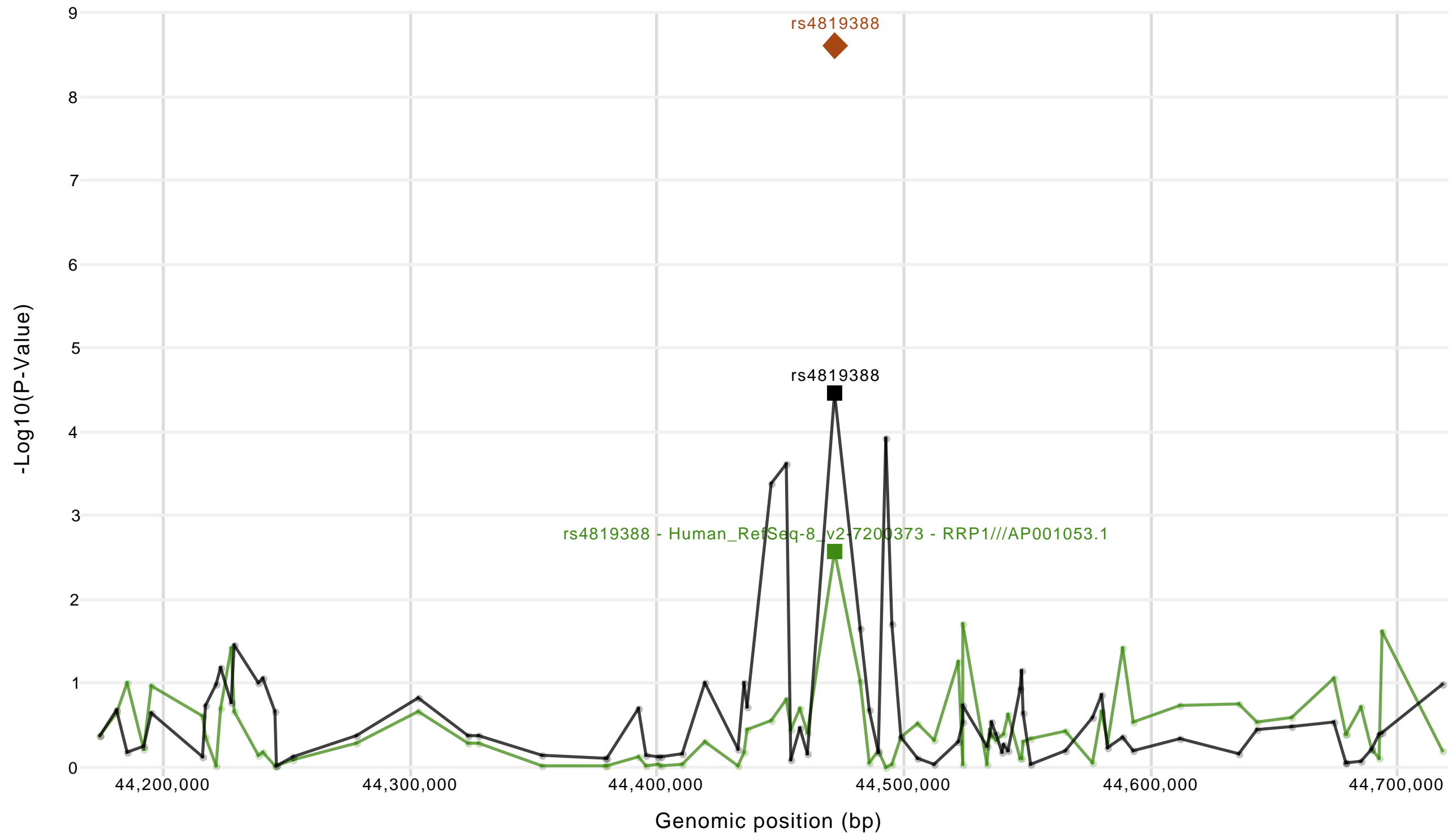
Chromosome 16



Chromosome 17

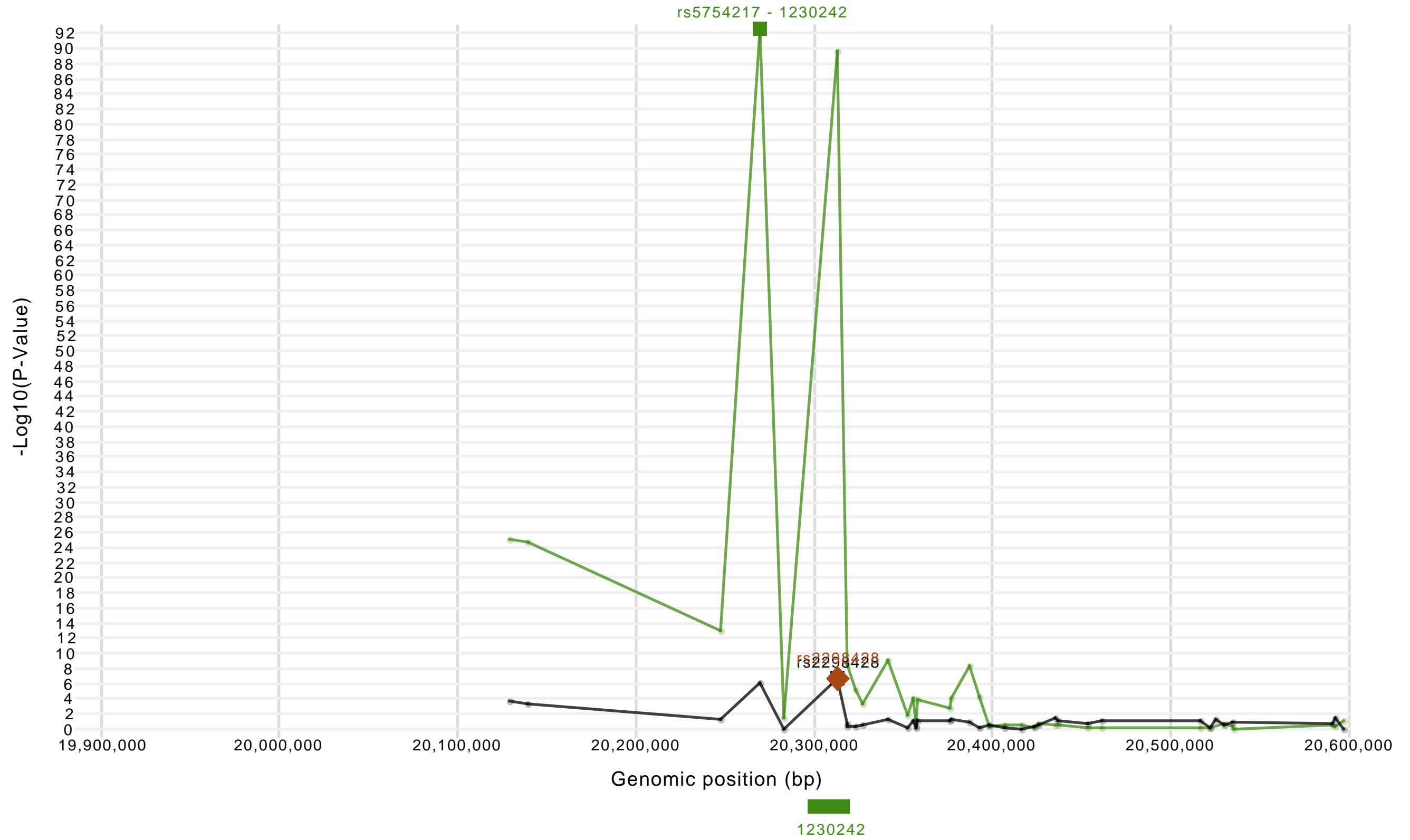


Chromosome 21

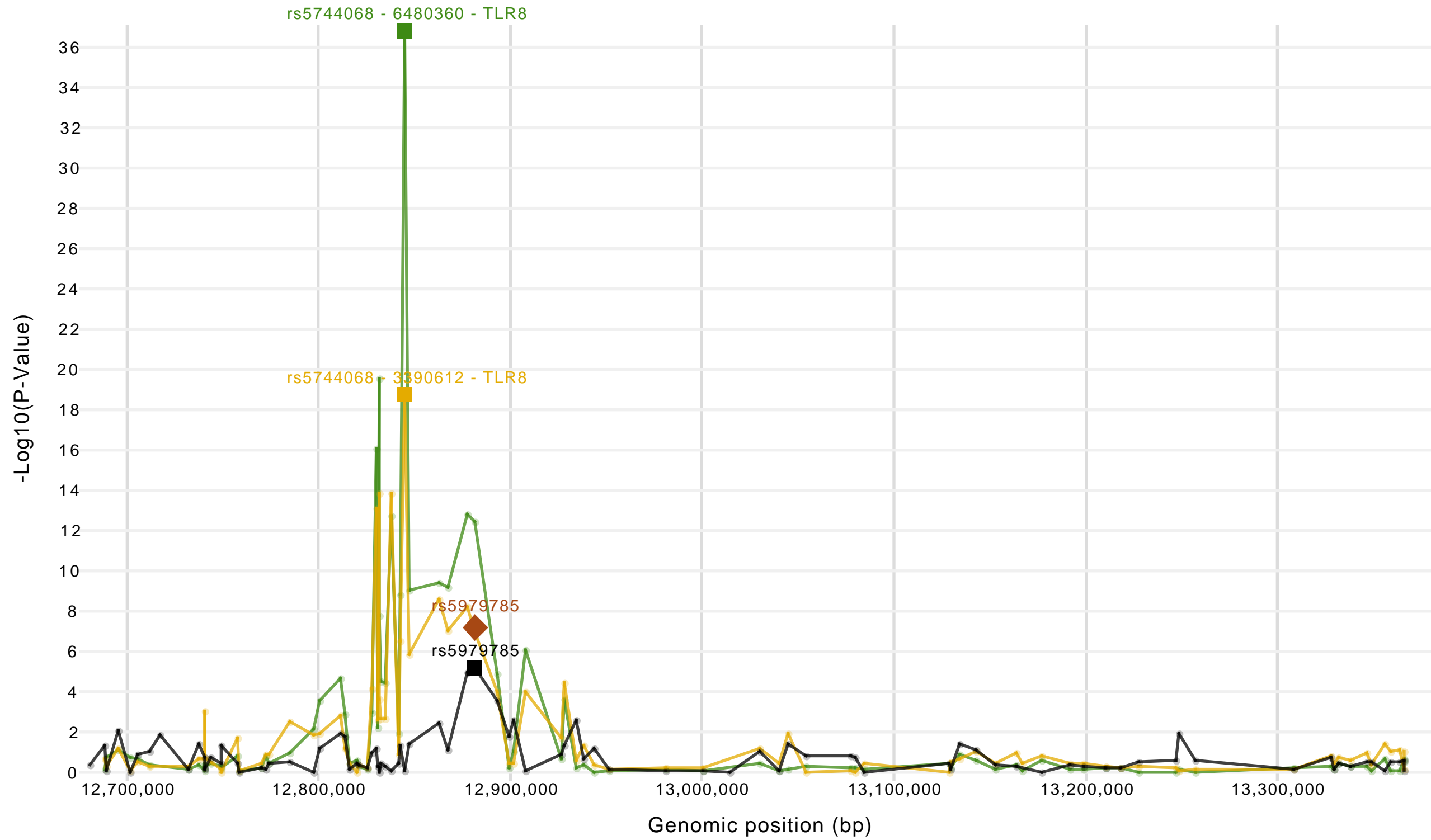


RRP1///AP001053.1

Chromosome 22



Chromosome 23



6480360 - TLR8
3390612 - TLR8