



# Genetics of circulating inflammatory proteins identifies drivers of immune-mediated disease risk and therapeutic targets

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## **Supplementary Material - Table of contents**

### i). Supplementary Notes

- Supplementary Note 1: Cohort details
- Supplementary Note 2: Comparison with pQTL study of Ferkingstad *et al.*
- Supplementary Note 3: Additional information on potential mechanisms underpinning *cis*-pQTLs
- Supplementary Note 4: TNFSF10 pQTL protein-protein network analysis
- Supplementary References

### ii). Supplementary Figure and Item Titles

### iii). Supplementary Figures

## **Supplementary Notes**

### **Supplementary Note 1: Cohort details**

**INTERVAL.** The INTERVAL study<sup>1</sup> is a prospective cohort study of blood donors. Volunteers were recruited and consented between 2012 and 2014 from 25 NHSBT (National Health Service Blood and Transplant) static donor centres across England. The INTERVAL study was approved by the Cambridge (East) Research Ethics Committee. A subset of 4,896 participants from INTERVAL with Olink inflammation panel data contributed to the present study. 2,907 were male and 1,989 female. These participants had an age range between 49 and 78 years (median 61, IQR=55-66). A complete list of the investigators and contributors to the INTERVAL trial is provided in reference<sup>2</sup>.

**Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy Trial (STABILITY).** STABILITY is a randomized, controlled trial conducted in 15,828 patients with chronic coronary heart disease (CHD) comparing darapladib or placebo, in addition to standard of care (<https://clinicaltrials.gov/ct2/show/NCT00799903>)<sup>3</sup>. Data from 2,951 individuals with Olink inflammation panel and genotyping data contributed to this pQTL study. All participants gave written informed consent to the biomarker and genetic sub-studies and the study was approved by the National Ethics Committees in the participating countries.

**Biomarkers For Identifying Neurodegenerative Disorders Early and Reliably (BioFINDER).** The BioFINDER study<sup>4</sup> is run by the Clinical Memory Research Unit and The Biomedical center, at Lund University, Sweden. Participants were recruited from the Memory and Neurology clinics at Skåne University Hospital and the Memory Clinic at Ängelholm's Hospital. Study participants comprised 1,496 individuals with mild cognitive symptoms, dementia or parkinsonian symptoms, and cognitively healthy elderly. The Ethics Committee of Lund University approved this study. All study participants gave written consent for participation in the study, which was performed in accordance with the Helsinki Declaration.

**Cooperative Health Research in the Region of Augsburg (KORA).** KORA is a series of independent population-based studies from the general population living in the region of Augsburg, Southern Germany. The KORA F4 study was conducted from 2006-2008 as a follow-up study to KORA S4 (1999-2001)<sup>5</sup>. 1,064 participants from KORA F4 contributed data to this study.

**Orkney Complex Disease Study (ORCADES).** The ORCADES is a family-based study in the isolated Scottish archipelago of Orkney, part of the Viking Genes studies ([ed.ac.uk/viking](http://ed.ac.uk/viking)). A total of 981 individuals with Olink inflammation panel data contributed to this pQTL study. All participants gave written informed consent and the study was approved by Research Ethics Committees in Orkney, Aberdeen (North of Scotland REC), and South East Scotland REC, NHS Lothian (reference: 12/SS/0151).

**Northern Sweden Population Health Study (NSPHS).** NSPHS is a cross-sectional study conducted in the communities of Karesuando (samples gathered in 2006) and Soppero (2009) in the subarctic region of the County of Norrbotten, Sweden<sup>6</sup>. Ethical approval was given by the local ethics committee at the University of Uppsala (Regionala Etikprövningsnämnden, Uppsala, Dnr 2005:325) in compliance with the Declaration of Helsinki. All participants gave

their written informed consent to the study. A total of 866 individuals with Olink inflammation panel data contributed to the present study.

**VIS.** CROATIA-Vis is a family-based, cross-sectional study in the island of Vis, Croatia. 899 participants with Olink Inflammation panel and genotyping data contributed to this pQTL study. All participants gave written informed consent and the study was approved by Research Ethics Committees in Croatia (Institutional Ethics Committee of the University of Split School of Medicine [protocol code 2181-198-03-04/10-11-0008] and Scotland).

**STANLEY (SWEBIC).** The SWEBIC cohort comprises participants meeting the diagnostic criteria for Bipolar disorder as per the DSM-IV recruited at Swedish sites in affiliation with the Stanley Medical Research Institute. In total, SWEBIC contributed 644 samples (cohort A [swe6]: 300, cohort B [lahl]: 344) with Olink inflammation panel data to this pQTL study. Ethical approval for SWEBIC was granted by the Regional Ethical Review Board in Stockholm, Sweden (2008/2009-31/2).

**Estonian Biobank (EstBB).** The EstBB cohort is a volunteer-based sample of the Estonian resident adult population (aged  $\geq$  18 years)<sup>7</sup>. A total of 487 participants contributed to this study. Ethical approval was given by the Estonian Committee on Bioethics and Human Research (1.1-12/624) and by the Research Ethics Committee of the University of Tartu (application number 262/T-3, October 2016), data extraction nr K29.

**RECOMBINE/EIRA.** The RECOMBINE/EIRA biobank was generated from participants with active rheumatoid arthritis recruited between February 2011 and May 2013 at the Karolinska University Hospital, Stockholm, Sweden as part of the Epidemiologic Investigation of Rheumatoid Arthritis (EIRA) study<sup>8</sup>. The study was approved by the Ethical Review Board at Karolinska Institutet, Stockholm, Sweden (reference numbers 2007-0889-31, 2007-1443-32 and 2015/1844-31/2). All participants gave written informed consent. At the time of recruitment, all participants were undergoing treatment initiation or escalation. 540 patients with Olink inflammation panel data contributed to this pQTL study.

**ARISTOTLE.** The Apixaban for reduction in stroke and other Thromboembolic events in atrial fibrillation (ARISTOTLE) trial was designed to investigate the safety and efficacy of the Factor Xa (FXa) inhibitor apixaban for secondary prevention of stroke in atrial fibrillation patients. Full details of the ARISTOTLE cohort are available at<sup>9,10</sup>. In total, ARISTOTLE contributed 1,585 samples with Olink inflammation panel data for comparison with the pQTL discovery meta-analysis findings. All participants gave written informed consent to the biomarker and genetic sub-studies and the study was approved by the National Ethics Committees in the participating countries.

#### **Supplementary Note 2: Comparison with pQTL study of Ferkingstad et al.**

In addition to testing the pQTLs from our discovery meta-analysis for replication in the ARISTOTLE study, we also compared our results to those from the study by Ferkingstad *et al*<sup>11</sup> from the deCODE group, hereafter referred to as the “deCODE study”. The deCODE study performed pQTL mapping in approximately 35,000 individuals from Iceland, with 4,907 proteins measured using the aptamer-based SomaScan V4 platform (whereas we used the

Olink Inflammation platform in our study).

72 of the 91 proteins in our study were measured in the deCODE study. Of the 180 significant locus-protein associations from our study, 158 were testable for replication in the deCODE summary statistics. Of these 158 variants, 75 were significant at  $P<5\times10^{-10}$ , 78 at  $P<5\times10^{-8}$ , and 96 at a more liberal  $P$ -value threshold of  $2.8\times10^{-4}$  (a Bonferroni-correction for the 180 pQTLs eligible for replication testing;  $P$ -values from linear regression). The numbers of pQTLs replicating in ARISTOTLE and in deCODE at varying  $P$ -value thresholds are shown in **Supplementary Note Table 1**. Overall, we replicated 126 (71%) of the 178 testable pQTLs in either ARISTOTLE or deCODE at  $P<2.8\times10^{-4}$ .

**Supplementary Note Table 1.** The numbers of pQTLs replicating in ARISTOTLE and in deCODE at varying  $P$ -value thresholds ( $P$ -values from linear regression).

P-value threshold	No. pQTLs replicated in ARISTOTLE	No. pQTLs replicated in deCODE	No. pQTLs replicated in either ARISTOTLE or deCODE
$5.0\times10^{-10}$	32	75	87
$5.0\times10^{-8}$	39	78	92
$2.78\times10^{-4}$	72	96	126
<b>Number of testable pQTLs</b>	<b>174</b>	<b>158</b>	<b>178</b>

Of note, 7 pQTLs replicated in ARISTOTLE with  $P<5\times10^{-8}$  and yet did not replicate in the deCODE study despite the larger sample size of the latter (**Supplementary Note Table 2**). 4 of these 7 were *cis*-pQTLs. Of the three *trans*-pQTLs, two have been reported in previous studies that use single protein ELISAs; i) the association of rs385076 with IL-18 levels was reported by Johansson *et al*<sup>12</sup>, and ii) rs2228145, a variant in *IL6R* (the gene encoding the interleukin-6 receptor), is well known to affect soluble IL6 levels<sup>13,14</sup>.

The lack of signal in the deCODE data (generated using the SomaScan platform), despite convincing evidence of a pQTL in these instances (in both Olink and ELISA-based studies), may reflect platform effects. Consistent with this, rs2228145 was not significantly associated with plasma IL6 levels in the study of Sun *et al*<sup>15</sup>, which used an earlier version of the SomaScan platform. There are a number of possible explanations for the absence of detecting a pQTL using the SomaScan: i) the specific aptamer may lack sensitivity; ii) aptamers do not always measure their canonical target protein, and instead may target a cleavage product or the protein bound in complex to another protein; iii) aptamers are more vulnerable to off-target binding than the Olink platform used in our study. This is because the Olink platform uses a pair of antibodies, each with a complementary oligonucleotide tag, for each protein target. If,

and only if, both antibodies bind then the oligonucleotides hybridise and a qPCR read-out is generated.

**Supplementary Note Table 2.** Details of pQTLs which replicated at  $P < 5 \times 10^{-8}$  in ARISTOTLE ( $n=1,585$ , Olink proteomics) but not in deCODE ( $n=35,556$ , SomaScan proteomics).  $P$ -values from linear regression.

Protein	rsID	P-value in ARISTOTLE	P-value in deCODE	Cis or trans
LTA	rs2229092	$5.8 \times 10^{-81}$	0.56	cis
CCL3	rs8951	$2.4 \times 10^{-25}$	0.0087	cis
GDNF	rs62360376	$1.6 \times 10^{-13}$	0.48	cis
CCL13	rs3136676	$3.1 \times 10^{-10}$	0.15	cis
IL18	rs385076	$5.1 \times 10^{-17}$	0.42	trans
TNFSF10	rs28929474	$1.6 \times 10^{-9}$	0.78	trans
IL6	rs2228145	$3.0 \times 10^{-8}$	0.0022	trans

**Supplementary Note 3: Additional information on potential mechanisms underpinning cis-pQTLs**

**Supplementary Note Table 3** provides information on whether the sentinel *cis*-pQTL variant was a protein-altering variant (PAV), or whether it was in high LD ( $r^2 \geq 0.8$ ) with a PAV, and whether there was a colocalising eQTL in at least one tissue or cell type.

Of the 11 *cis*-pQTLs with sentinel variants that are PAVs, only 2 had a corresponding colocalising (PP H4  $> 0.8$ ) *cis*-eQTL. These were pQTLs for IL15RA and PLA2U. The remaining 9 did not (*cis*-pQTLs for ADA, CCL8, CCL25, CXCL10, HGF, LTA, MMP10, SIRT2, TGFB1).

For a further 10 *cis*-pQTLs, the sentinel variants were not themselves PAVs but were in high LD ( $r^2 \geq 0.8$ ) with a PAV. However, 3 of these PAVs were not in the gene encoding the target protein but were instead in another nearby gene, and thus protein-altering effects could not account for the pQTL. Of the remaining 7 *cis*-pQTLs, 4 have a colocalising corresponding *cis*-eQTL (CD6, CCL11, CST5, CXCL5), whereas 3 do not (TNFSF14, CCL4, CASP8).

There were 27 *cis*-pQTLs without a corresponding colocalising *cis*-eQTL. 12 of the 27 *cis*-pQTLs without a colocalising eQTL are potentially explaining by PAVs, leaving 15 unexplained

by current available eQTL data.

**Supplementary Note Table 3.** Annotation of *cis*-pQTLs. The target protein is denoted by the non-italicised gene symbol of the encoding gene. PAV = protein-altering variant. LD = linkage disequilibrium. PP H4 = posterior probability of hypothesis 4 from coloc.

Sentinel pQTL variant	Target protein	Sentinel pQTL is a PAV	Sentinel pQTL is in high LD ( $r^2 \geq 0.8$ ) with a PAV	Colocalising eQTL in at least 1 tissue (PP H4 $\geq 0.8$ )
rs11555566	ADA	<b>Yes</b>	N/A	No
rs6328	NGF	No	No	<b>Yes</b>
rs56328050	CASP8	No	<b>Yes</b>	No
rs79722574	CCL11	No	<b>Yes</b>	<b>Yes</b>
rs11574915	CCL19	No	Yes but in a different gene to that encoding target protein ( <i>FAM205A</i> )	No
rs10207134	CCL20	No	No	<b>Yes</b>
rs712048	CCL23	No	No	No
rs2032887	CCL25	<b>Yes</b>	N/A	No
rs8064426	CCL4	No	<b>Yes</b>	No
rs11265493	CD244	No	No	<b>Yes</b>
rs1883832	CD40	No	No	<b>Yes</b>
rs674379	CD5	No	No	<b>Yes</b>
rs2074227	CD6	No	<b>Yes</b>	<b>Yes</b>
rs2276862	CDCP1	No	No	<b>Yes</b>
rs17610659	CSF1	No	No	<b>Yes</b>
rs4815244	CST5	No	<b>Yes</b>	<b>Yes</b>
rs671623	CX3CL1	No	No	<b>Yes</b>
rs1366949	CXCL1	No	No	<b>Yes</b>
rs11548618	CXCL10	<b>Yes</b>	N/A	No
rs6827617	CXCL11	No	Yes but in a different gene to that encoding target protein	No

			(SDAD1)	
rs450373	CXCL5	No	<b>Yes</b>	<b>Yes</b>
rs16850073	CXCL6	No	No	<b>Yes</b>
rs4241577	CXCL9	No	Yes but in a different gene to that encoding target protein (NAA)	<b>Yes</b>
rs62193248	DNER	No	No	<b>Yes</b>
rs3014874	S100A12	No	No	<b>Yes</b>
rs838131	FGF21	No	No	No
rs12509595	FGF5	No	No	<b>Yes</b>
rs62360376	GDNF	No	No	No
rs5745687	HGF	<b>Yes</b>	N/A	No
rs12123181	IL10	No	No	No
rs2266590	IL10RB	No	No	<b>Yes</b>
rs10076557	IL12B	No	No	No
rs2228059	IL15RA	<b>Yes</b>	No	<b>Yes</b>
rs17700884	IL17C	No	No	No
rs5744249	IL18	No	No	<b>Yes</b>
rs2270297	IL18R1	No	No	<b>Yes</b>
rs112359206	IL7	No	No	<b>Yes</b>
rs6446951	IL8	No	No	No
rs1800472	TGFB1	<b>Yes</b>	N/A	No
rs1133763	CCL8	<b>Yes</b>	N/A	No
rs7213460	CCL7	No	No	No
rs3136676	CCL13	No	No	No
rs8951	CCL3	No	No	<b>Yes</b>
rs471994	MMP1	No	No	<b>Yes</b>
rs17860955	MMP10	<b>Yes</b>	N/A	No
rs2247769	TNFRSF11B	No	No	No
rs822335	CD274	No	No	<b>Yes</b>

rs144373891	SIRT2	<b>Yes</b>	N/A	No
rs60094514	SLAMF1	No	No	No
rs149278	SULT1A1	No	No	<b>Yes</b>
rs72912115	TGFA	No	No	<b>Yes</b>
rs2229092	LTA	<b>Yes</b>	N/A	No
rs1776354	TNFRSF9	No	No	<b>Yes</b>
rs344562	TNFSF14	No	<b>Yes</b>	No
rs574044675	TNFSF10	No	No	No
rs4512994	TNFSF11	No	No	<b>Yes</b>
rs34790908	TNFSF12	No	No	<b>Yes</b>
rs55744193	PLAU	<b>Yes</b>	No	<b>Yes</b>
rs6921438	VEGFA	No	No	No

#### **Supplementary Note 4: Protein-protein network analysis for TNFSF10**

Plasma levels of TNFSF10 were associated with 7 genetic loci. To help identify the mediating genes at each of these loci, we constructed a protein-protein interaction network based on the candidate mediating genes at each loci and TNFSF10 itself using STRINGdb. We observed a cluster of eight interacting proteins (**Extended Data Figure 7a**), representing proteins encoded by 5 of the 7 loci with pQTLs for TNFSF10. The genes encoding these proteins highlight the plasminogen-activating system as a common feature. The relation of the trans-pQTLs for TNFSF10 and these are as follows: (i) rs4760 is a missense variant in *PLAUR*, which encodes the plasminogen-activator urokinase receptor; (ii) rs5030044 is intronic in *KNG1*, encoding kininogen 1 which is involved in bradykinin formation, which is regulated by plasmin; (iii) rs28929474 is a missense variant in *SERPINA1*, which encodes alpha1-antitrypsin, an anti-protease which can bind plasmin; (iv) rs8178824 is intronic to *APOH*, which encodes a cofactor for plasminogen activation<sup>16,17</sup>; and (v) rs654488 is upstream of *MEP1B*, encoding meprin A, which is activated by the plasmin<sup>18</sup>. Together, these findings highlight the most likely mediating genes at 5 of the 7 regulatory loci and links TNFSF10 to the plasminogen-activating system.

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## **Supplementary Figure Titles**

**Supplementary Figure 1. Manhattan plots for the 91 proteins.**

**Supplementary Figure 2. Forest plots and regional association plots for the 180 pQTLs.**

**Supplementary Figure 3. Regional association plots comparing plasma *cis*-pQTLs and blood *cis*-eQTLs for the gene encoding the corresponding protein.**

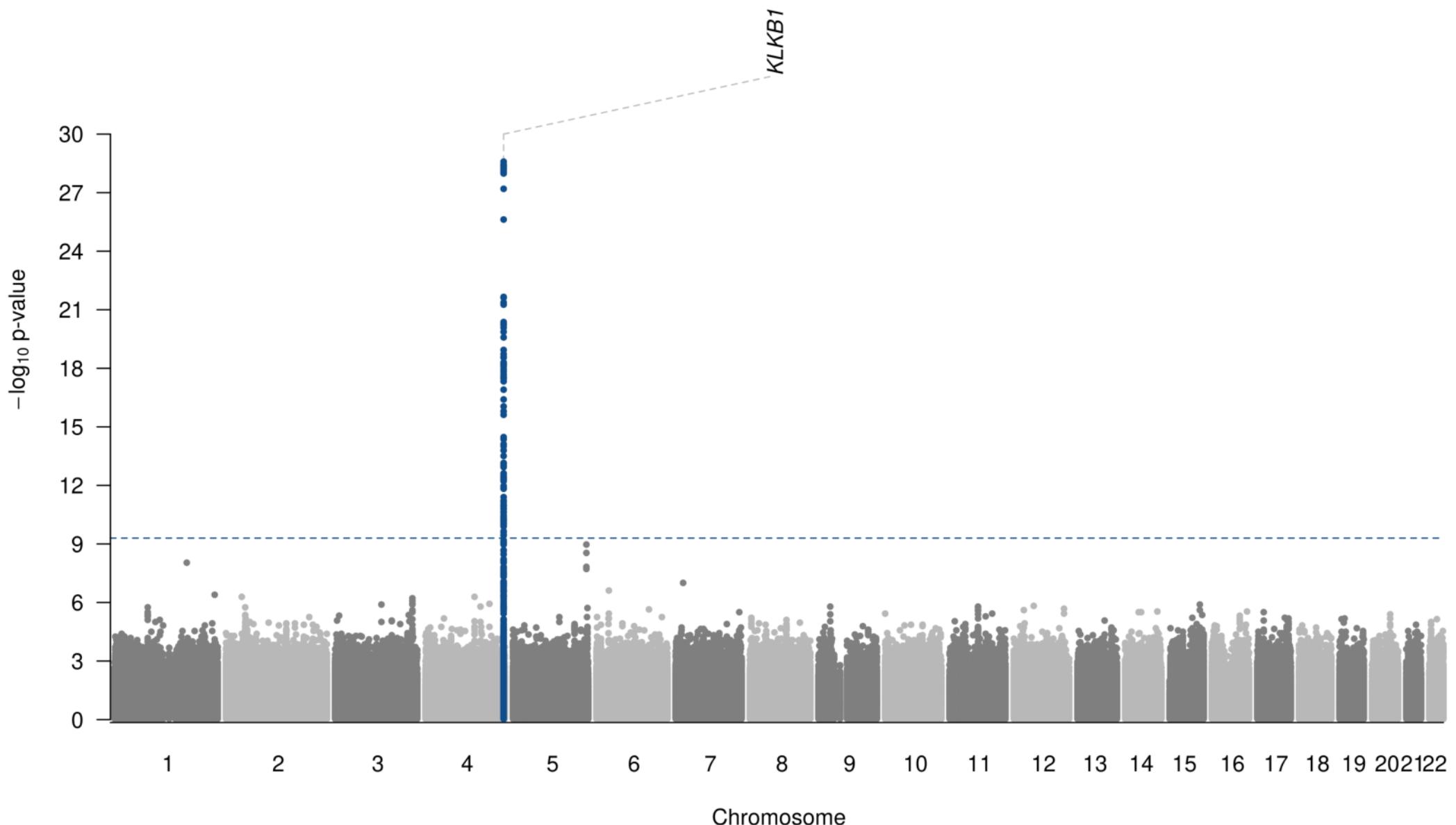
**Supplementary Figure 4. Regional association plots comparing plasma *cis*-pQTLs and disease associations.**

**Supplementary Item. 3-dimensional interactive genomic map of pQTLs.**

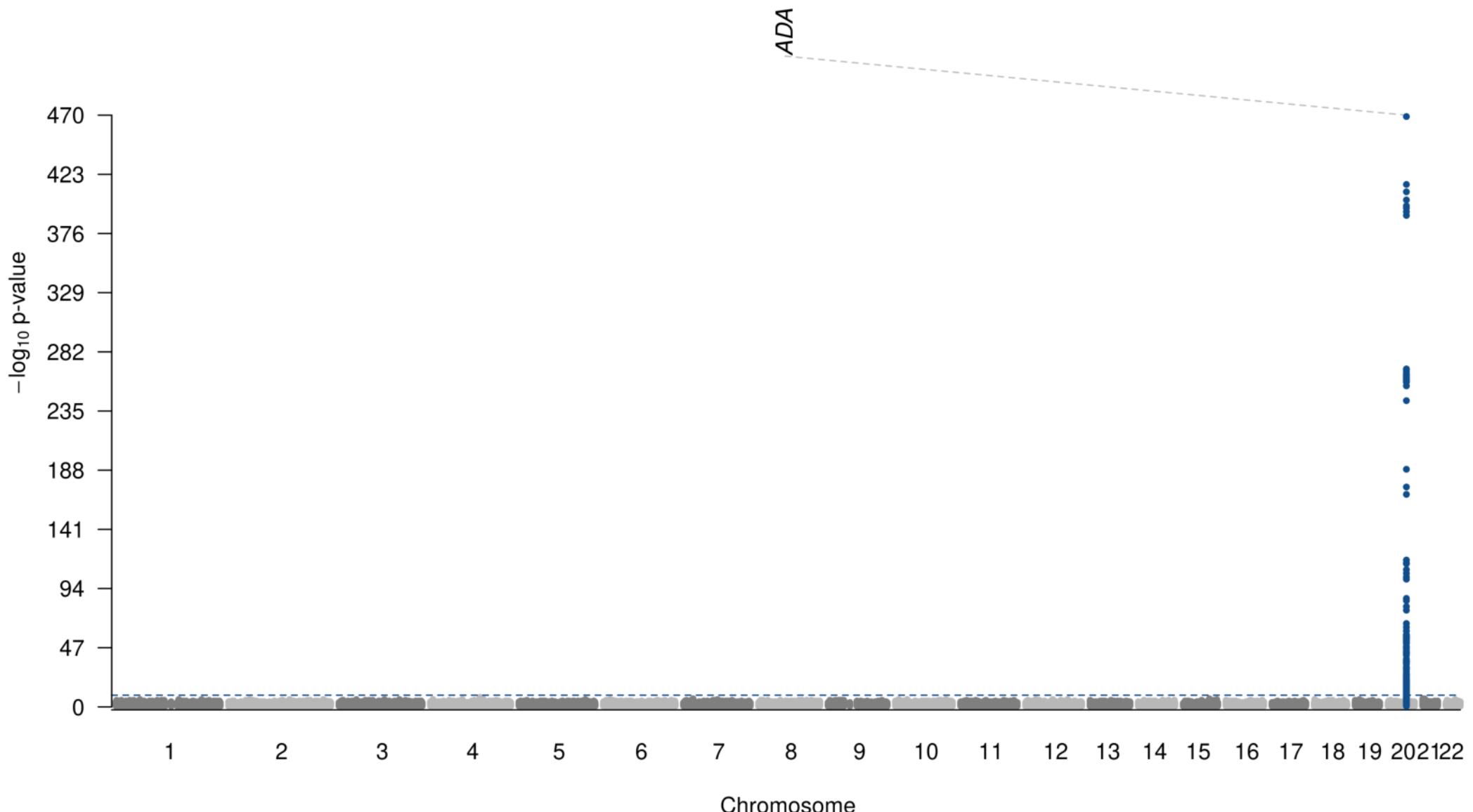
The html file (supplied separately) shows pQTL sentinel variant position in relation to the gene encoding the target protein and the strength of the statistical association (two-sided *P*-values are from meta-analysis of linear regression estimates). Hover over a point to see detailed information. The image can be rotated by holding at left clicking the mouse.

**Supplementary Figure 1.** Manhattan plots for the 91 proteins. Proteins are labelled with both the label provided by Olink, and with the encoding gene symbol in parentheses. Two-sided  $P$ -values are from meta-analysis of linear regression estimates. Horizontal dash blue line =  $P=5\times10^{-10}$  (genome-wide significance after Bonferroni-correction for testing multiple proteins).

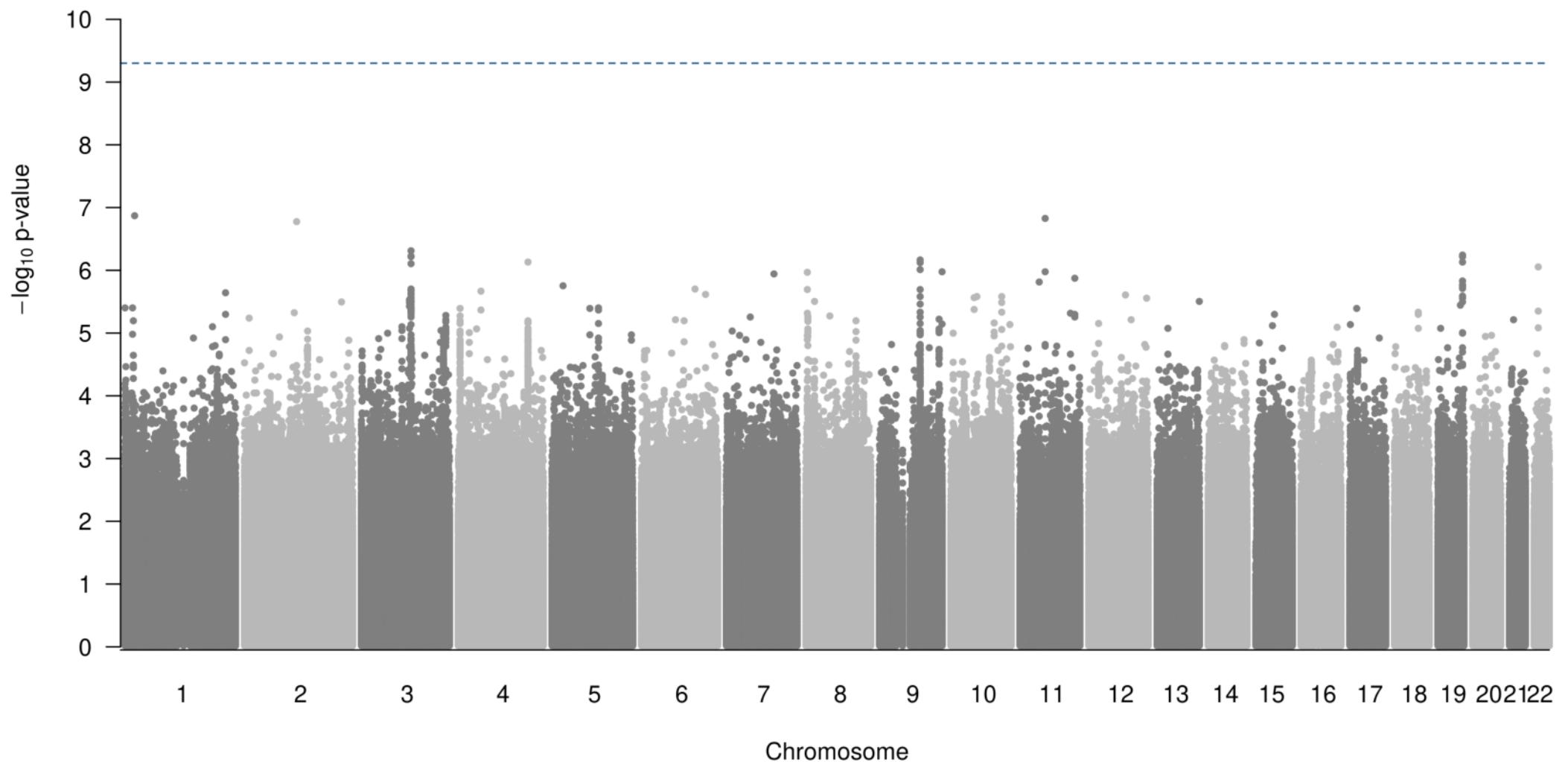
## 4EBP1 (EIF4EBP1)



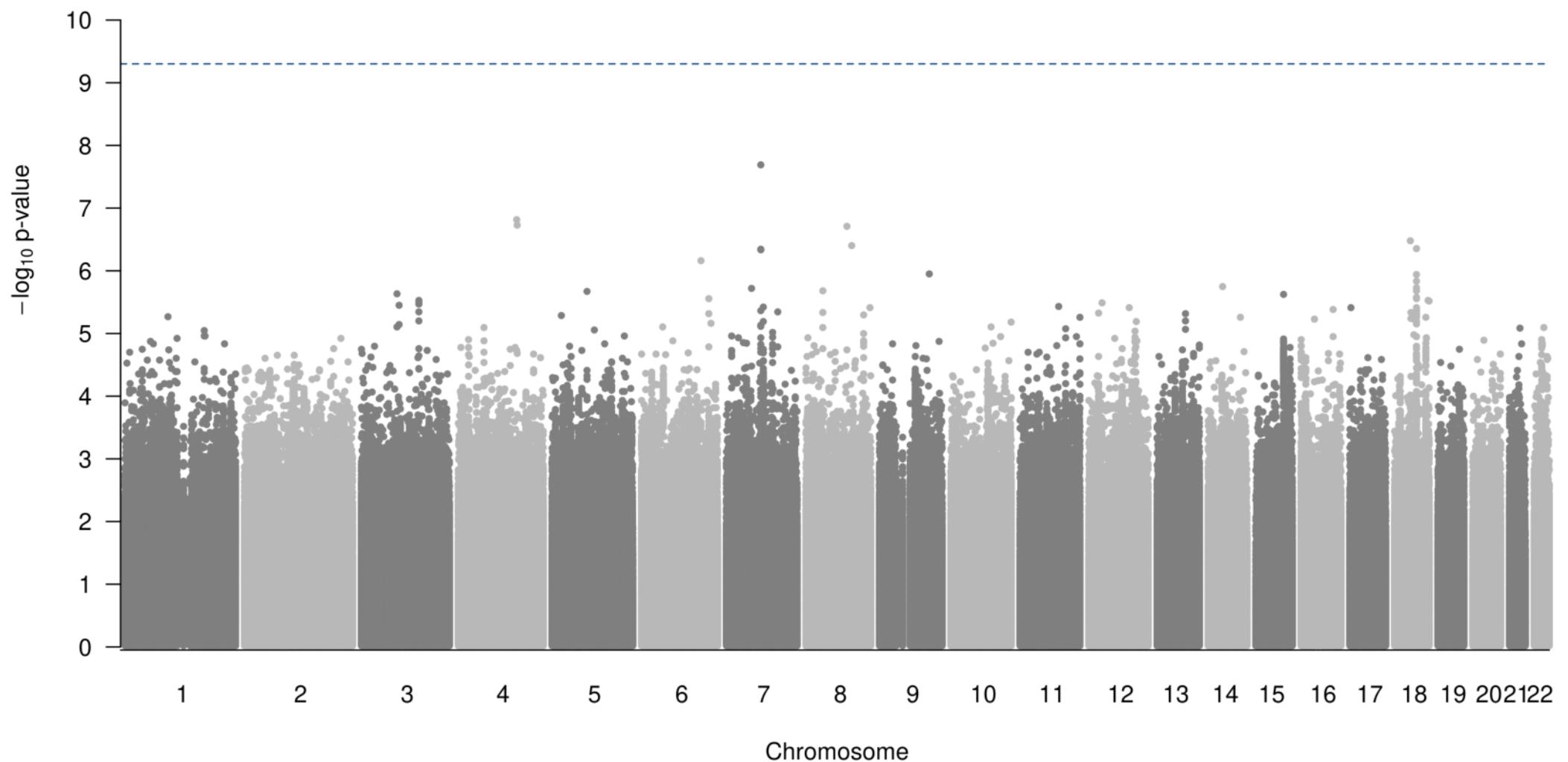
# ADA (ADA)



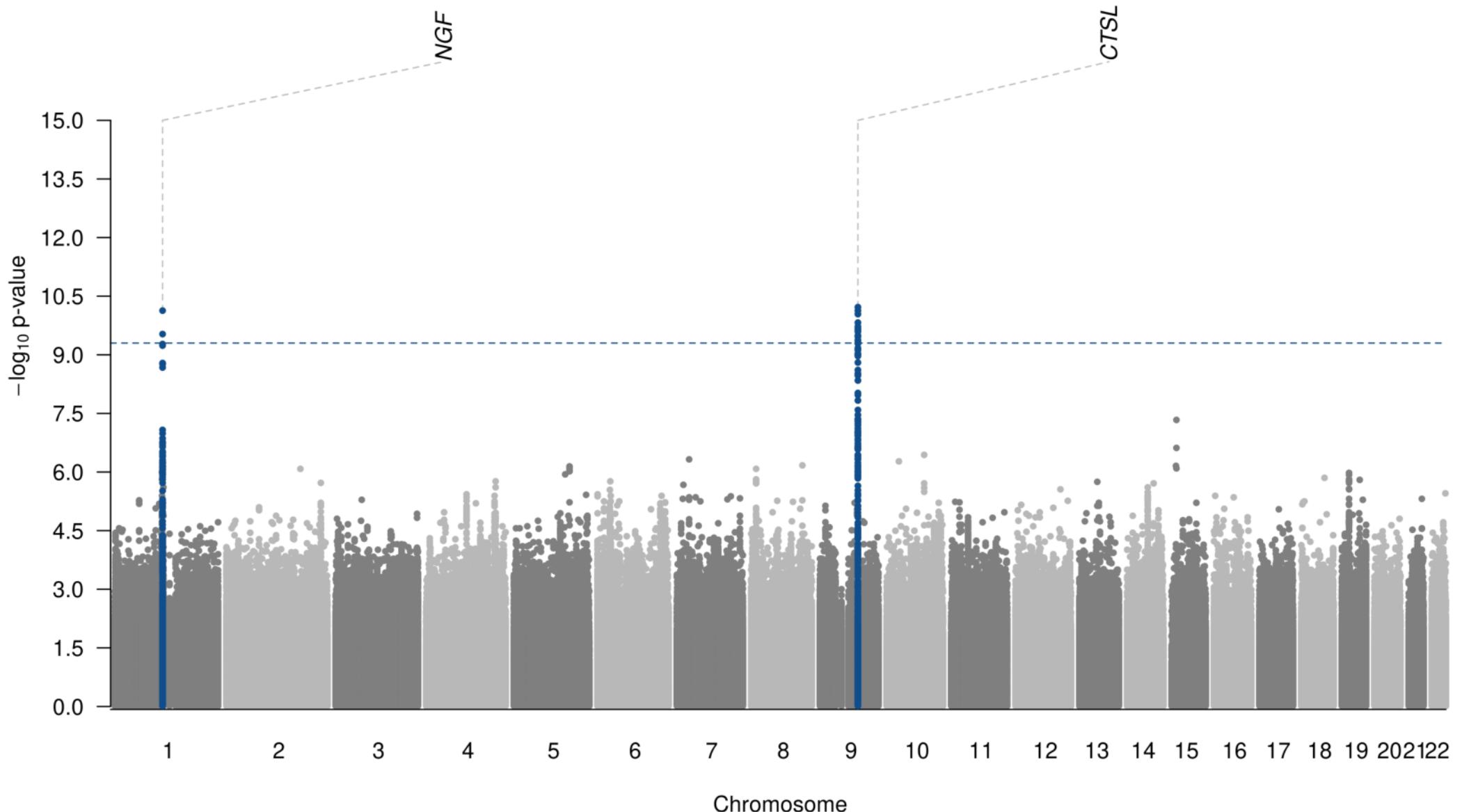
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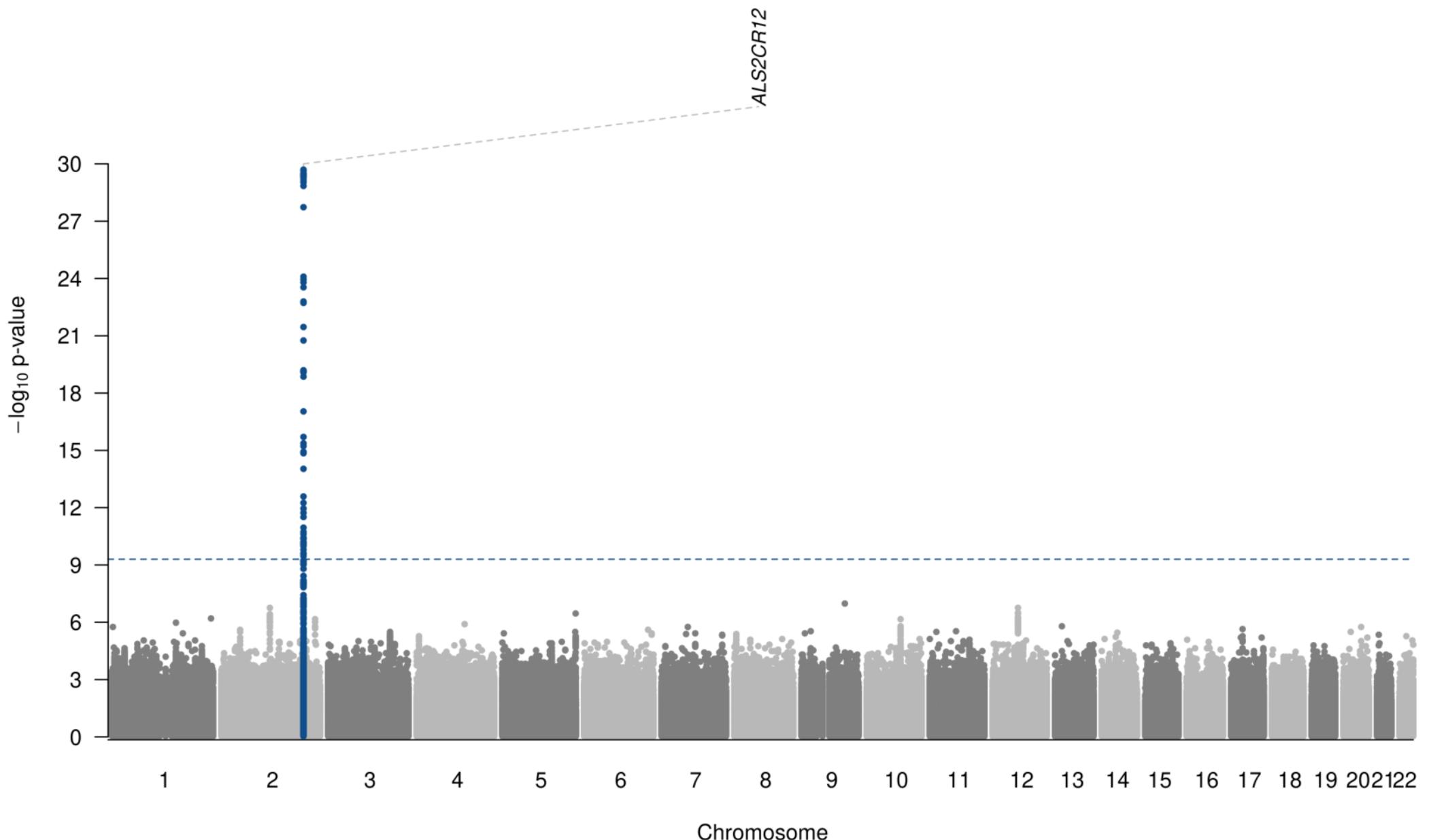
# **AXIN1 (AXIN1)**



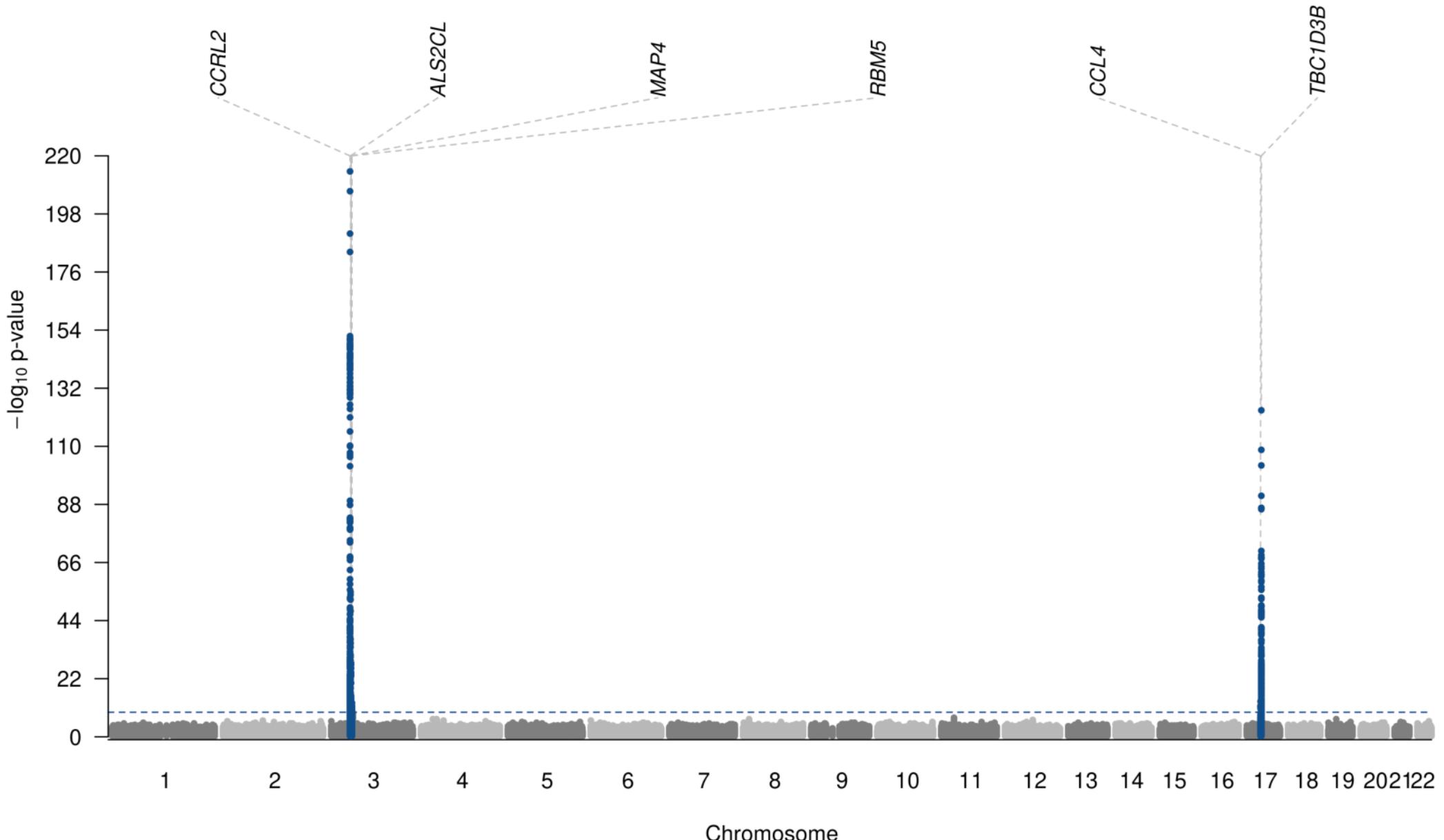
## Beta-NGF (NGF)



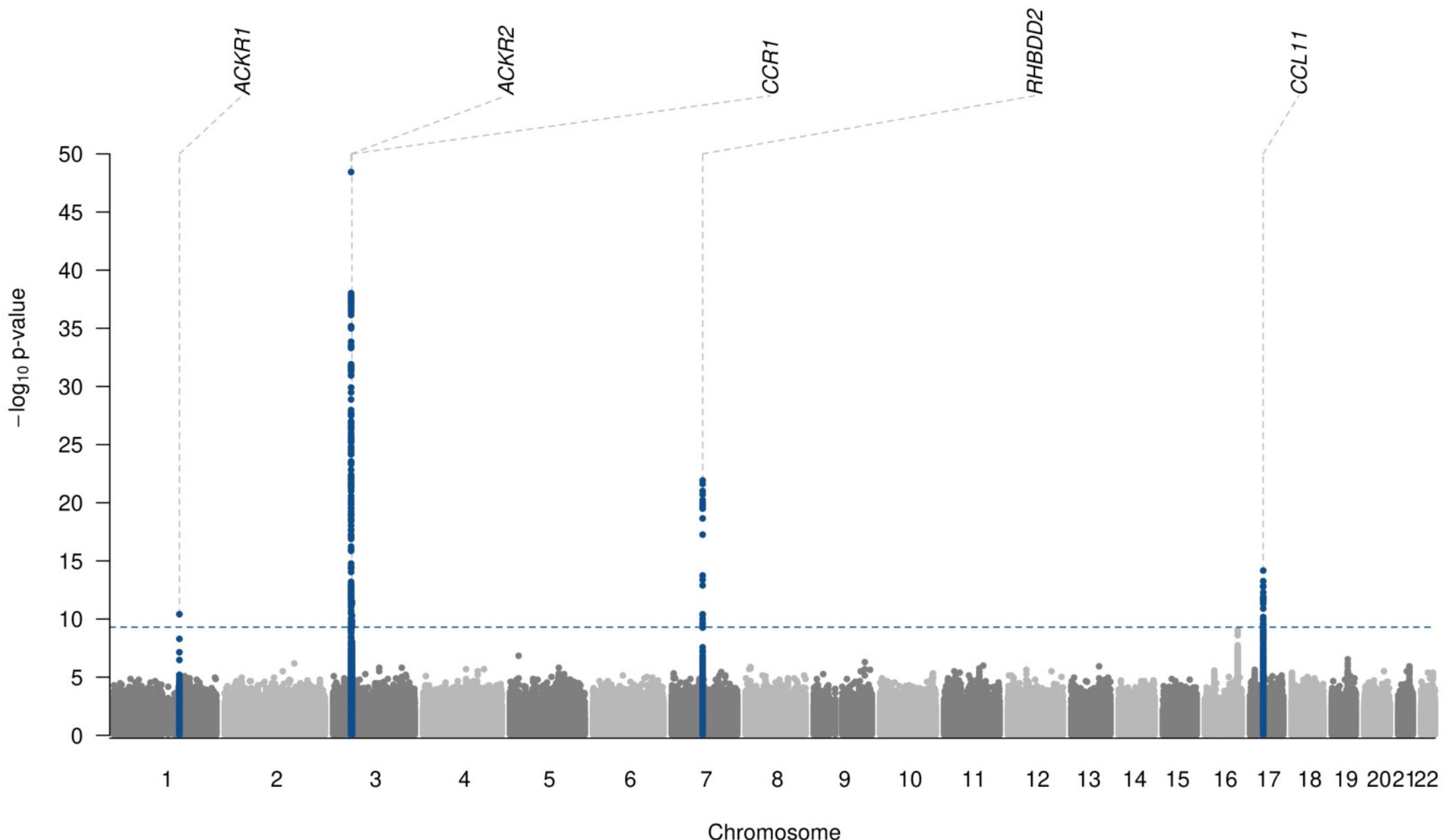
## CASP-8 (CASP8)



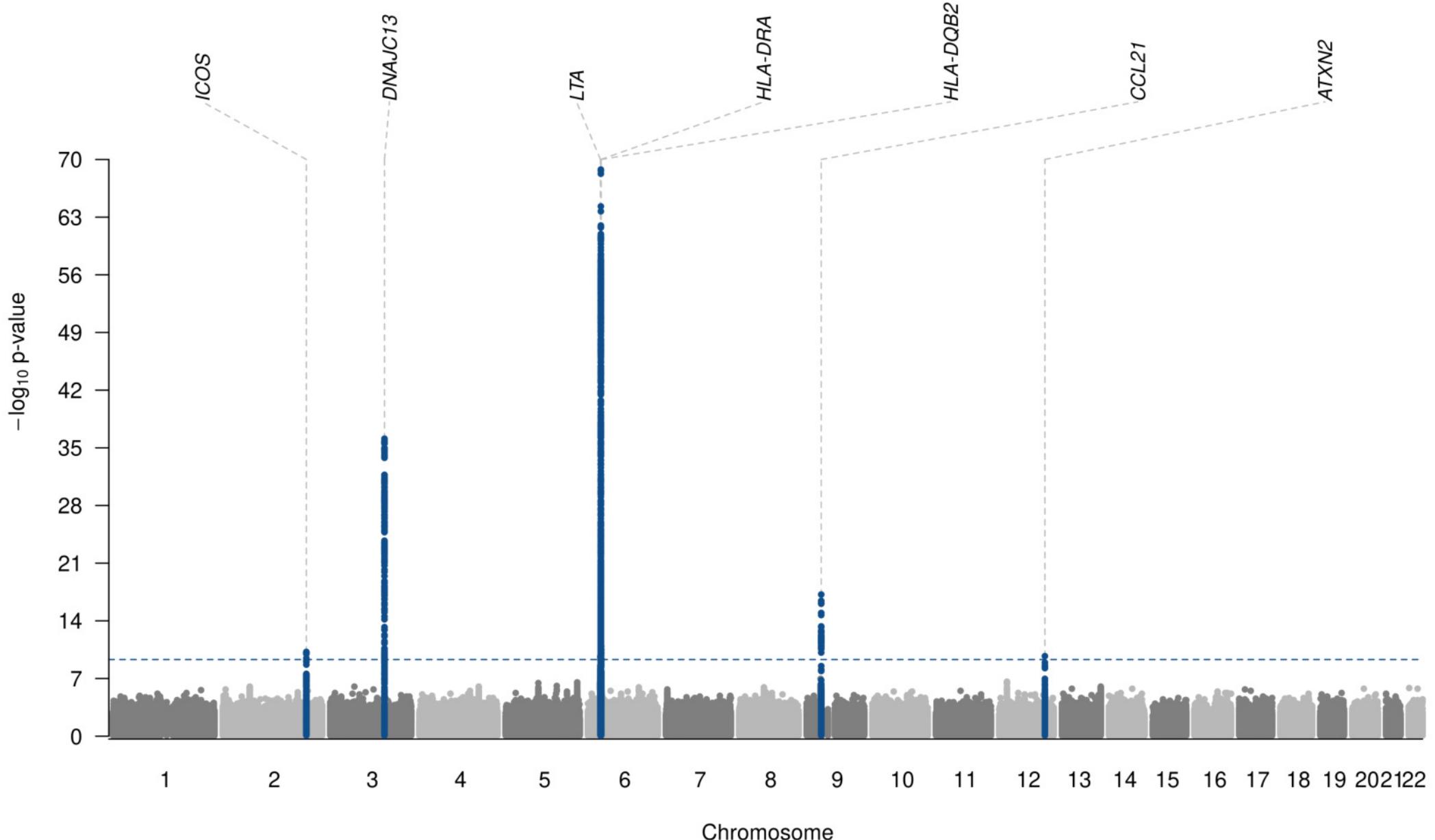
## CCL4 (CCL4)



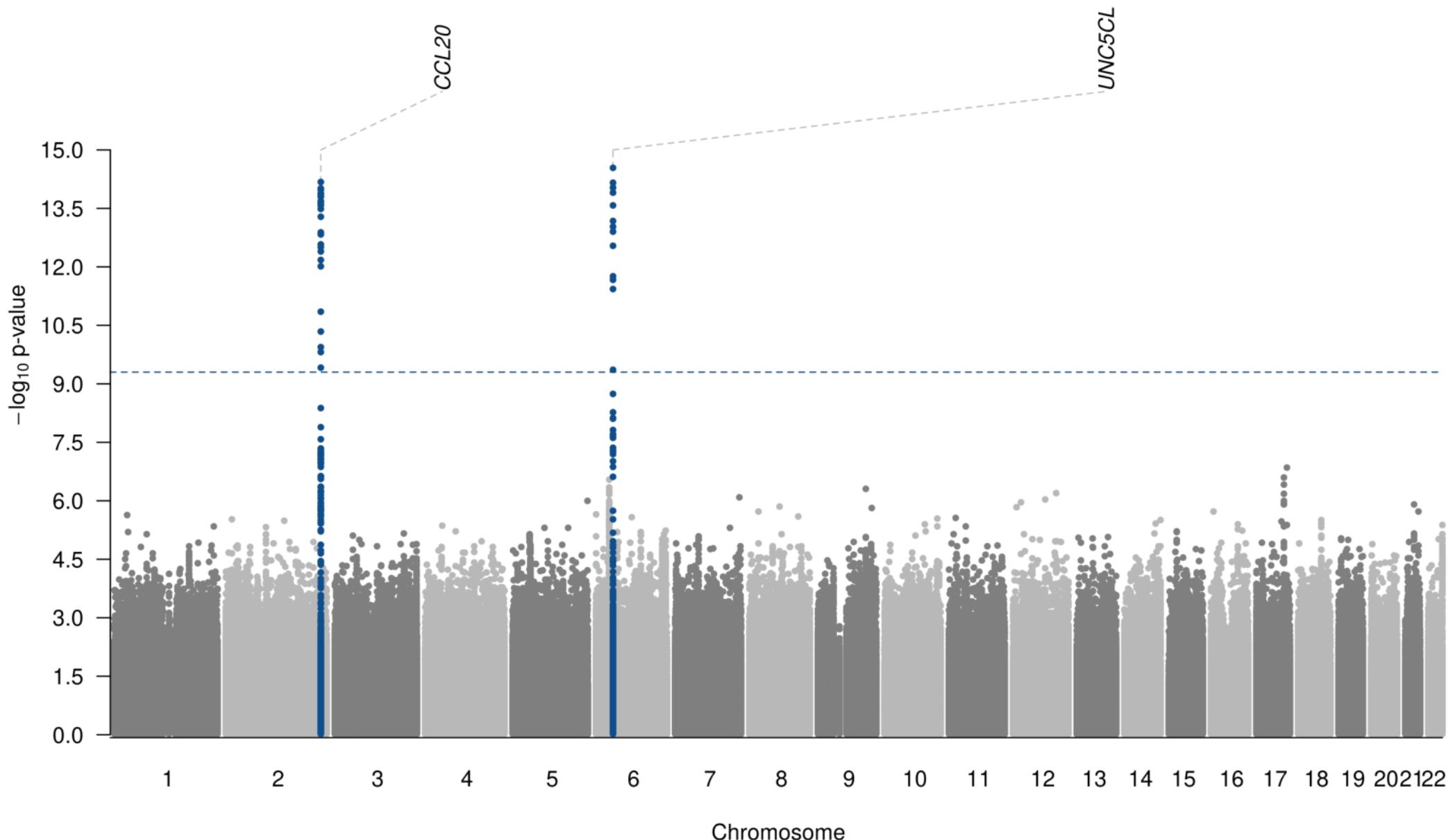
## CCL11 (CCL11)



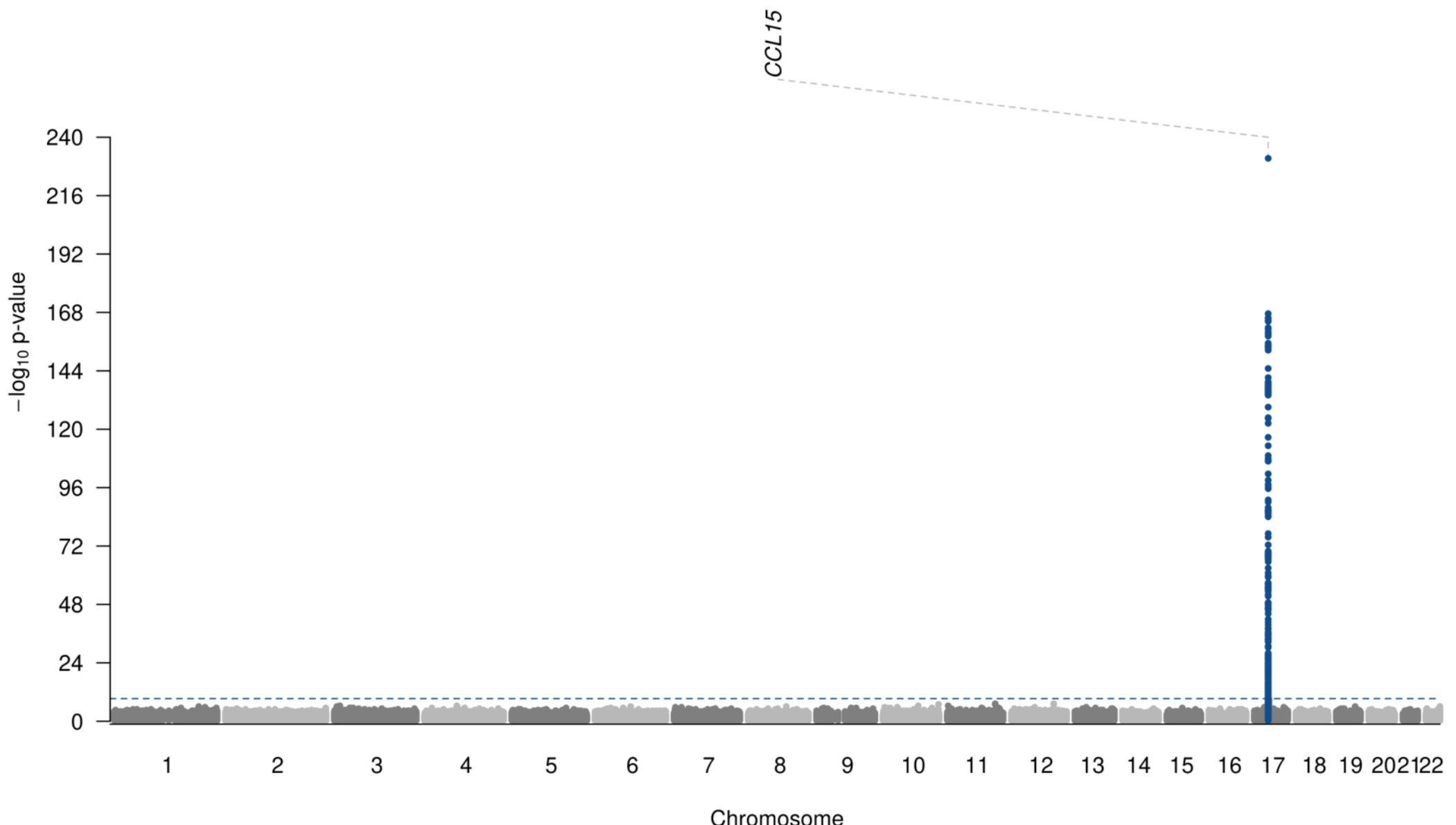
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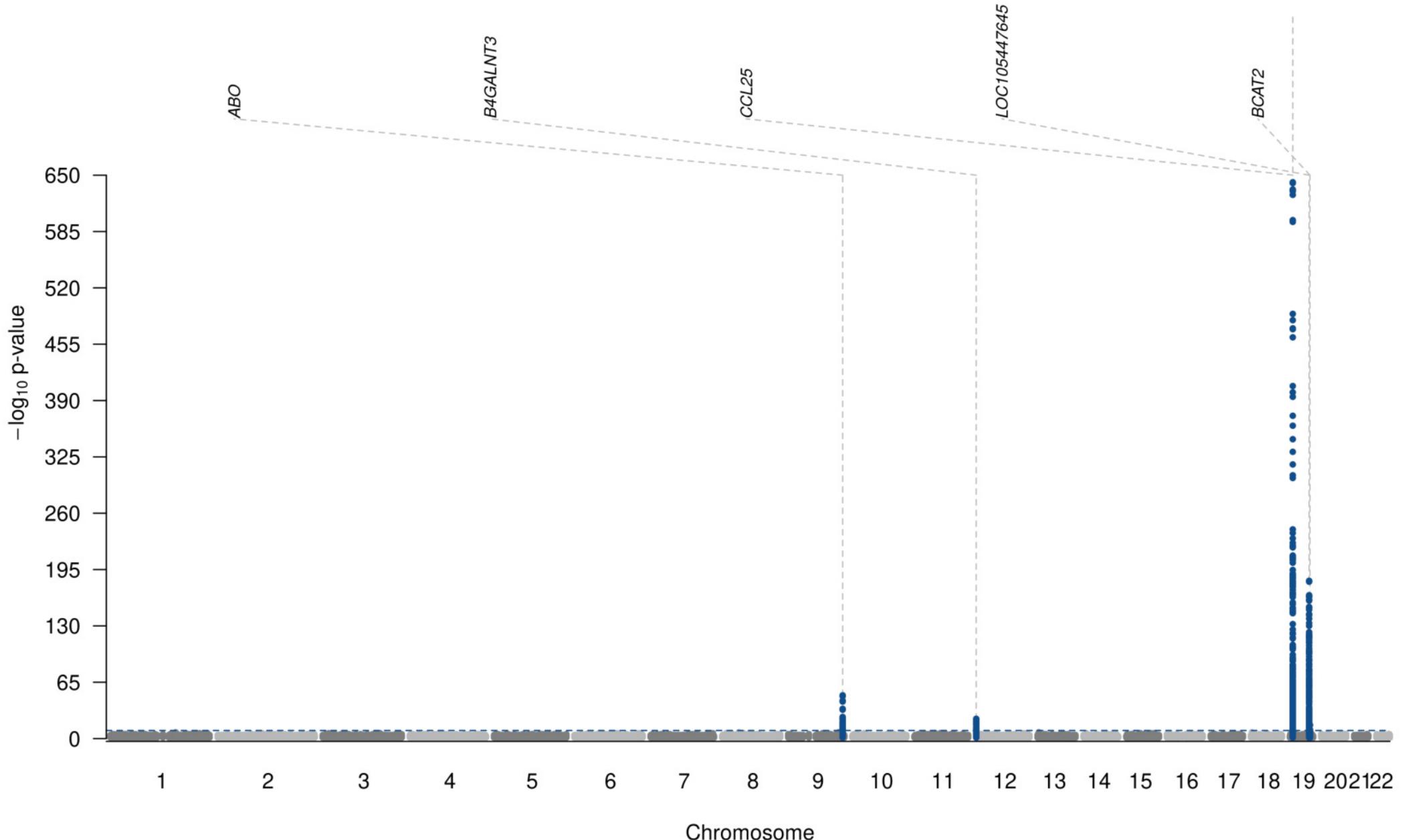
## CCL20 (CCL20)



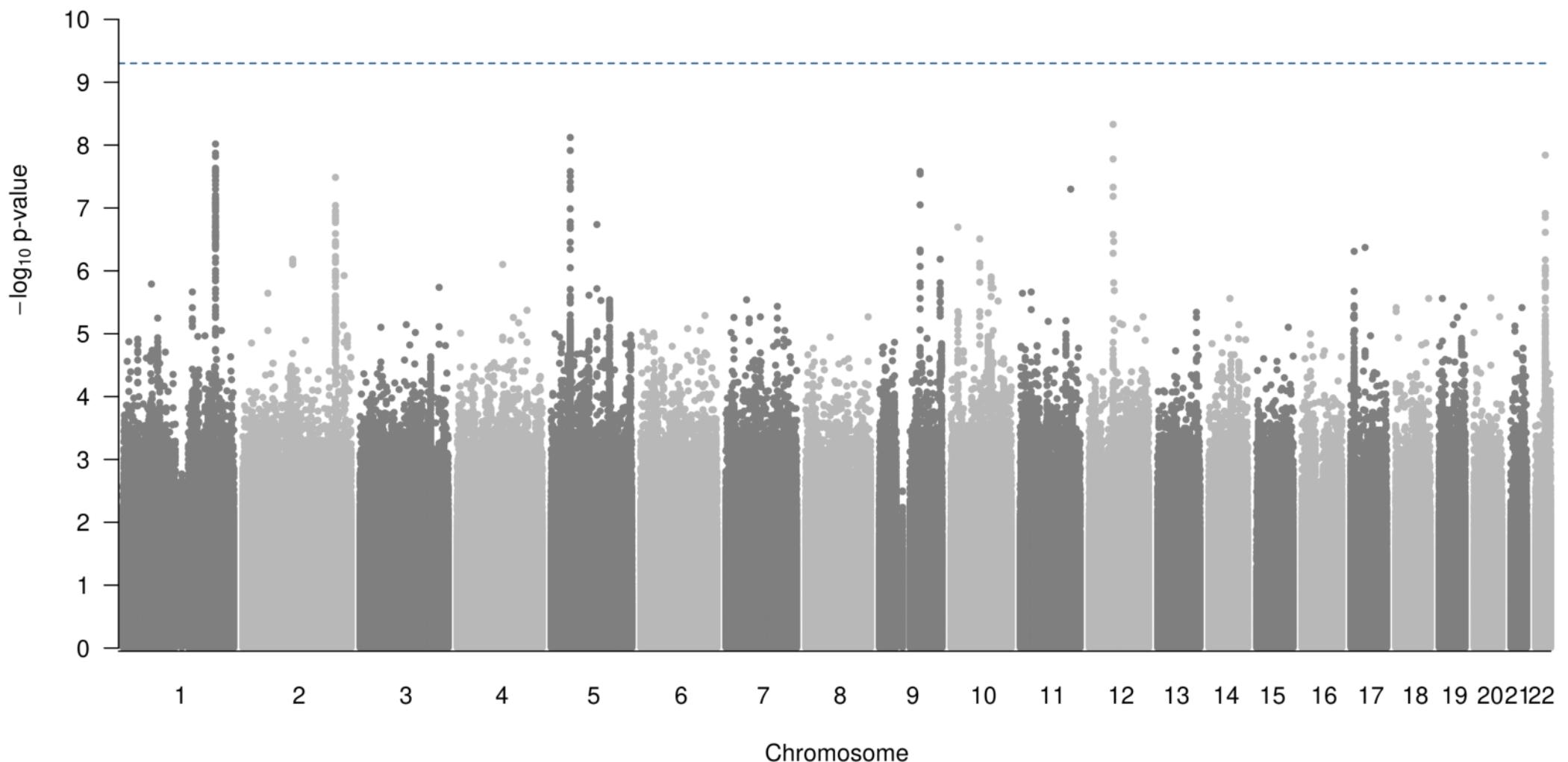
## CCL23 (CCL23)



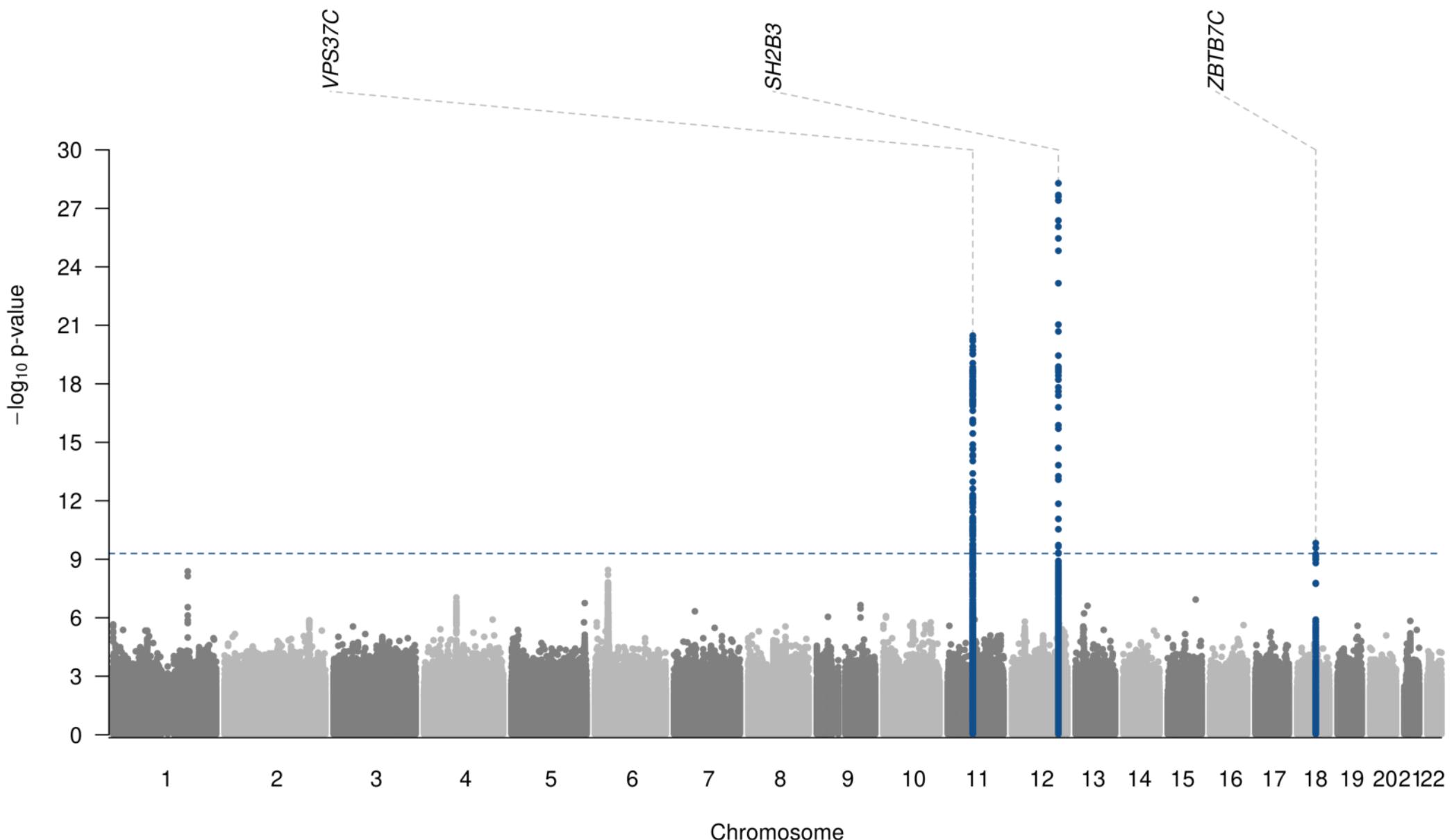
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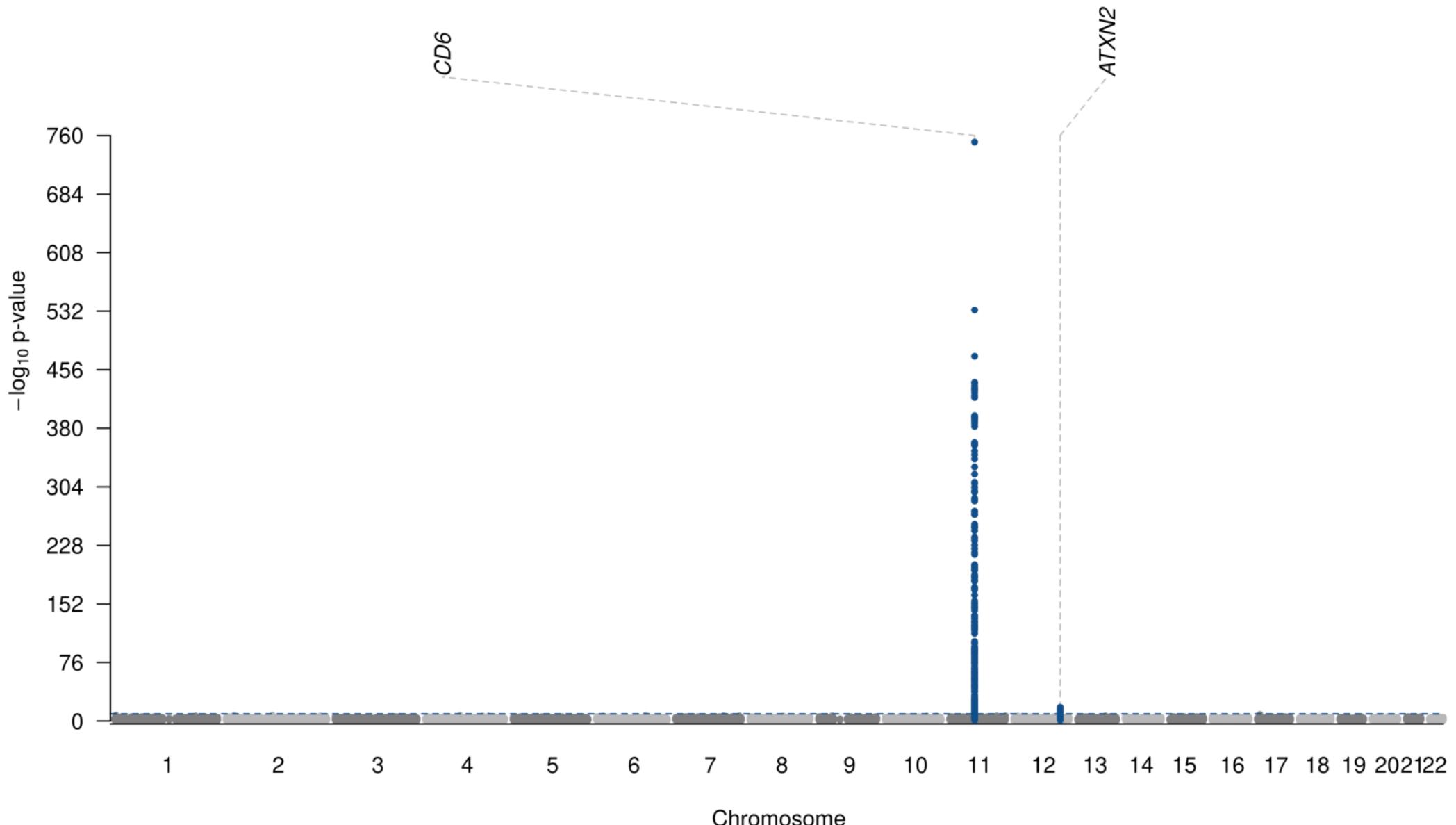
## CCL28 (CCL28)



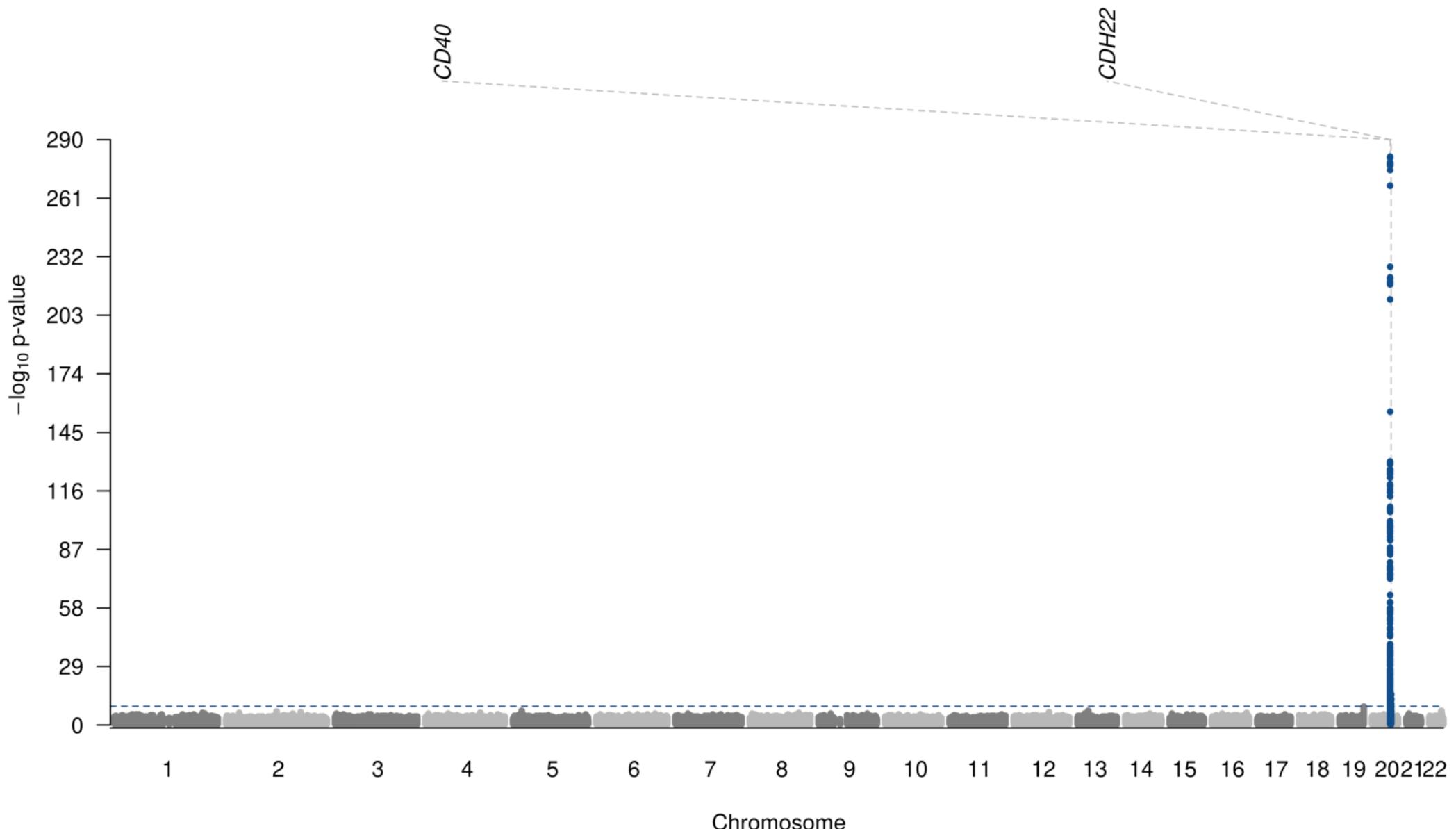
## CD5 (CD5)



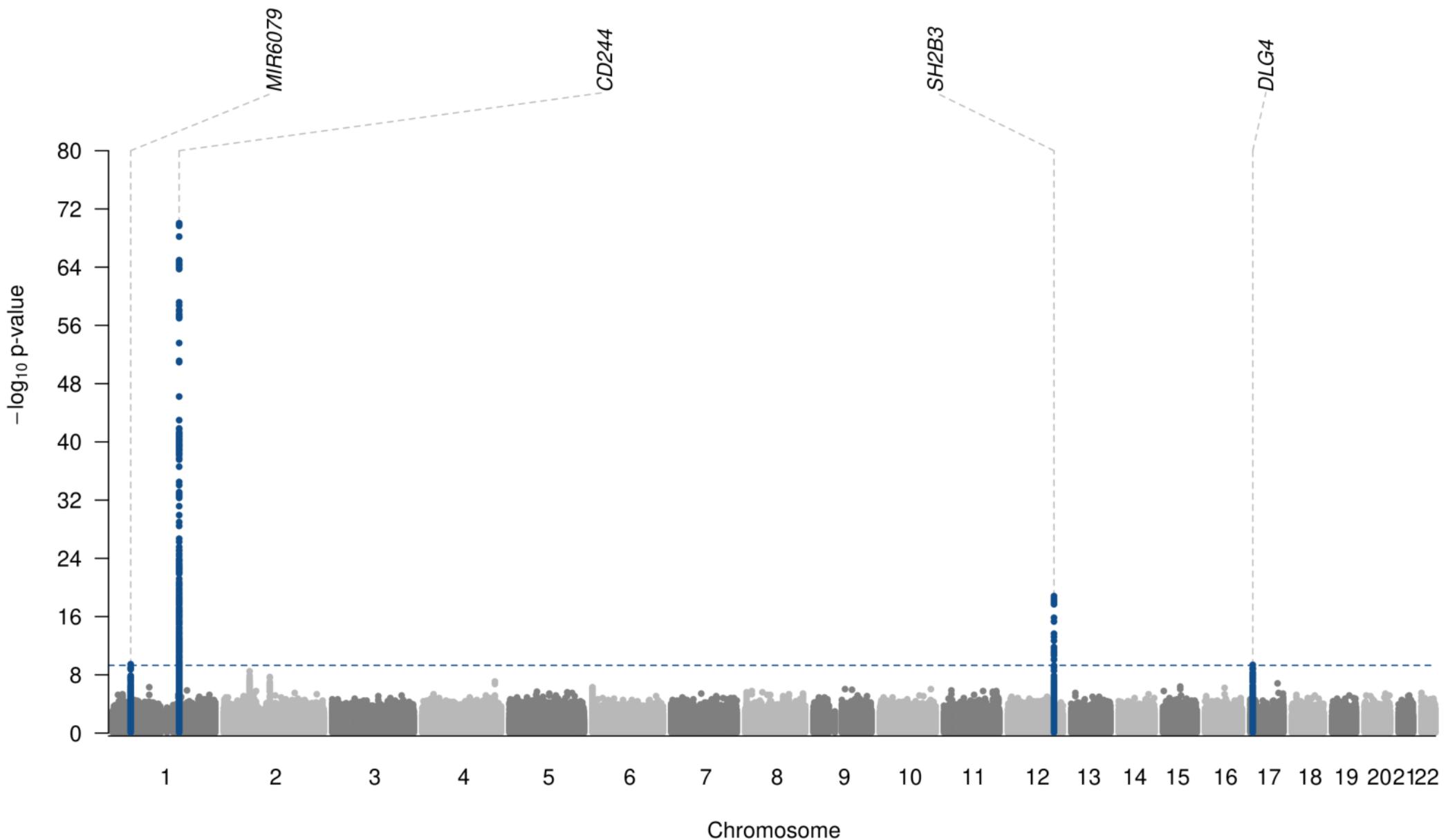
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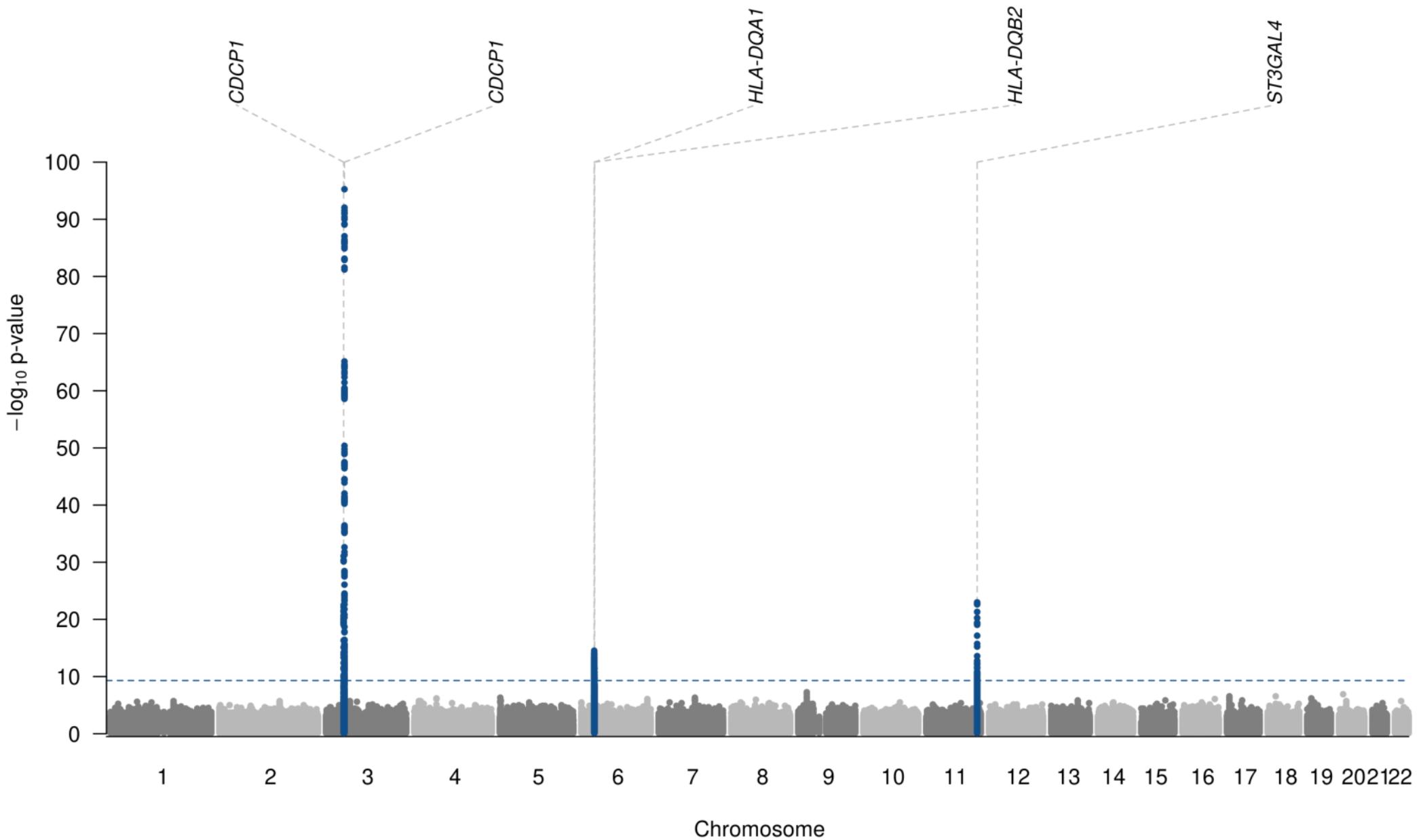
## **CD40 (CD40)**



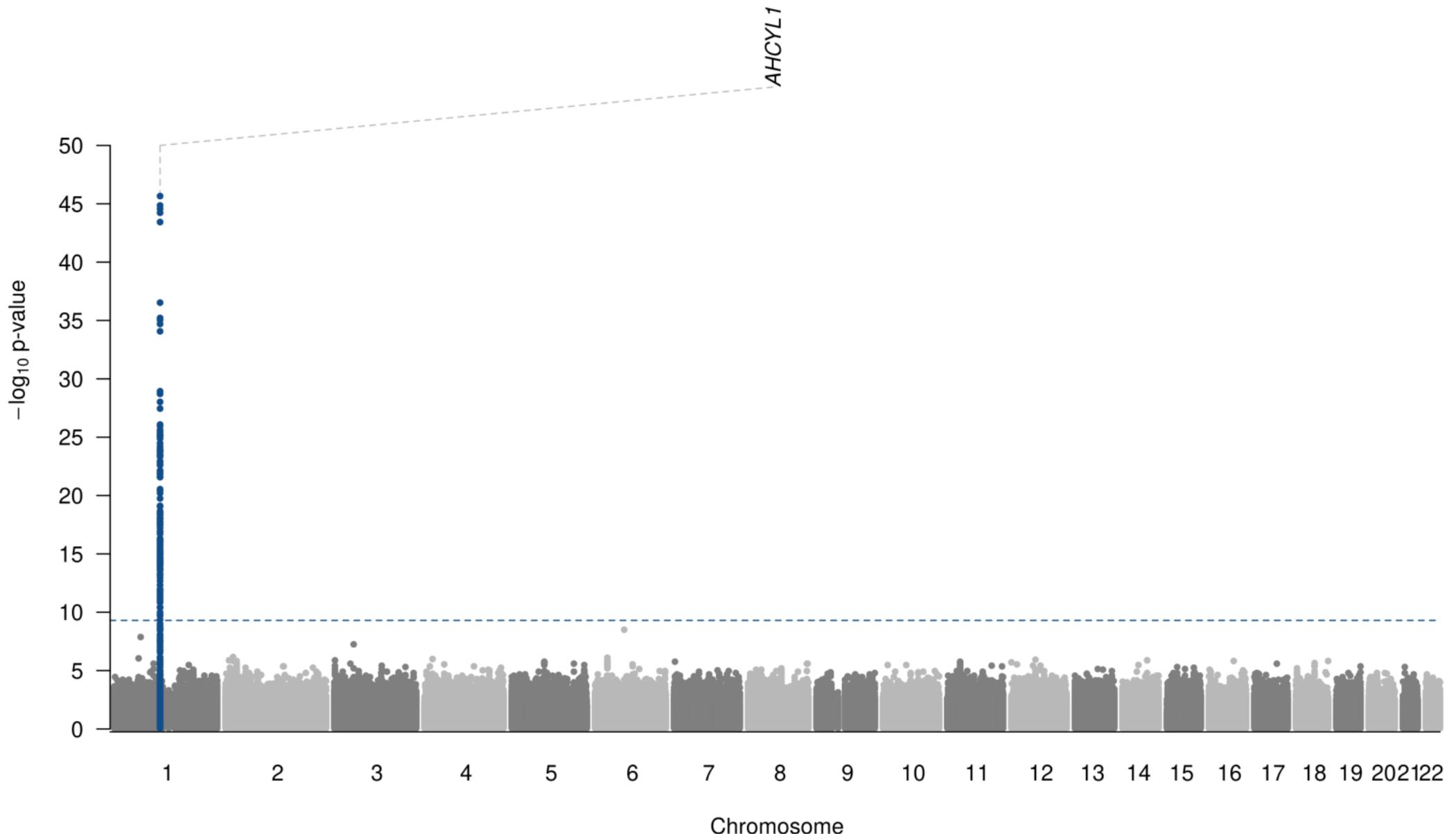
## CD244 (CD244)



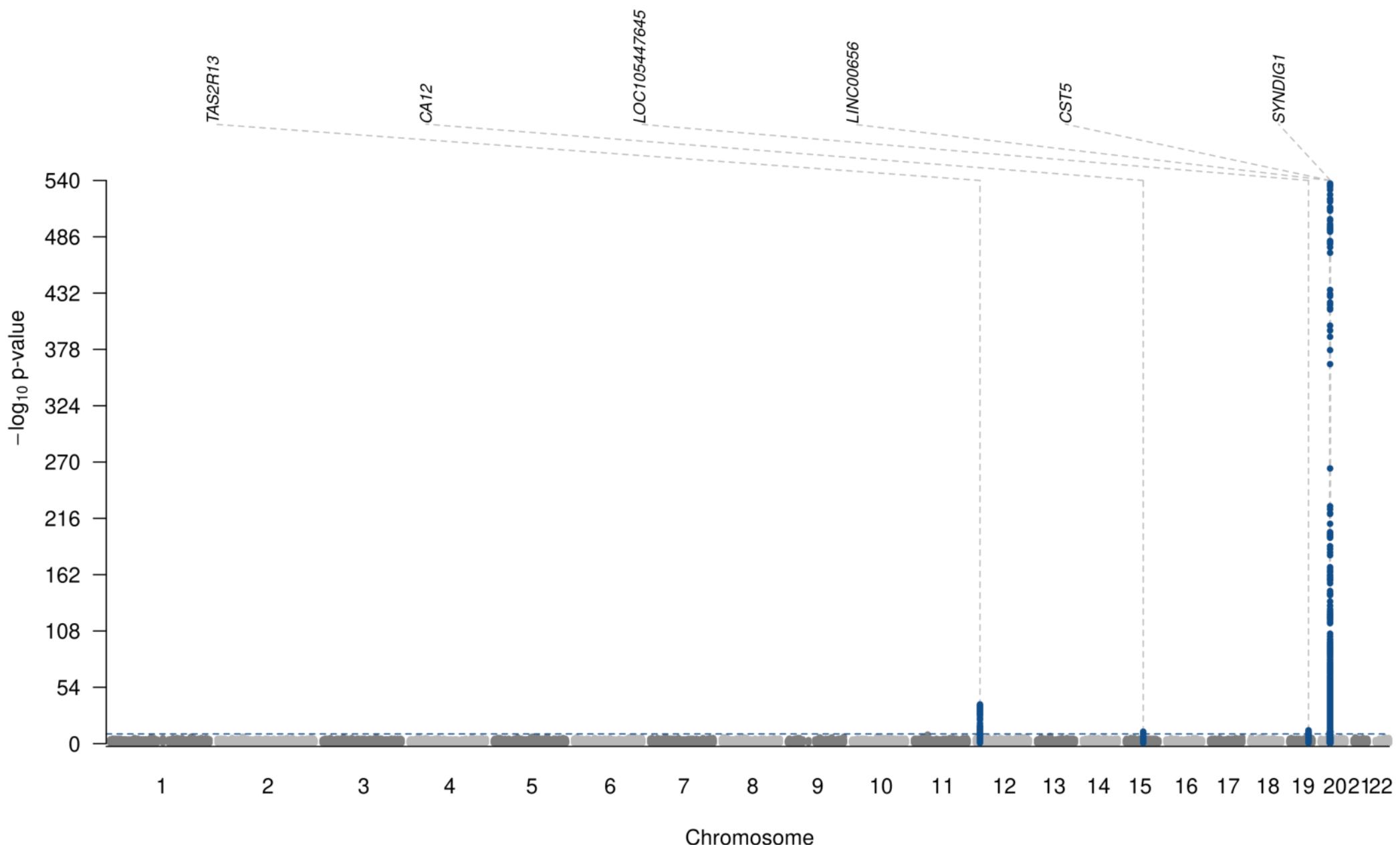
# CDCP1 (CDCP1)



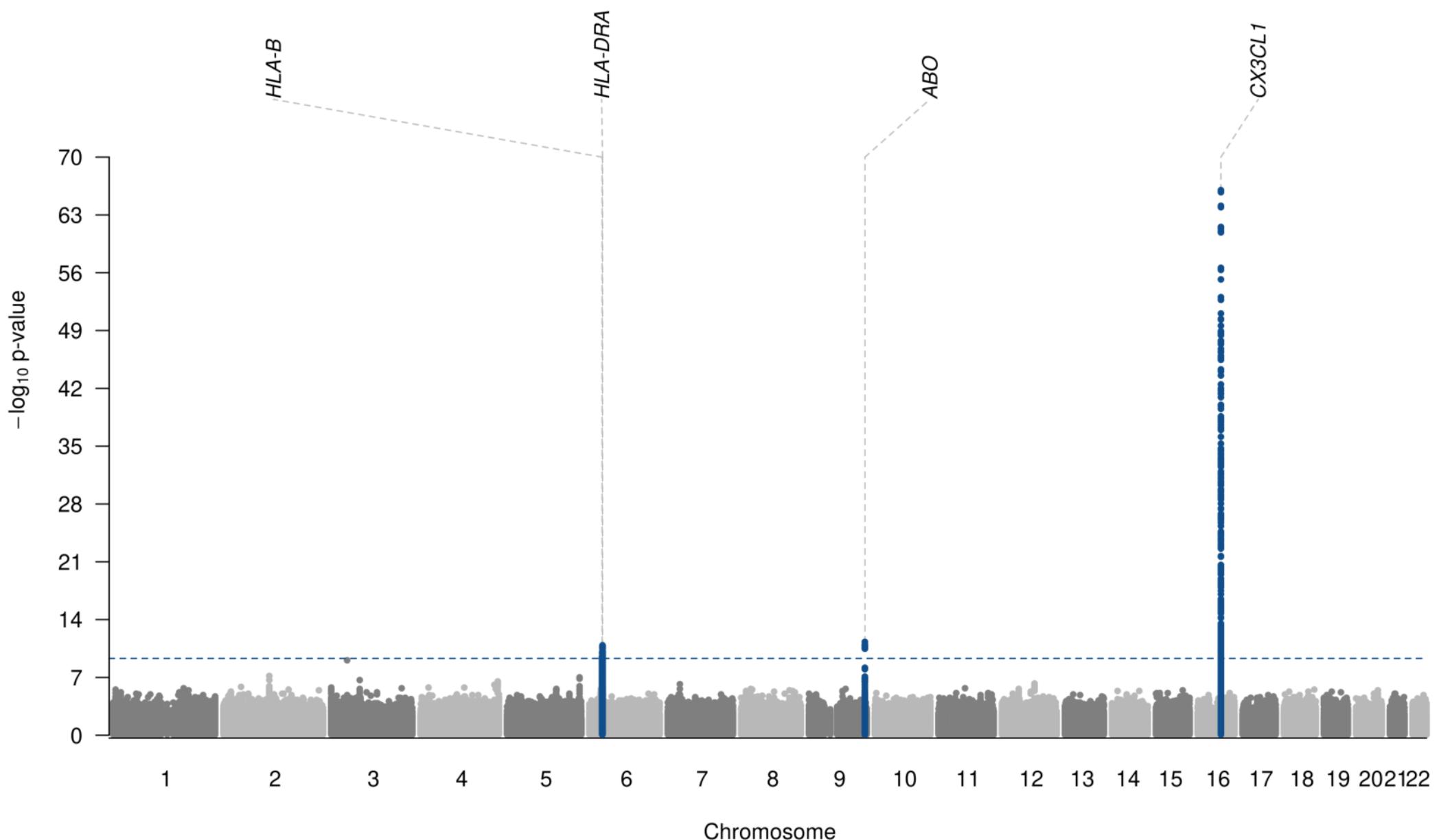
## CSF-1 (CSF1)



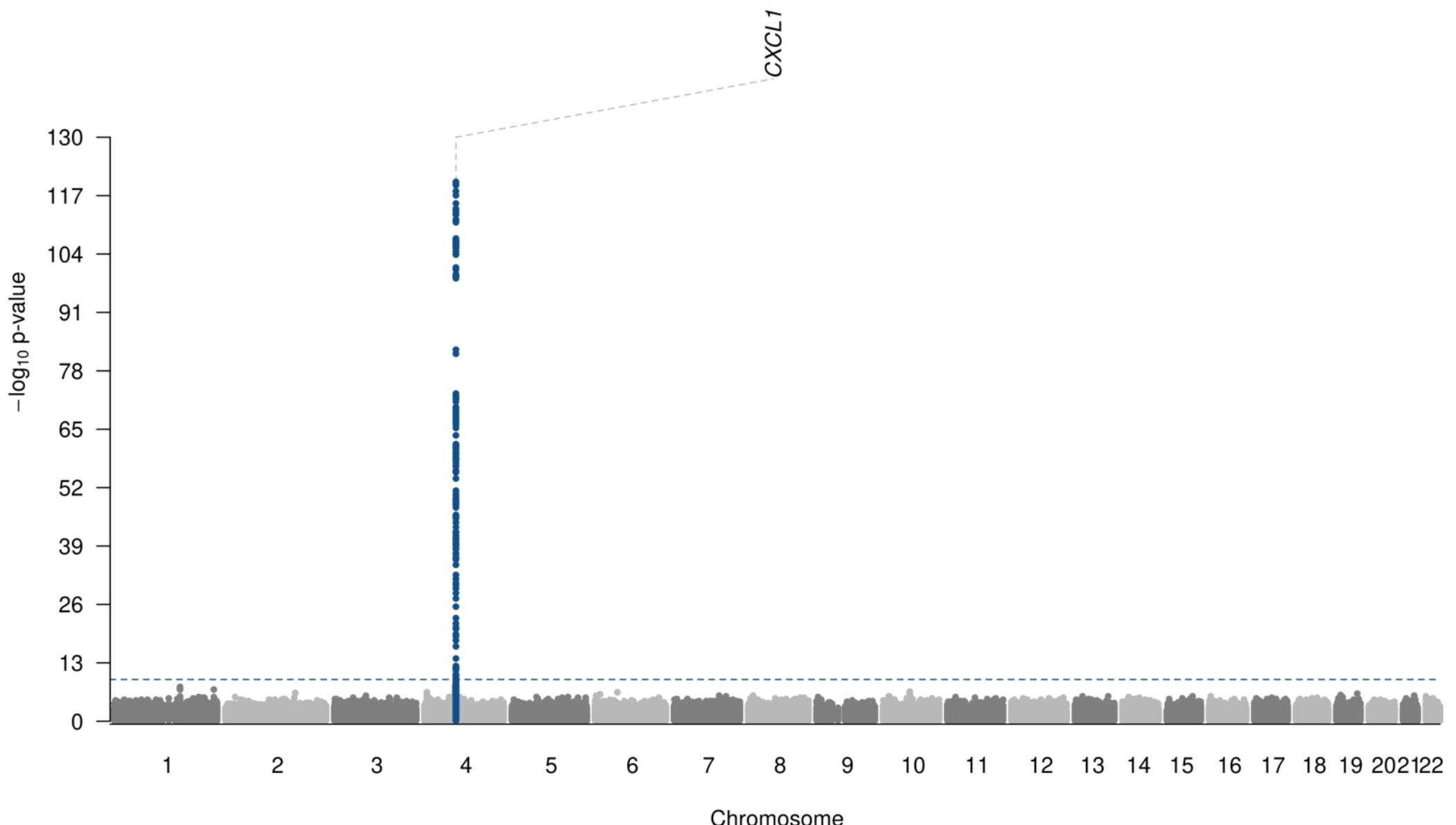
## CST5 (CST5)



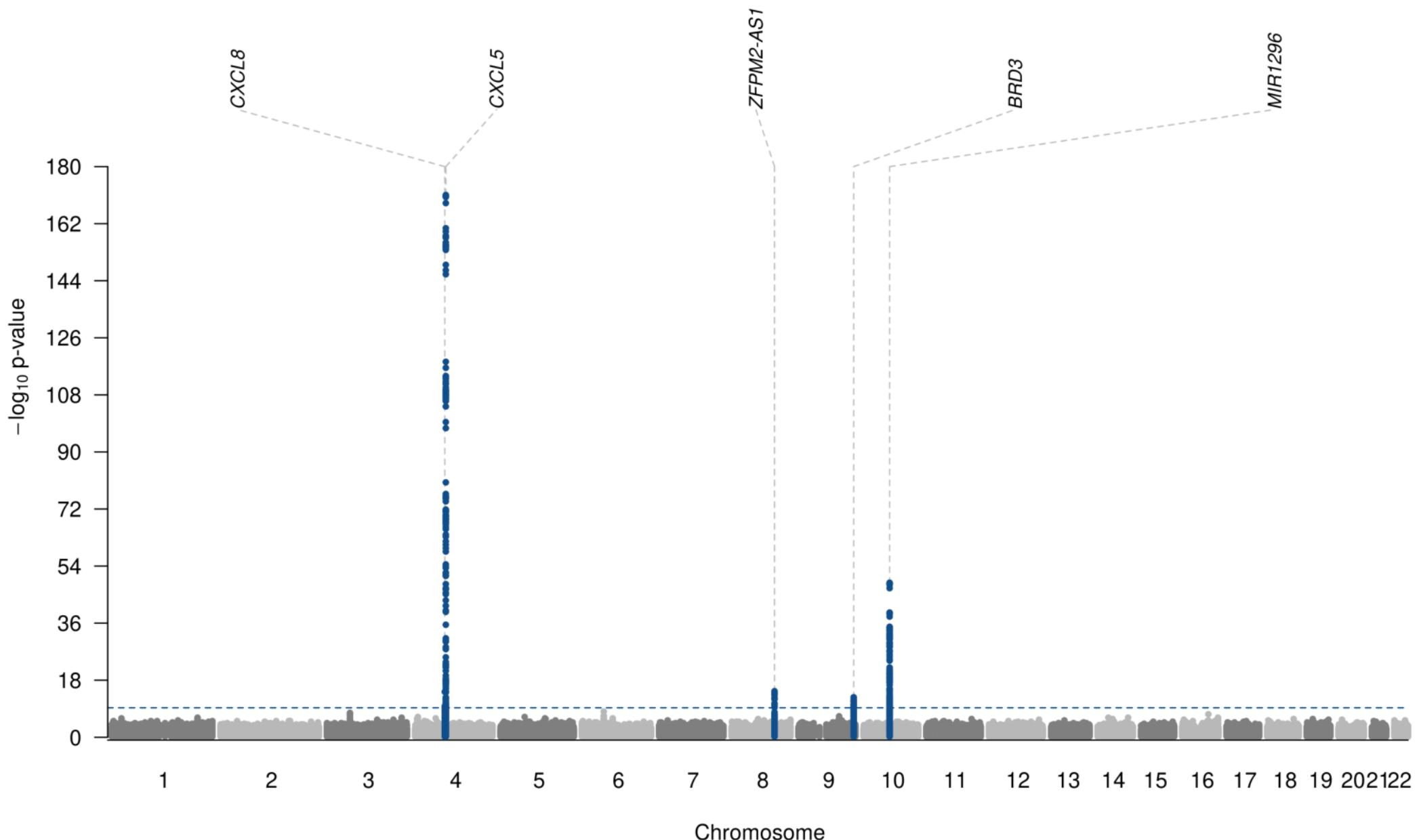
# CX3CL1 (CX3CL1)



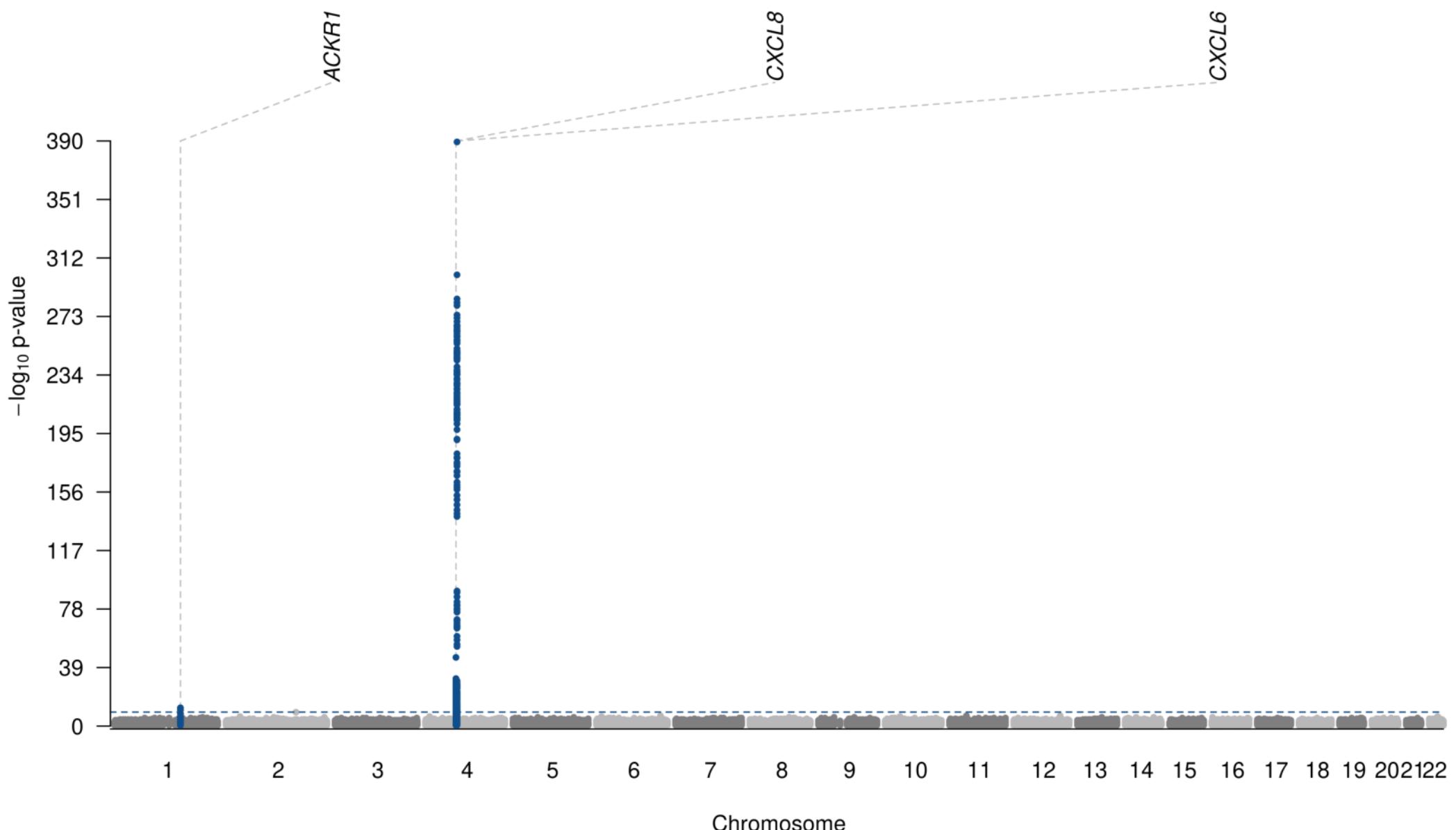
## CXCL1 (CXCL1)



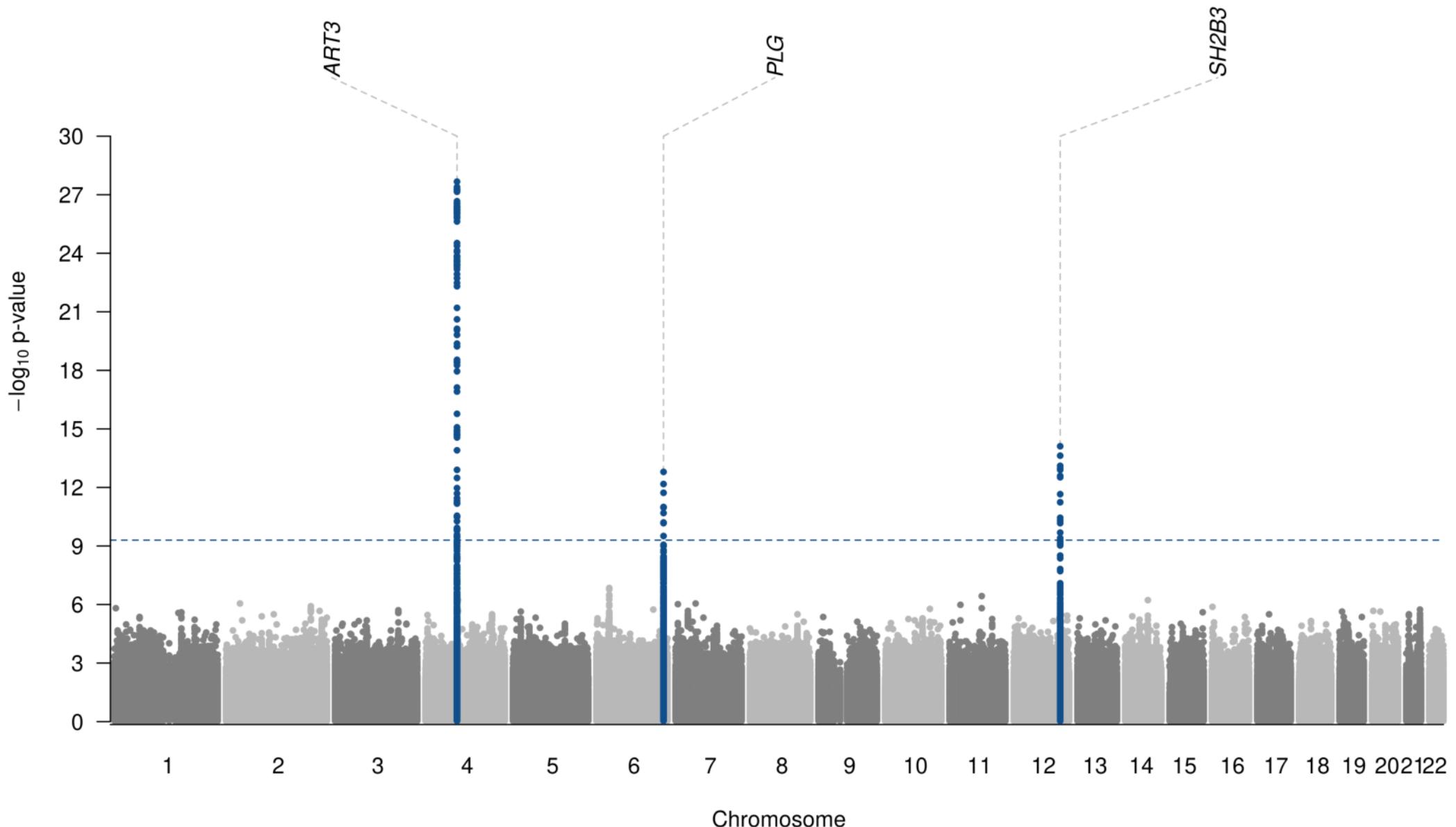
## CXCL5 (CXCL5)



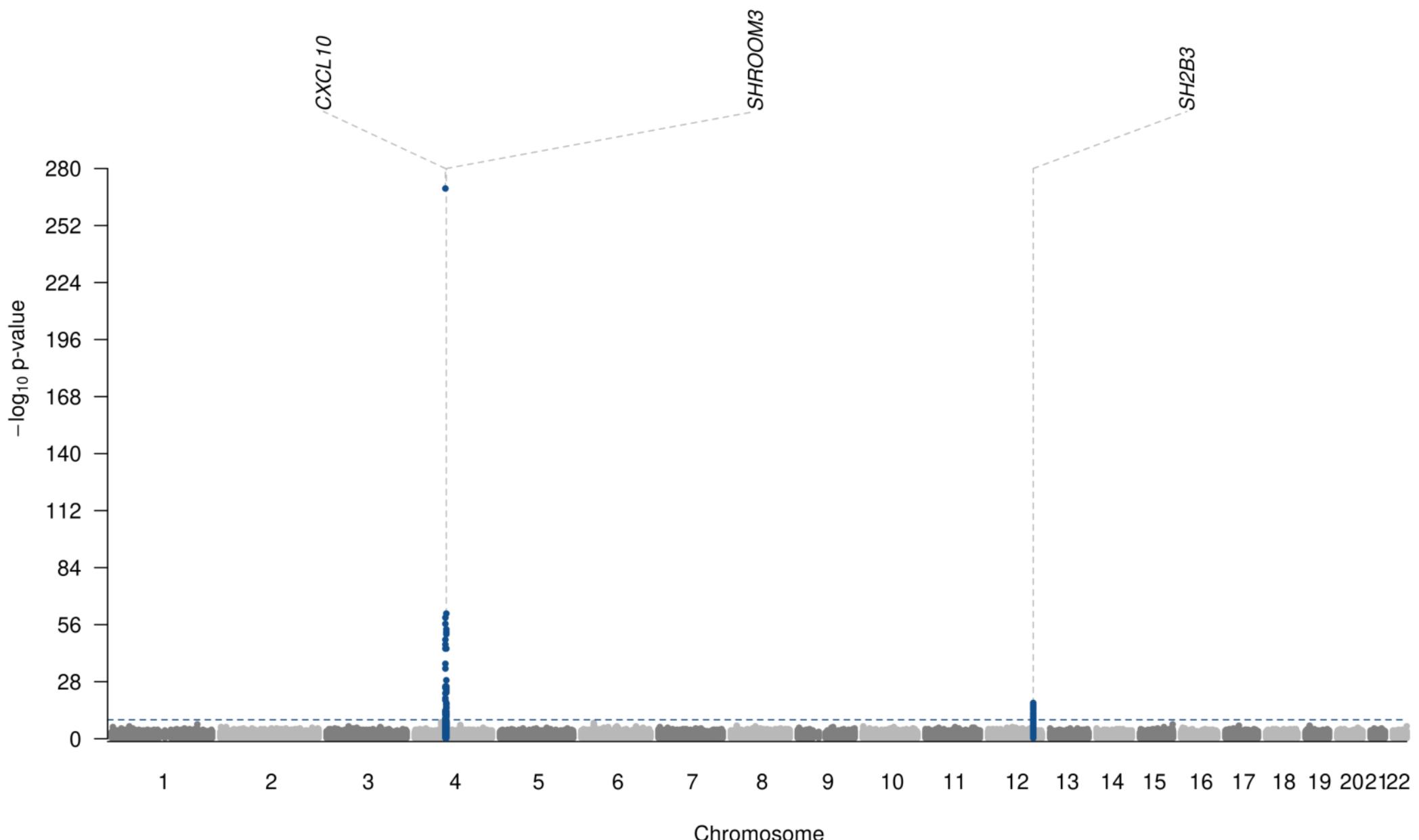
## CXCL6 (CXCL6)



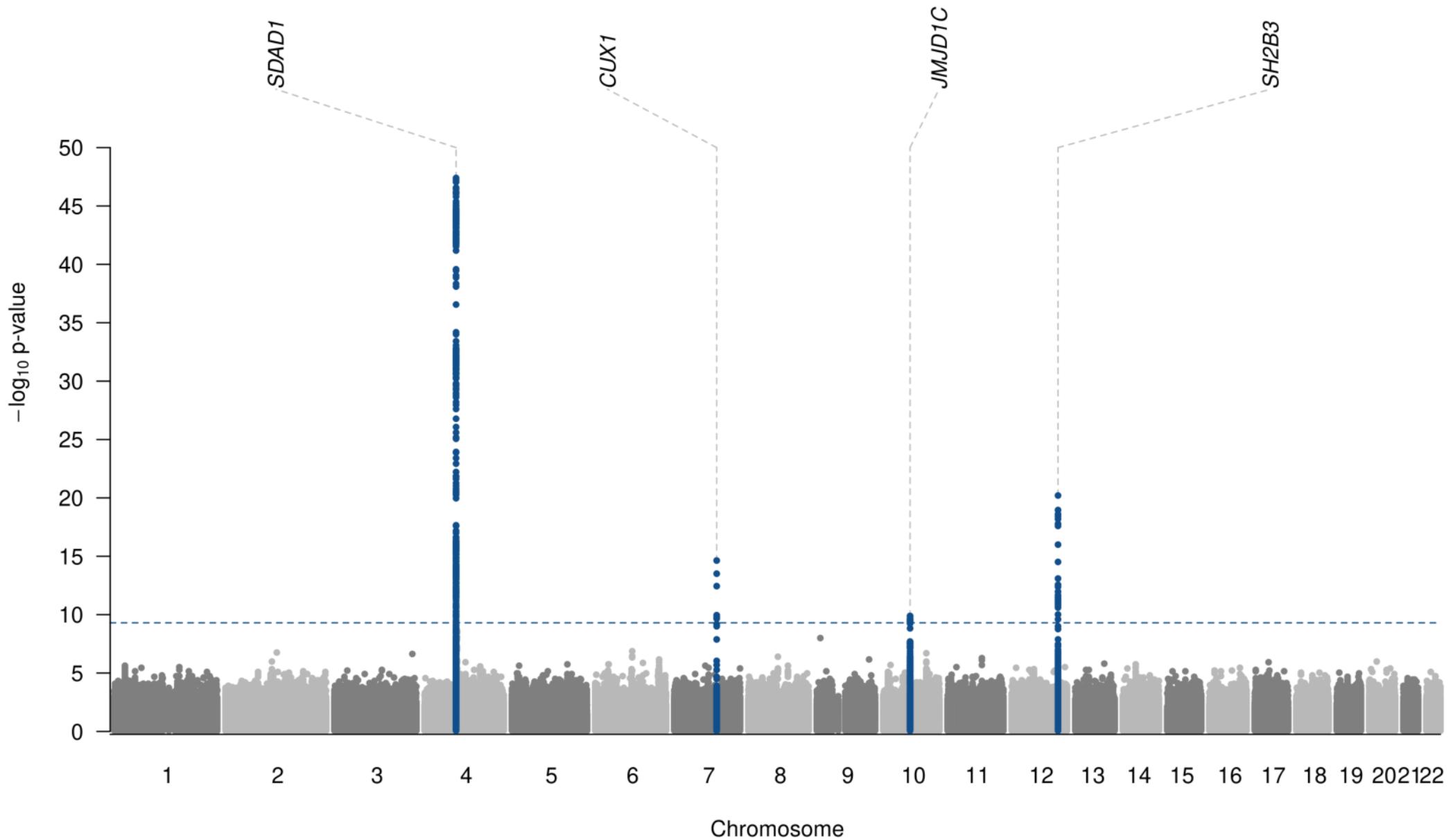
# CXCL9 (CXCL9)



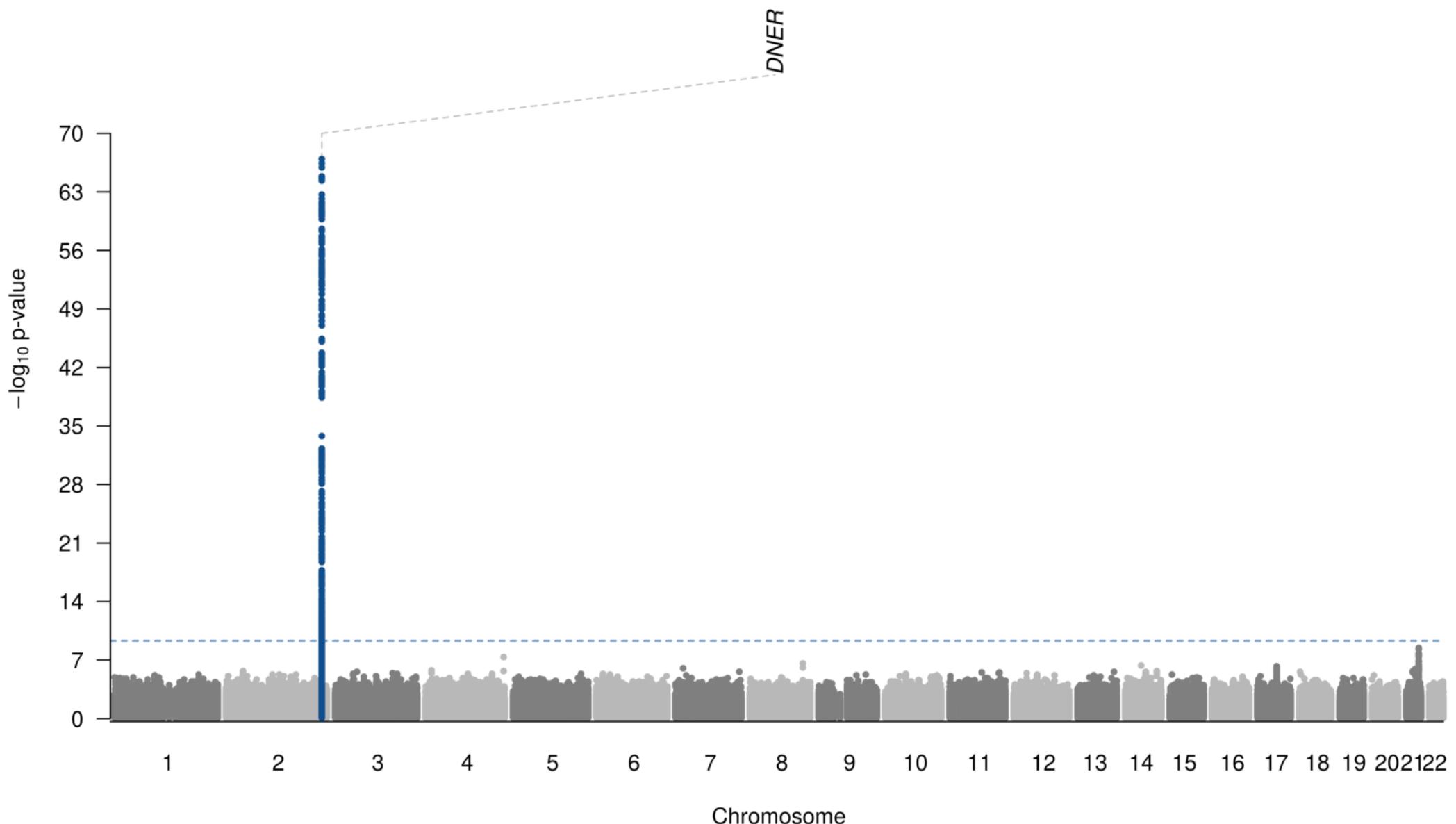
## CXCL10 (CXCL10)



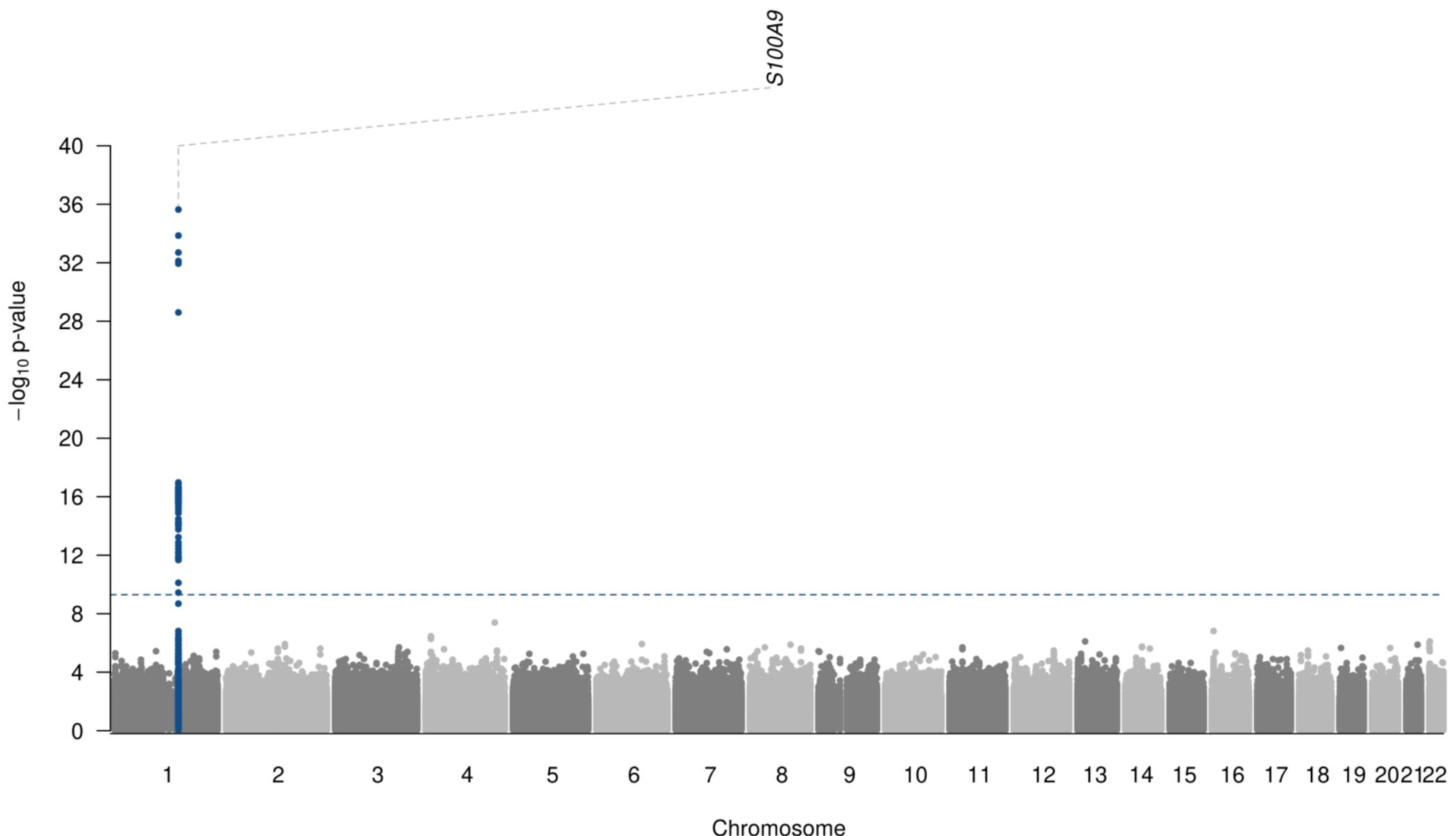
# CXCL11 (CXCL11)



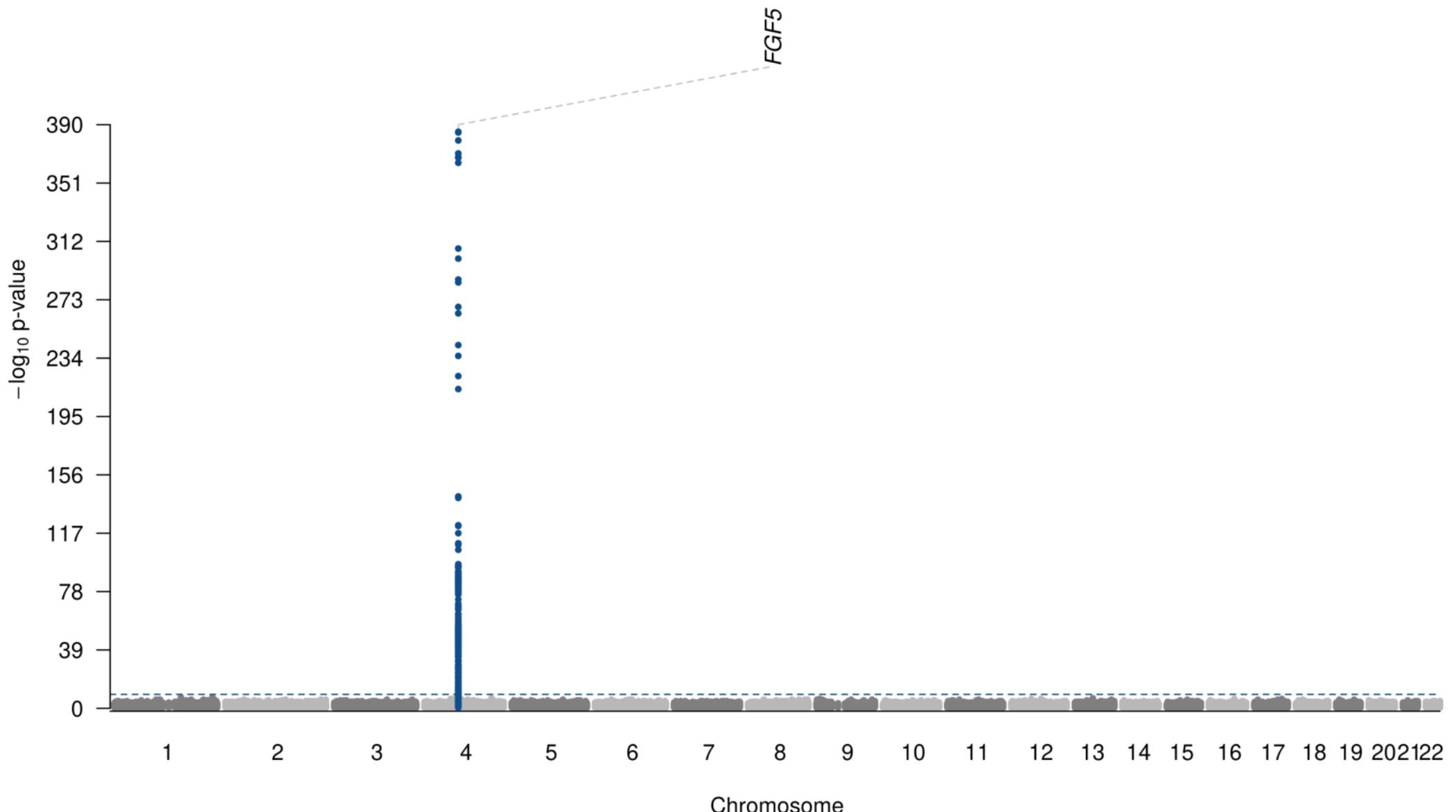
## DNER (DNER)



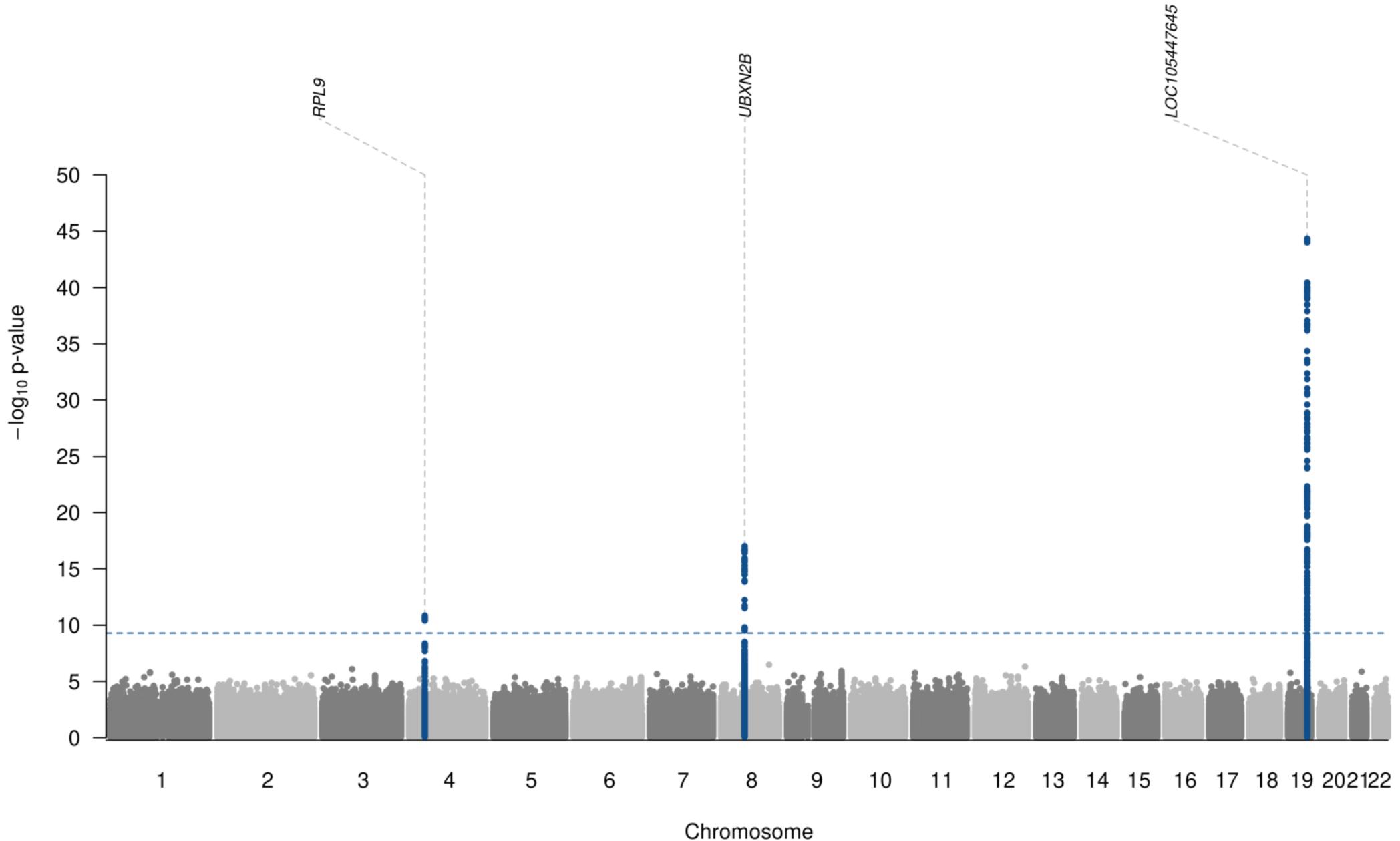
# EN-RAGE (S100A12)



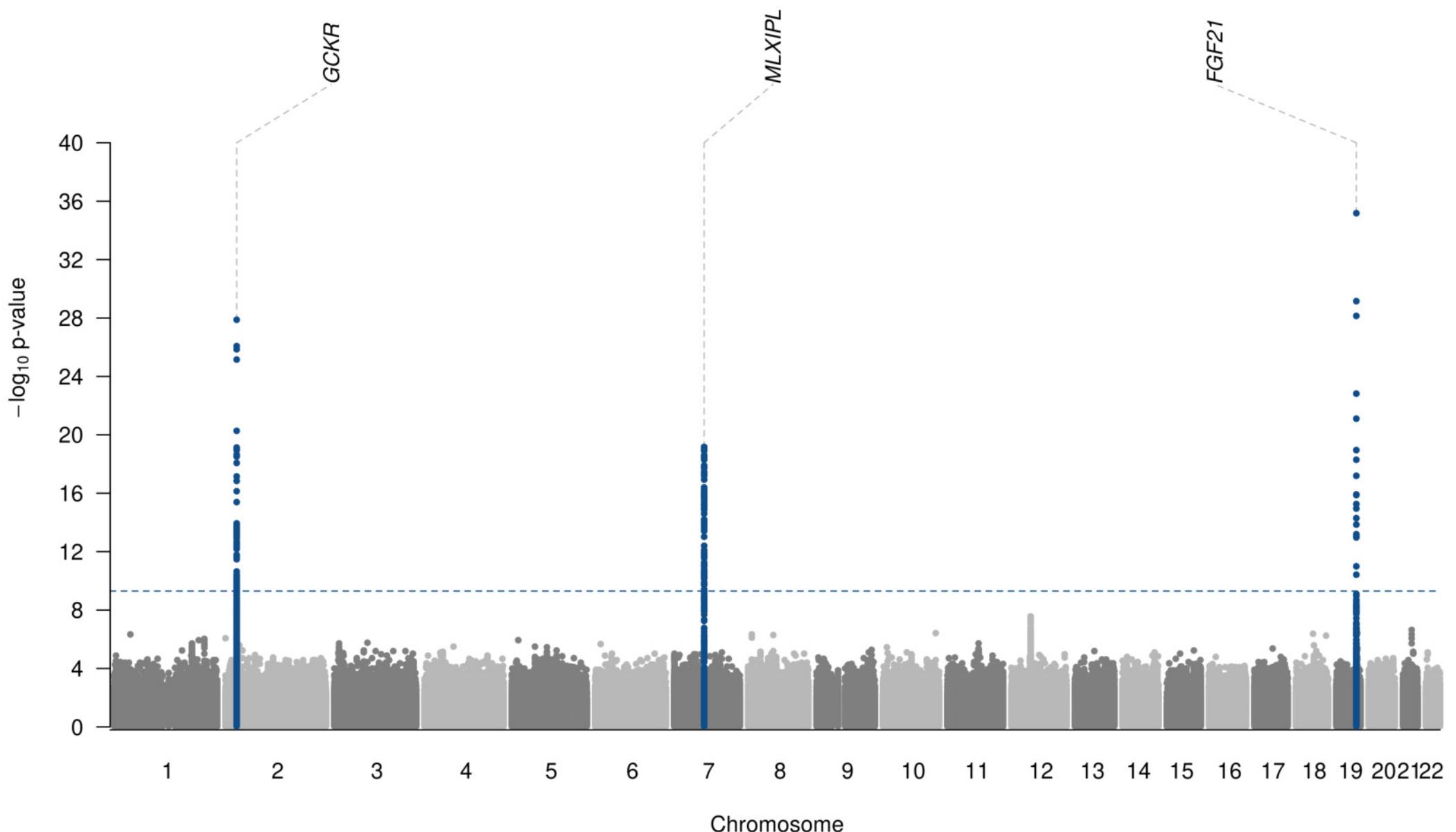
## FGF-5 (FGF5)



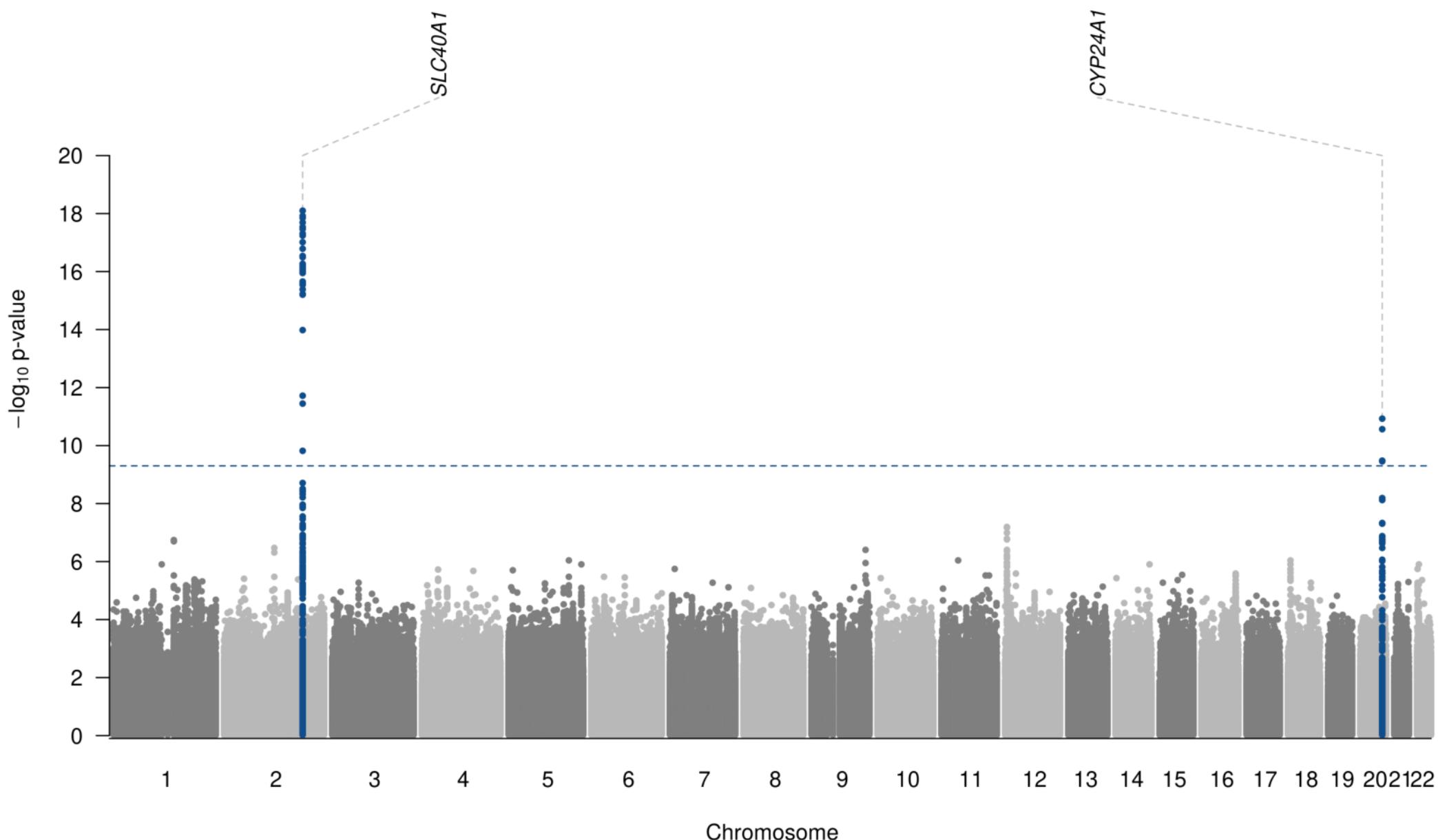
## FGF-19 (FGF19)



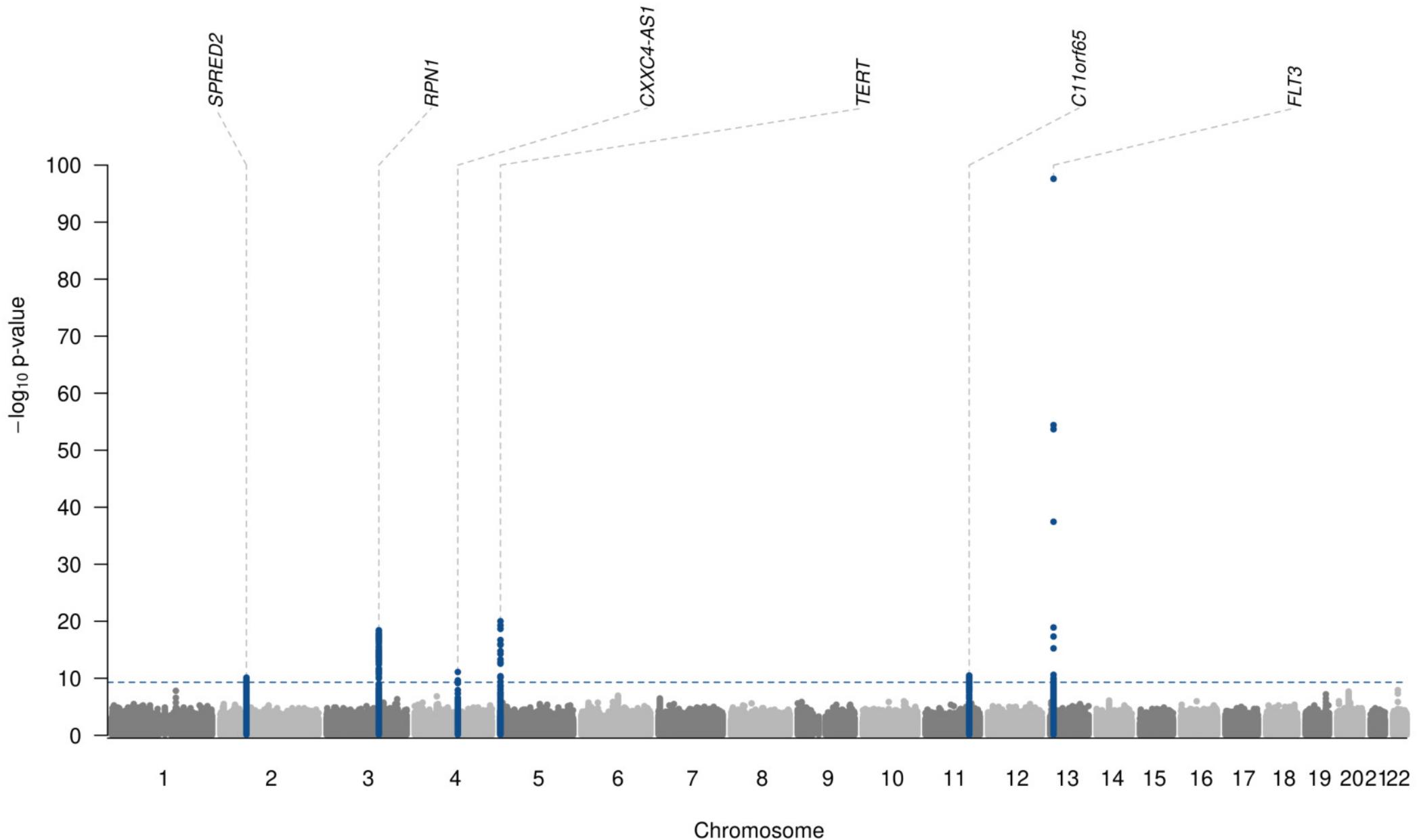
## FGF-21 (FGF21)



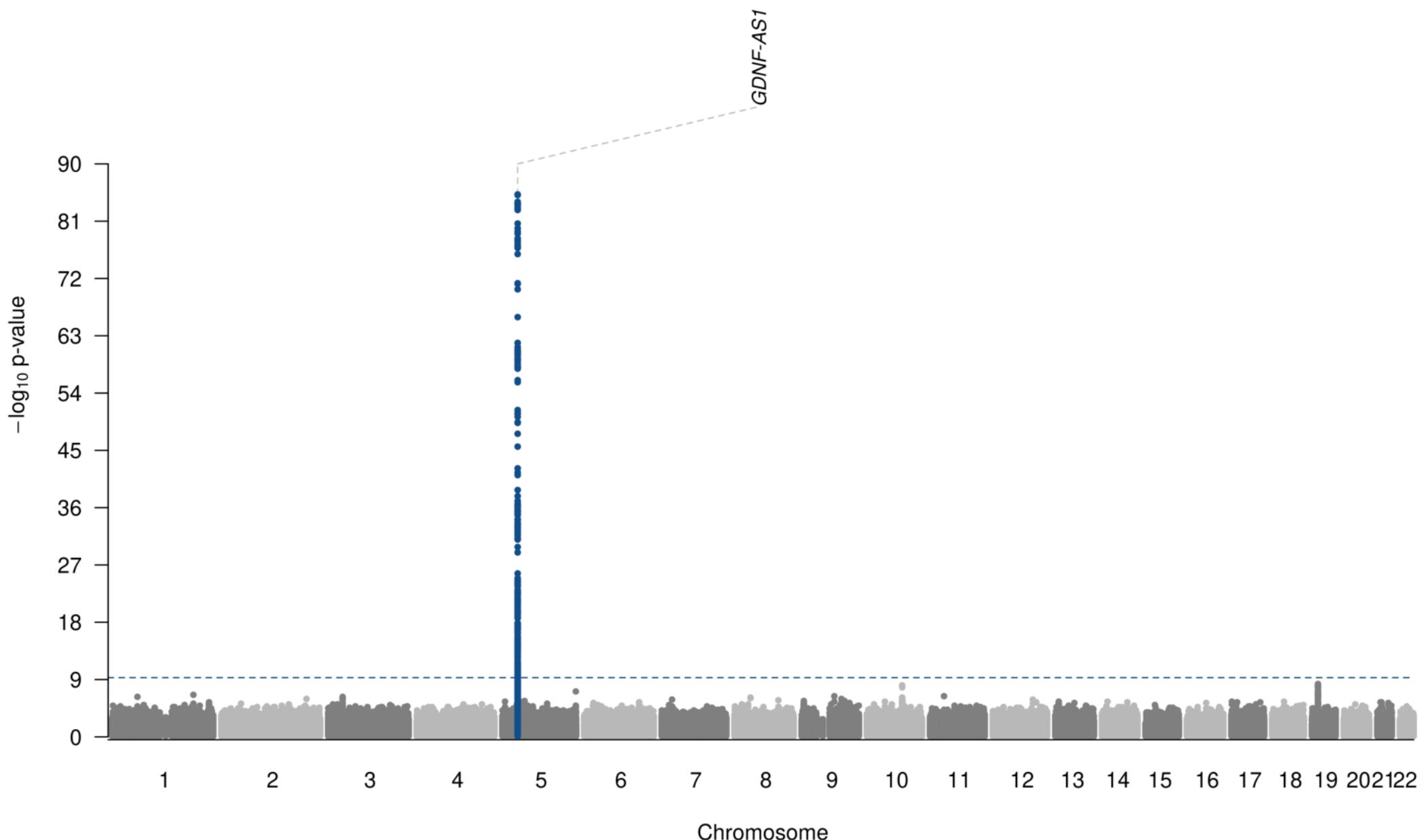
## FGF-23 (FGF23)



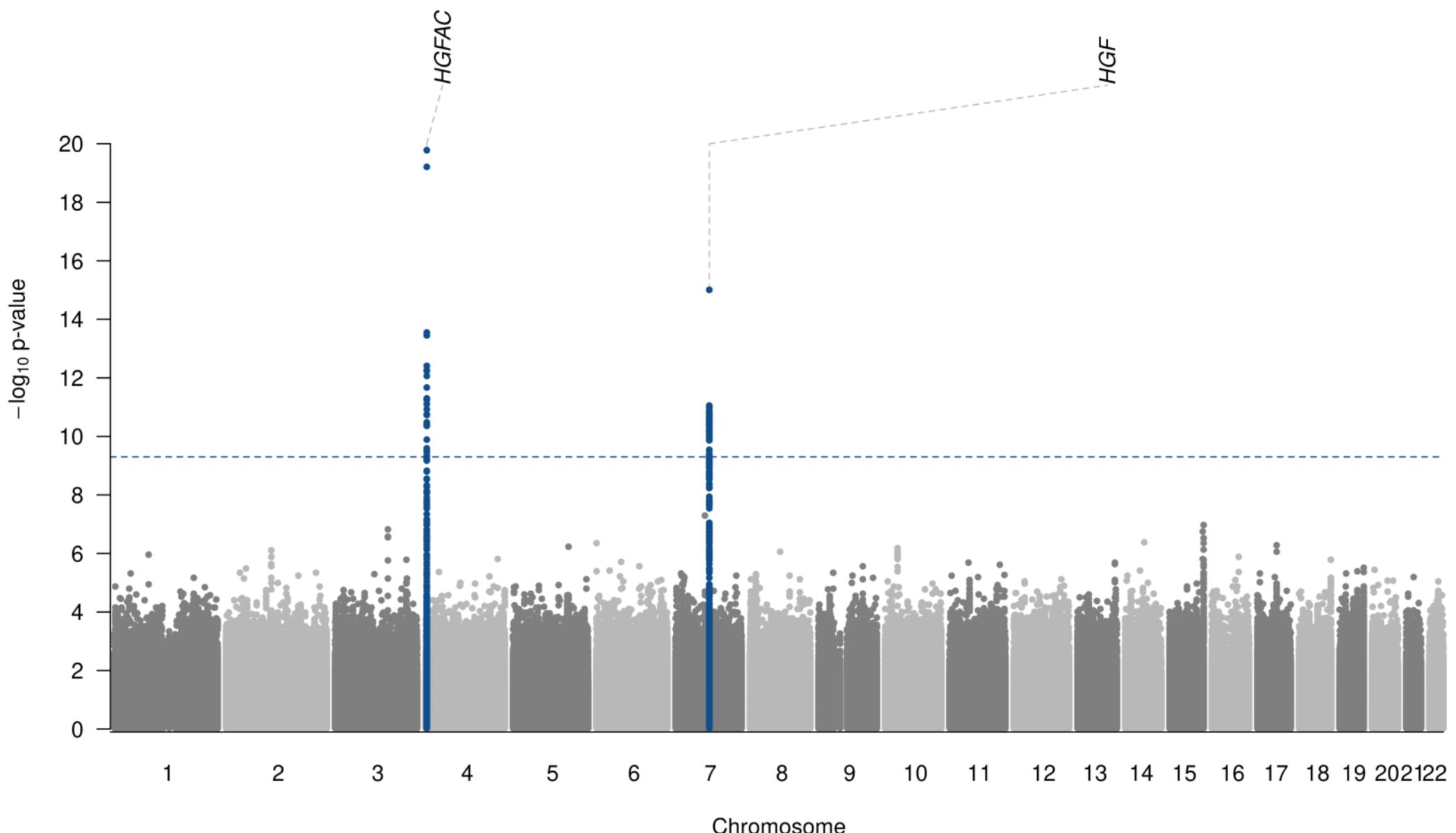
# Flt3L (FLT3LG)



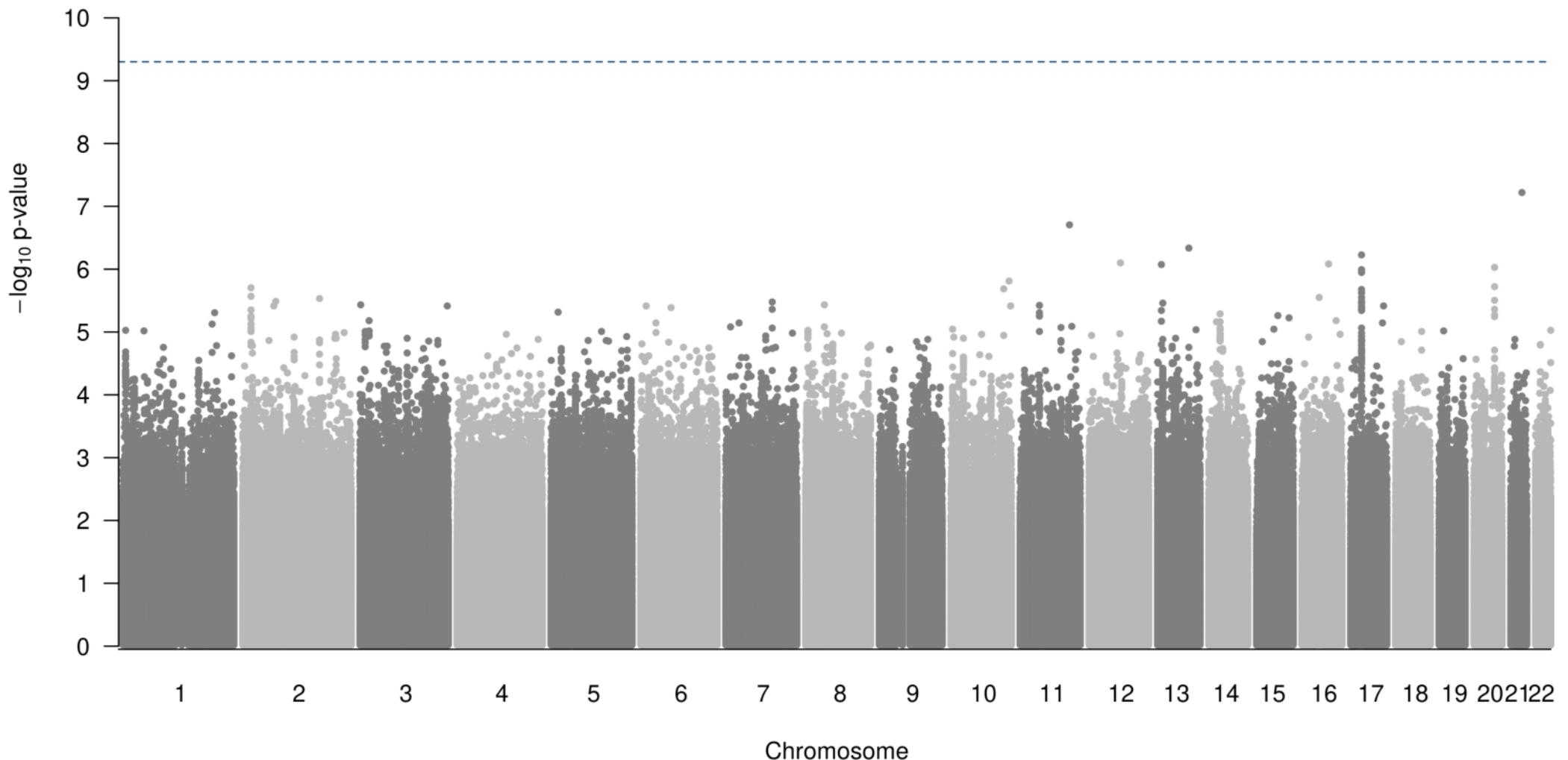
## hGDNF (GDNF)



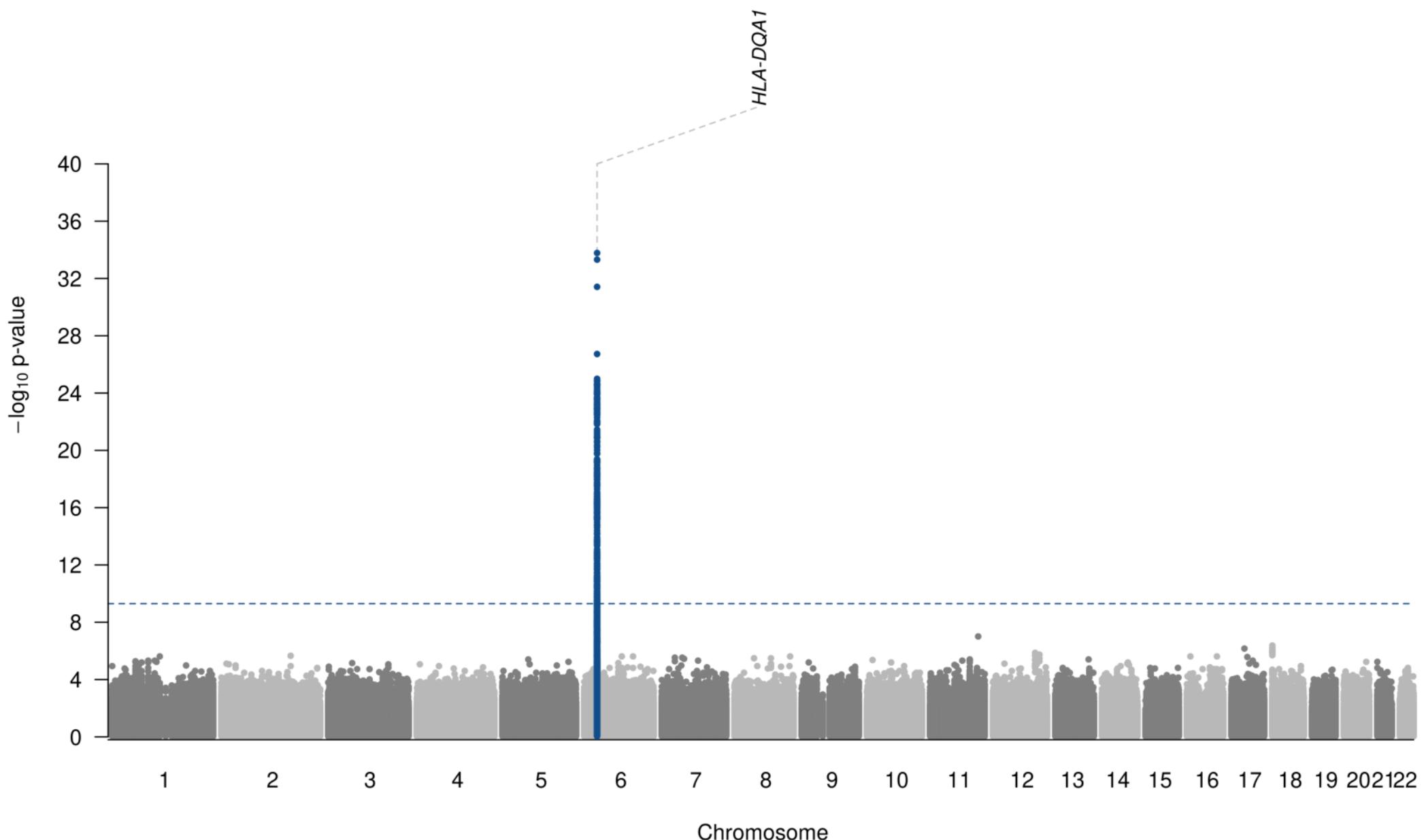
## HGF (HGF)



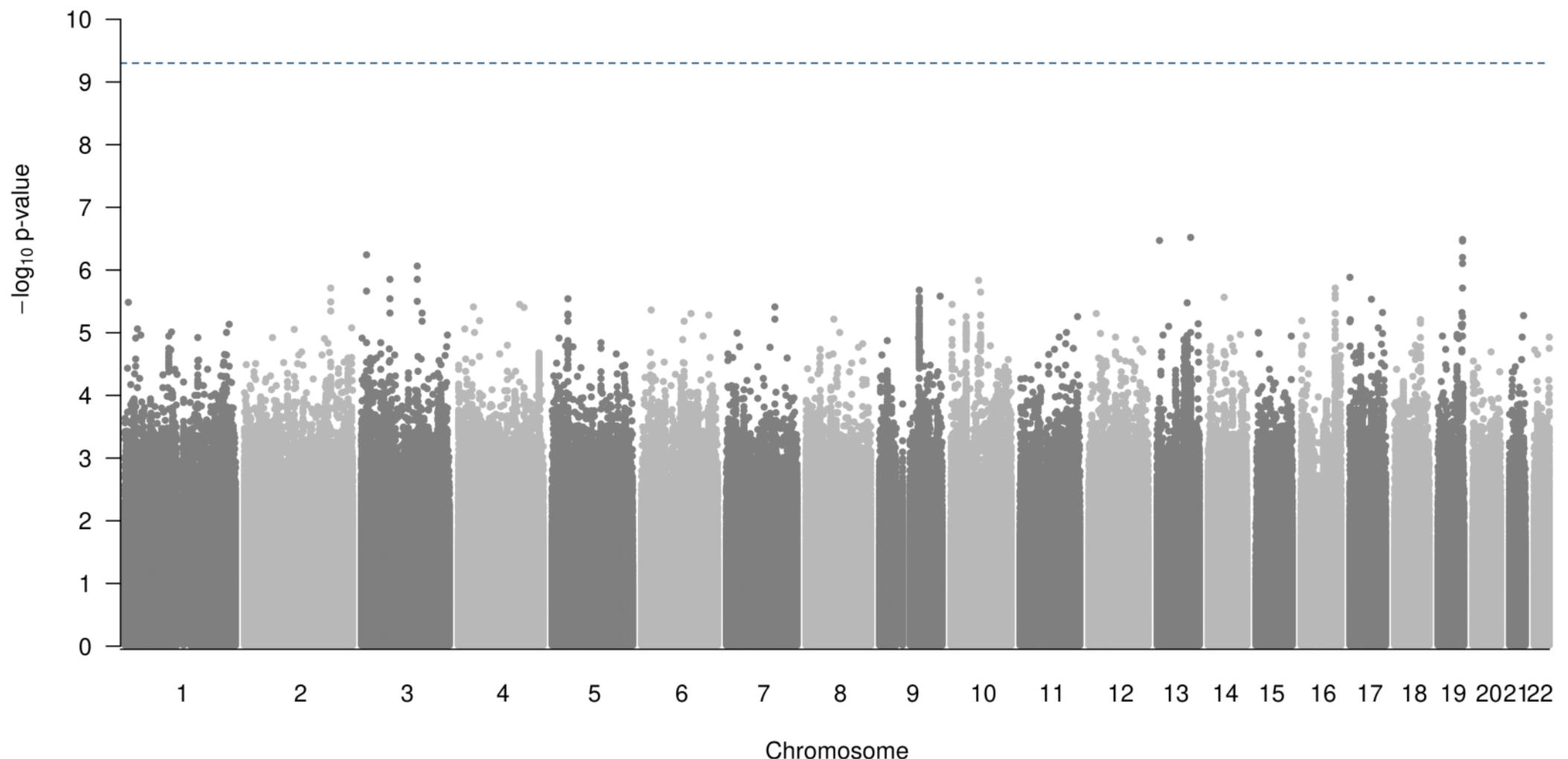
## IFN-gamma (IFNG)



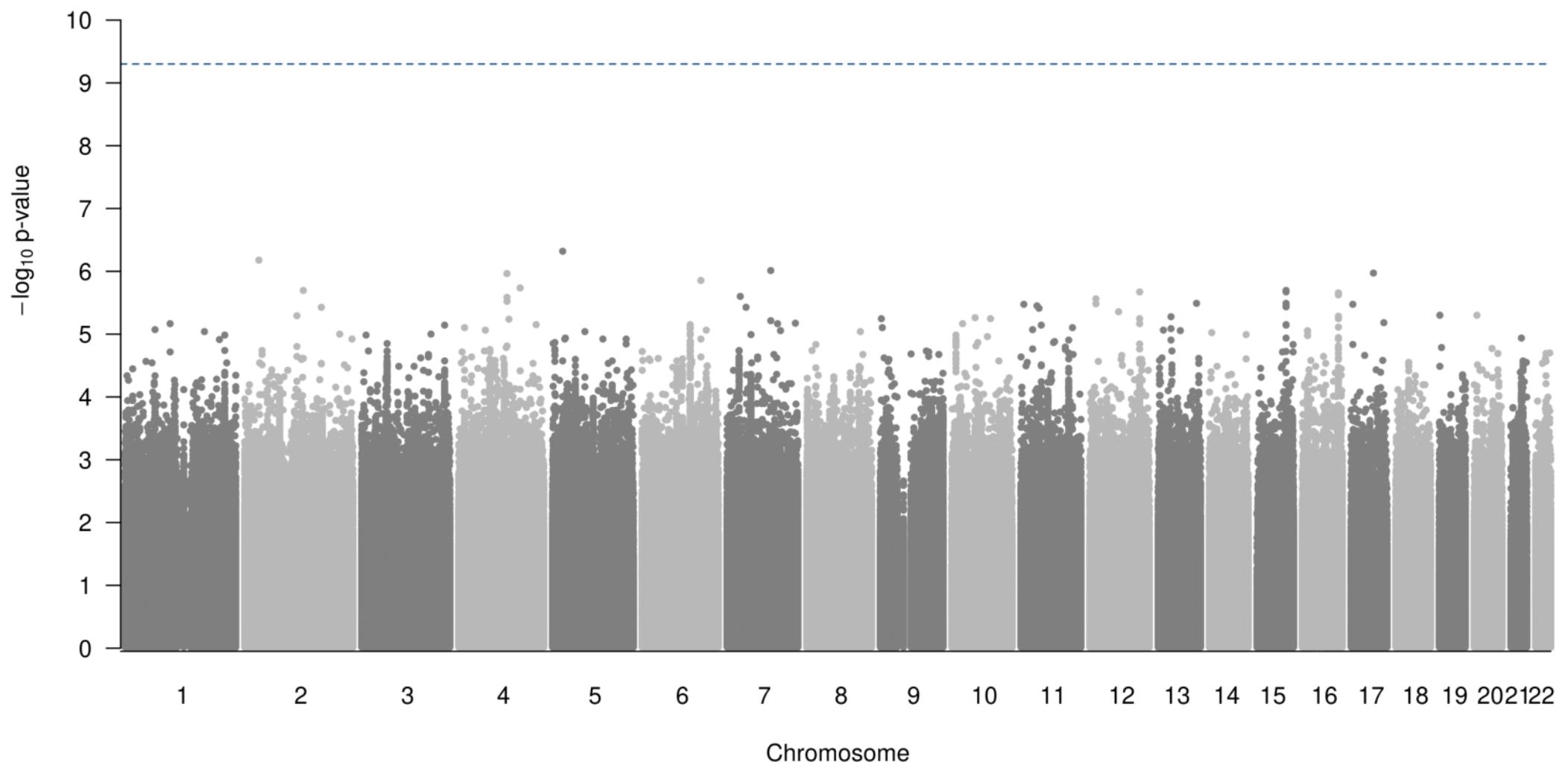
# IL-1 (IL1A)



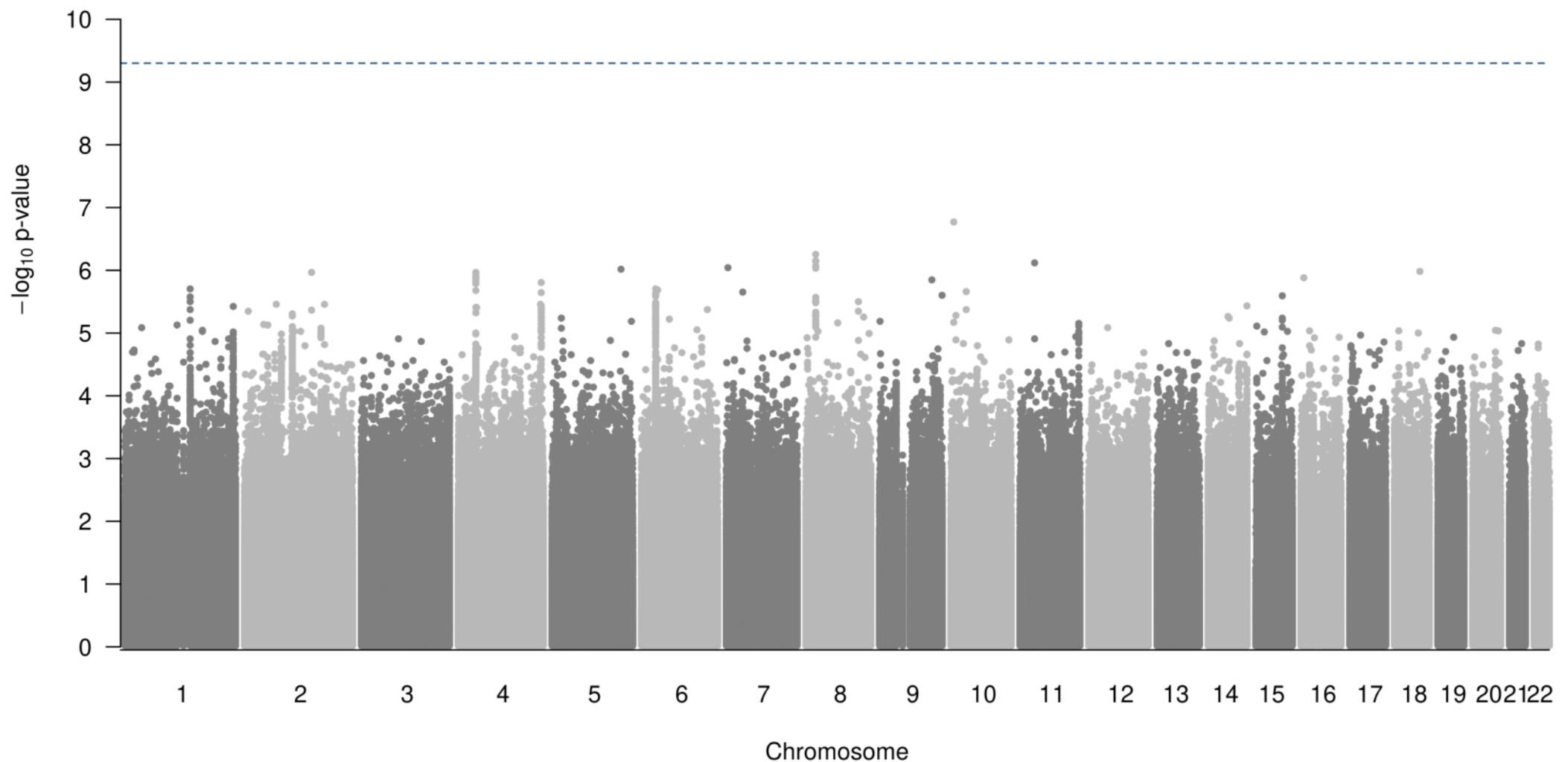
## IL-2 (IL2)



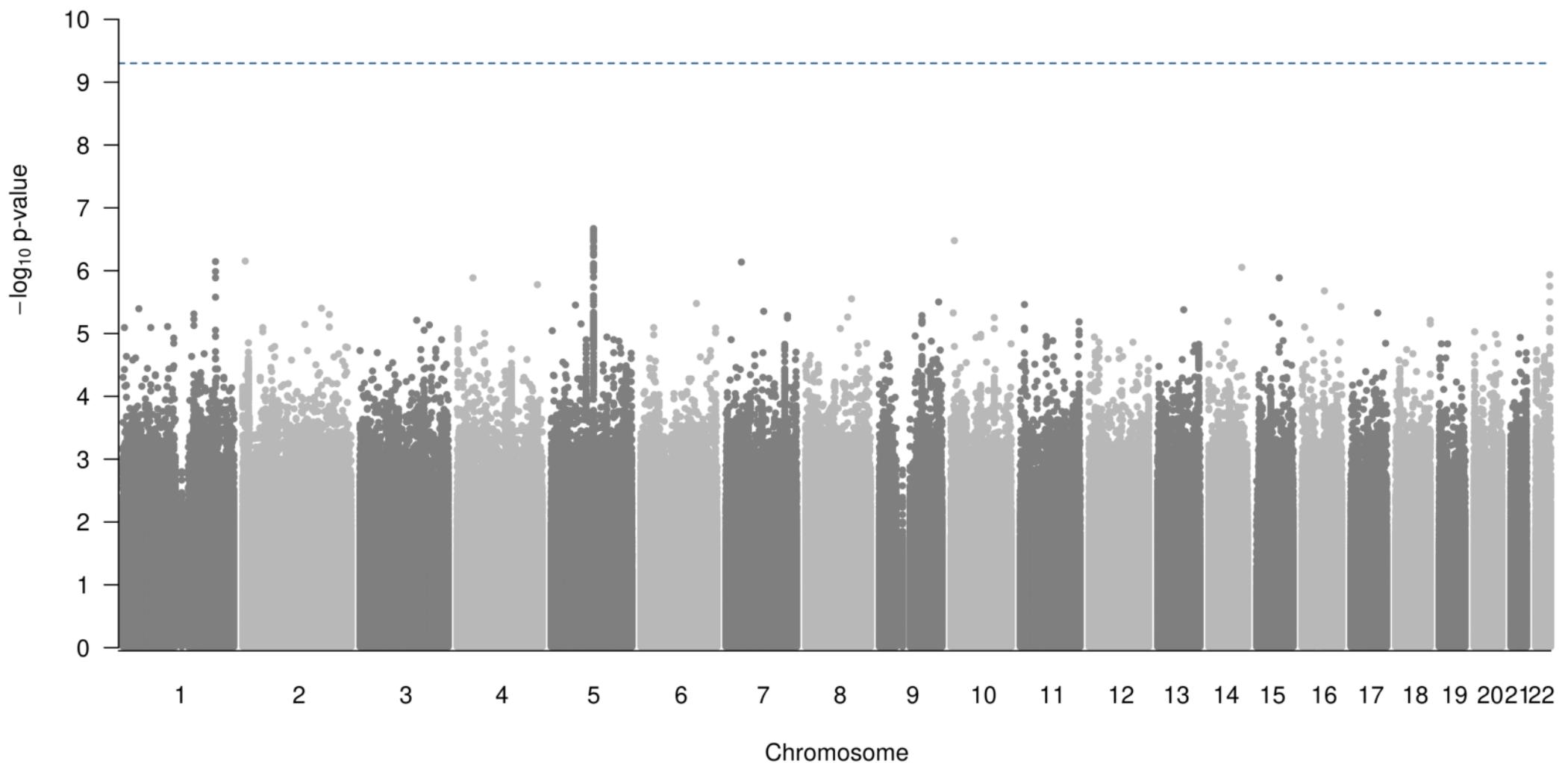
## IL-2RB (IL2RB)



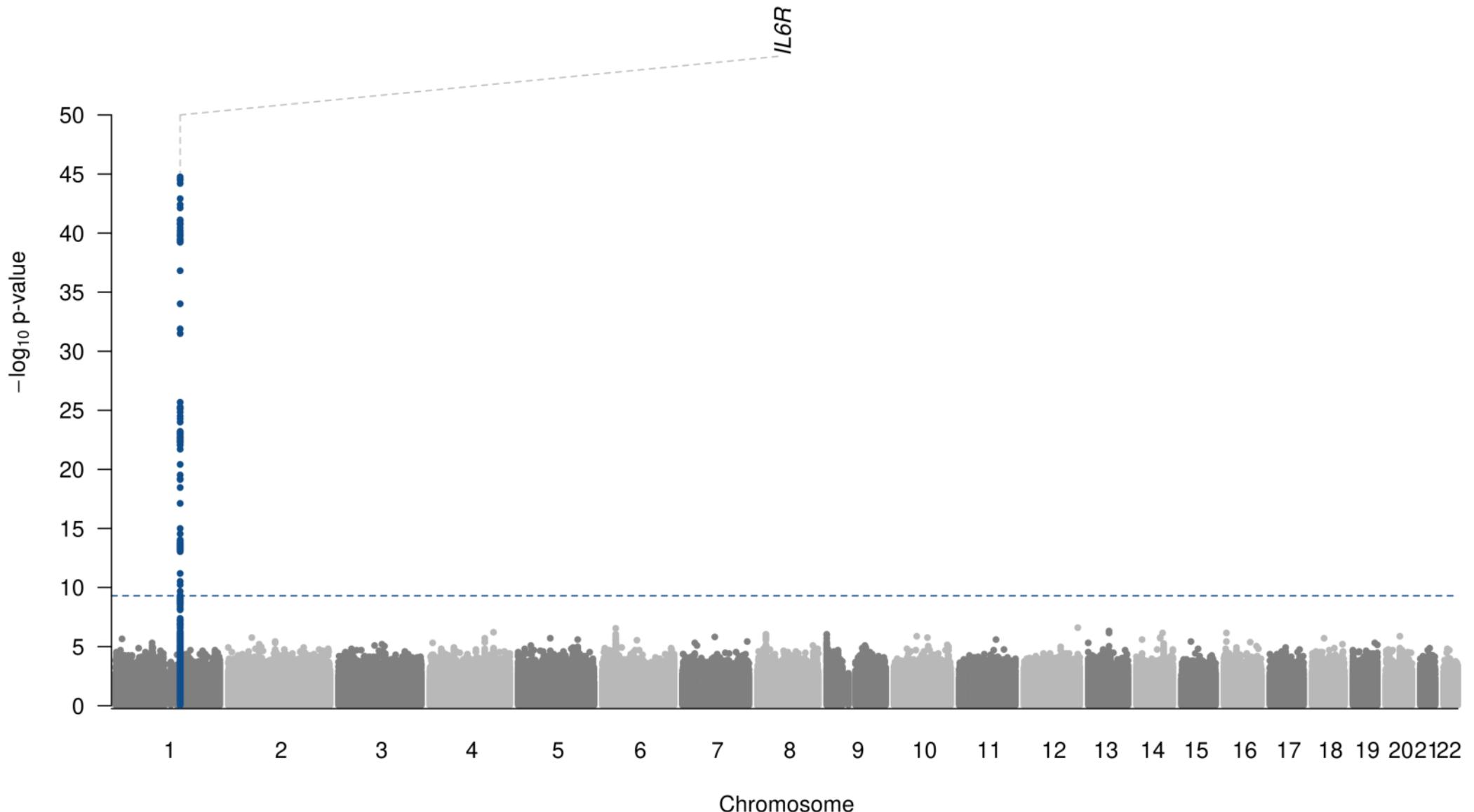
## IL-4 (IL4)



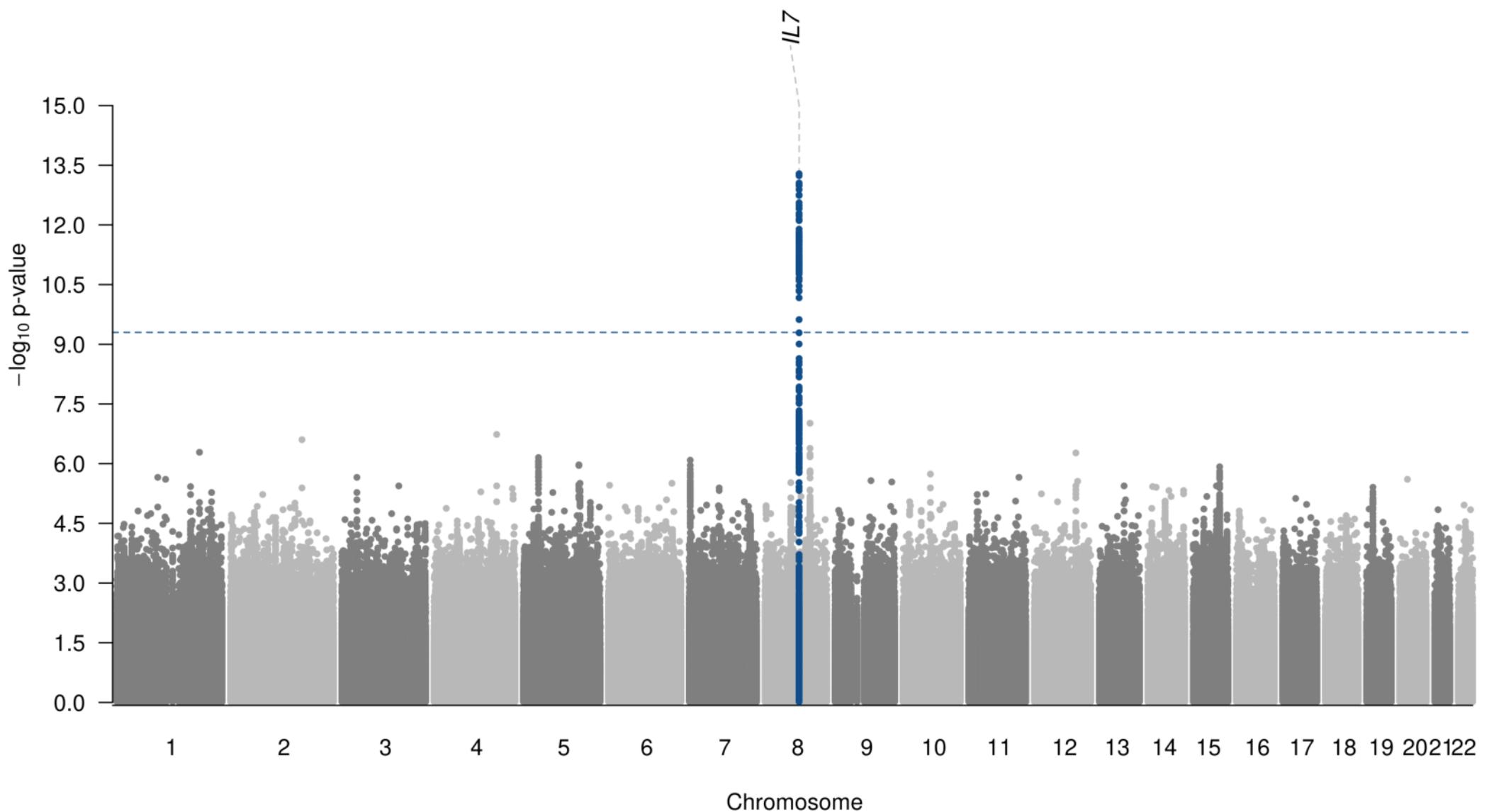
# IL-5 (IL5)



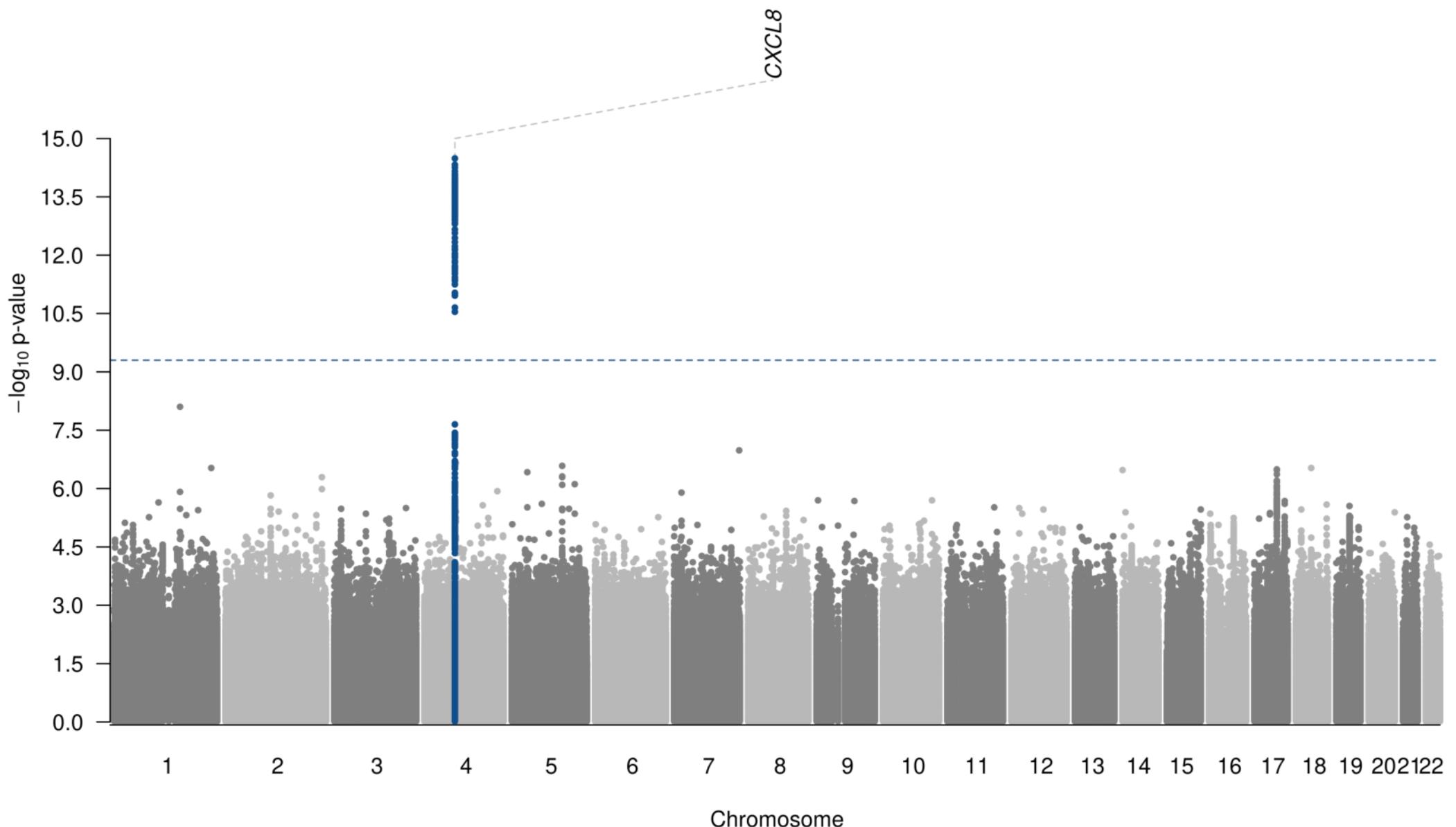
# IL-6 (IL6)



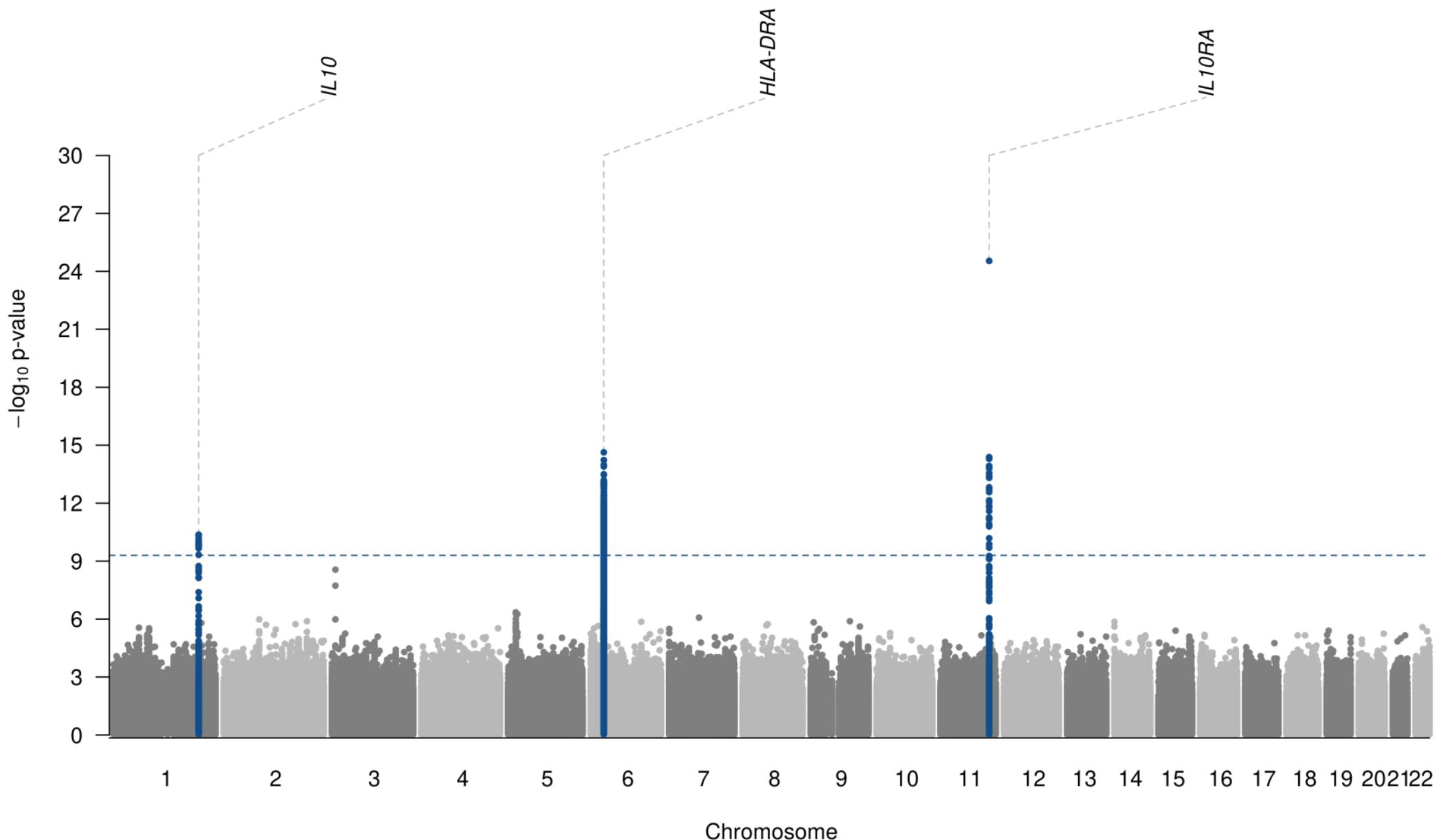
# IL-7 (IL7)



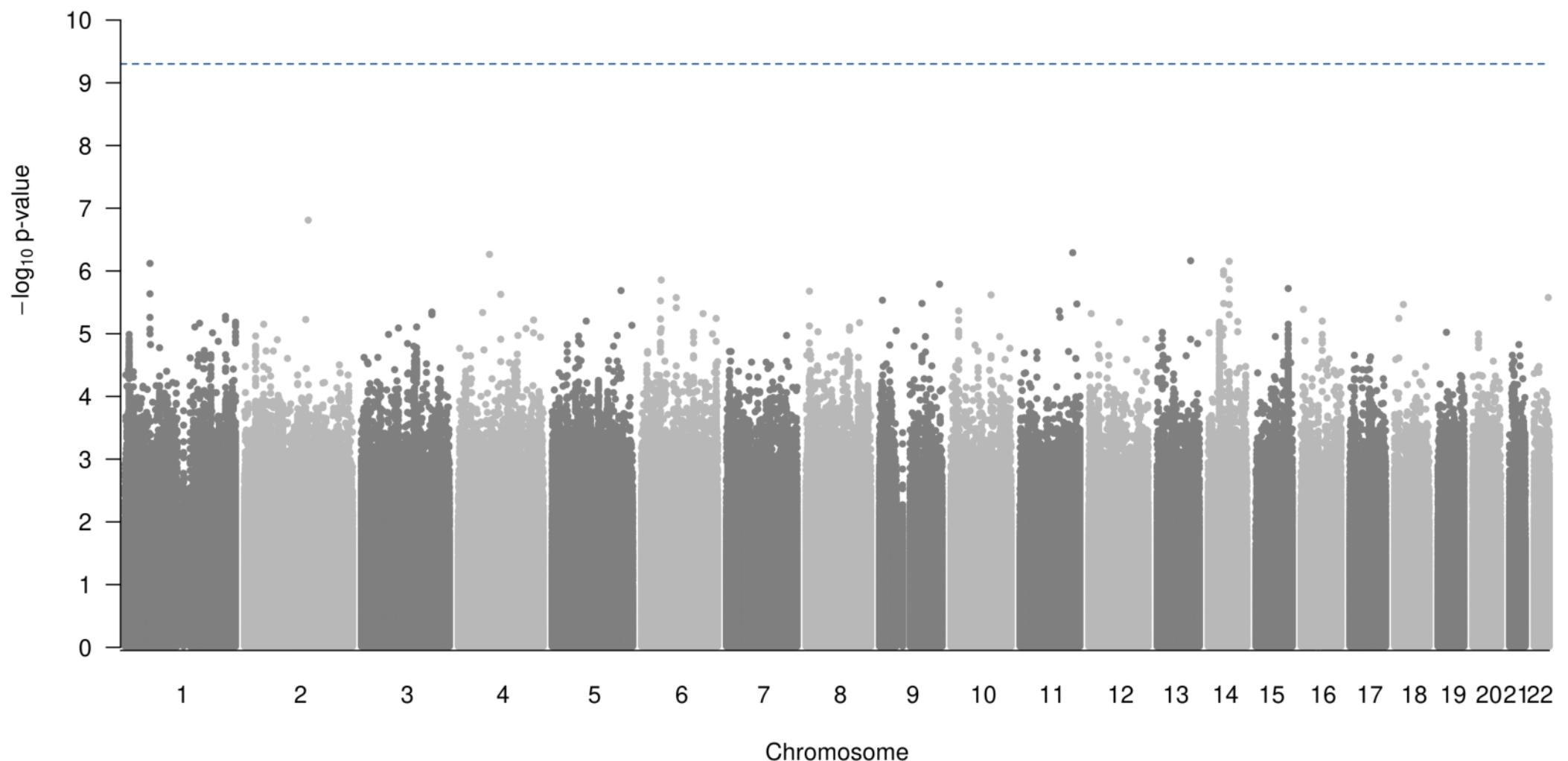
# IL-8 (IL8)



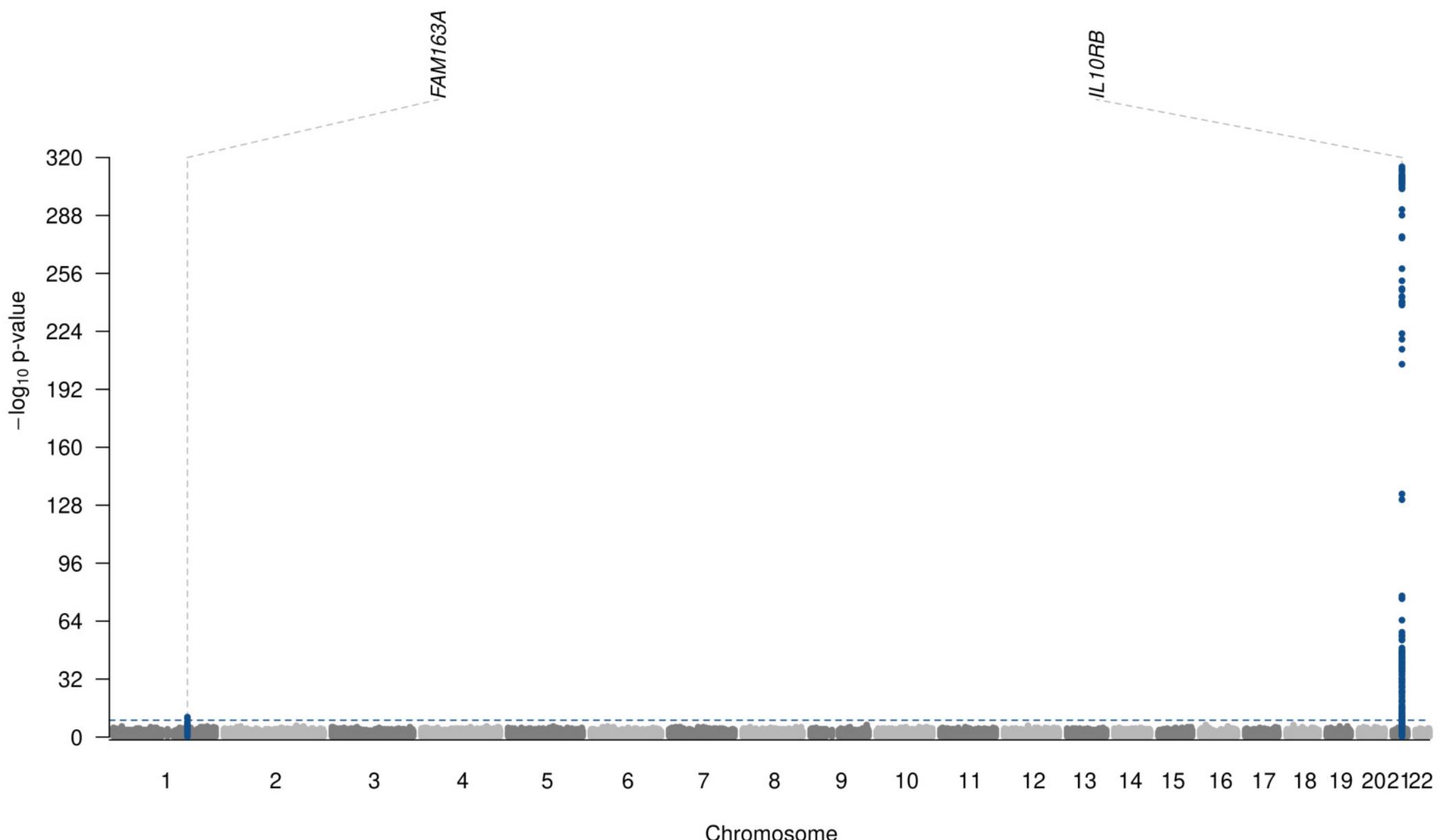
# IL-10 (IL10)



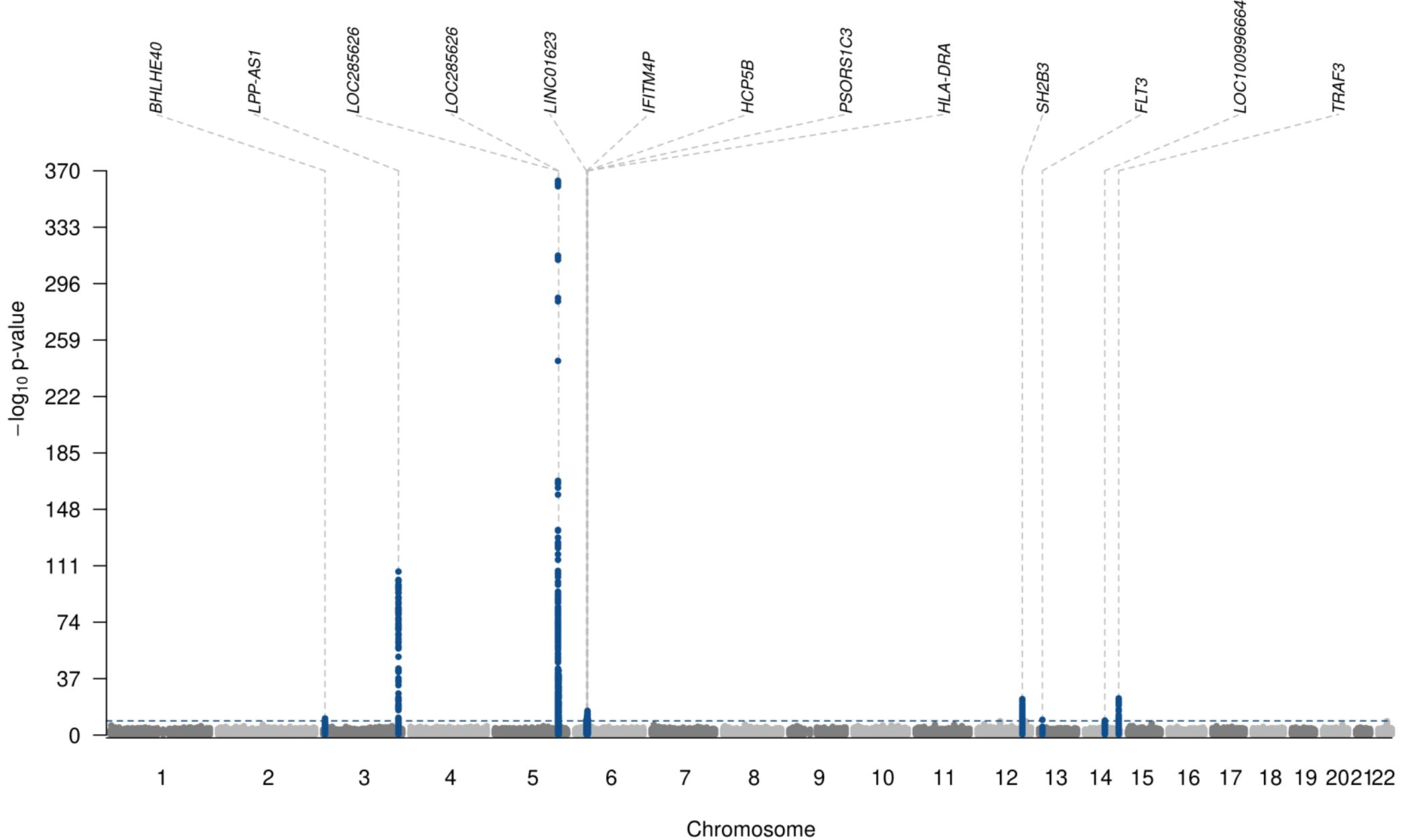
## IL-10RA (IL10RA)



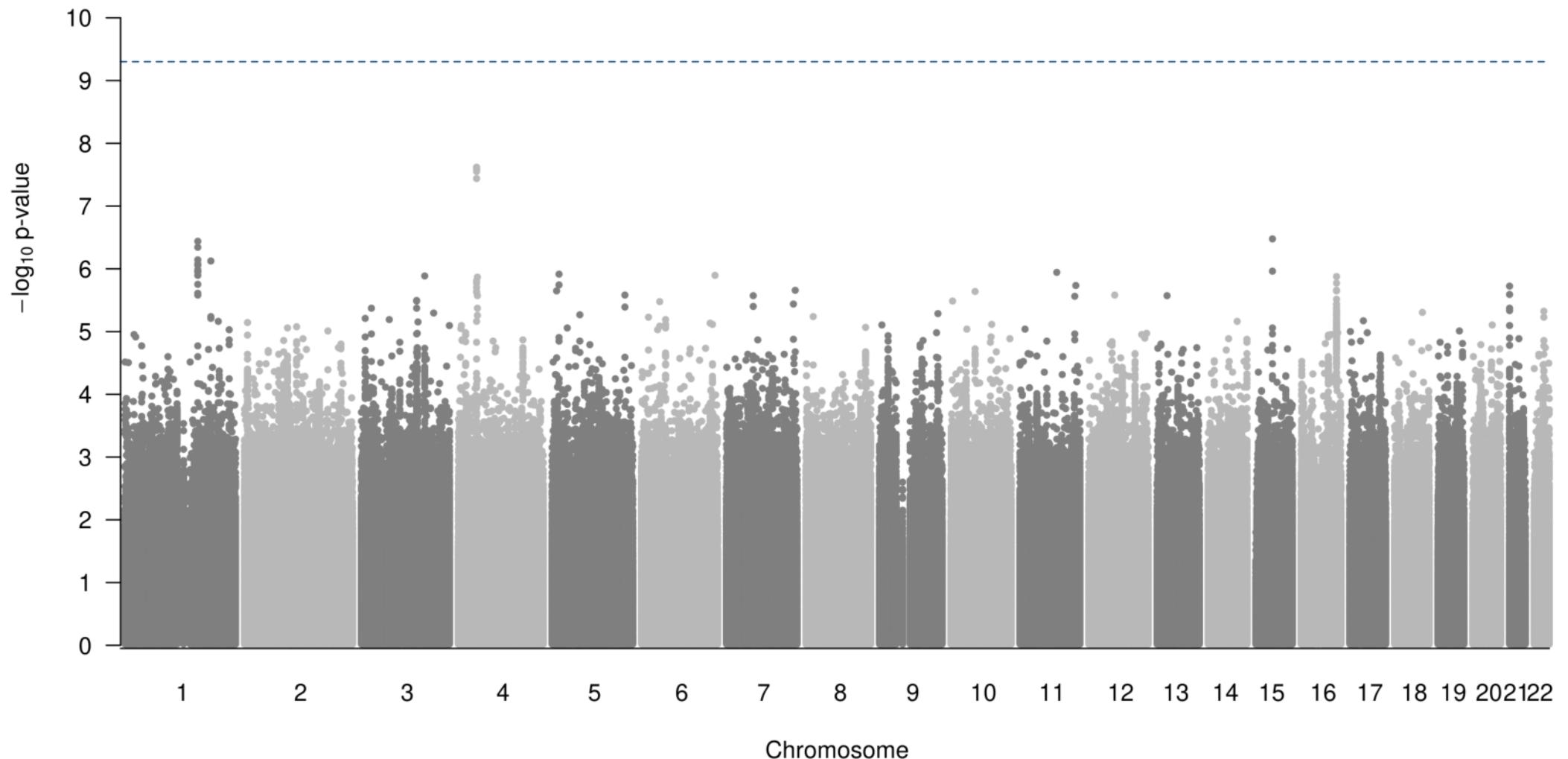
## IL10RB (IL10RB)



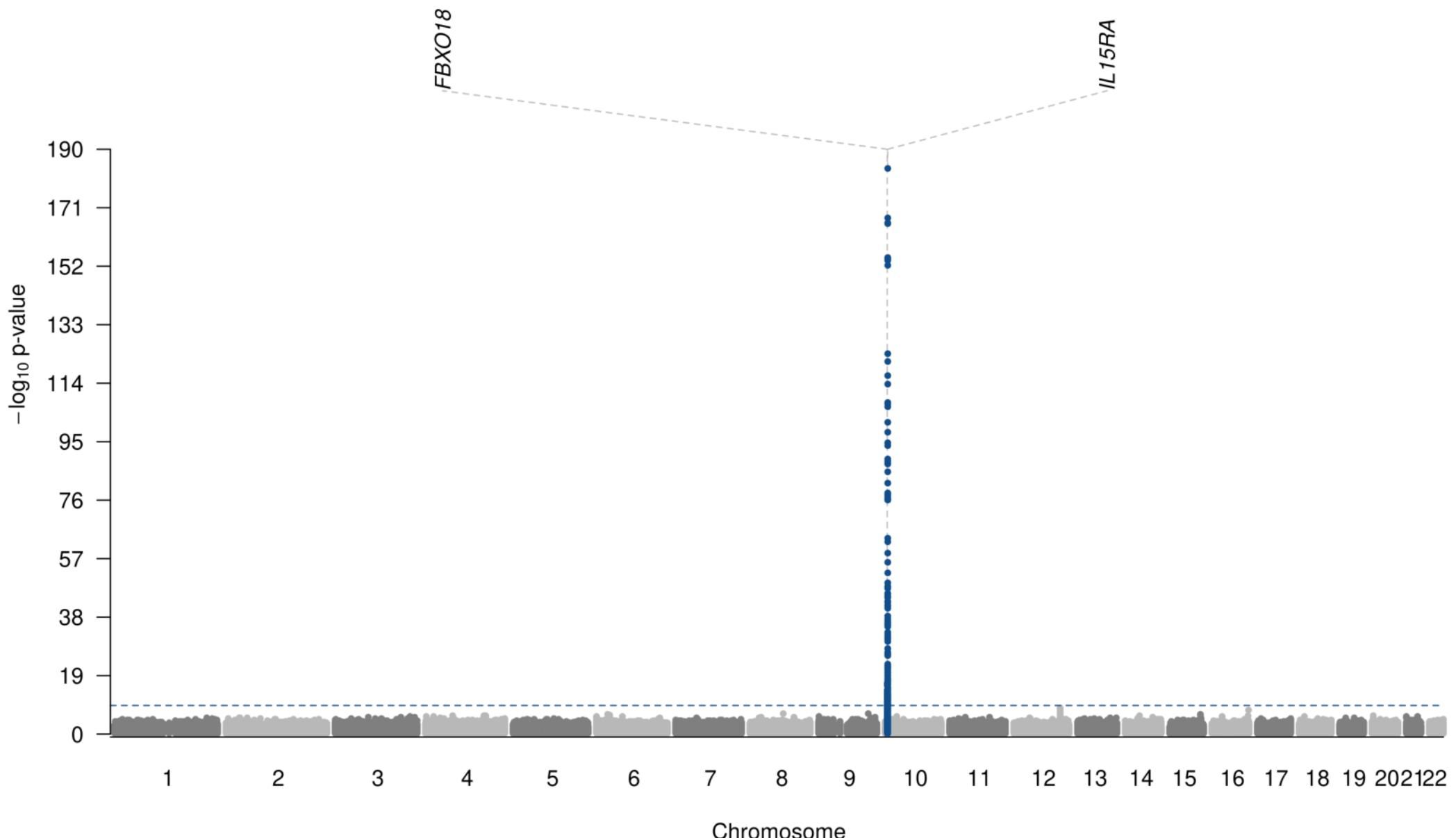
## IL-12B (IL12B)



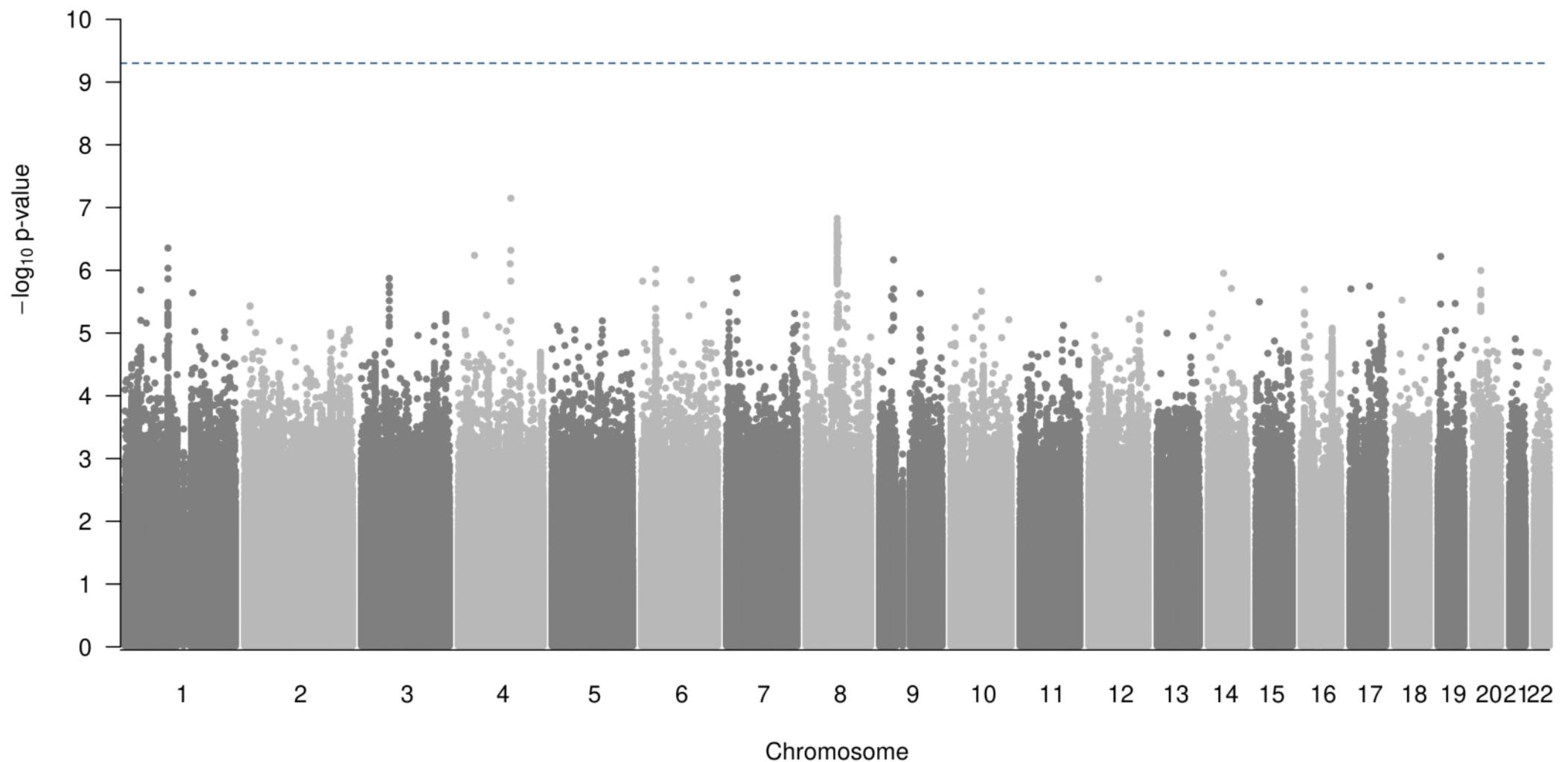
# IL-13 (IL13)



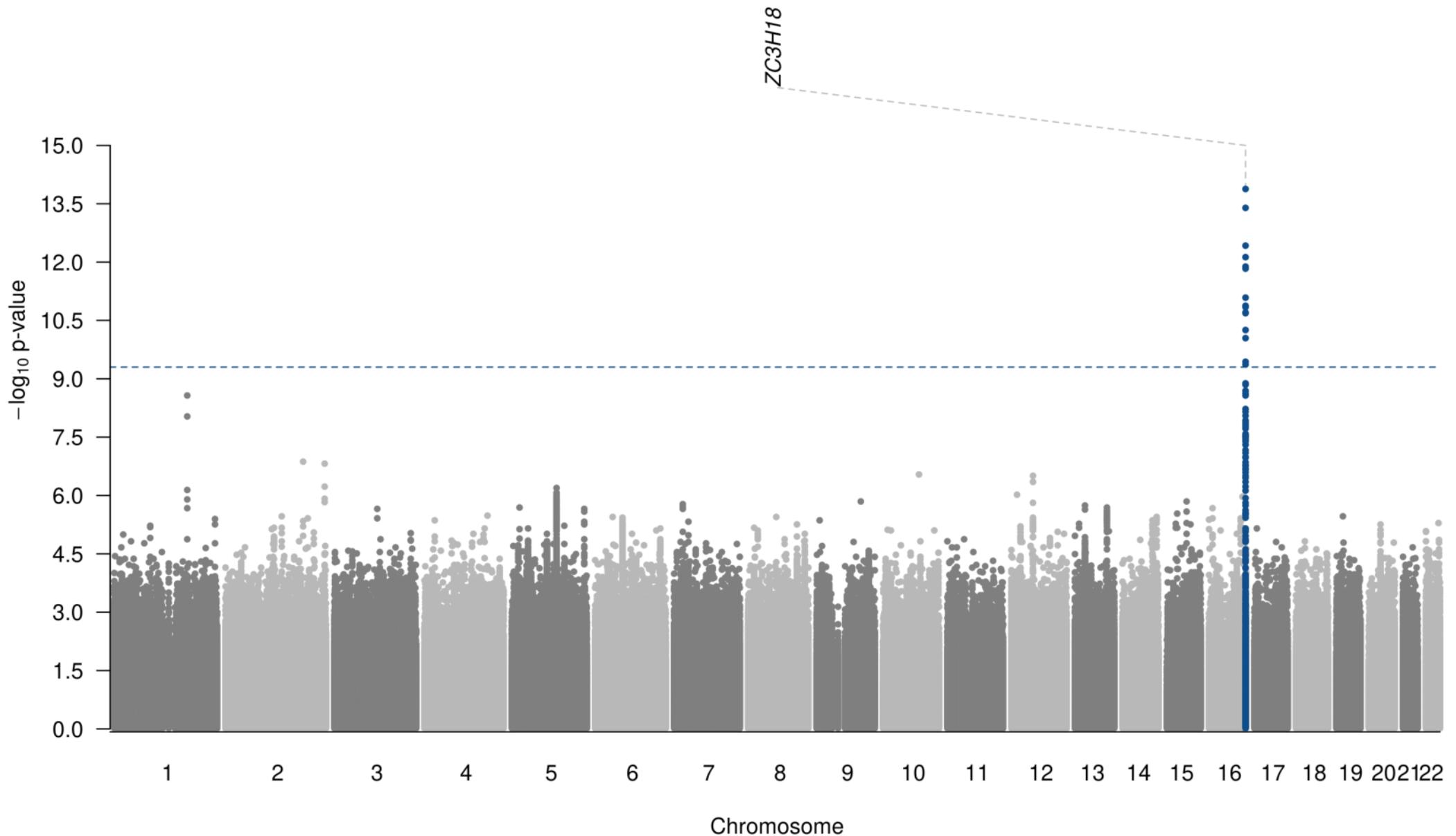
## IL-15RA (IL15RA)



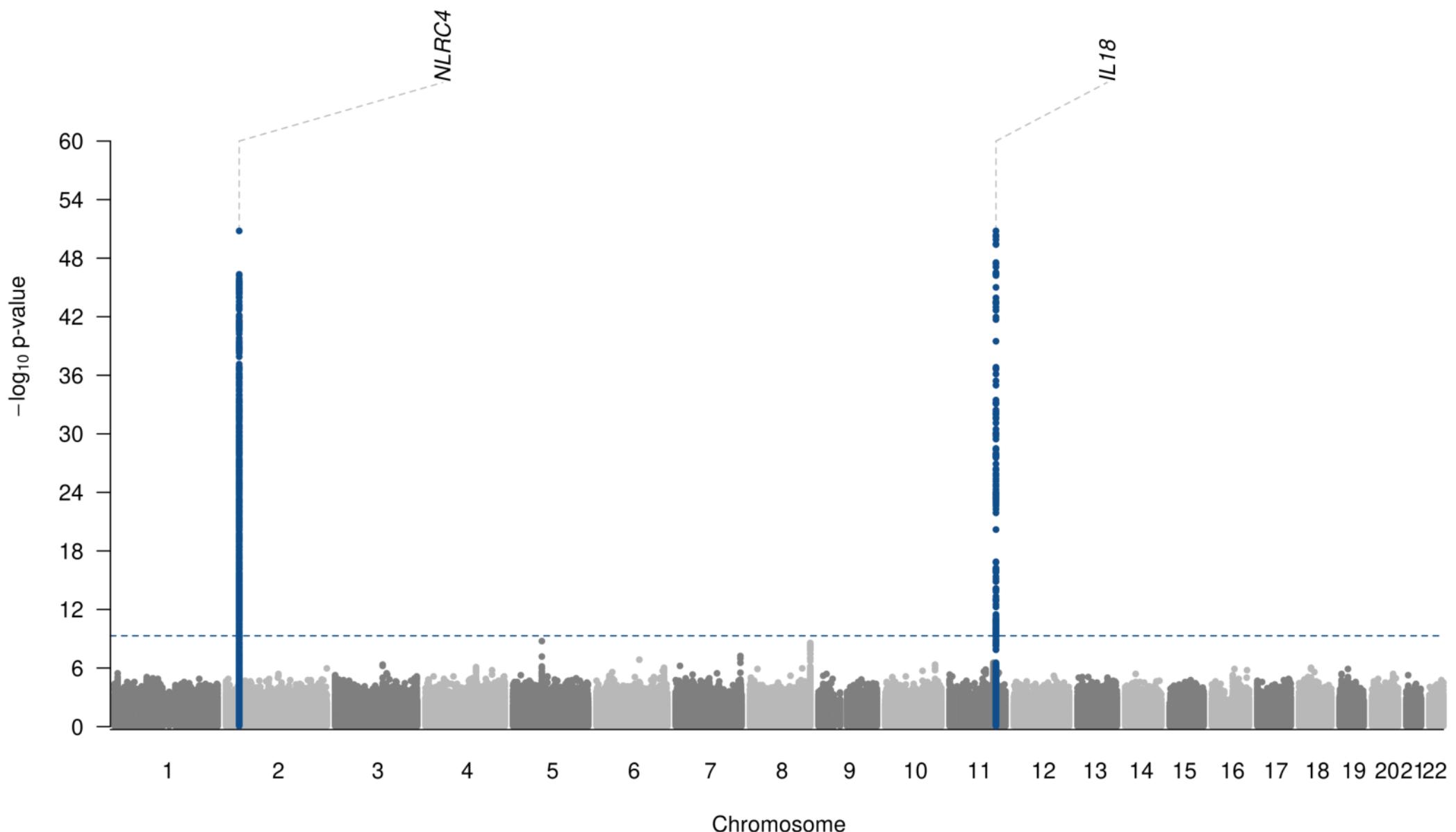
# IL-17A (IL17A)



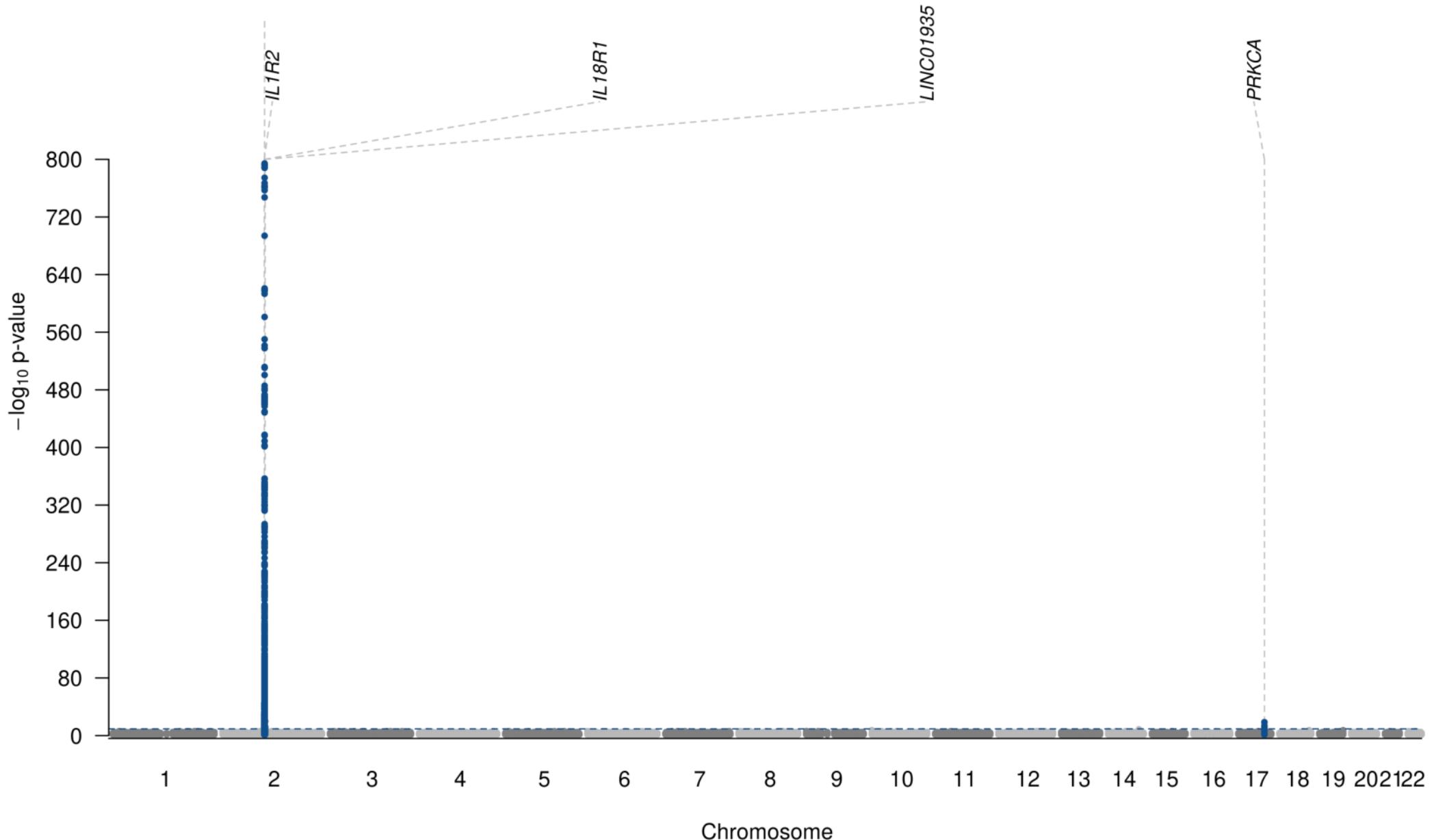
# IL-17C (IL17C)



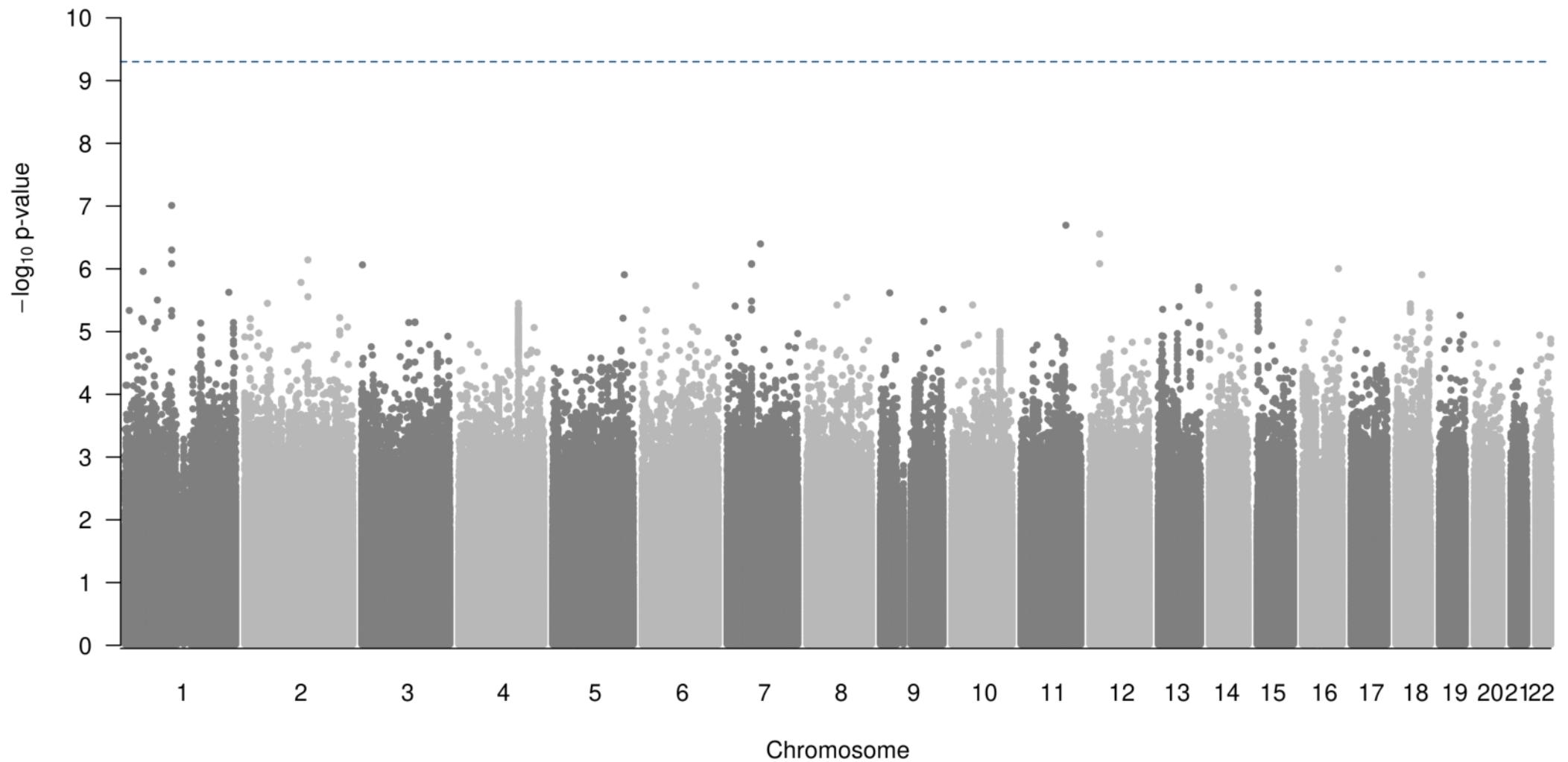
### **IL-18 (IL18)**



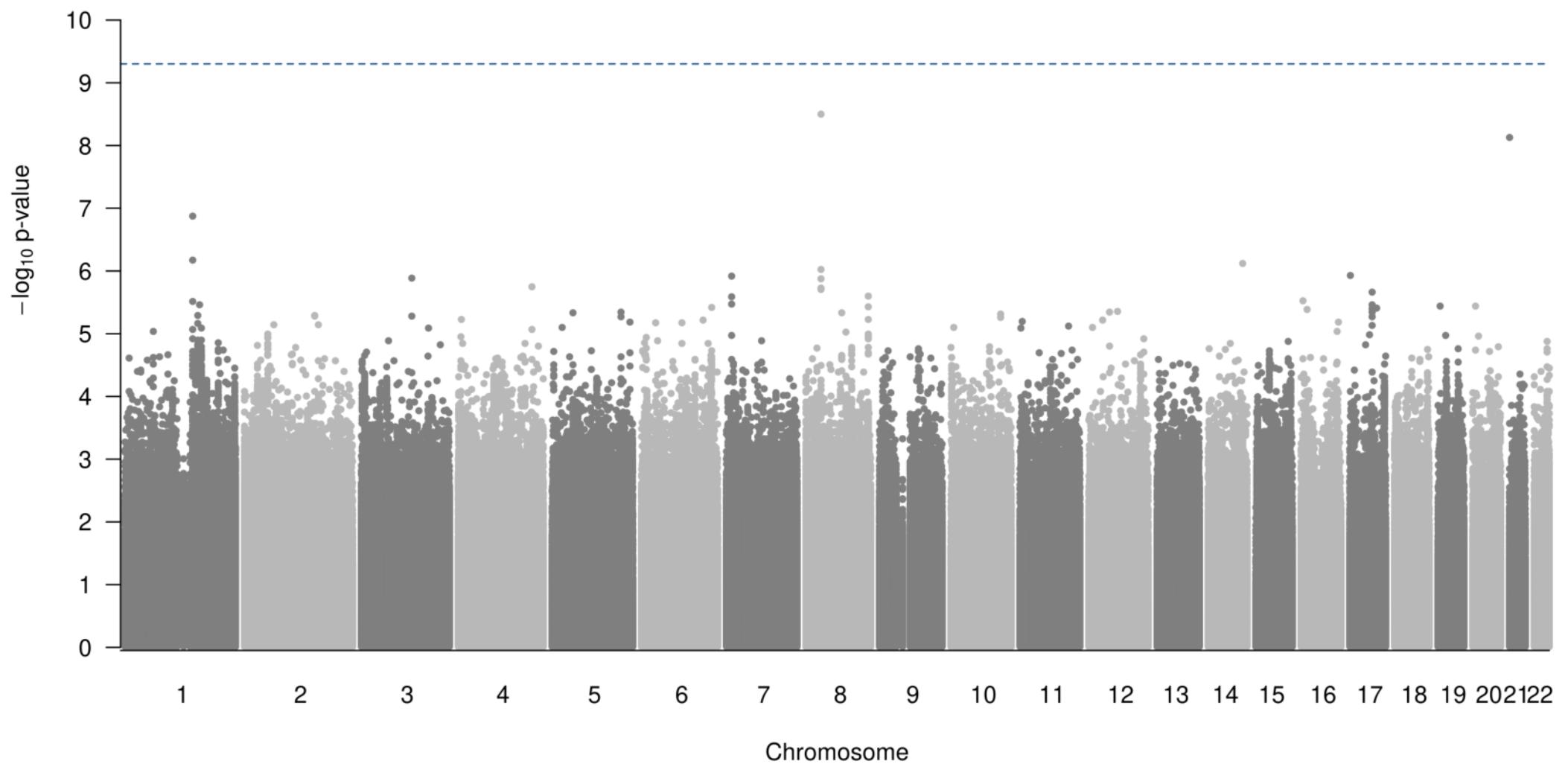
## IL-18R1 (IL18R1)



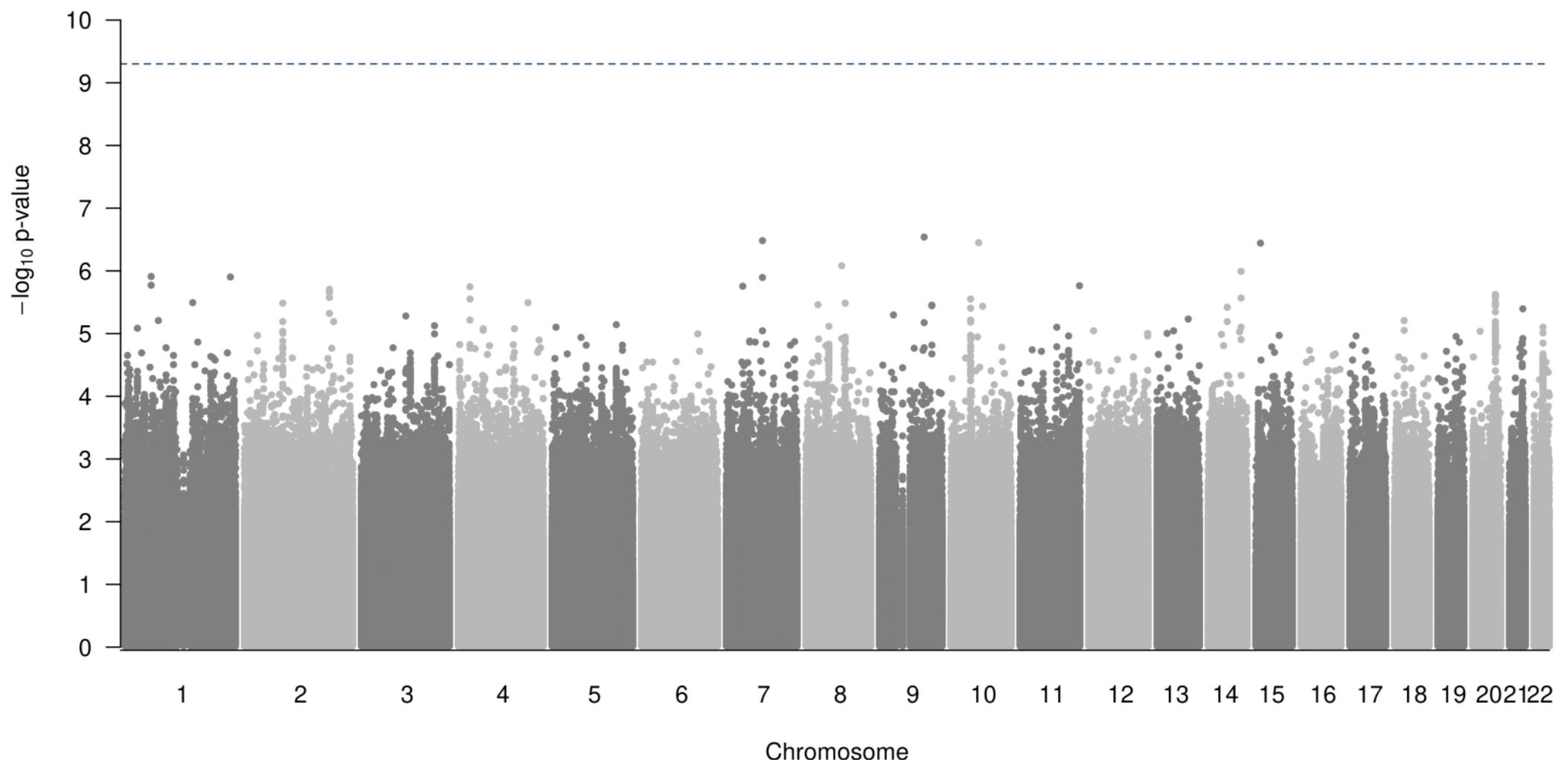
## IL-20 (IL20)



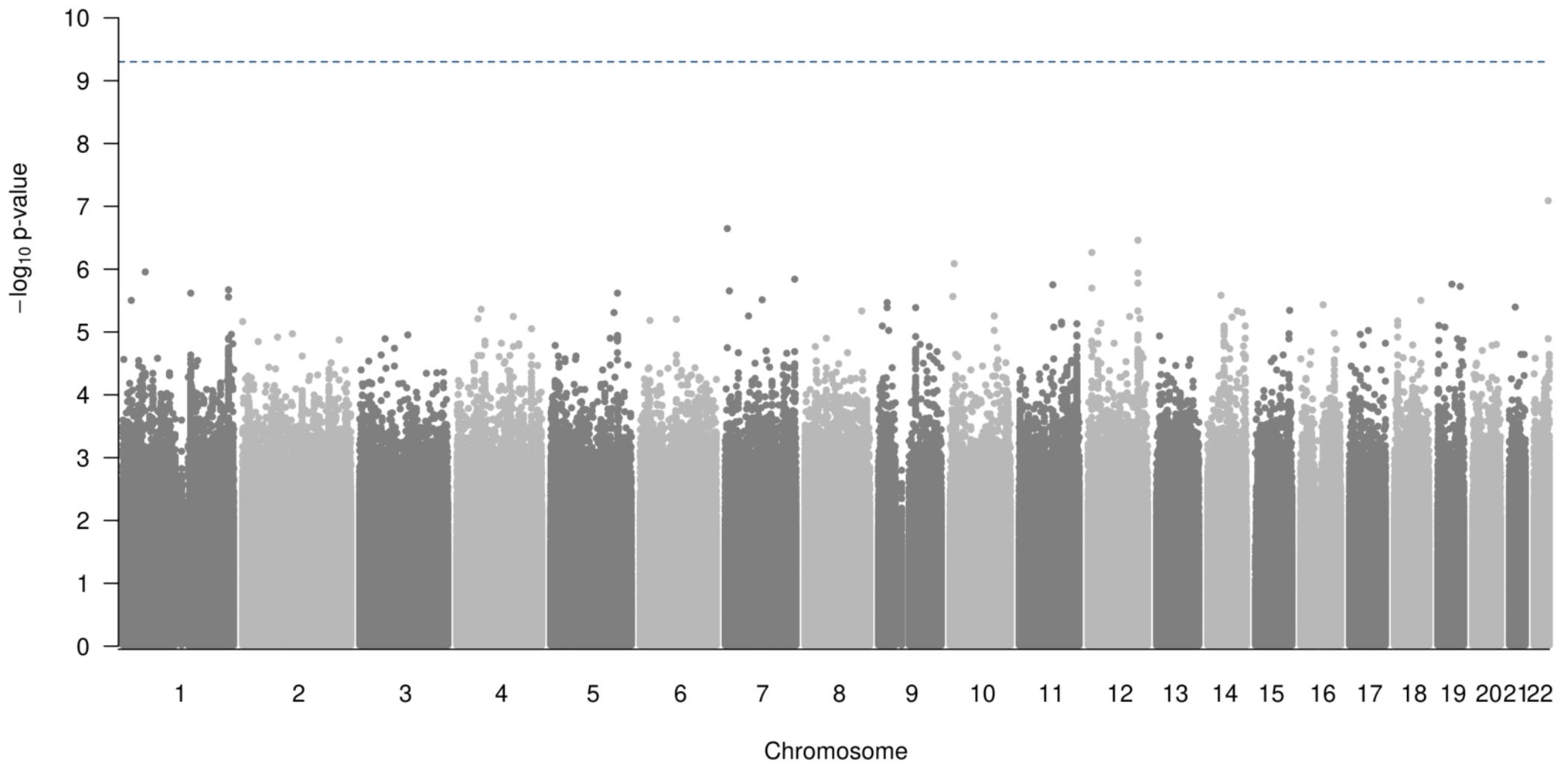
## IL-20RA (IL20RA)



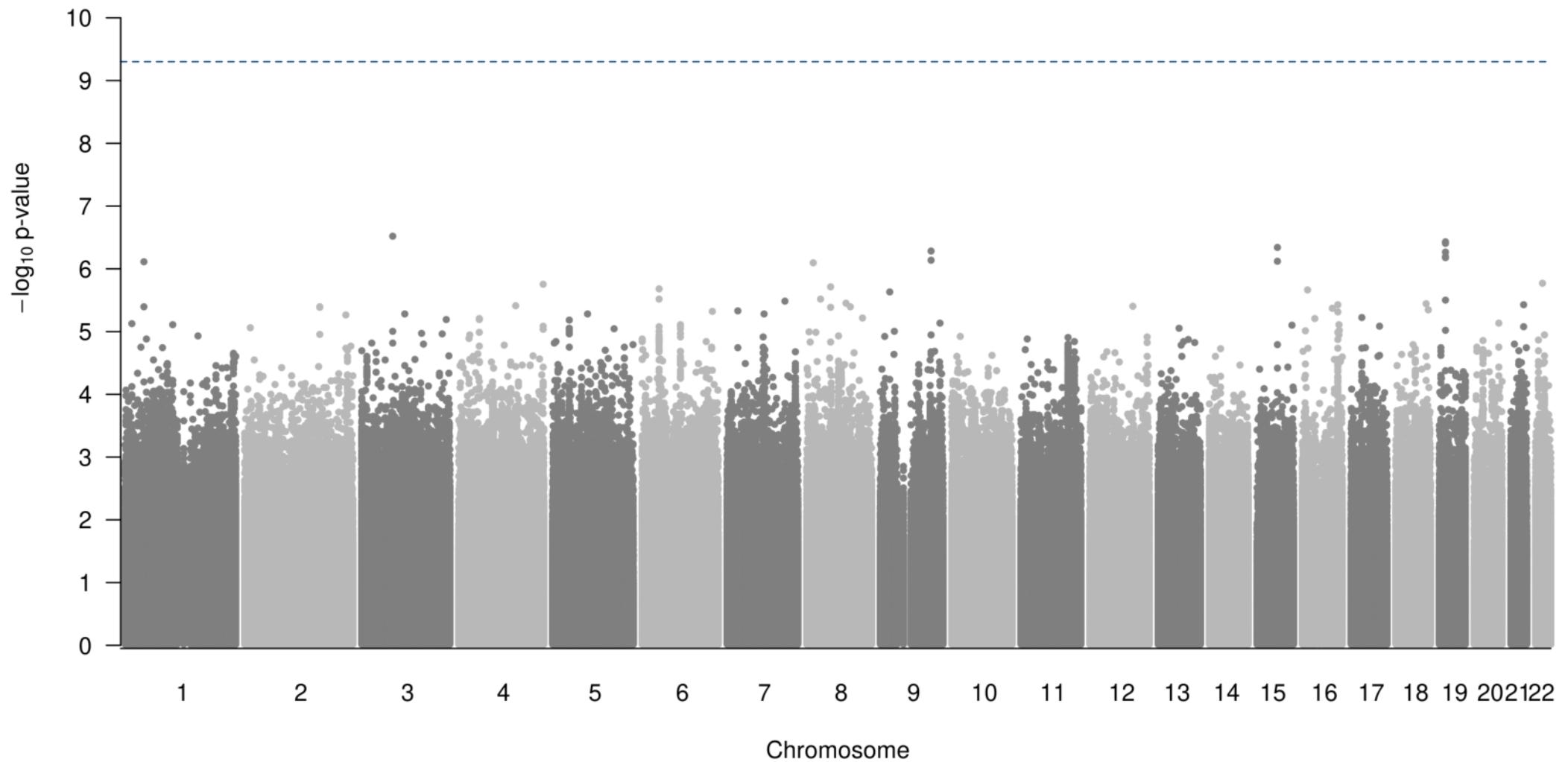
## IL-22RA1 (IL22RA1)



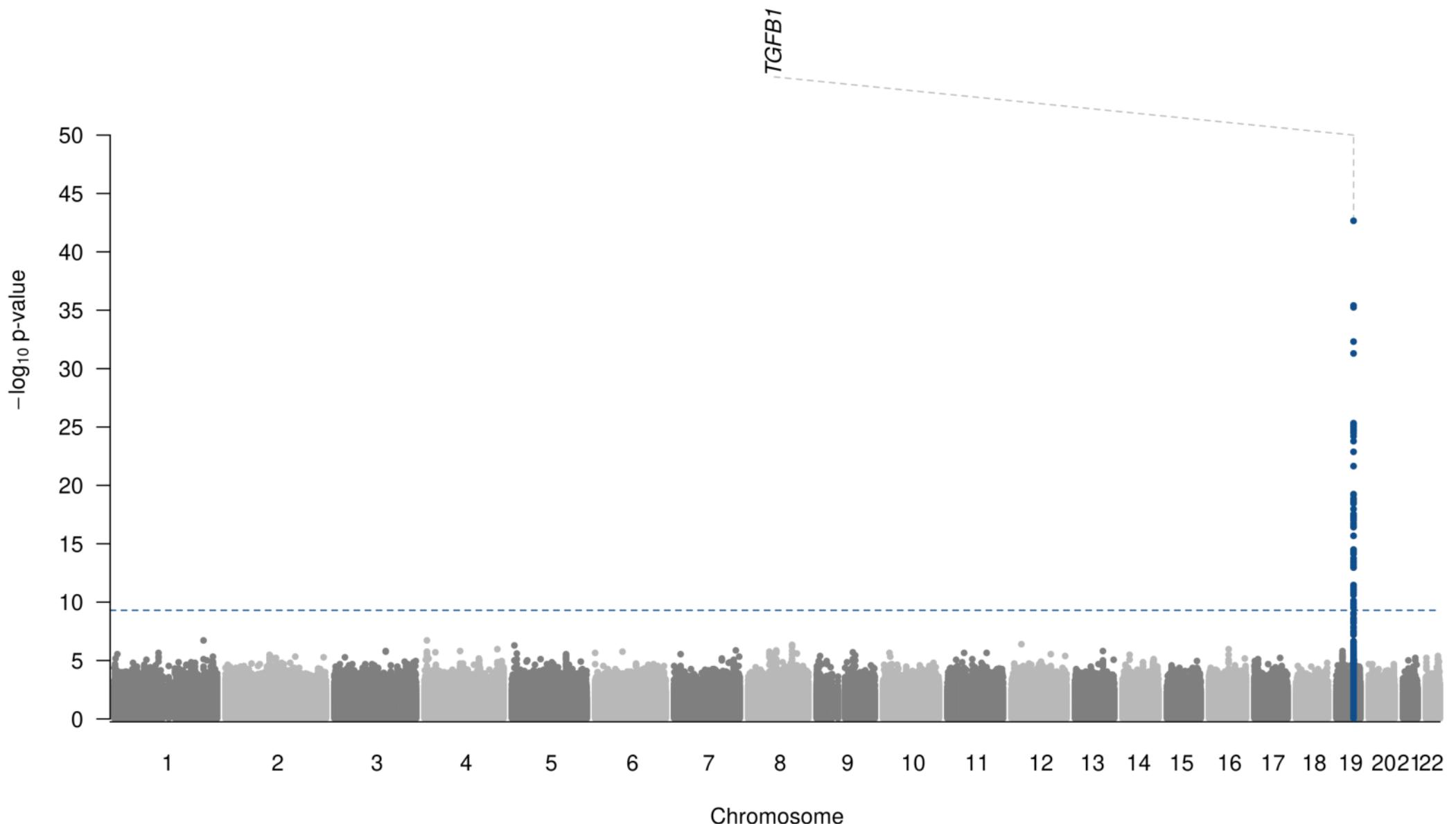
## IL-24 (IL24)



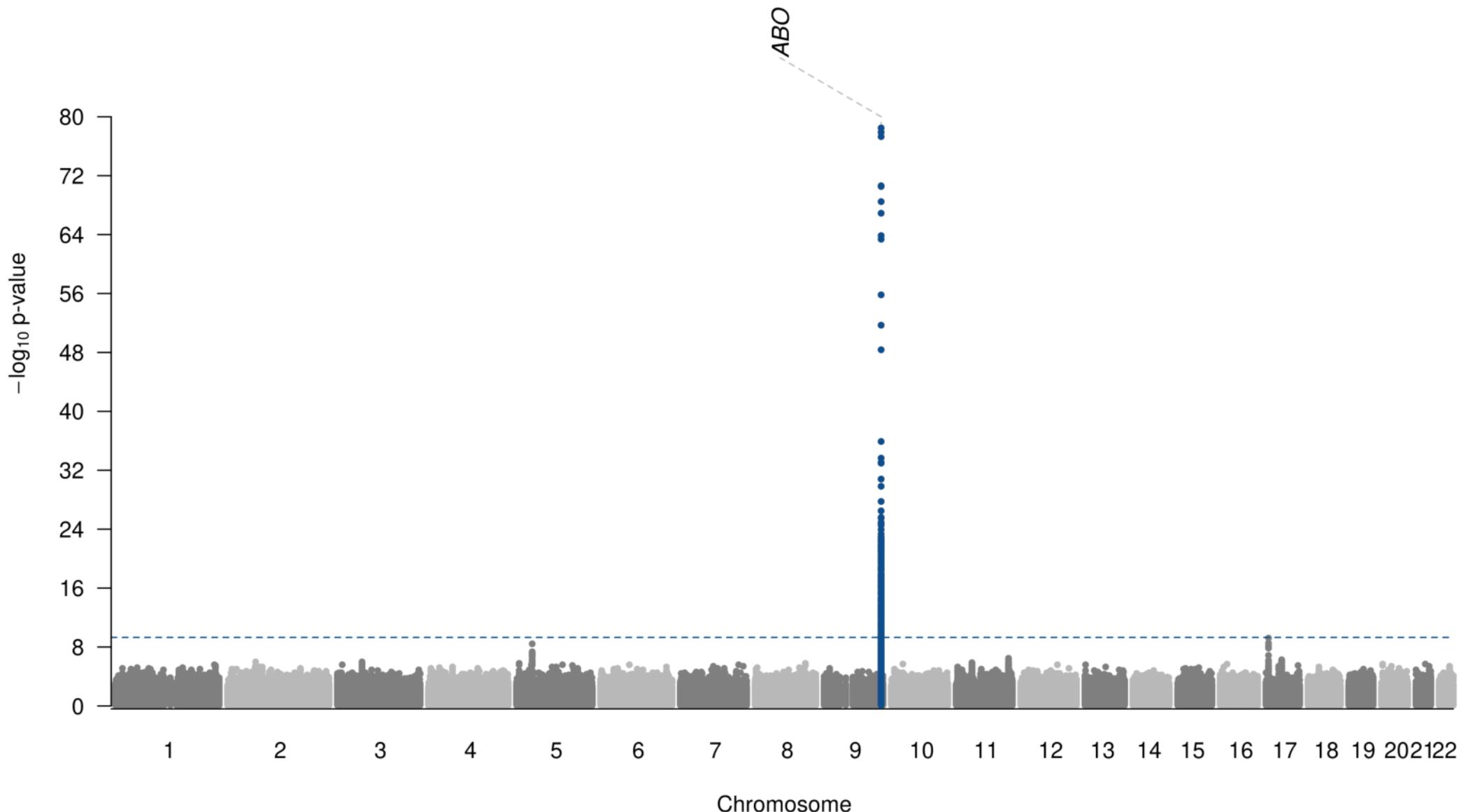
### IL-33 (IL33)



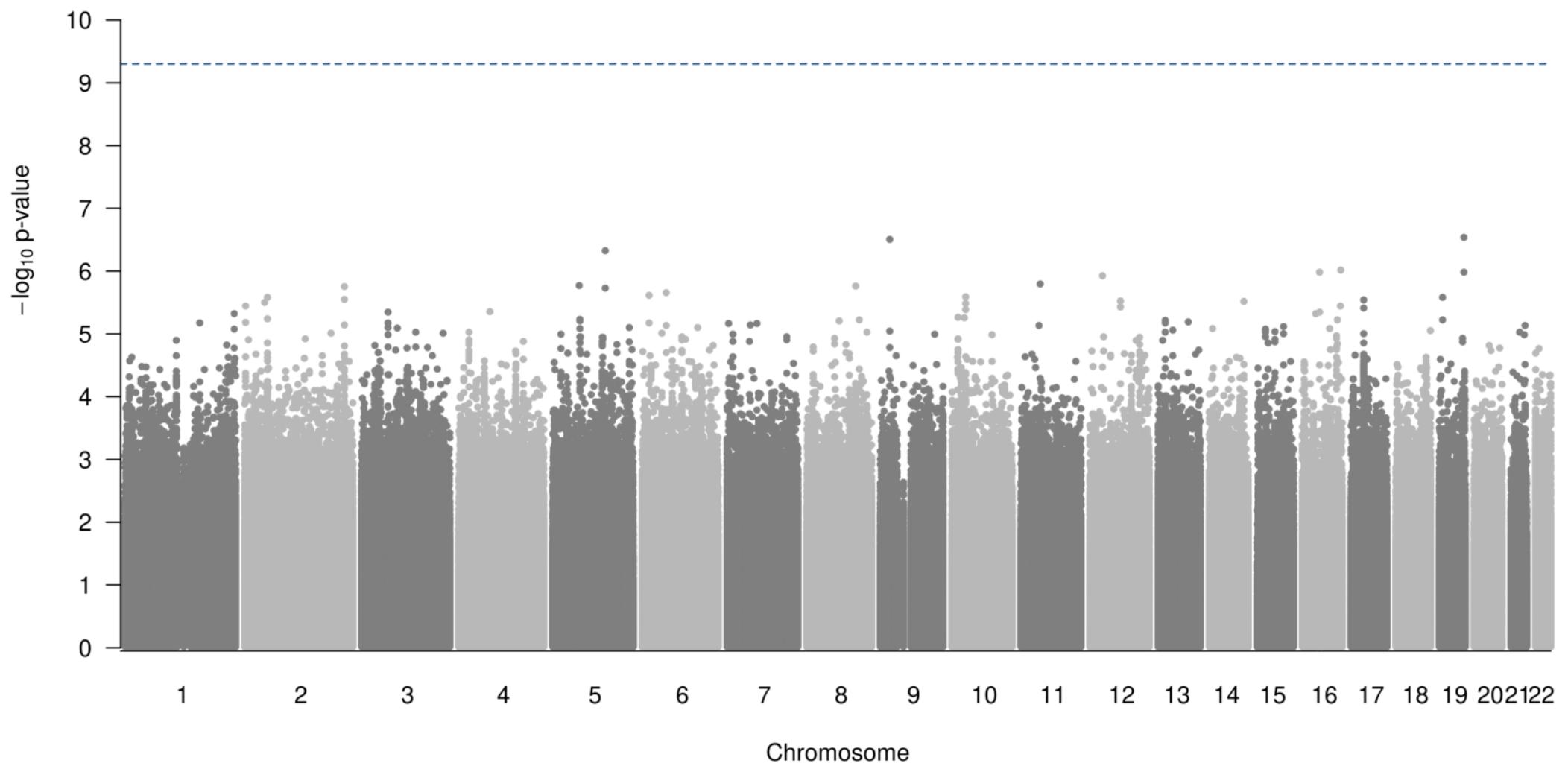
# LAP (TGFB1)



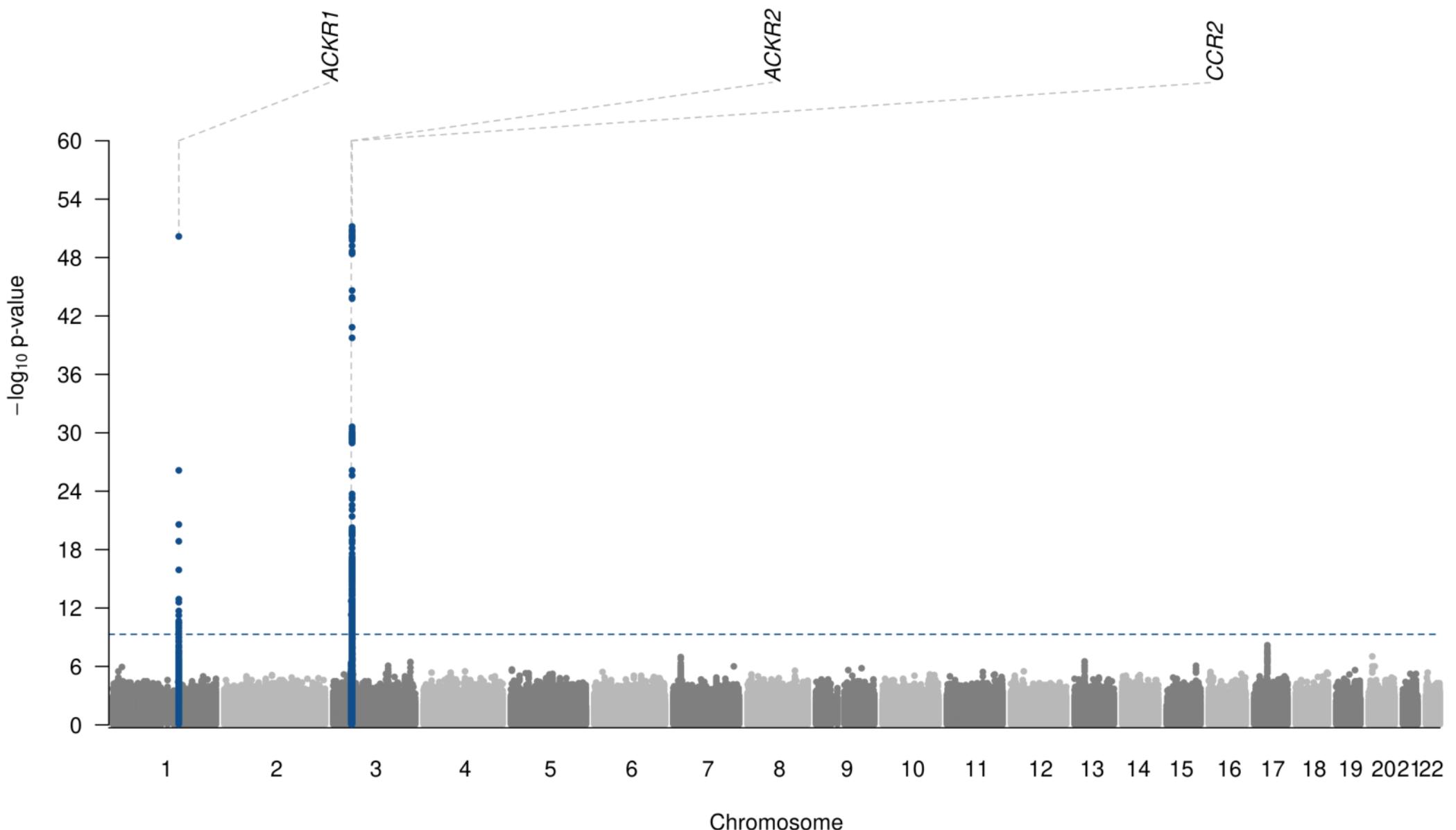
# LIF-R (LIFR)



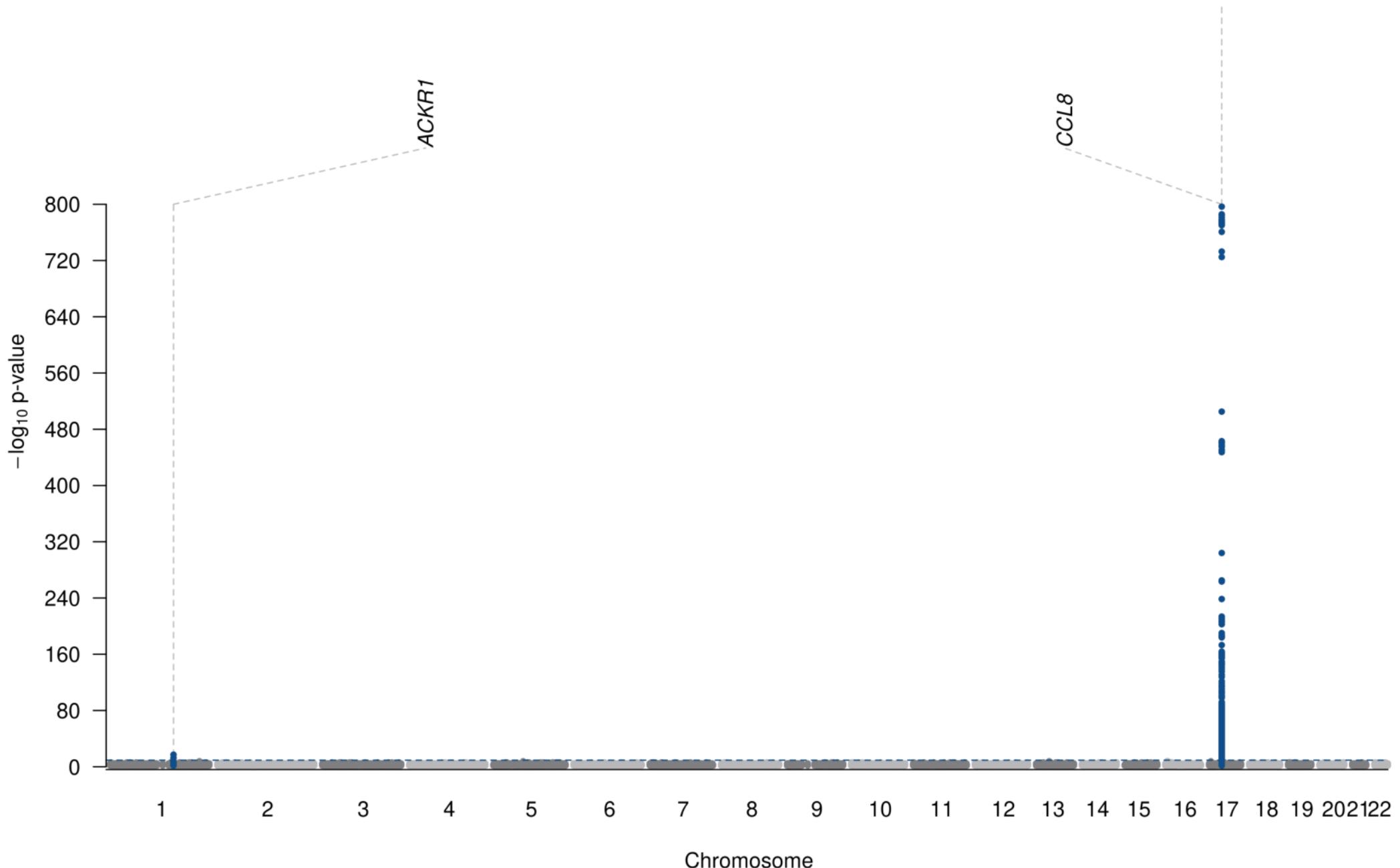
## LIF (LIF)



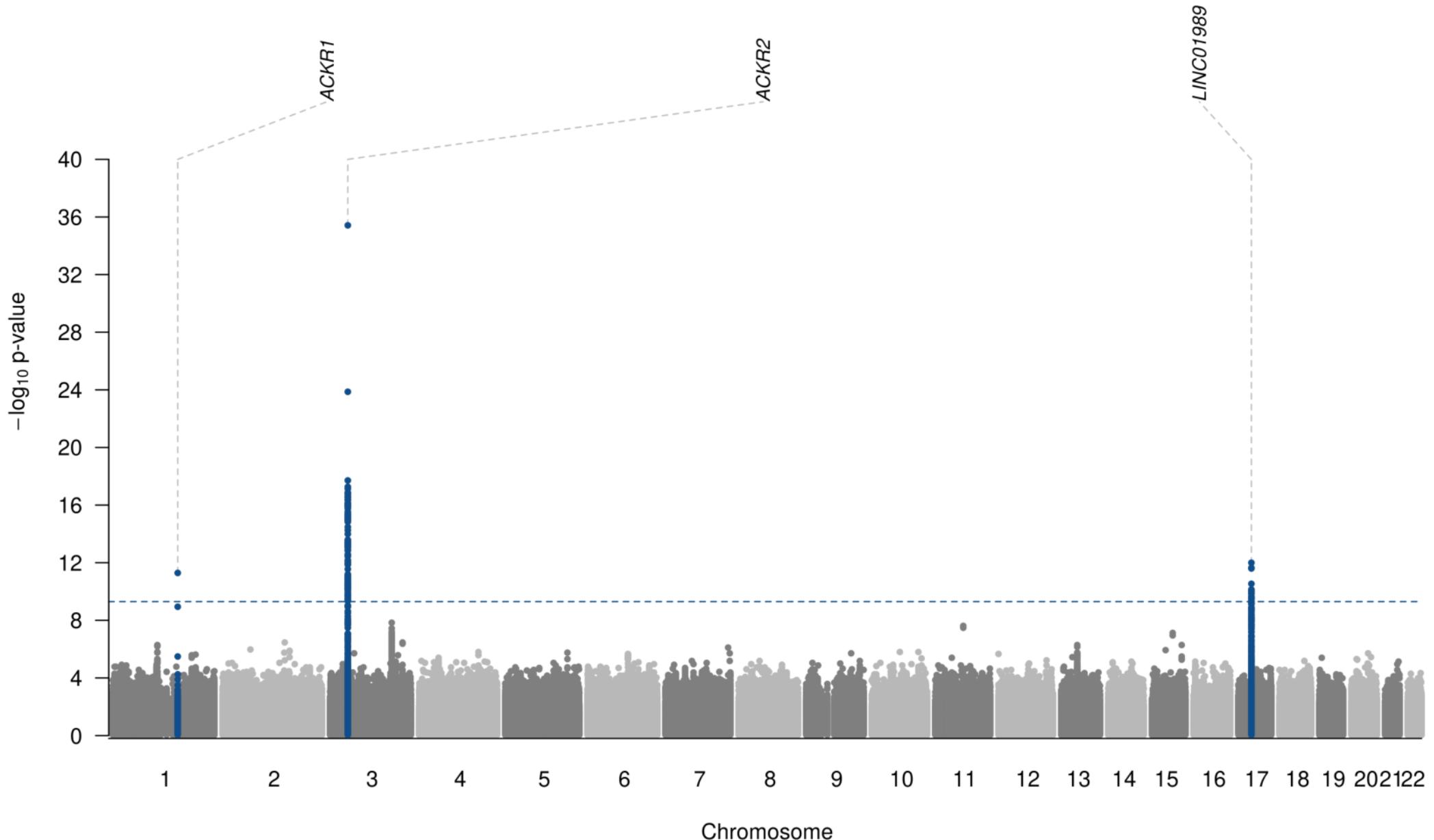
## MCP-1 (CCL2)



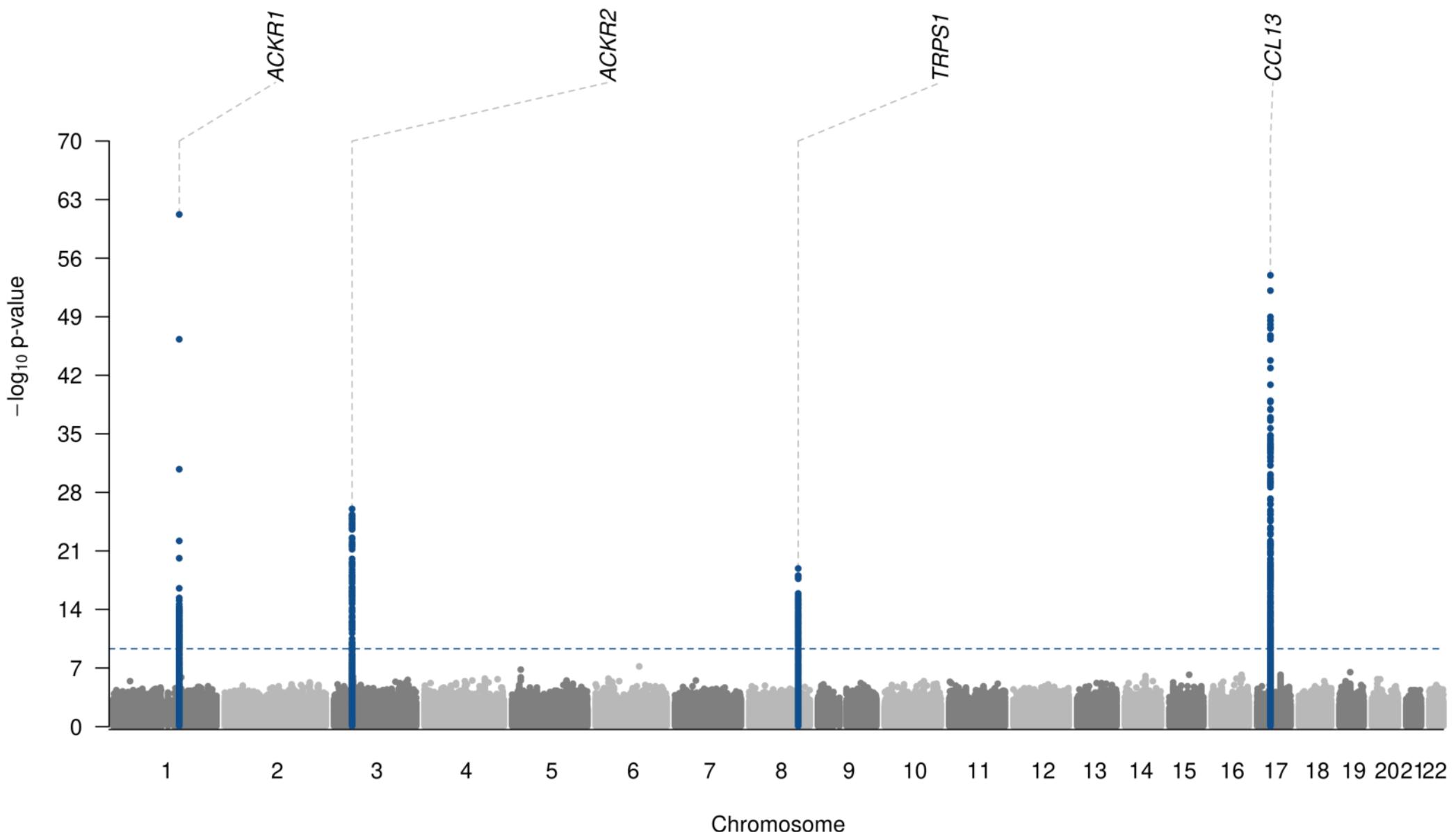
## MCP-2 (CCL8)



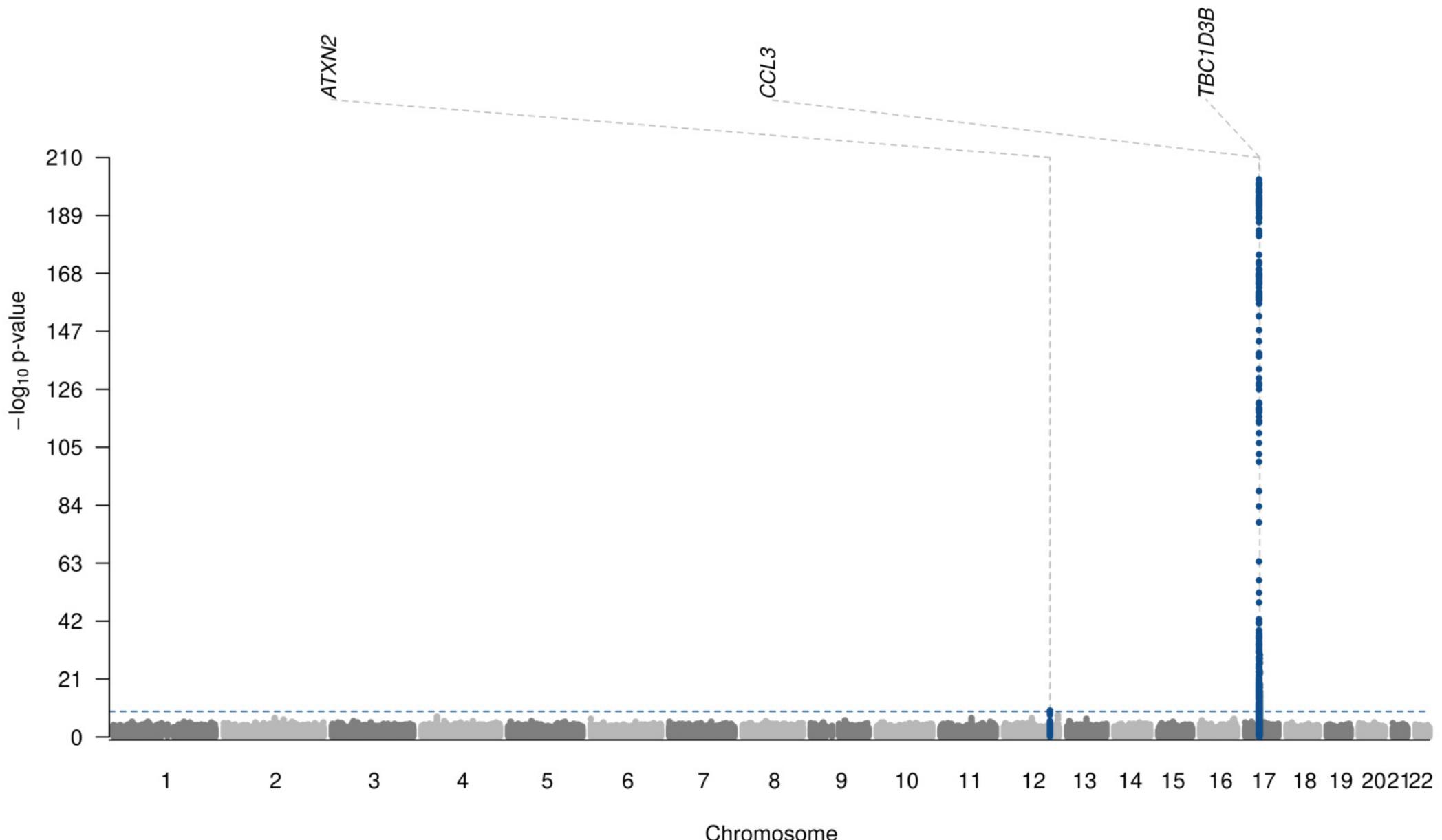
## MCP-3 (CCL7)



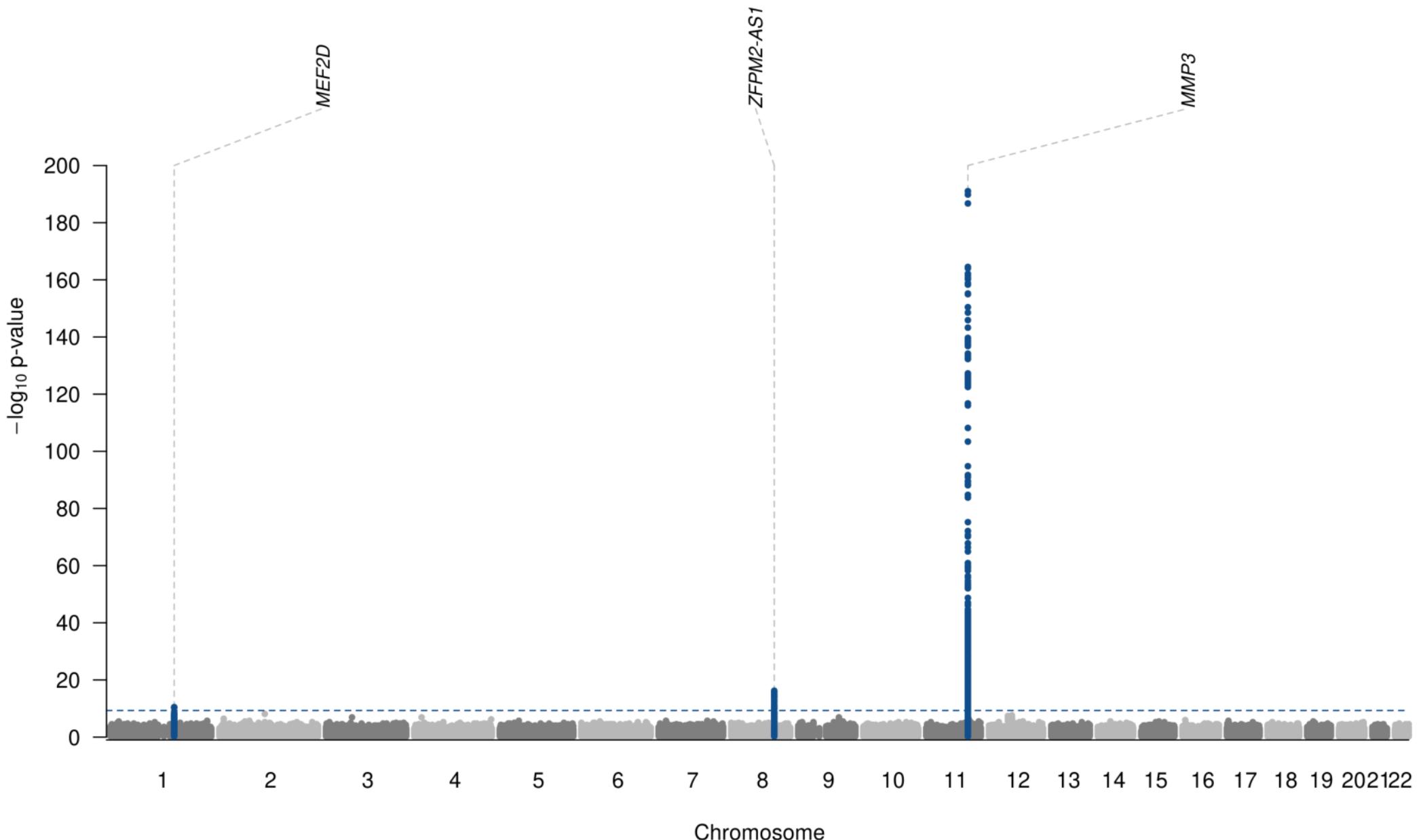
## MCP-4 (CCL13)



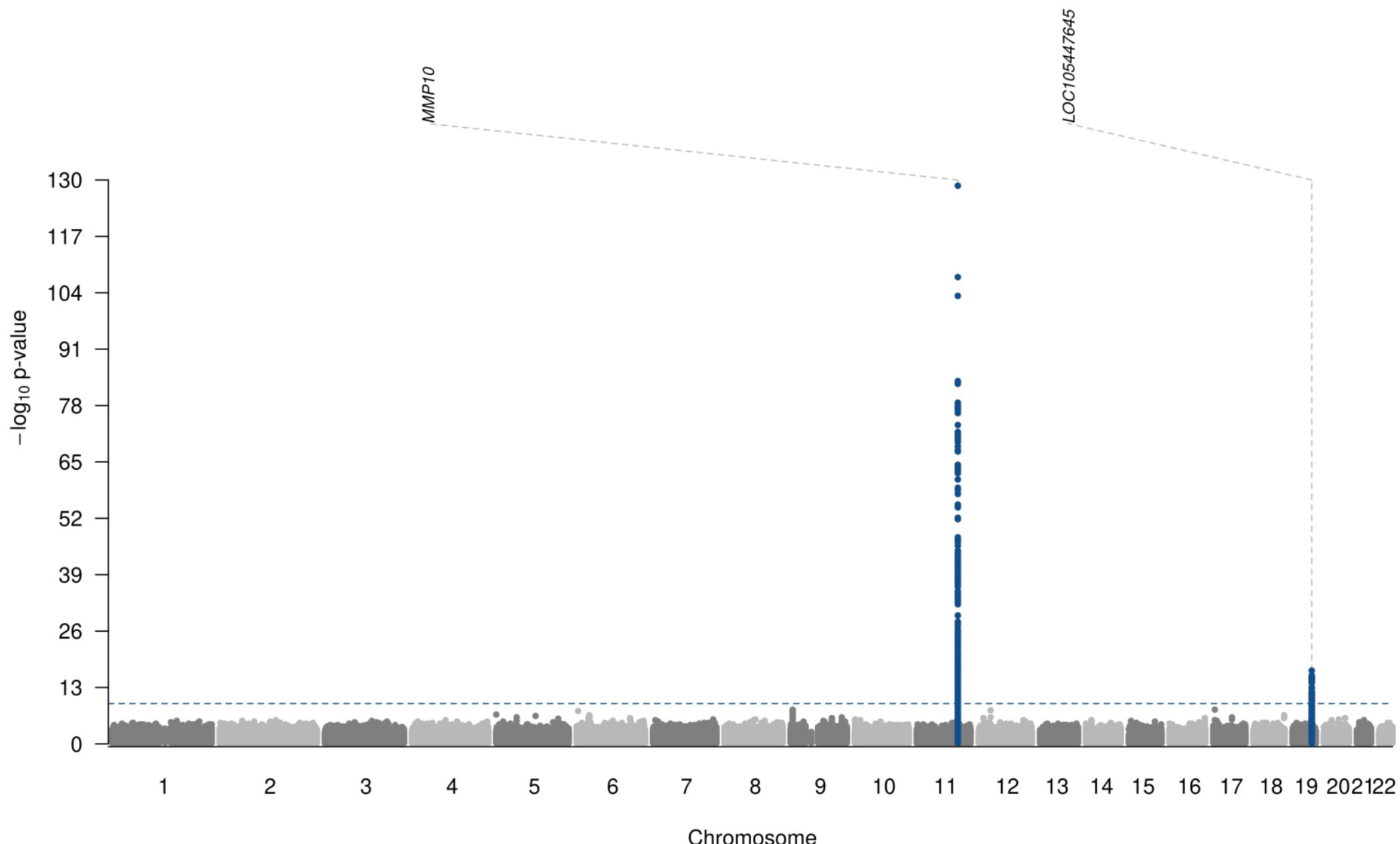
# MIP-1 (CCL3)



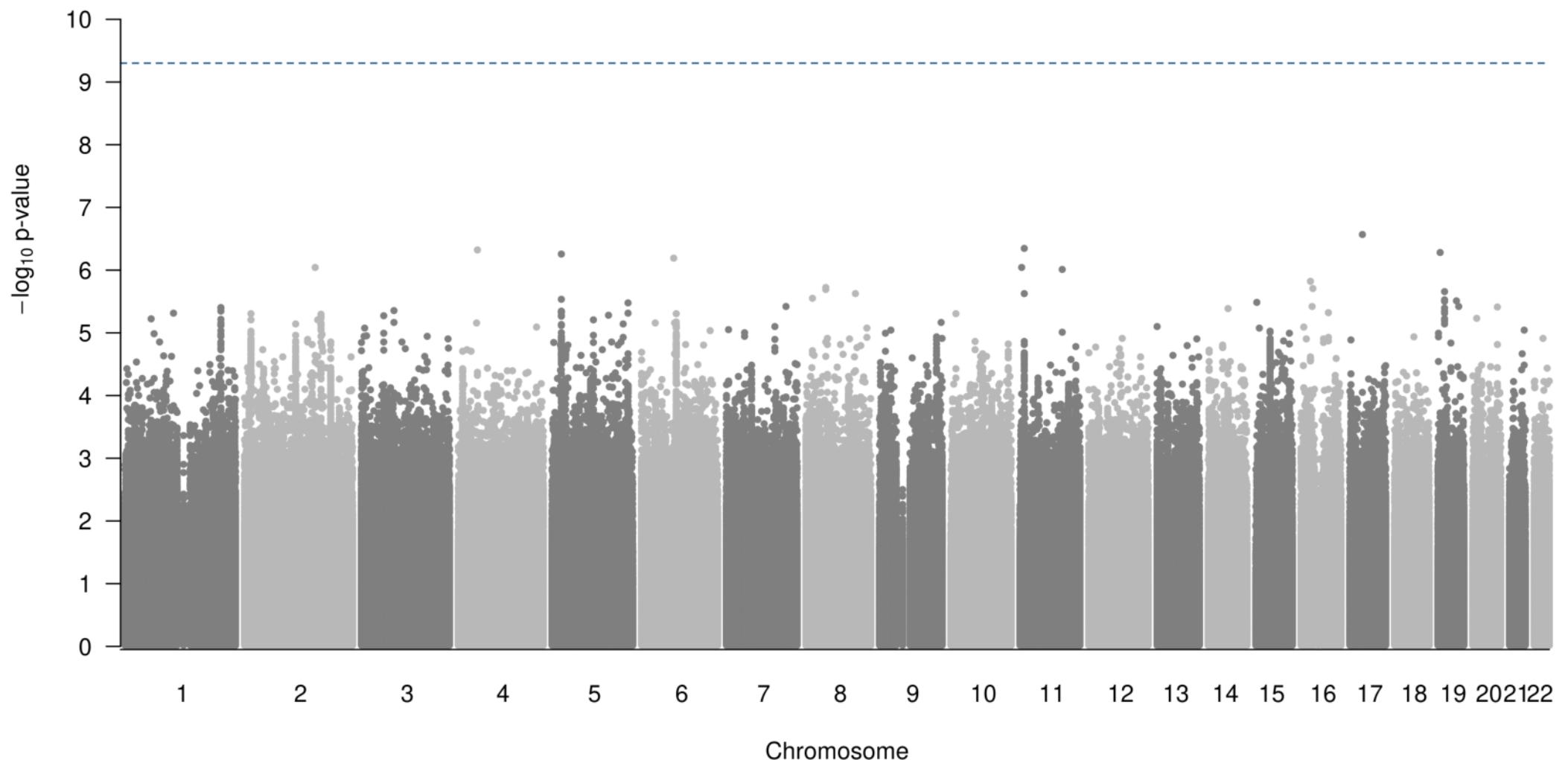
## MMP-1 (MMP1)



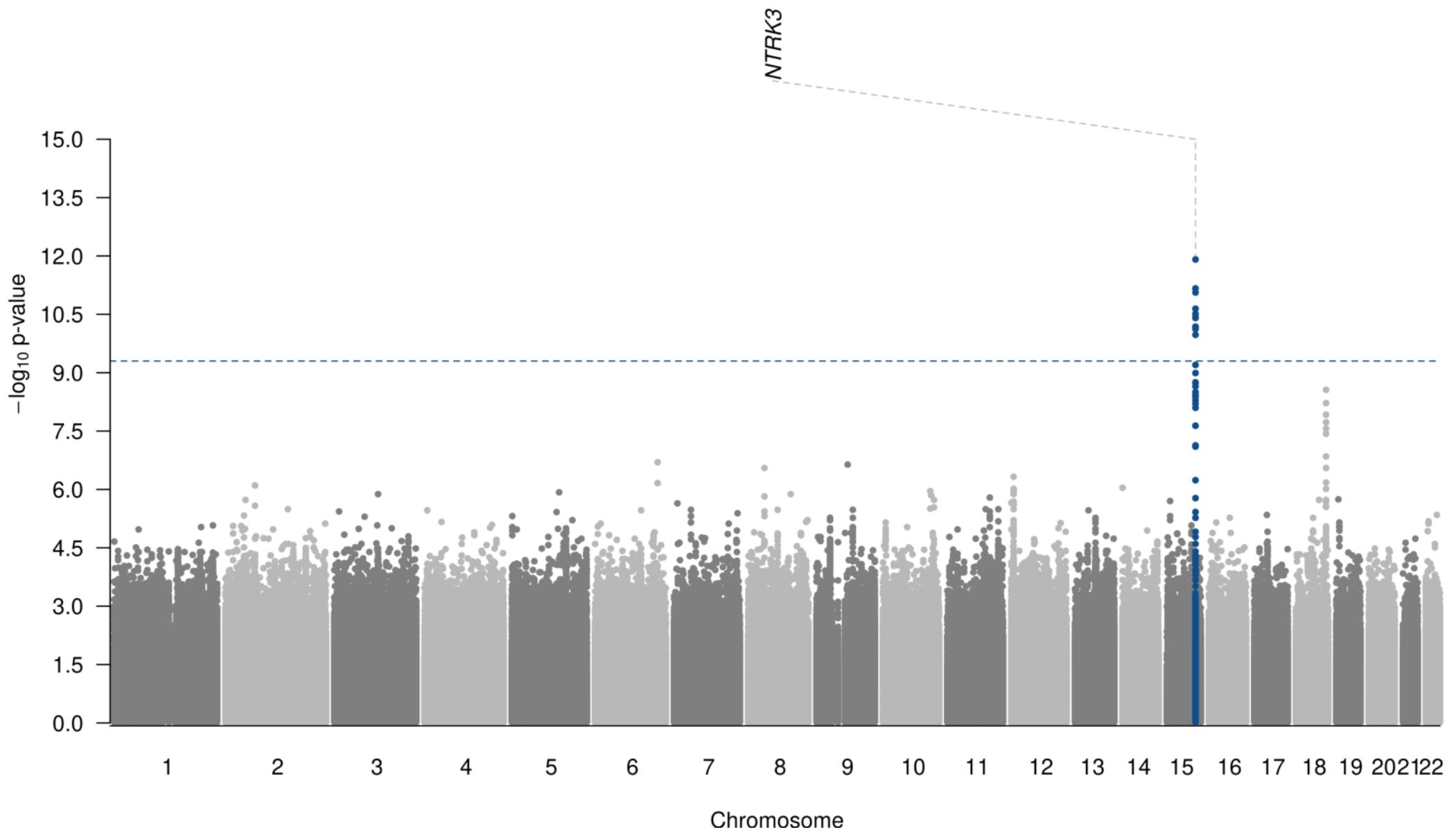
## MMP-10 (MMP10)



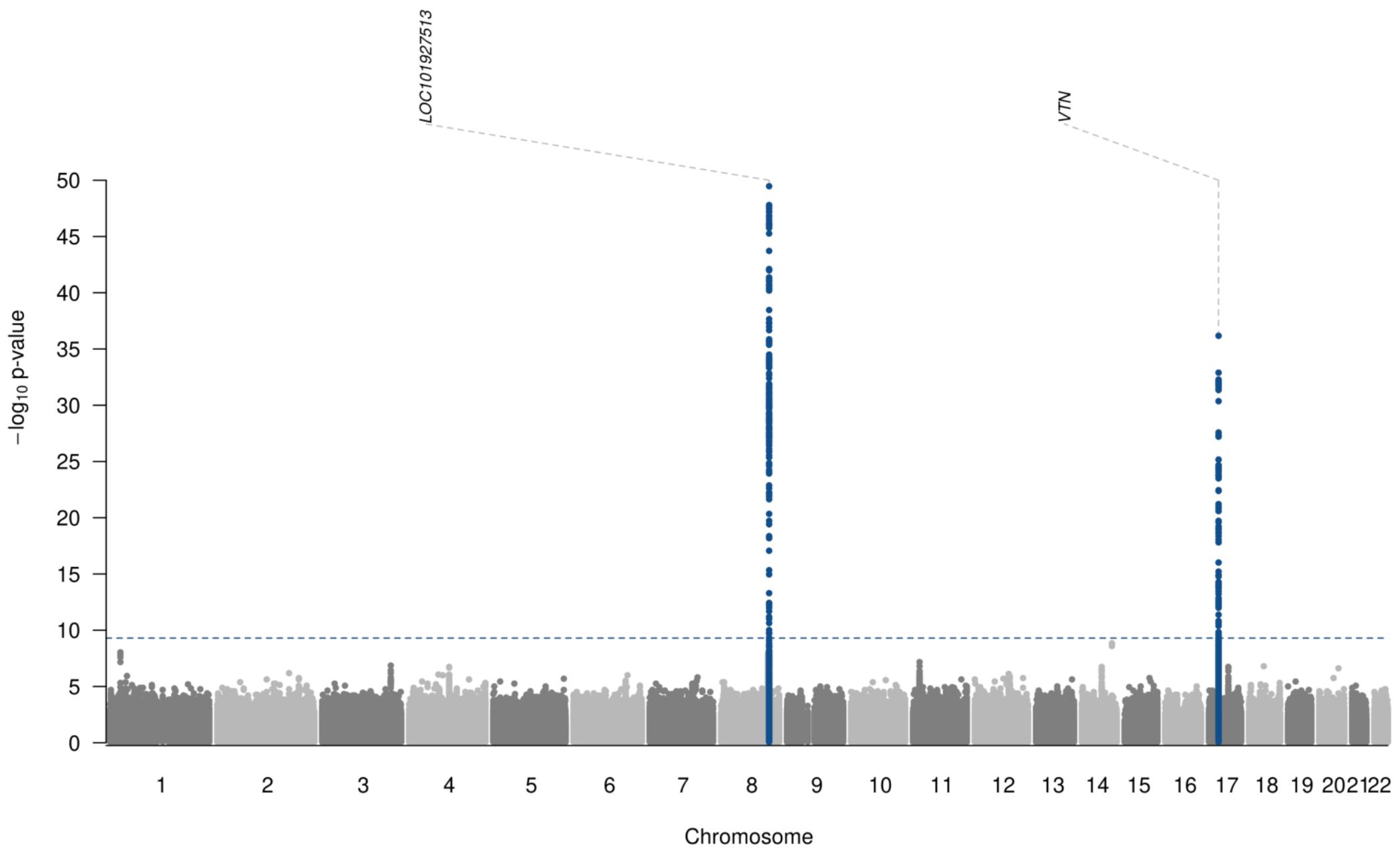
## NRTN (NRTN)



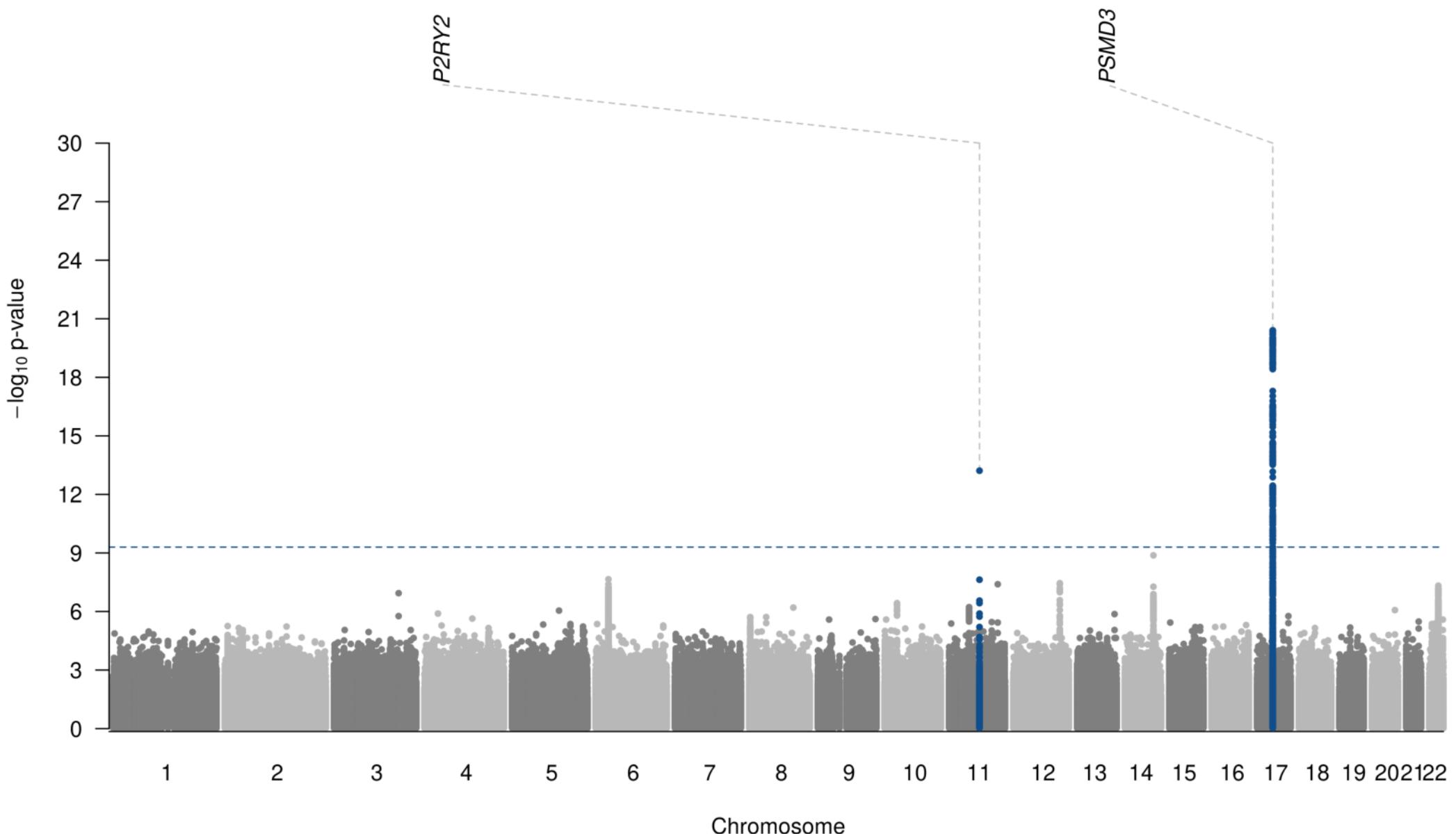
# NT-3 (NTF3)



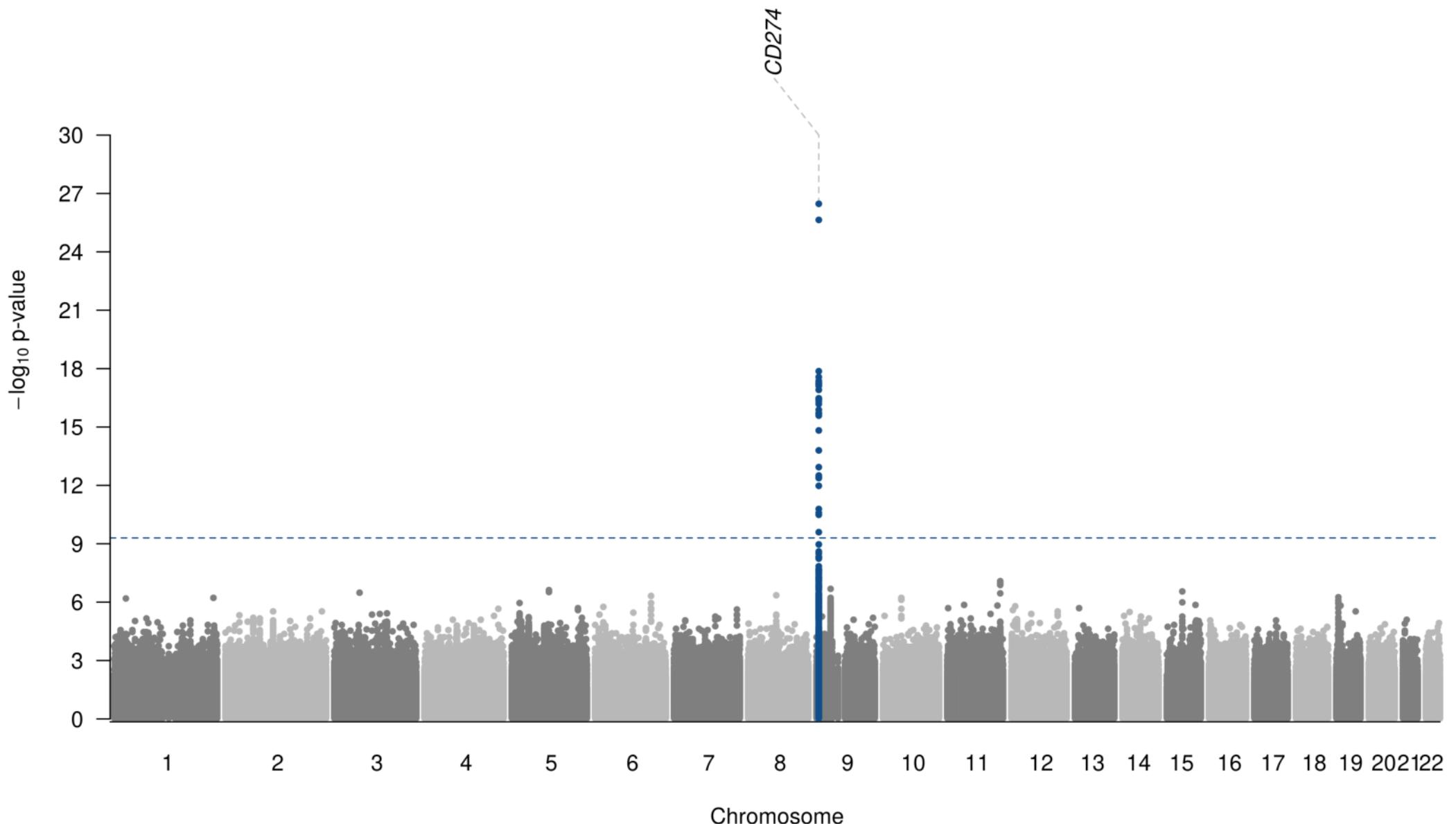
# OPG (TNFRSF11B)



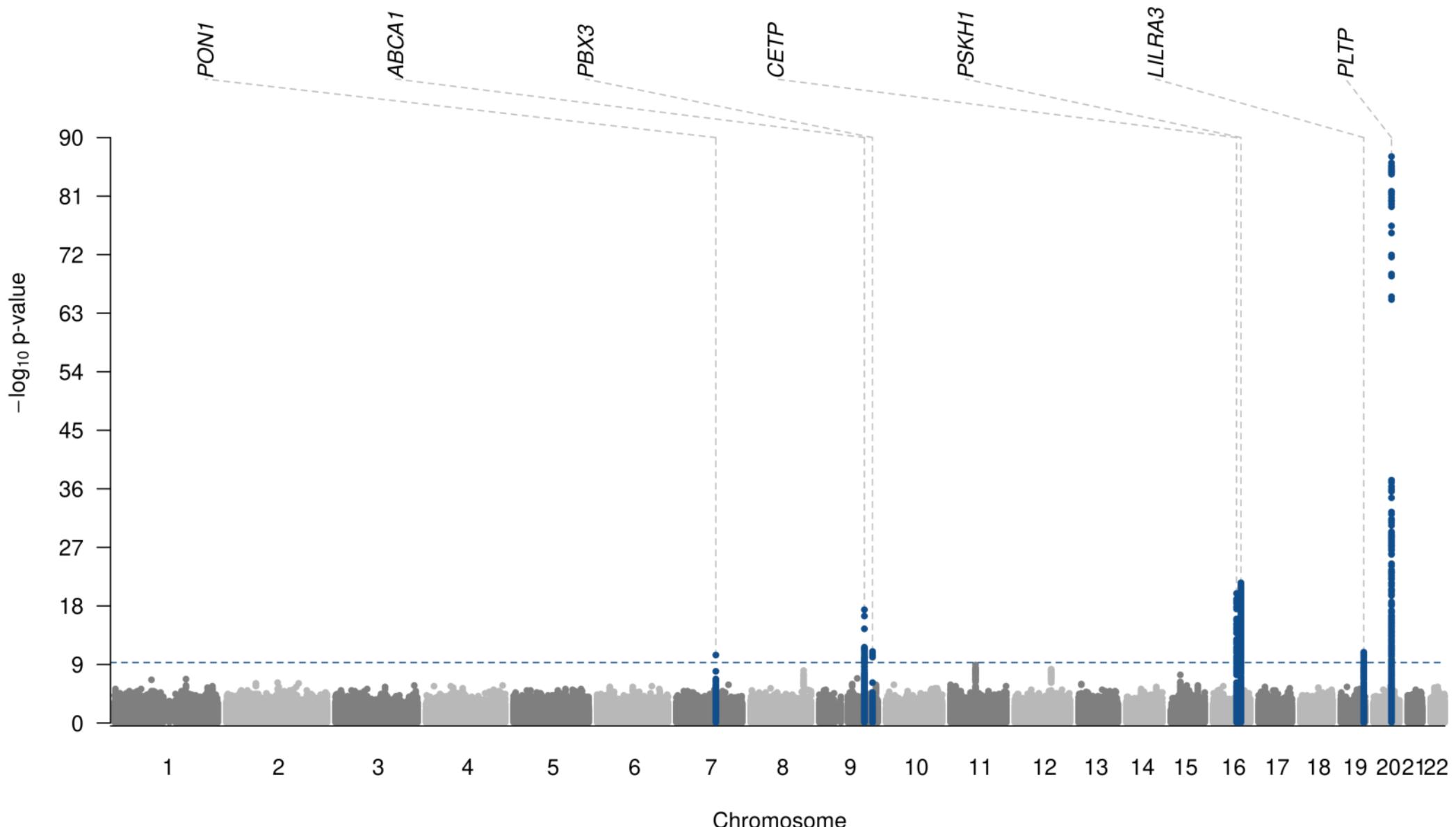
## OSM (OSM)



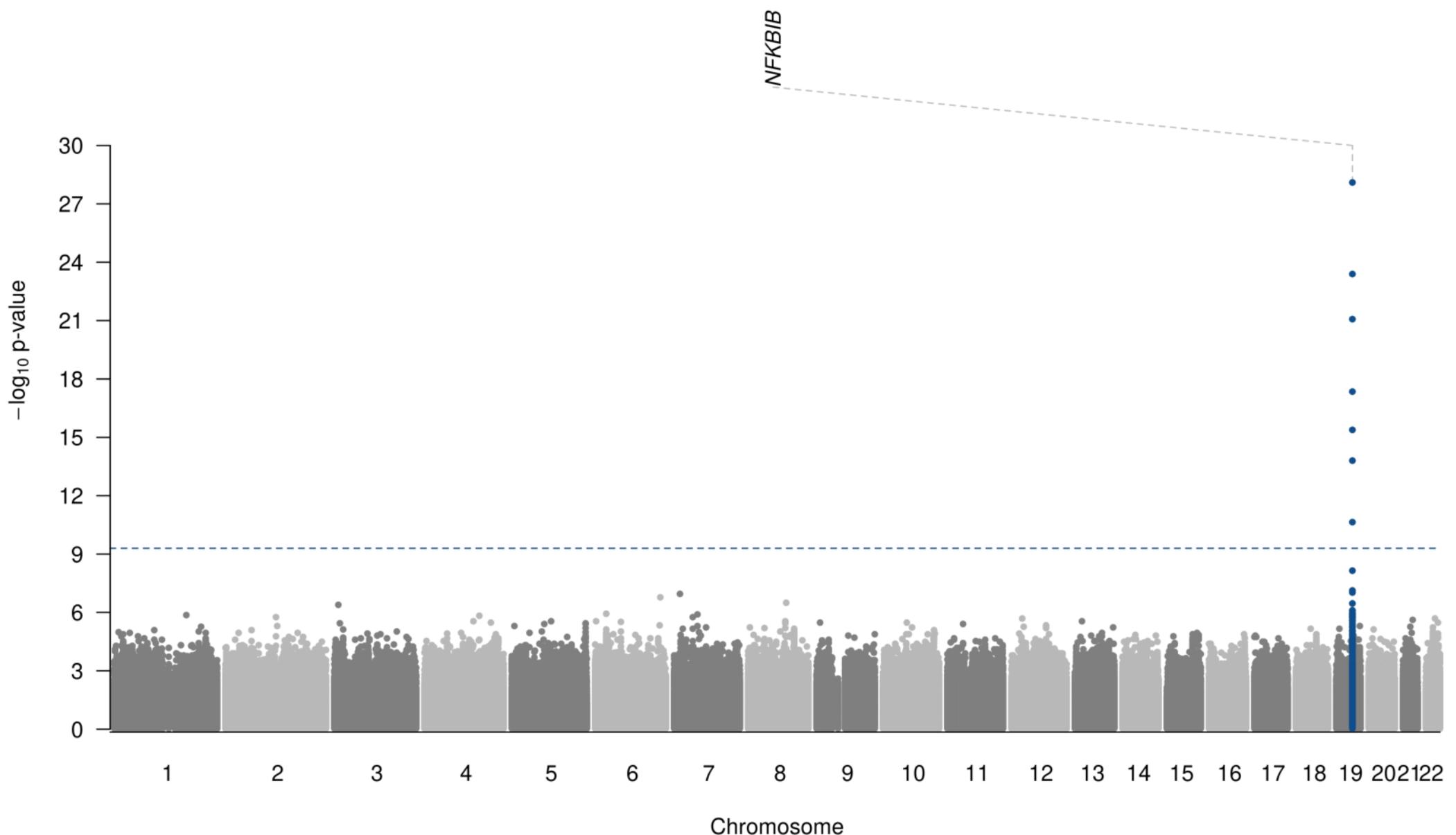
## PD-L1 (CD274)



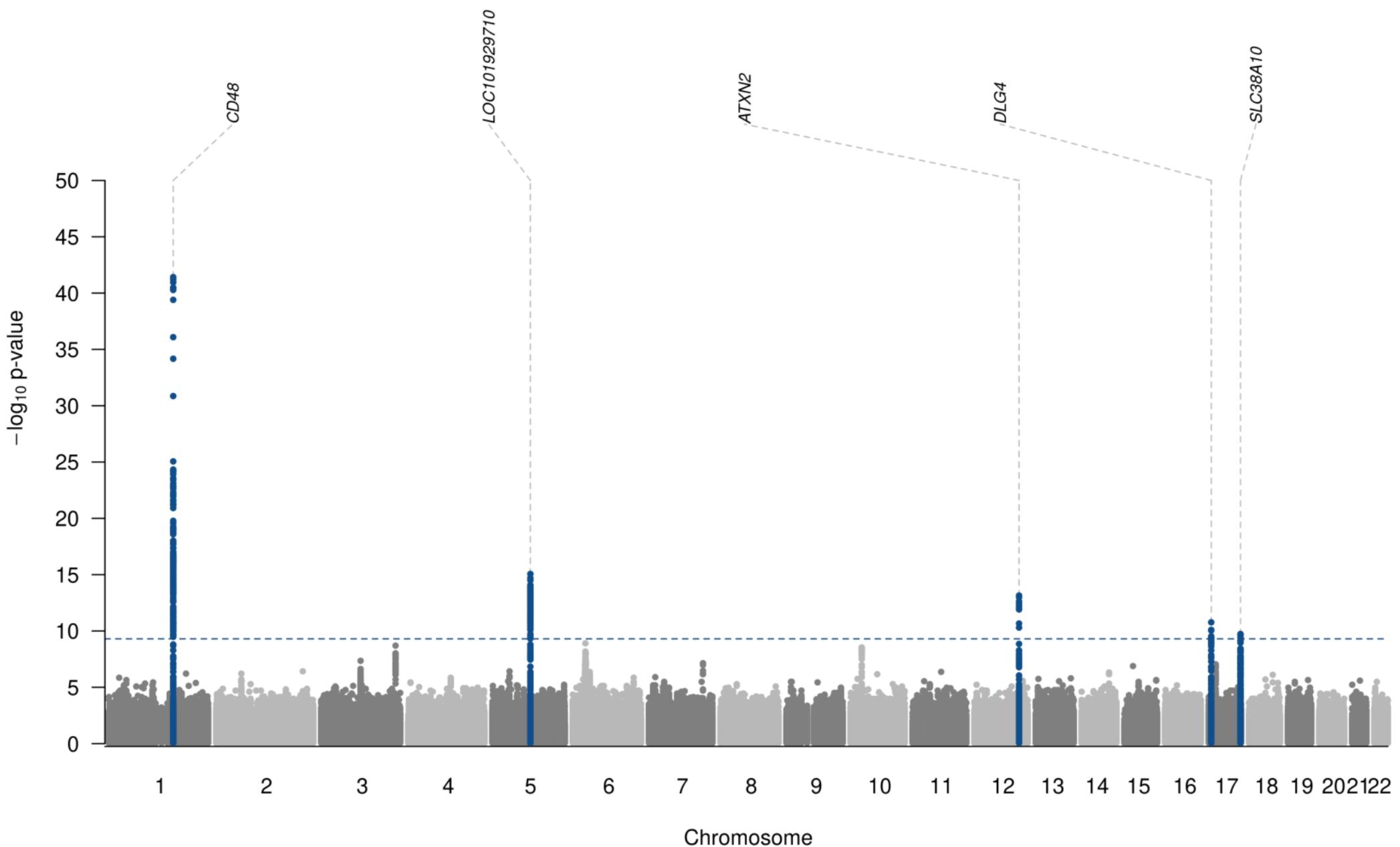
## SCF (KITLG)



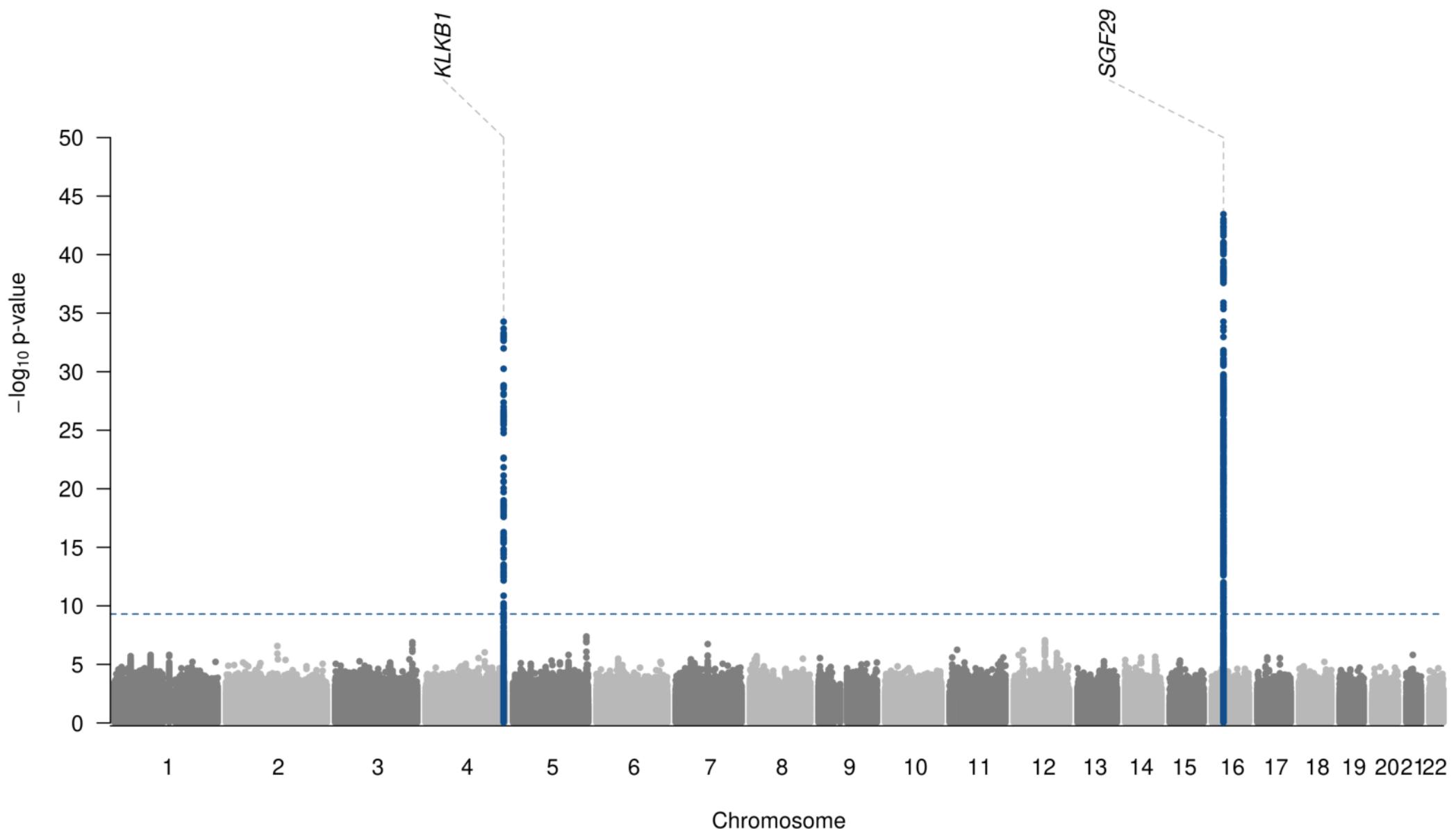
## SIRT2 (SIRT2)



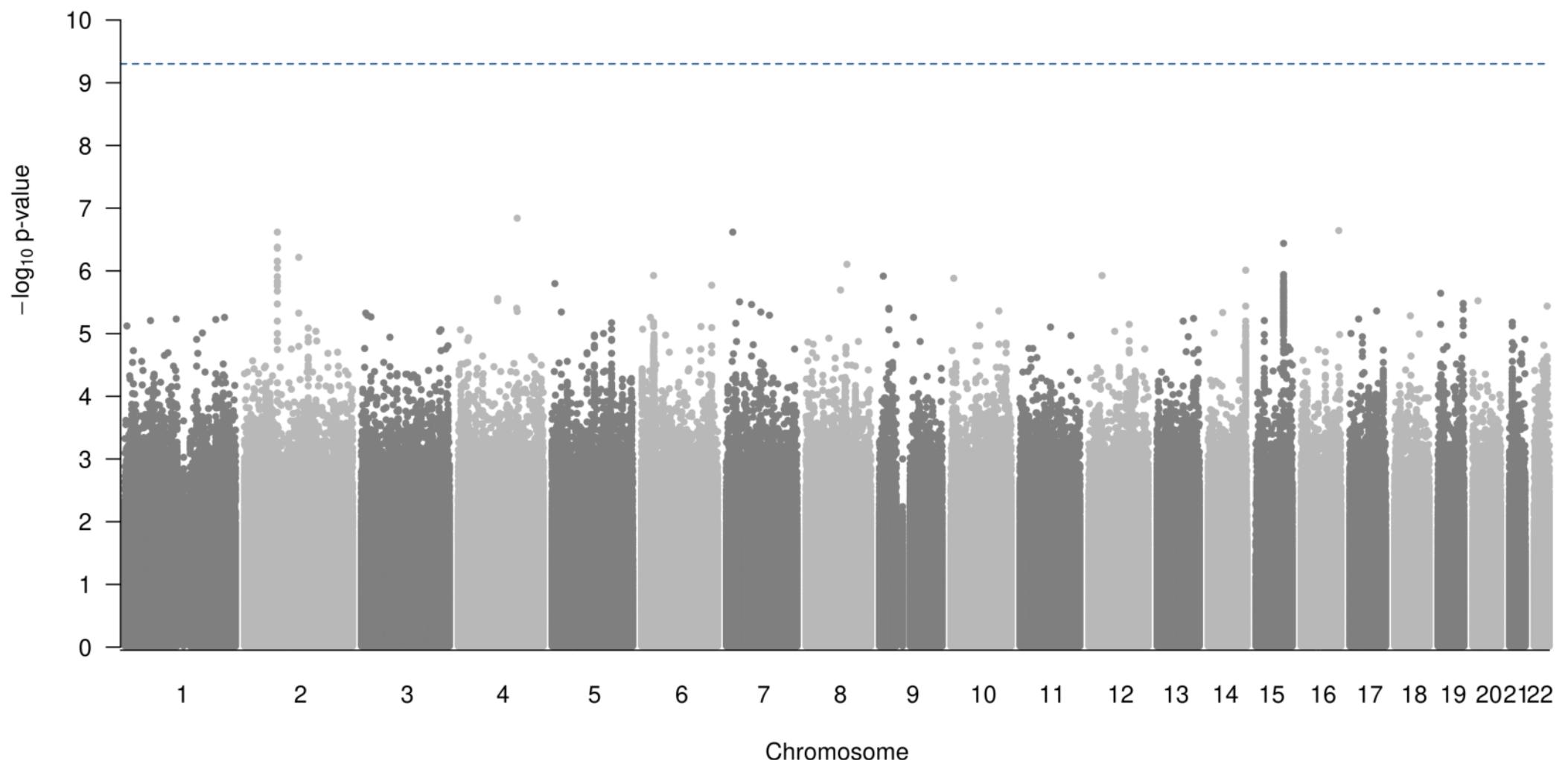
# SLAMF1 (SLAMF1)



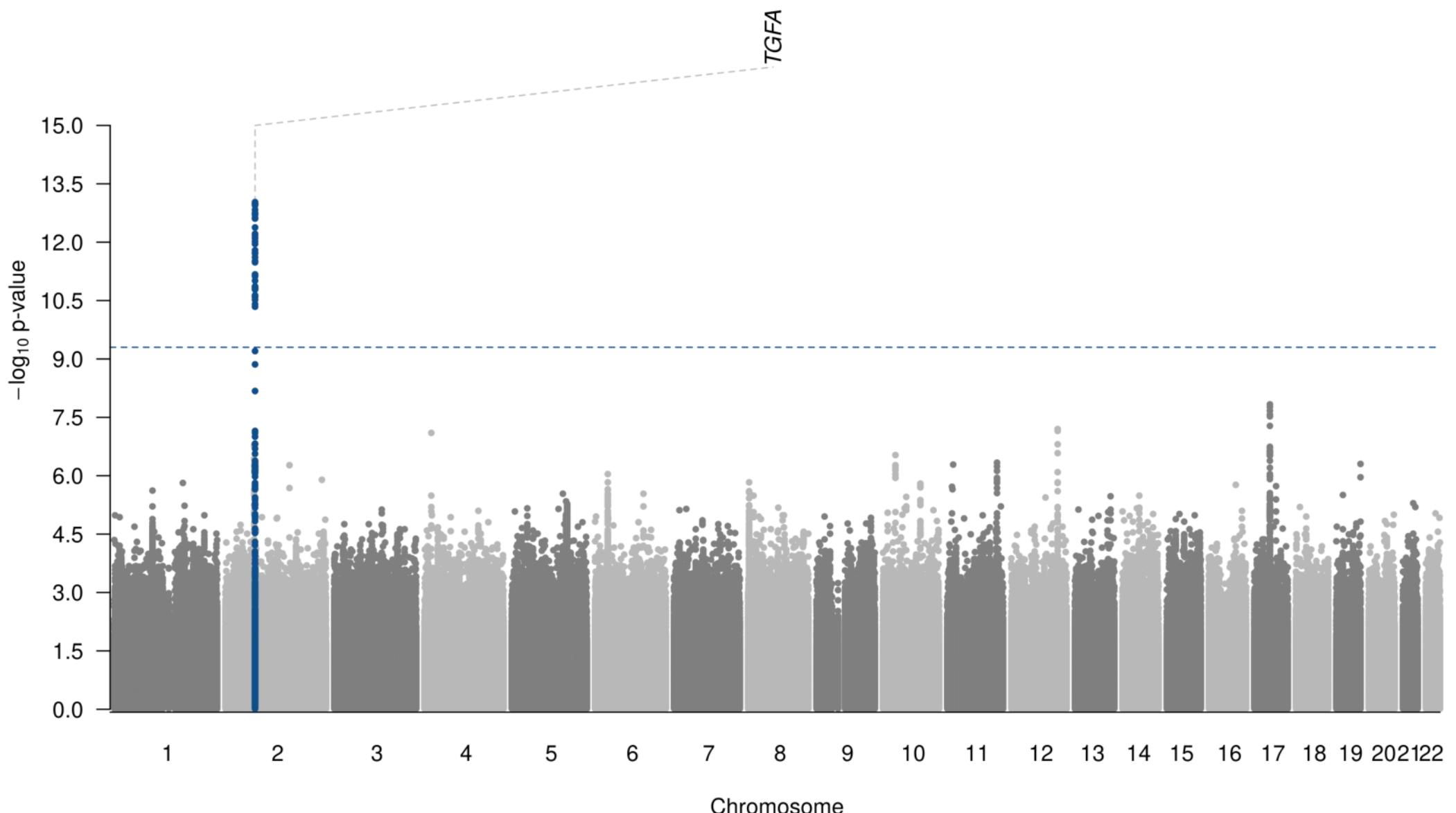
# ST1A1 (SULT1A1)



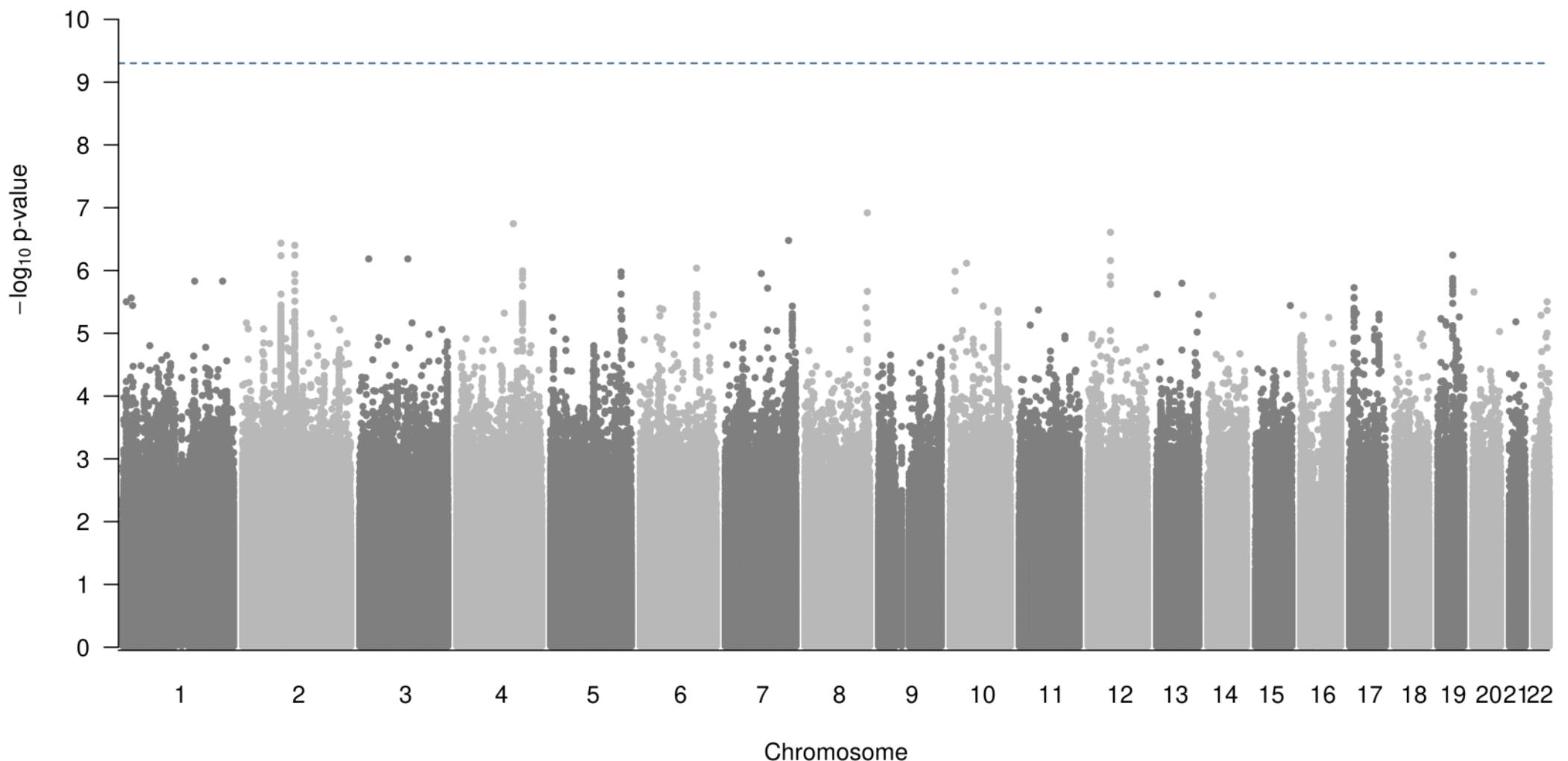
## STAMPB (STAMBP)



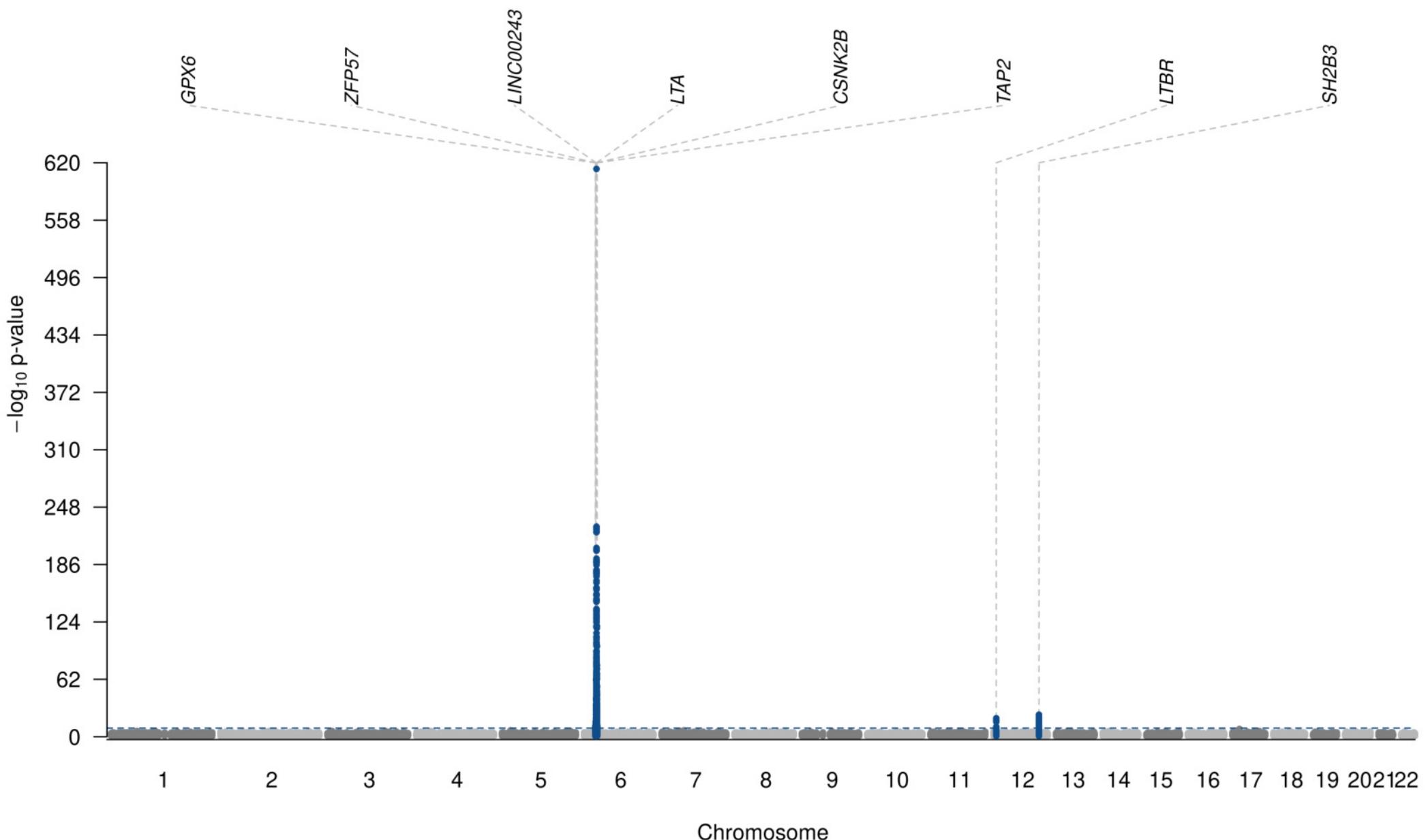
## TGF-alpha (TGFA)



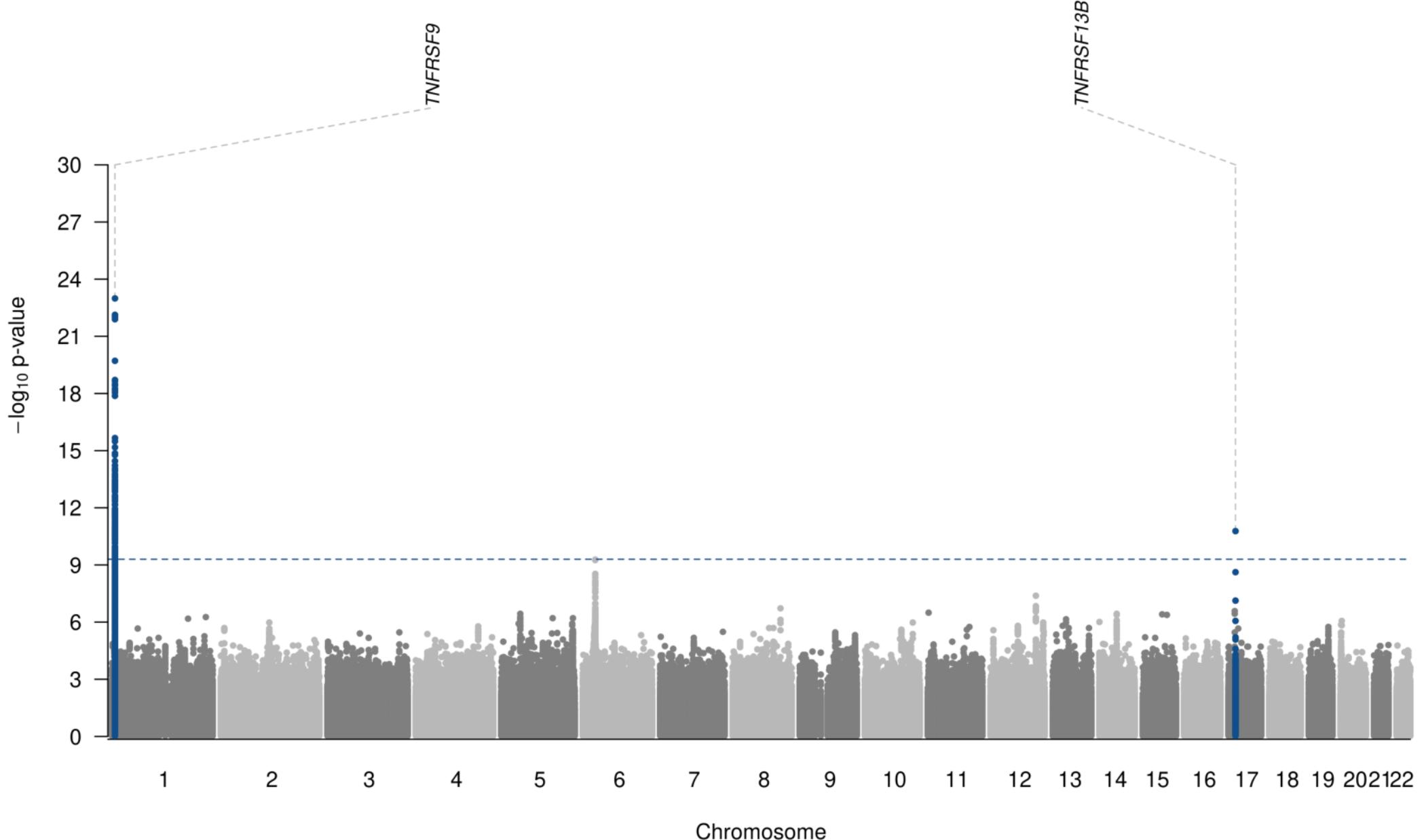
## TNF (TNF)



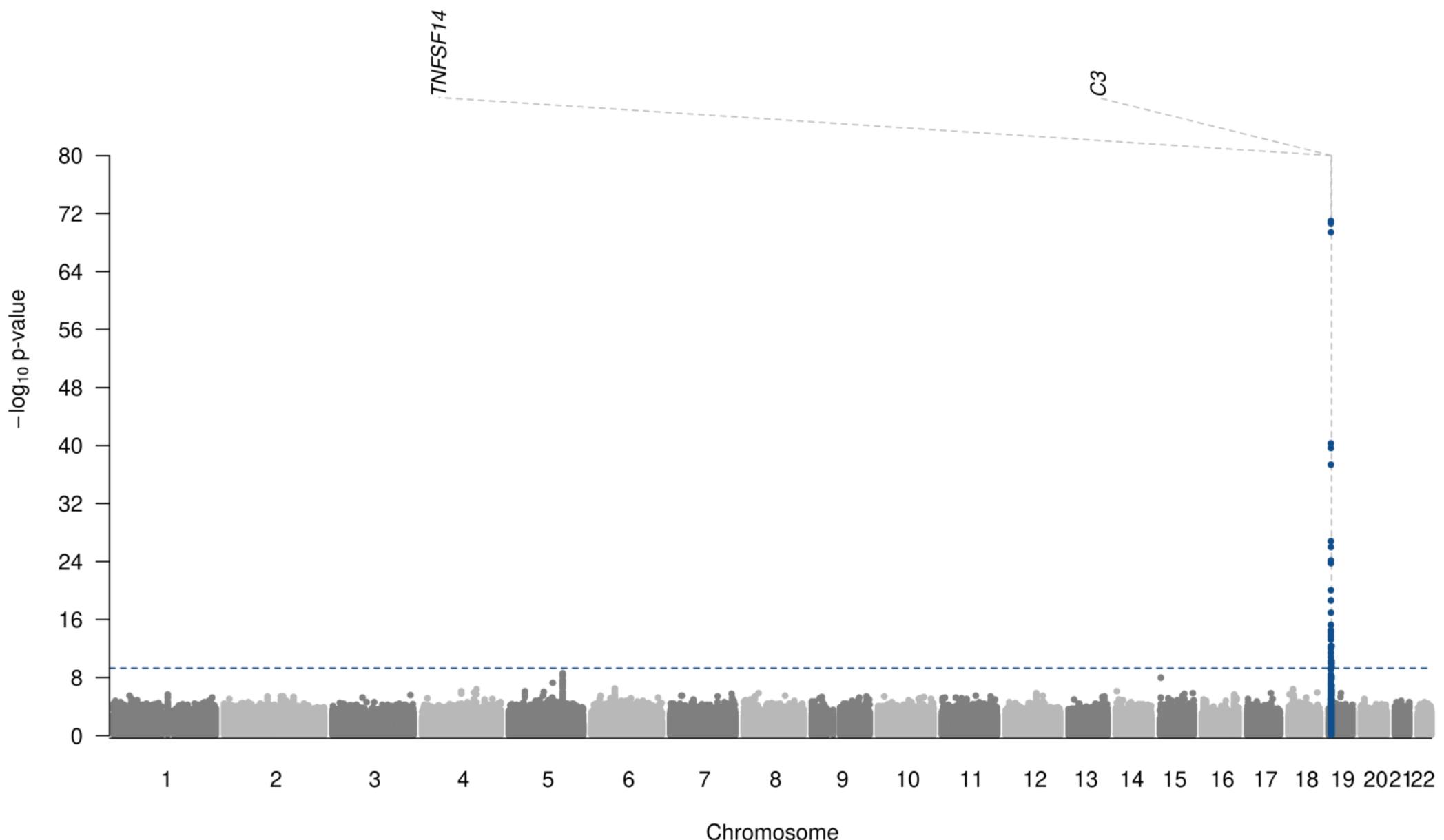
## TNFB (LTA)



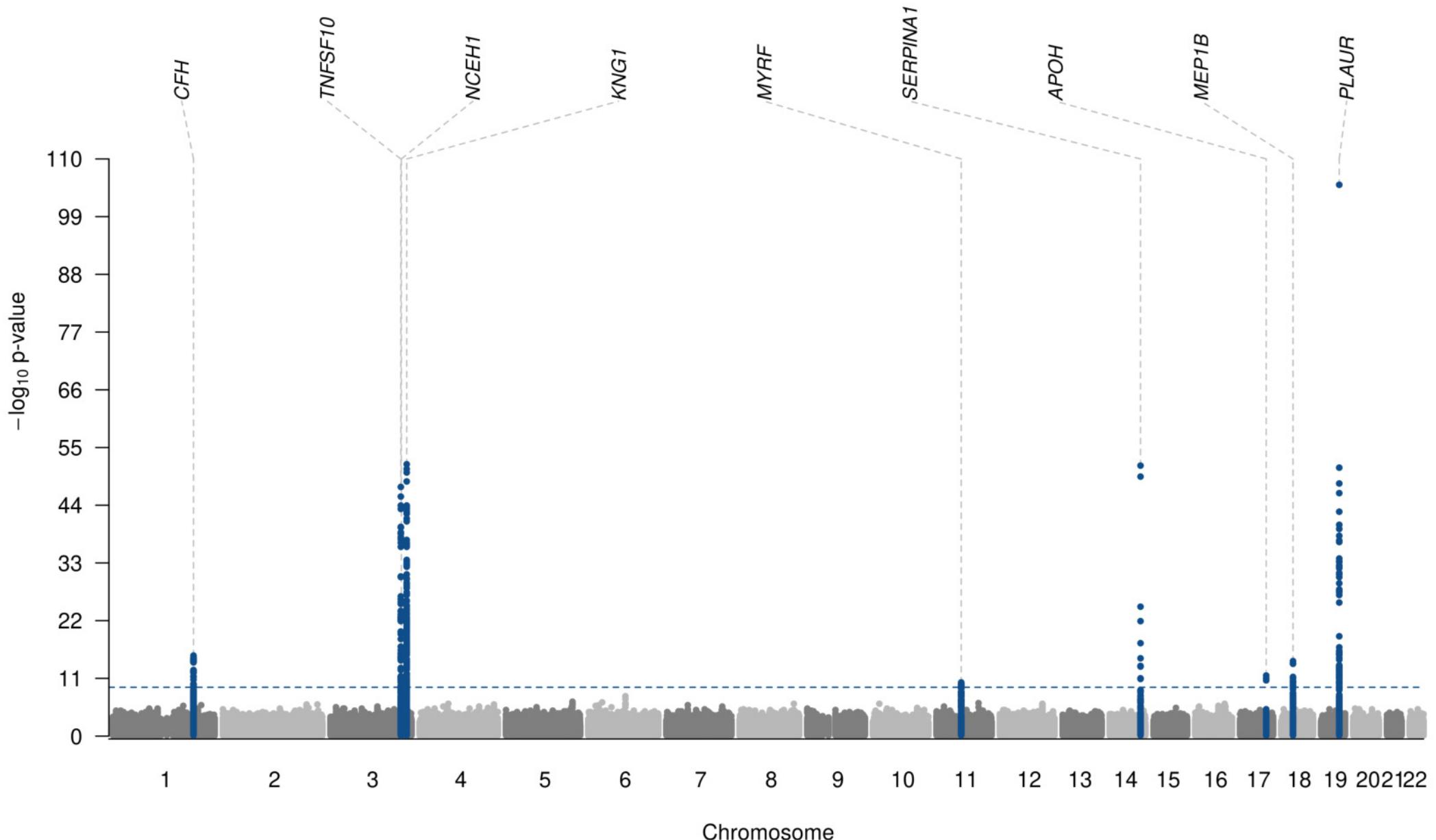
## TNFRSF9 (TNFRSF9)



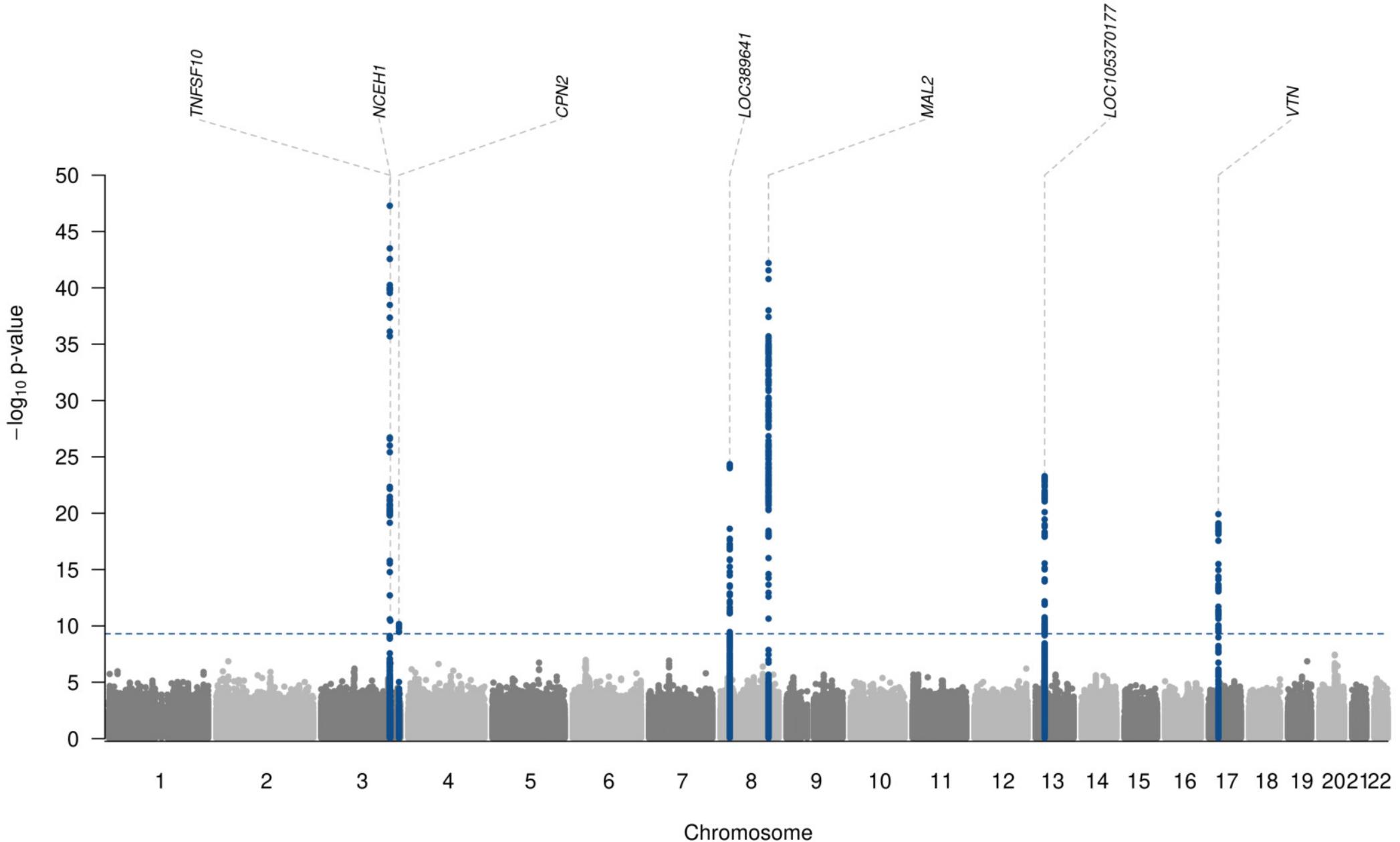
## TNFSF14 (TNFSF14)



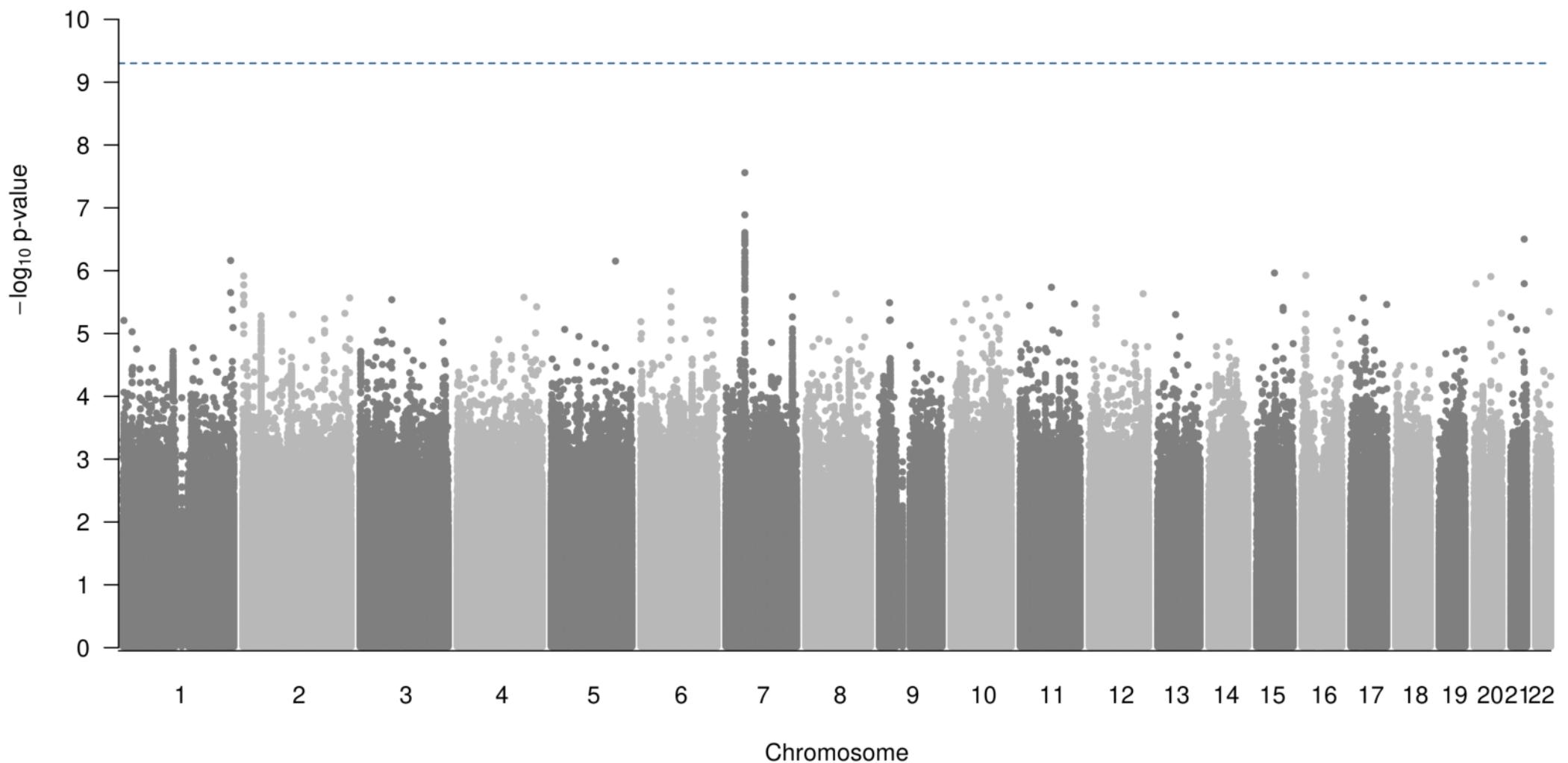
## TRAIL (TNFSF10)



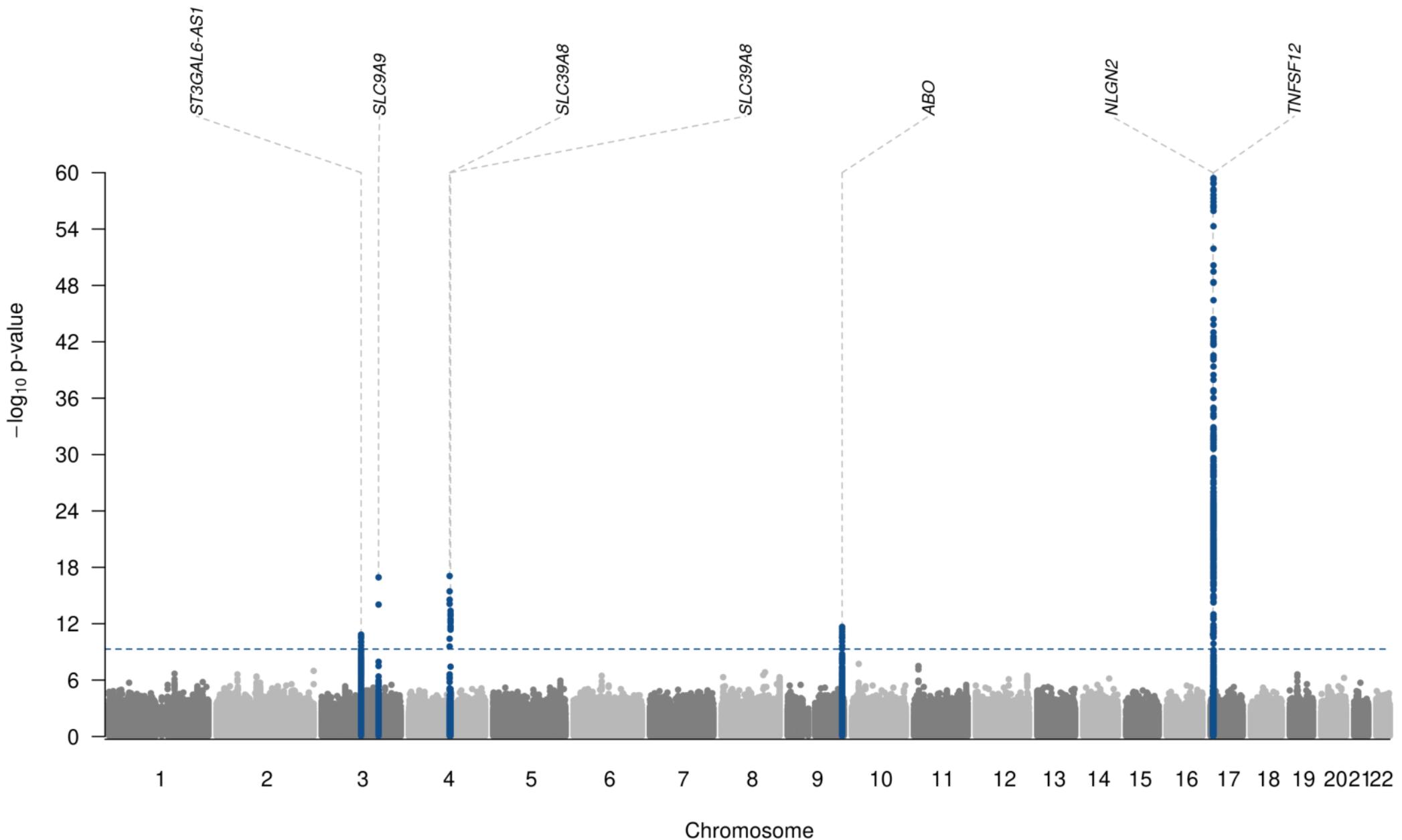
# TRANCE (TNFSF11)



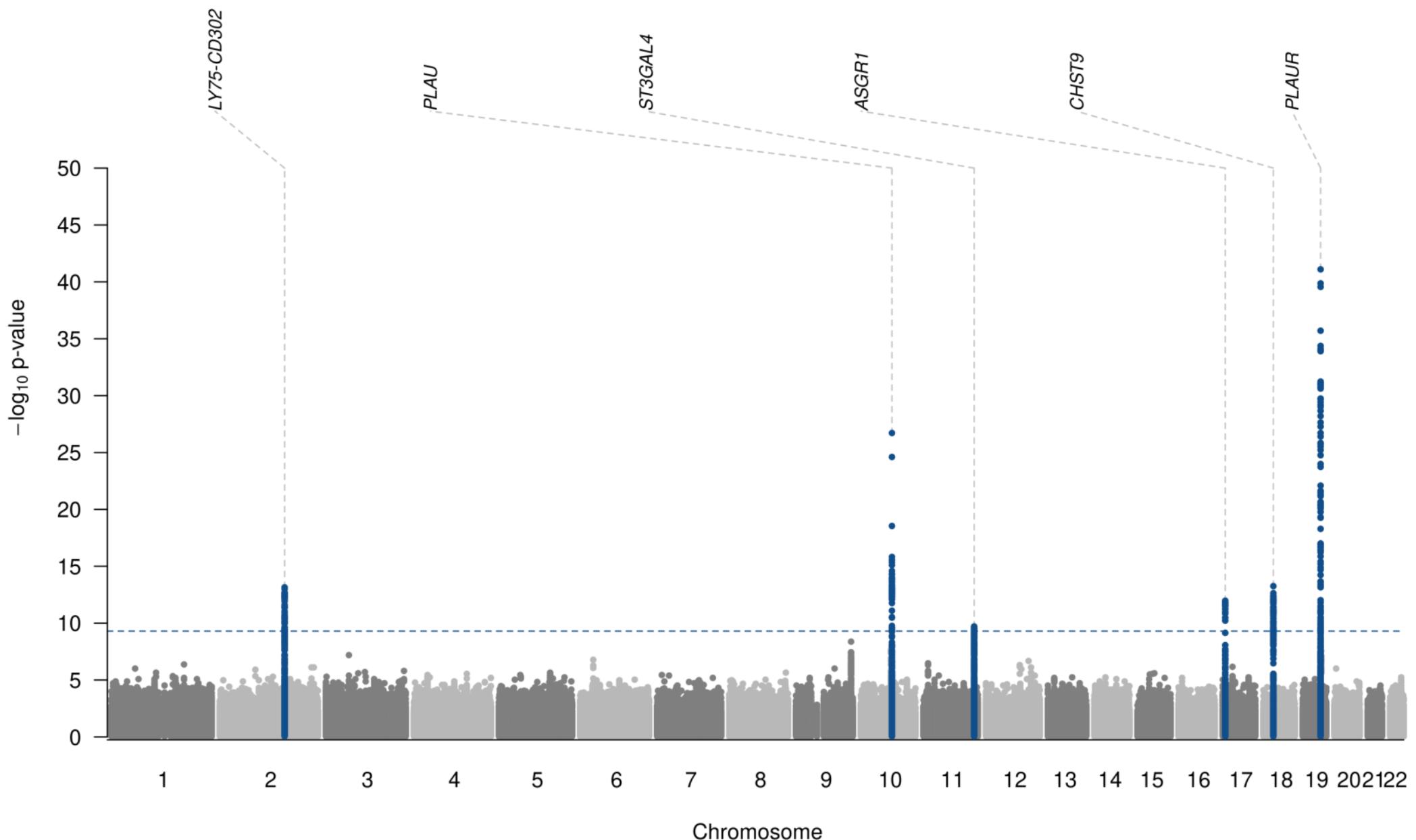
## TSLP (TSLP)



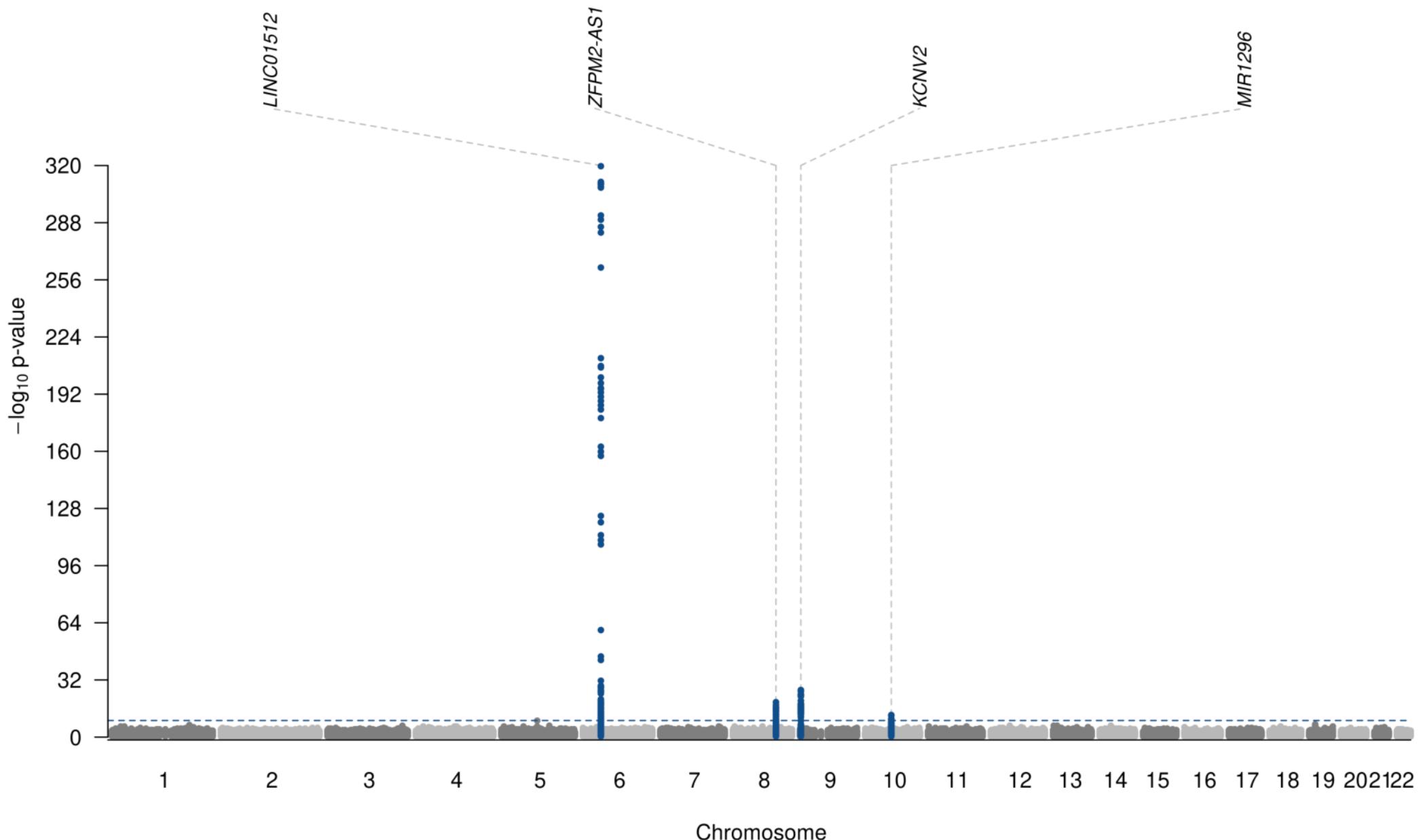
# TWEAK (TNFSF12)



## uPA (PLAU)

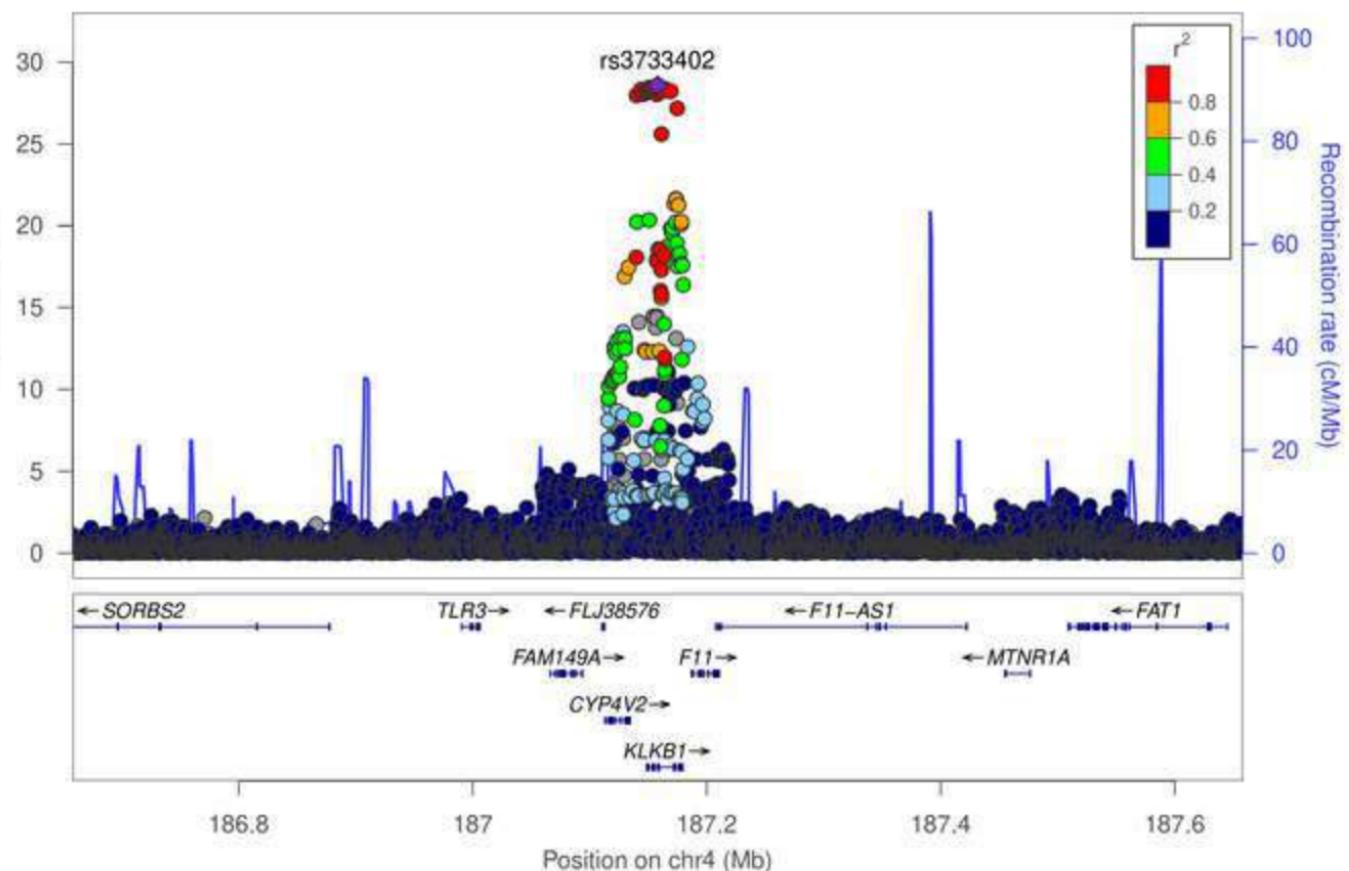
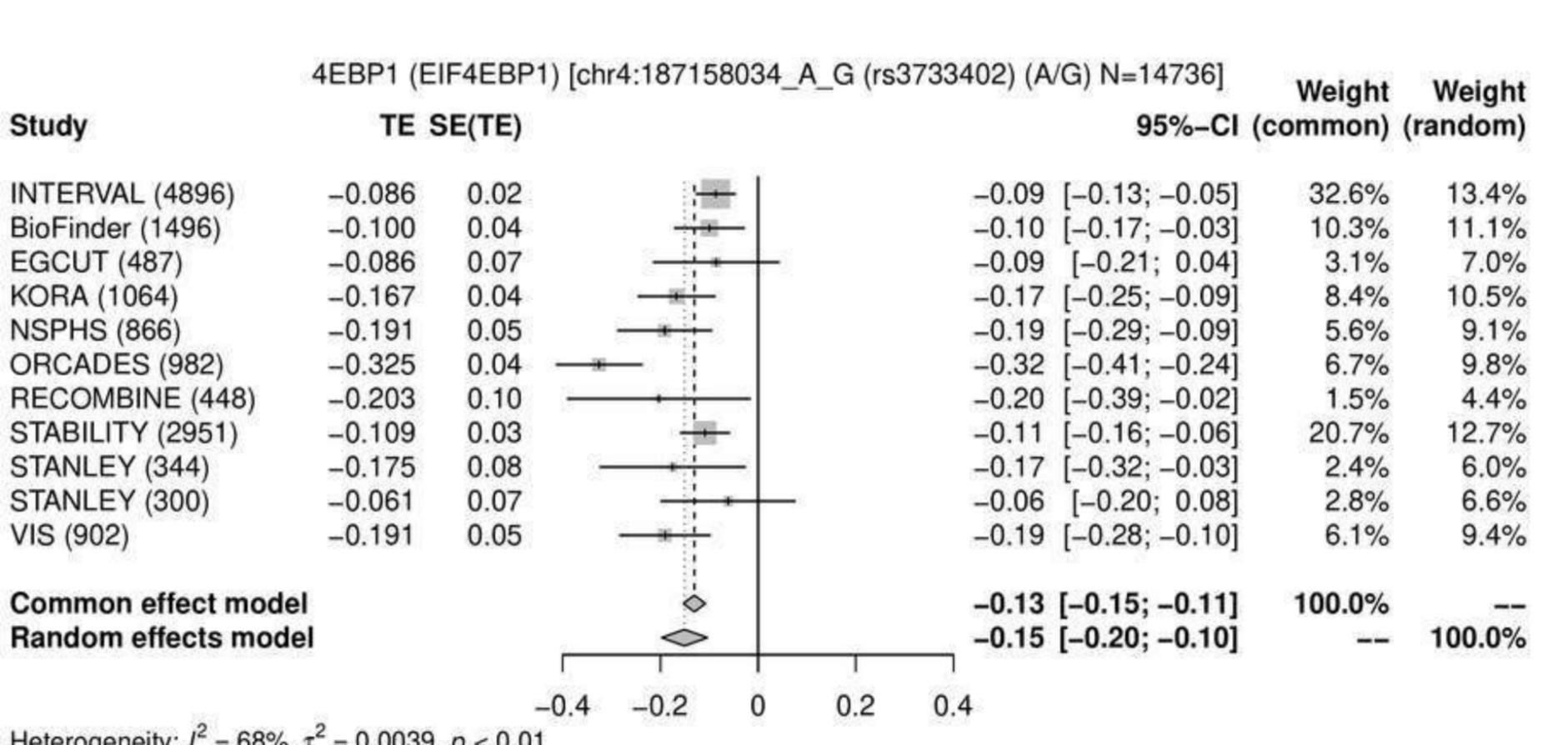


# VEGF\_A (VEGFA)

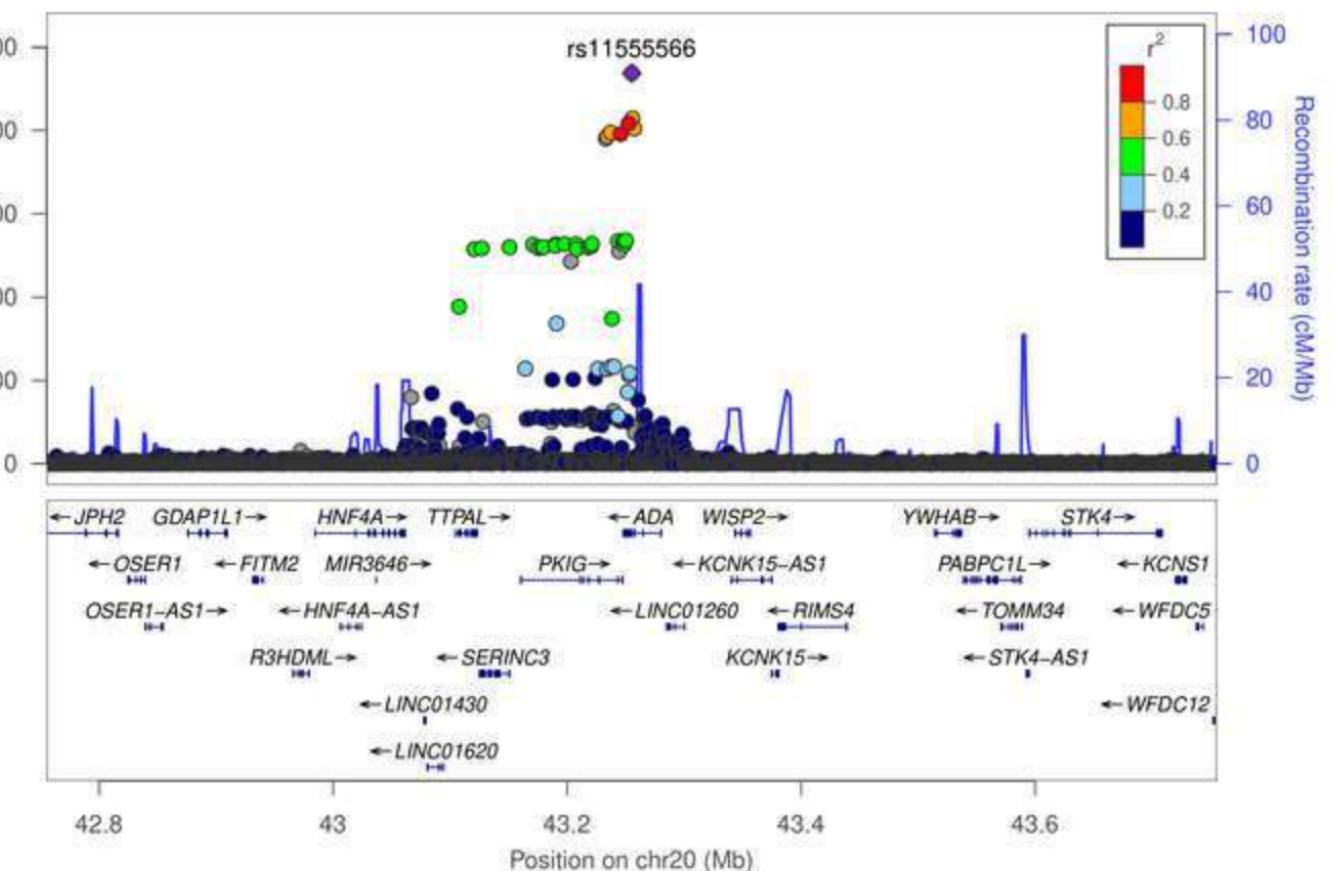
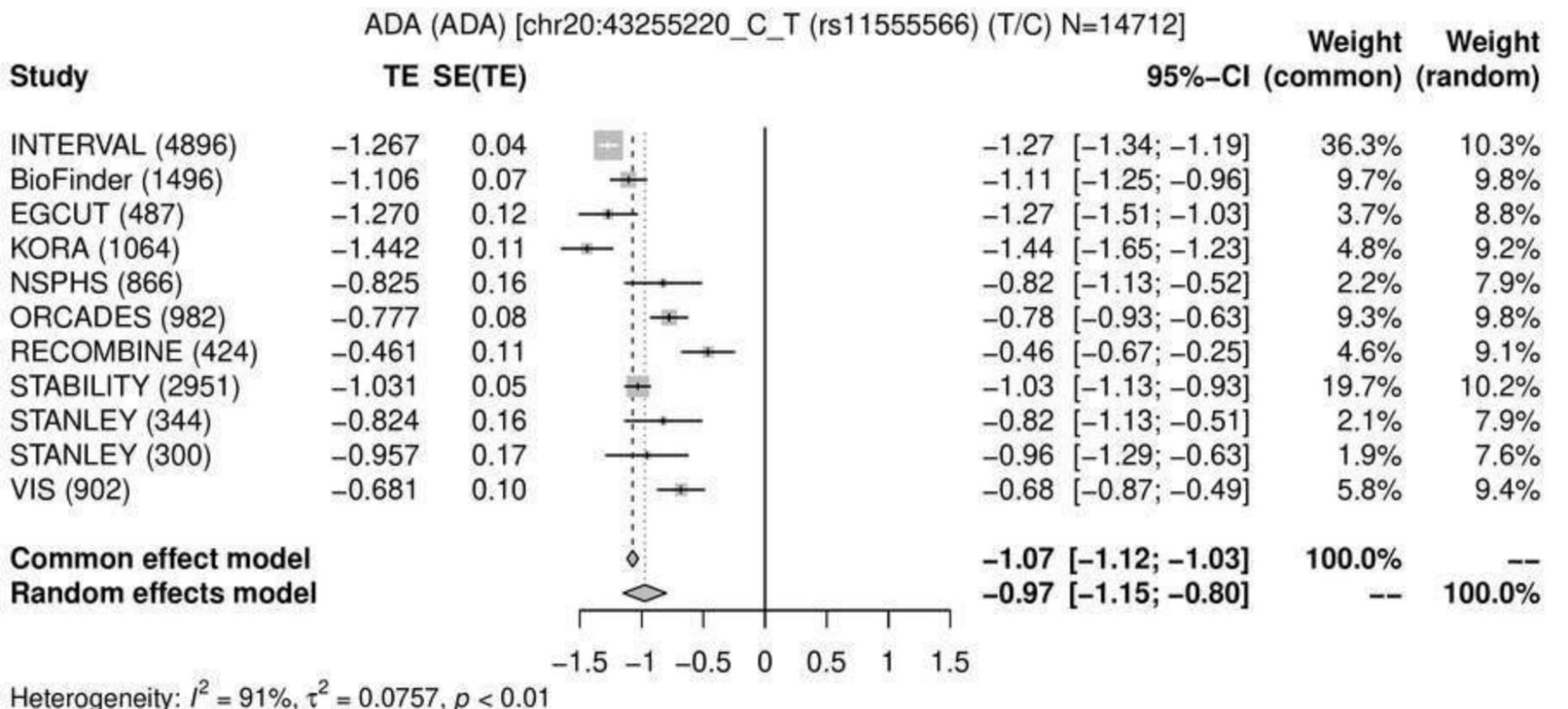


**Supplementary Figure 2.** Forest plots and regional association plots for the 180 pQTLs. Left panels: forest plots show the effect estimate and 95% confidence intervals in each cohort. Metrics of heterogeneity are provided. N= number of individuals. Right panels: locuszoom plots of the regional associations. Proteins are labelled with both the label provided by Olink, and with the encoding gene symbol in parentheses. Two-sided *P*-values are from meta-analysis of linear regression estimates.

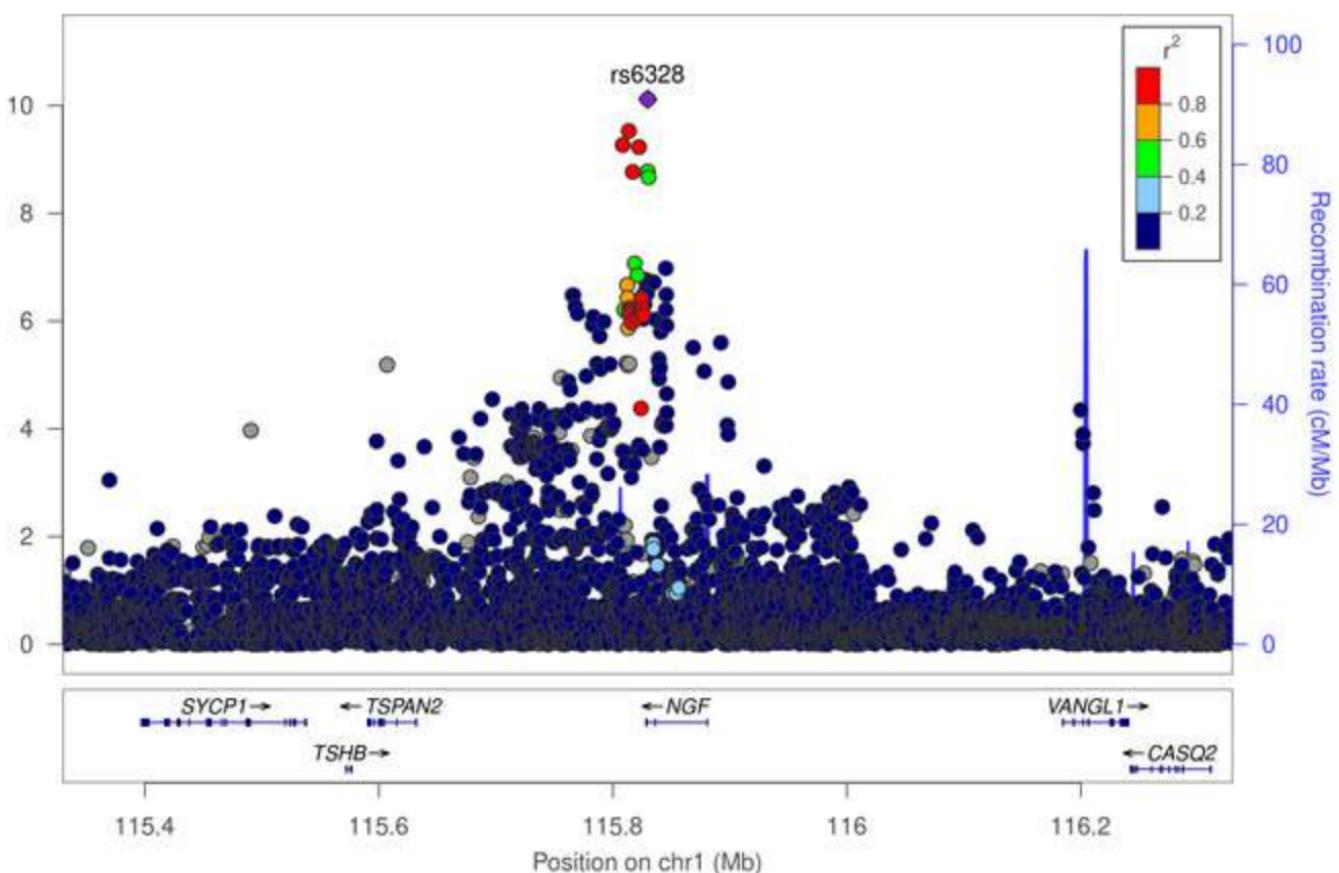
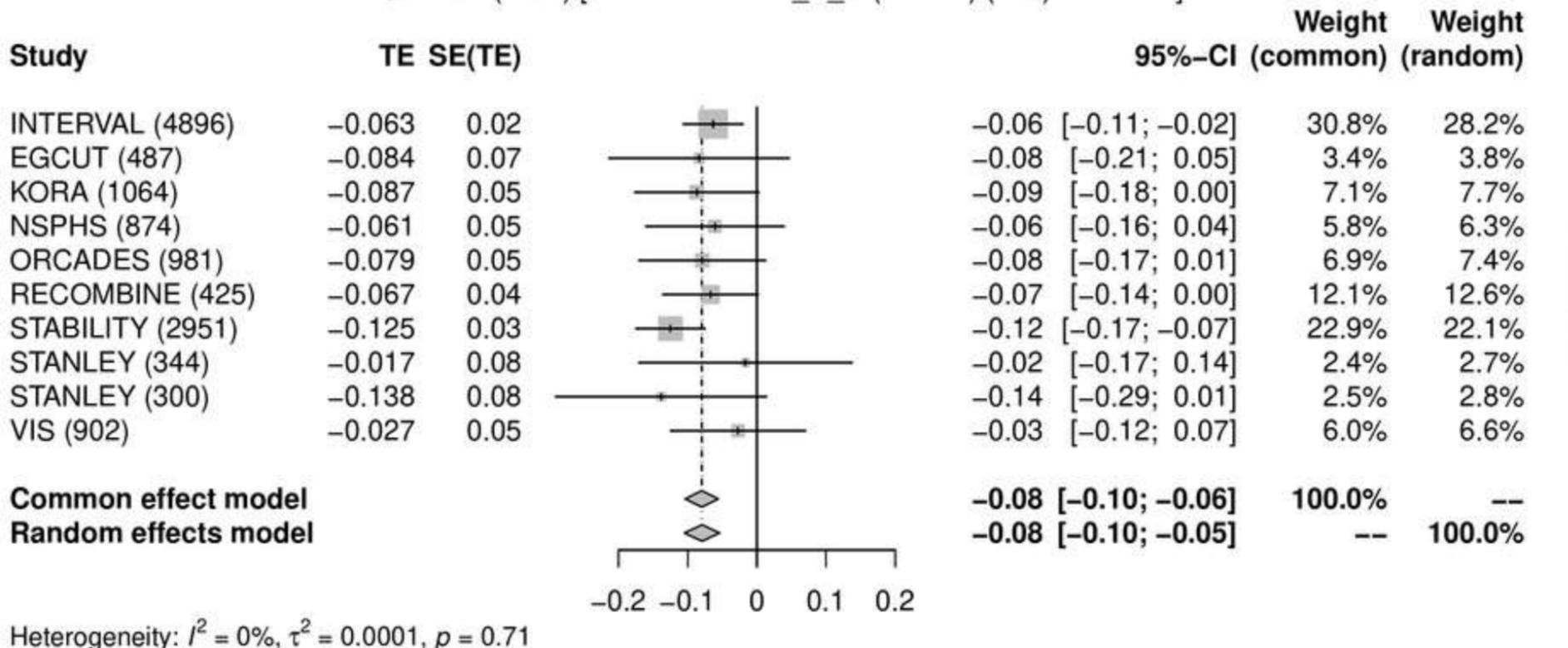
# 4EBP1 (EIF4EBP1)-rs3733402



# ADA (ADA)-rs11555566

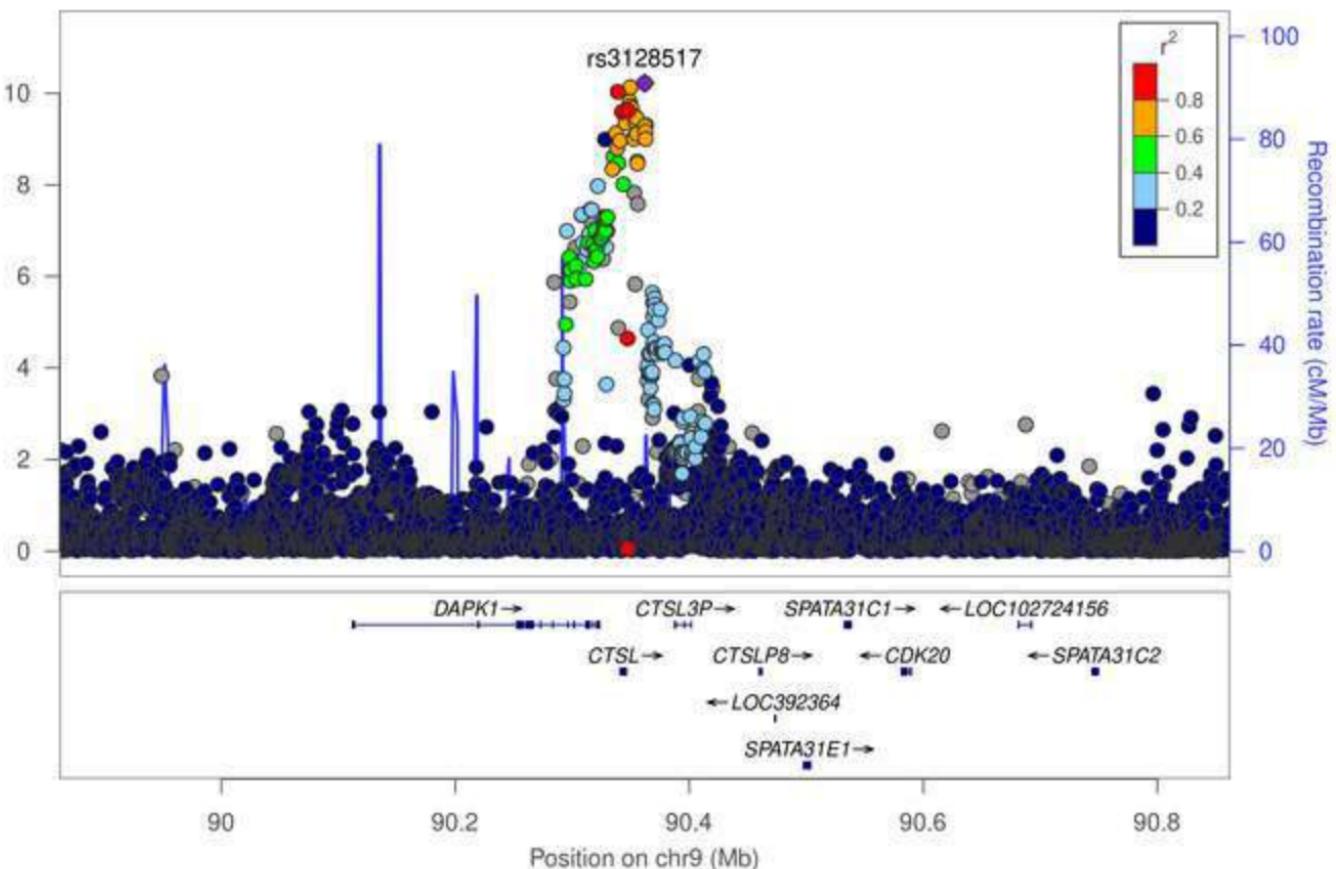
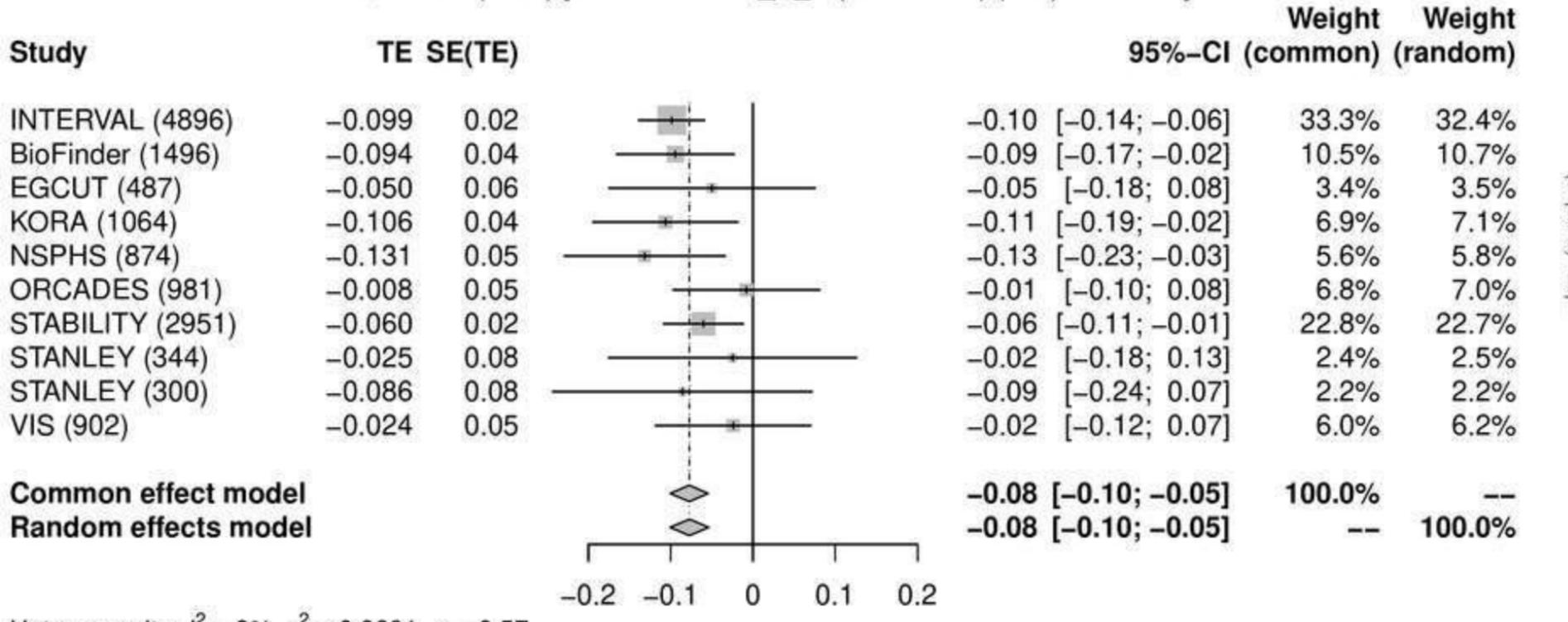


# Beta-NGF (NGF)-rs6328

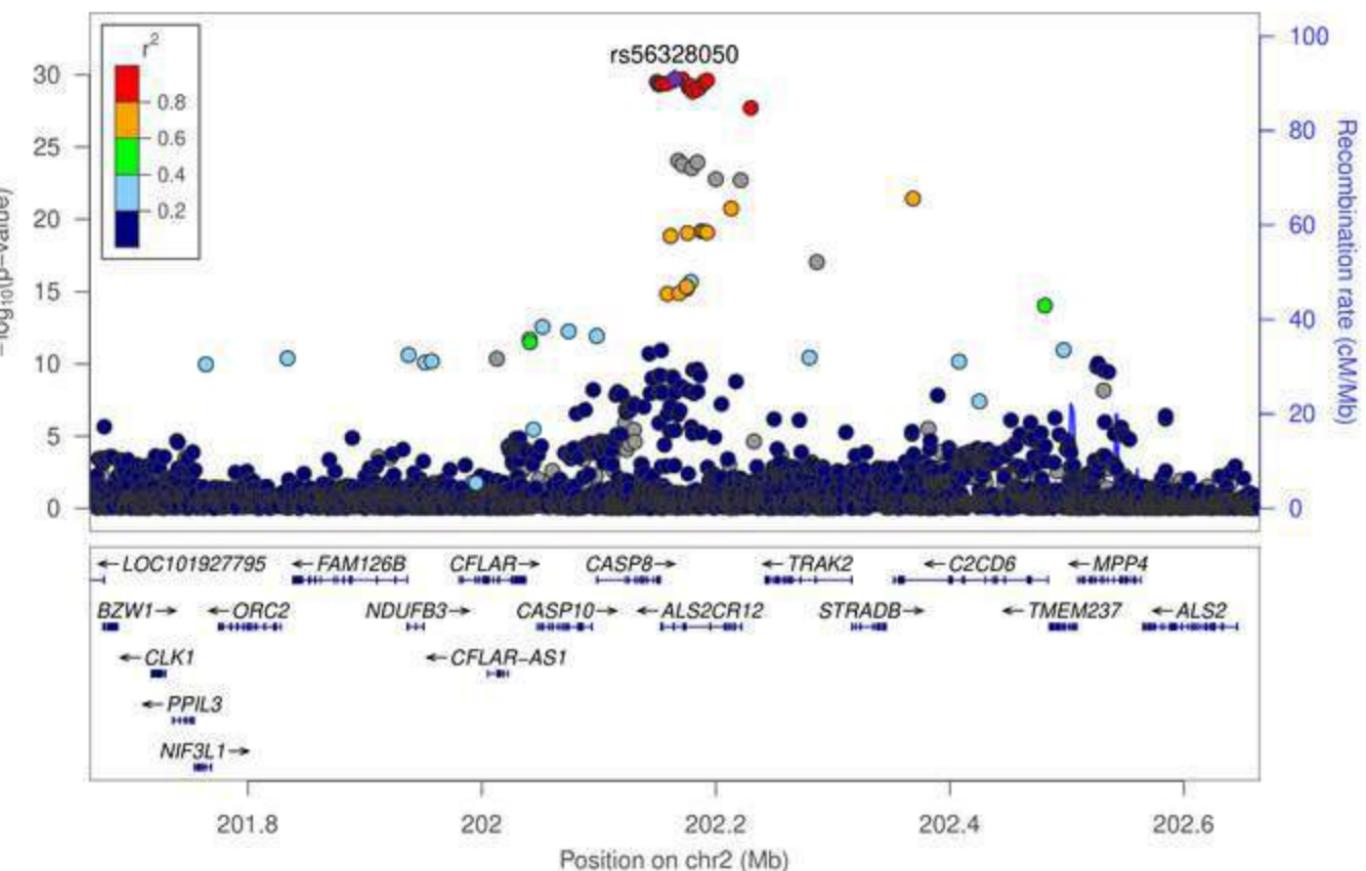
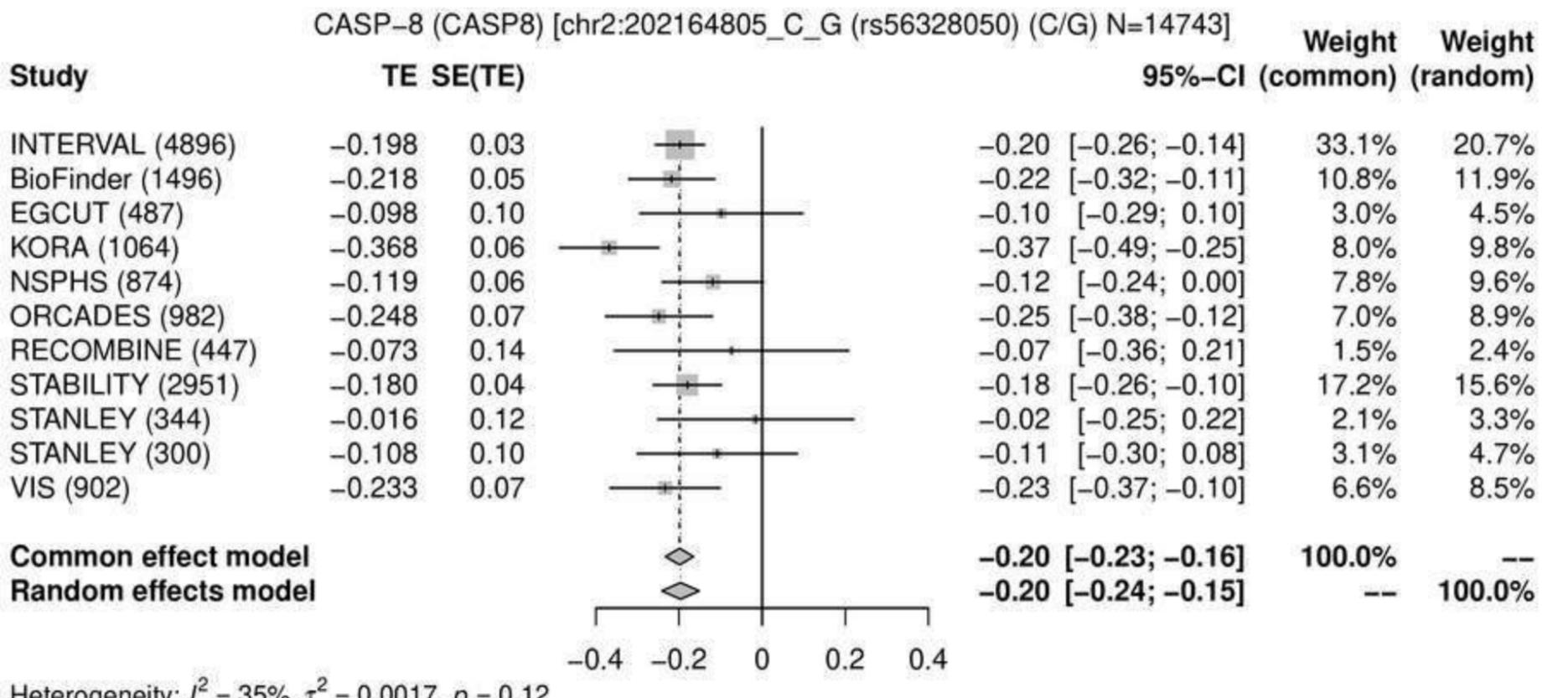


# Beta-NGF (NGF)-rs3128517

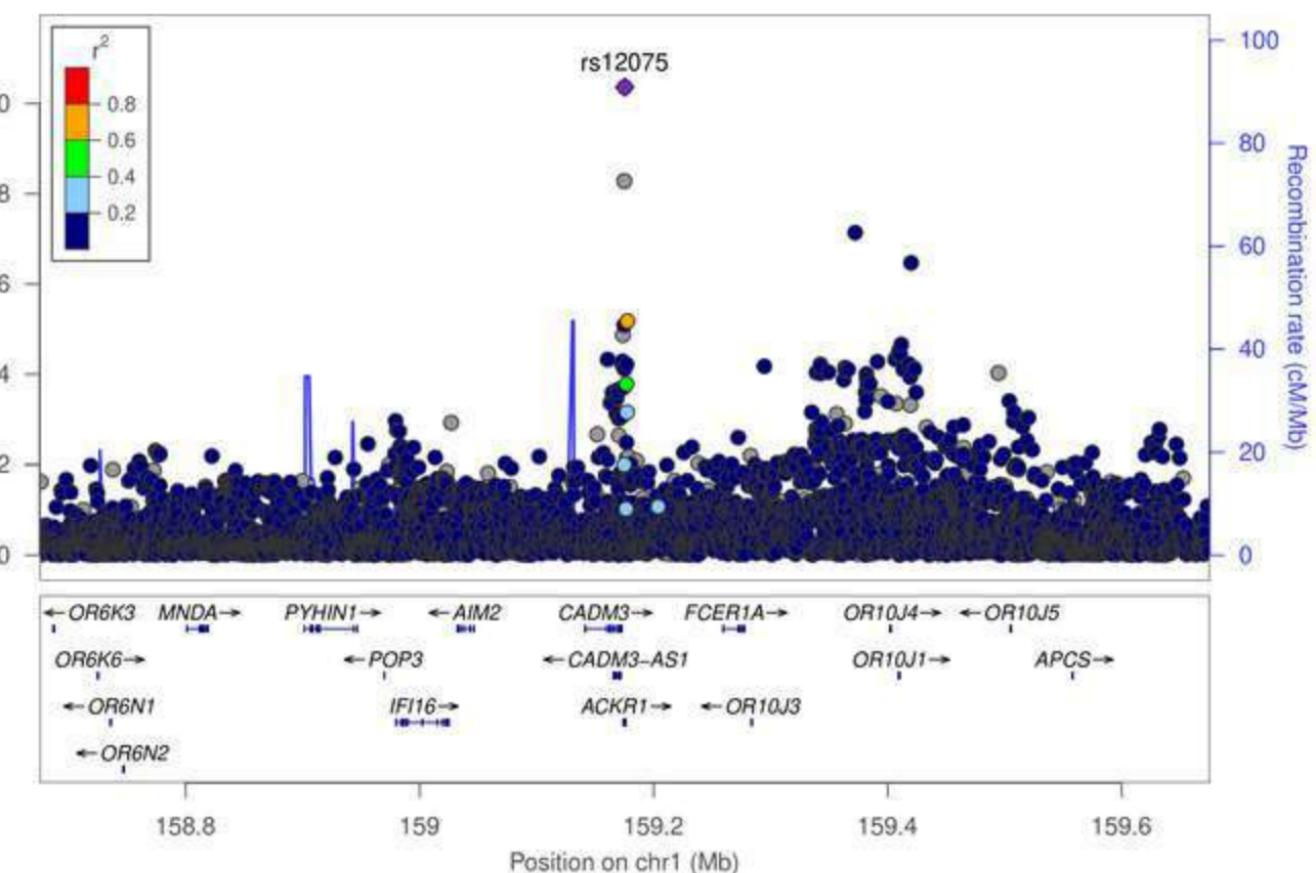
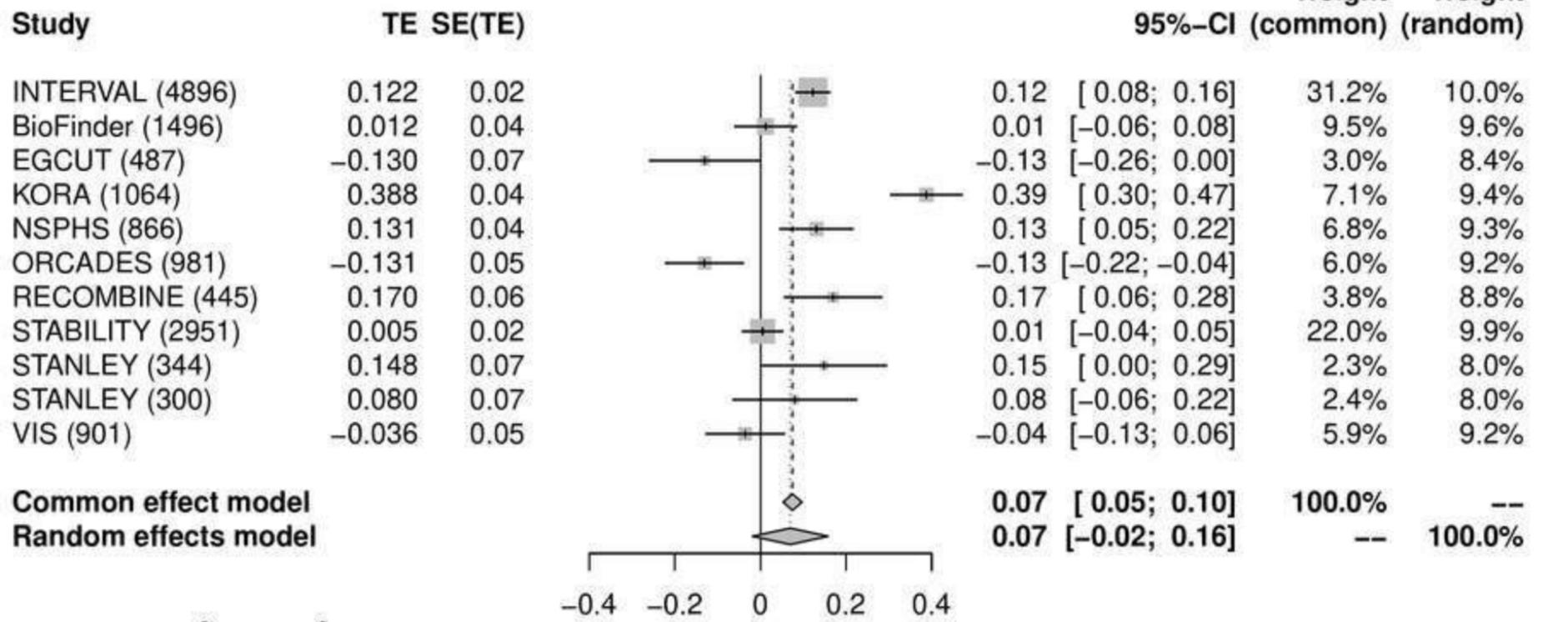
Beta-NGF (NGF) [chr9:90362040\_C\_T (rs3128517) (T/C) N=14295]



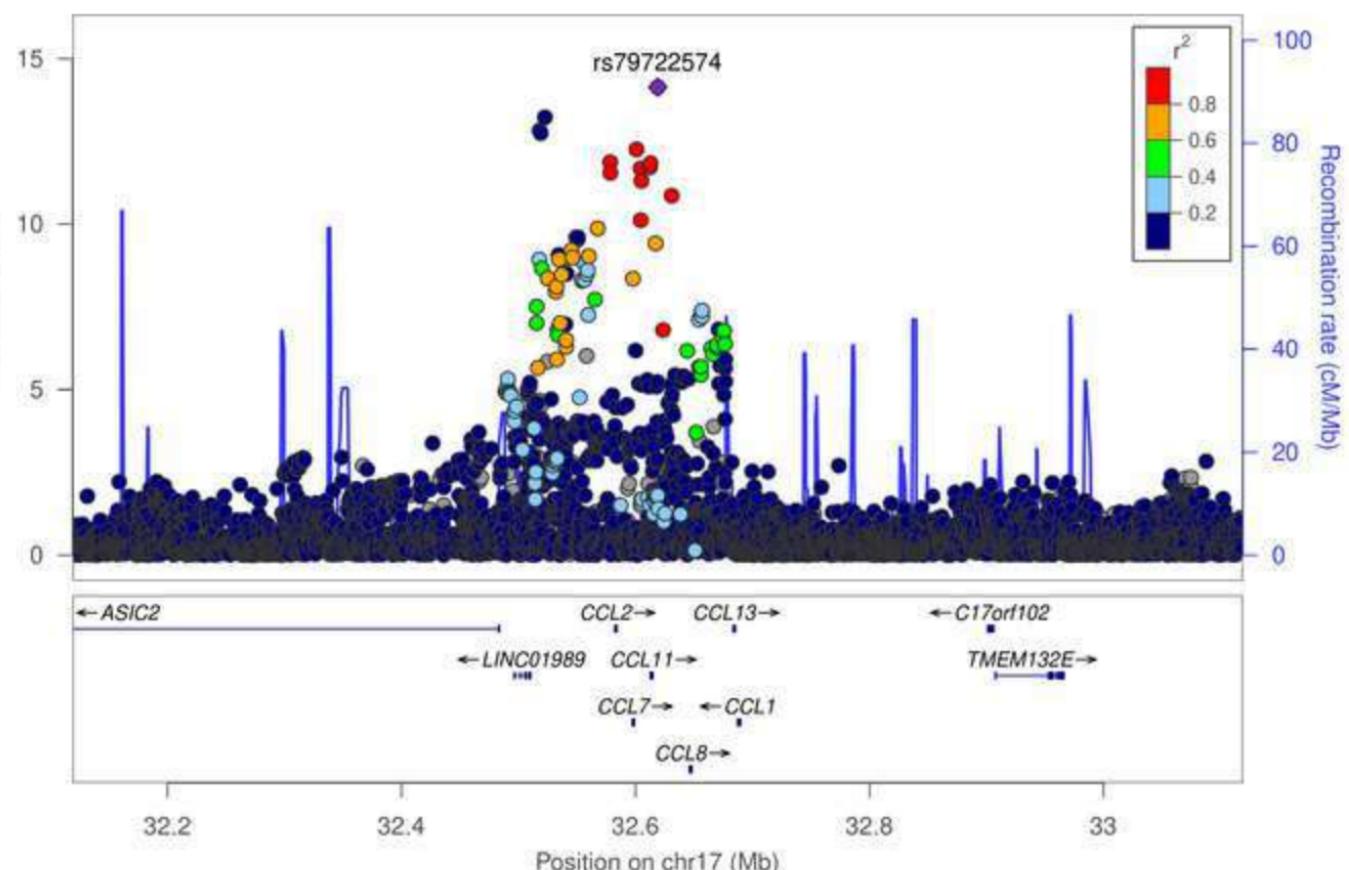
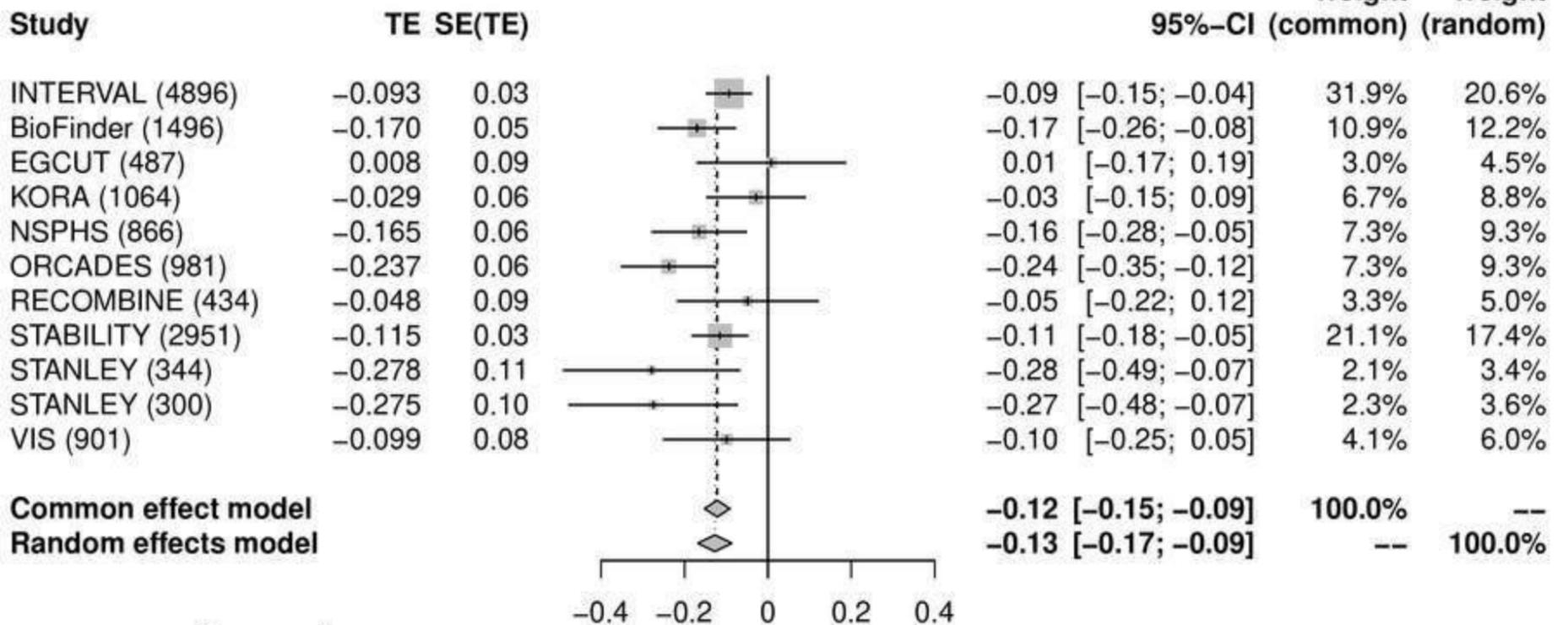
# CASP-8 (CASP8)-rs56328050



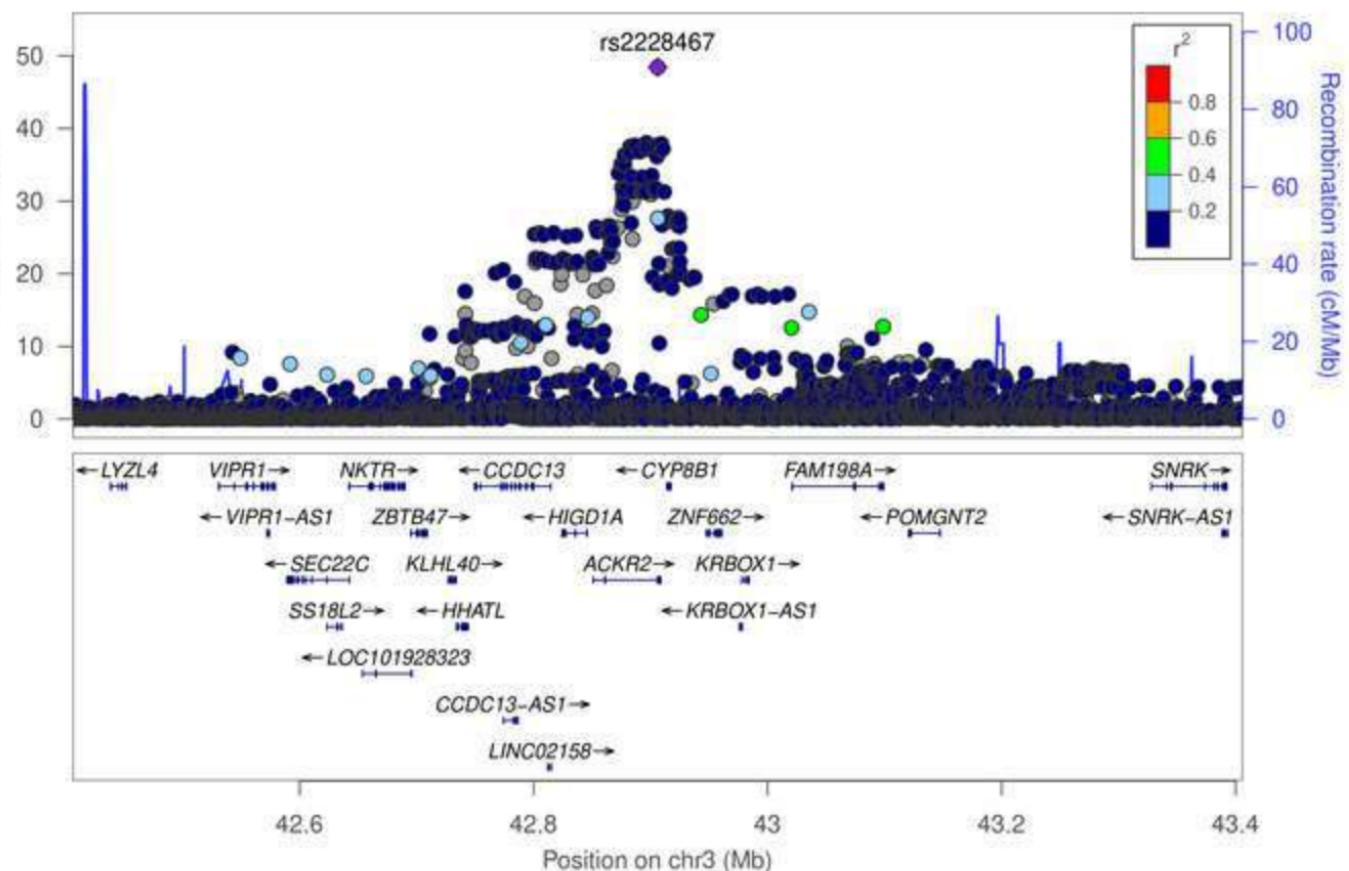
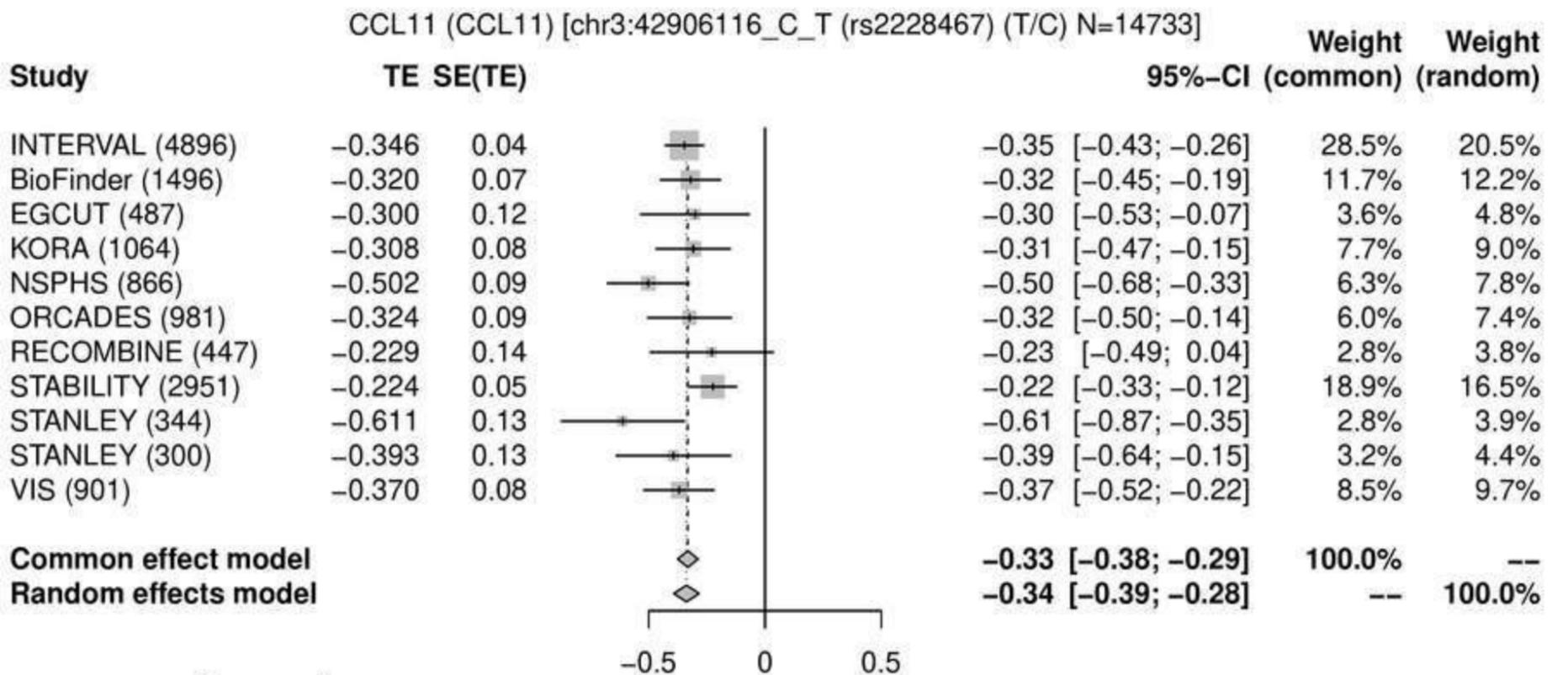
# CCL11 (CCL11)-rs12075



# CCL11 (CCL11)-rs79722574

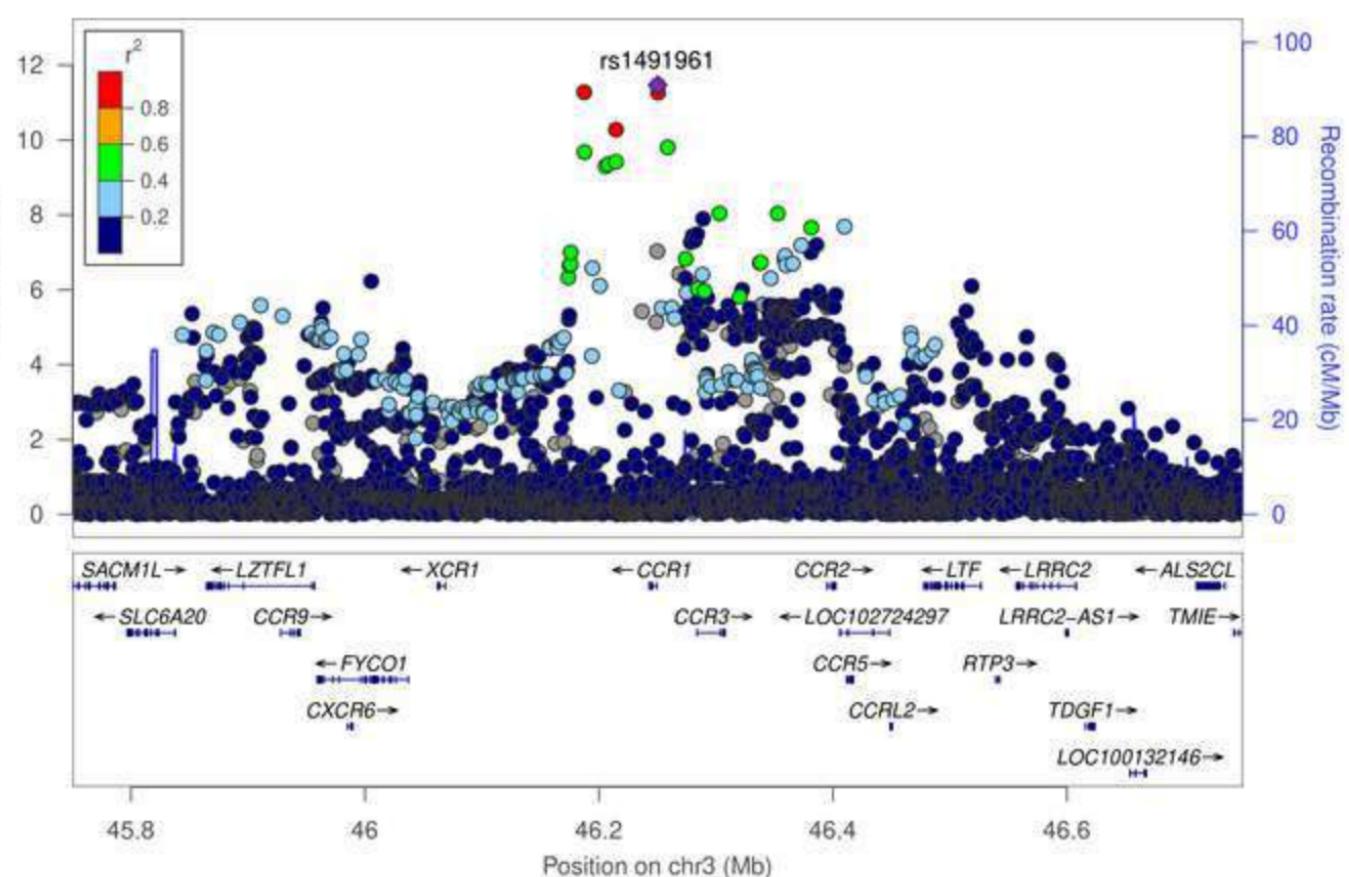
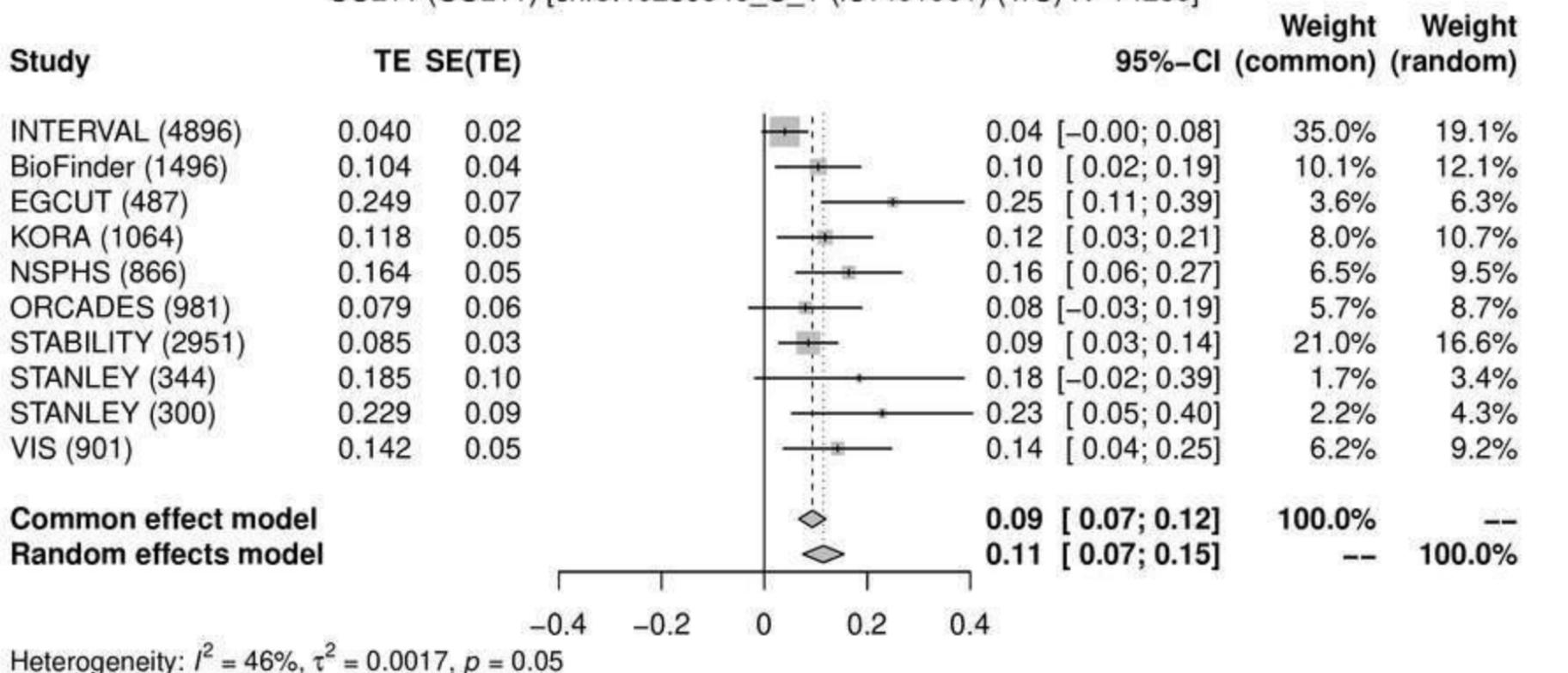


# CCL11 (CCL11)-rs2228467

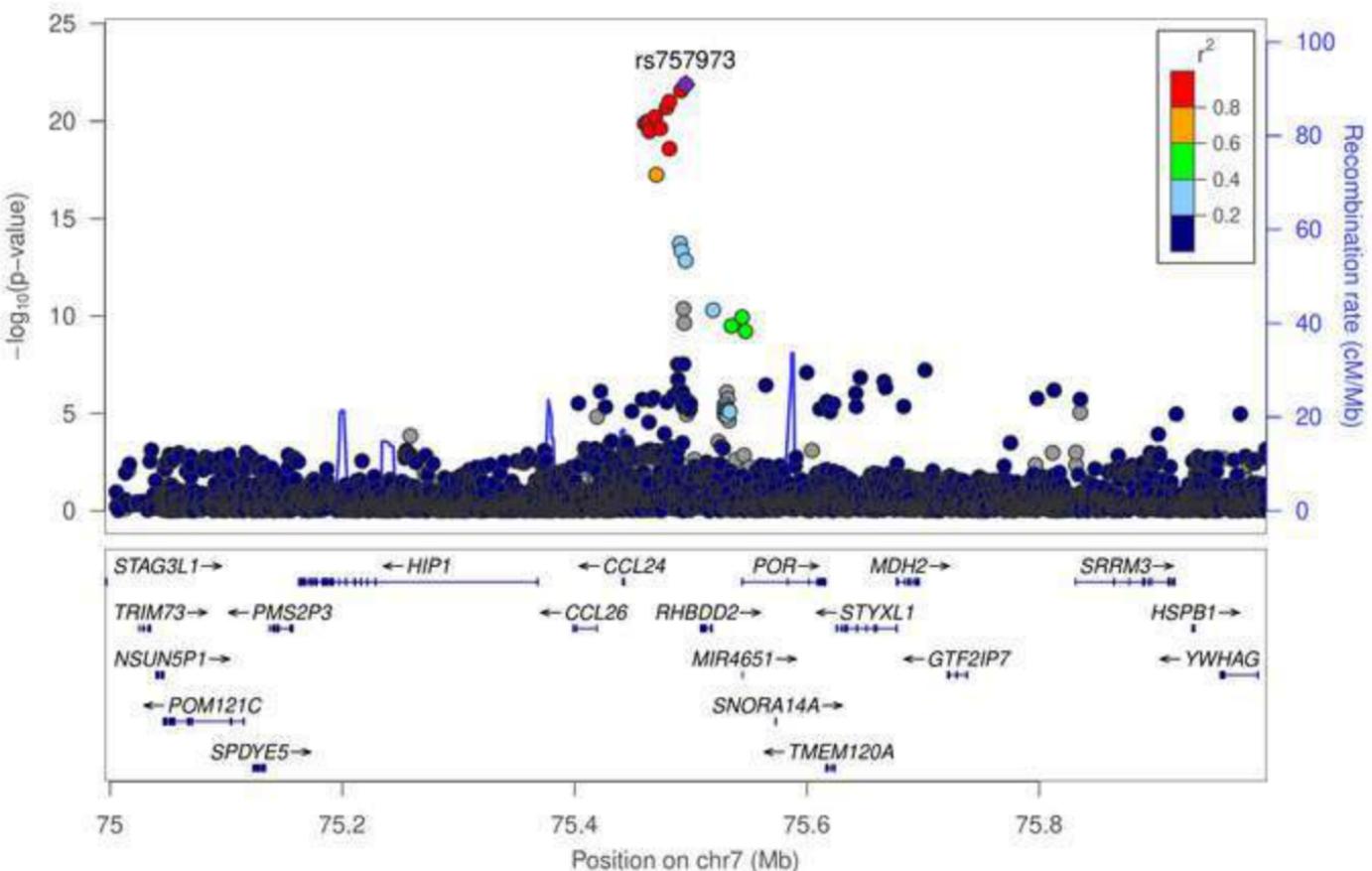
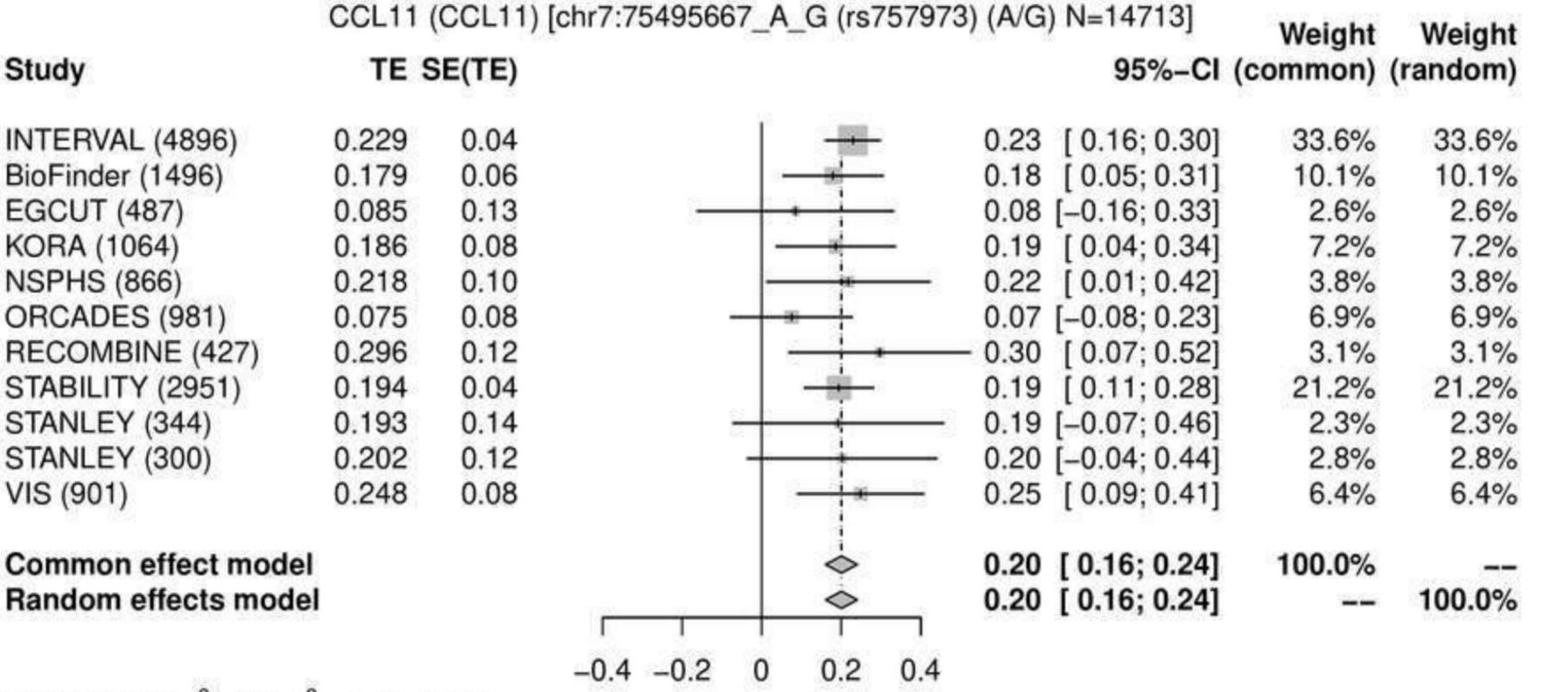


# CCL11 (CCL11)-rs1491961

CCL11 (CCL11) [chr3:46250348\_C\_T (rs1491961) (T/C) N=14286]



# CCL11 (CCL11)-rs757973



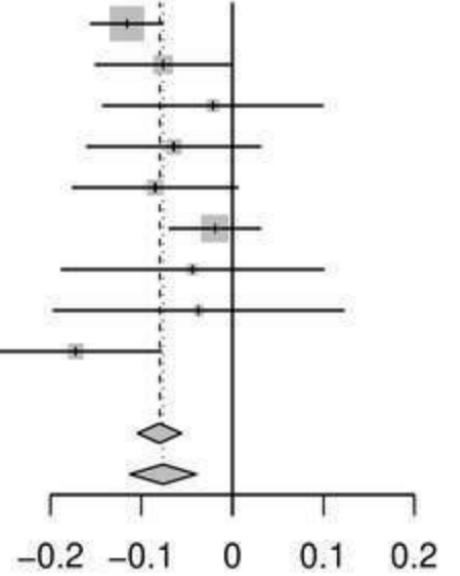
# CCL19 (CCL19)-rs13010492

CCL19 (CCL19) [chr2:204776176\_C\_G (rs13010492) (C/G) N=13422]

## Study

INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
ORCADES (982)  
STABILITY (2951)  
STANLEY (344)  
STANLEY (300)  
VIS (902)

**TE SE(TE)**



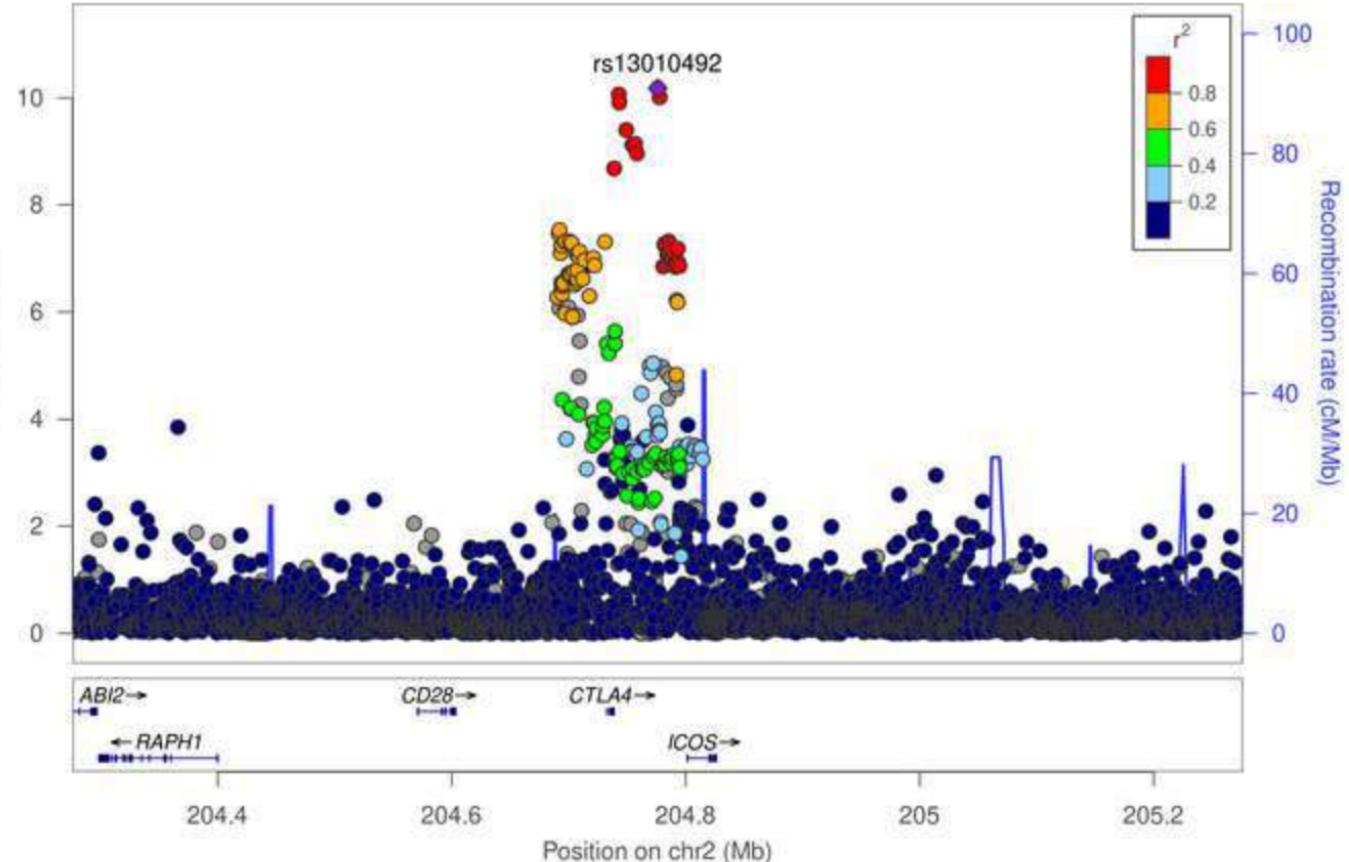
**Weight  
95%-CI (common) (random)**

	Weight 95%-CI (common) (random)
-0.12 [-0.16; -0.08]	37.3% 21.5%
-0.08 [-0.15; -0.00]	10.6% 13.2%
-0.02 [-0.14; 0.10]	4.0% 6.9%
-0.06 [-0.16; 0.03]	6.4% 9.7%
-0.08 [-0.18; 0.01]	7.0% 10.4%
-0.02 [-0.07; 0.03]	23.1% 18.7%
-0.04 [-0.19; 0.10]	2.8% 5.3%
-0.04 [-0.20; 0.12]	2.3% 4.4%
-0.17 [-0.27; -0.08]	6.6% 9.9%

100.0%  
--  
100.0%

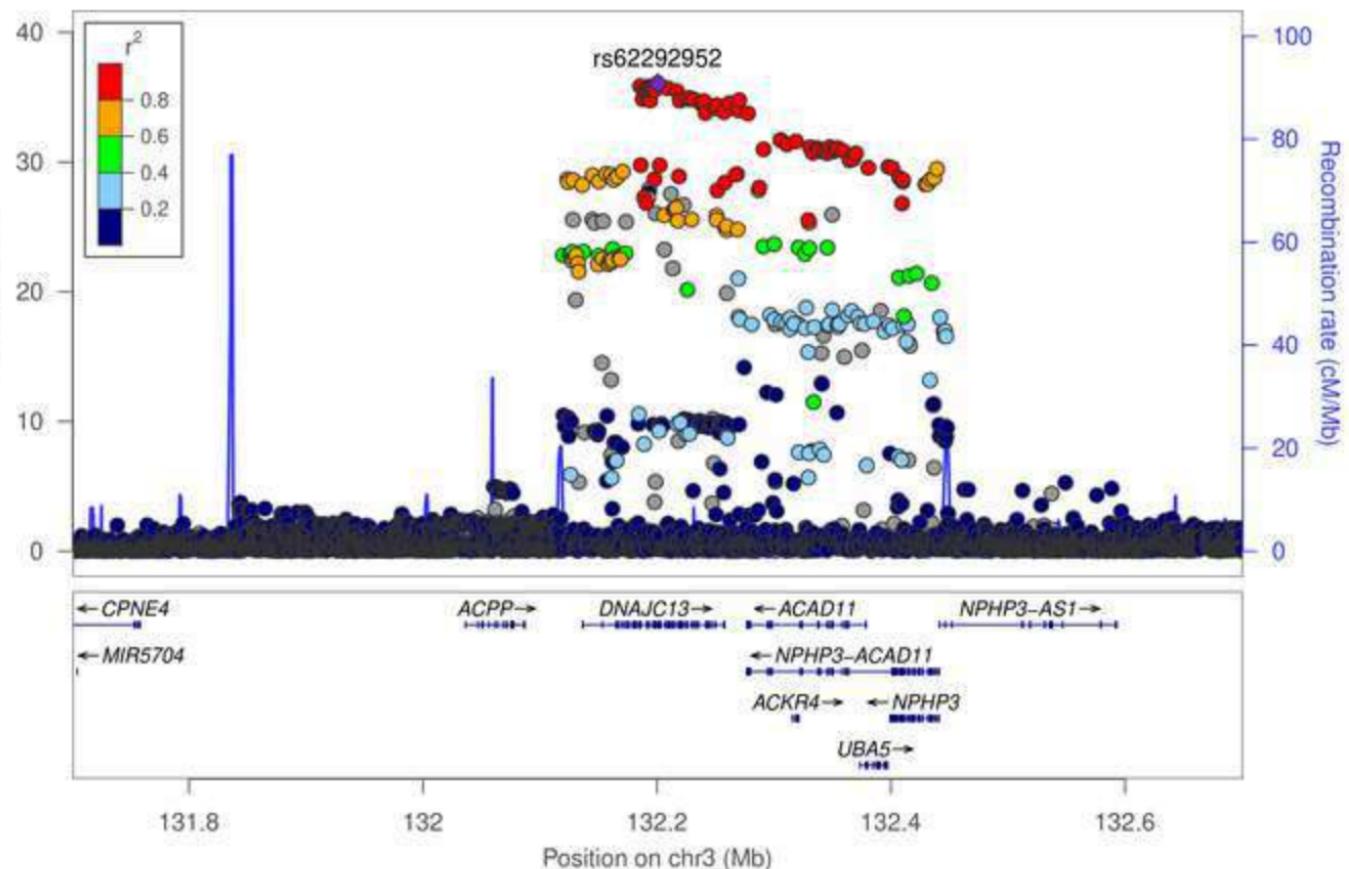
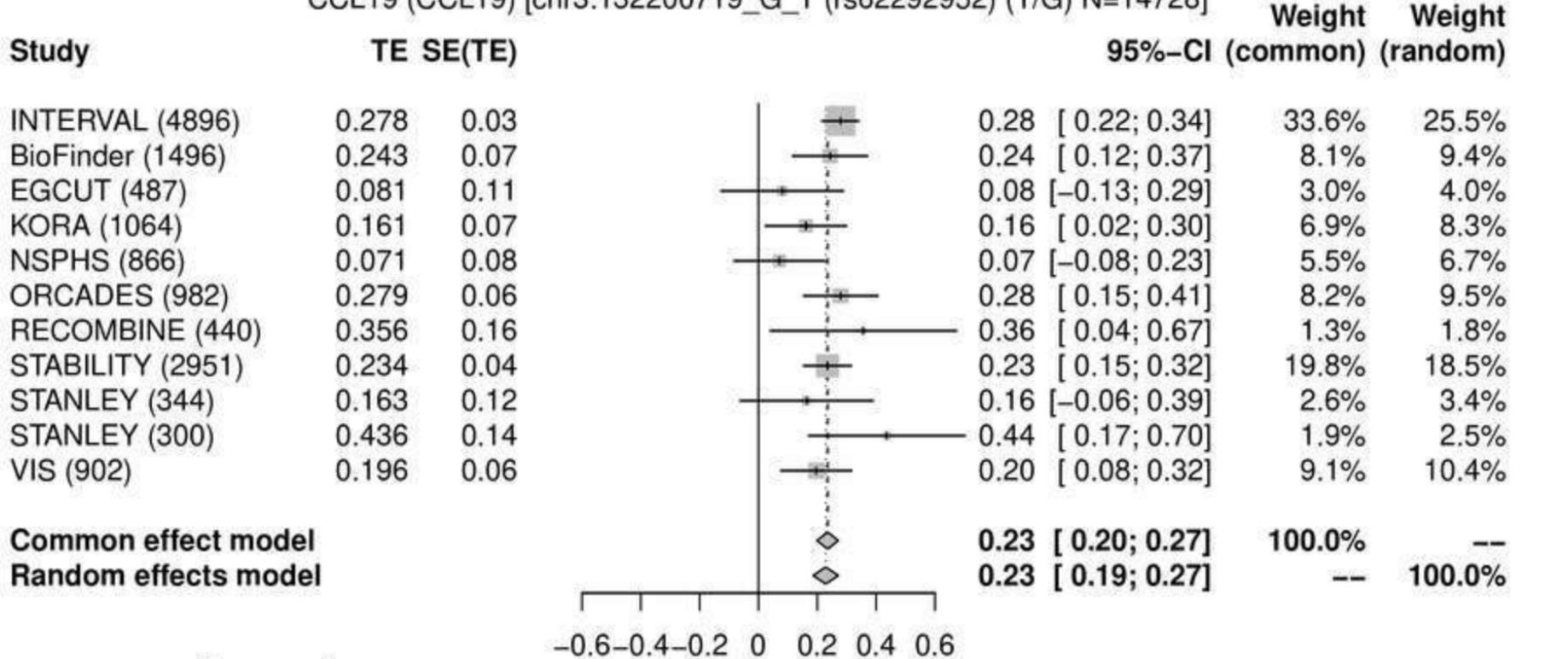
**Common effect model**  
**Random effects model**

Heterogeneity:  $I^2 = 43\%, \tau^2 = 0.0012, p = 0.08$

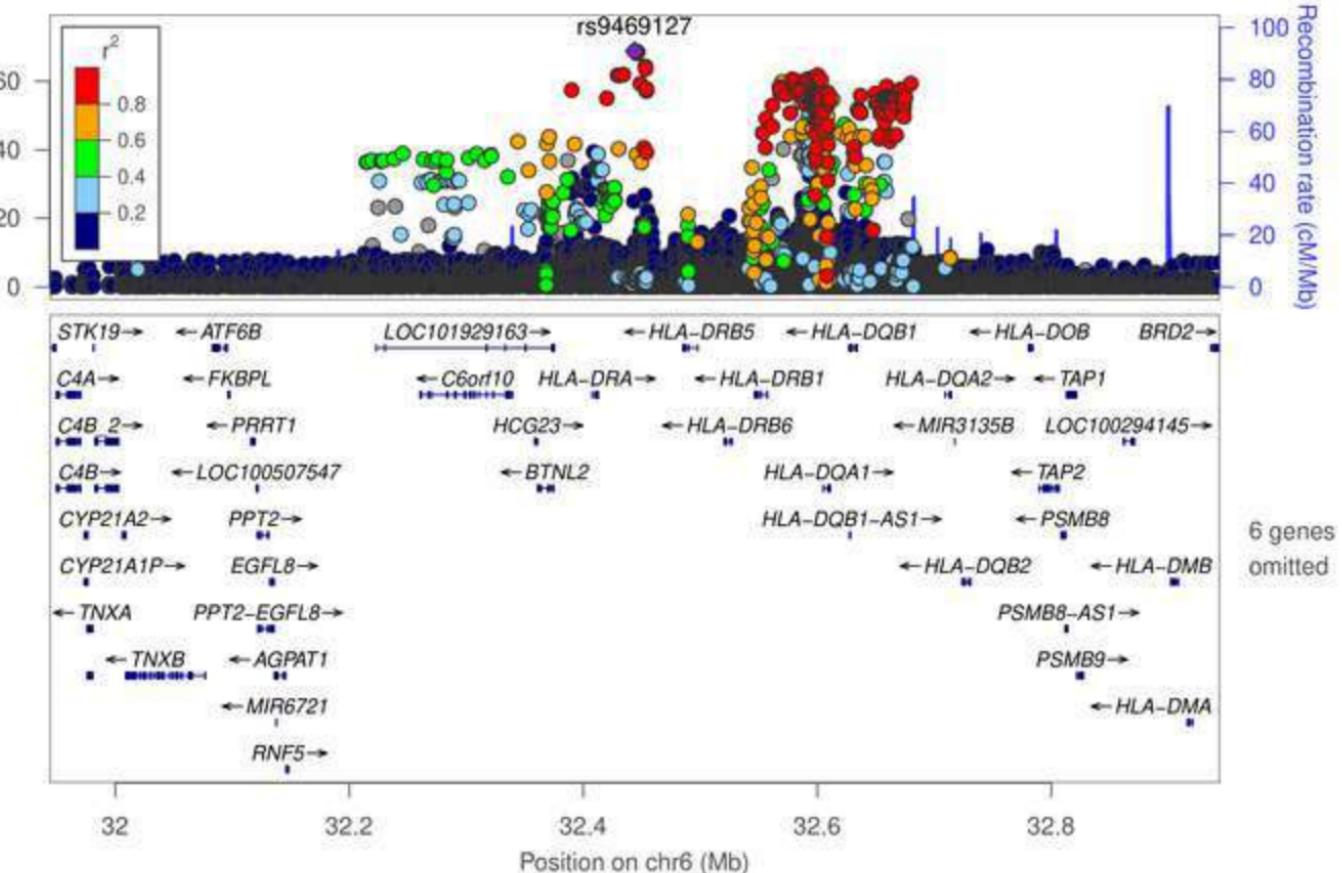
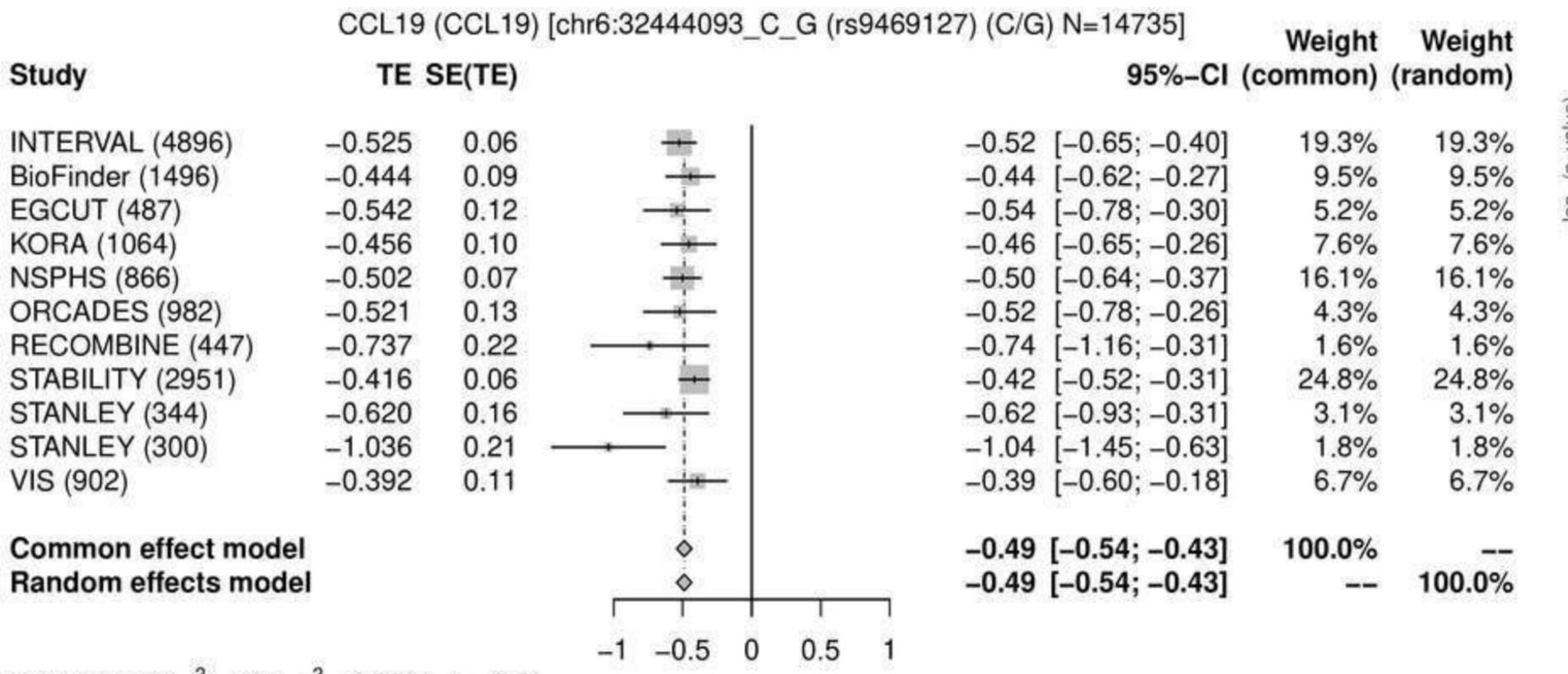


# CCL19 (CCL19)-rs62292952

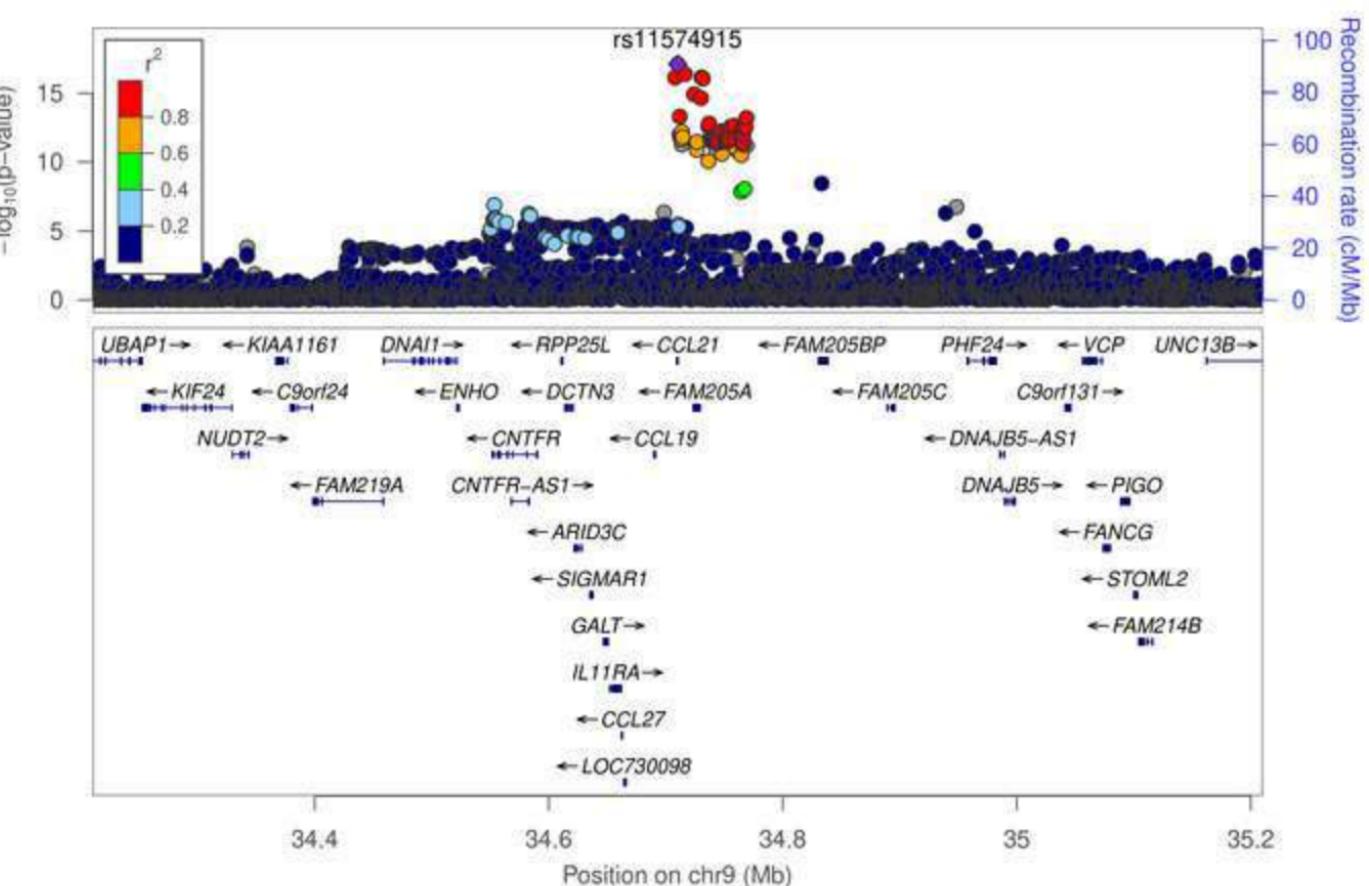
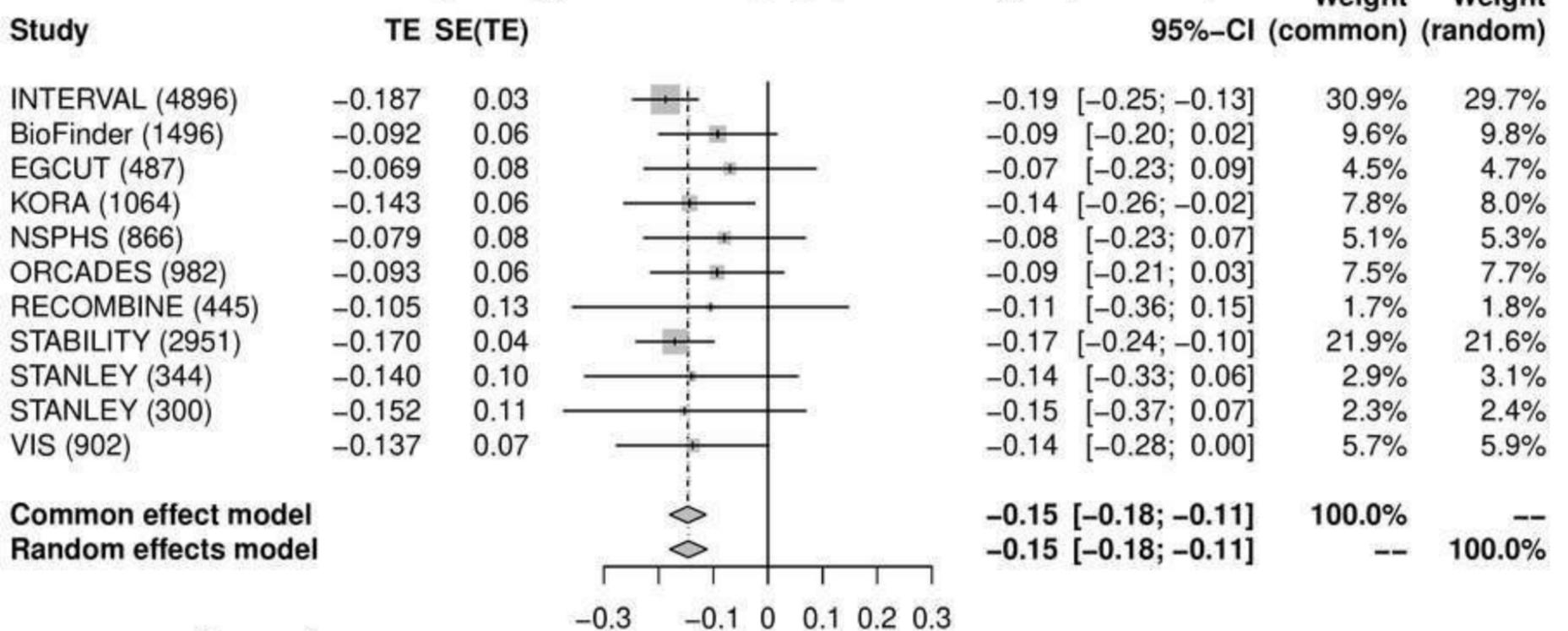
CCL19 (CCL19) [chr3:132200719\_G\_T (rs62292952) (T/G) N=14728]



# CCL19 (CCL19)-rs9469127

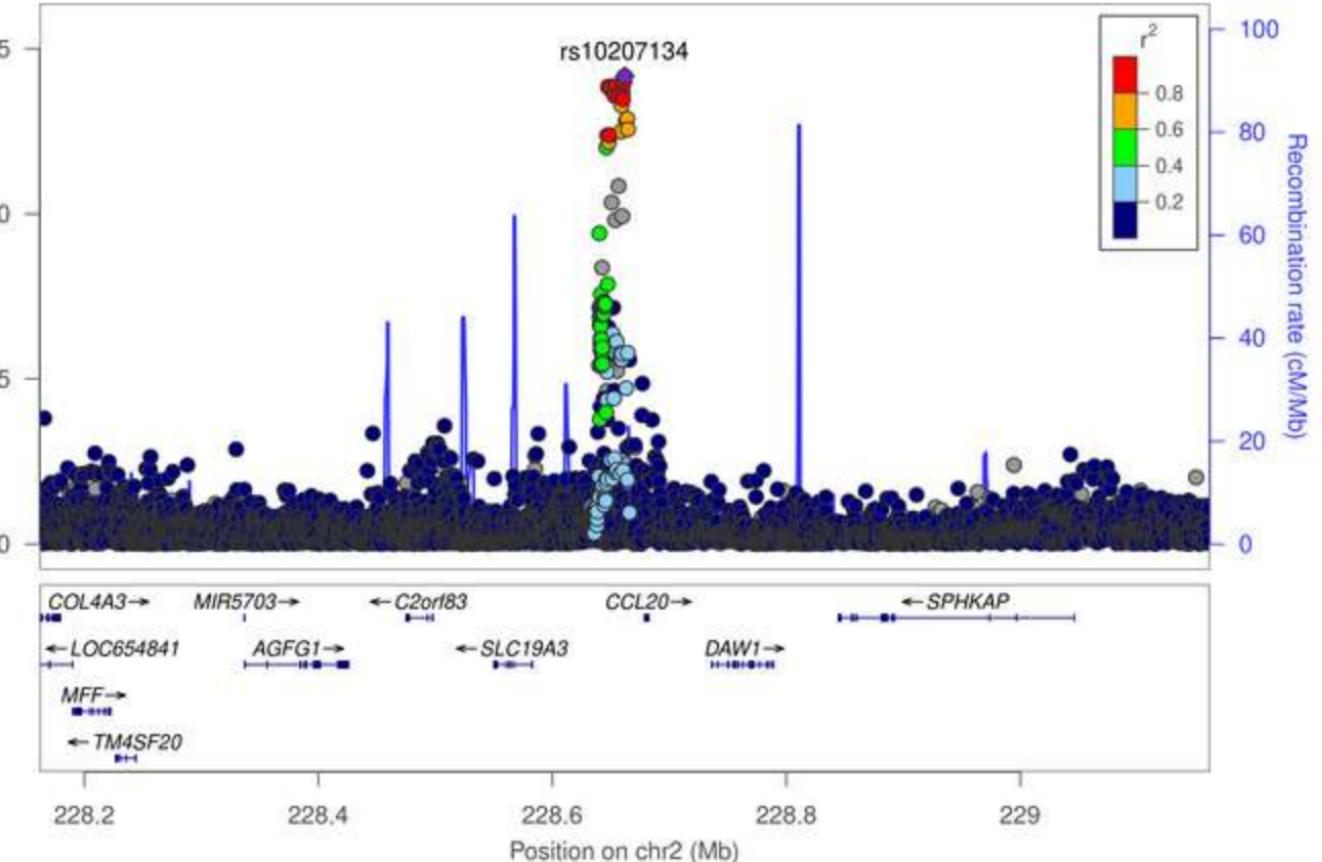
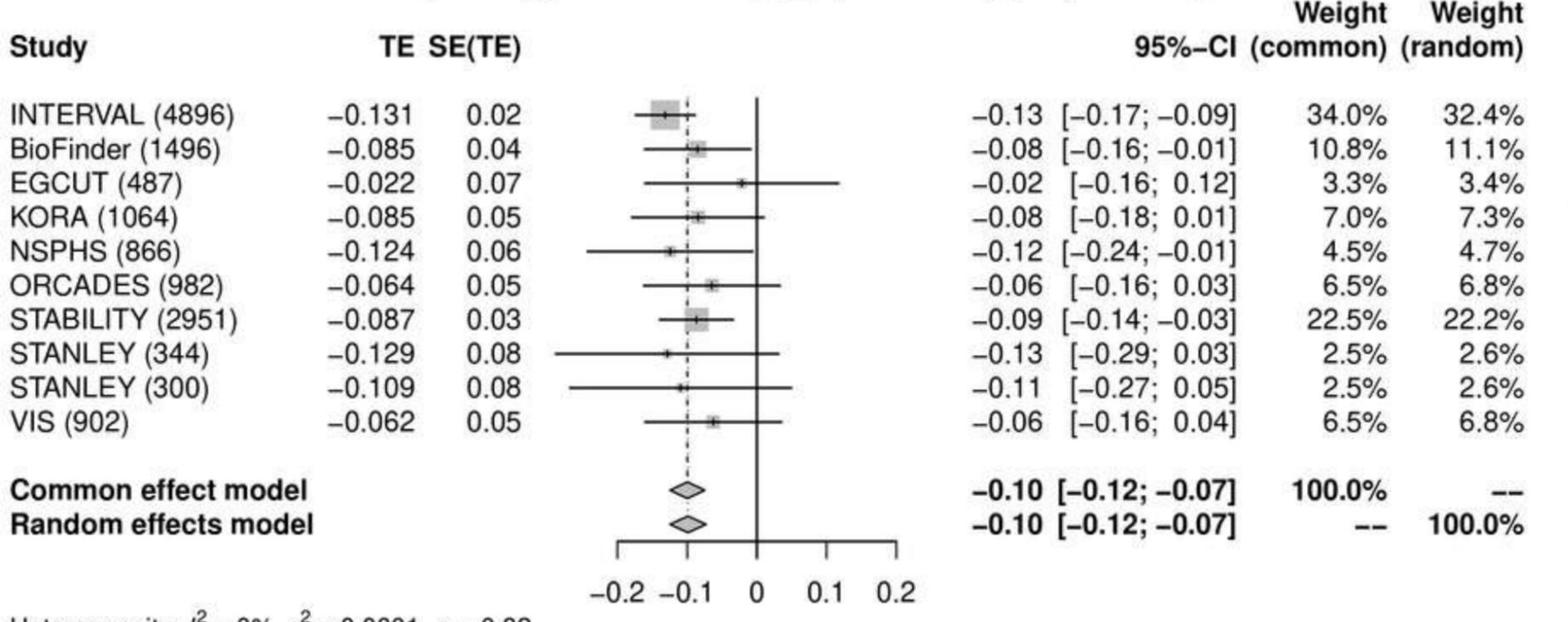


# CCL19 (CCL19)-rs11574915

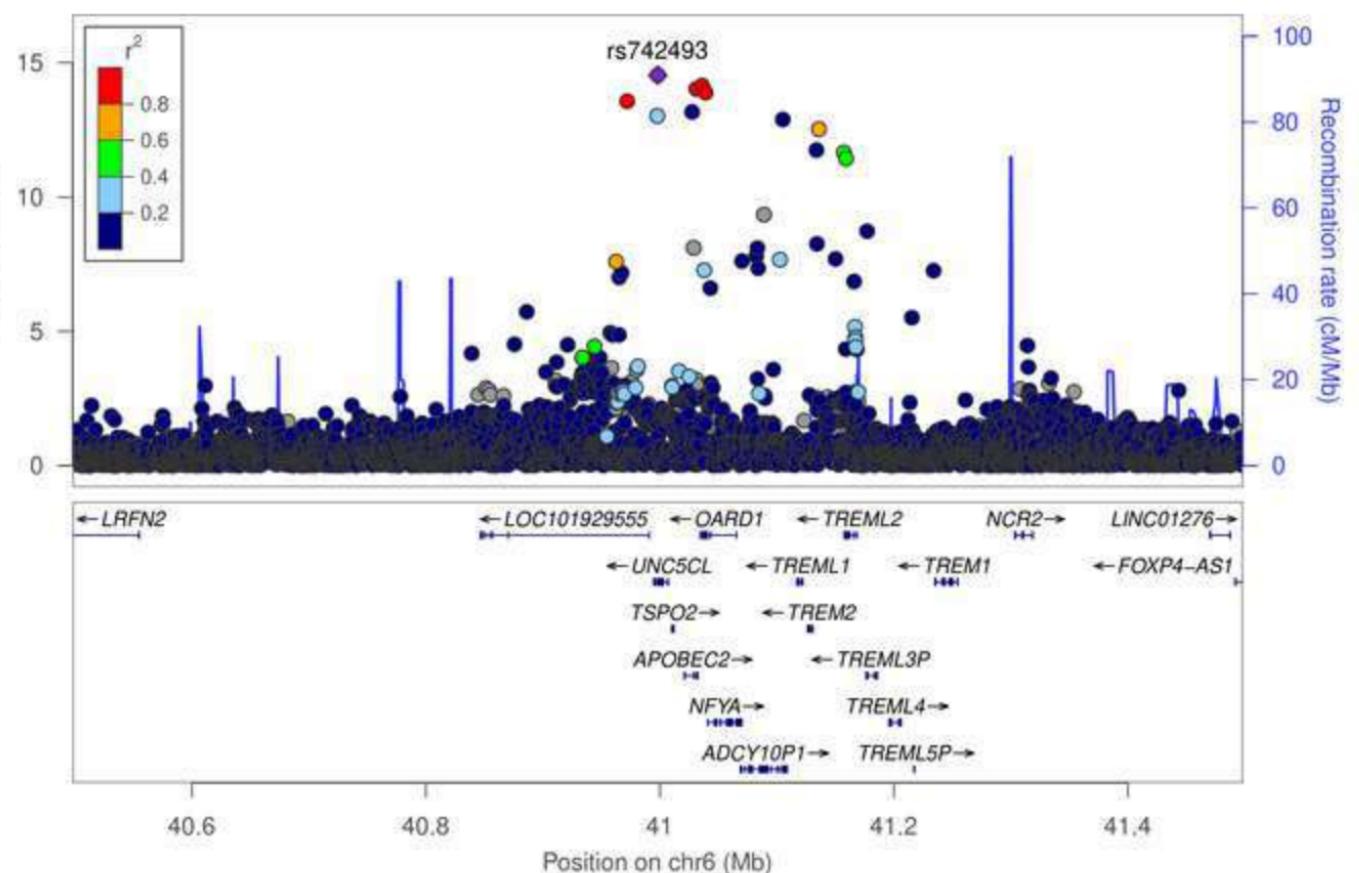
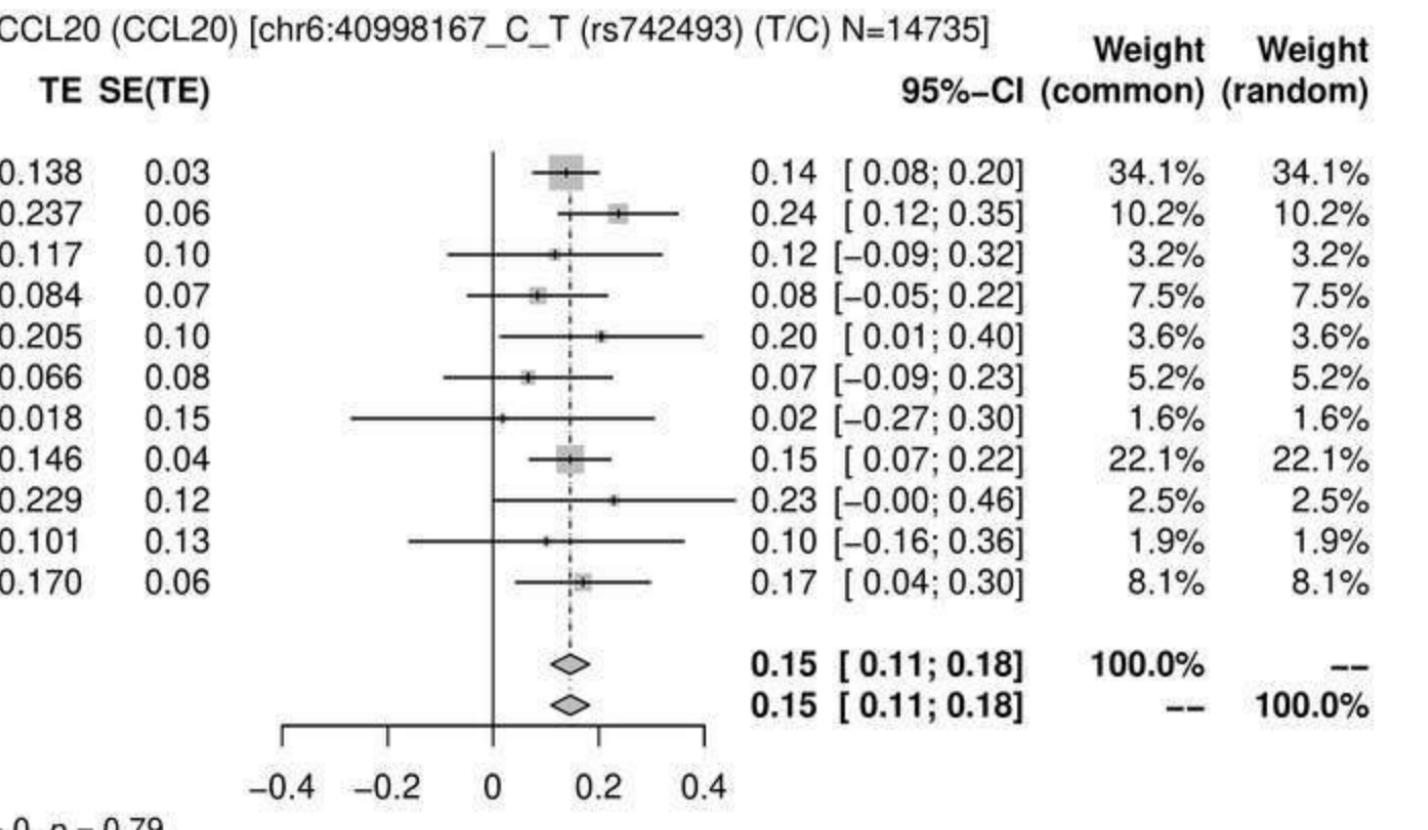


# CCL20 (CCL20)-rs10207134

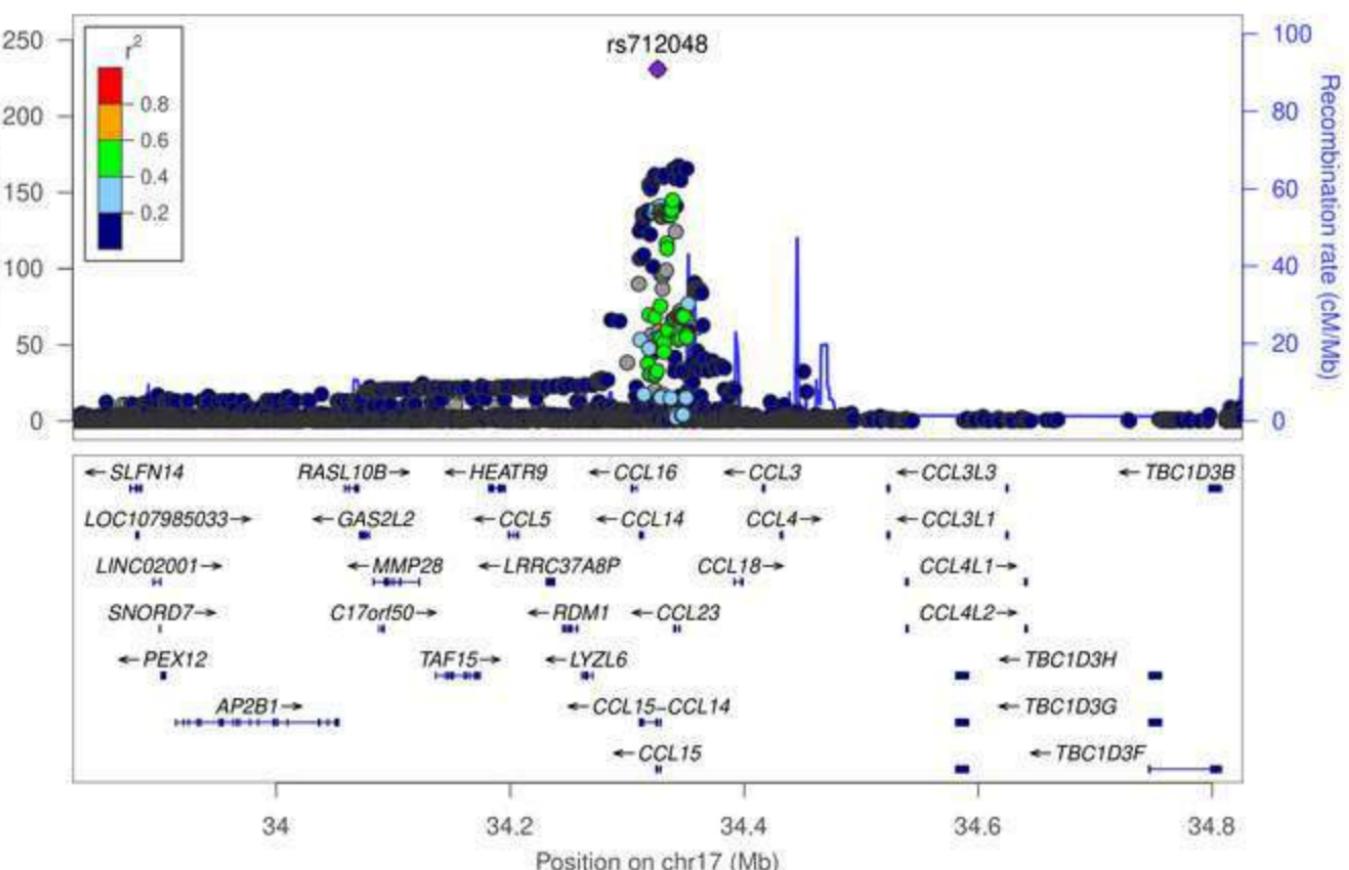
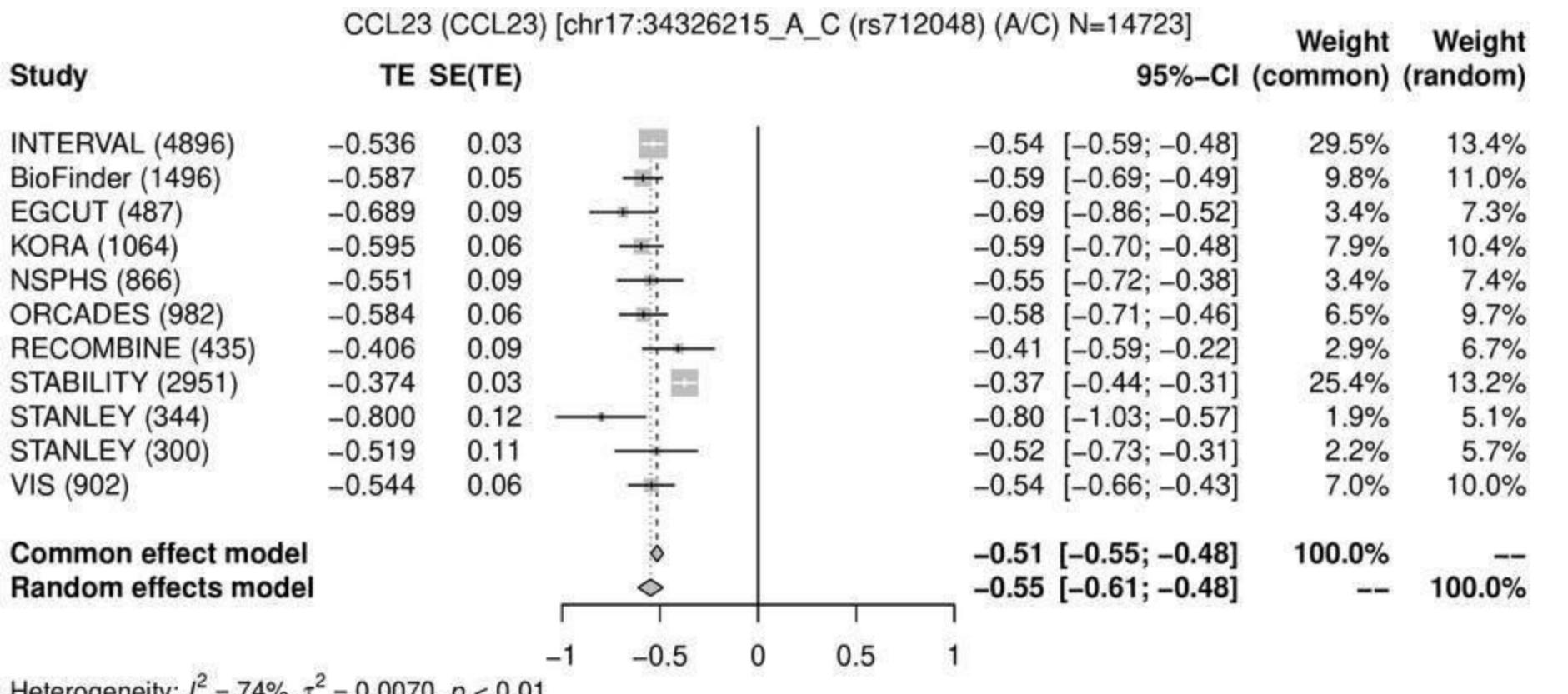
CCL20 (CCL20) [chr2:228661828\_C\_T (rs10207134) (T/C) N=14288]



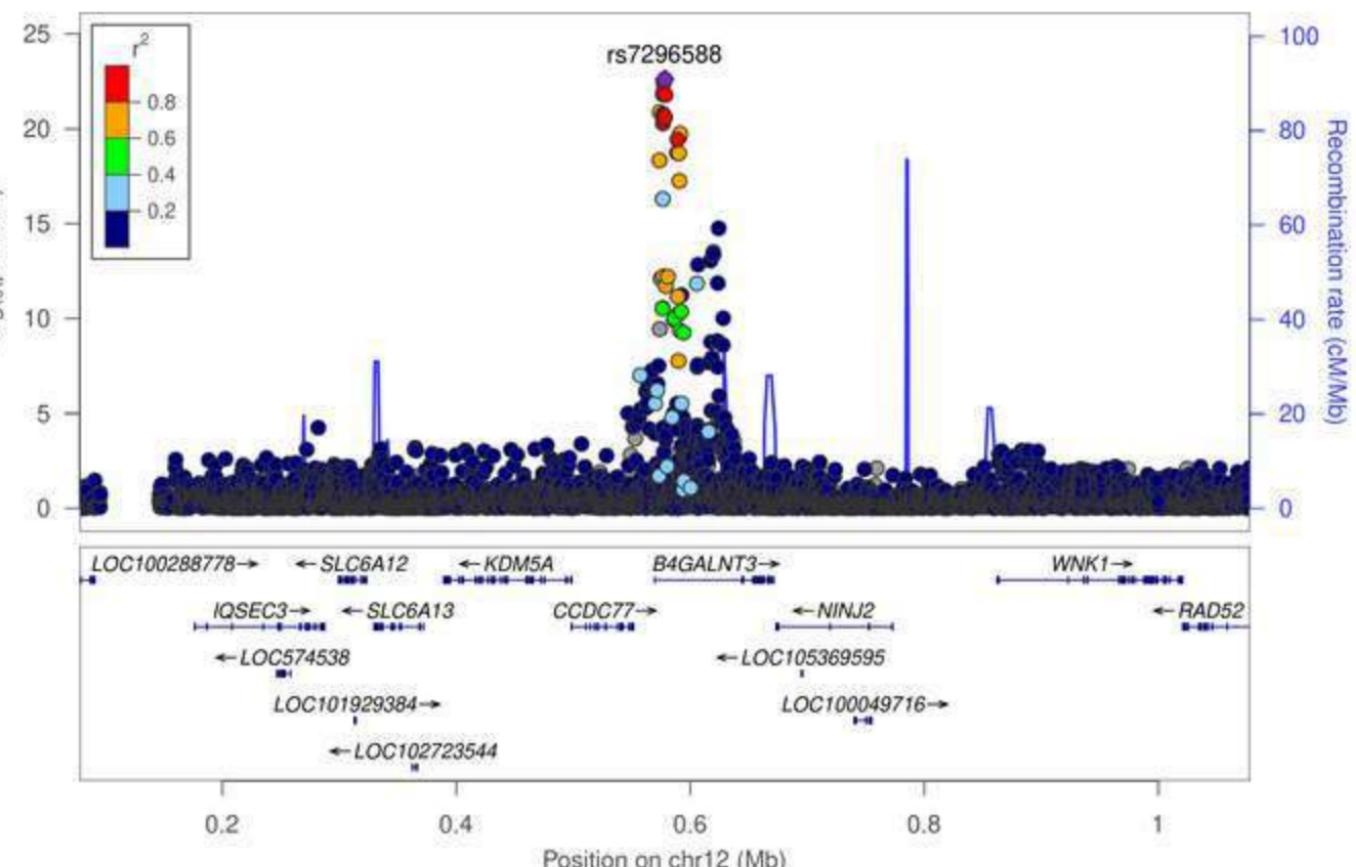
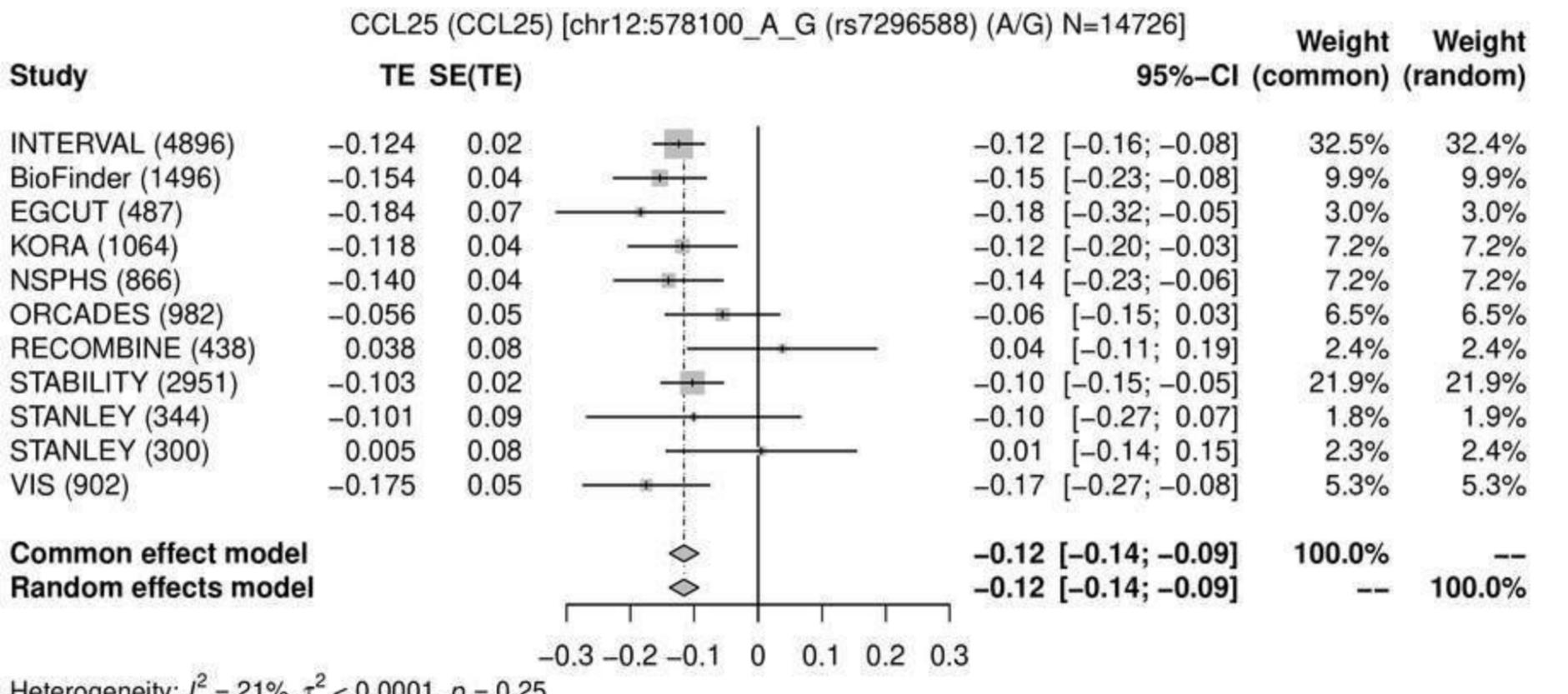
# CCL20 (CCL20)-rs742493



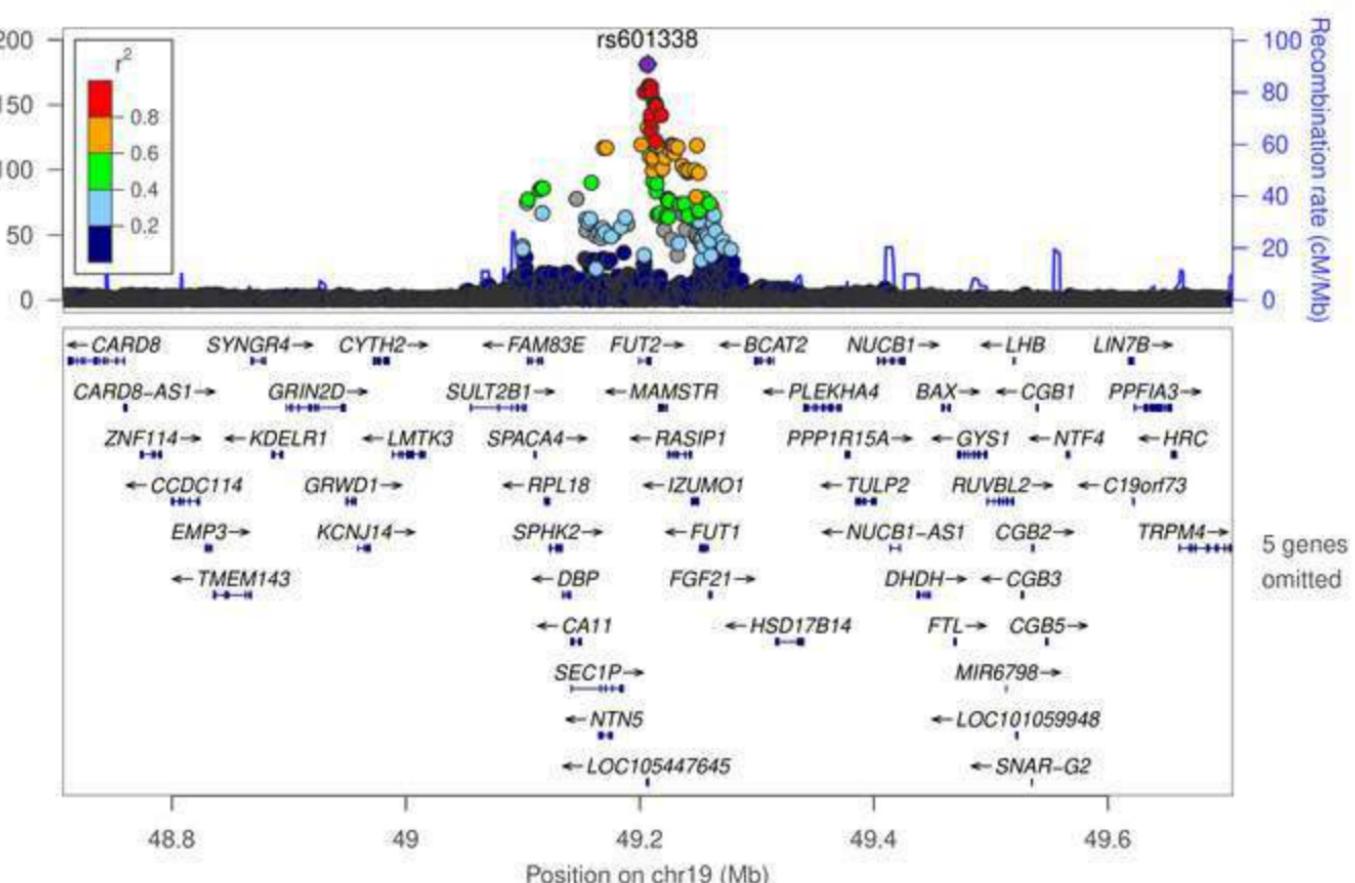
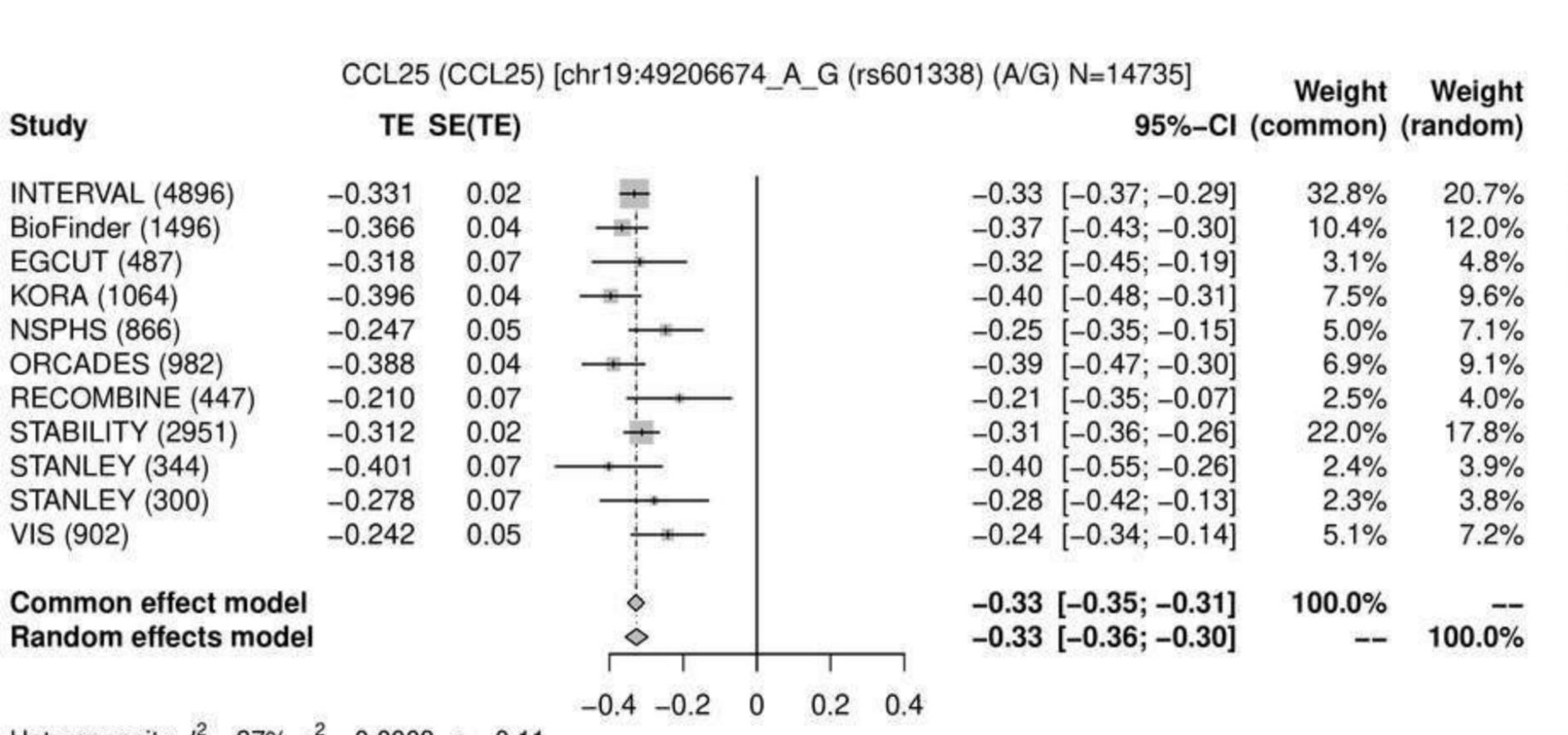
# CCL23 (CCL23)-rs712048



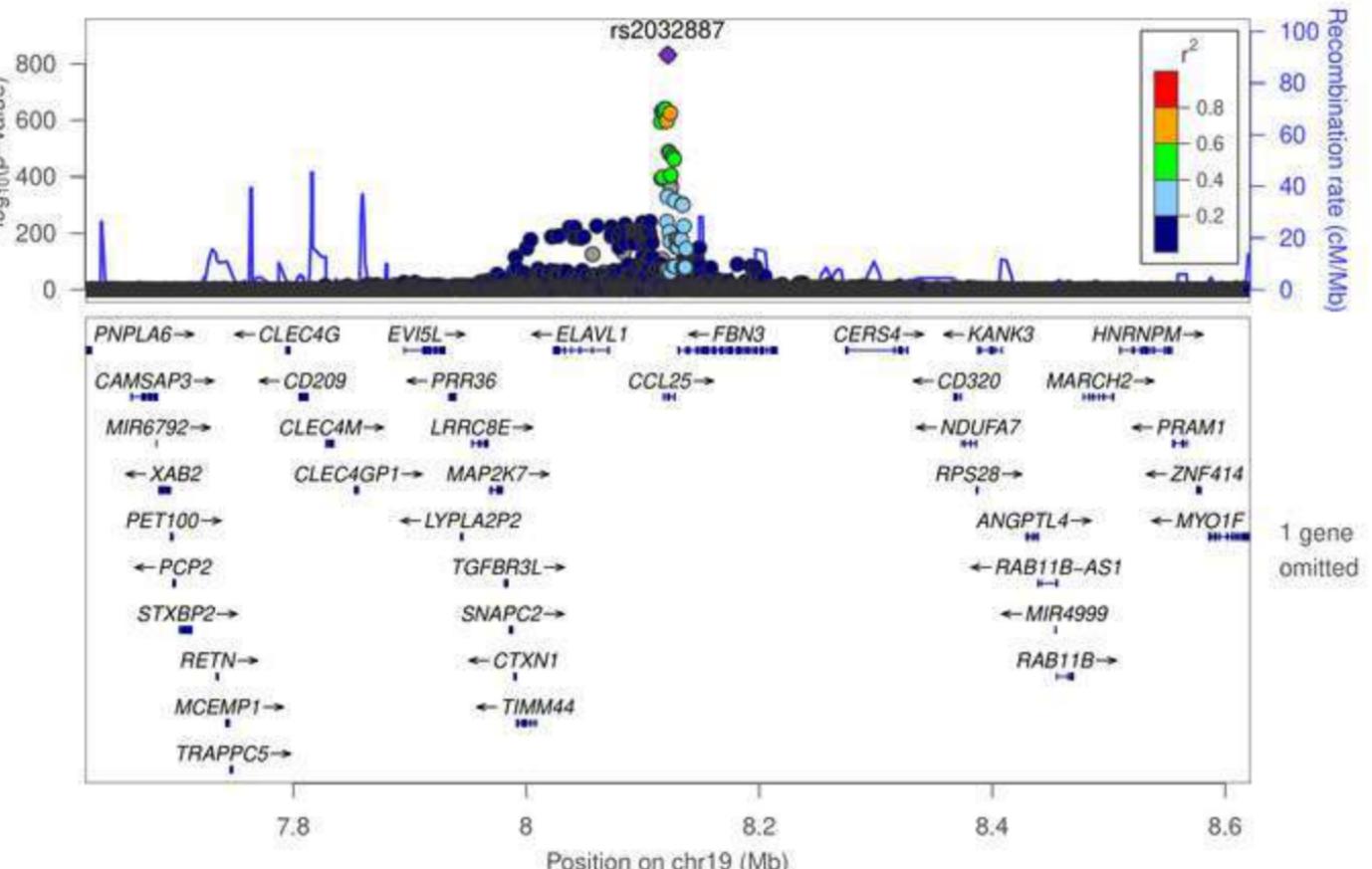
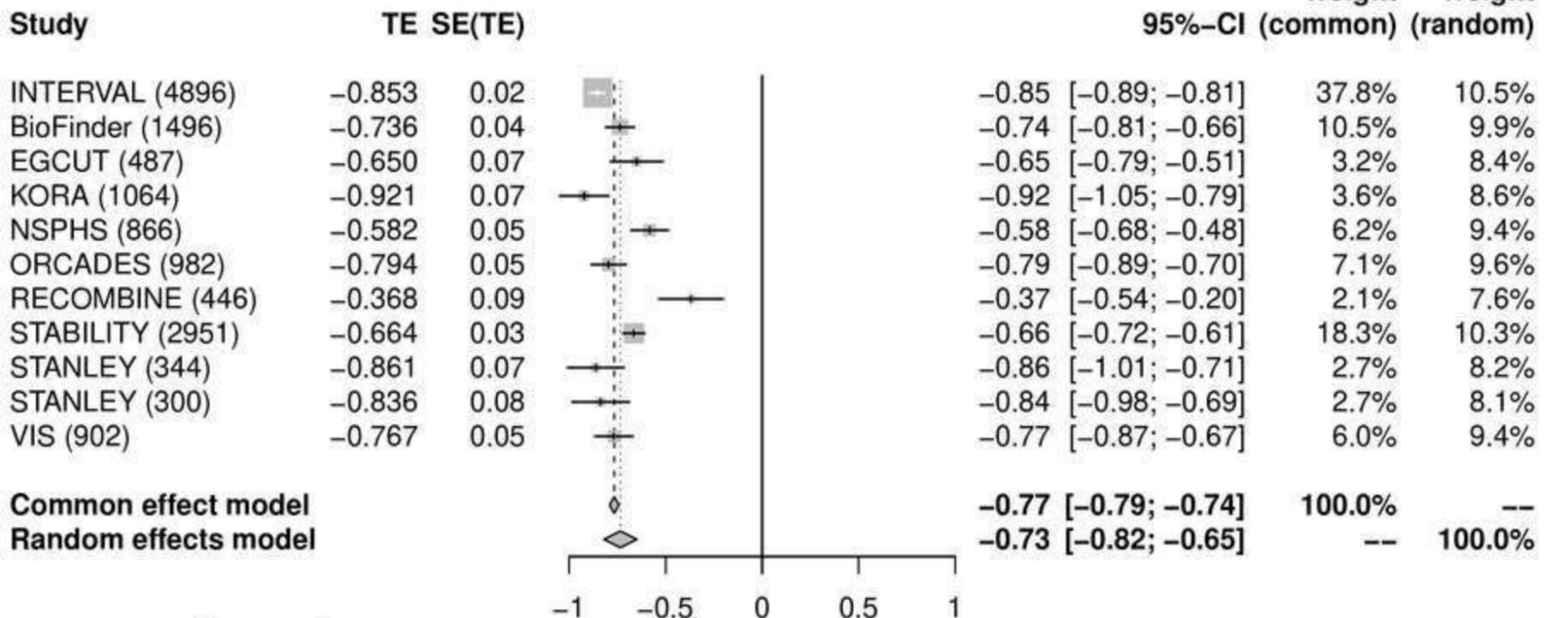
# CCL25 (CCL25)-rs7296588



# CCL25 (CCL25)-rs601338

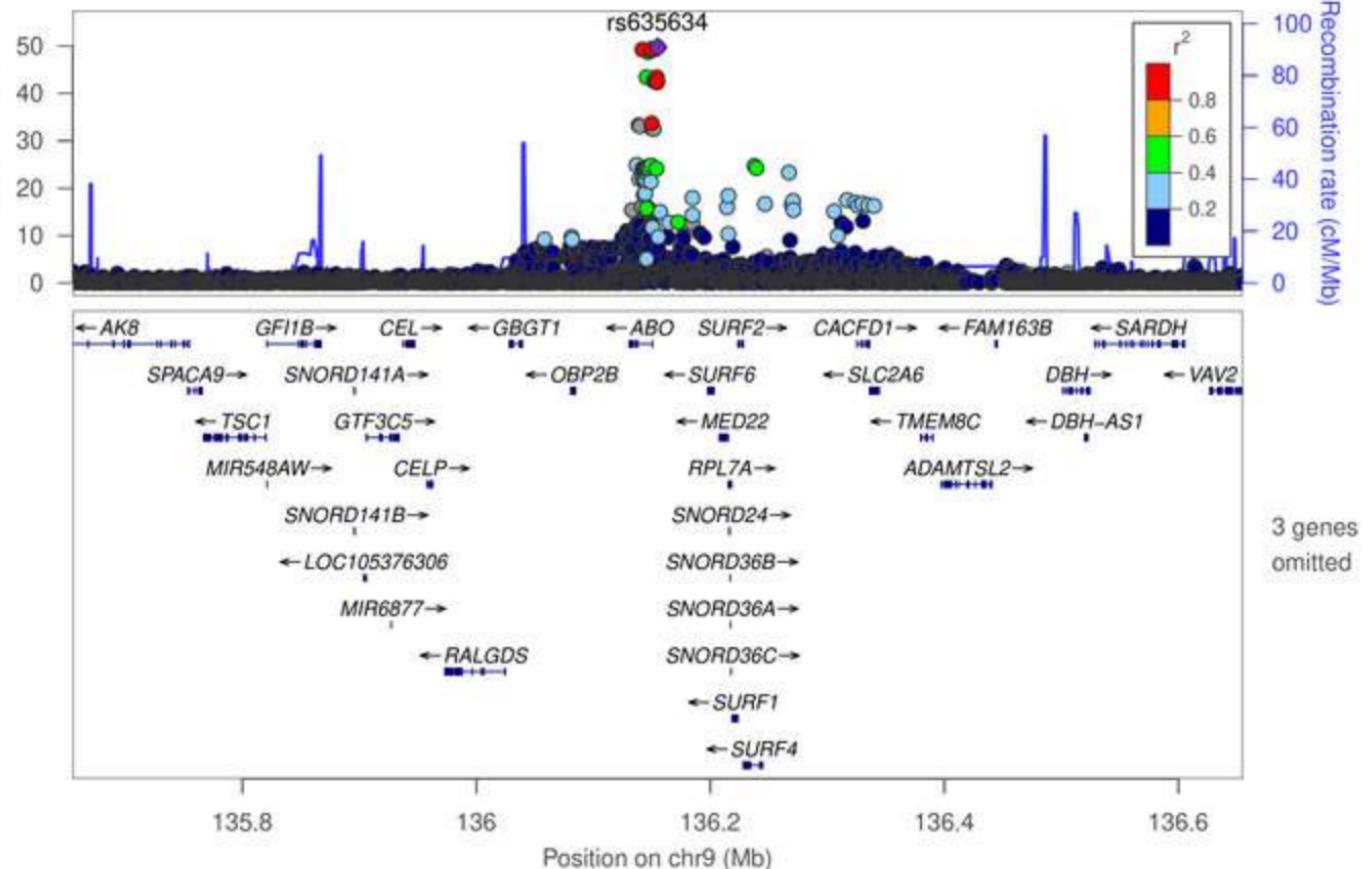
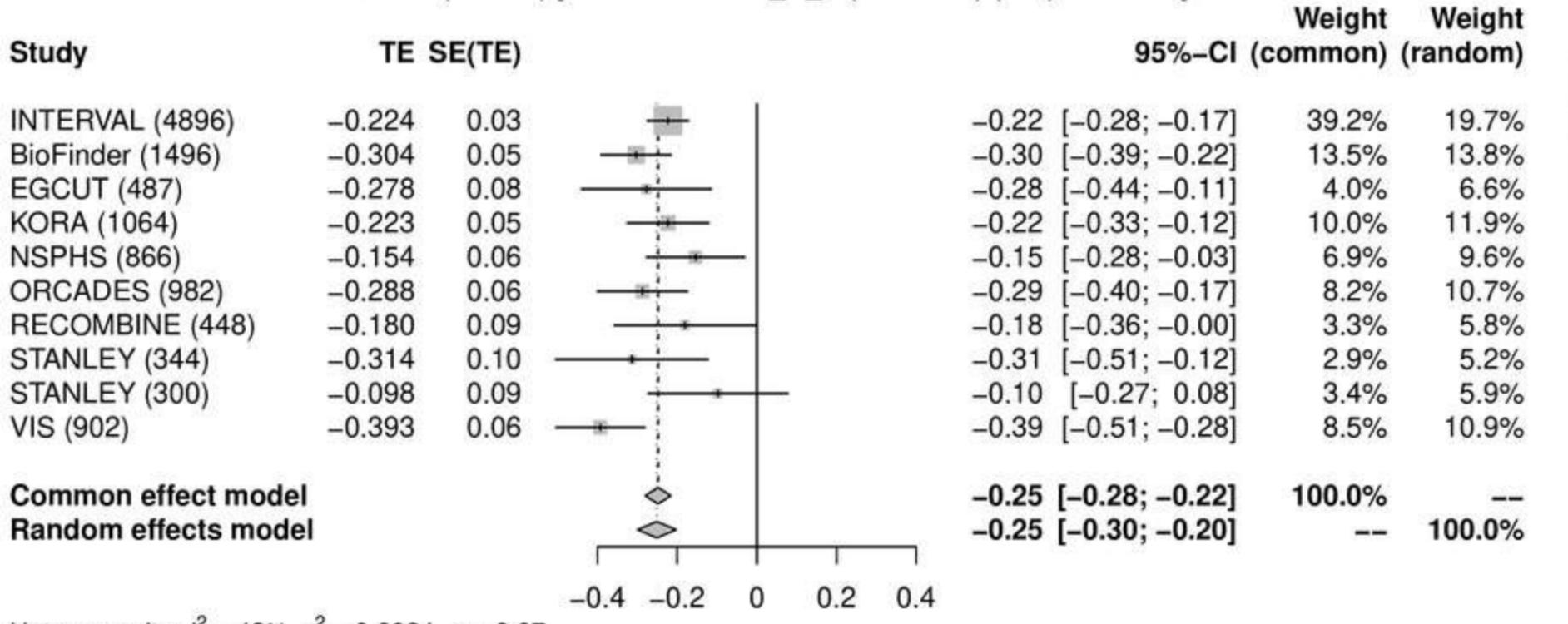


# CCL25 (CCL25)-rs2032887



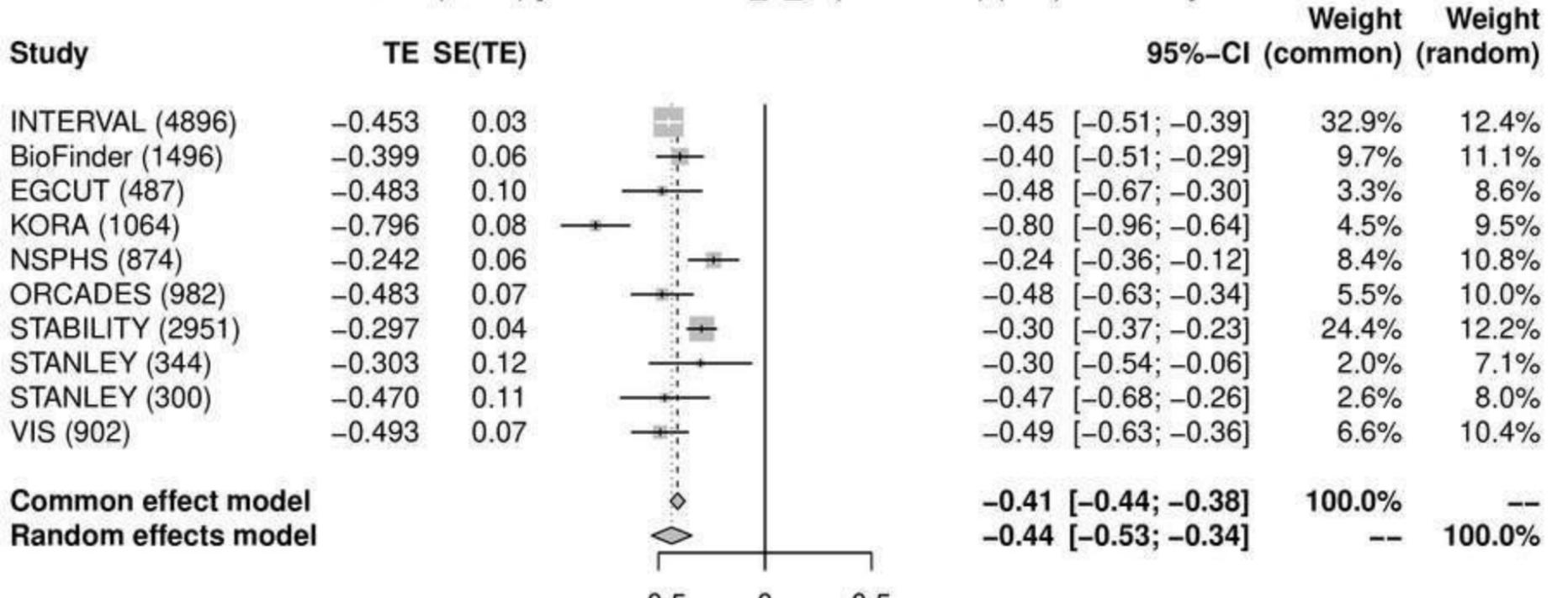
# CCL25 (CCL25)-rs635634

CCL25 (CCL25) [chr9:136155000\_C\_T (rs635634) (T/C) N=11785]

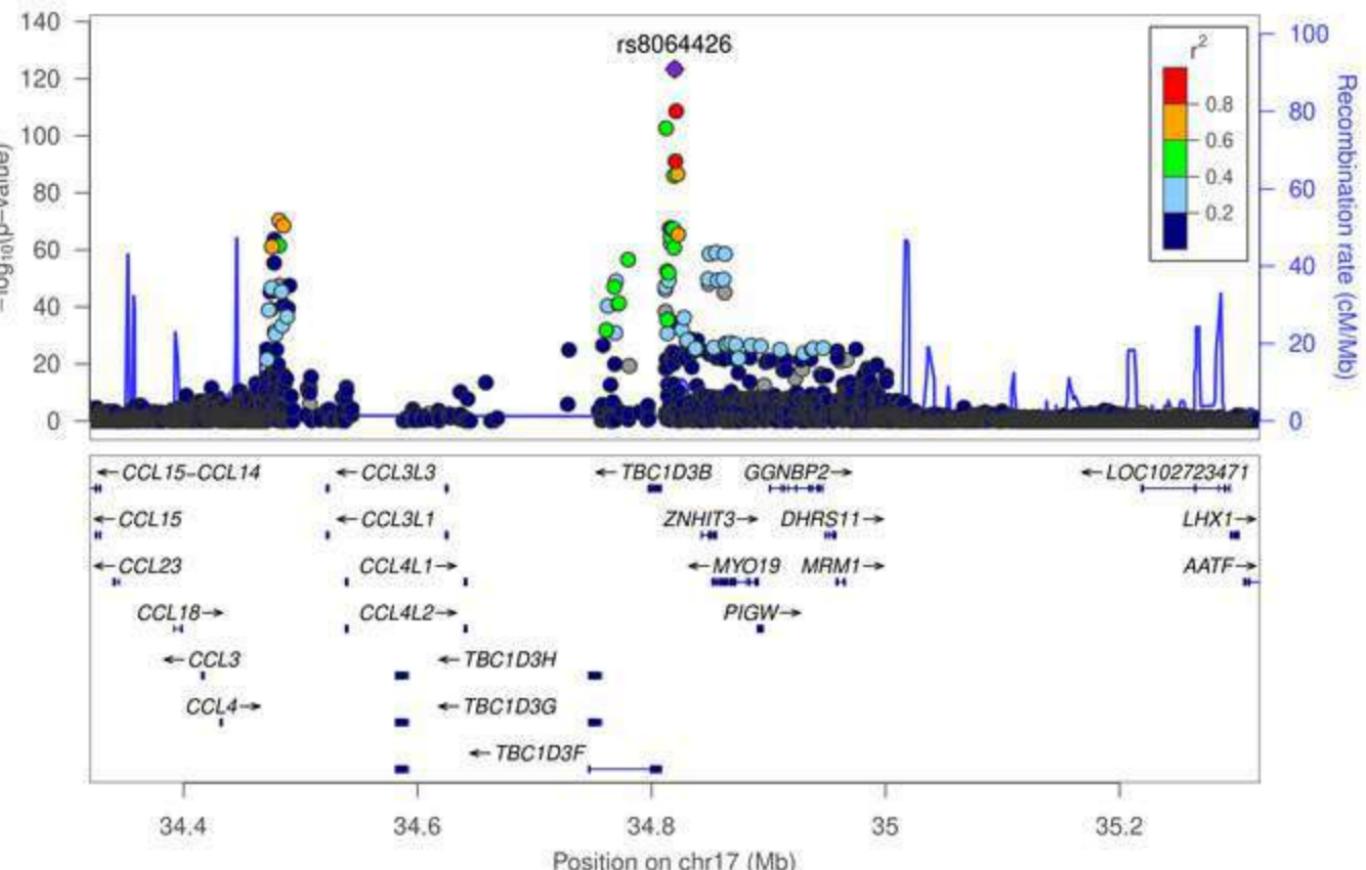


# CCL4 (CCL4)-rs8064426

CCL4 (CCL4) [chr17:34819750\_A\_G (rs8064426) (A/G) N=14296]

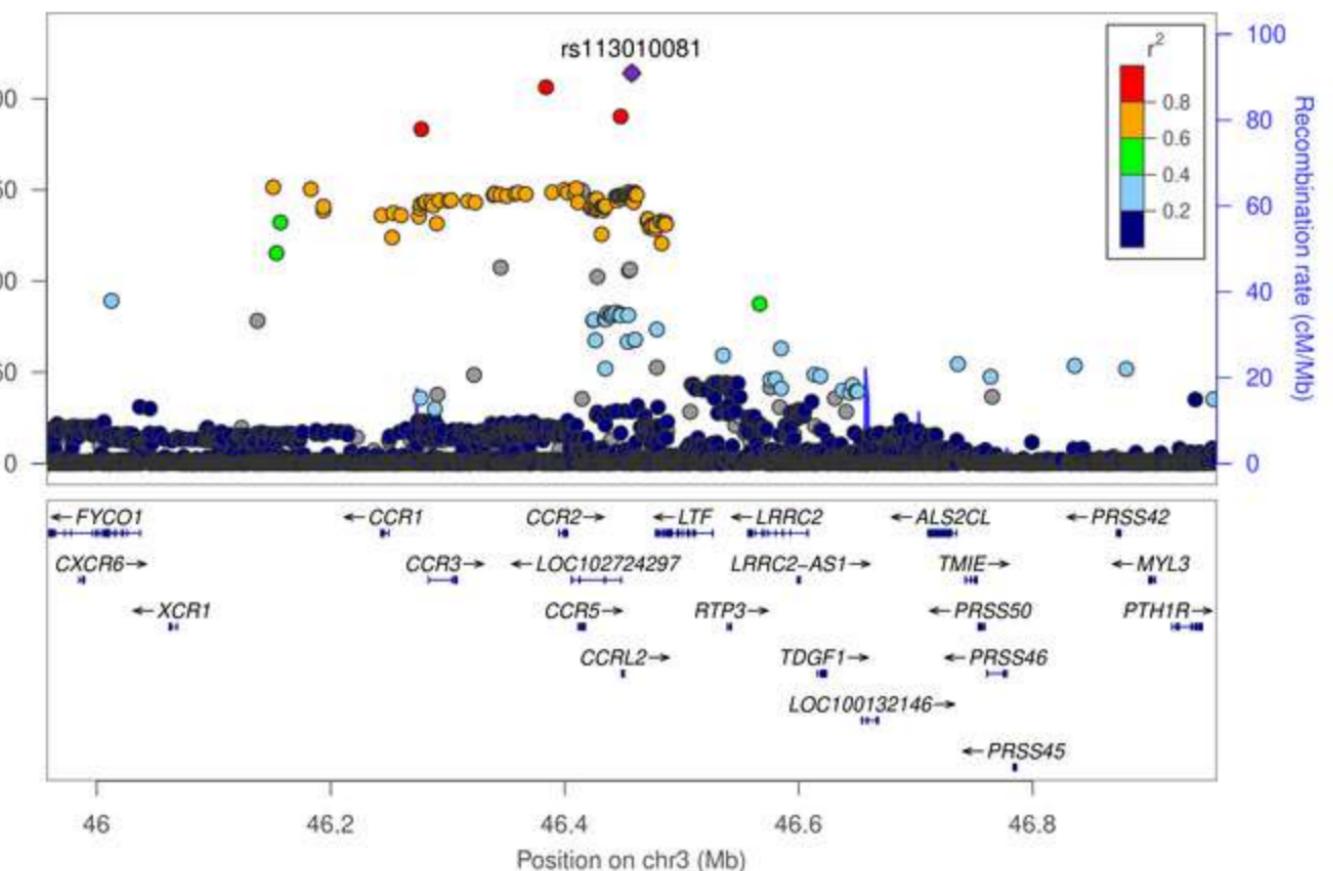
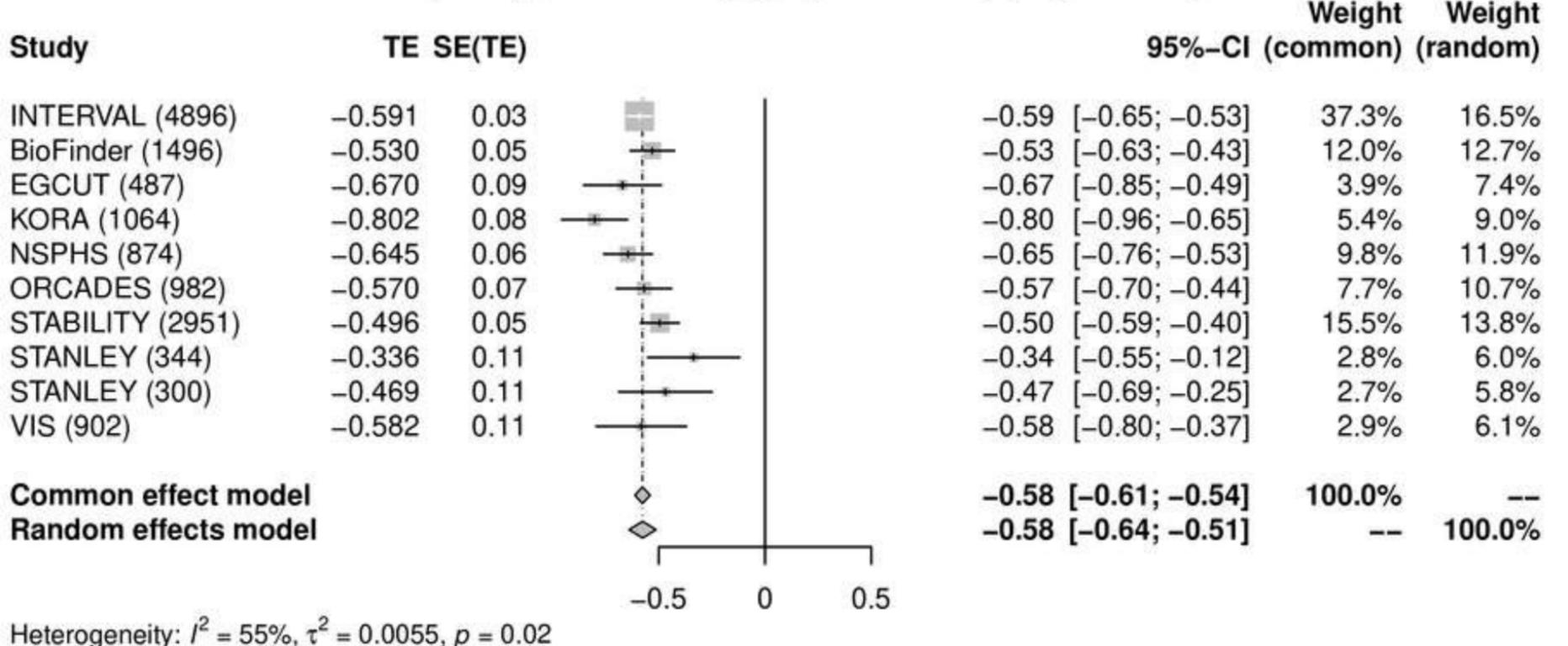


Heterogeneity:  $I^2 = 81\%$ ,  $\tau^2 = 0.0178$ ,  $p < 0.01$

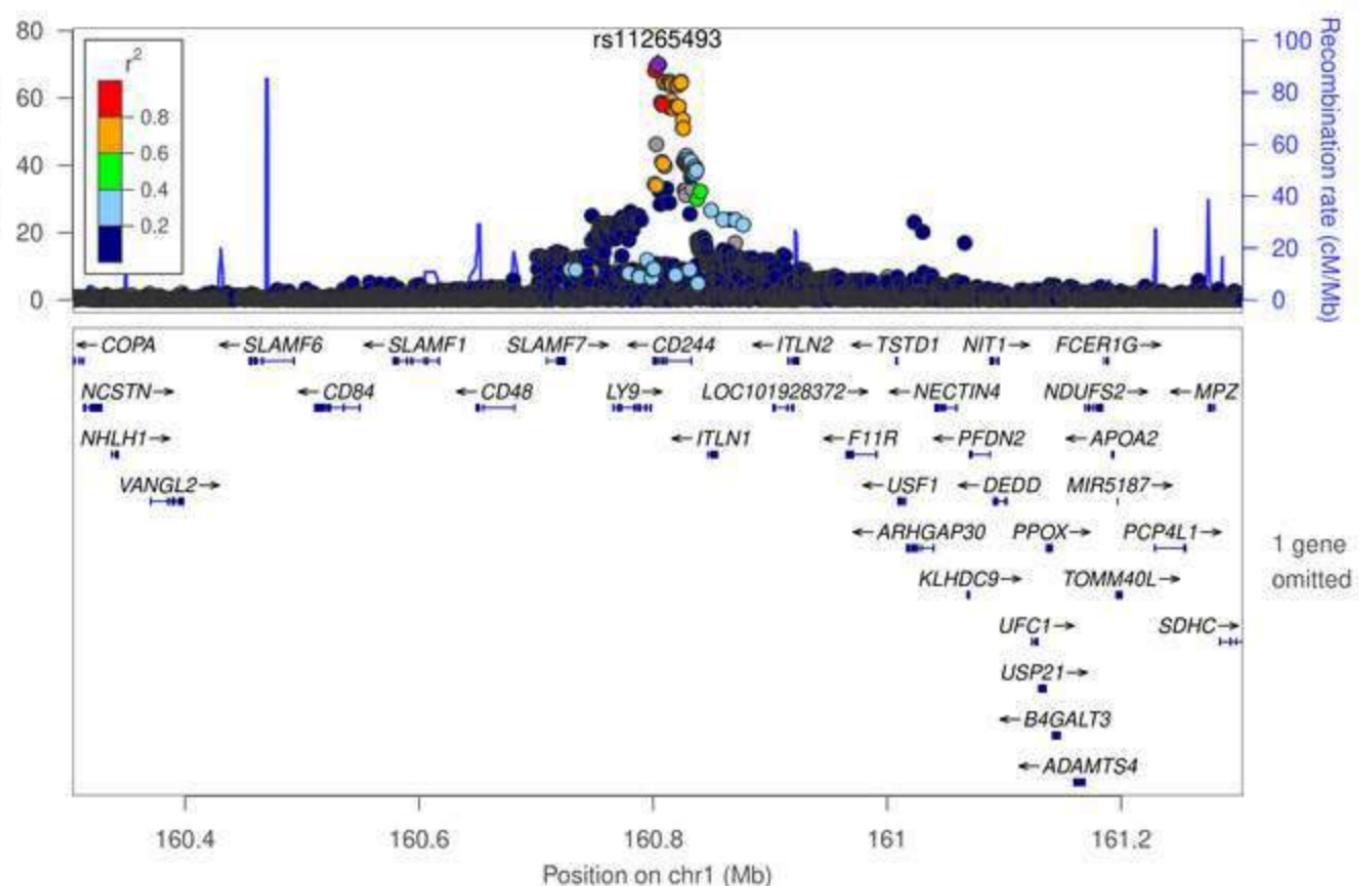
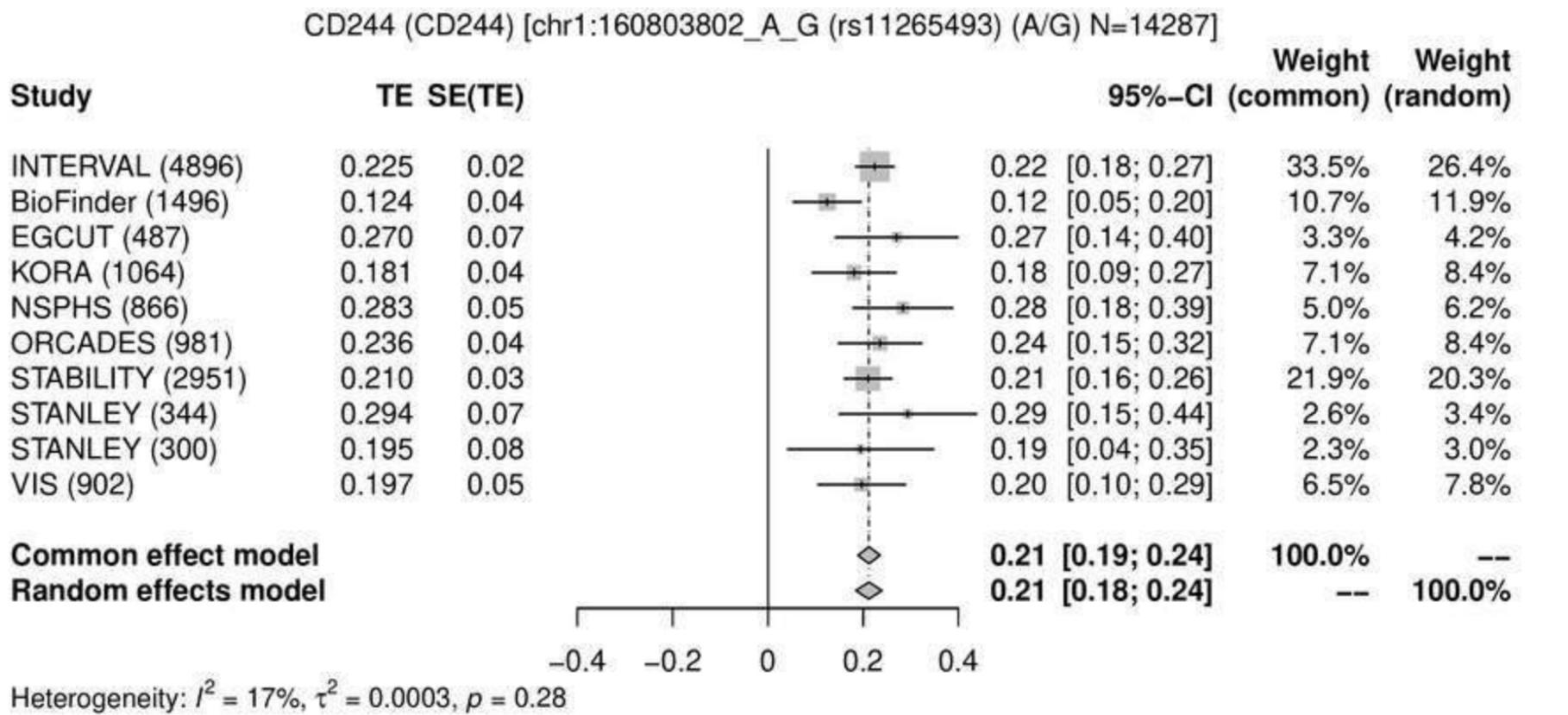


# CCL4 (CCL4)-rs113010081

CCL4 (CCL4) [chr3:46457412\_C\_T (rs113010081) (T/C) N=14296]

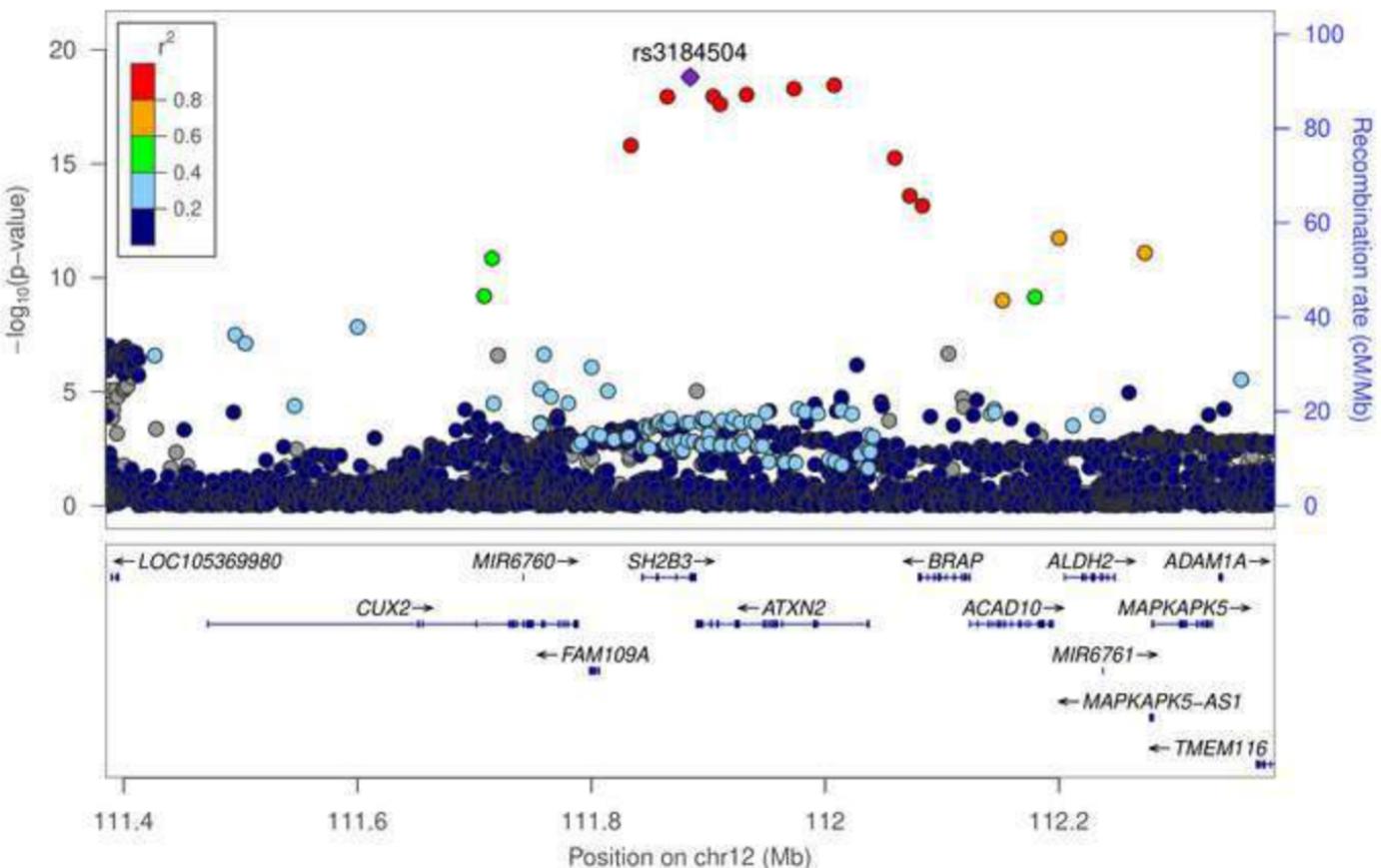
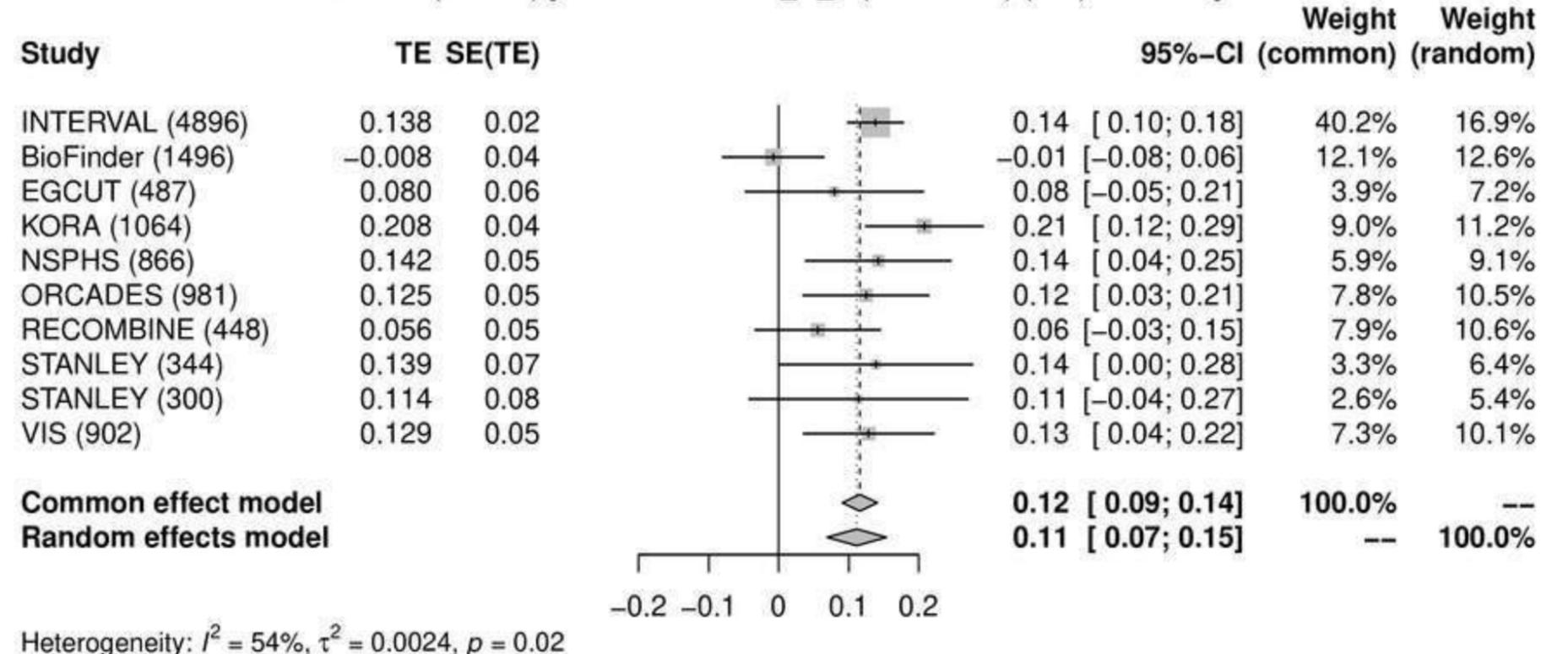


# CD244 (CD244)-rs11265493



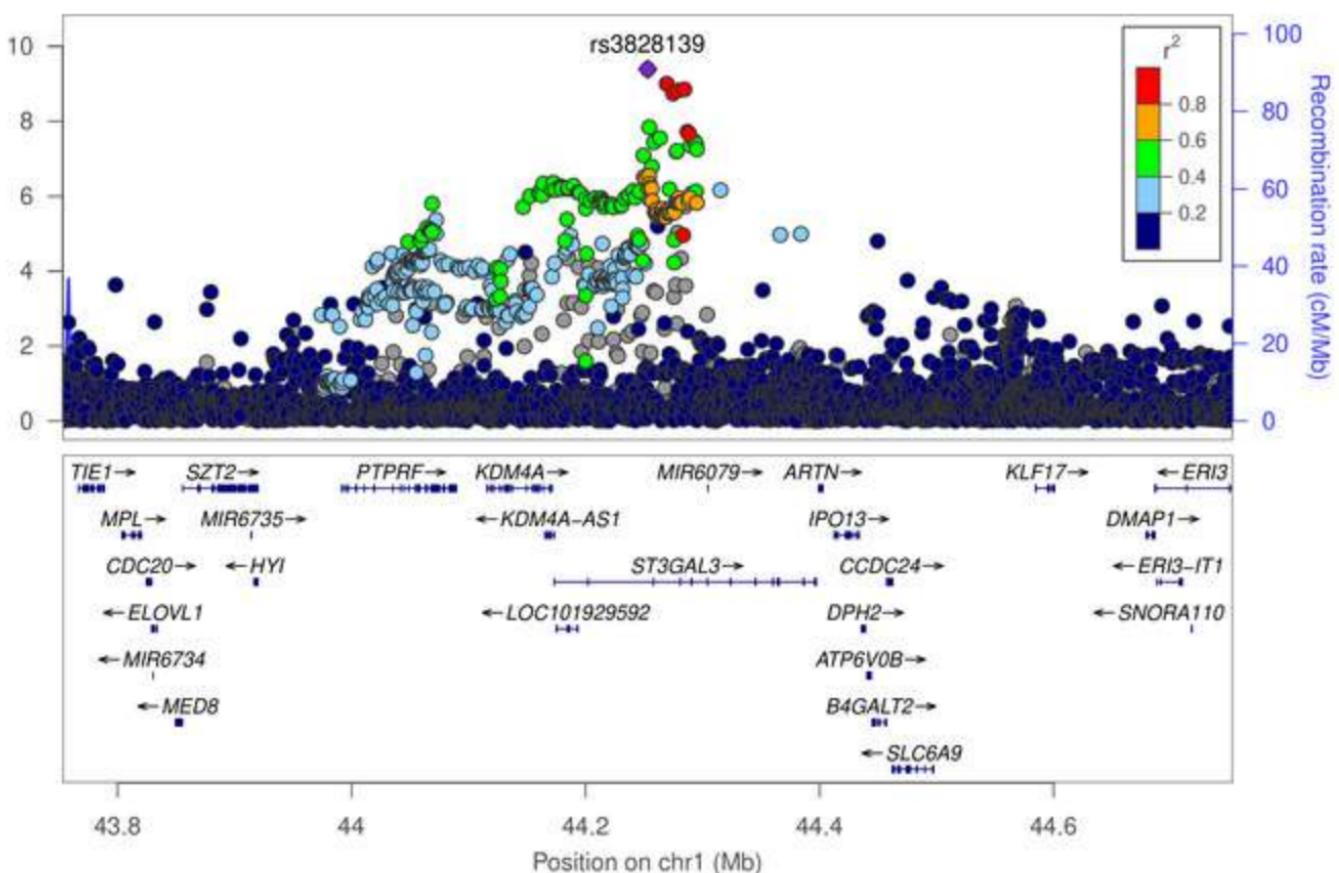
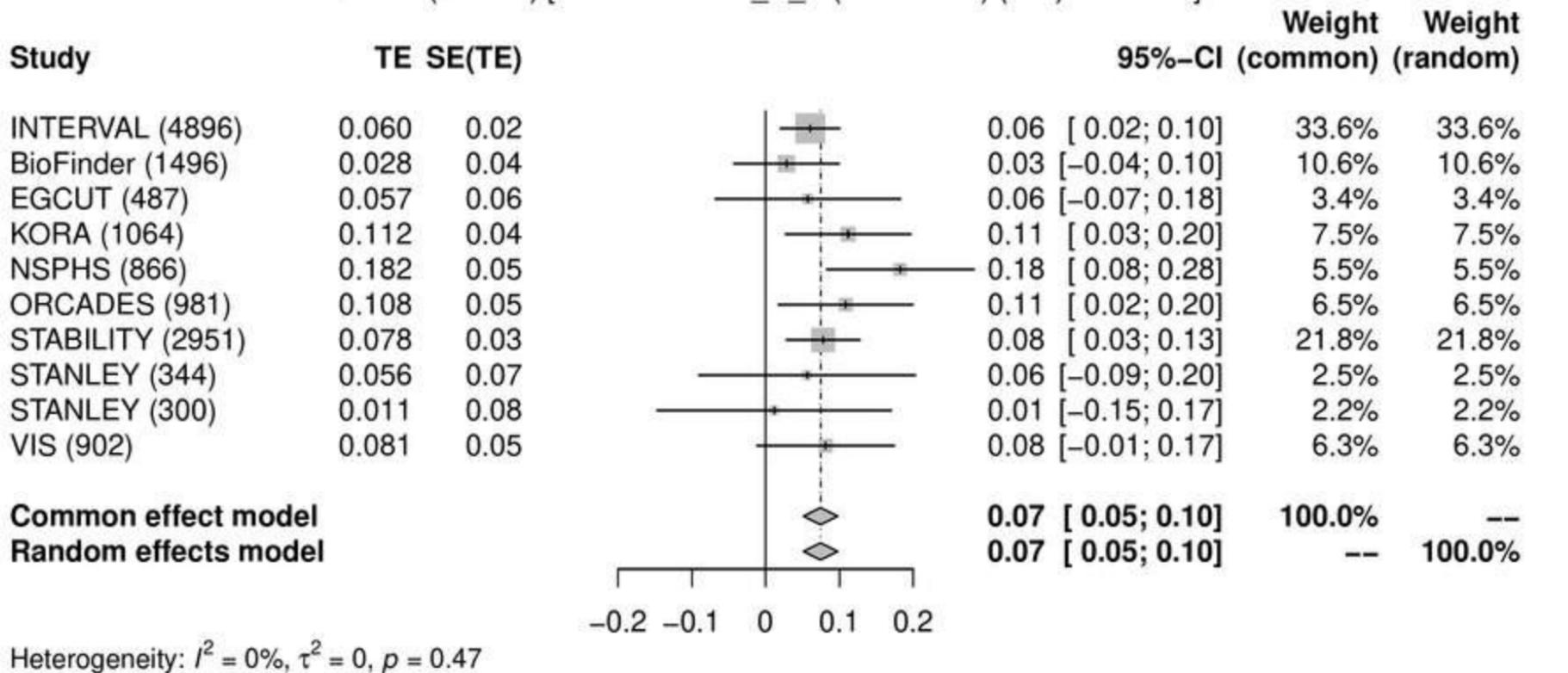
# CD244 (CD244)-rs3184504

CD244 (CD244) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11784]



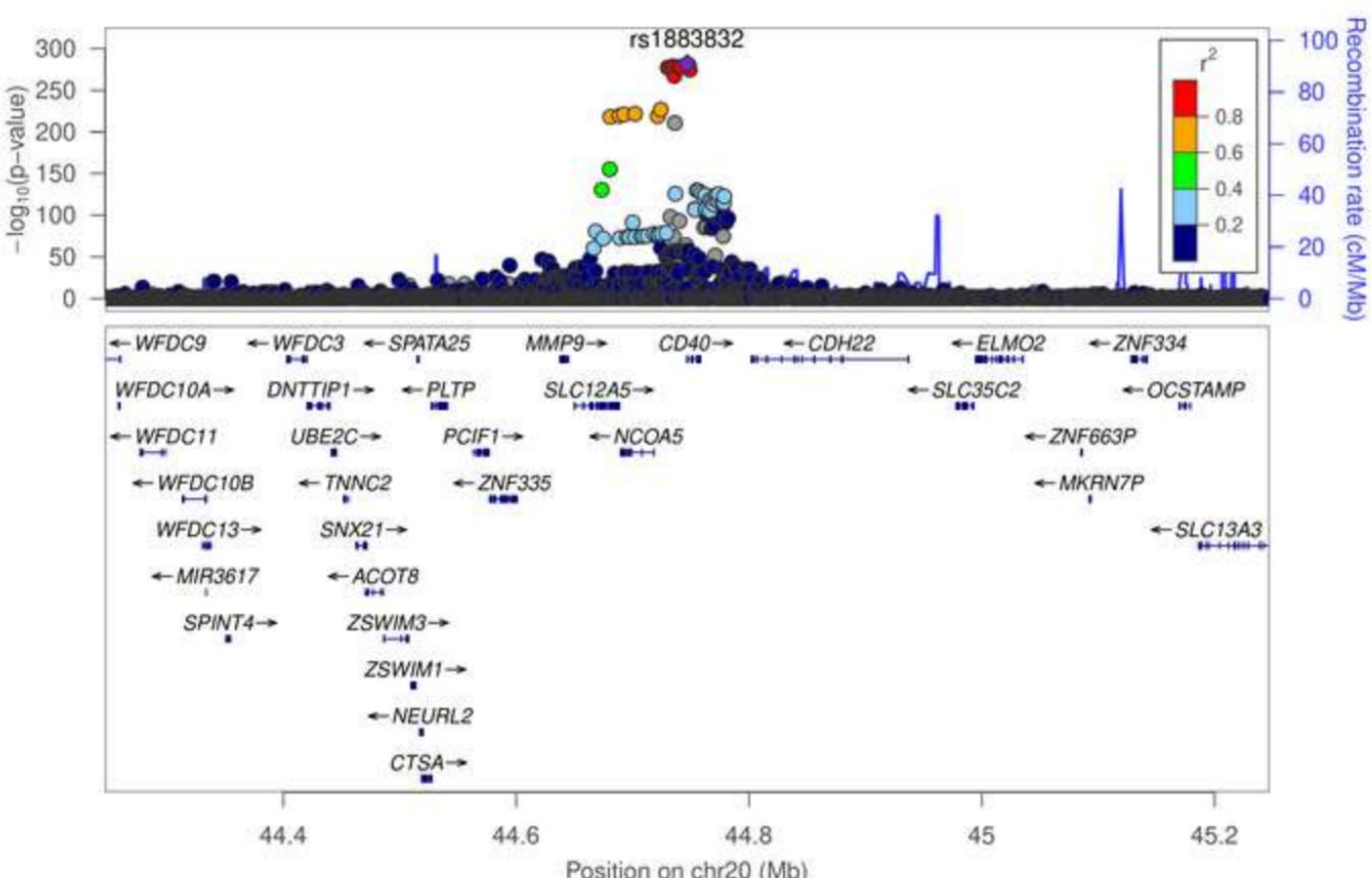
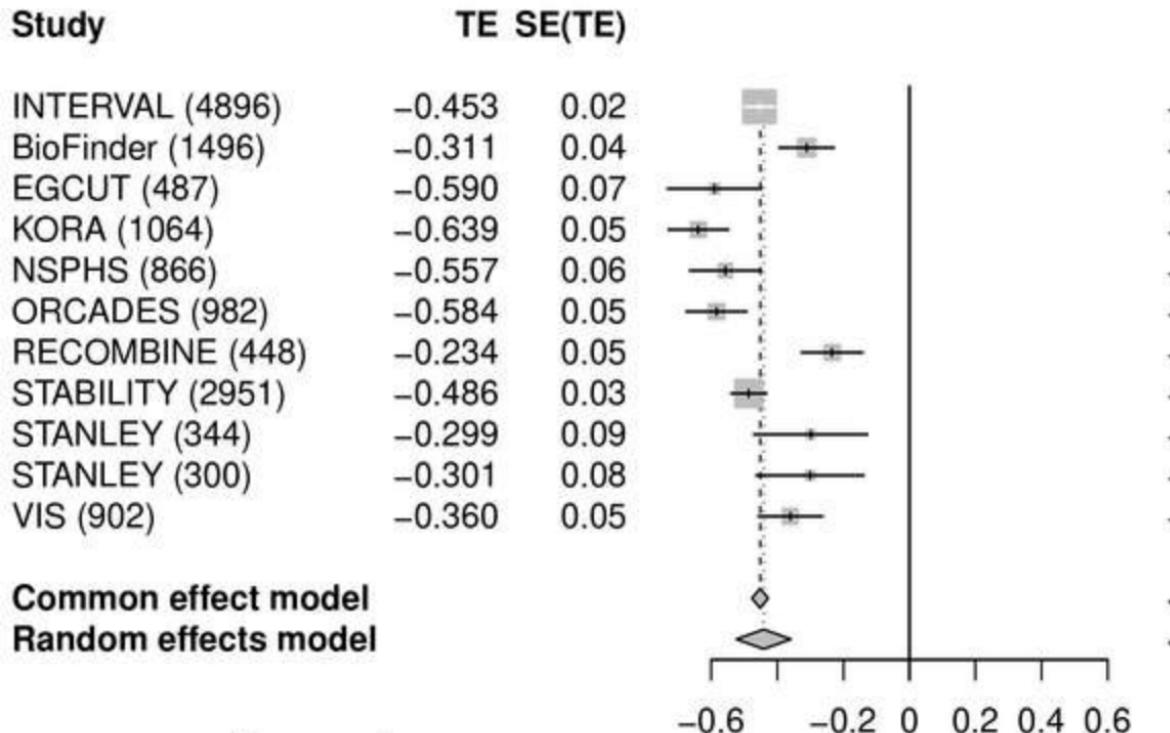
# CD244 (CD244)-rs3828139

CD244 (CD244) [chr1:44253015\_C\_T (rs3828139) (T/C) N=14287]



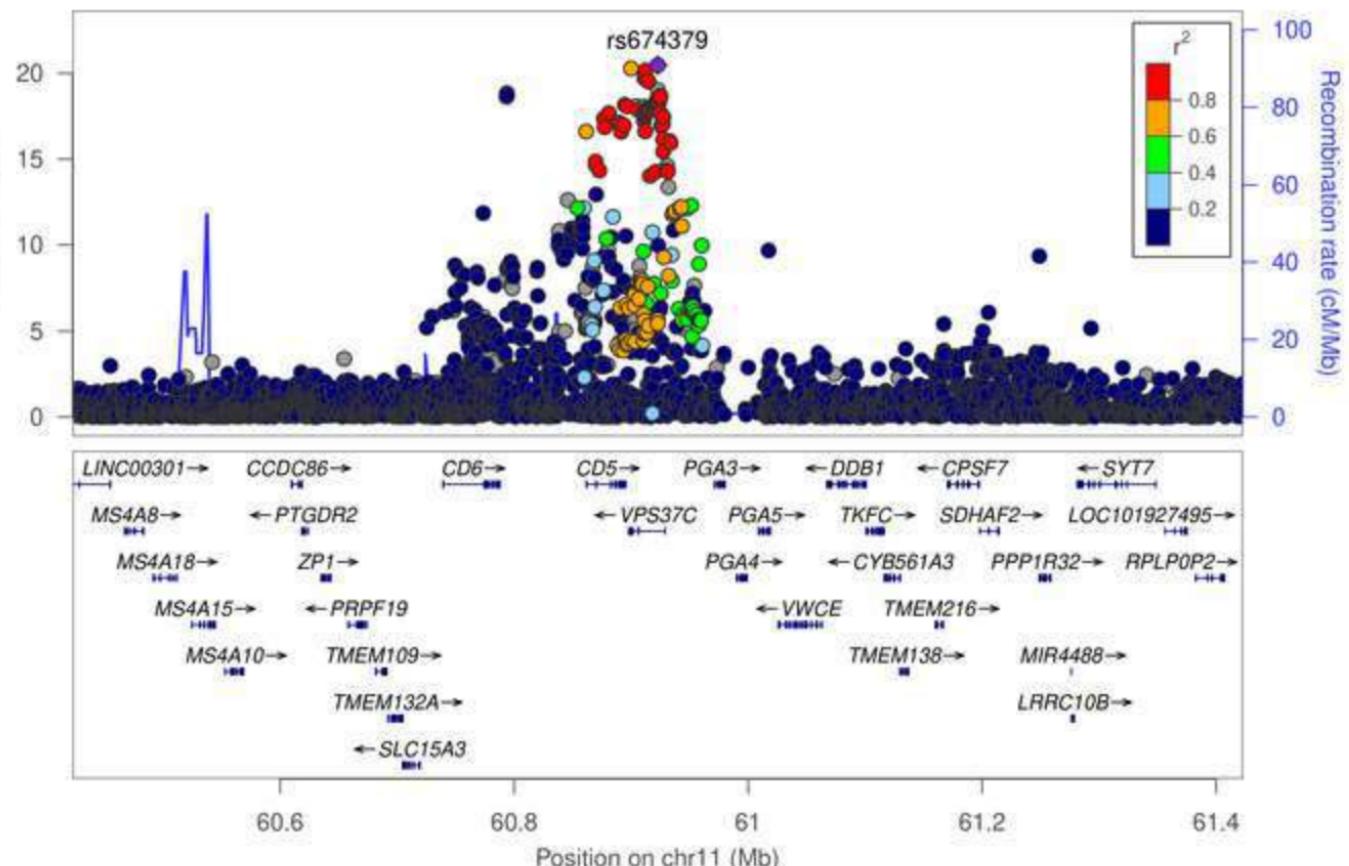
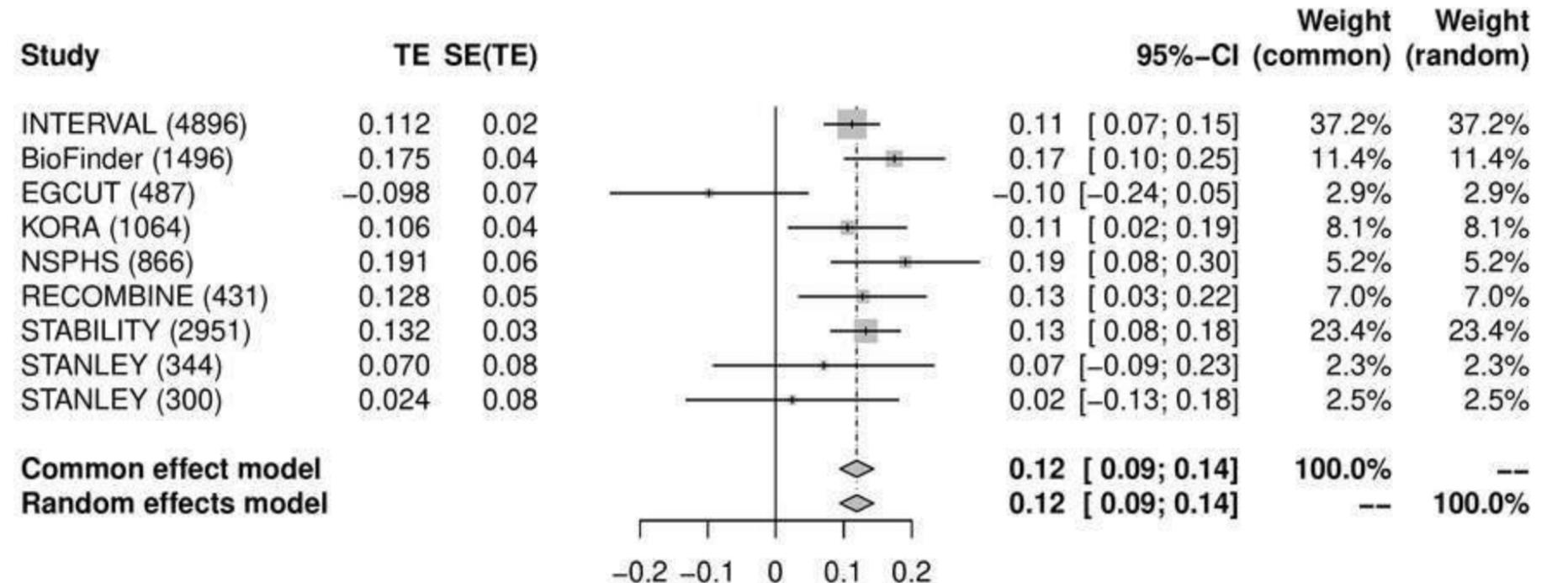
# CD40 (CD40)-rs1883832

## Study



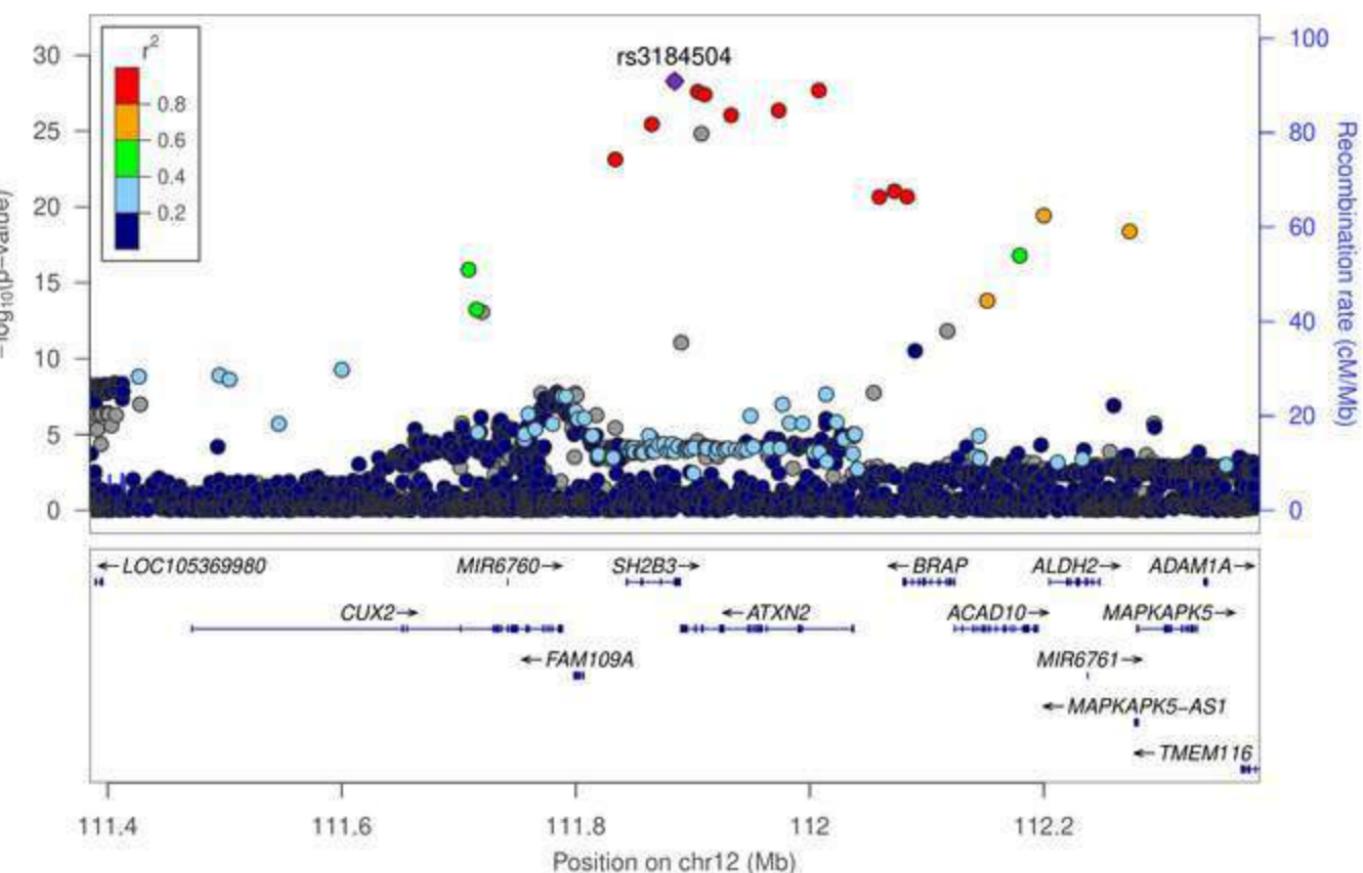
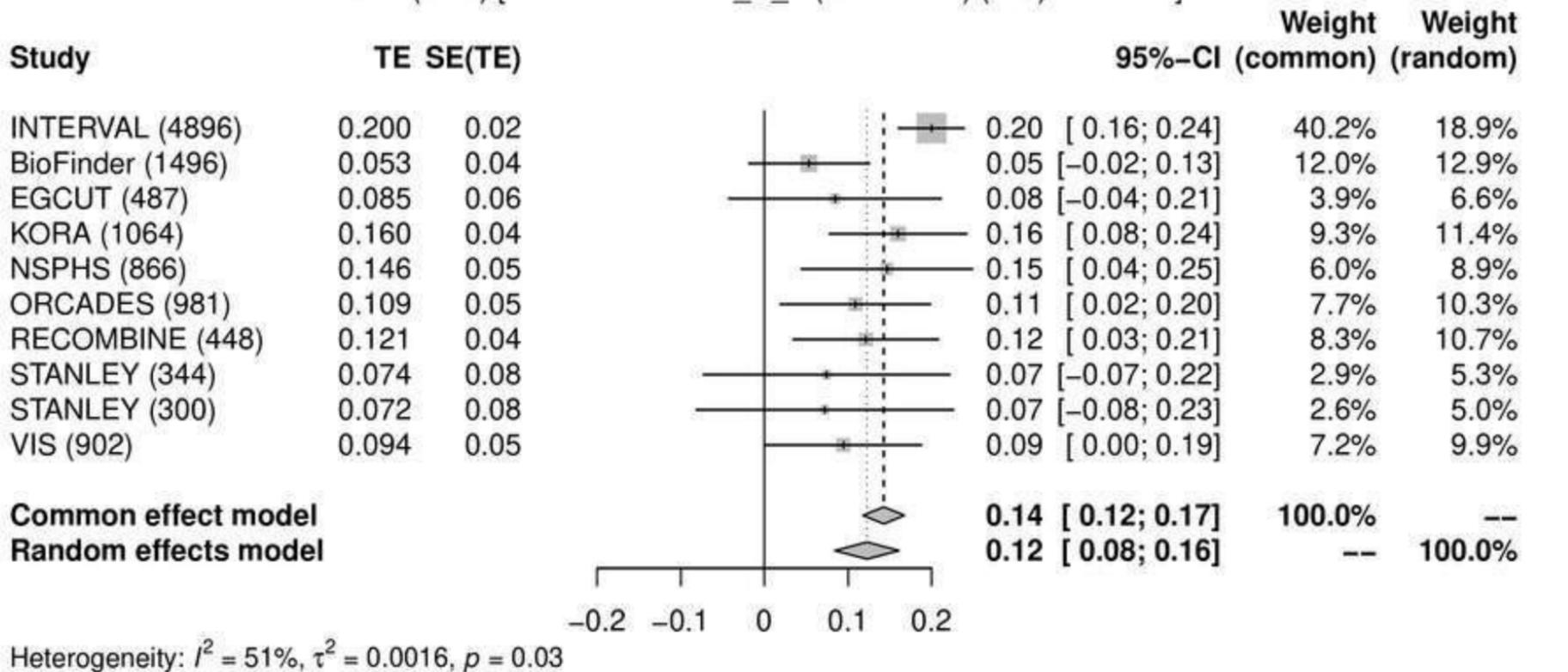
# CD5 (CD5)-rs674379

CD5 (CD5) [chr11:60922561\_C\_G (rs674379) (C/G) N=12835]

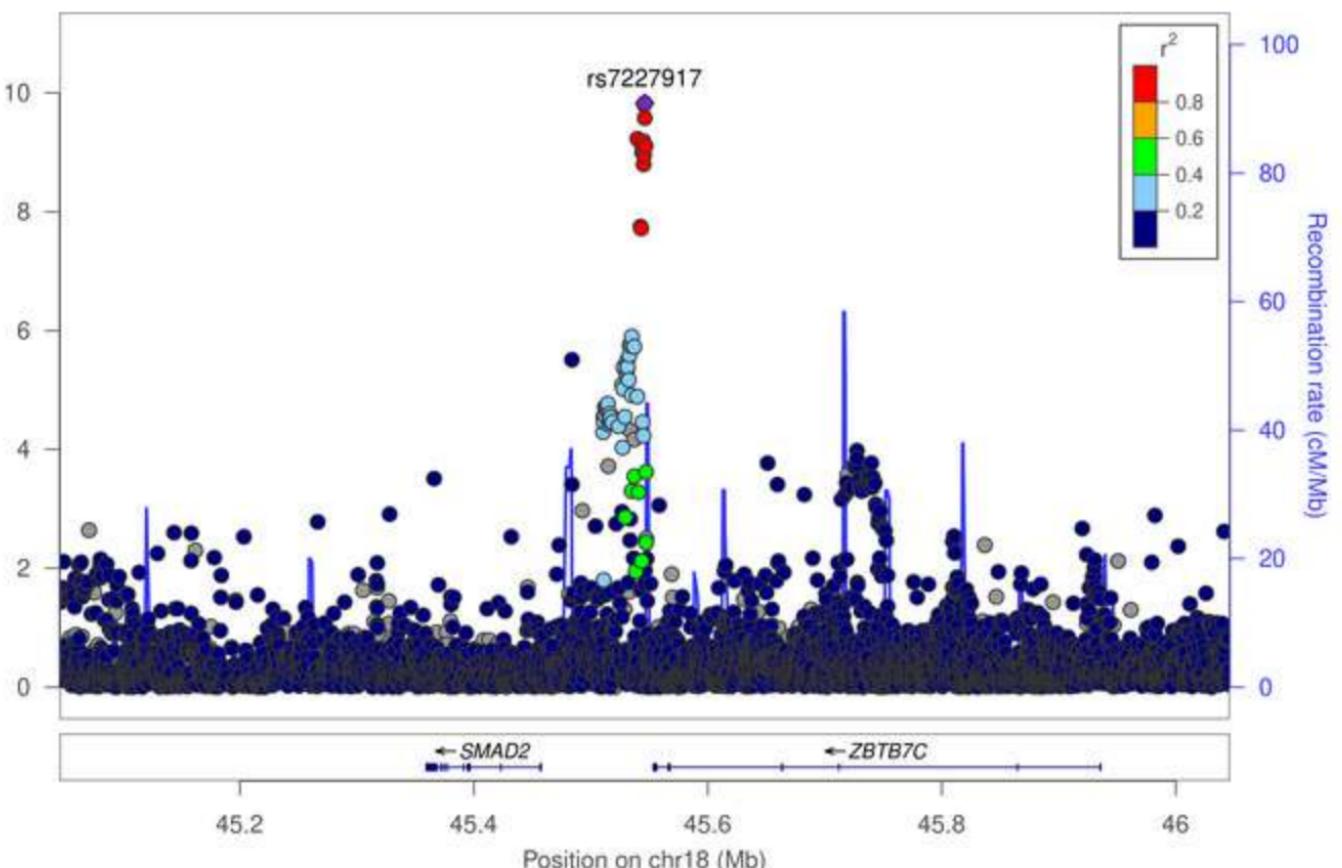
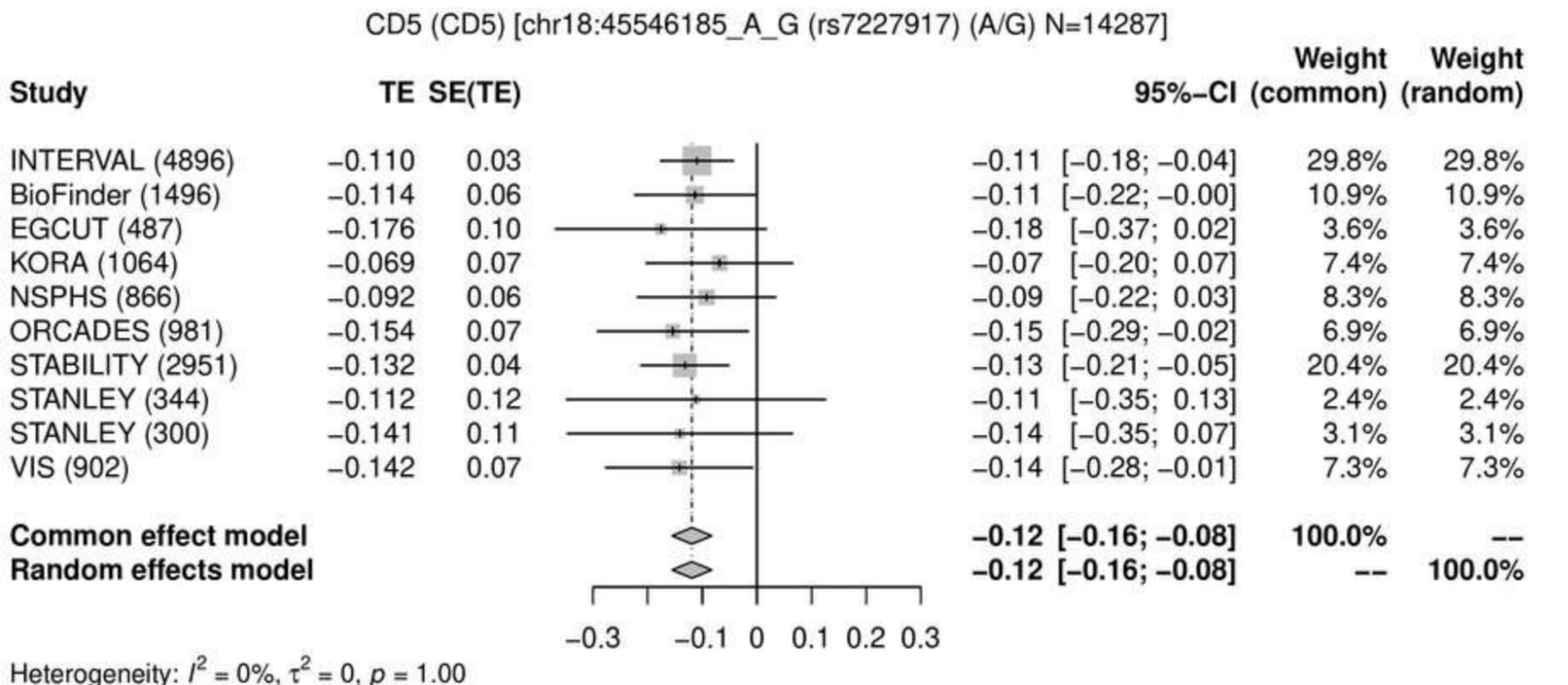


# CD5 (CD5)-rs3184504

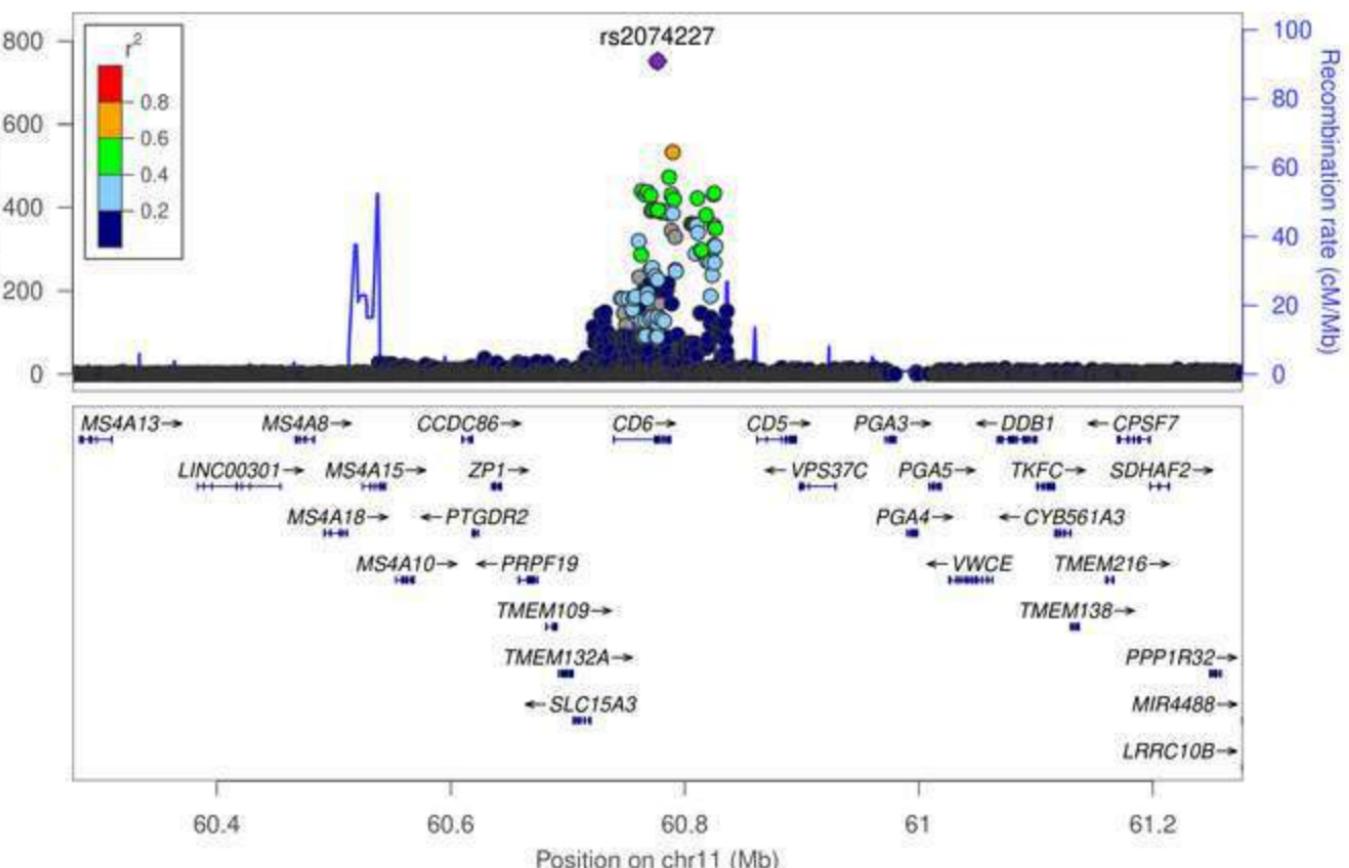
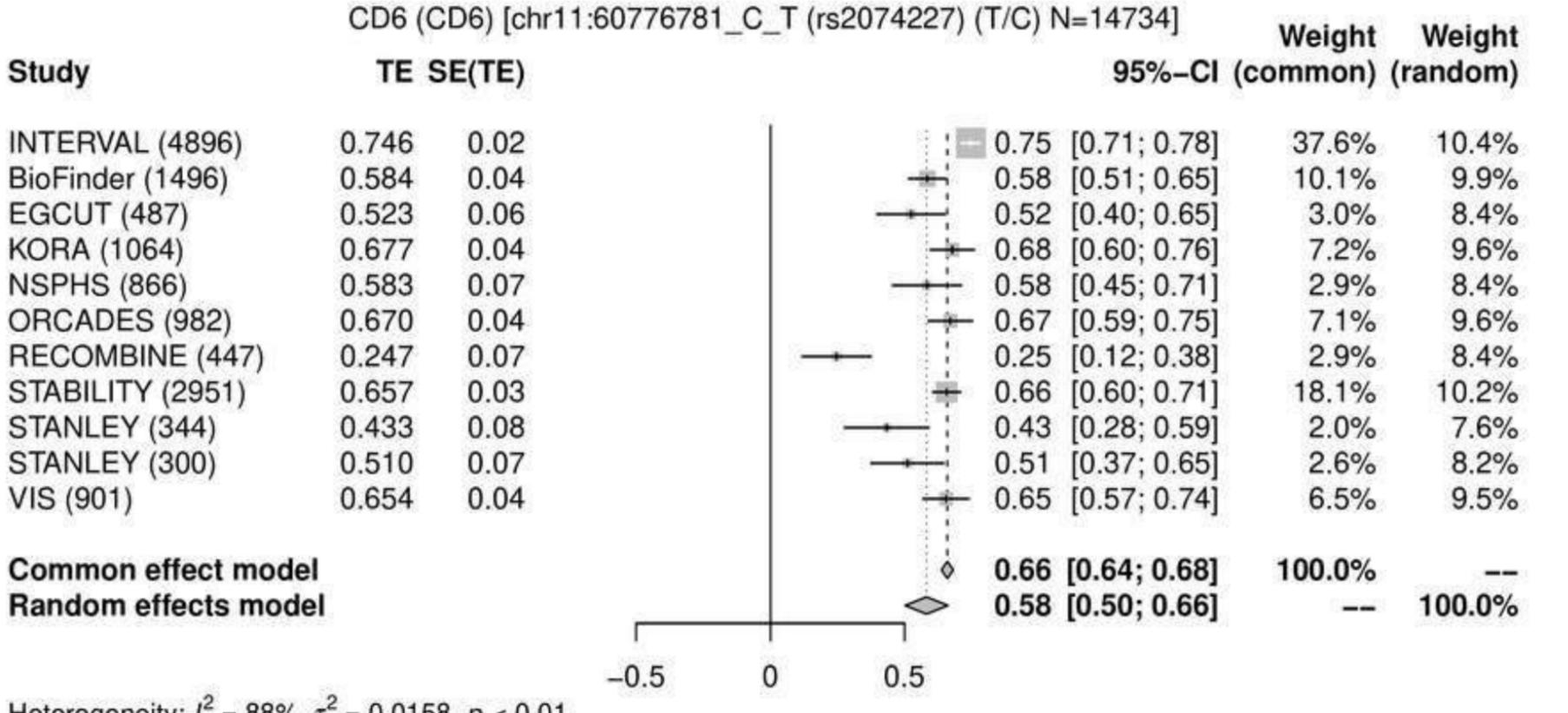
CD5 (CD5) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11784]



# CD5 (CD5)-rs7227917

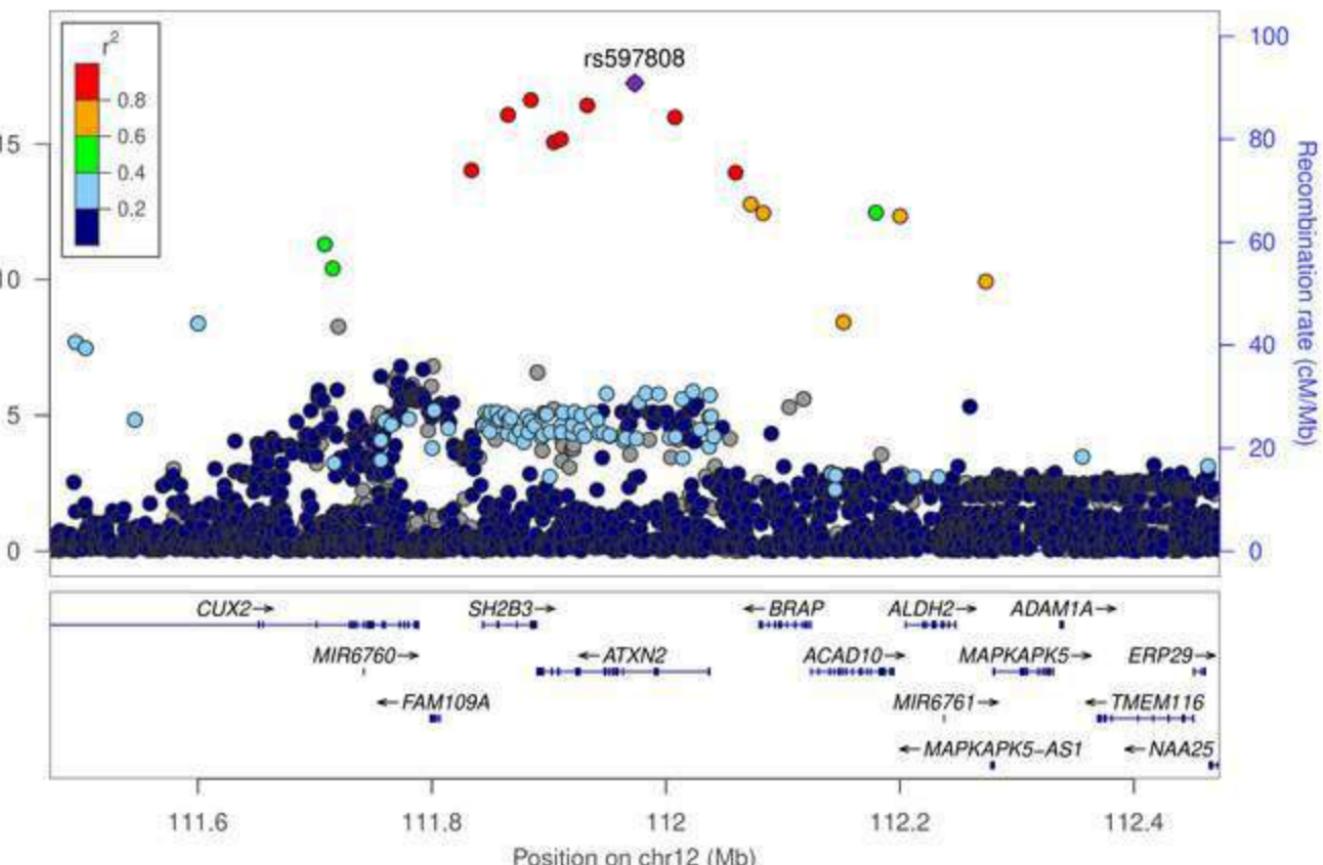
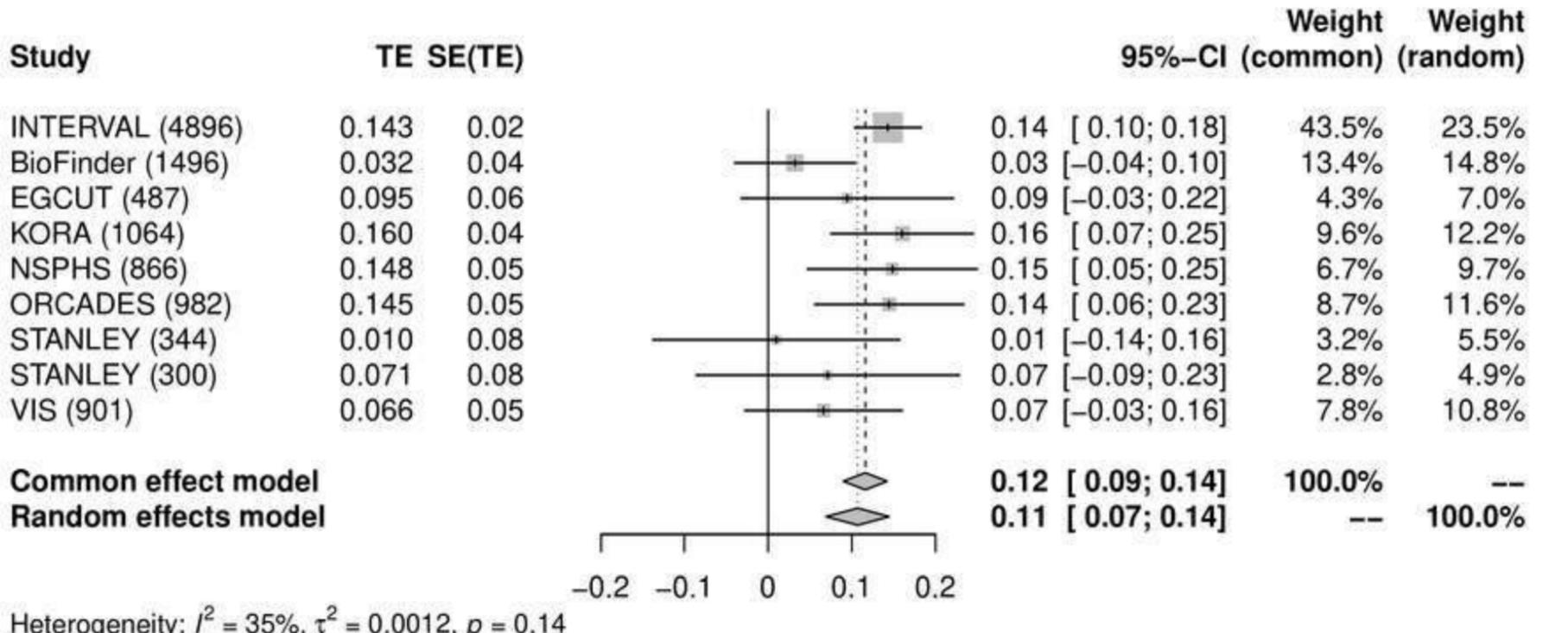


# CD6 (CD6)-rs2074227

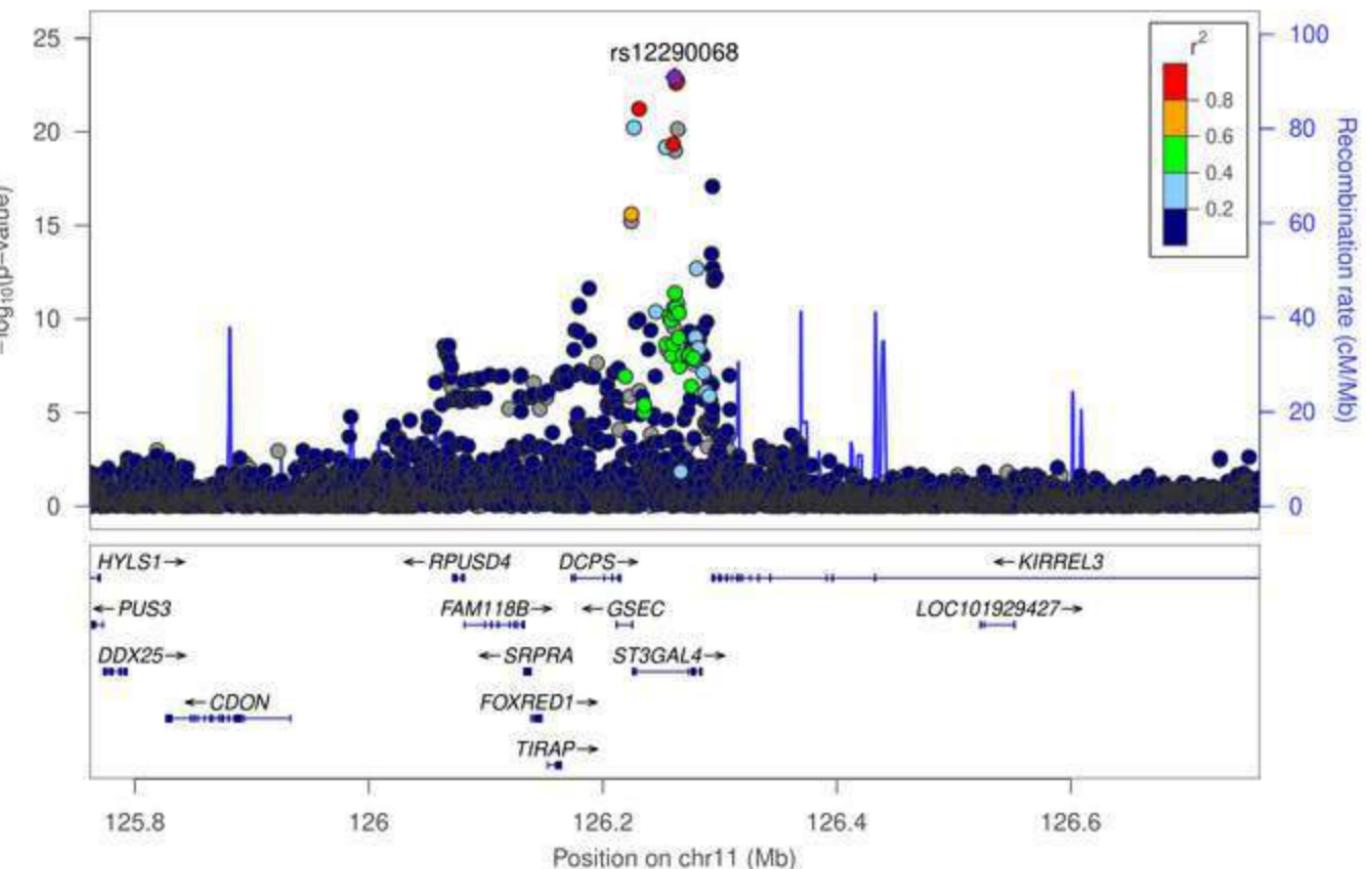
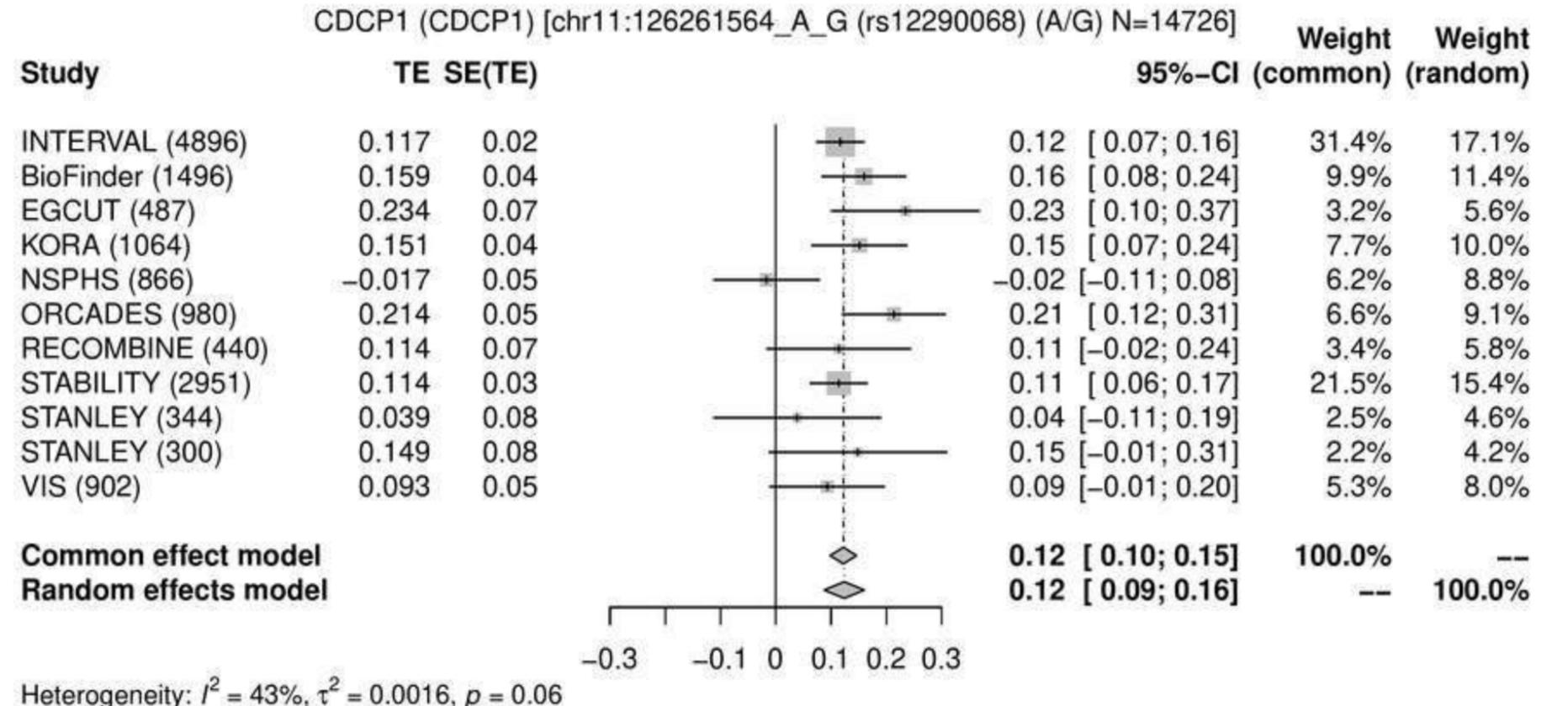


# CD6 (CD6)-rs597808

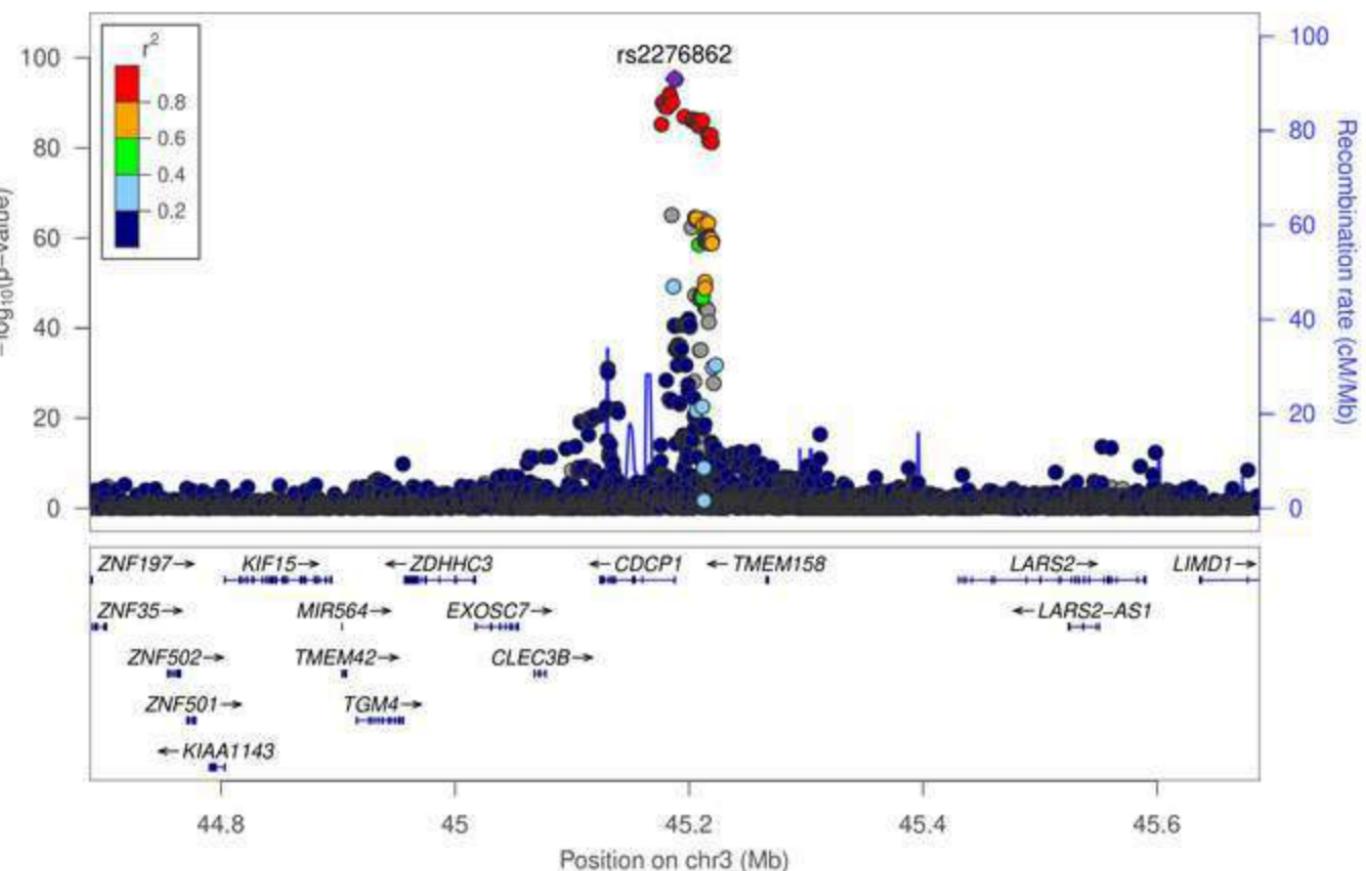
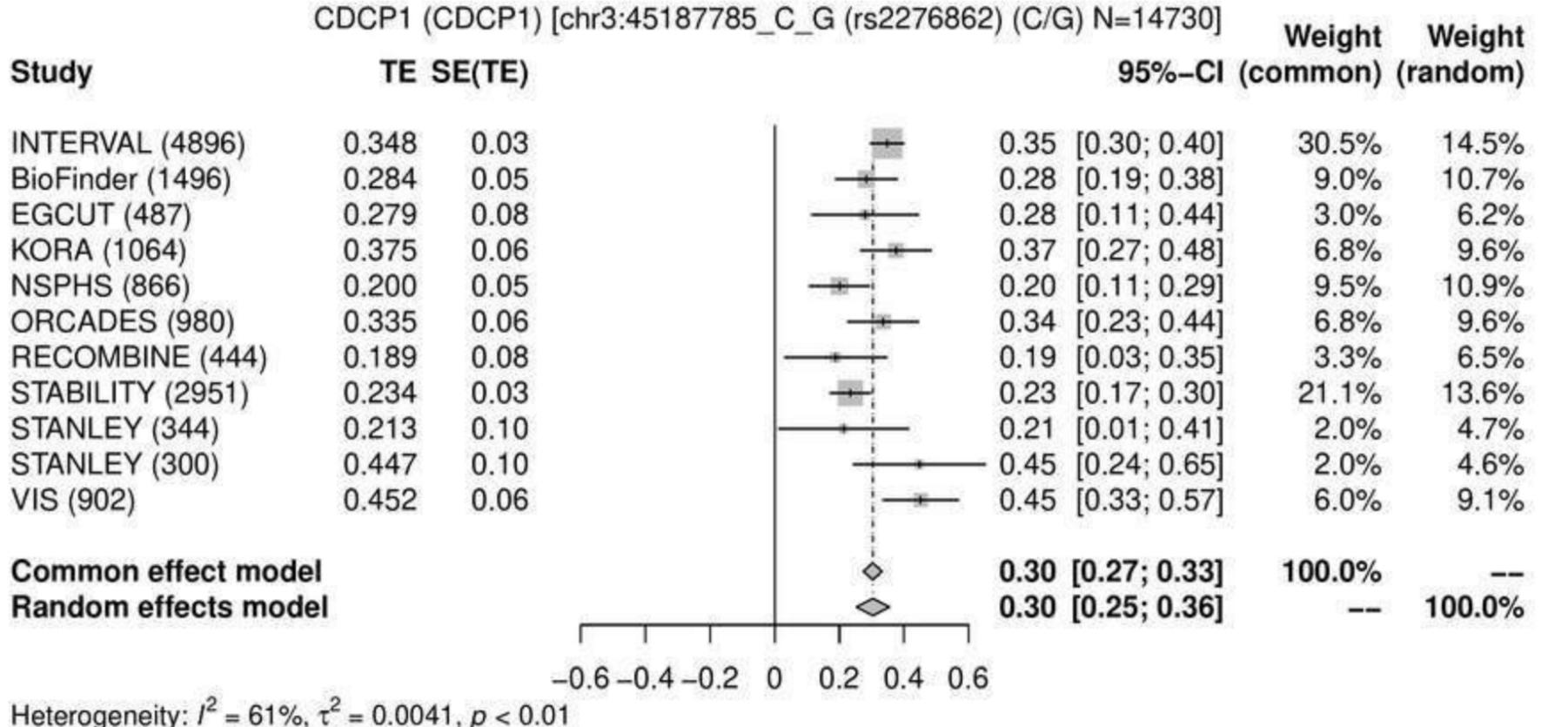
CD6 (CD6) [chr12:111973358\_A\_G (rs597808) (A/G) N=11336]



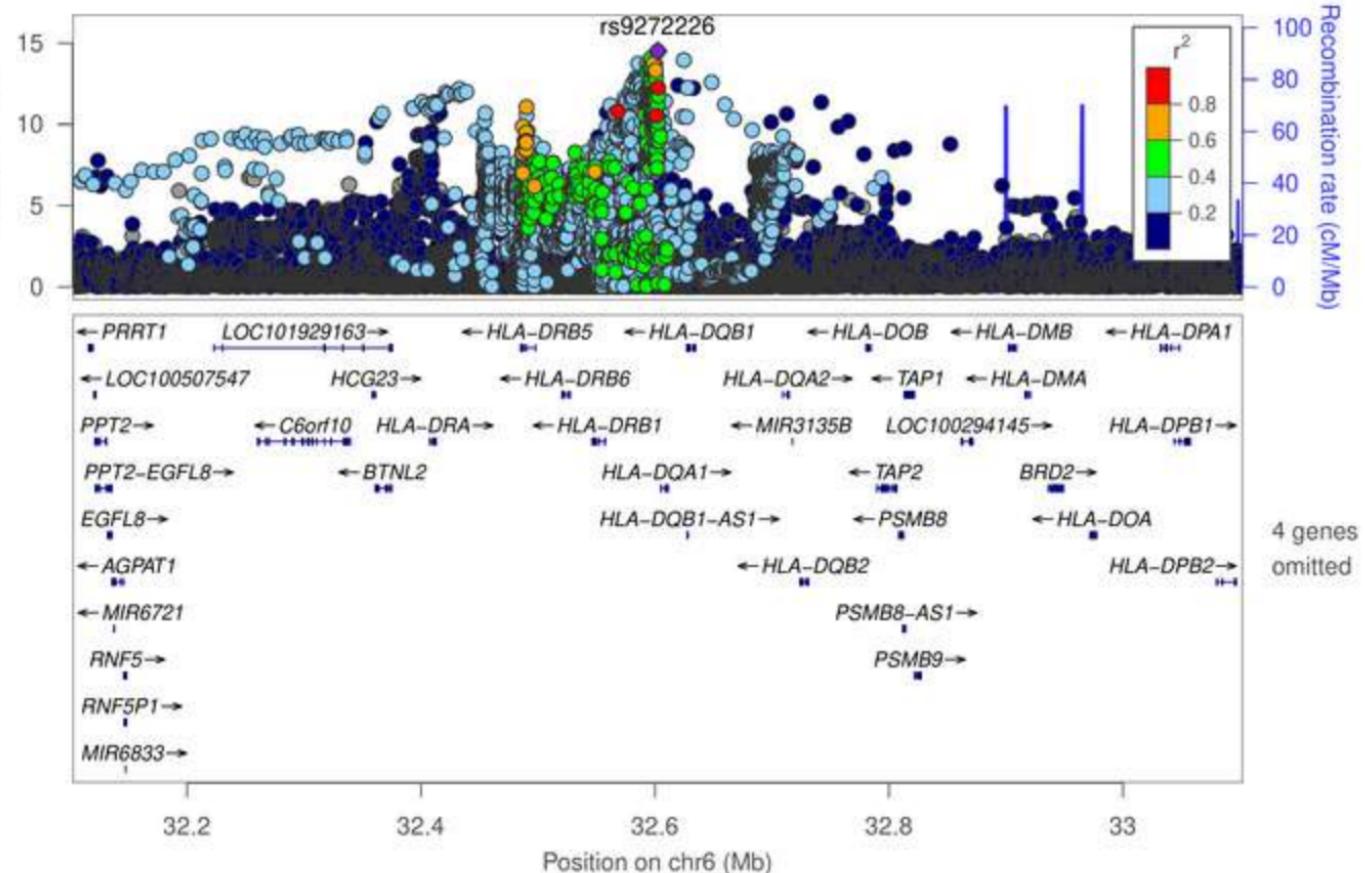
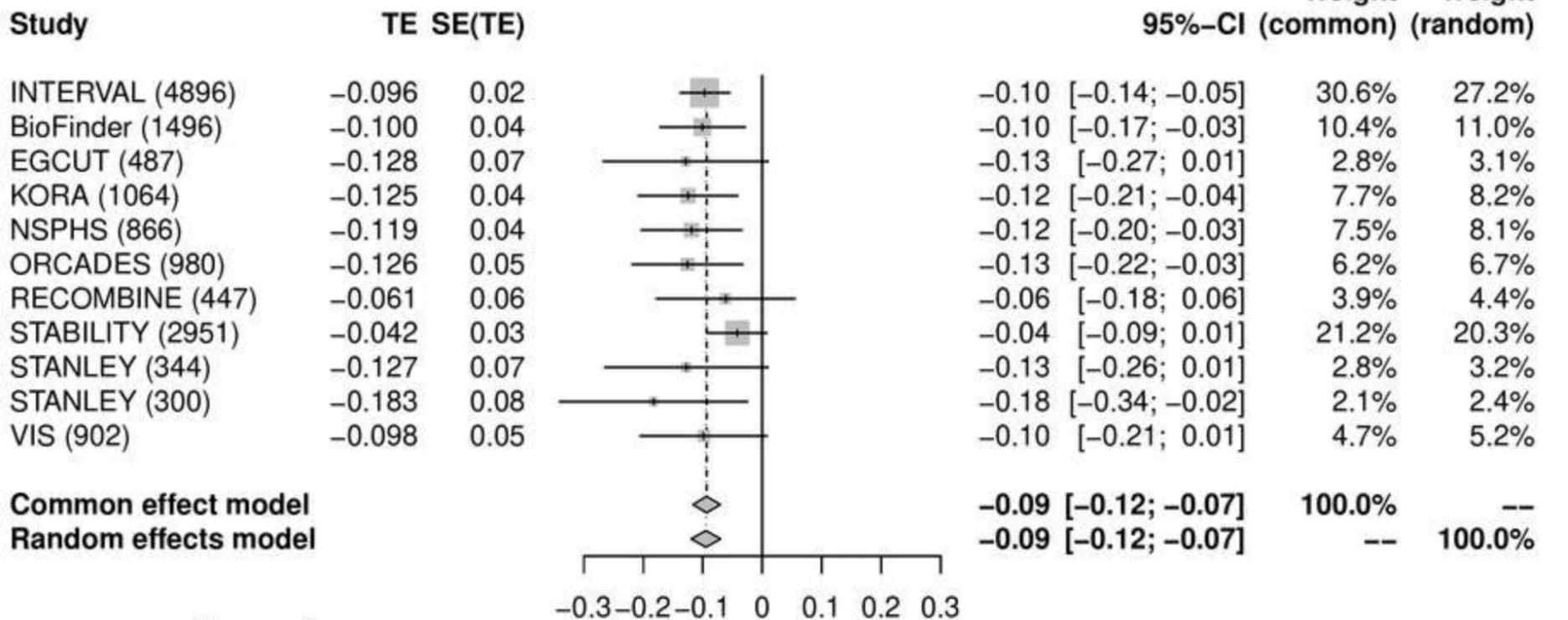
# CDCP1 (CDCP1)-rs12290068



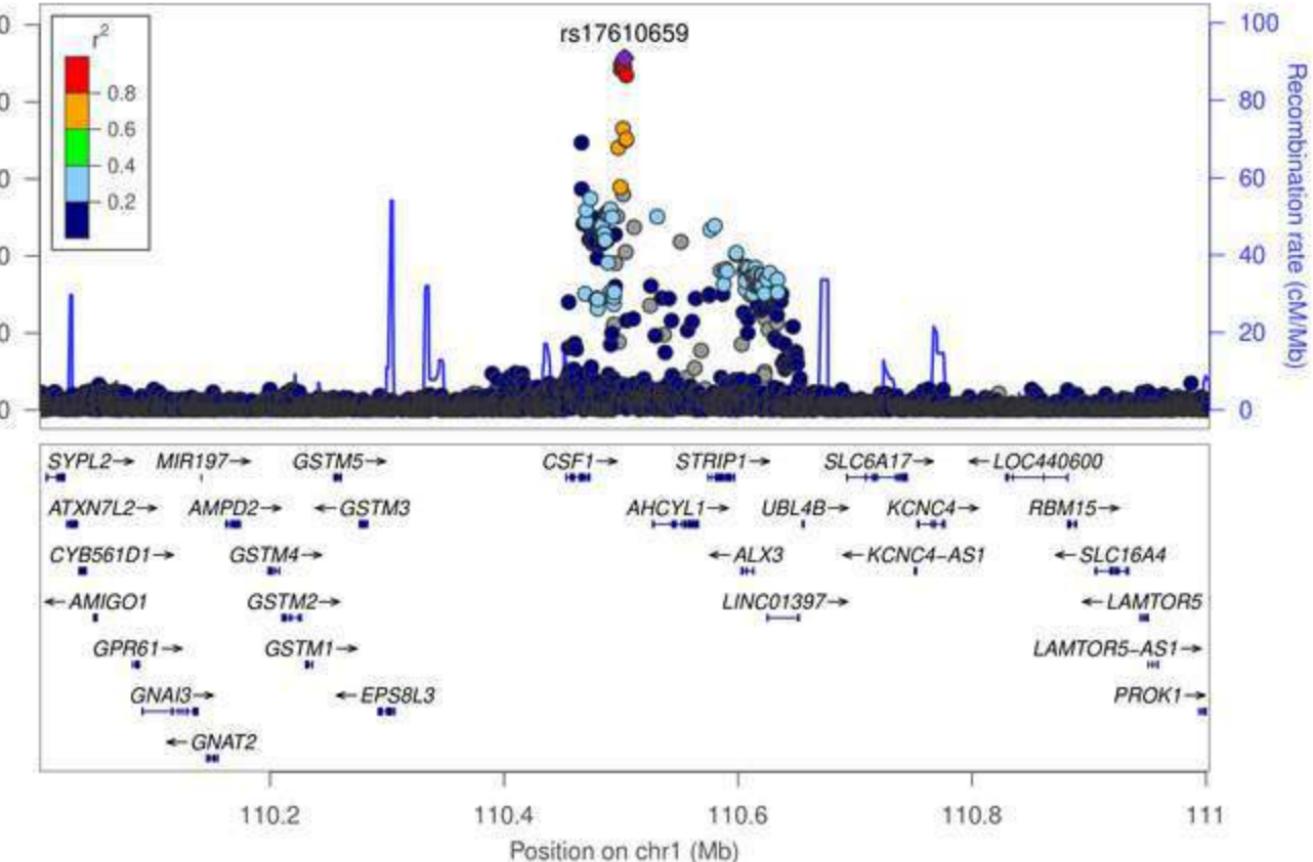
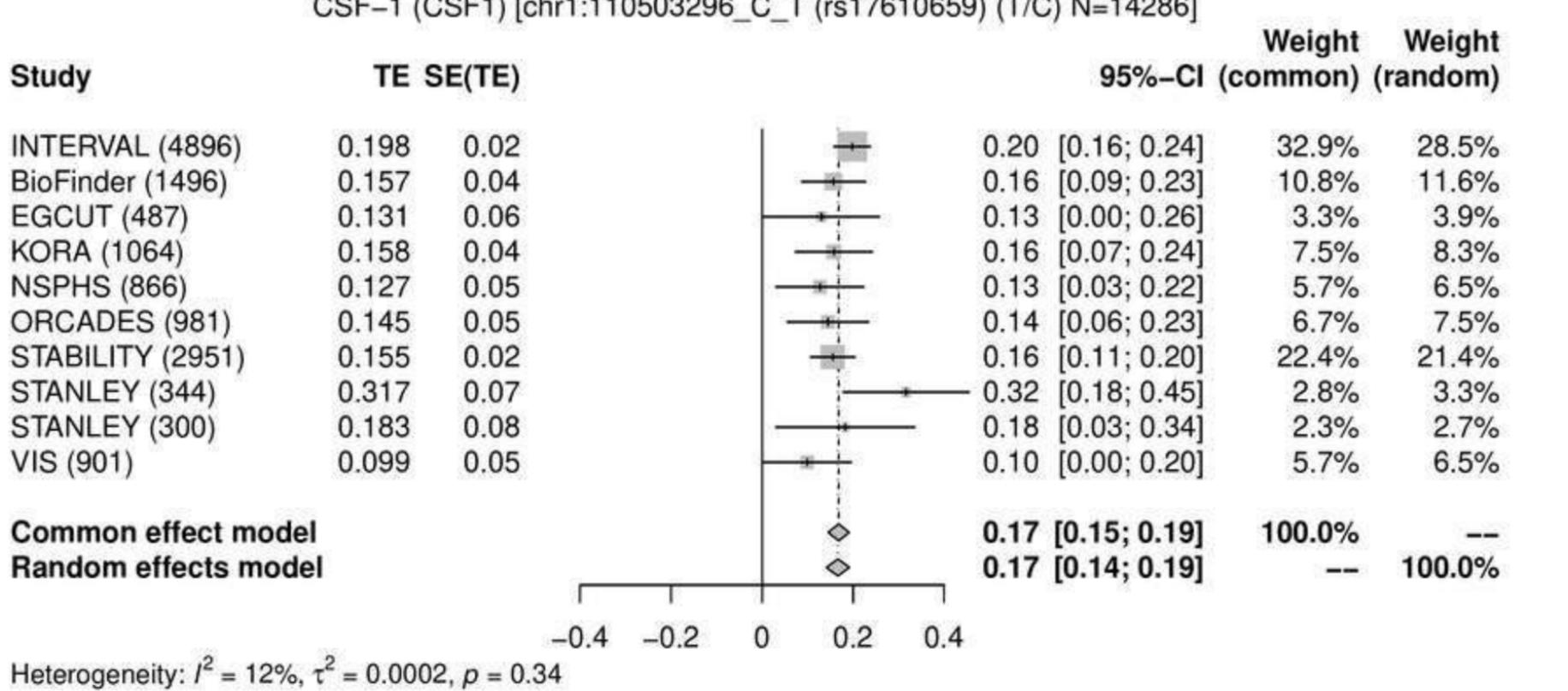
# CDCP1 (CDCP1)-rs2276862



# CDCP1 (CDCP1)-rs9272226

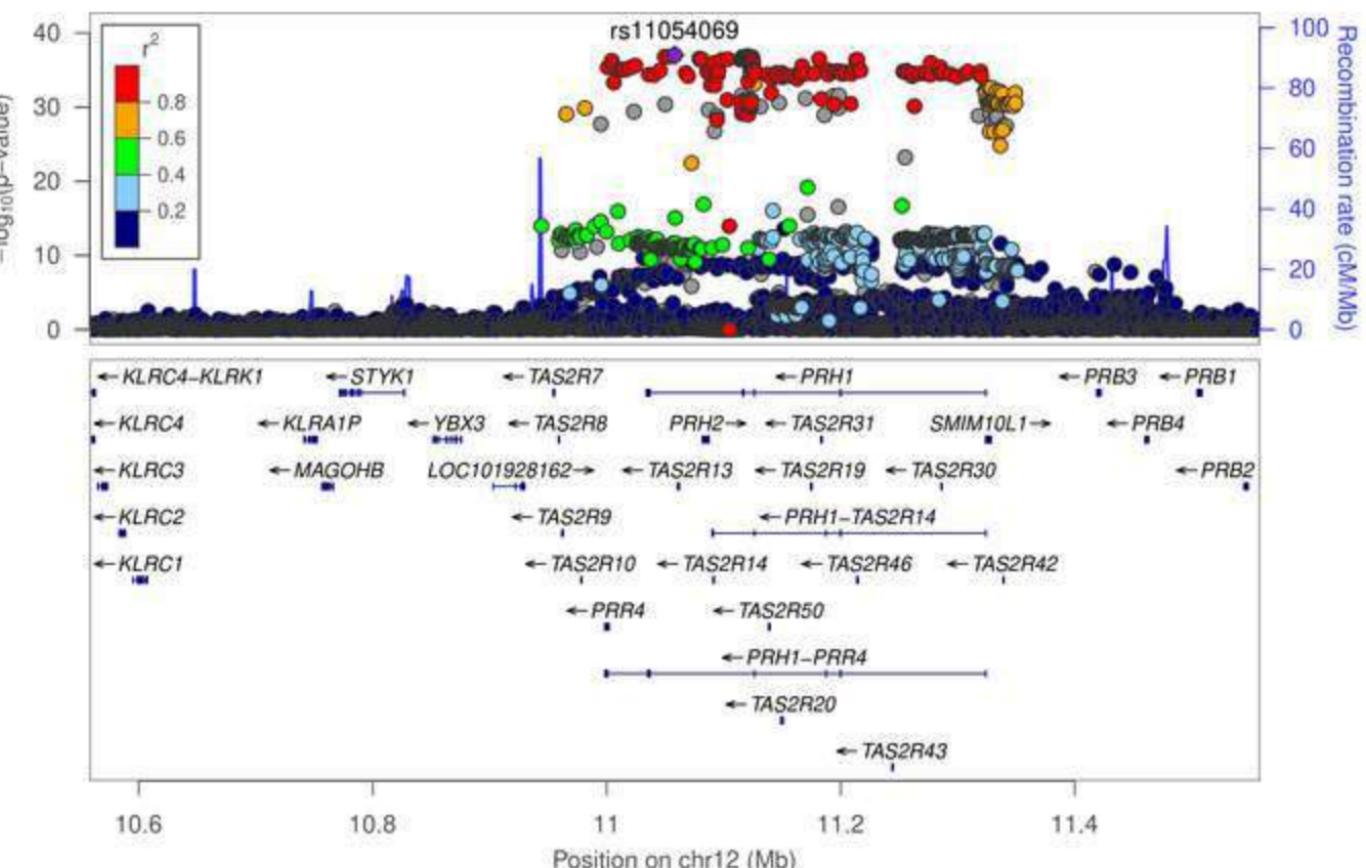
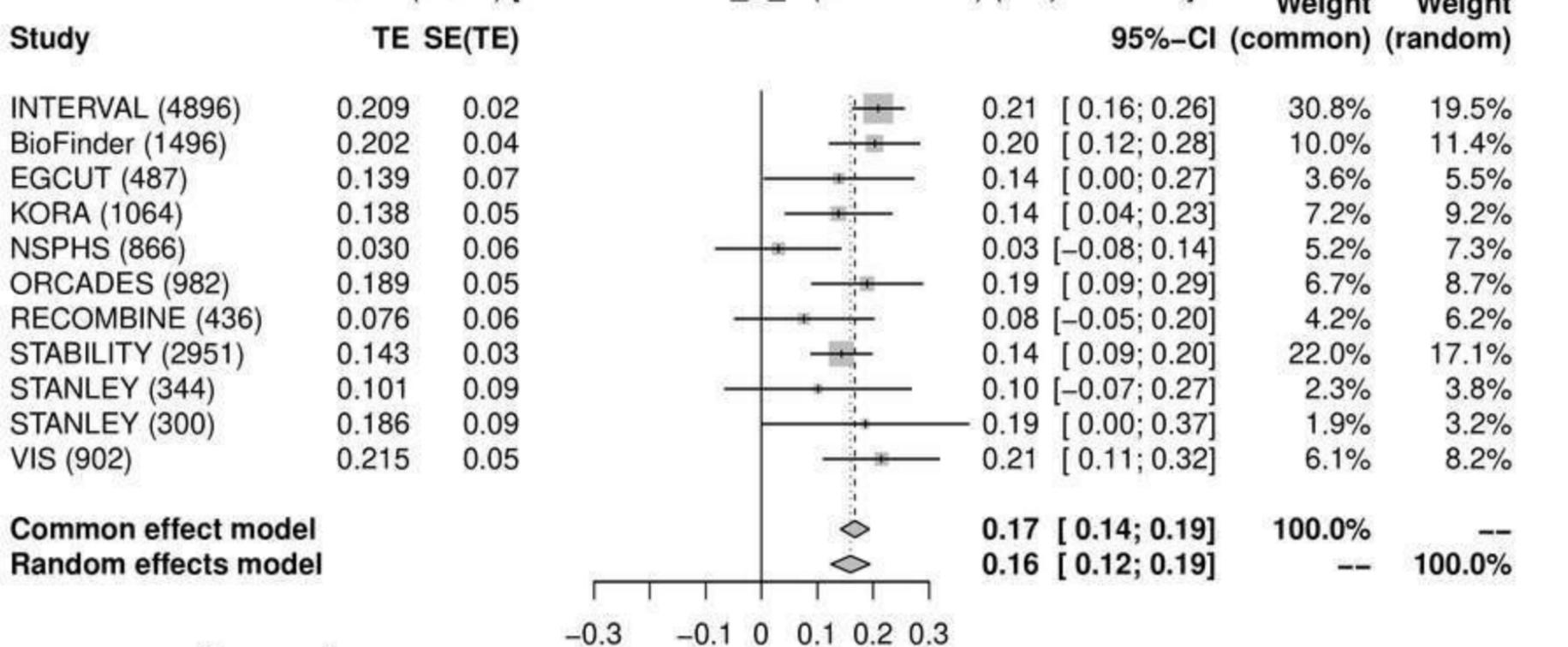


# CSF-1 (CSF1)-rs17610659

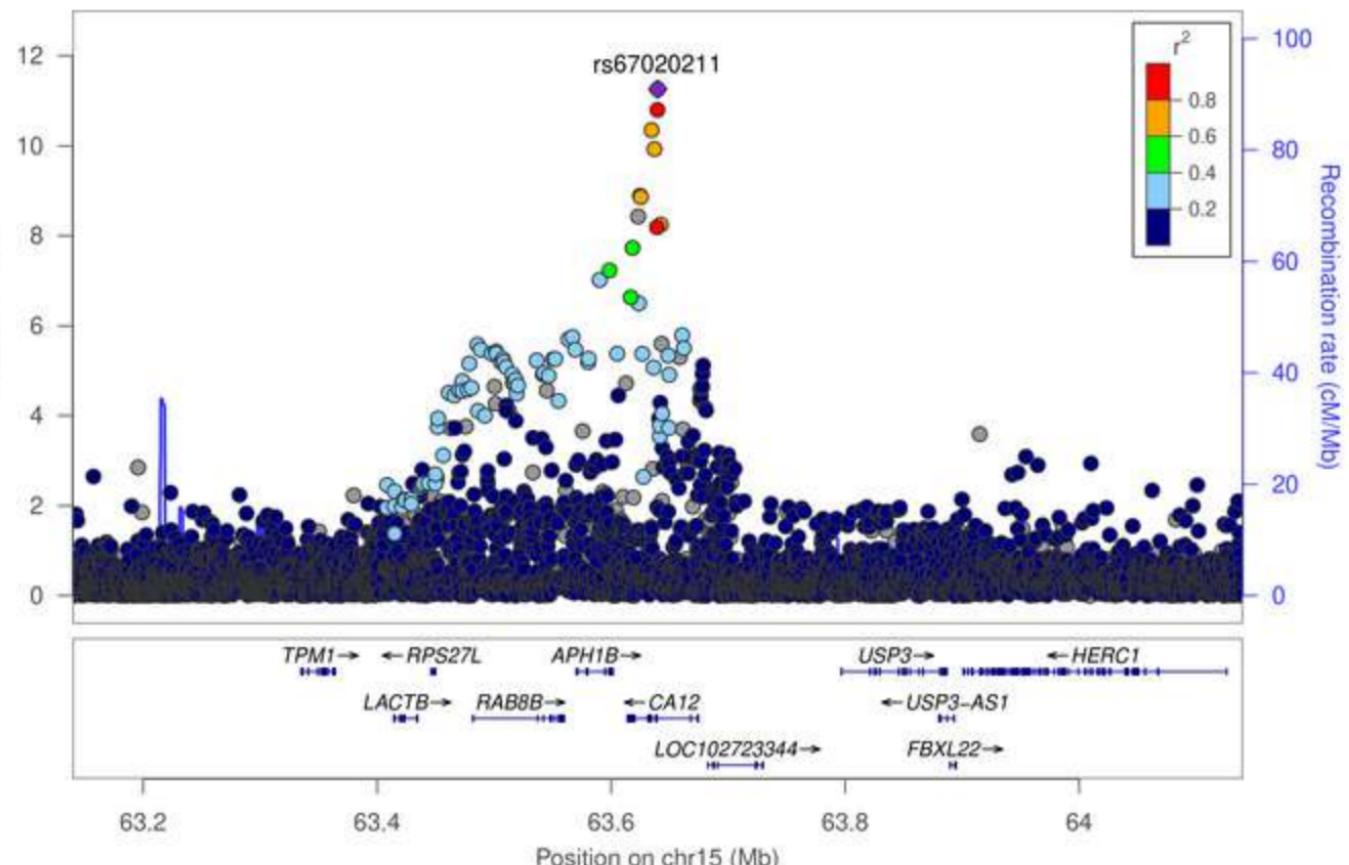
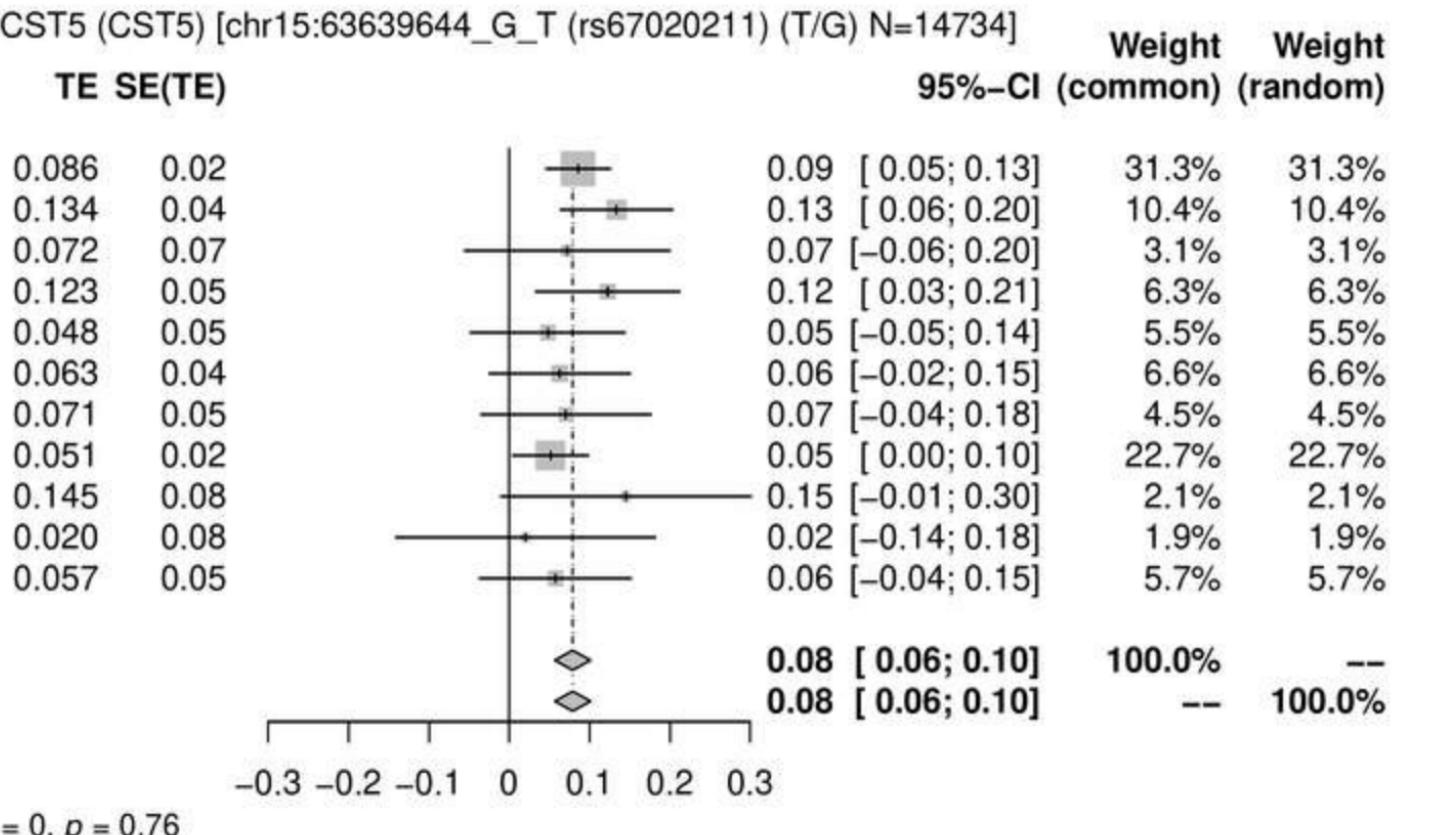


# CST5 (CST5)-rs11054069

CST5 (CST5) [chr12:11058117\_C\_T (rs11054069) (T/C) N=14724]

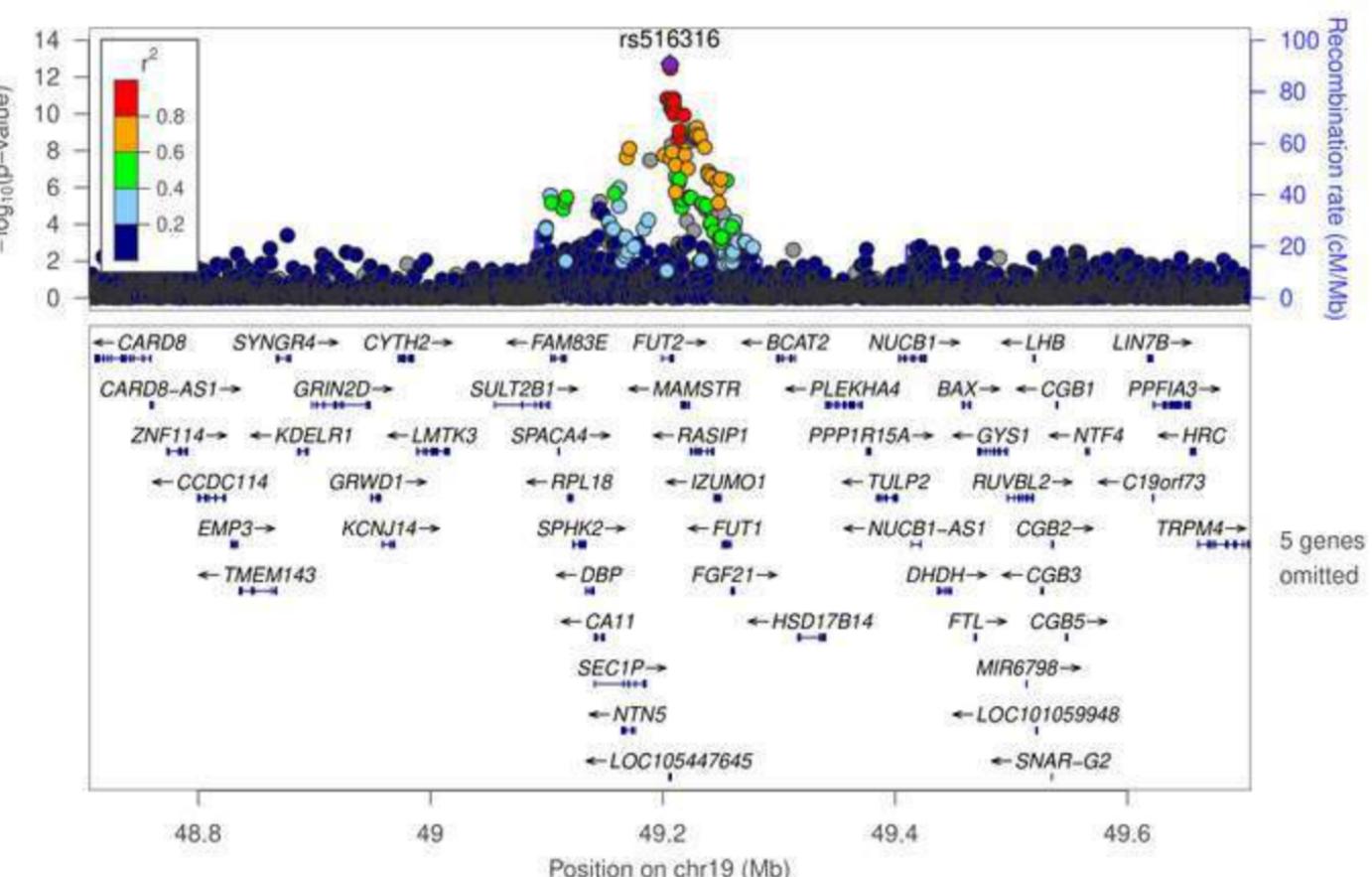
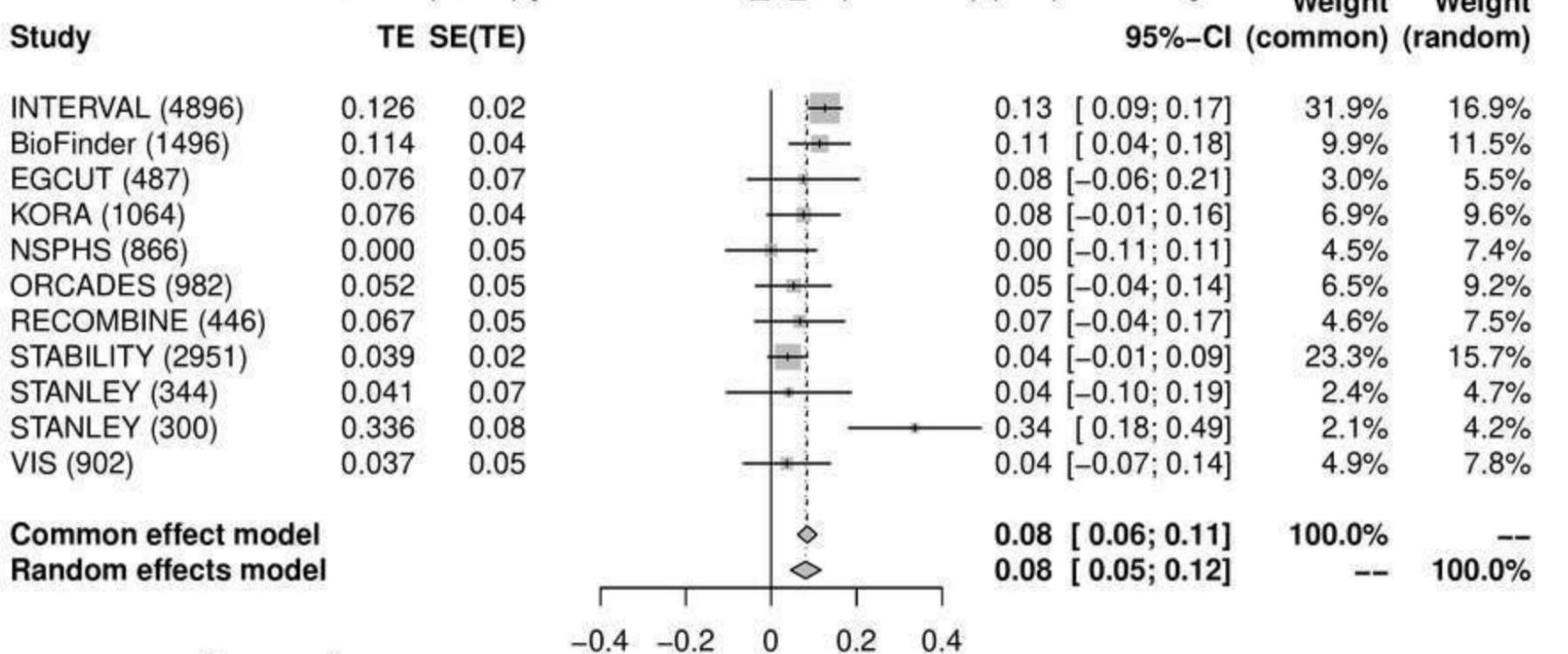


# CST5 (CST5)-rs67020211

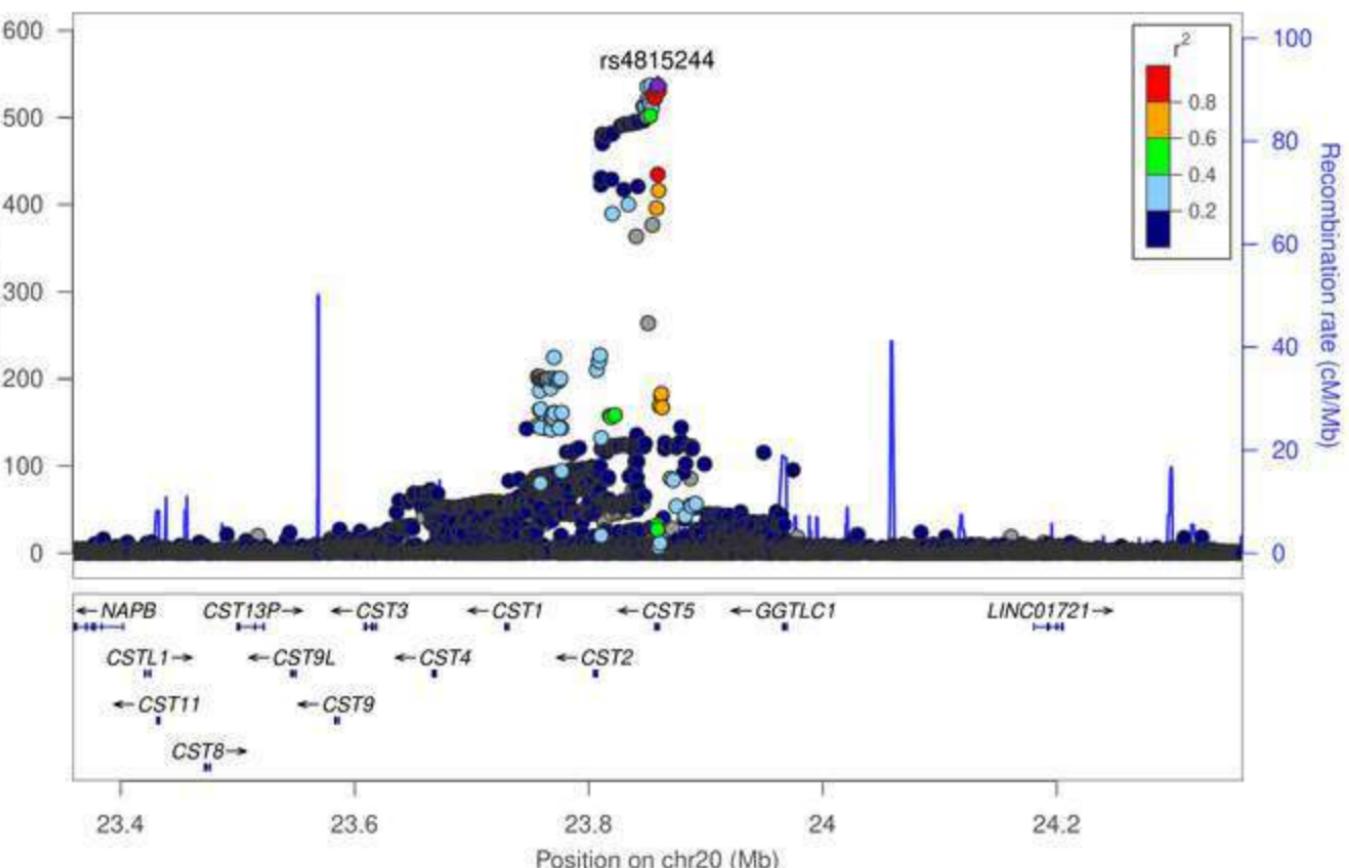
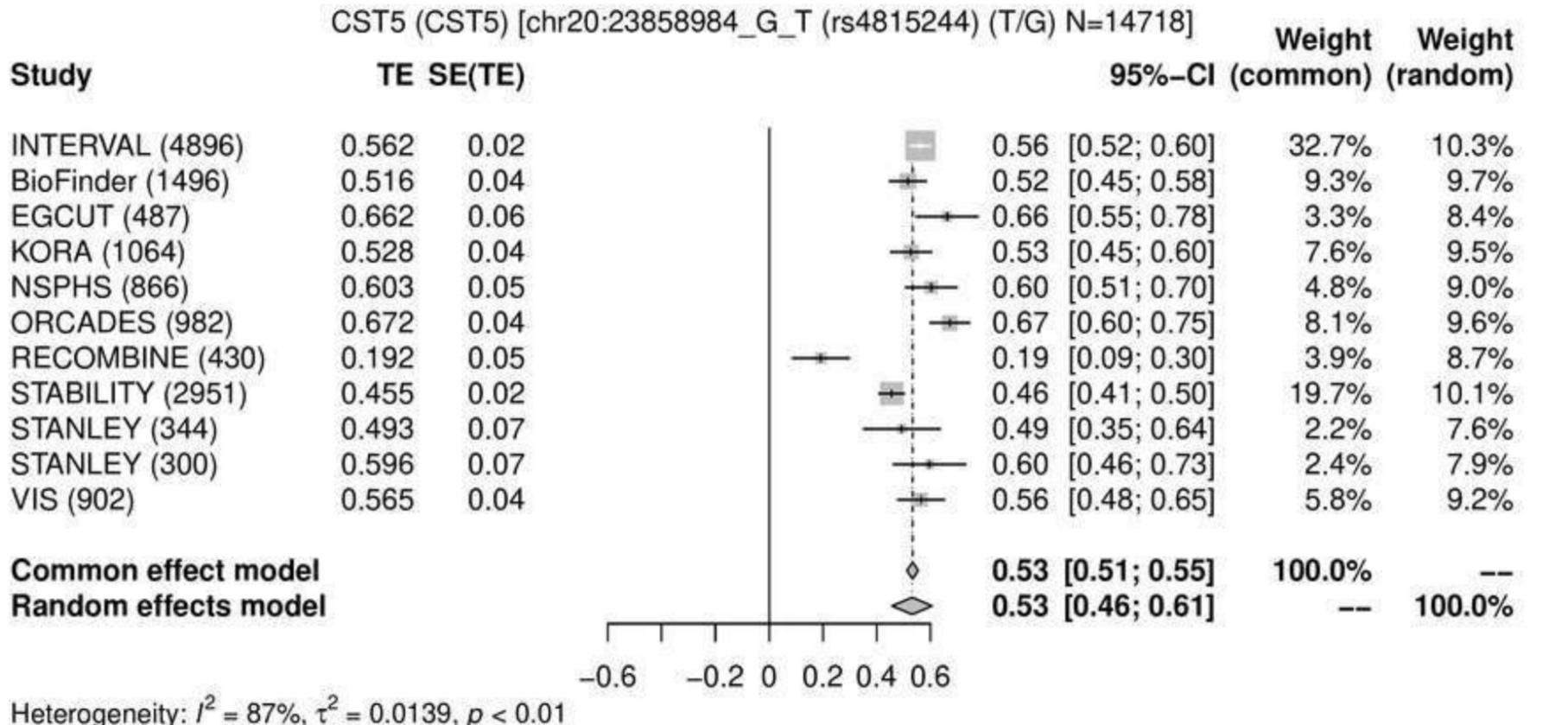


# CST5 (CST5)-rs516316

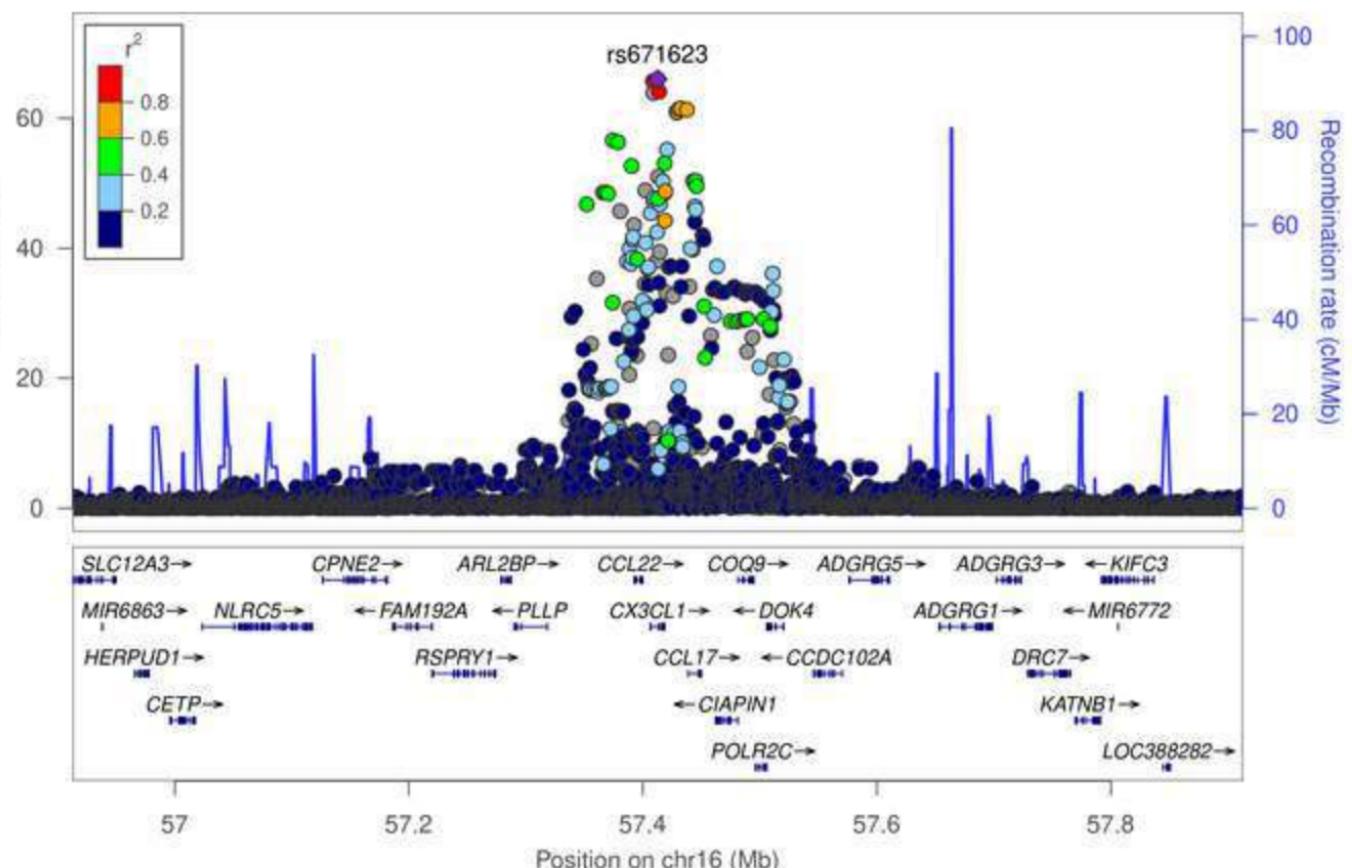
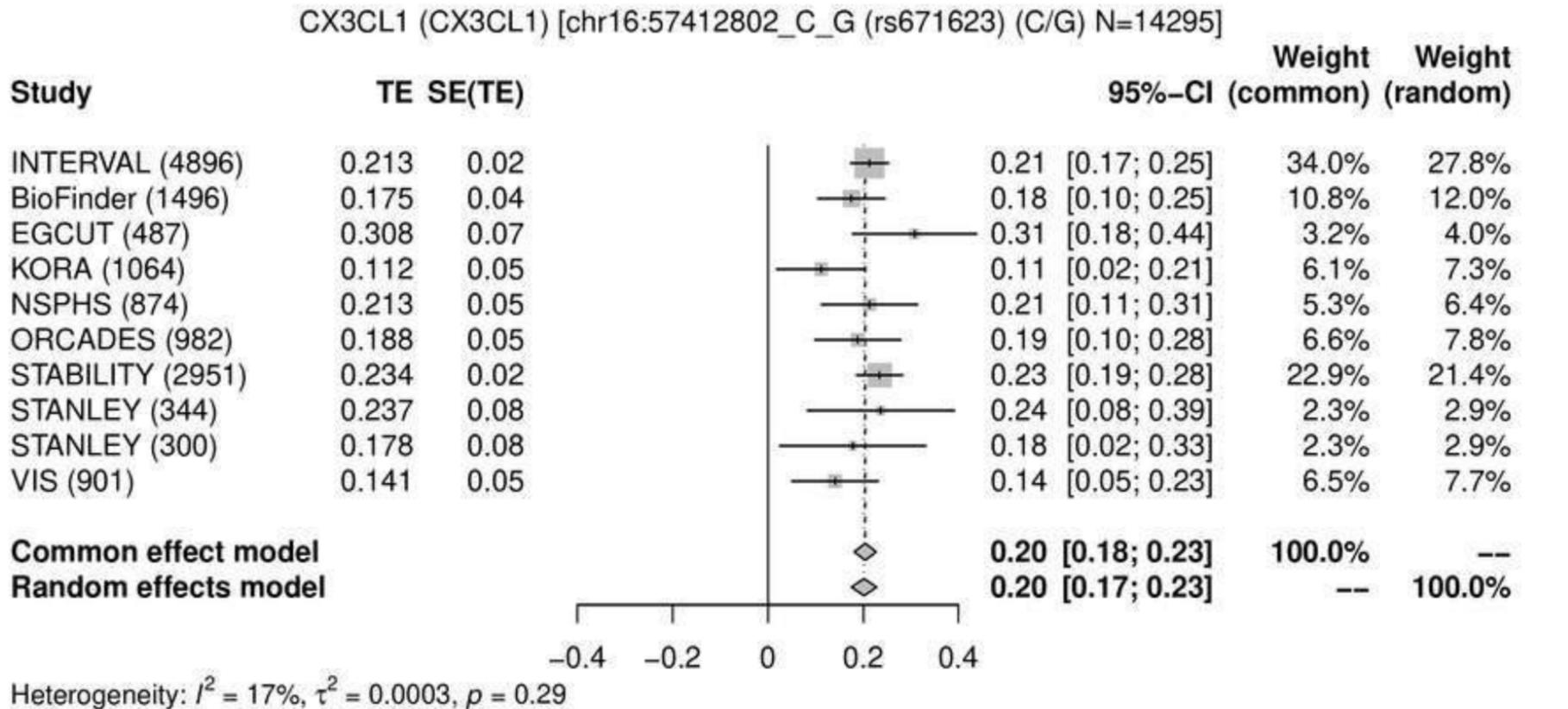
CST5 (CST5) [chr19:49206145\_C\_G (rs516316) (C/G) N=14734]



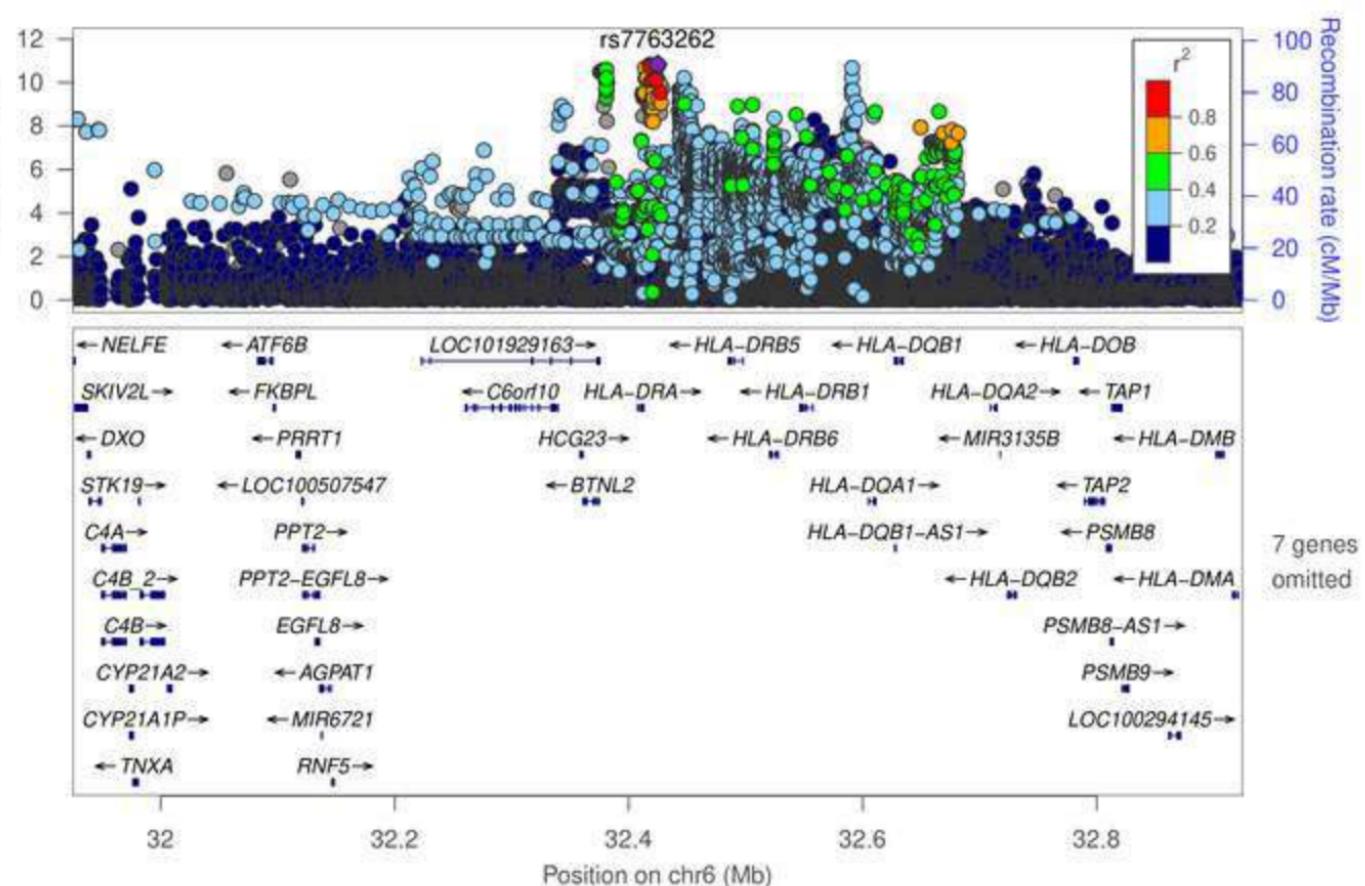
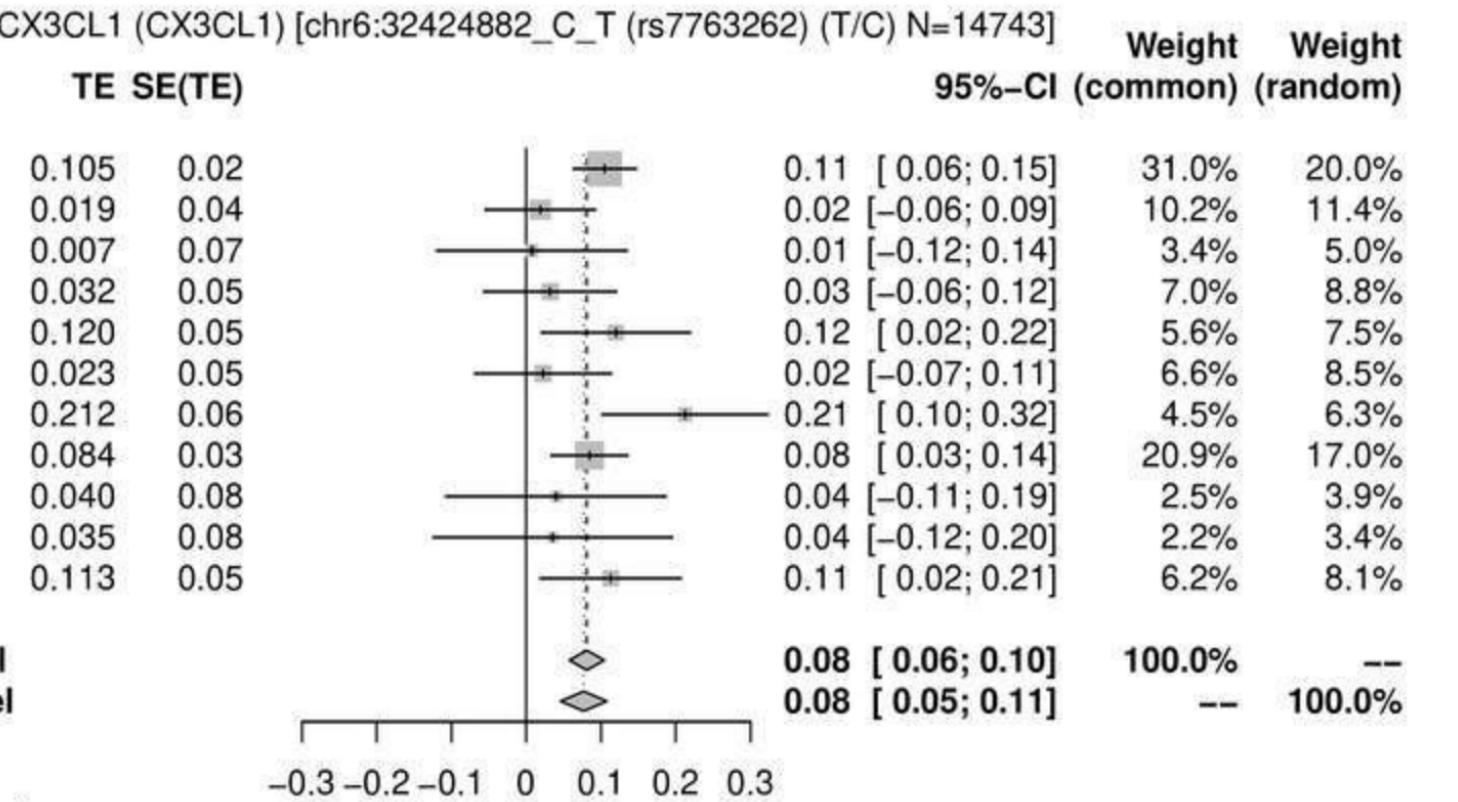
# CST5 (CST5)-rs4815244



# CX3CL1 (CX3CL1)-rs671623

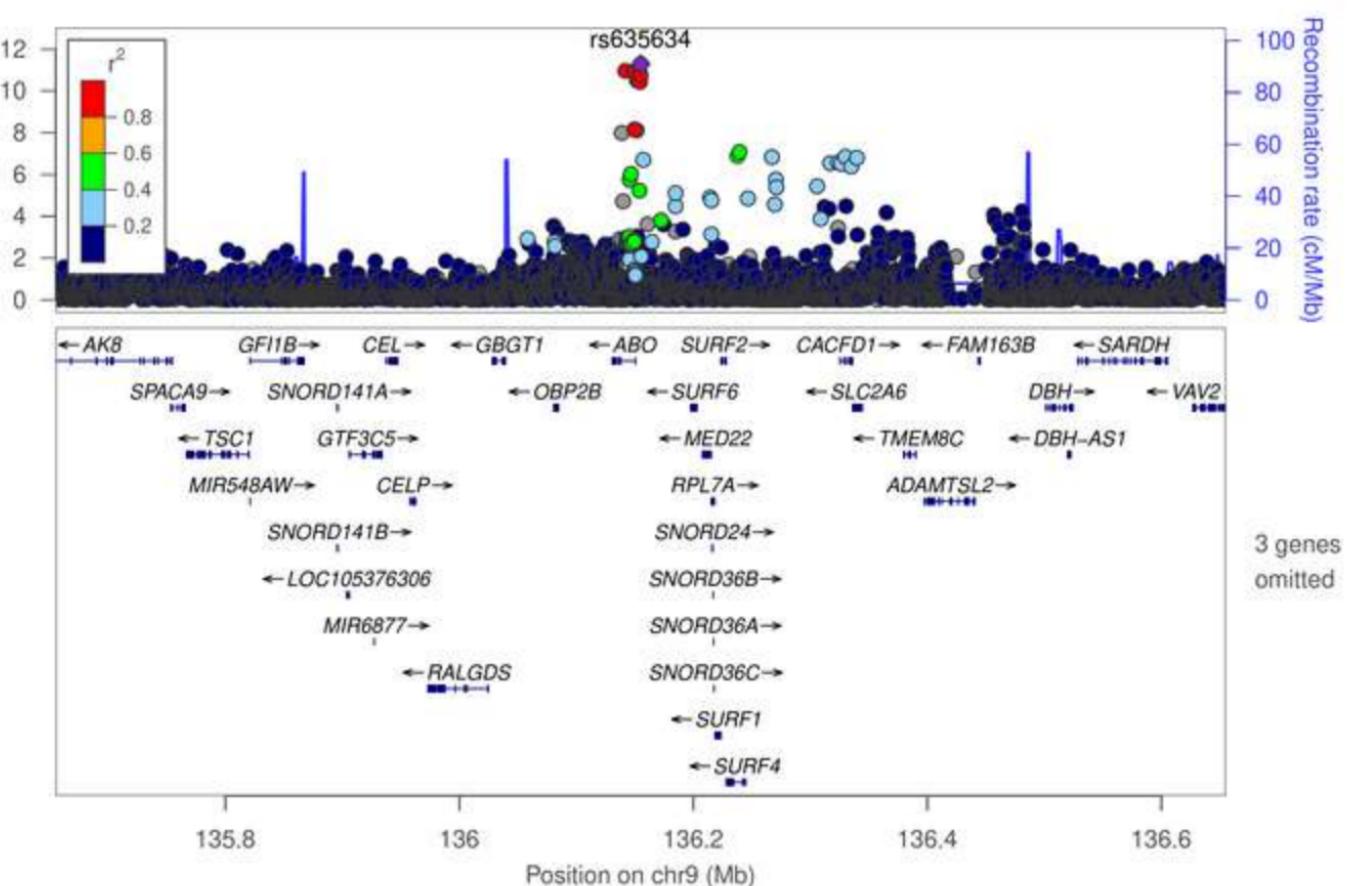
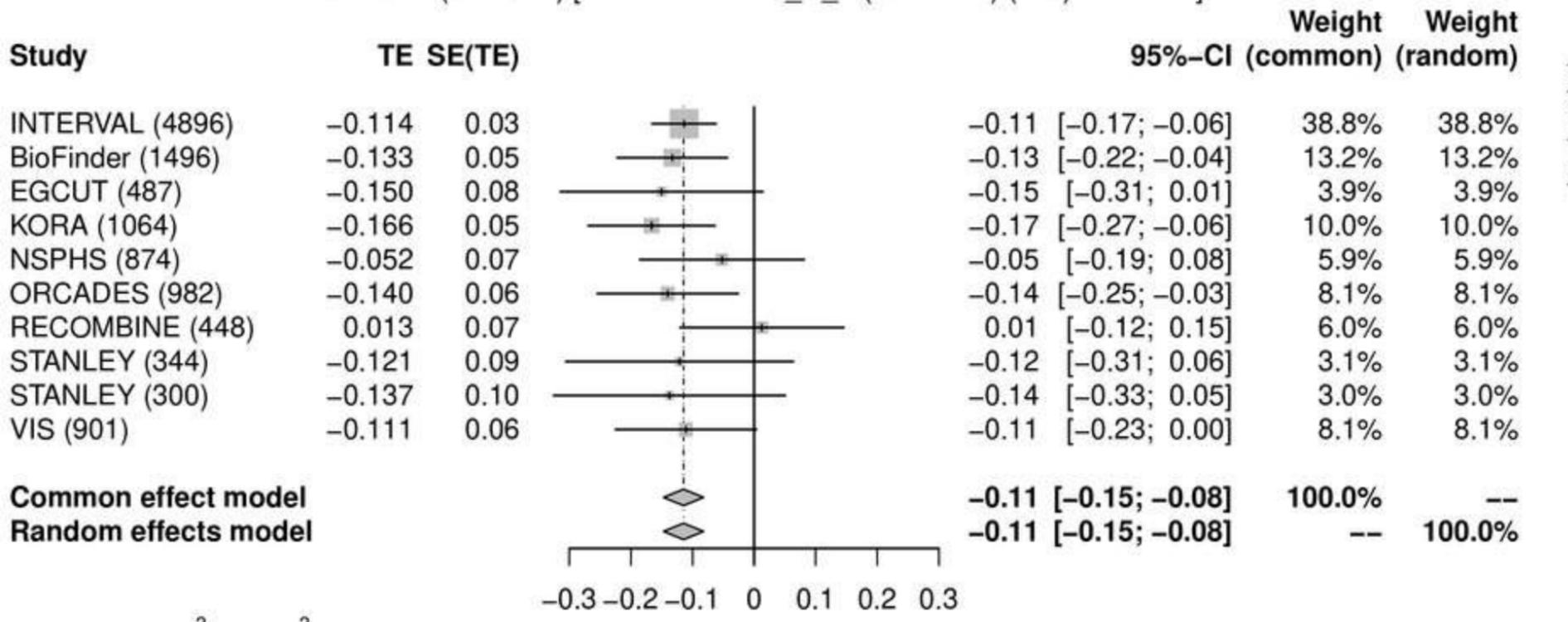


# CX3CL1 (CX3CL1)-rs7763262



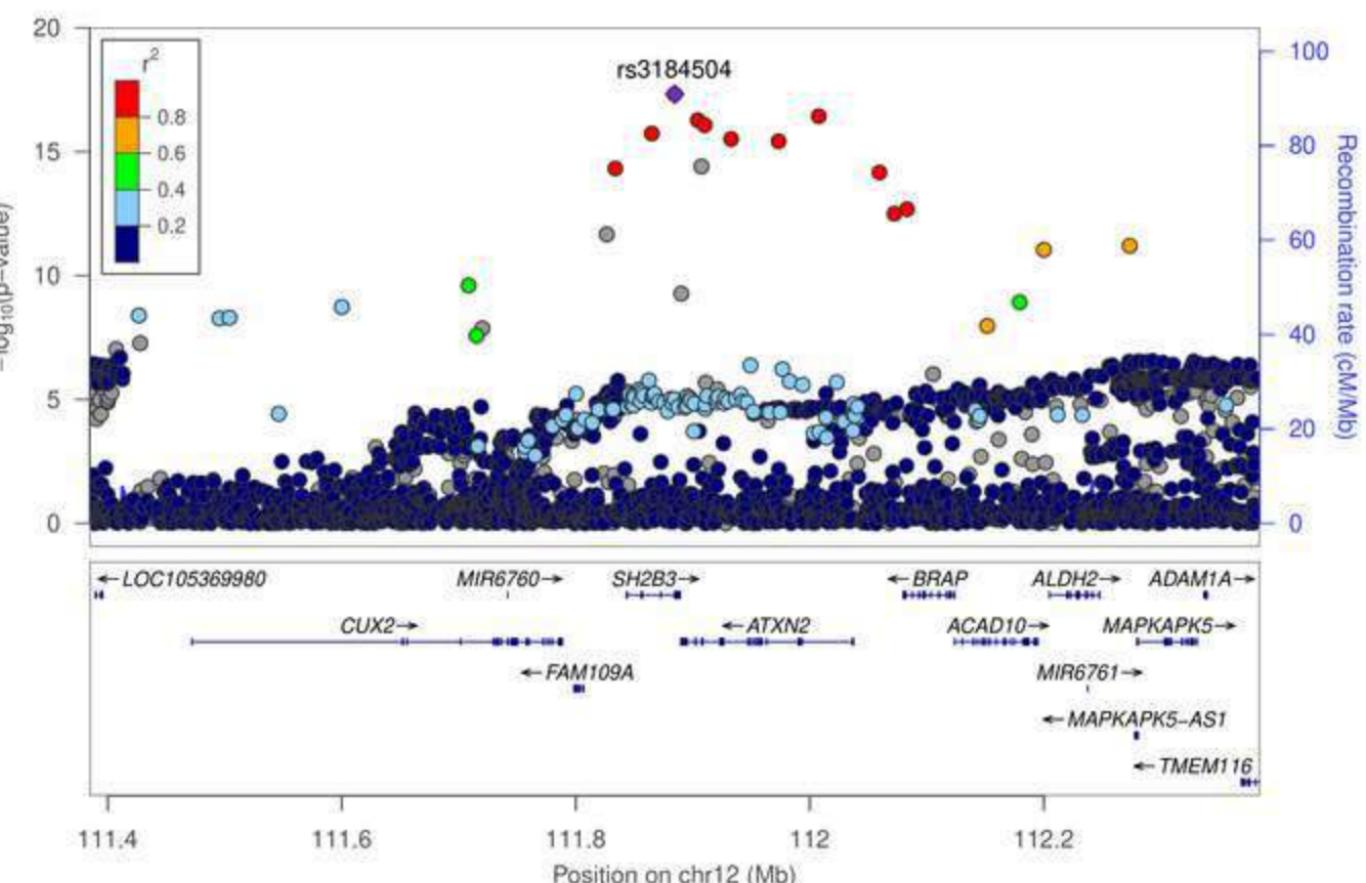
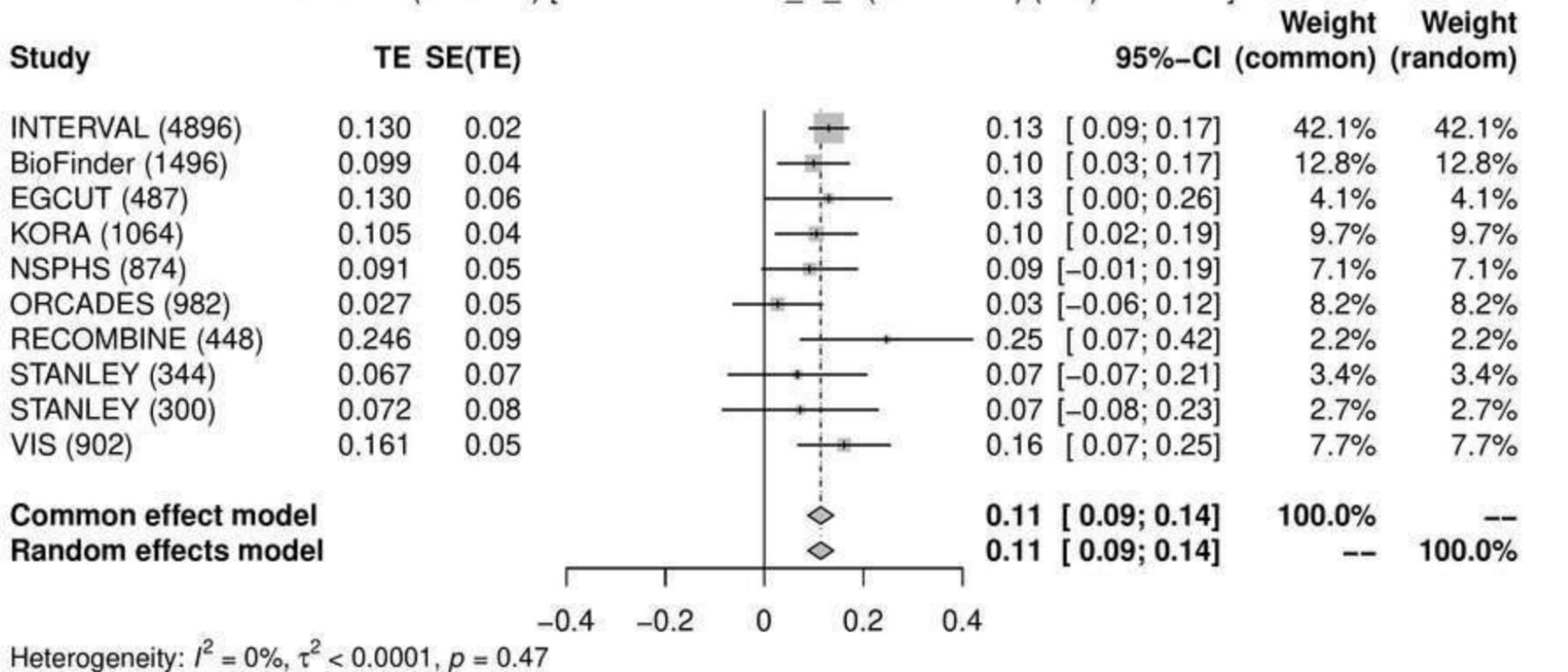
# CX3CL1 (CX3CL1)-rs635634

CX3CL1 (CX3CL1) [chr9:136155000\_C\_T (rs635634) (T/C) N=11792]



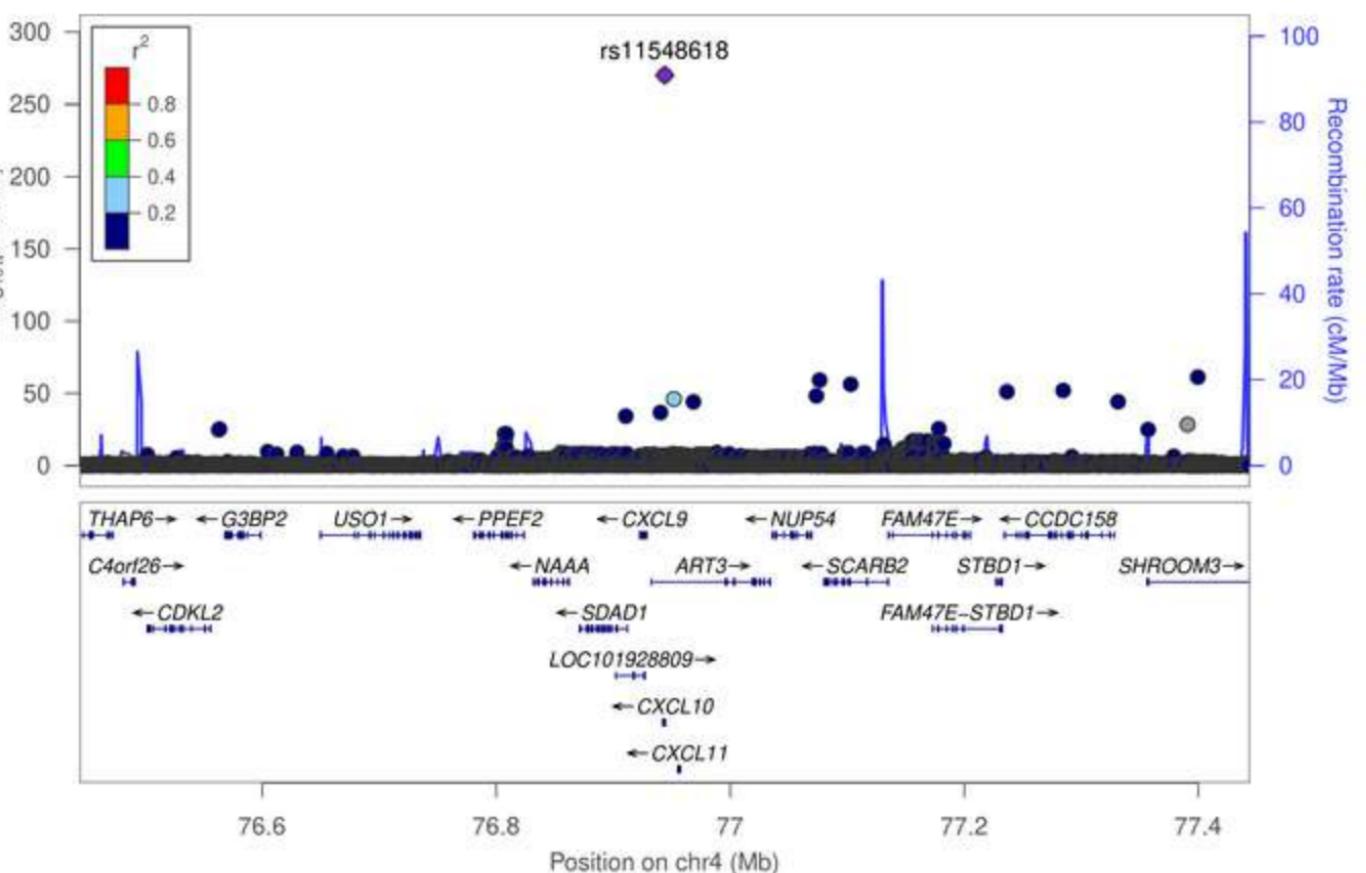
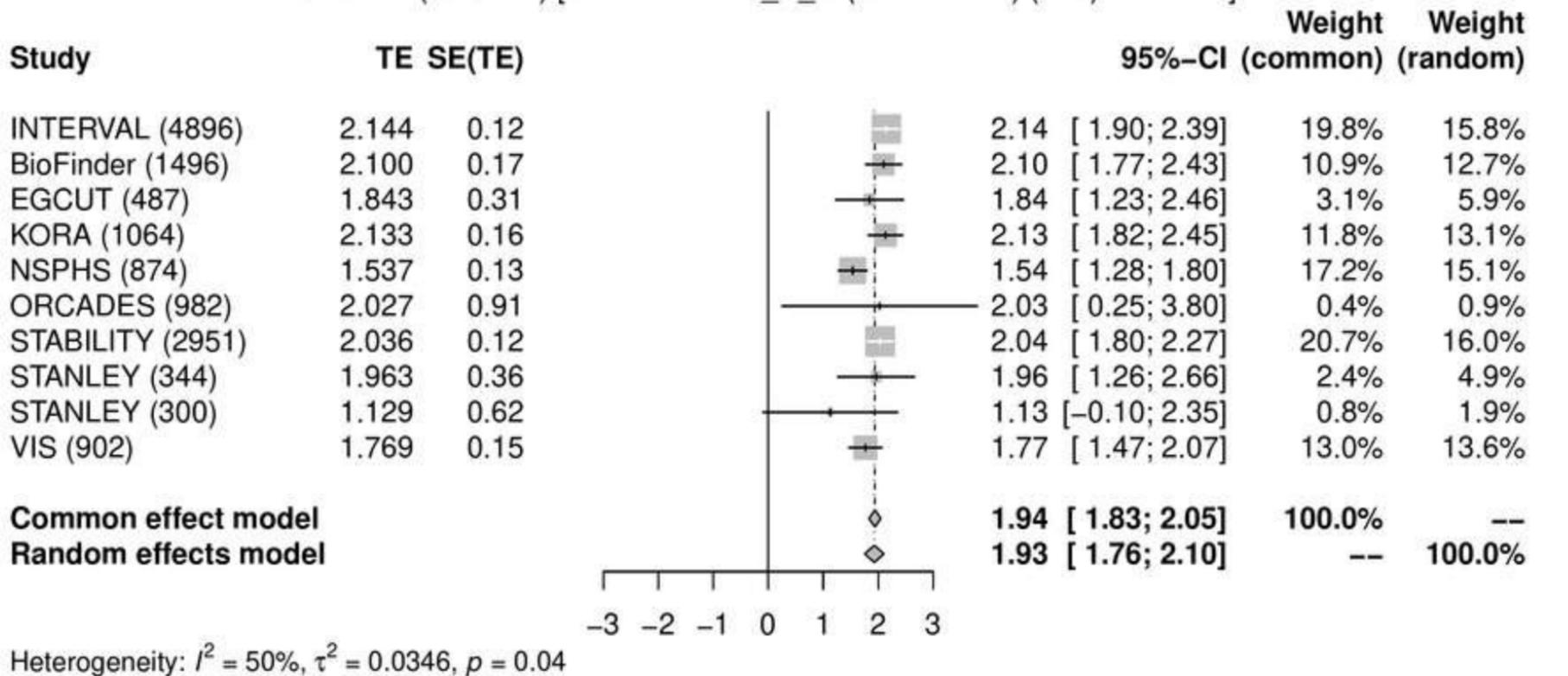
# CXCL10 (CXCL10)-rs3184504

CXCL10 (CXCL10) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11793]



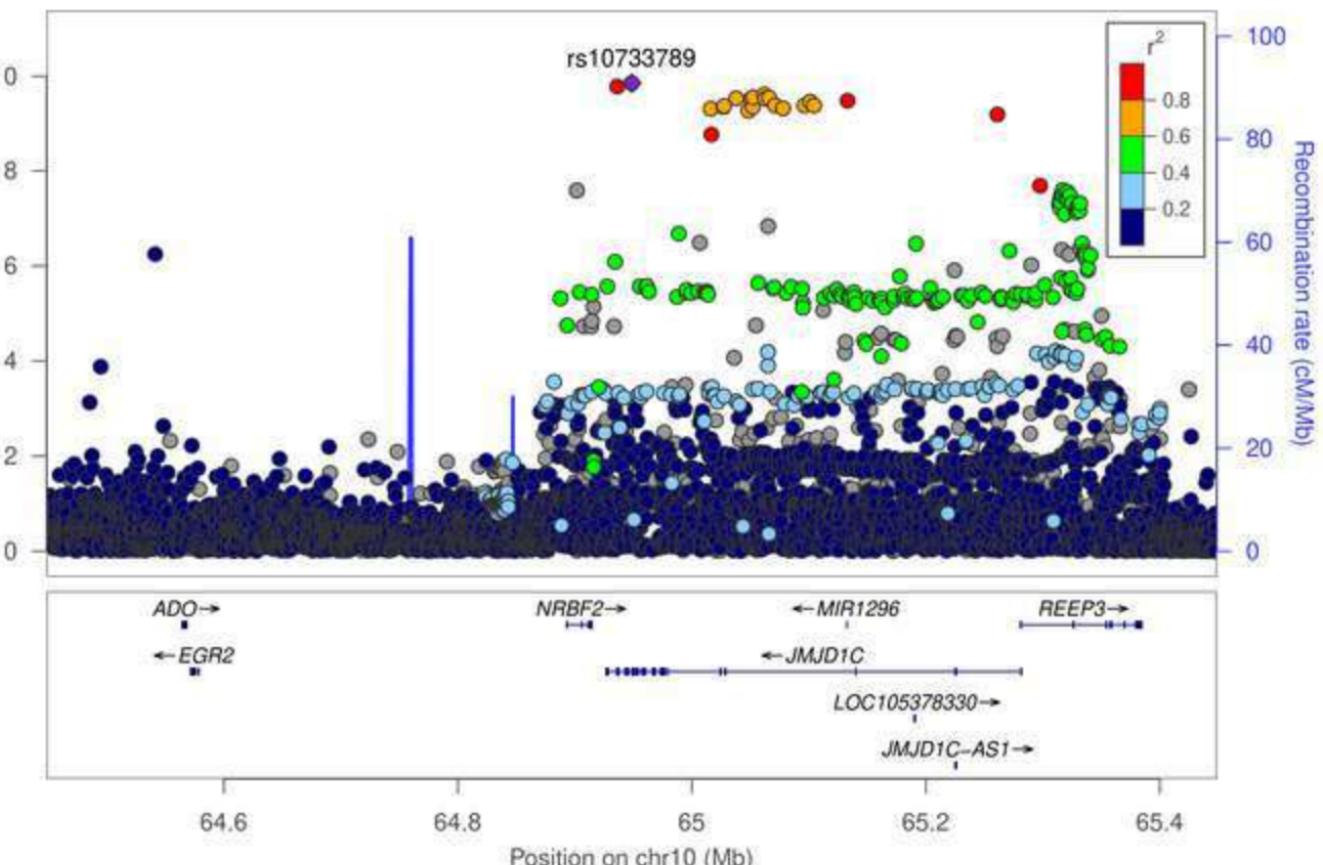
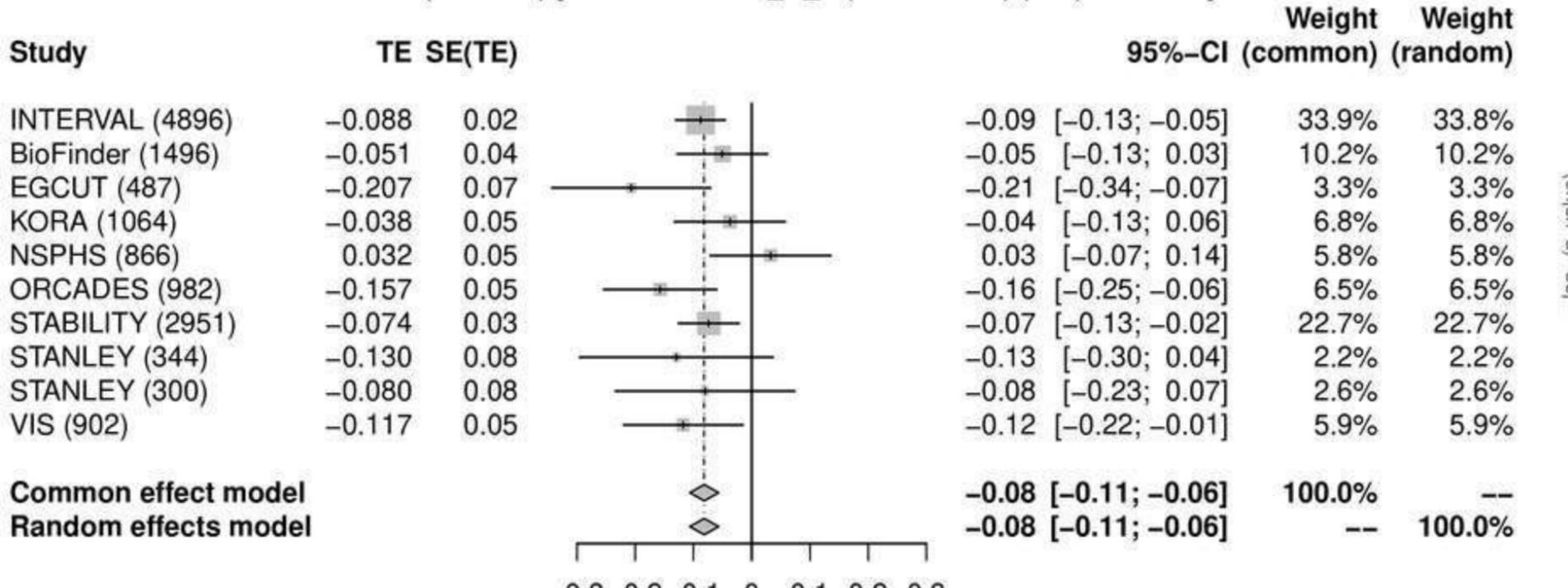
# CXCL10 (CXCL10)-rs11548618

CXCL10 (CXCL10) [chr4:76943947\_A\_G (rs11548618) (A/G) N=14296]



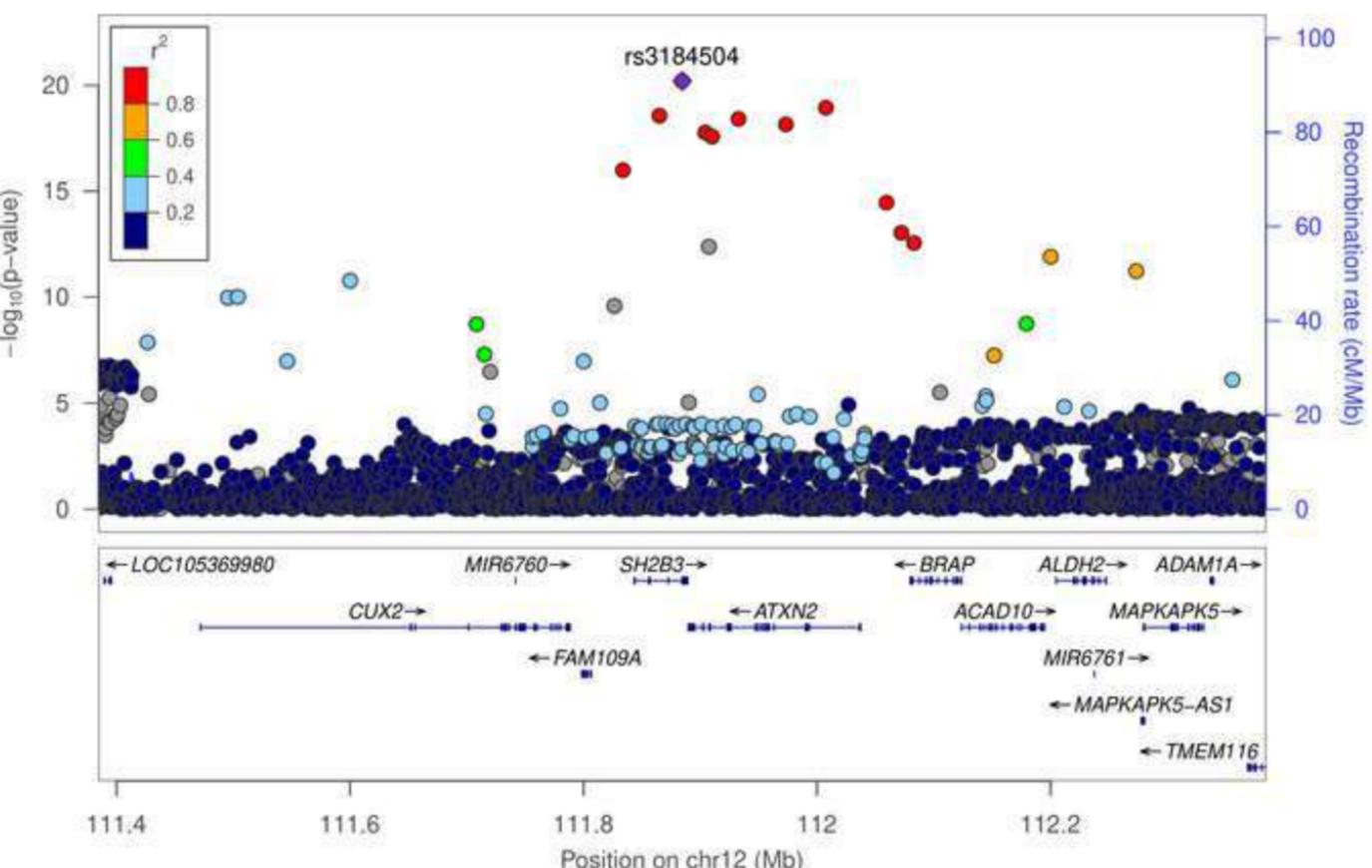
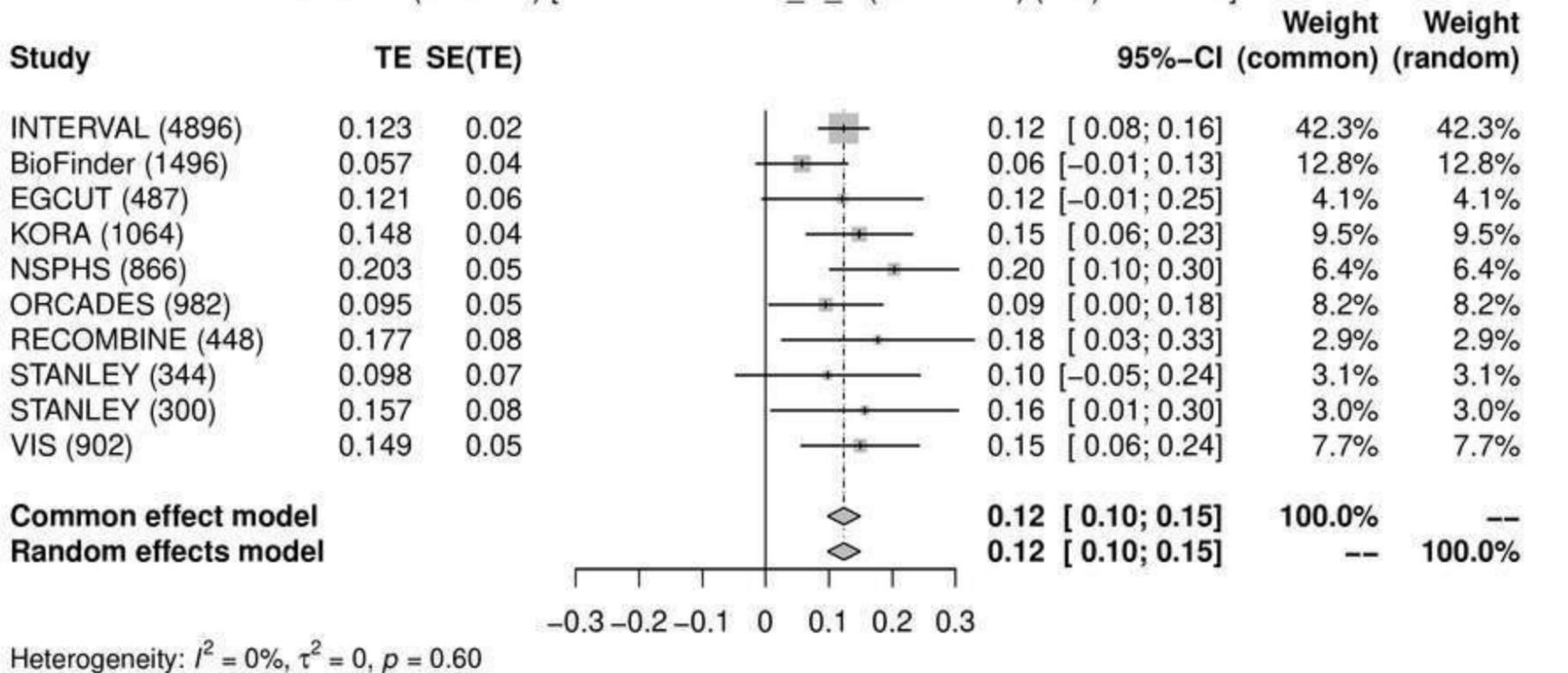
# CXCL11 (CXCL11)-rs10733789

CXCL11 (CXCL11) [chr10:64948684\_C\_T (rs10733789) (T/C) N=14288]

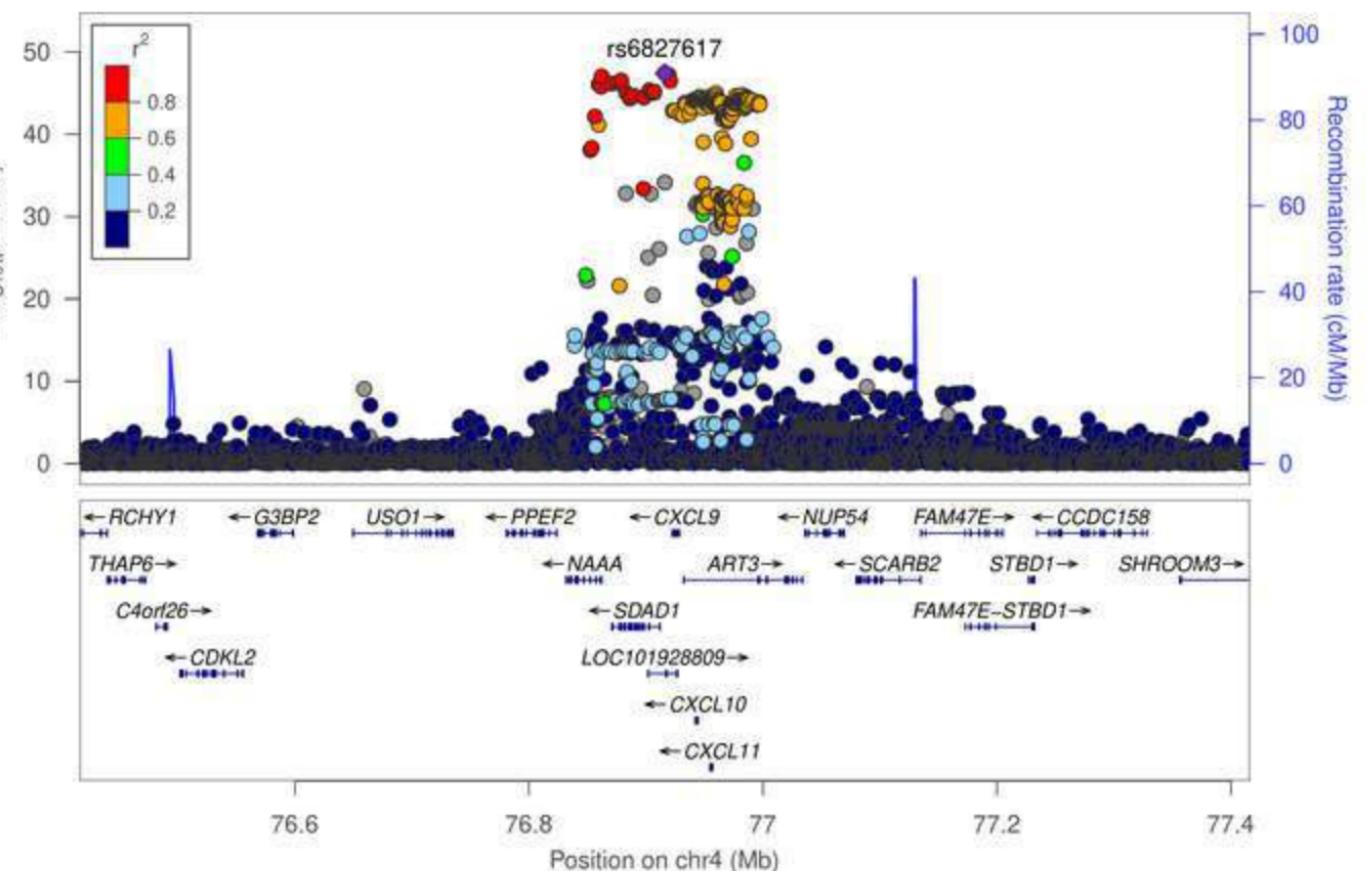
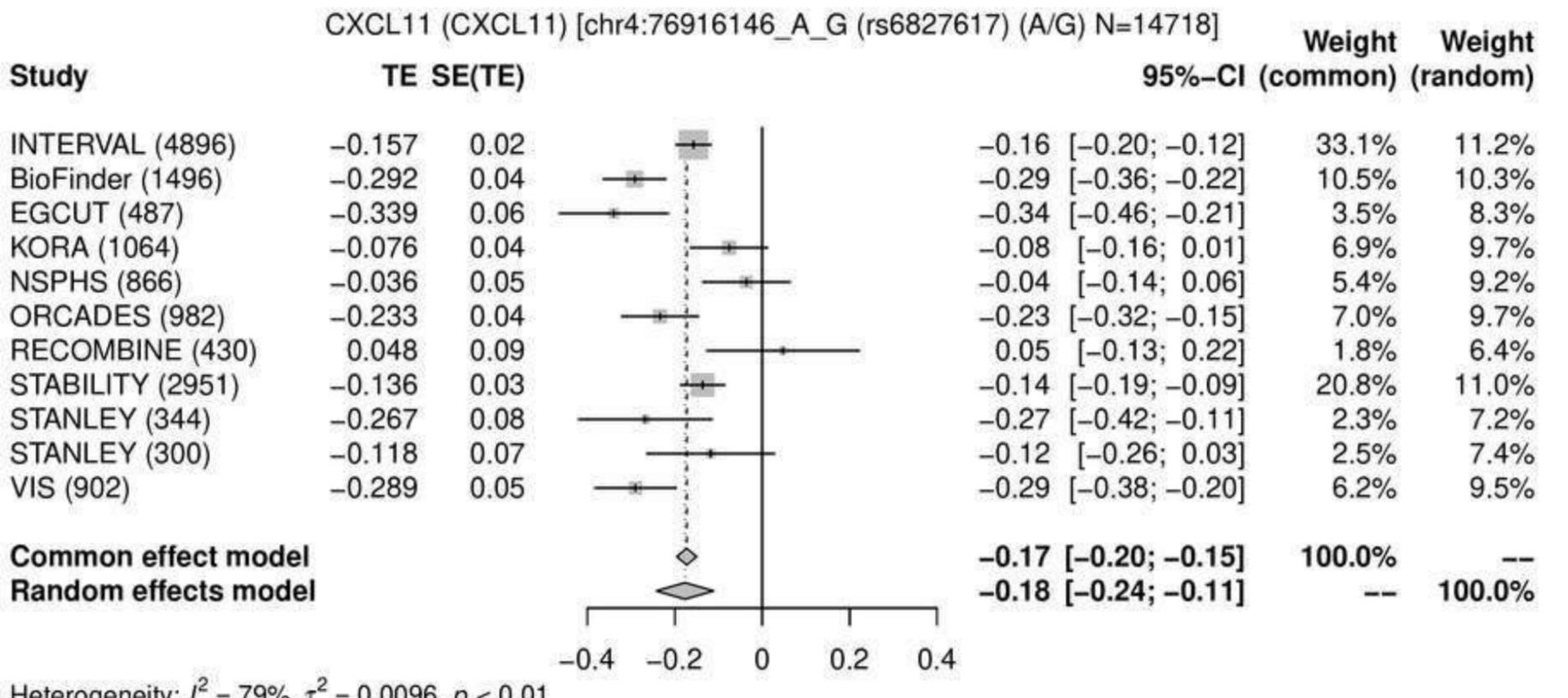


# CXCL11 (CXCL11)-rs3184504

CXCL11 (CXCL11) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11785]

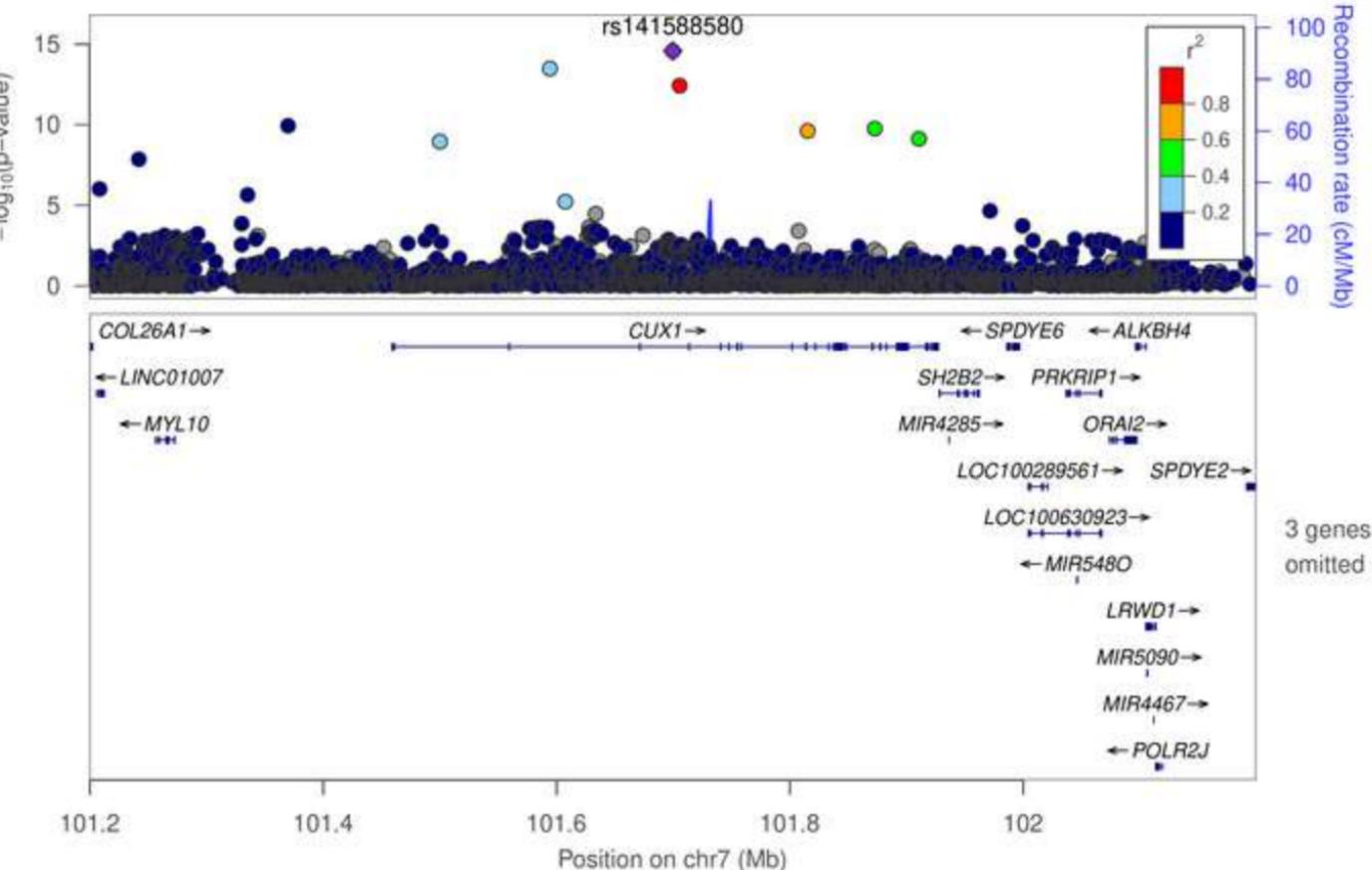
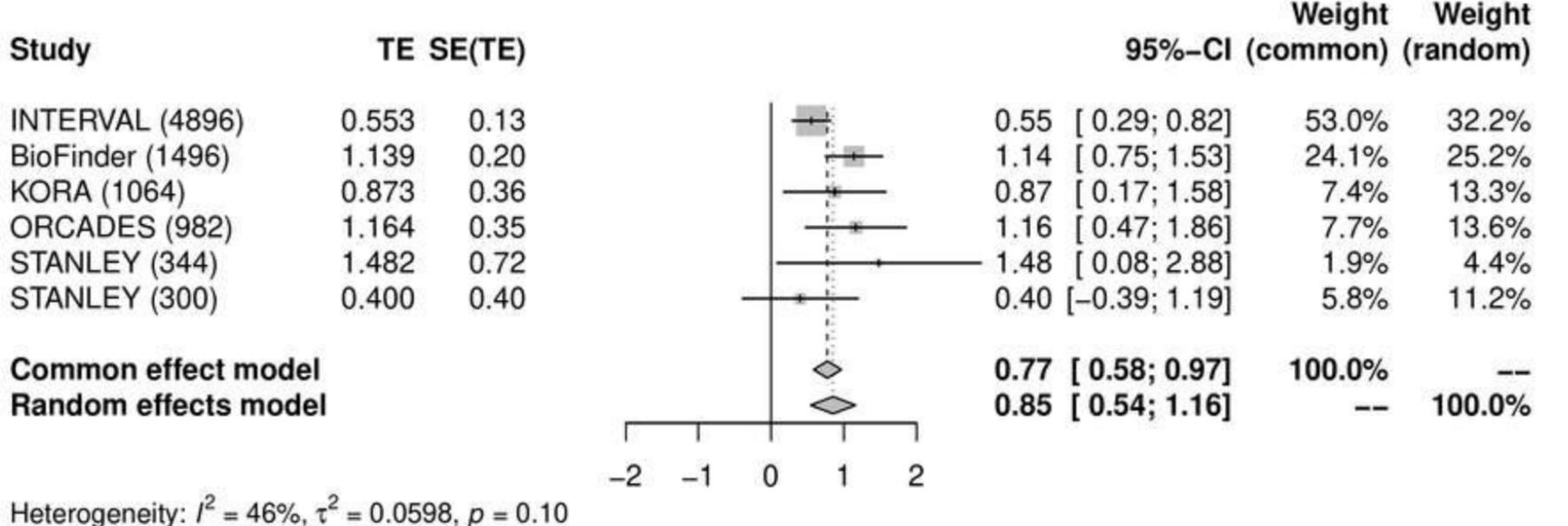


# CXCL11 (CXCL11)-rs6827617

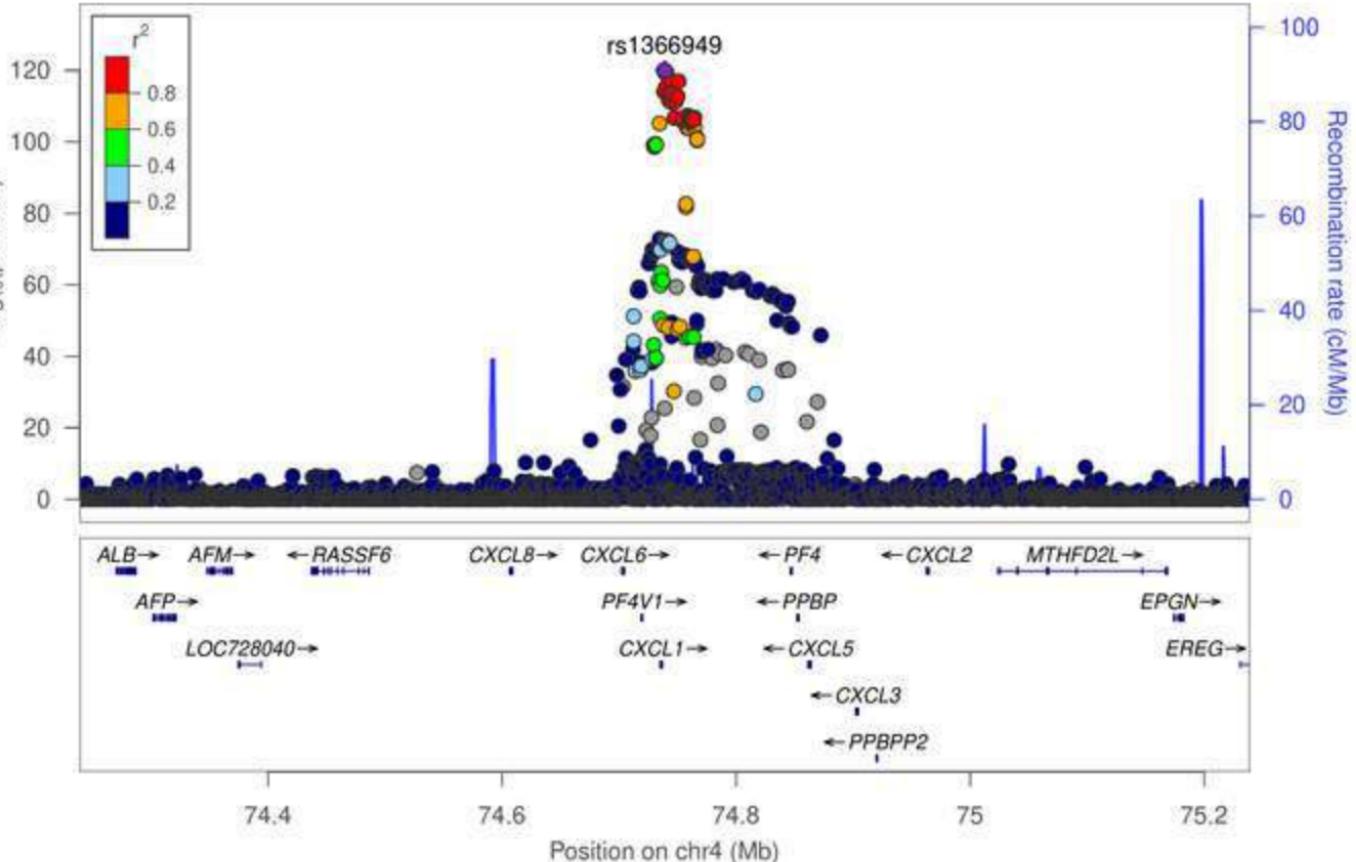
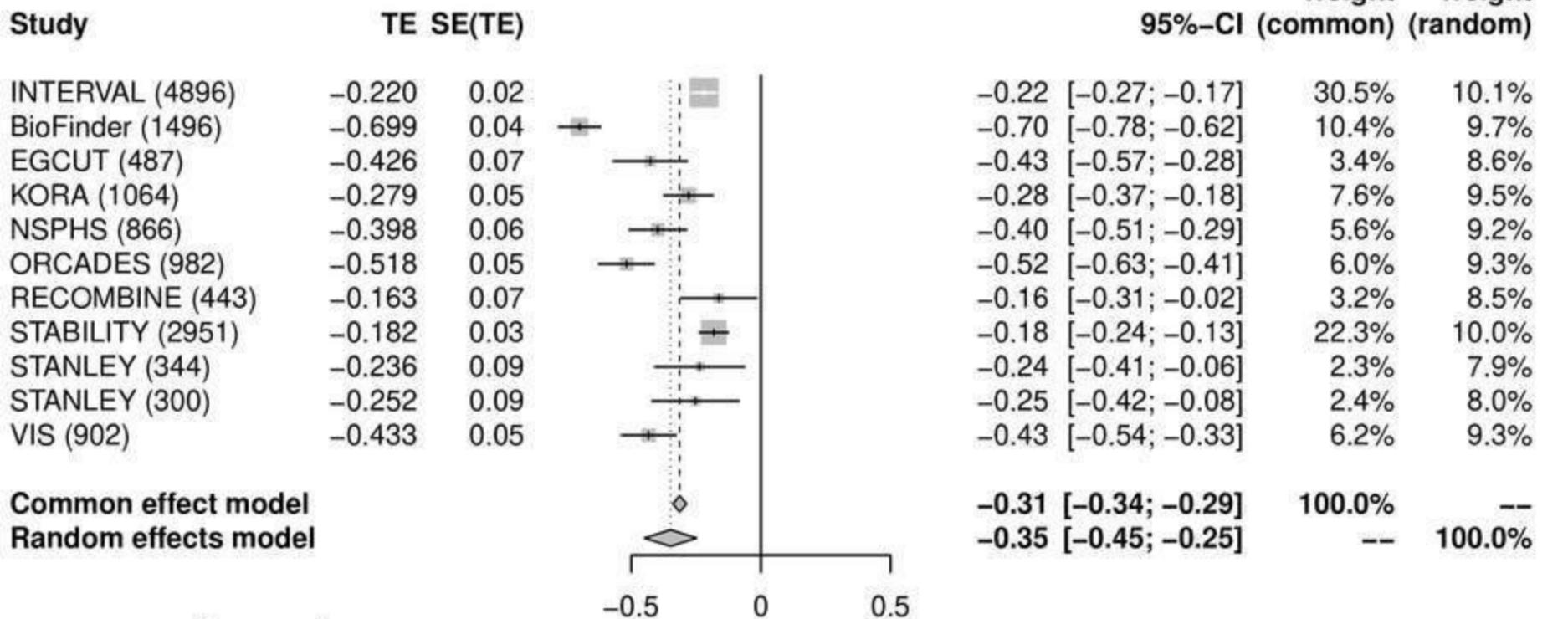


# CXCL11 (CXCL11)-rs141588580

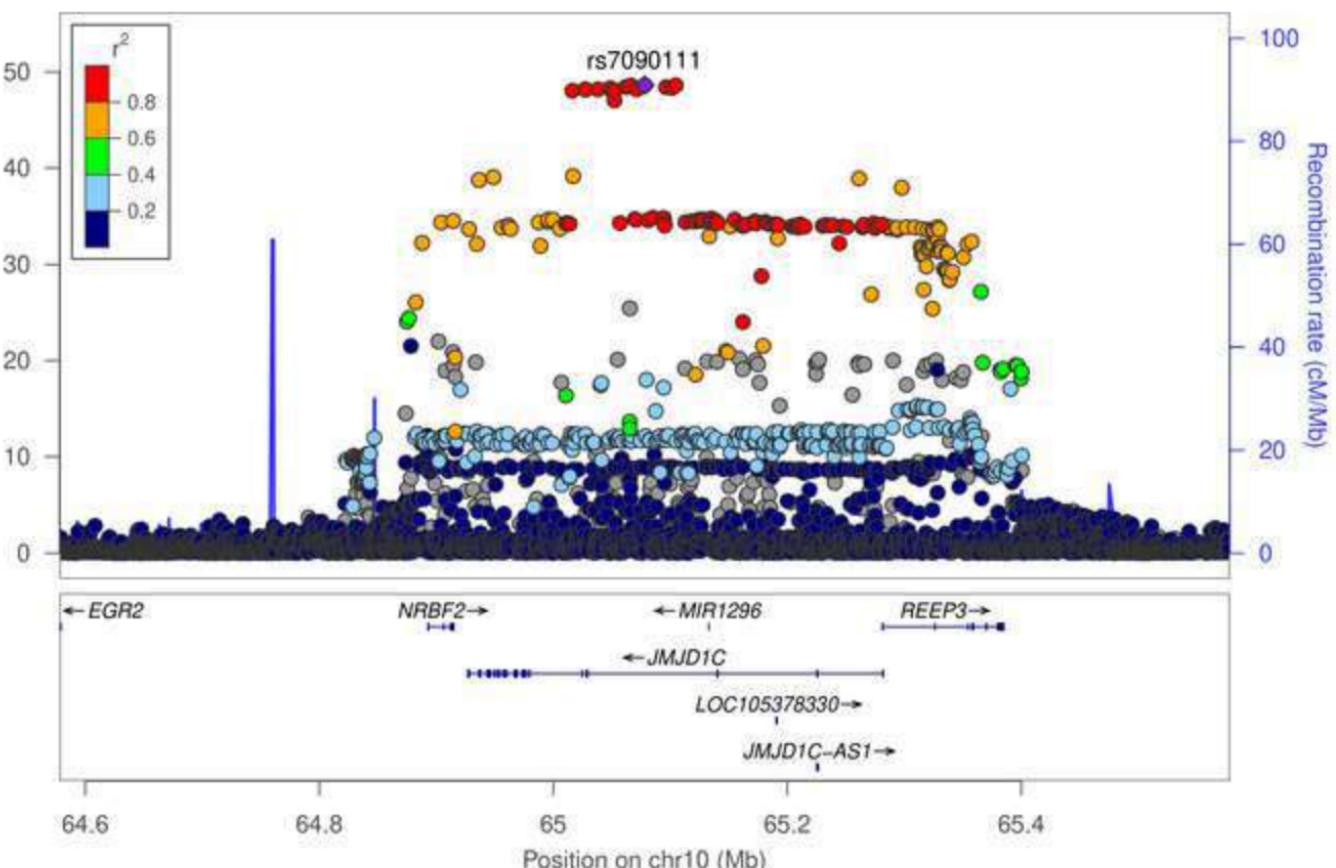
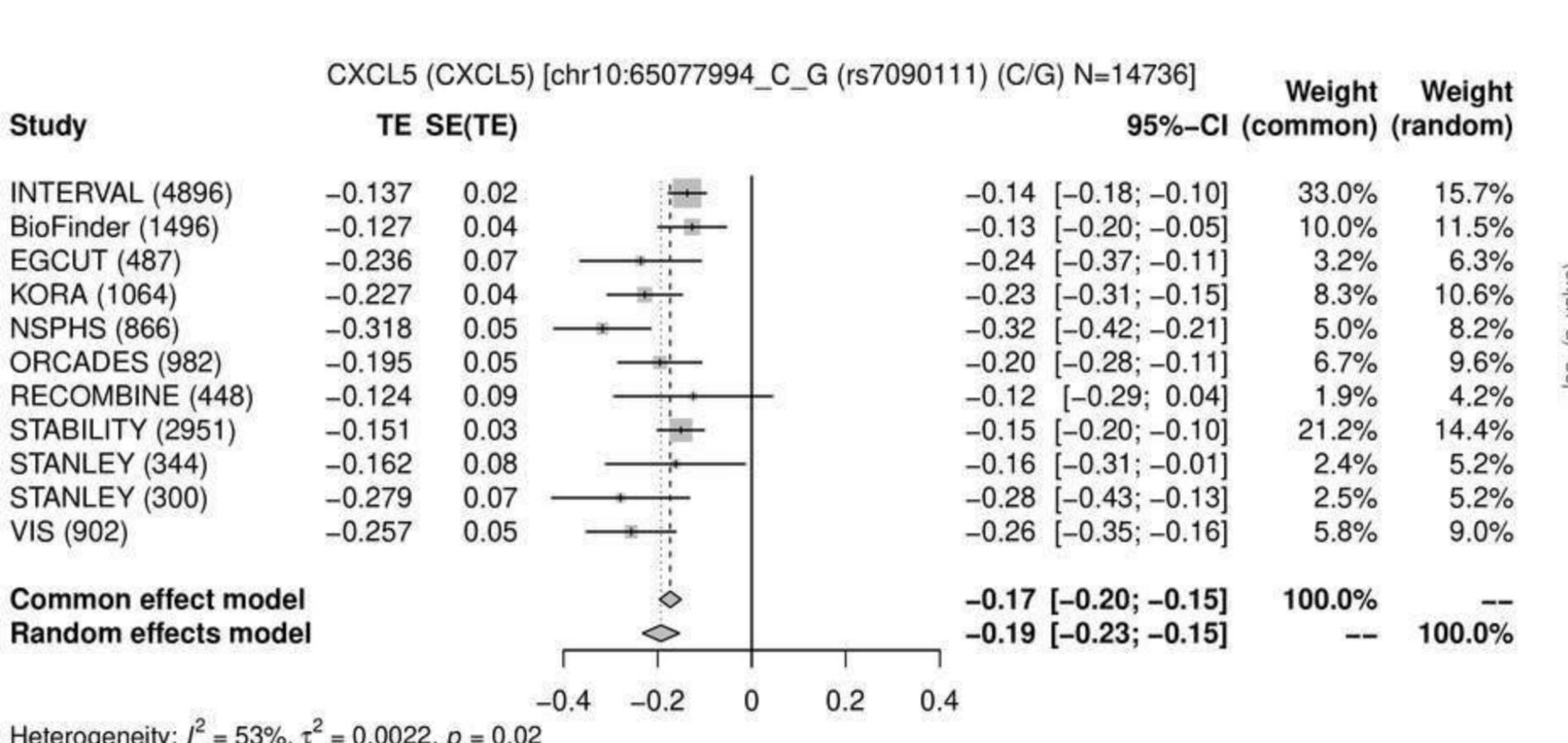
CXCL11 (CXCL11) [chr7:101699589\_G\_T (rs141588580) (T/G) N=9082]



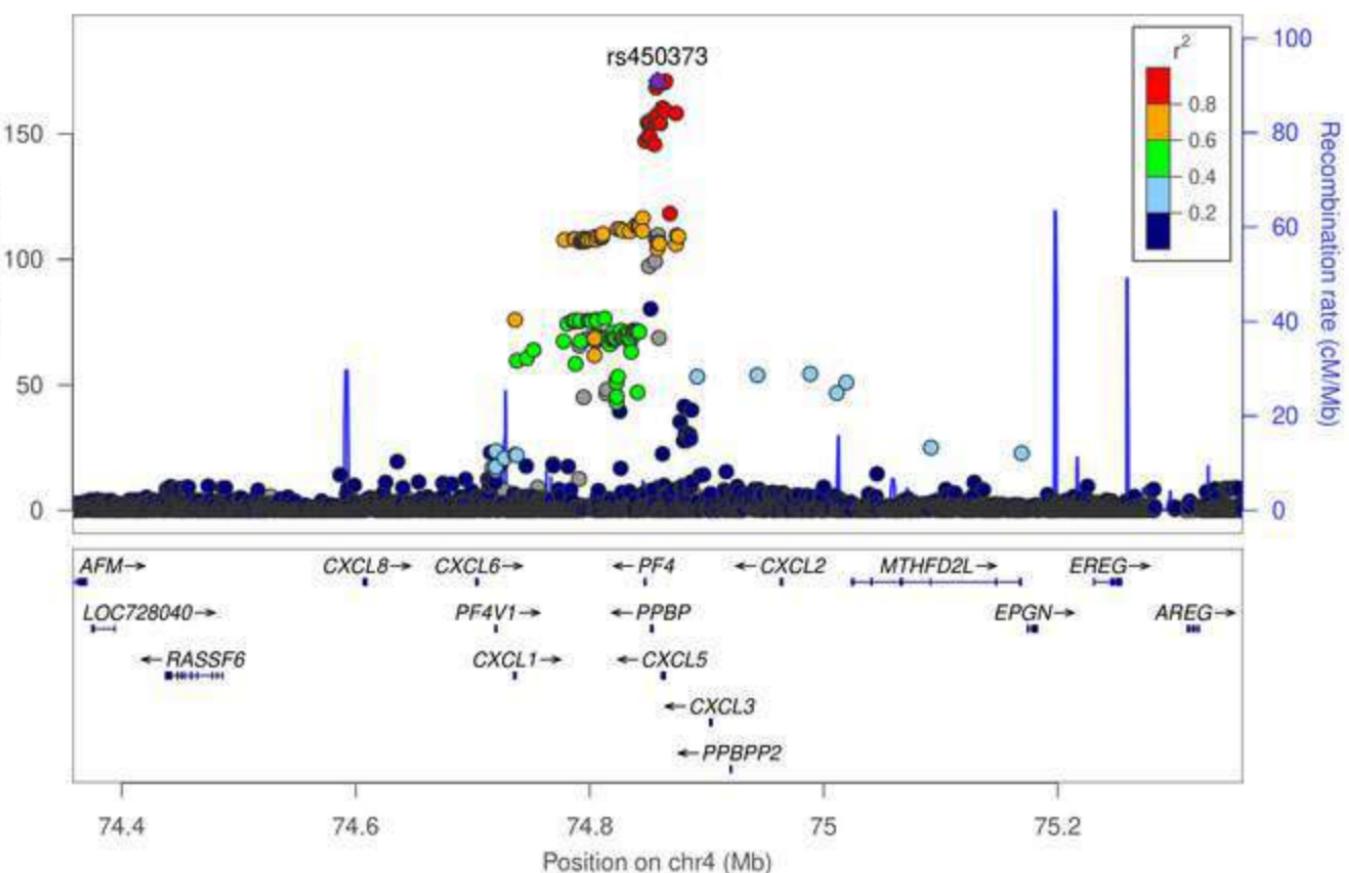
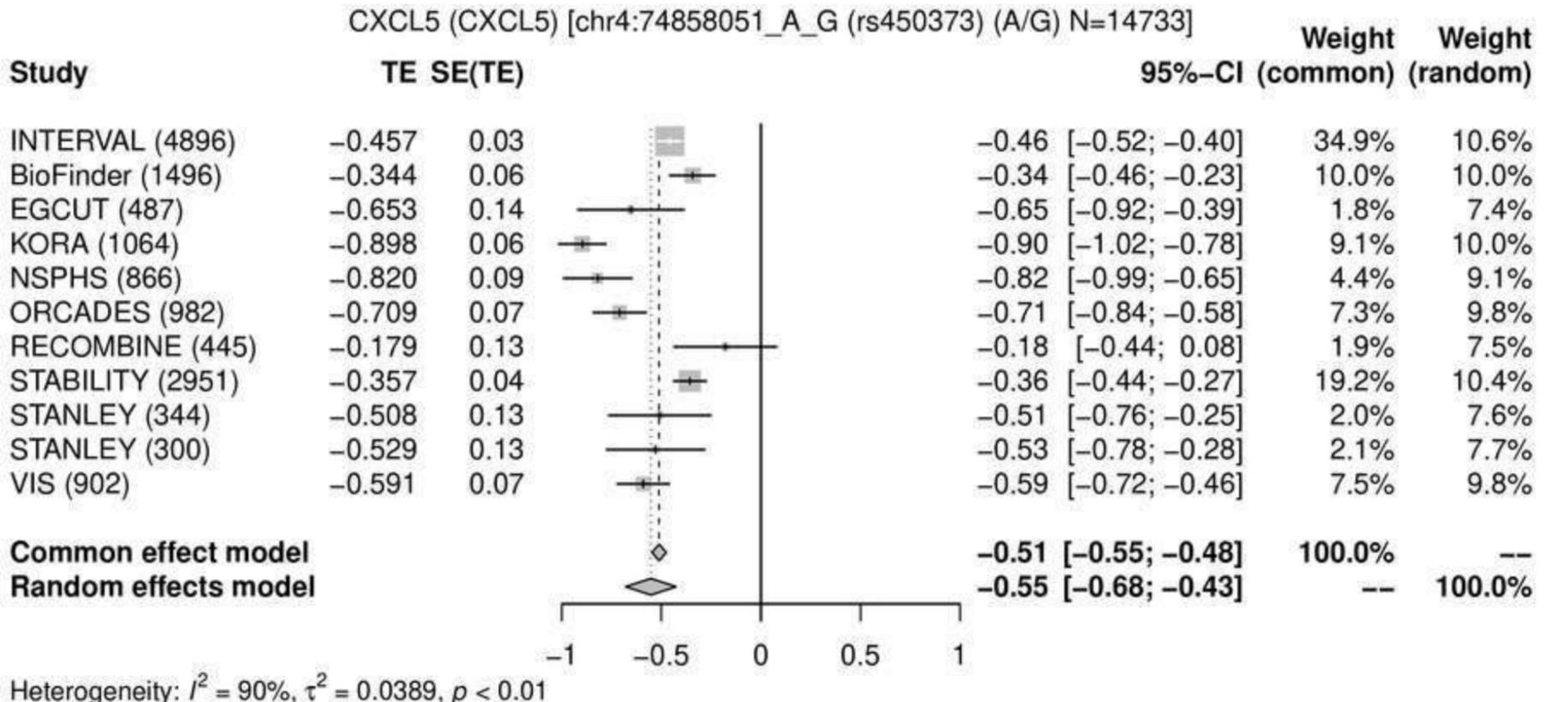
# CXCL1 (CXCL1)-rs1366949



# CXCL5 (CXCL5)-rs7090111

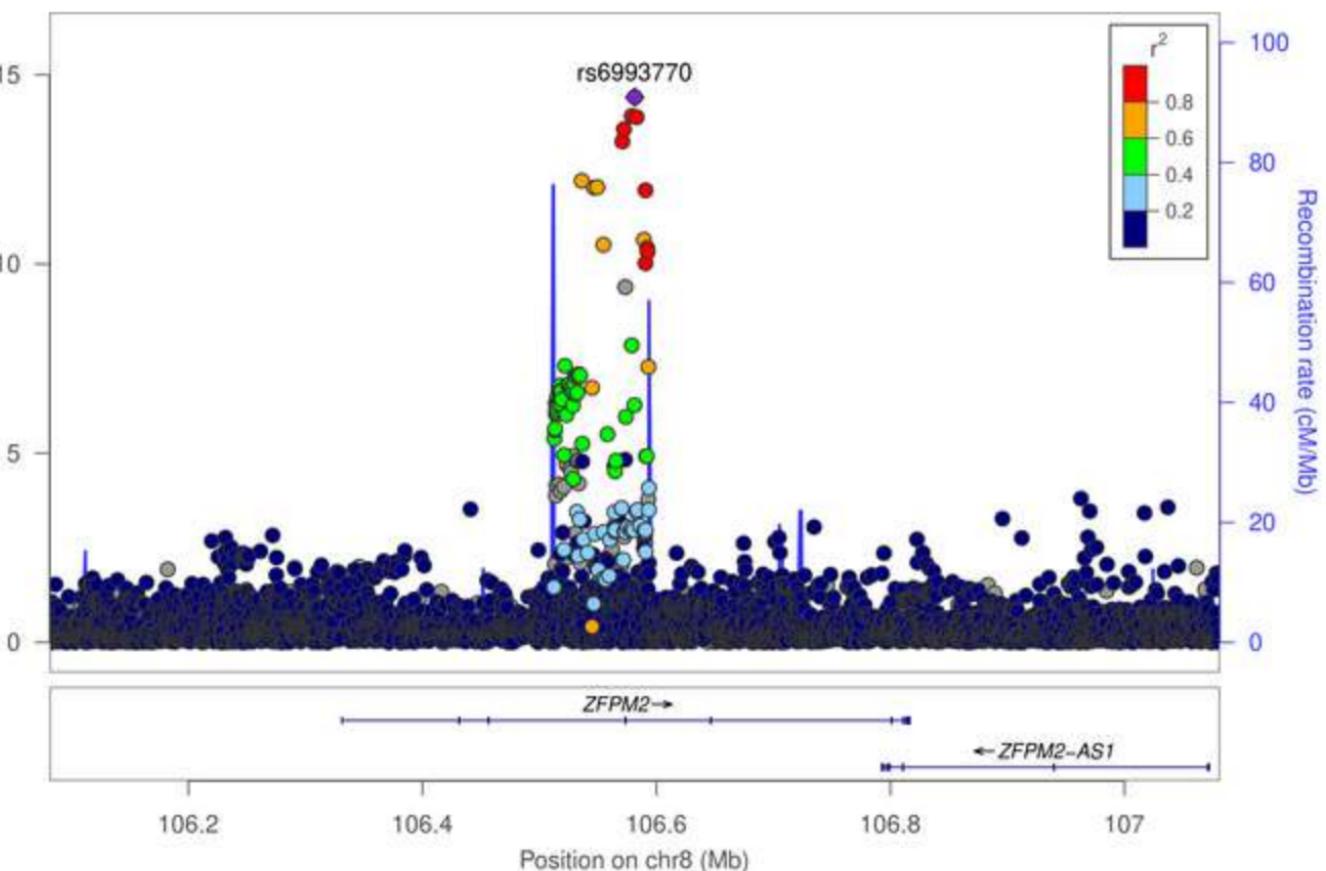
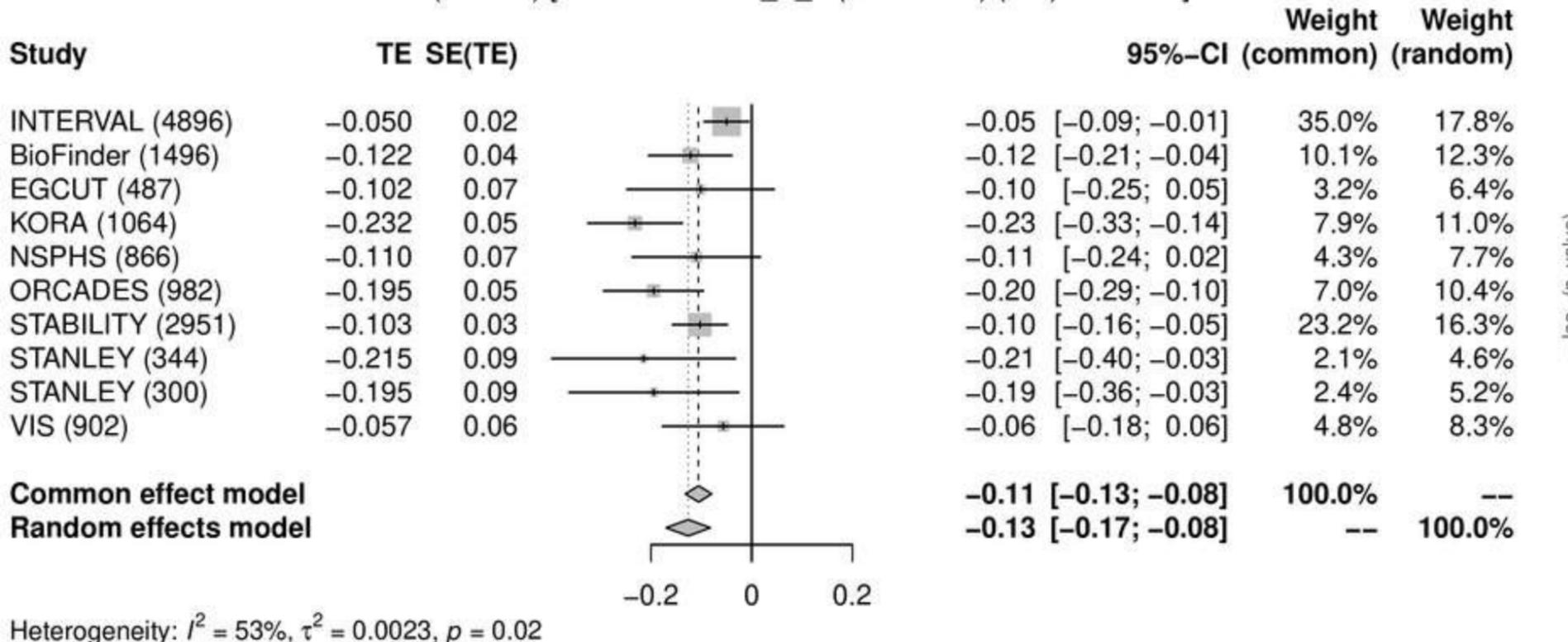


# CXCL5 (CXCL5)-rs450373



# CXCL5 (CXCL5)-rs6993770

CXCL5 (CXCL5) [chr8:106581528\_A\_T (rs6993770) (A/T) N=14288]



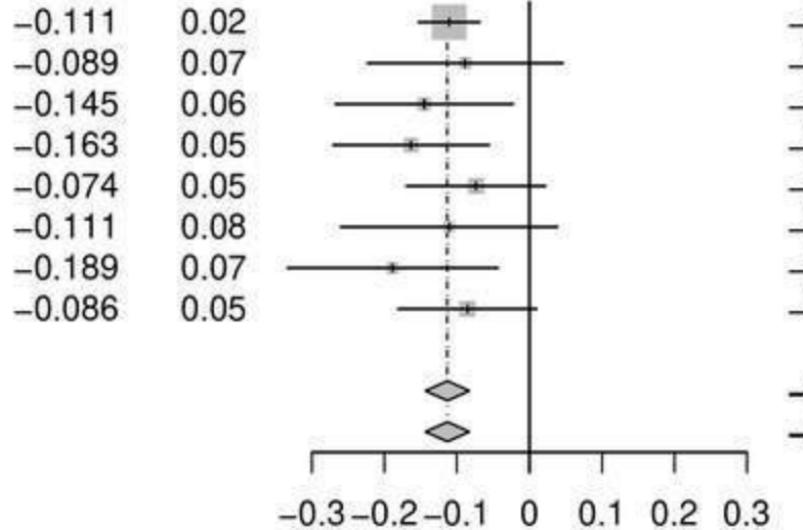
# CXCL5 (CXCL5)-rs10821552

CXCL5 (CXCL5) [chr9:136939992\_A\_C (rs10821552) (A/C) N=9841]

## Study

INTERVAL (4896)  
EGCUT (487)  
KORA (1064)  
NSPHS (866)  
ORCADES (982)  
STANLEY (344)  
STANLEY (300)  
VIS (902)

TE SE(TE)



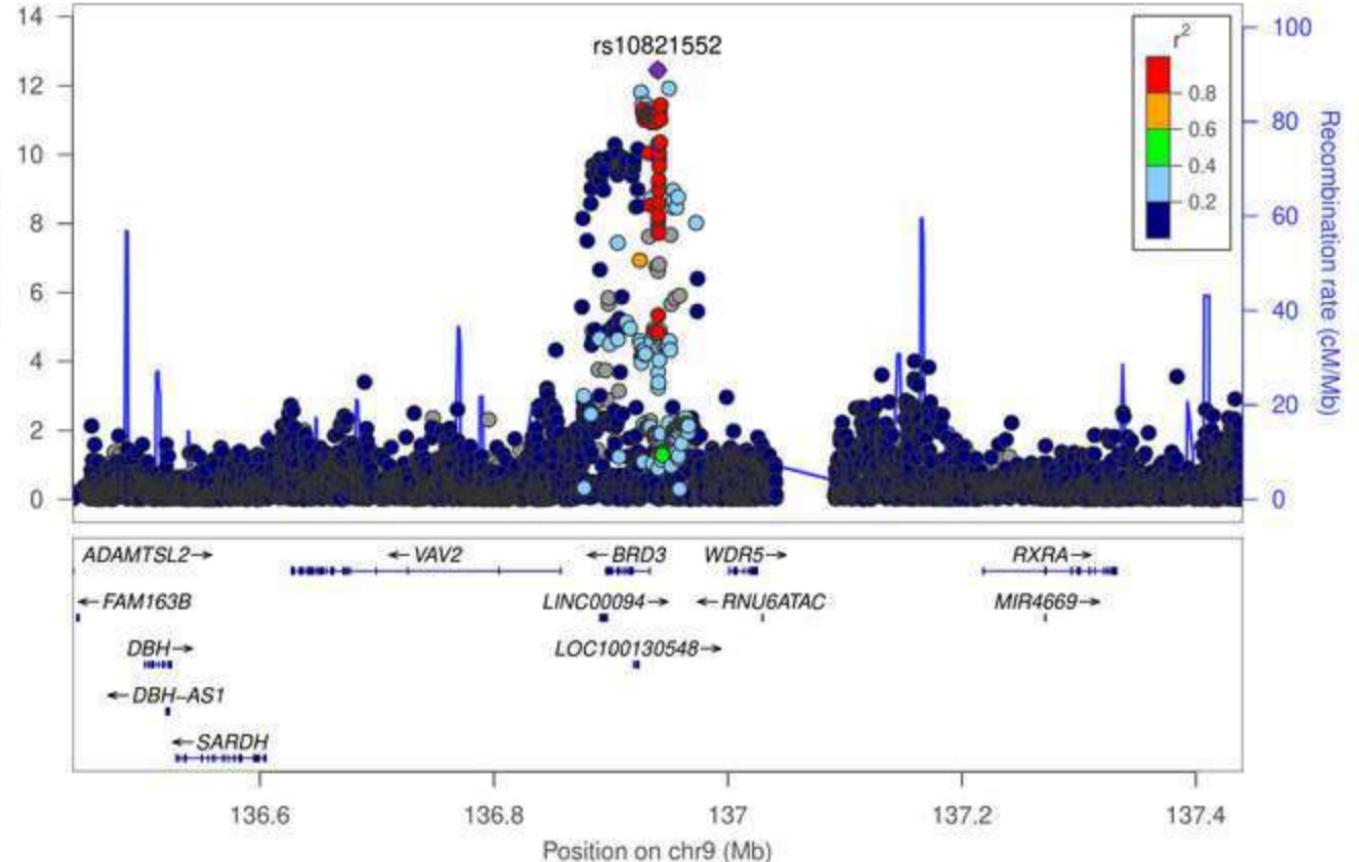
Common effect model  
Random effects model

Heterogeneity:  $I^2 = 0\%$ ,  $\tau^2 = 0$ ,  $p = 0.86$

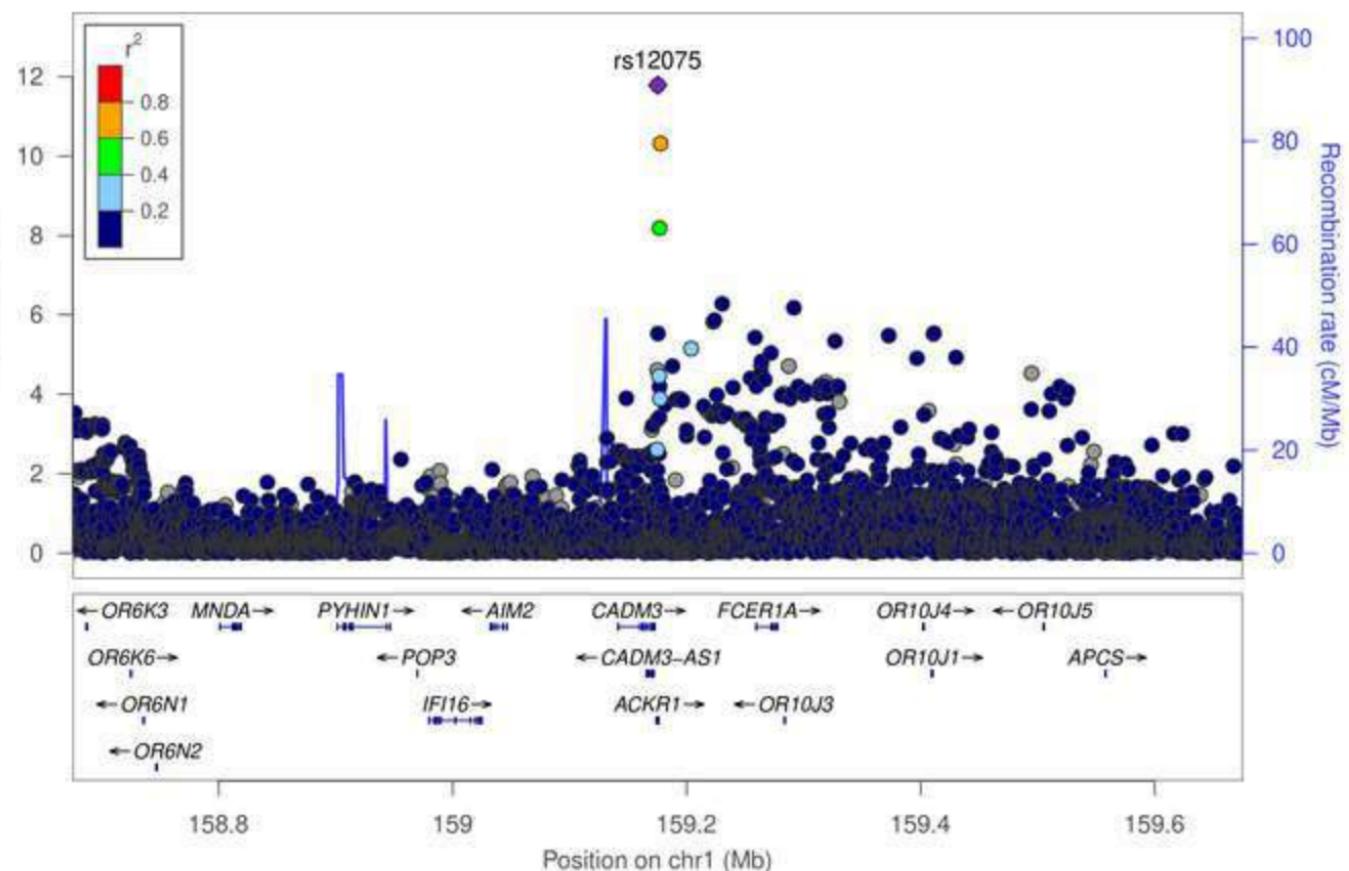
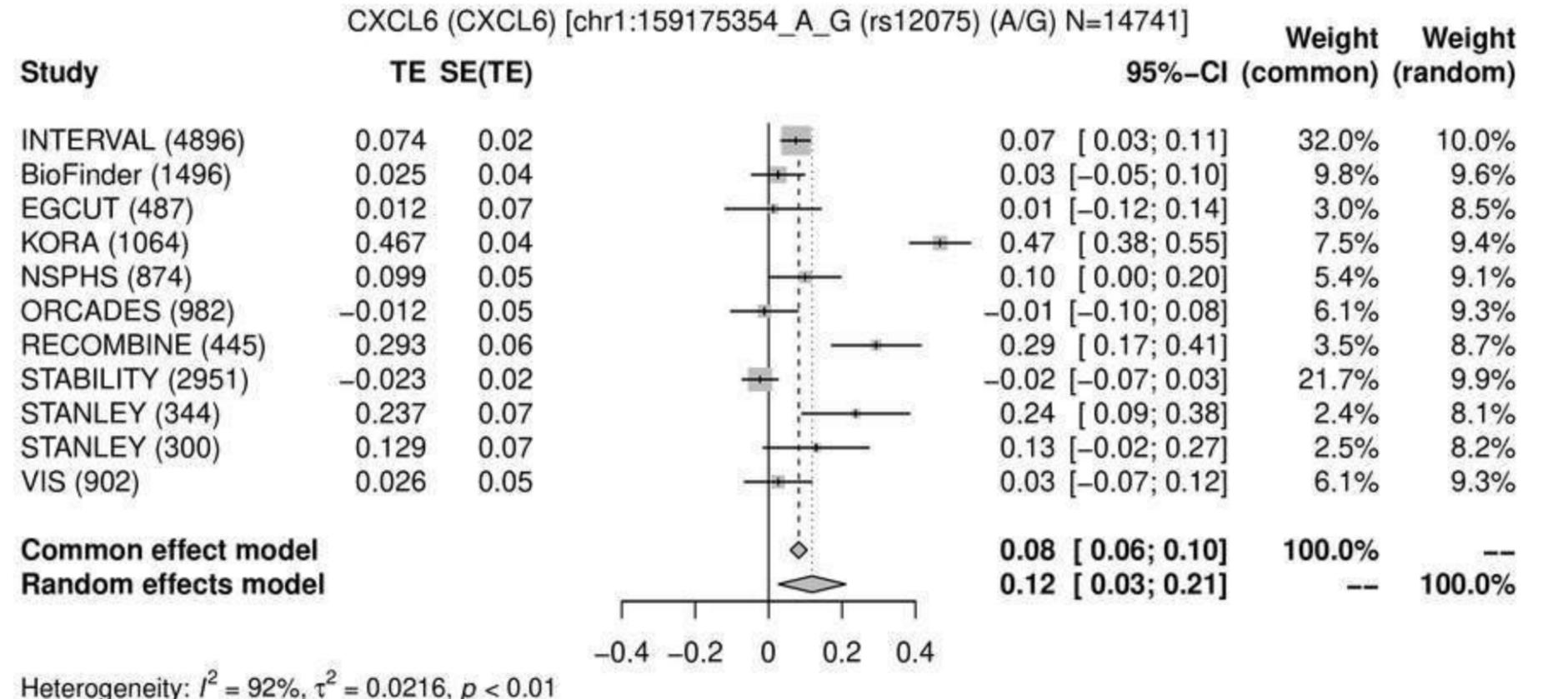
Weight  
95%-CI (common) (random)

-0.11	[-0.15; -0.07]	51.9%	51.9%
-0.09	[-0.22; 0.05]	5.1%	5.1%
-0.15	[-0.27; -0.02]	6.2%	6.2%
-0.16	[-0.27; -0.06]	8.0%	8.0%
-0.07	[-0.17; 0.02]	10.1%	10.1%
-0.11	[-0.26; 0.04]	4.1%	4.1%
-0.19	[-0.33; -0.04]	4.4%	4.4%
-0.09	[-0.18; 0.01]	10.2%	10.2%

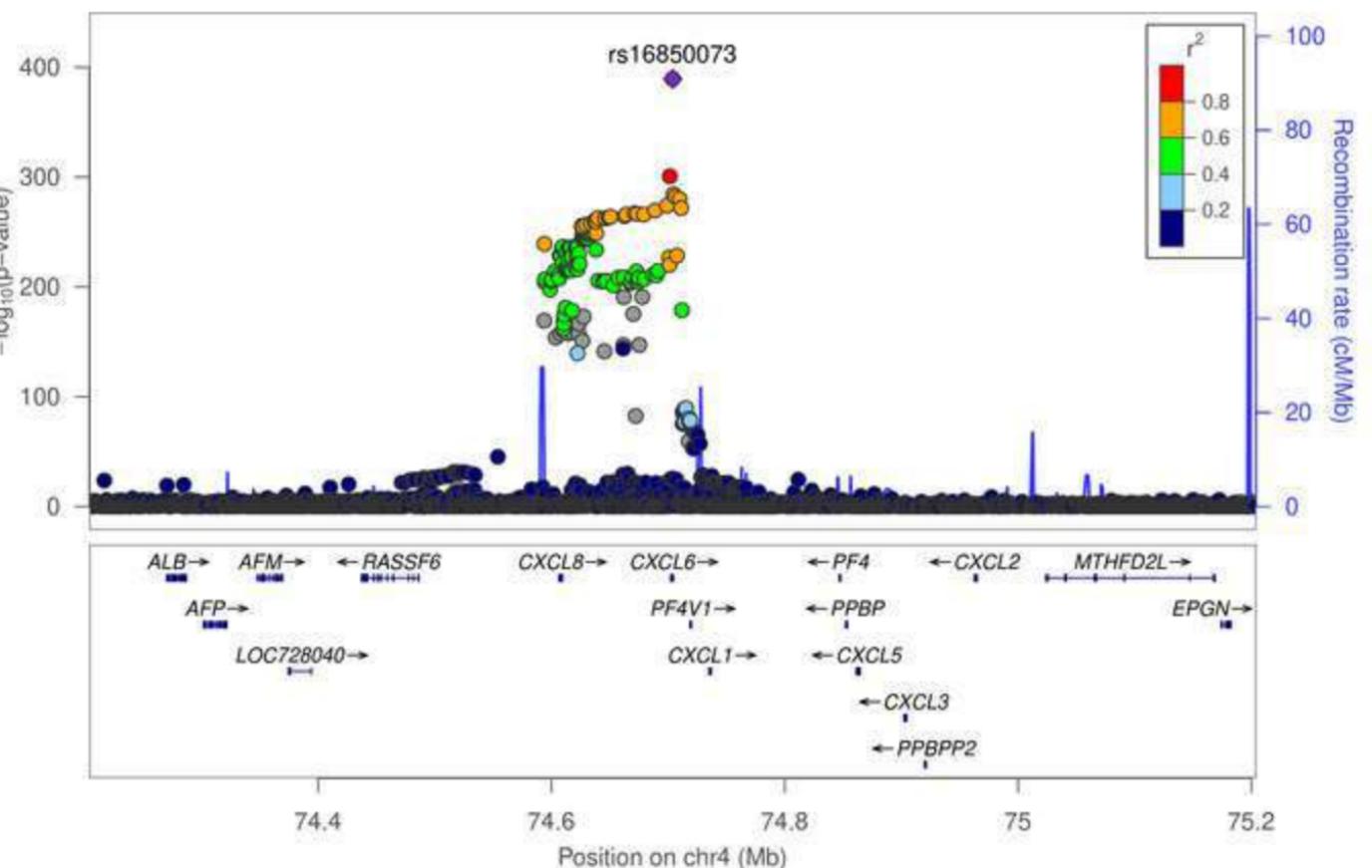
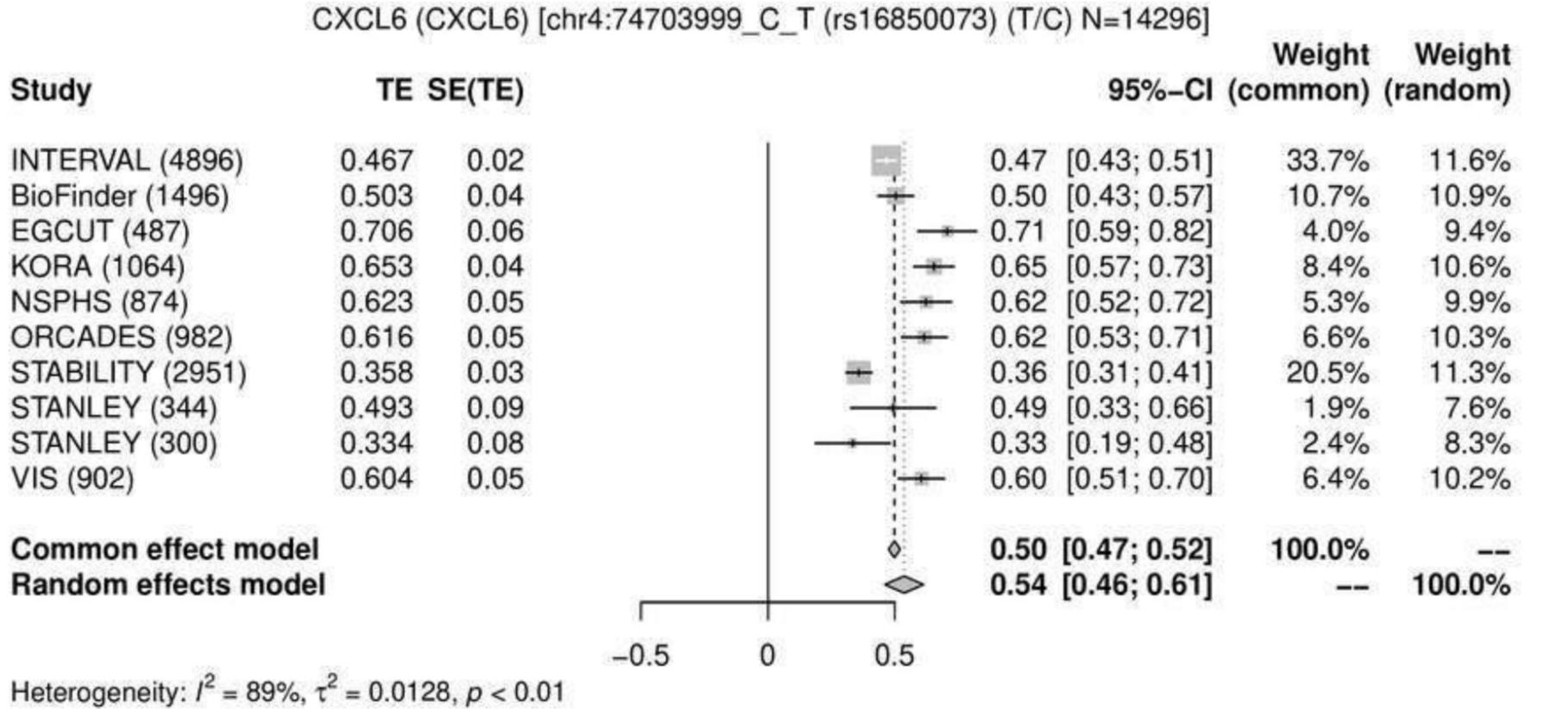
100.0% -- 100.0%



## CXCL6 (CXCL6)-rs12075

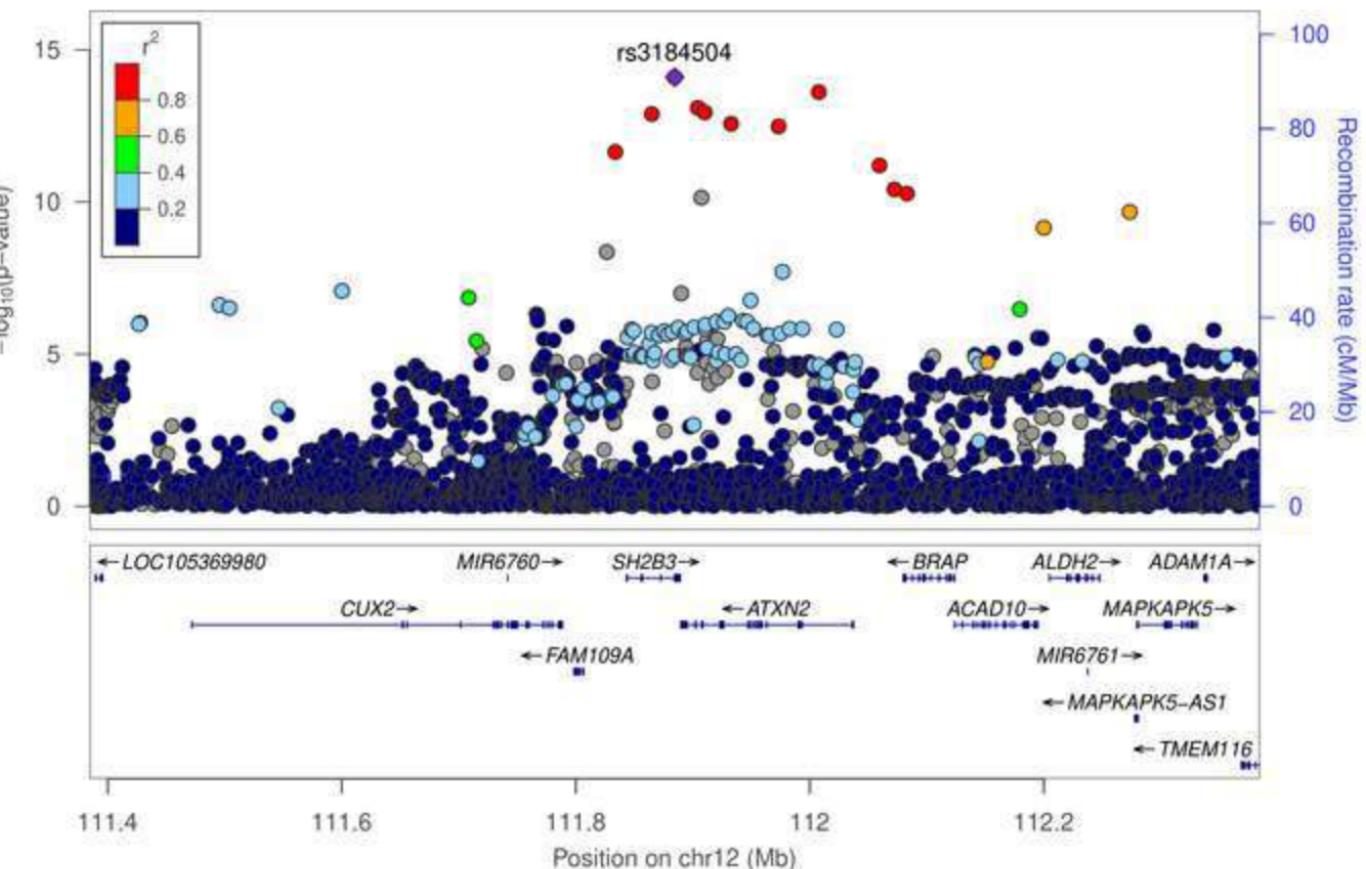
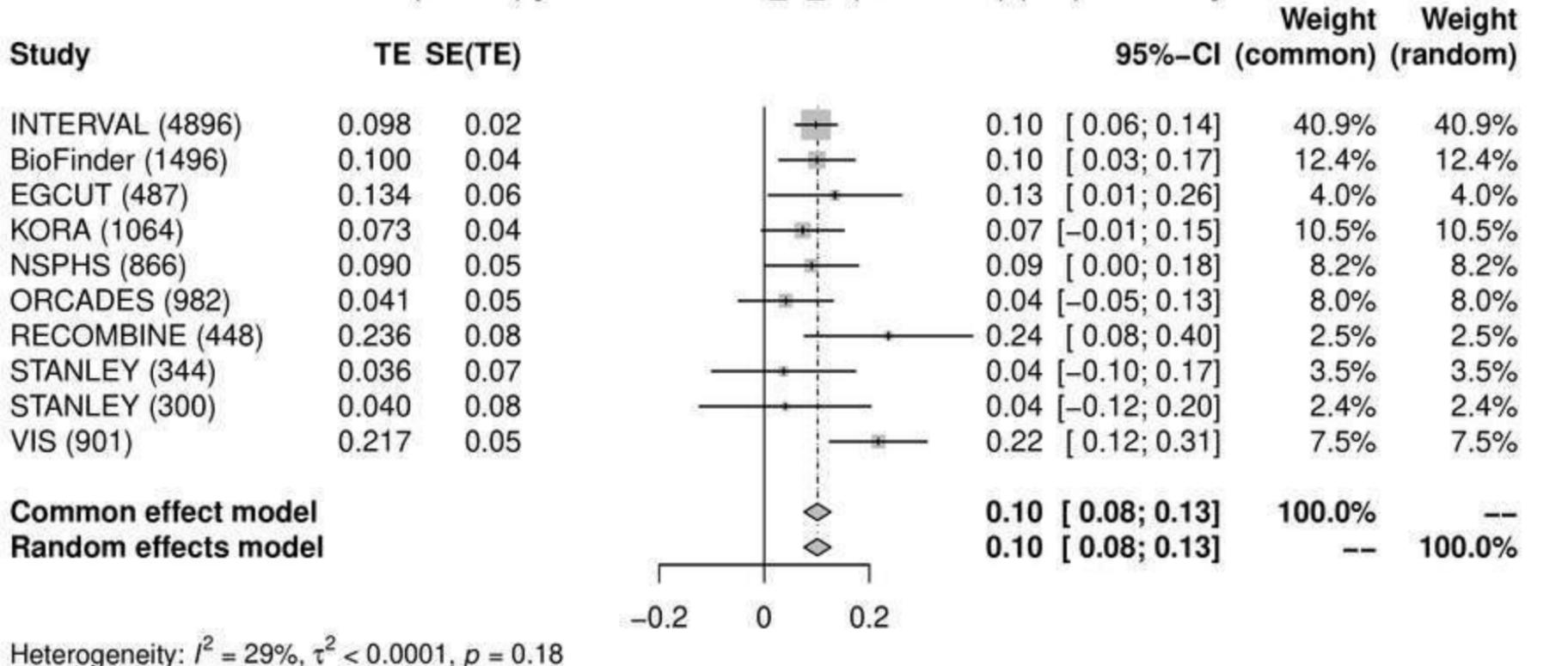


# CXCL6 (CXCL6)-rs16850073

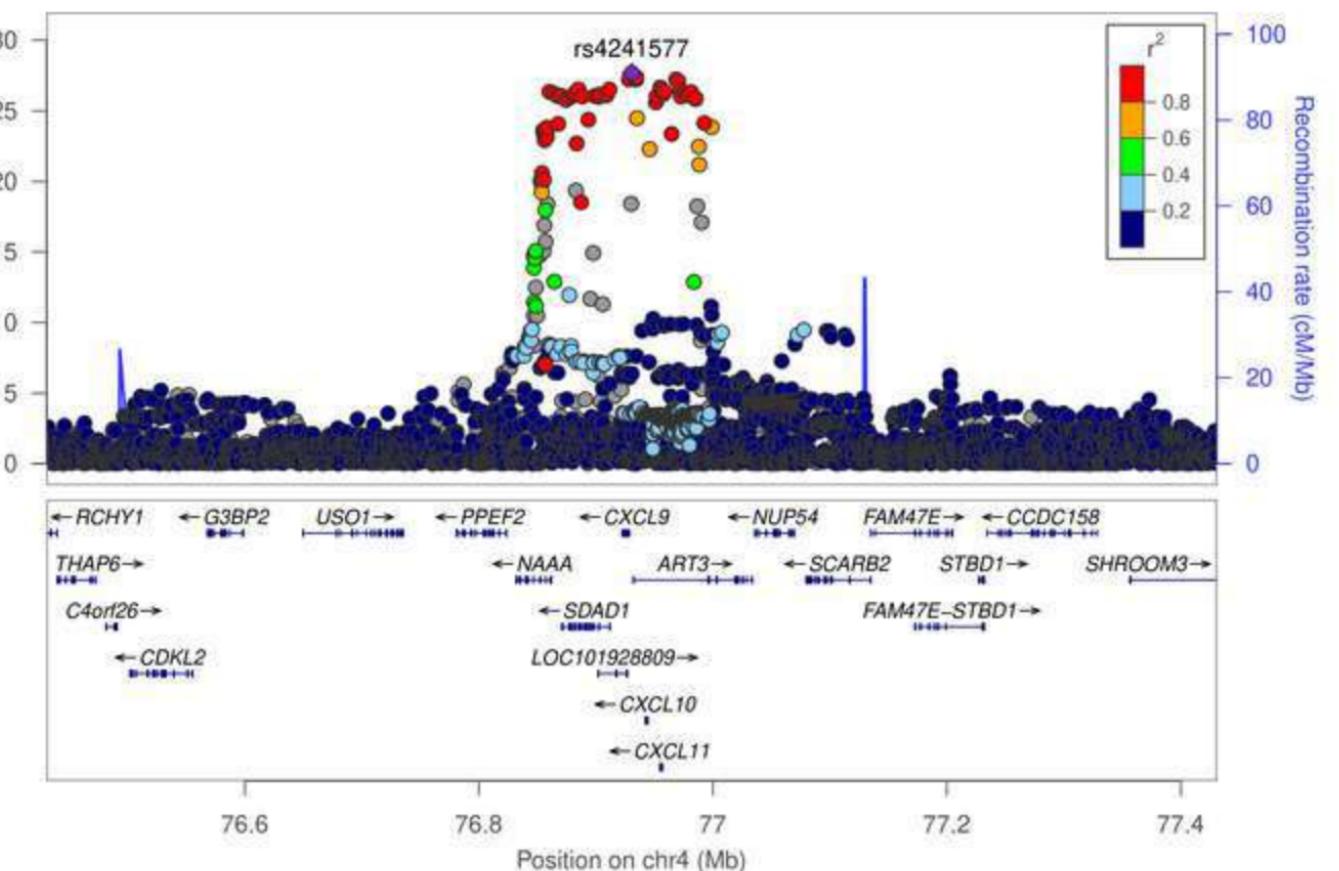
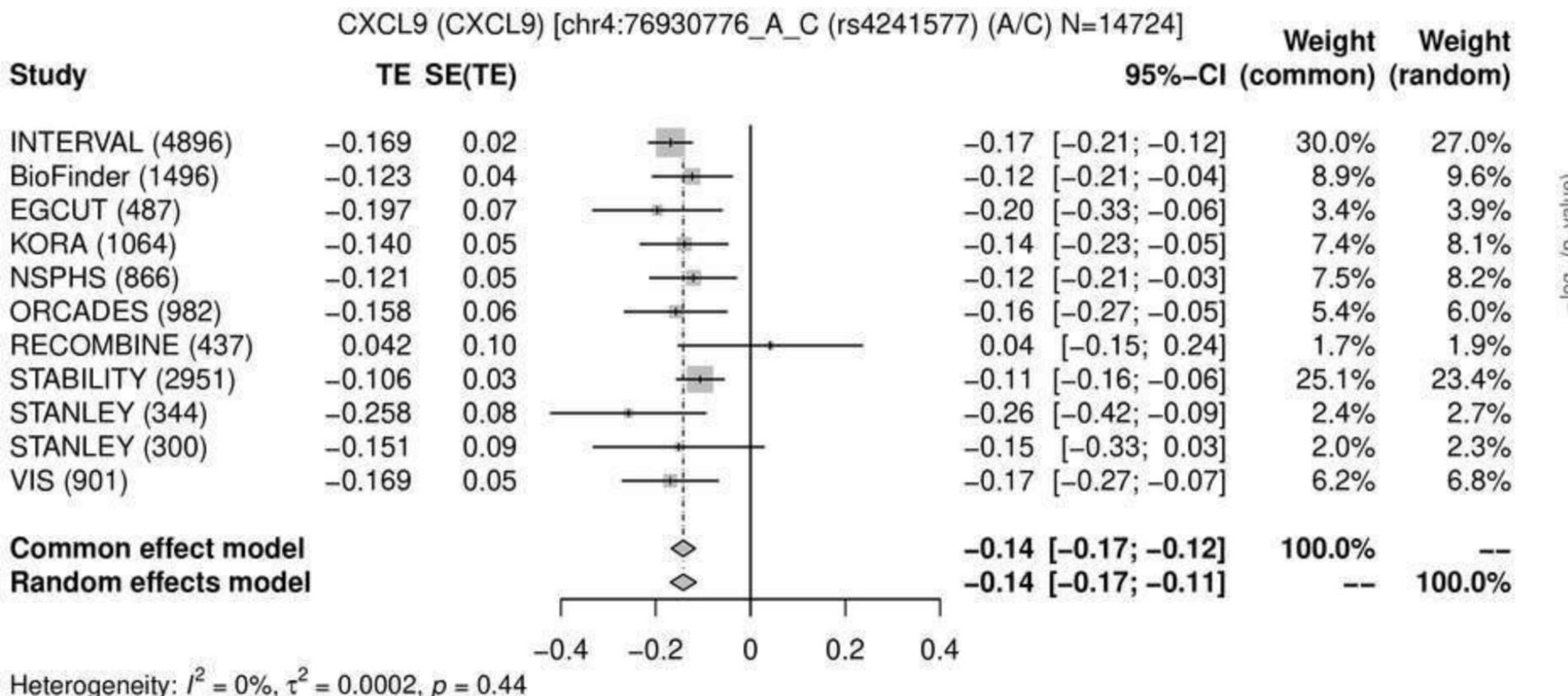


# CXCL9 (CXCL9)-rs3184504

CXCL9 (CXCL9) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11784]

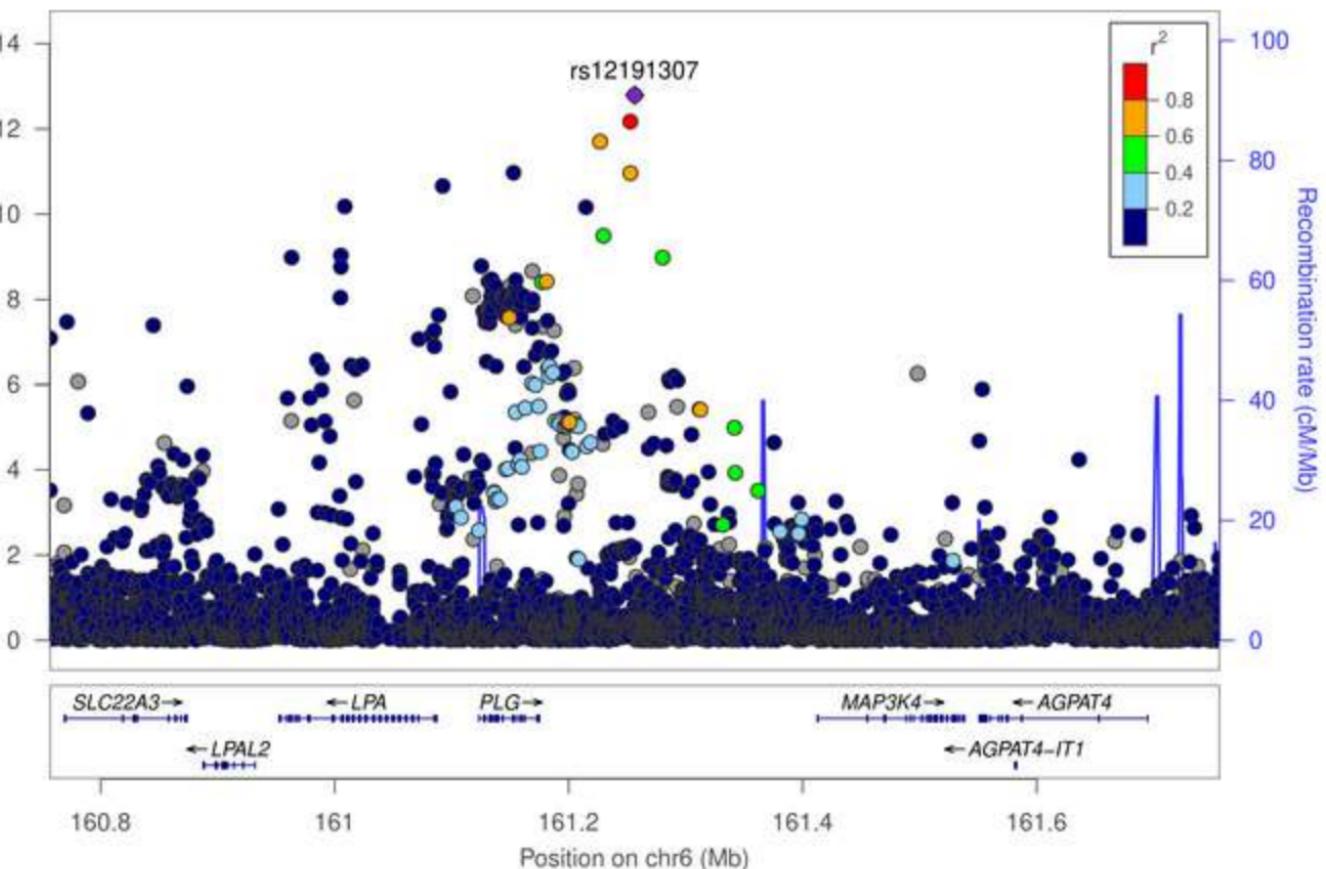
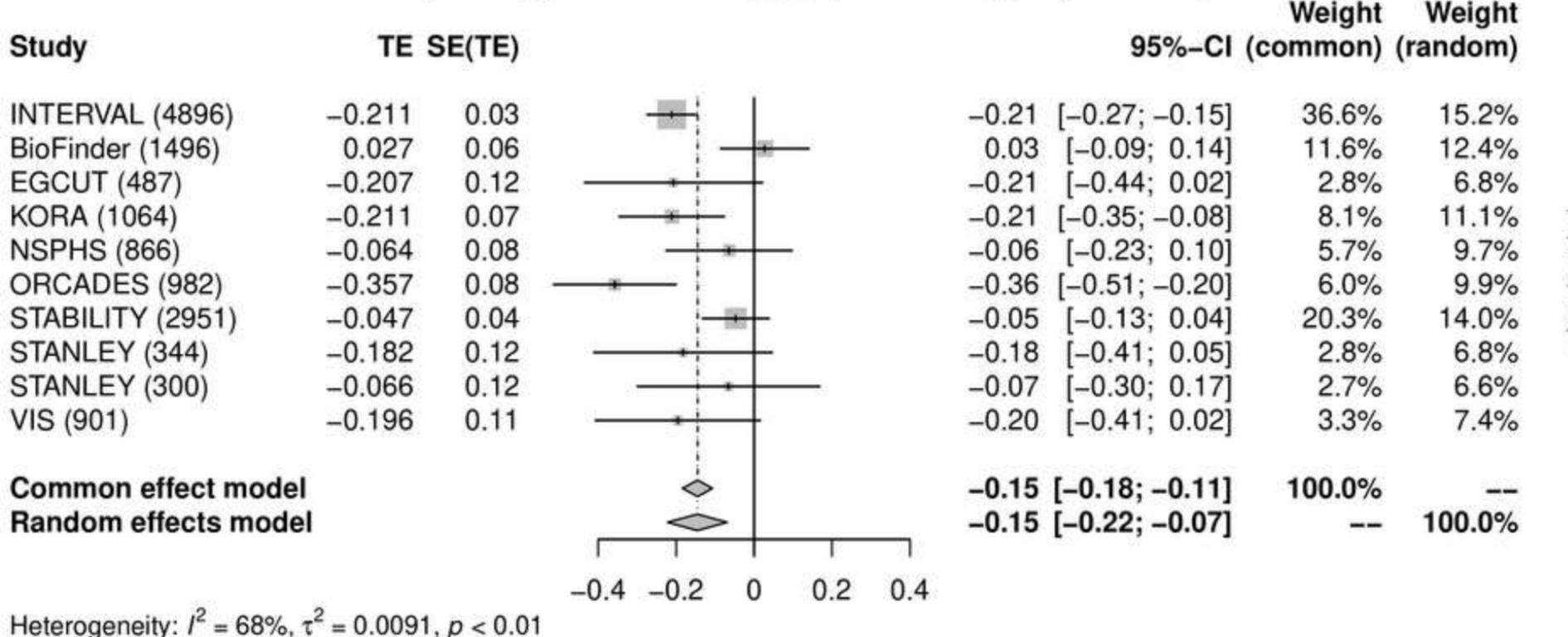


# CXCL9 (CXCL9)-rs4241577



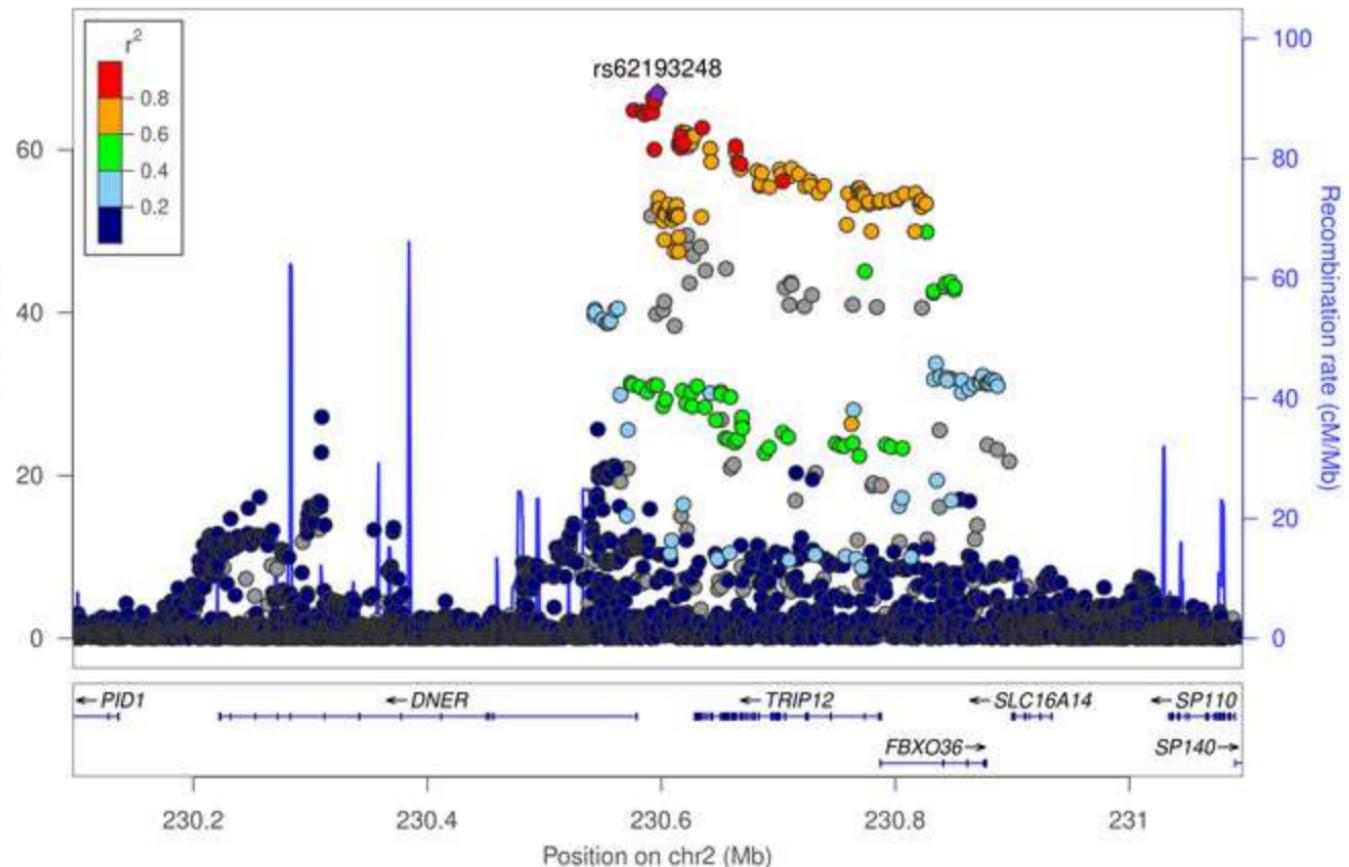
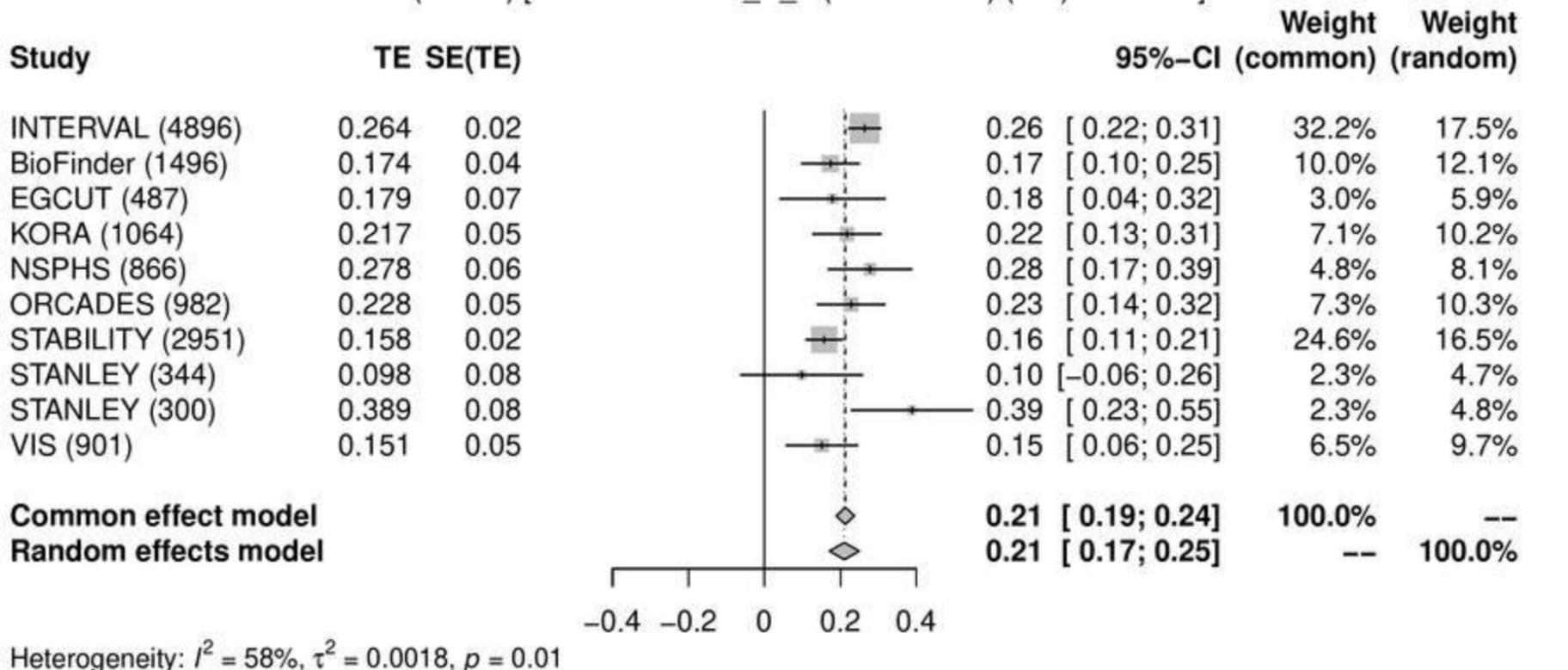
# CXCL9 (CXCL9)-rs12191307

CXCL9 (CXCL9) [chr6:161256529\_A\_G (rs12191307) (A/G) N=14287]

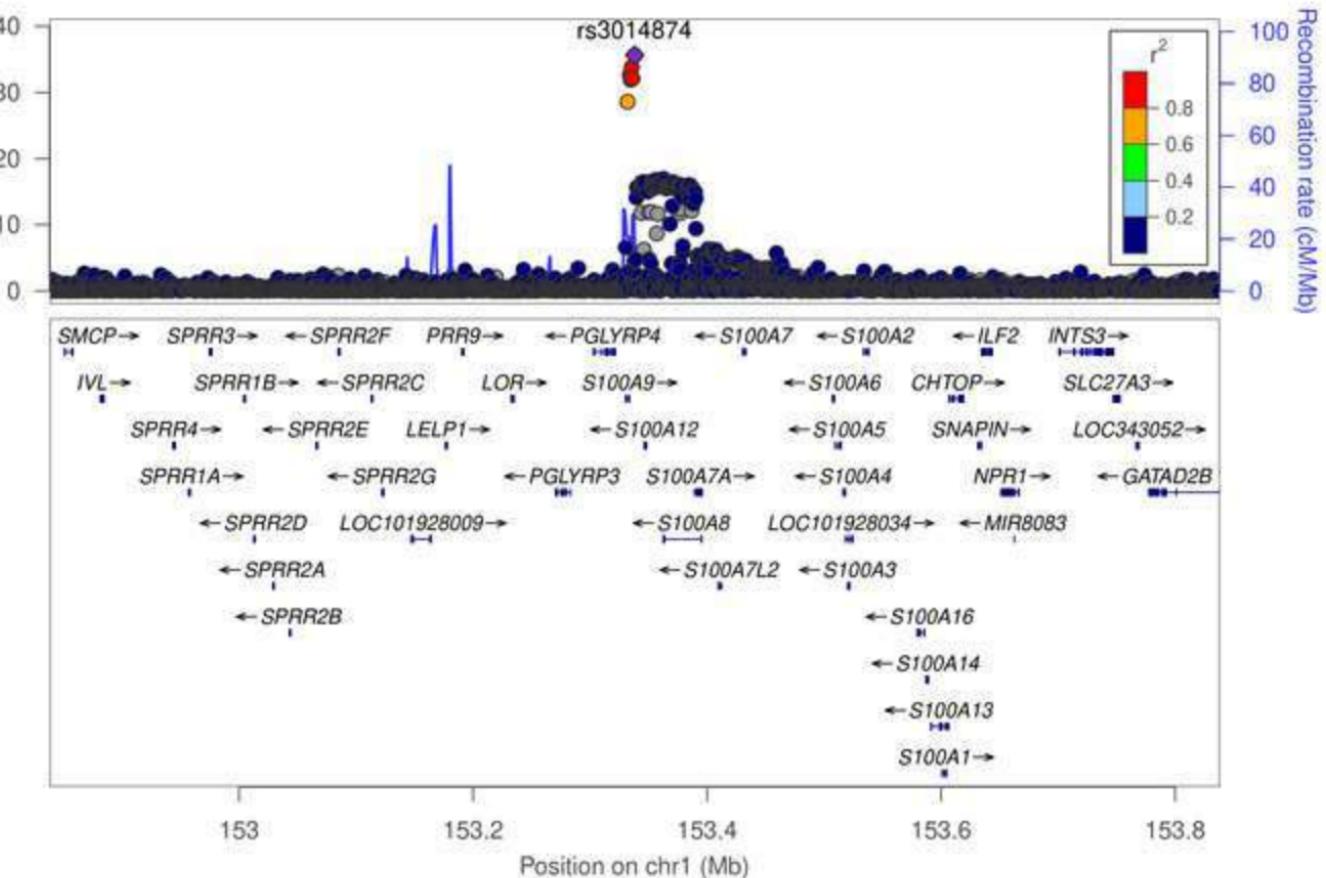
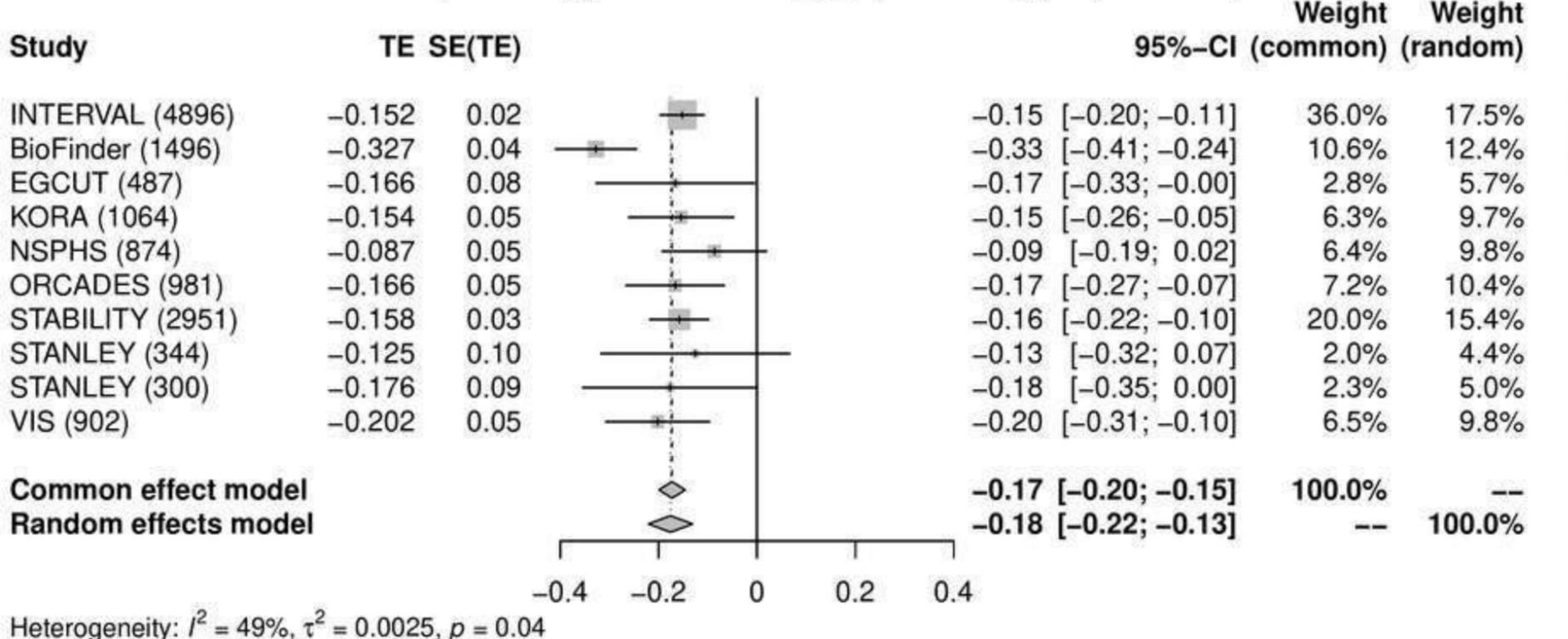


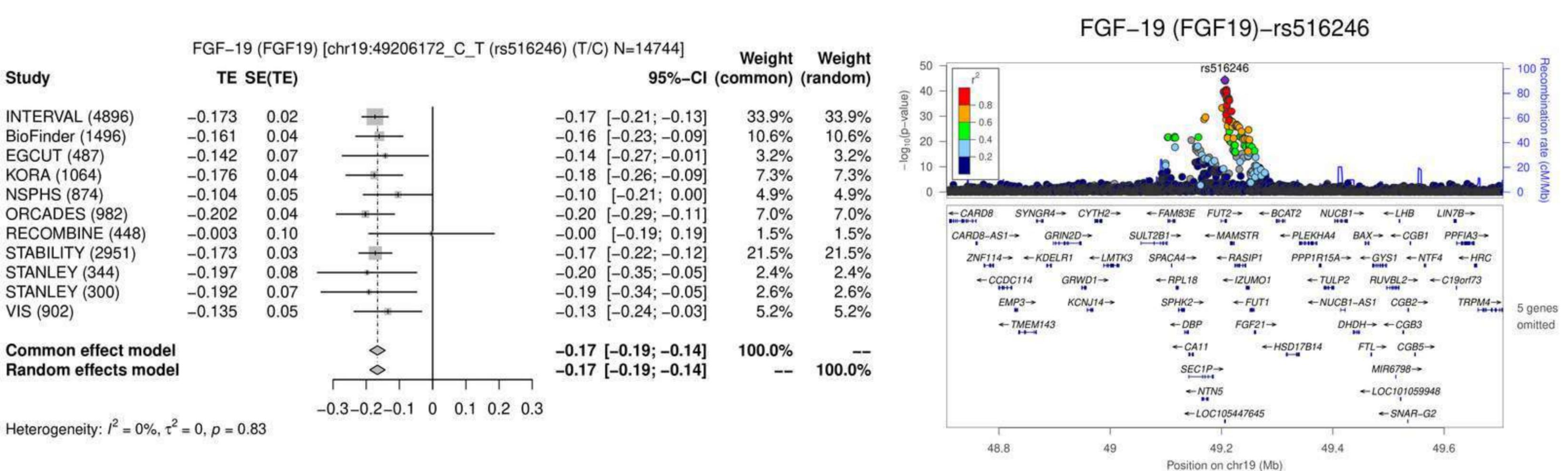
# DNER (DNER)-rs62193248

DNER (DNER) [chr2:230596917\_A\_T (rs62193248) (A/T) N=14287]



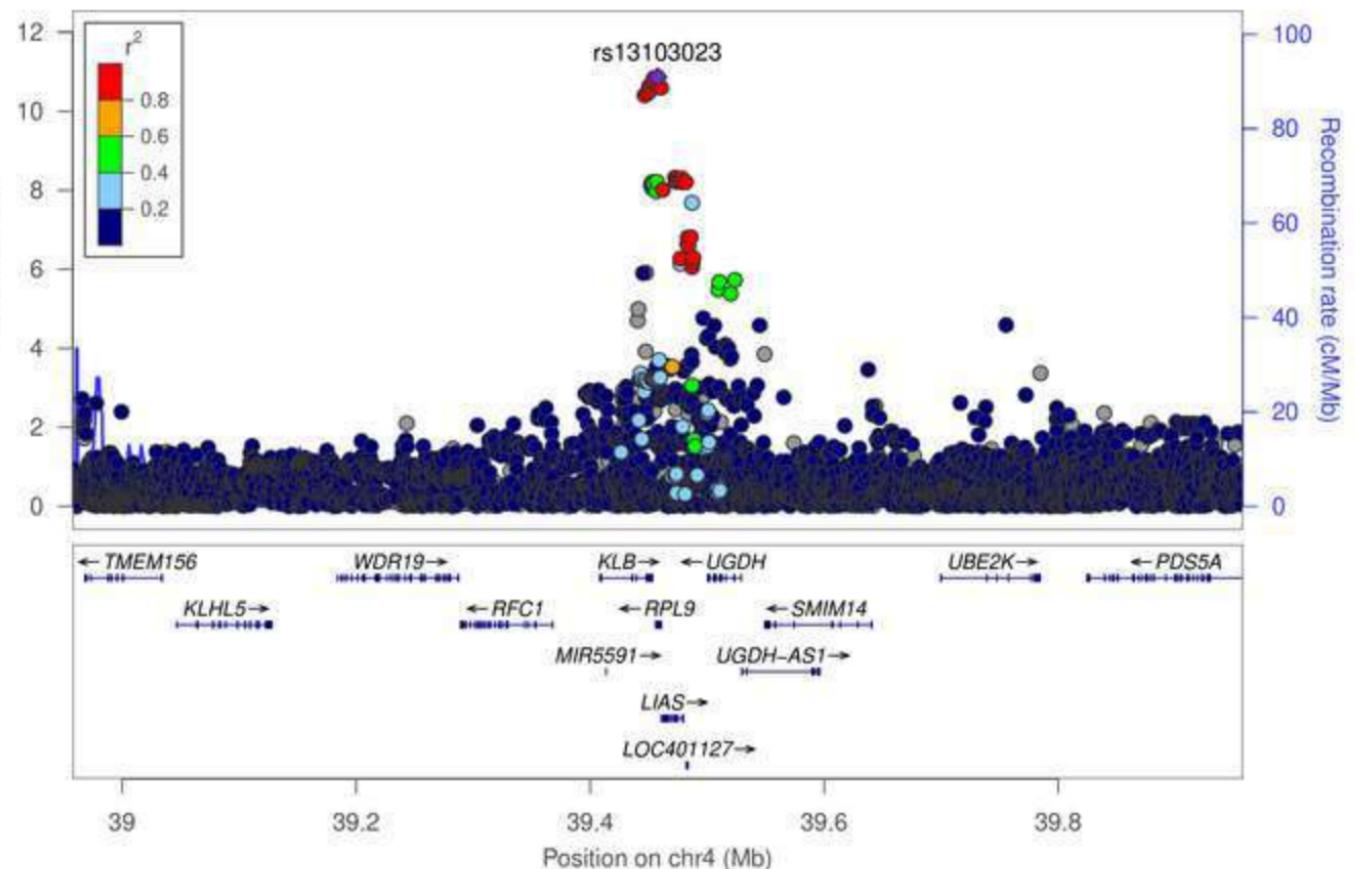
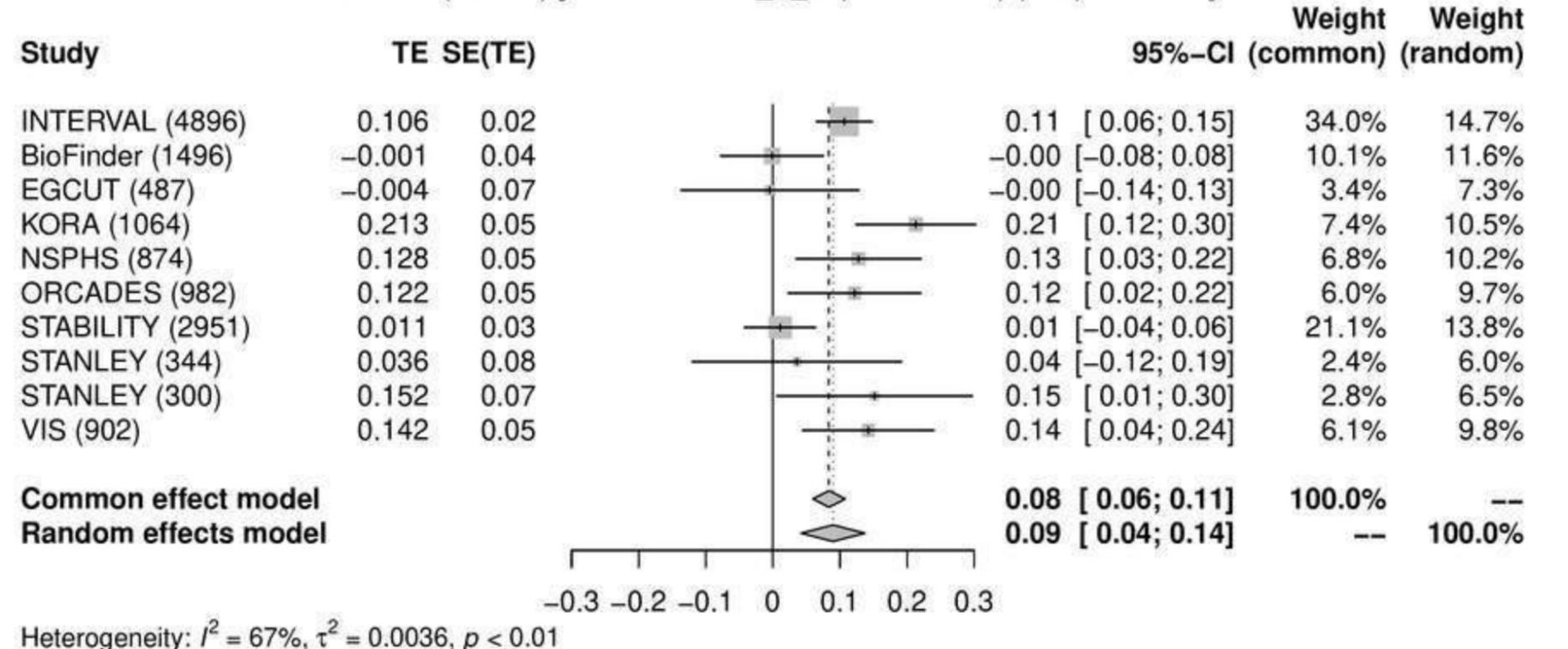
# EN-RAGE (S100A12)-rs3014874



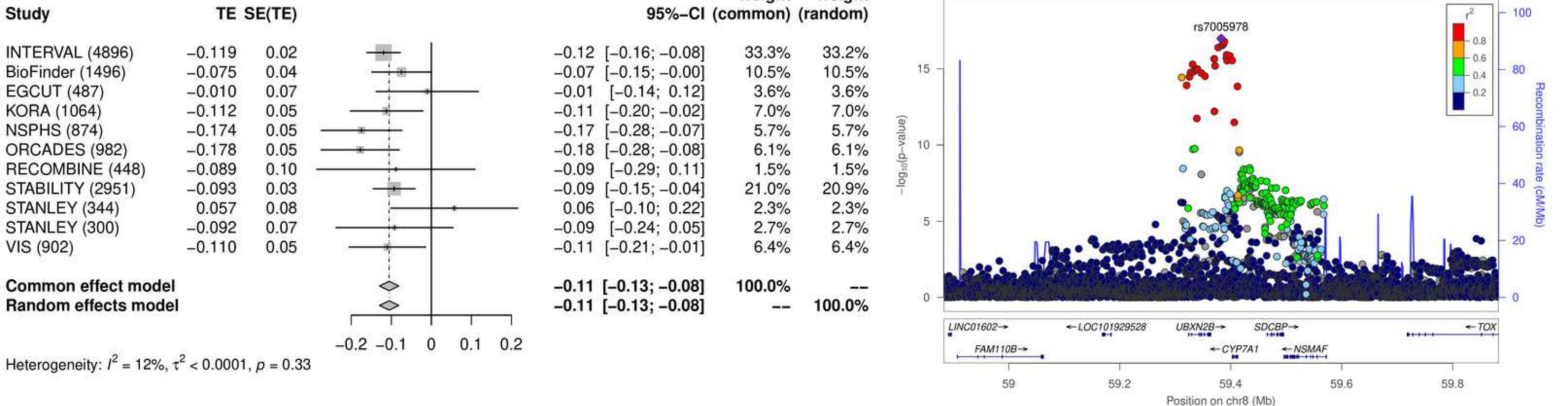


# FGF-19 (FGF19)-rs13103023

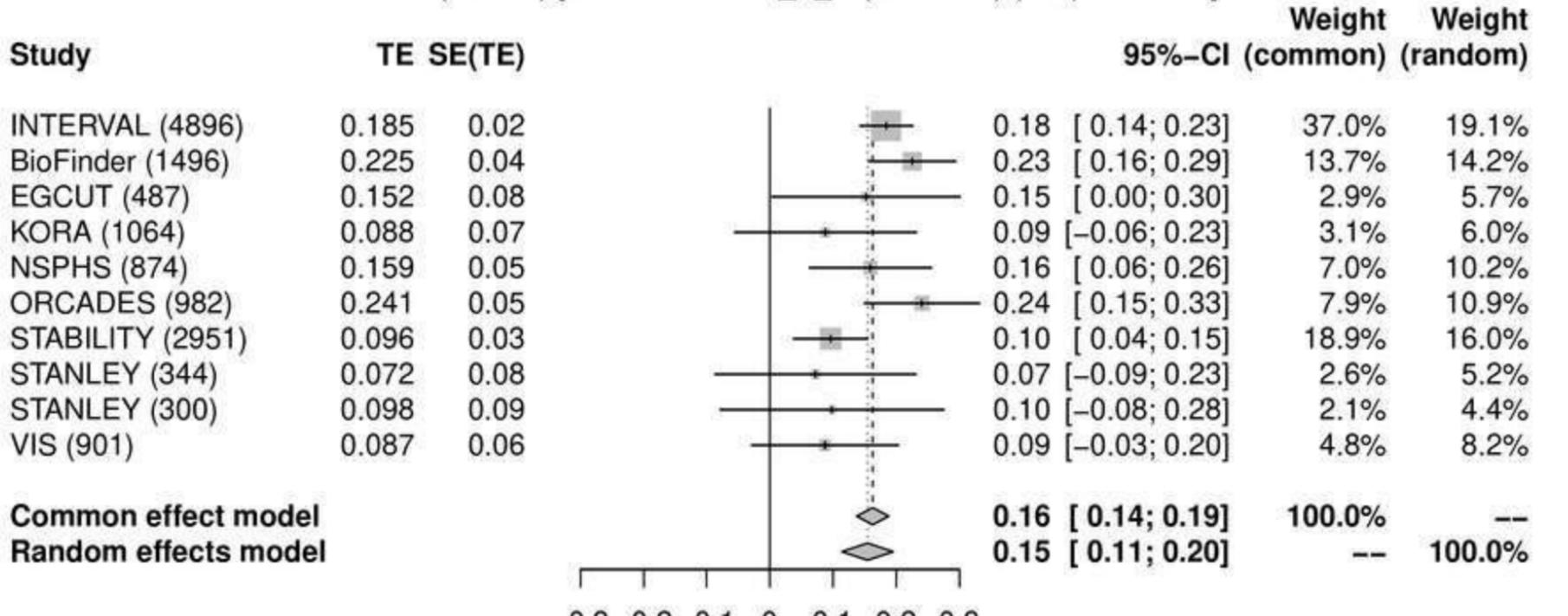
FGF-19 (FGF19) [chr4:39457617\_A\_G (rs13103023) (A/G) N=14296]



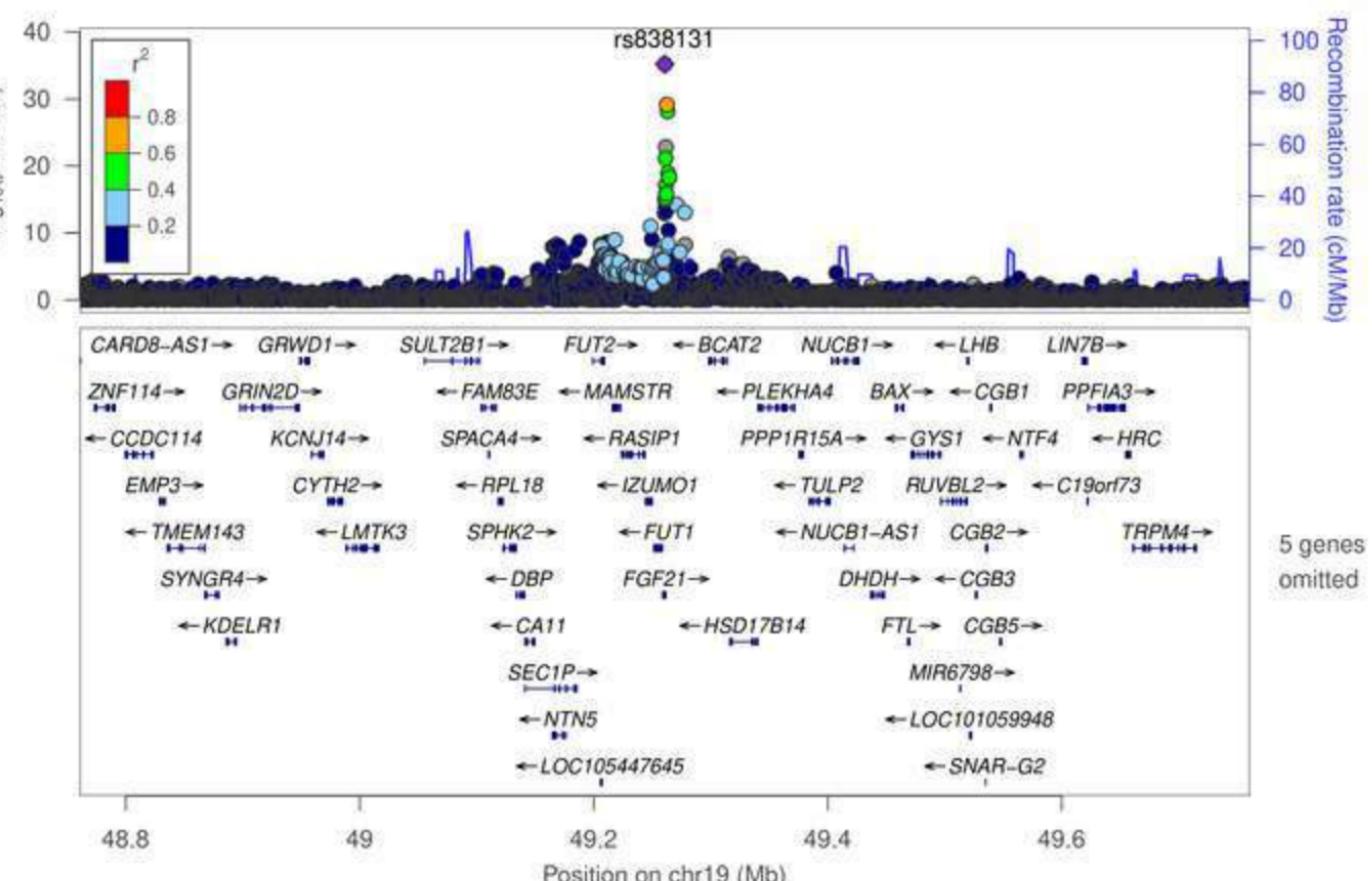
# FGF-19 (FGF19)-rs7005978



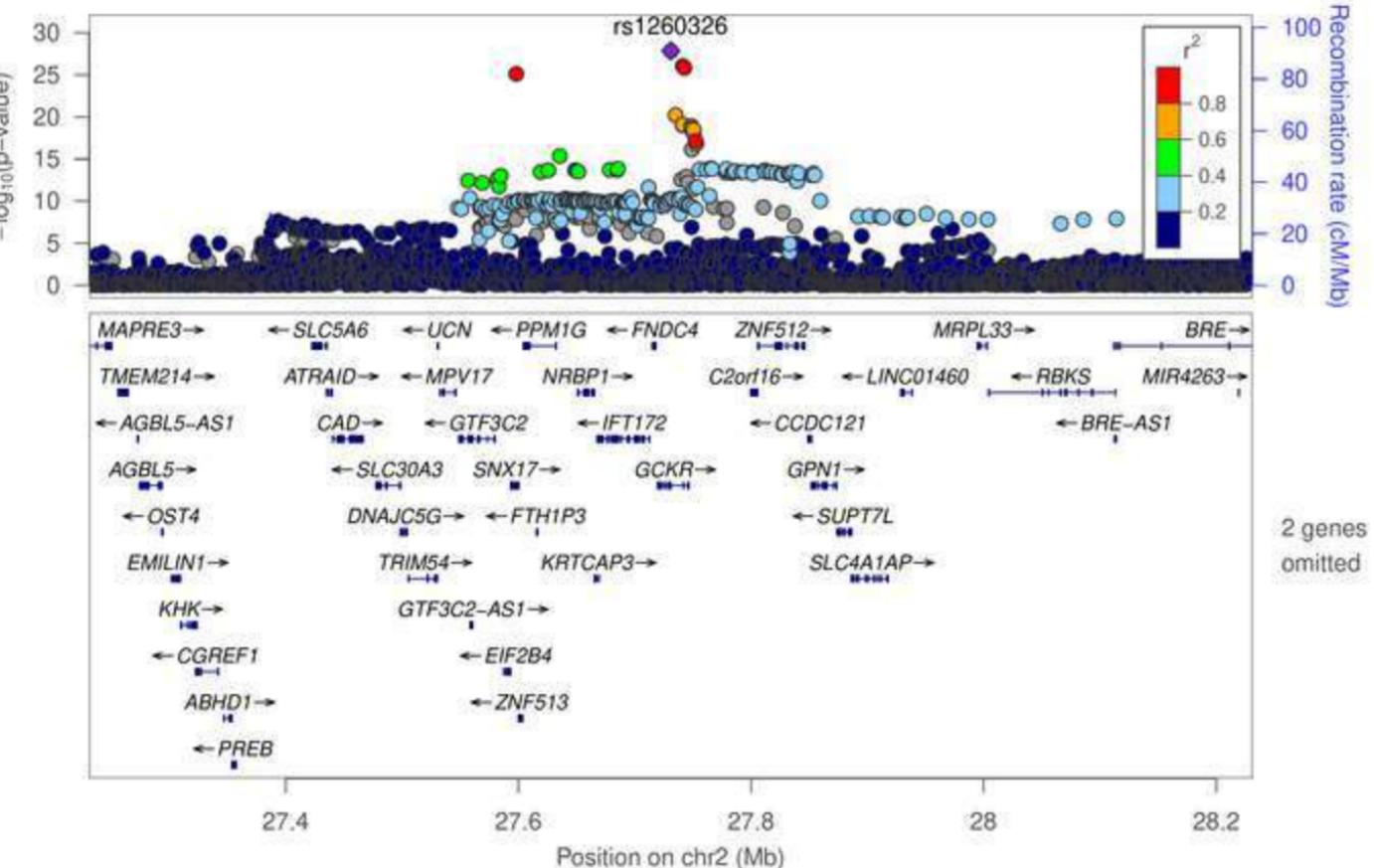
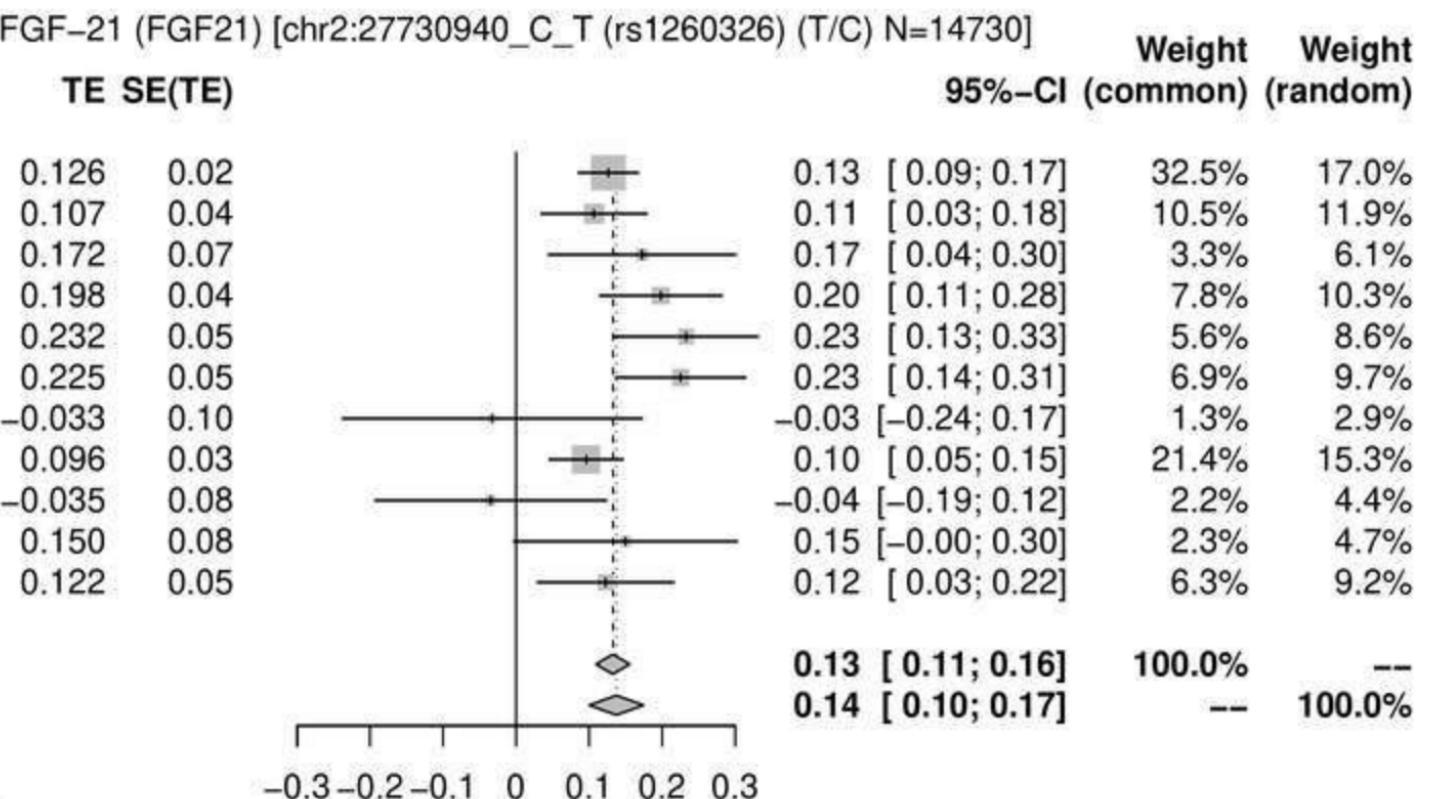
FGF-21 (FGF21) [chr19:49260677\_A\_C (rs838131) (A/C) N=14295]



FGF-21 (FGF21)-rs838131

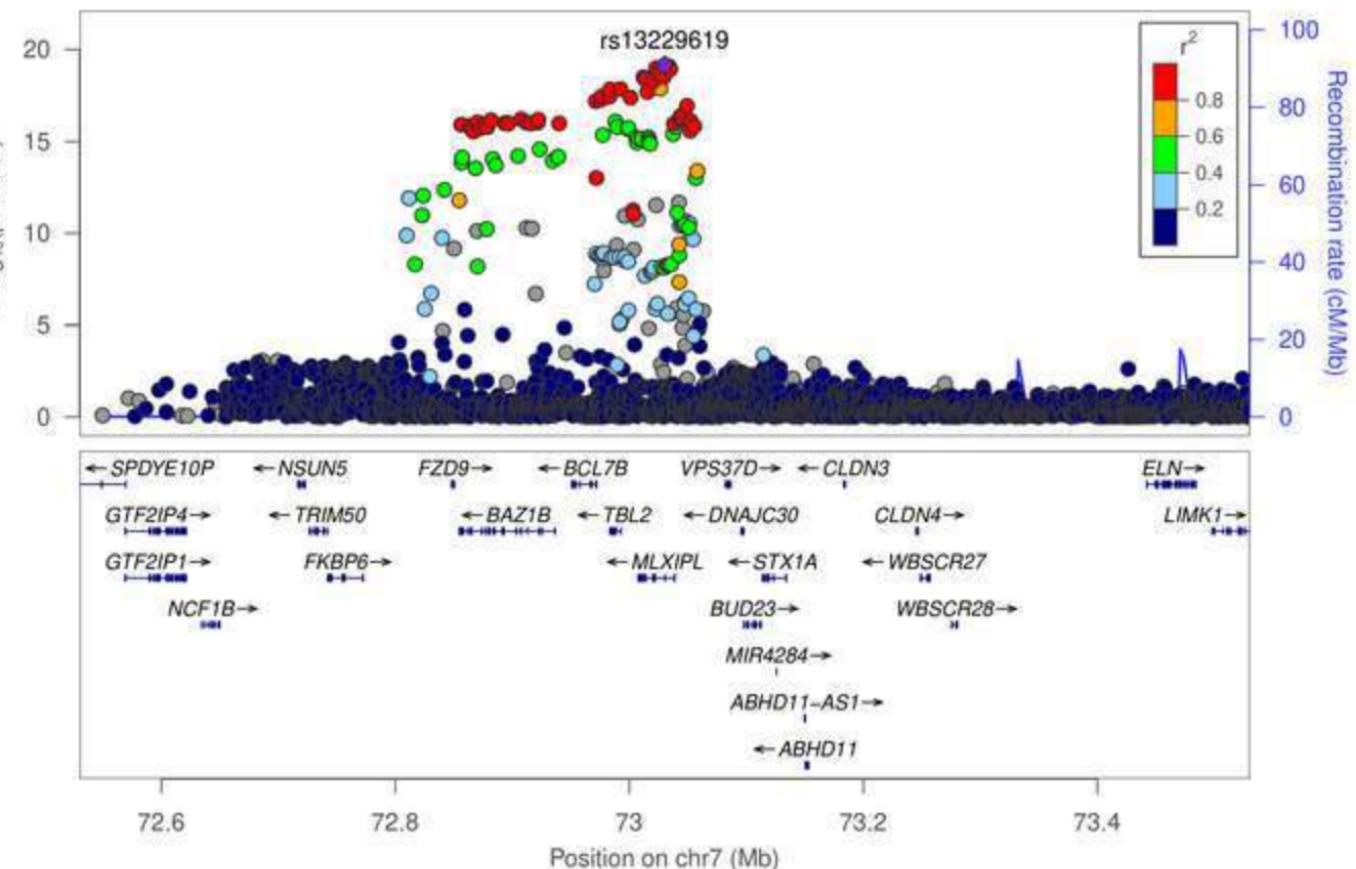
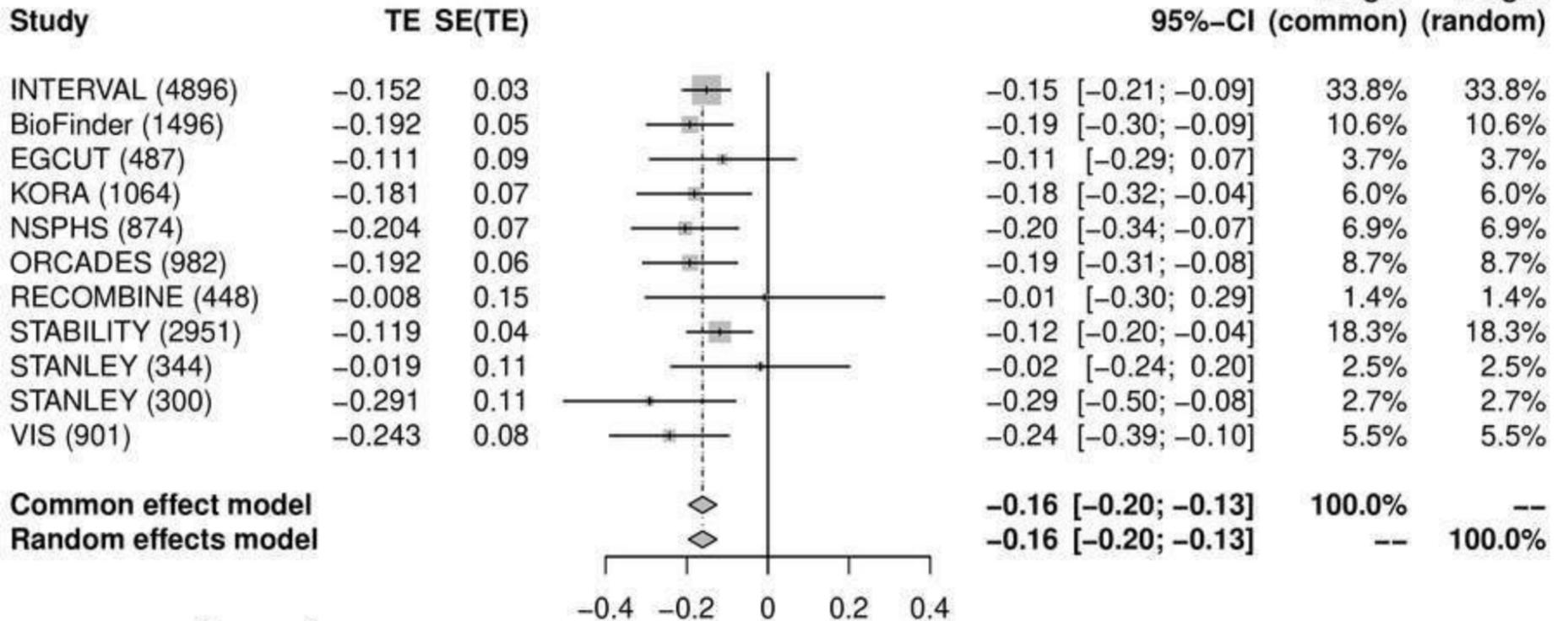


# FGF-21 (FGF21)-rs1260326



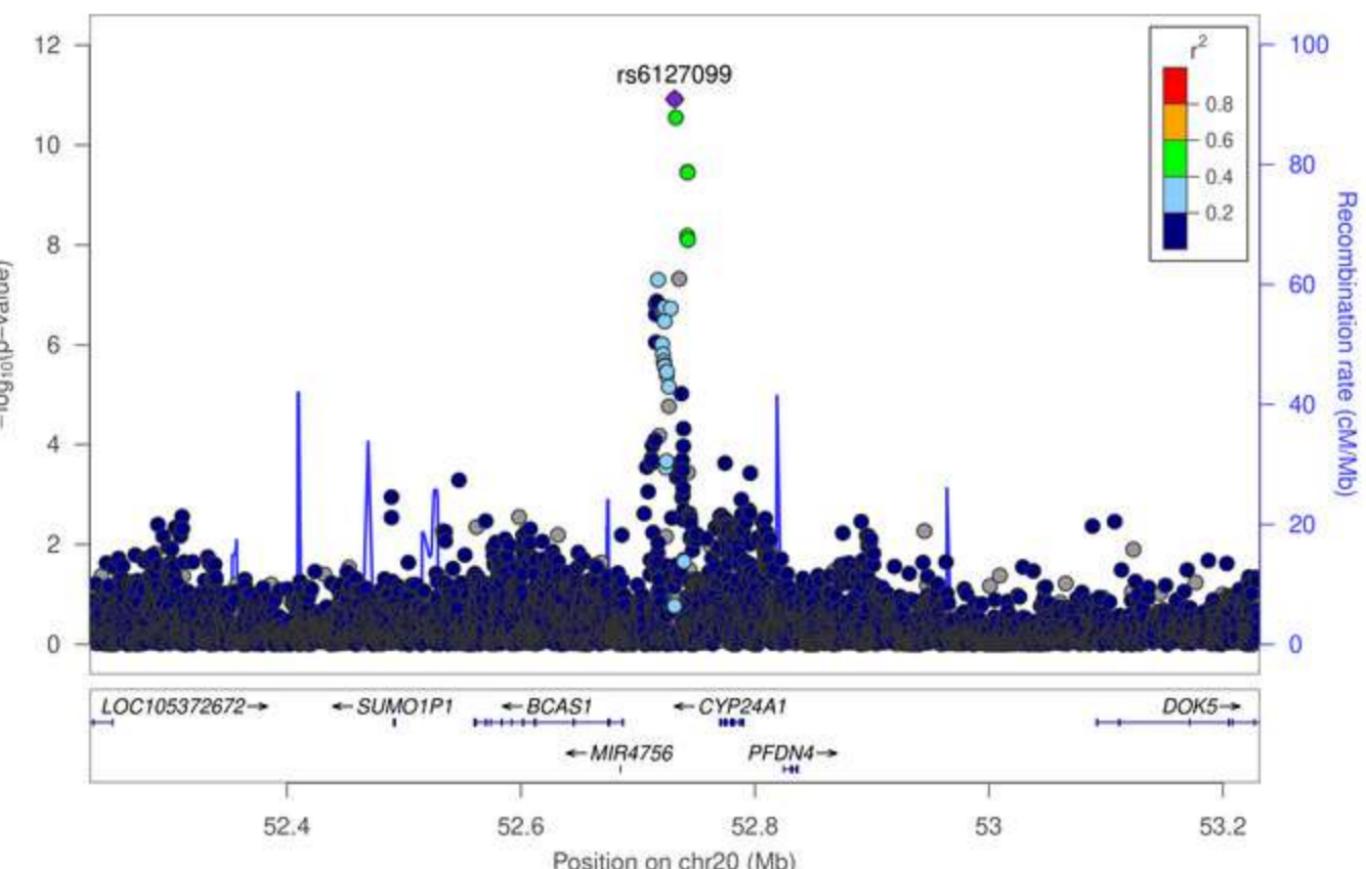
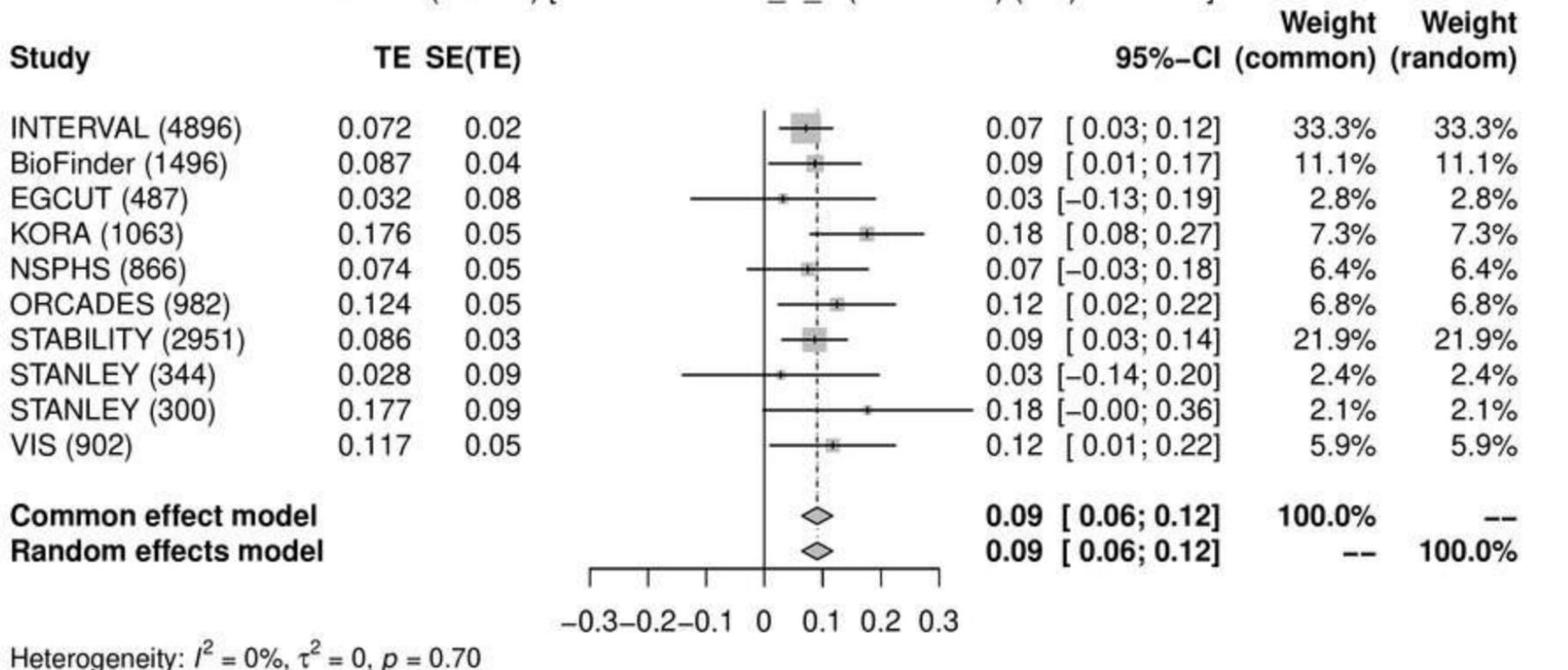
# FGF-21 (FGF21)-rs13229619

FGF-21 (FGF21) [chr7:73030175\_A\_G (rs13229619) (A/G) N=14743]



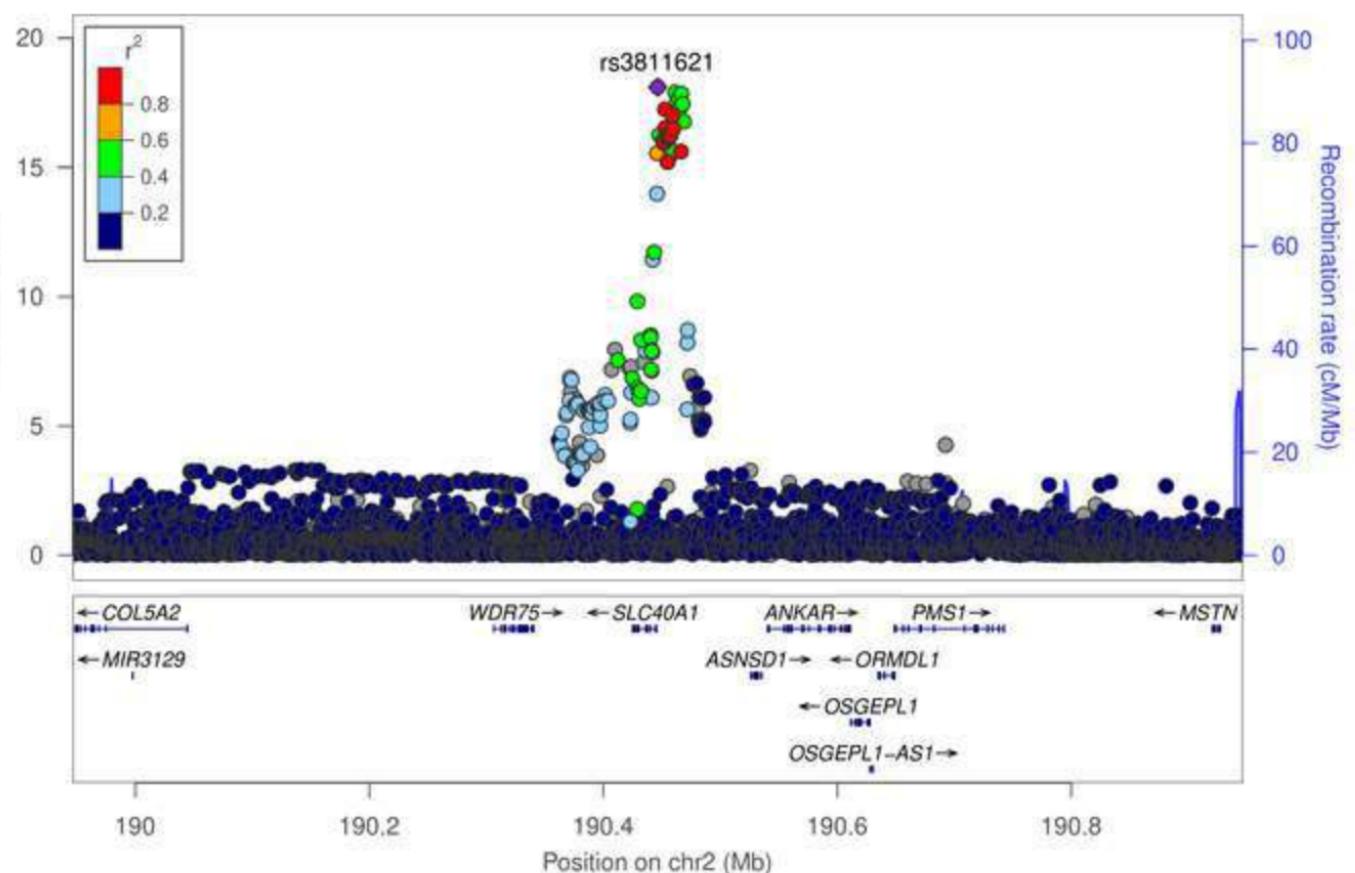
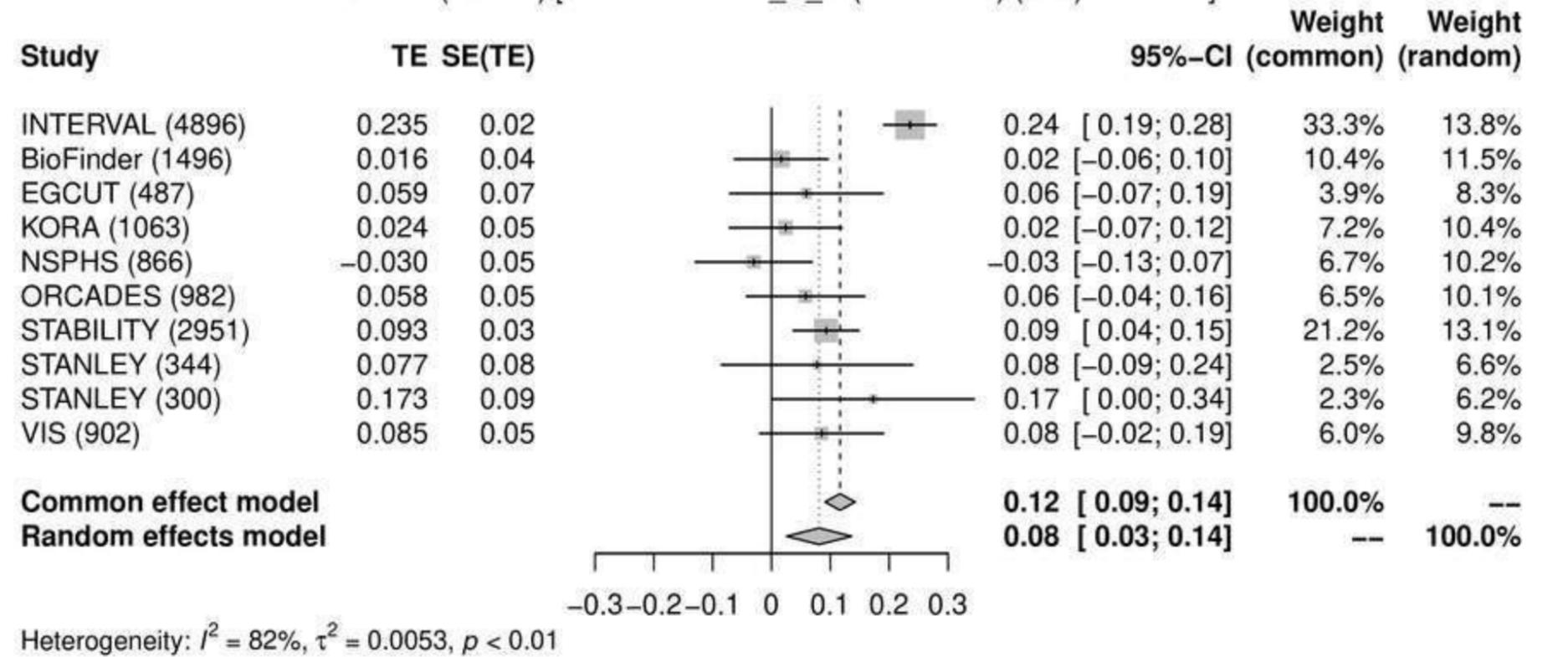
# FGF-23 (FGF23)-rs6127099

FGF-23 (FGF23) [chr20:52731402\_A\_T (rs6127099) (A/T) N=14287]



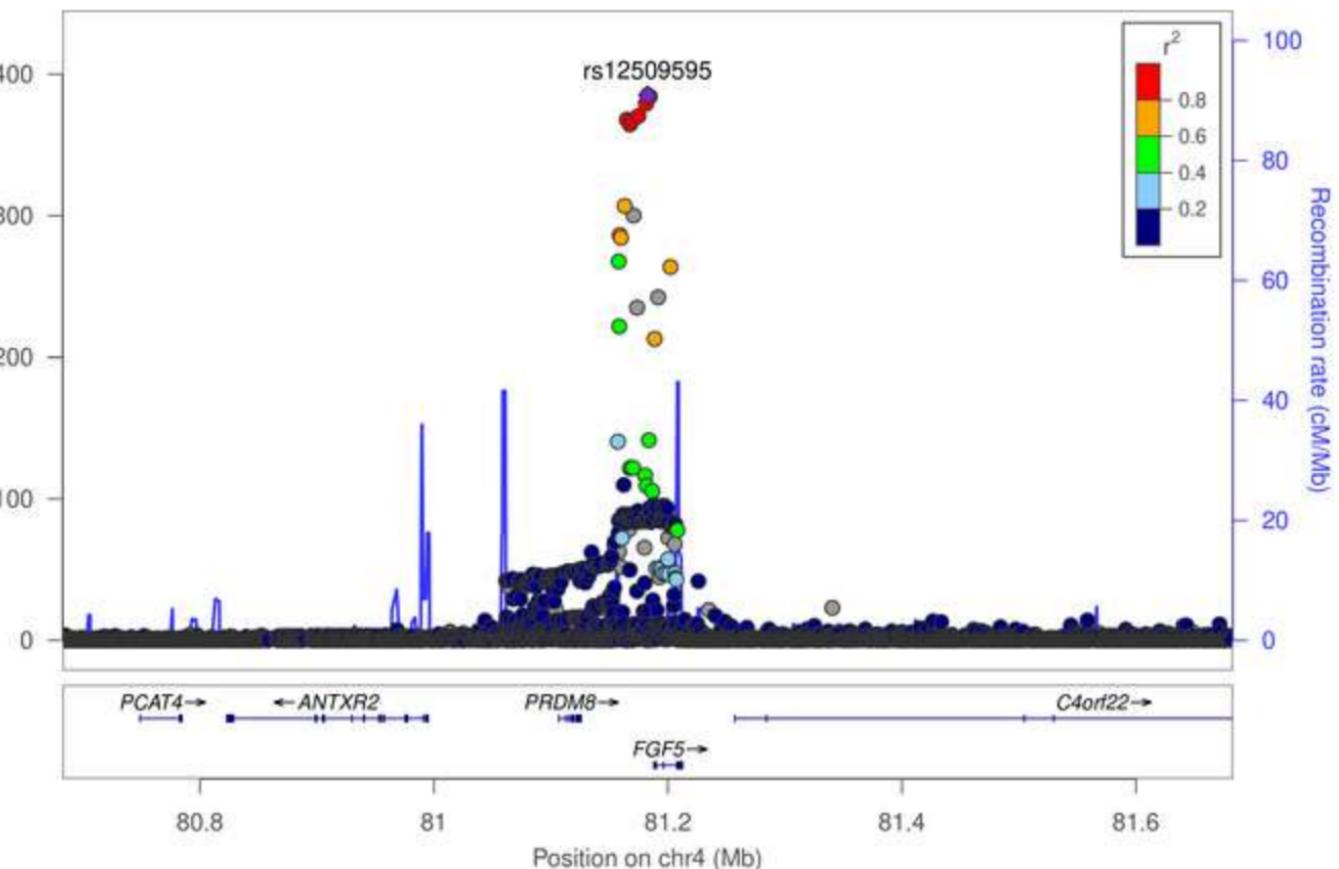
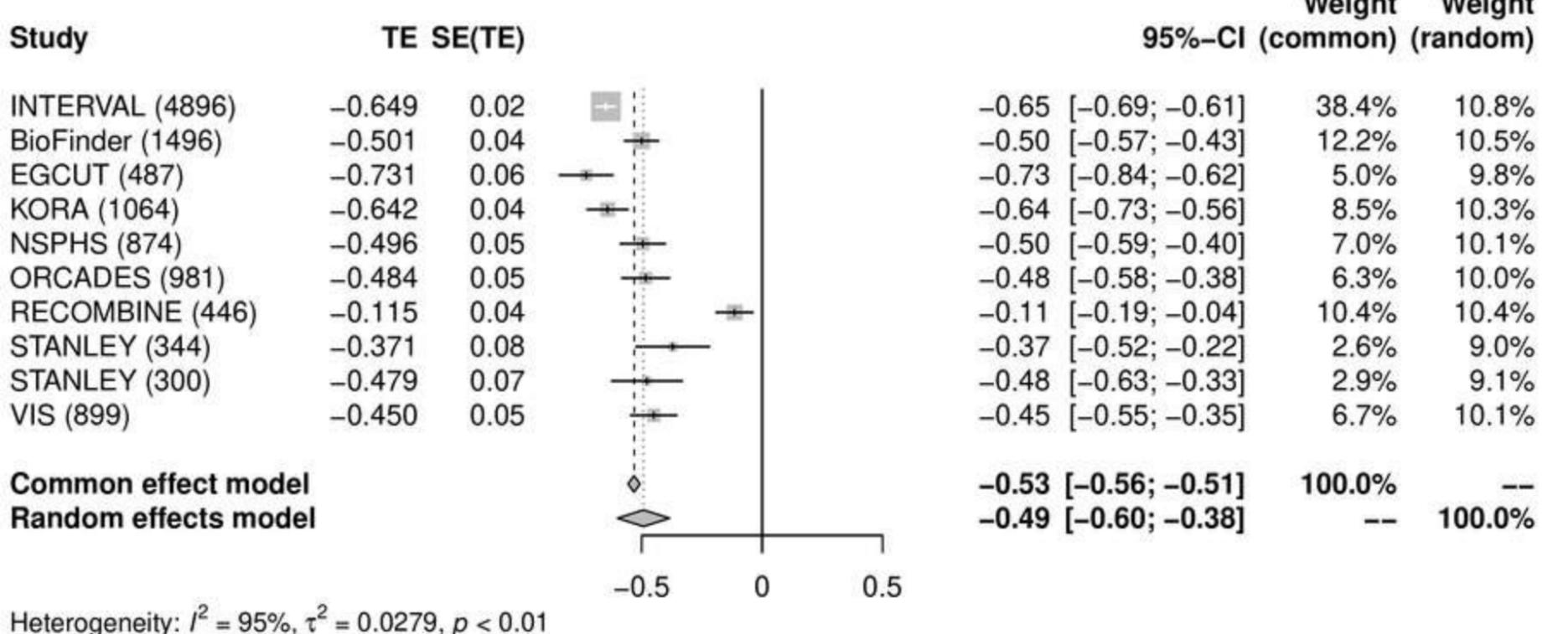
# FGF-23 (FGF23)-rs3811621

FGF-23 (FGF23) [chr2:190446541\_C\_G (rs3811621) (C/G) N=14287]



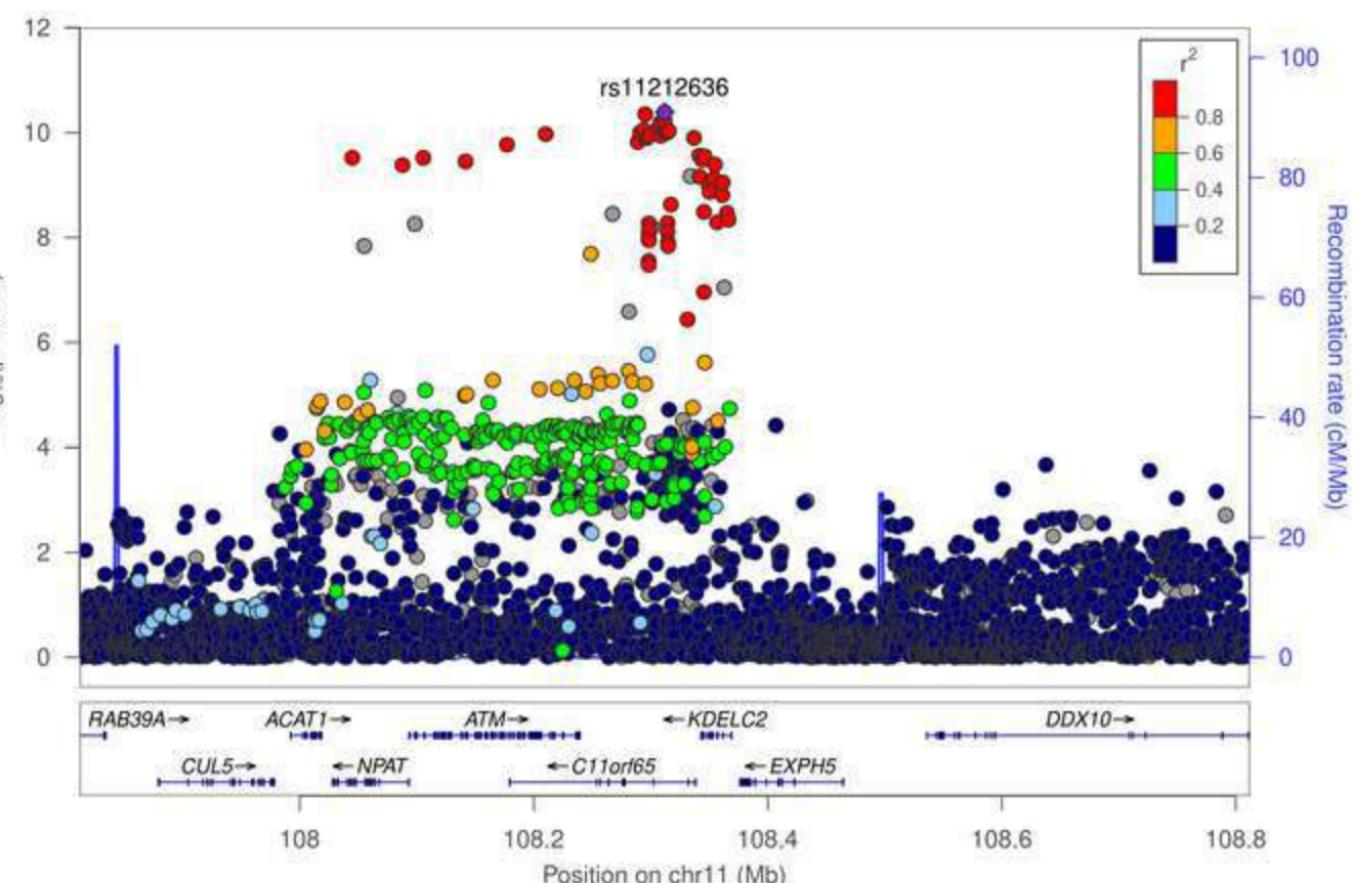
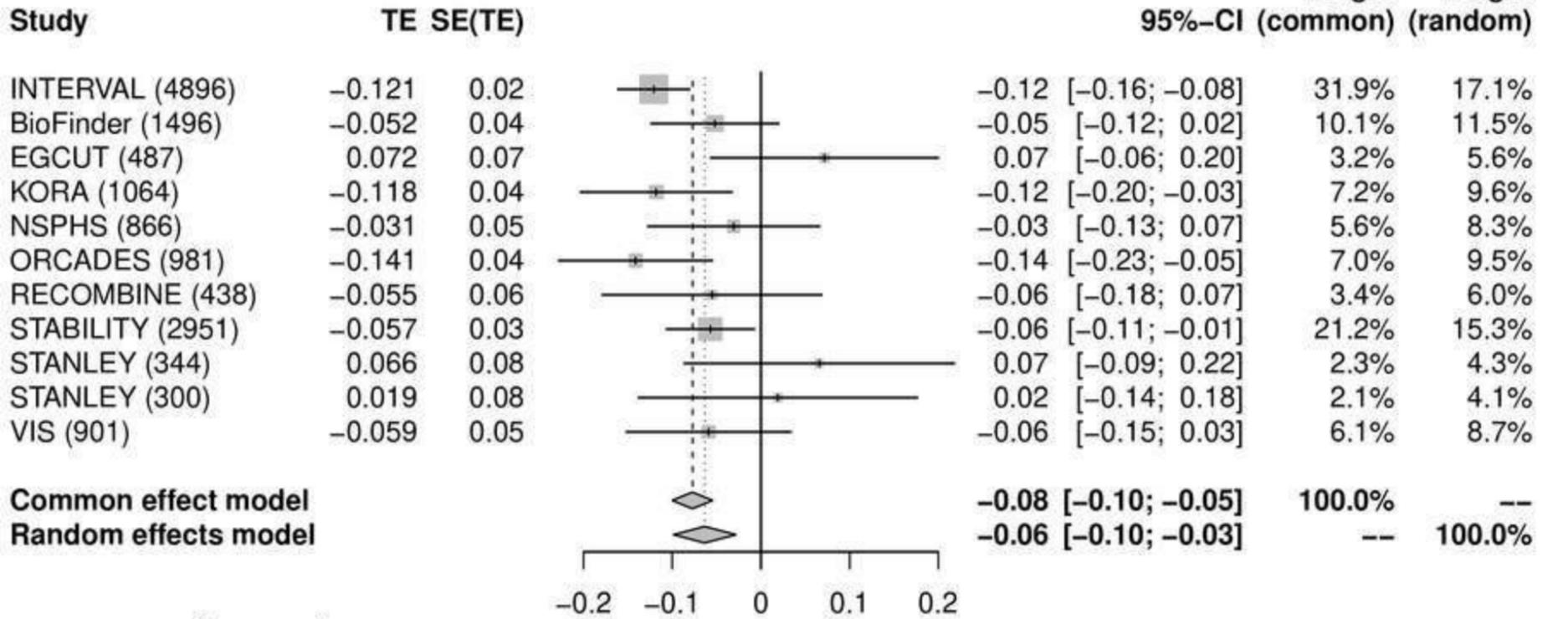
# FGF-5 (FGF5)-rs12509595

FGF-5 (FGF5) [chr4:81182554\_C\_T (rs12509595) (T/C) N=11787]



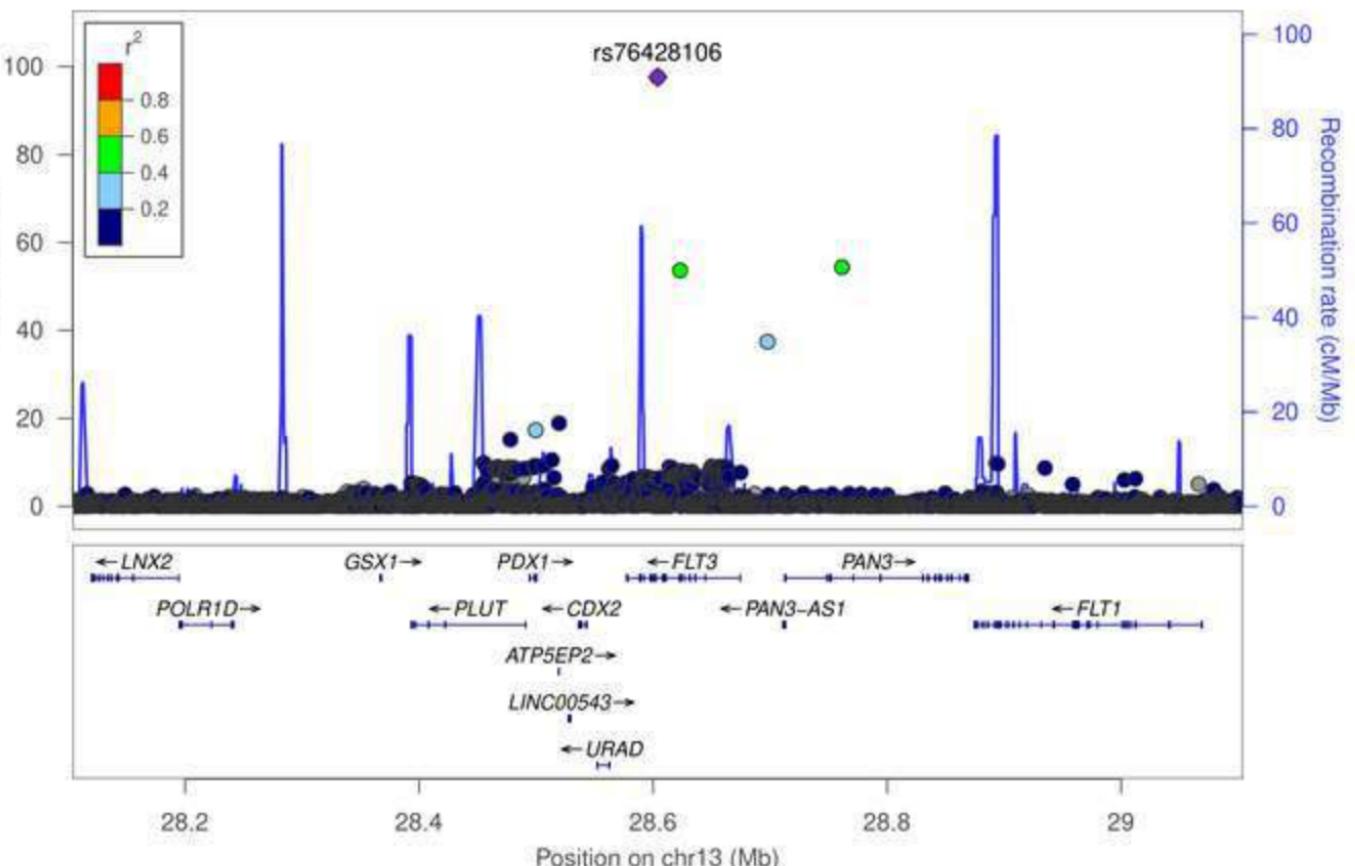
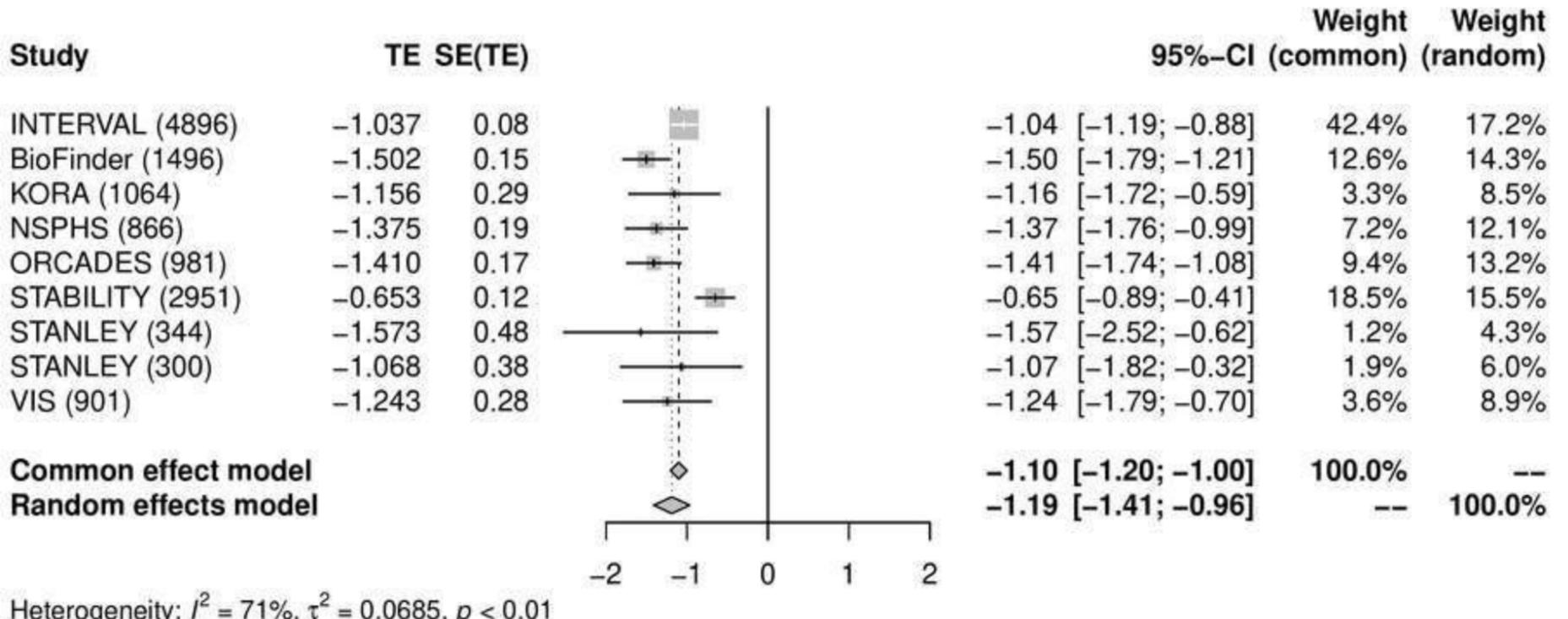
# Flt3L (FLT3LG)-rs11212636

**Study**



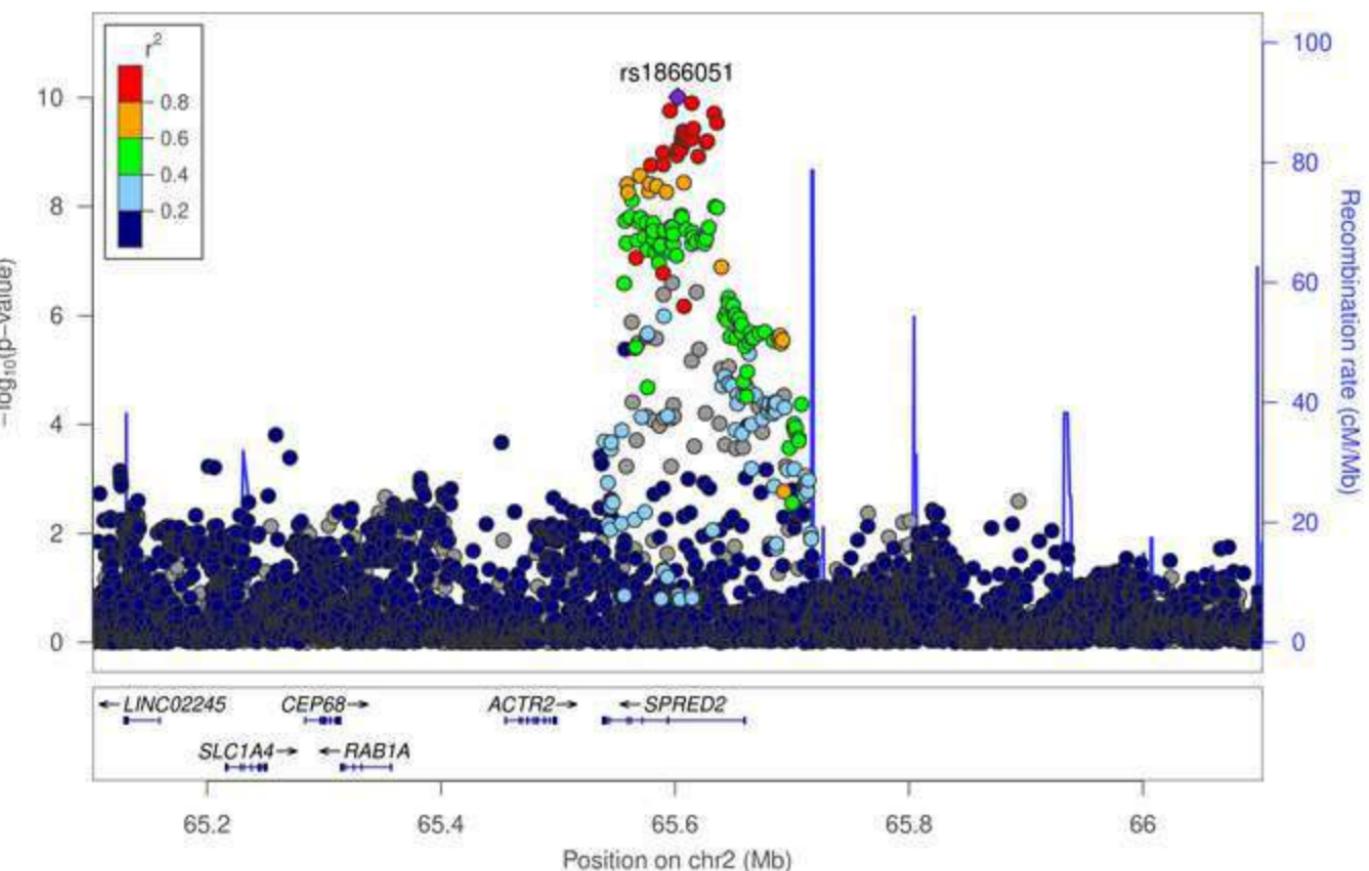
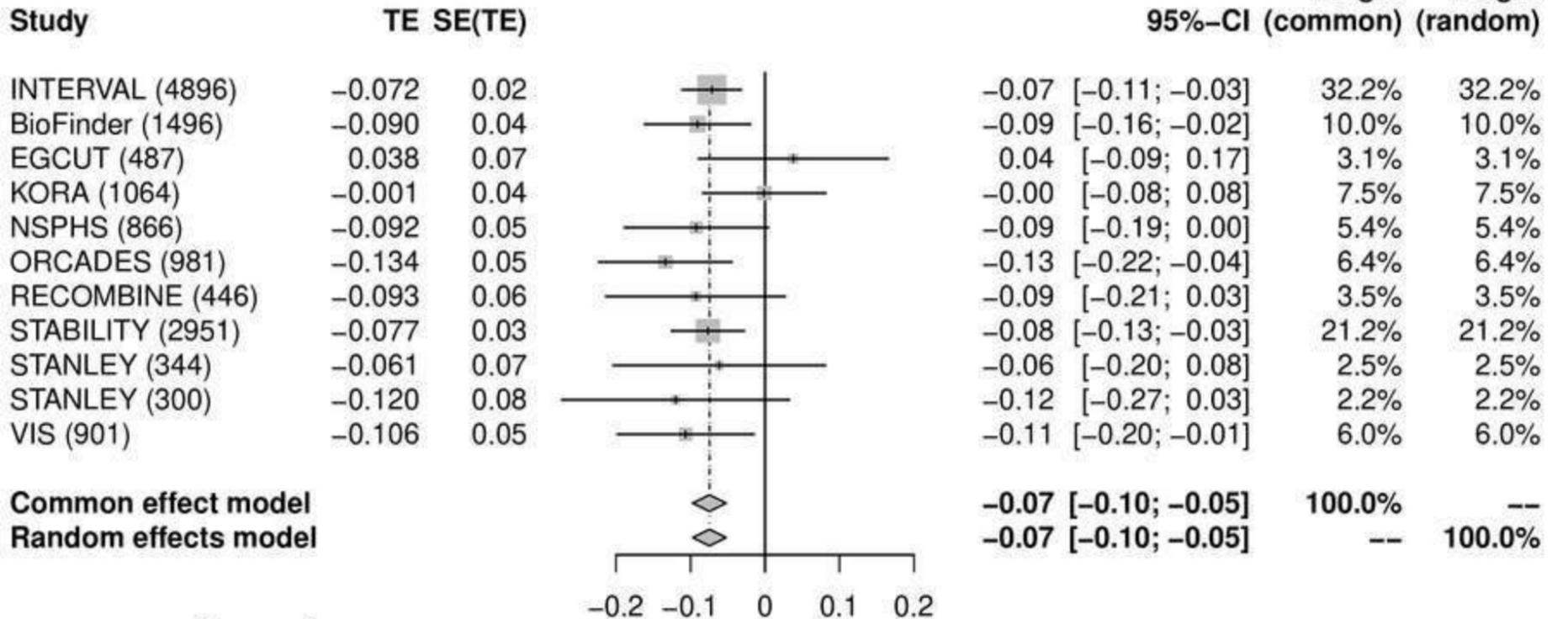
# Flt3L (FLT3LG)-rs76428106

Flt3L (FLT3LG) [chr13:28604007\_C\_T (rs76428106) (T/C) N=13799]

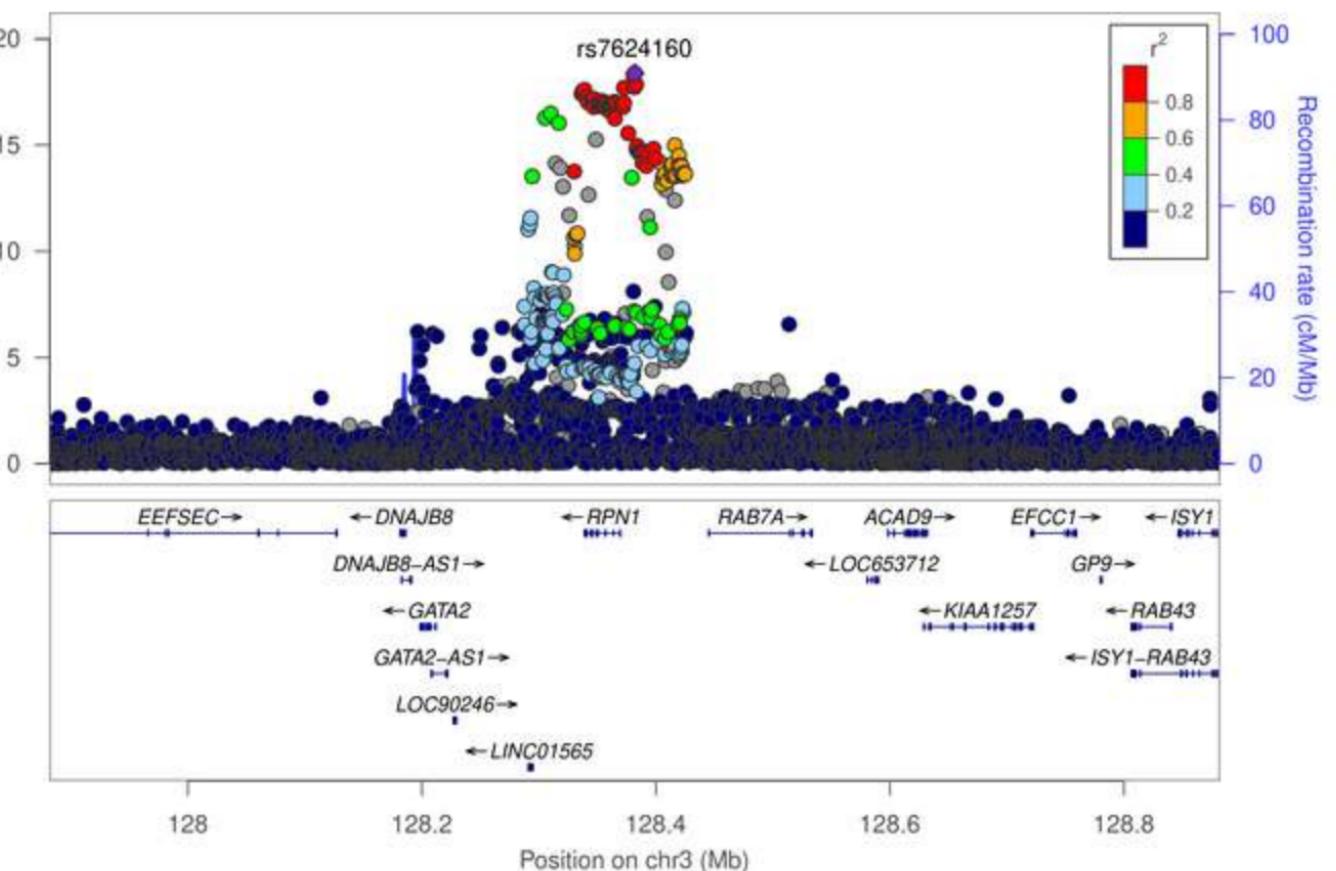
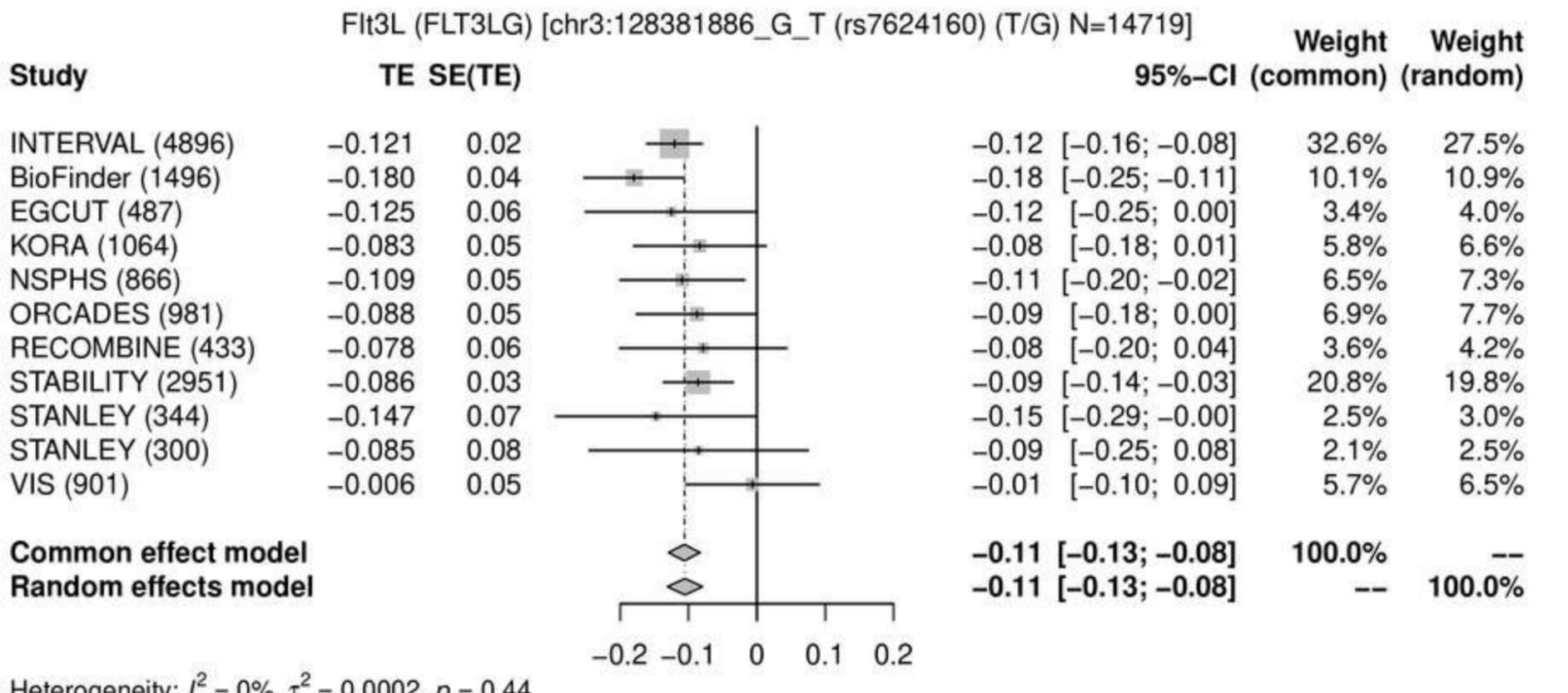


# Flt3L (FLT3LG)-rs1866051

## Study



# Flt3L (FLT3LG)-rs7624160



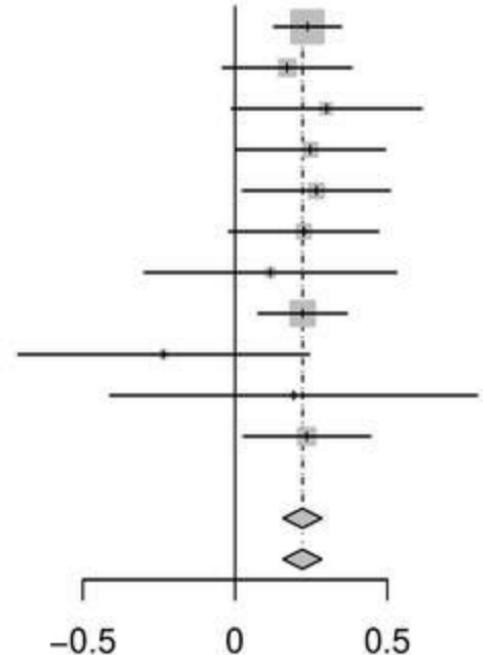
# Flt3L (FLT3LG)-rs144317085

Flt3L (FLT3LG) [chr4:105806108\_A\_T (rs144317085) (A/T) N=14722]

## Study

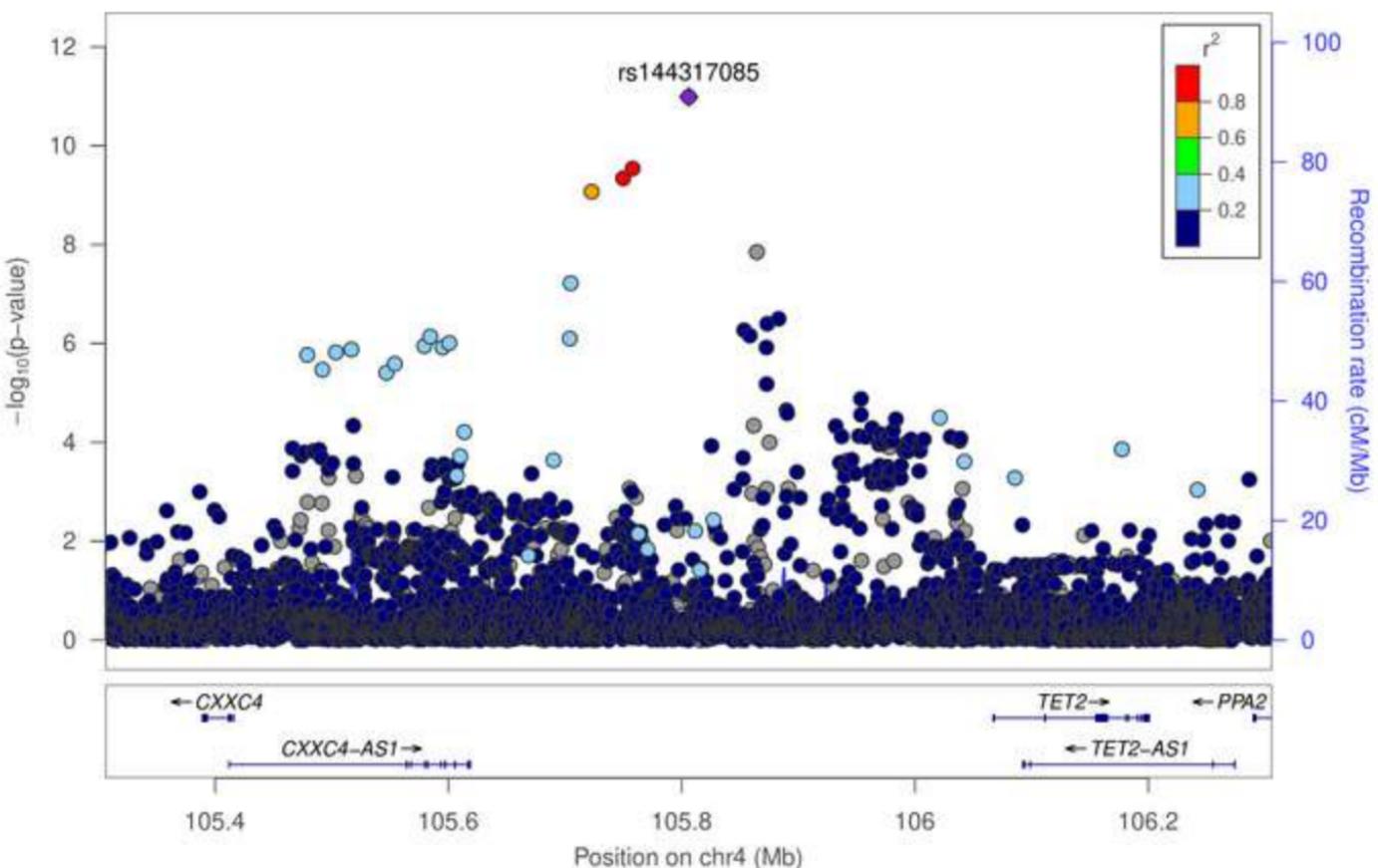
INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
NSPHS (866)  
ORCADES (981)  
RECOMBINE (436)  
STABILITY (2951)  
STANLEY (344)  
STANLEY (300)  
VIS (901)

TE SE(TE)

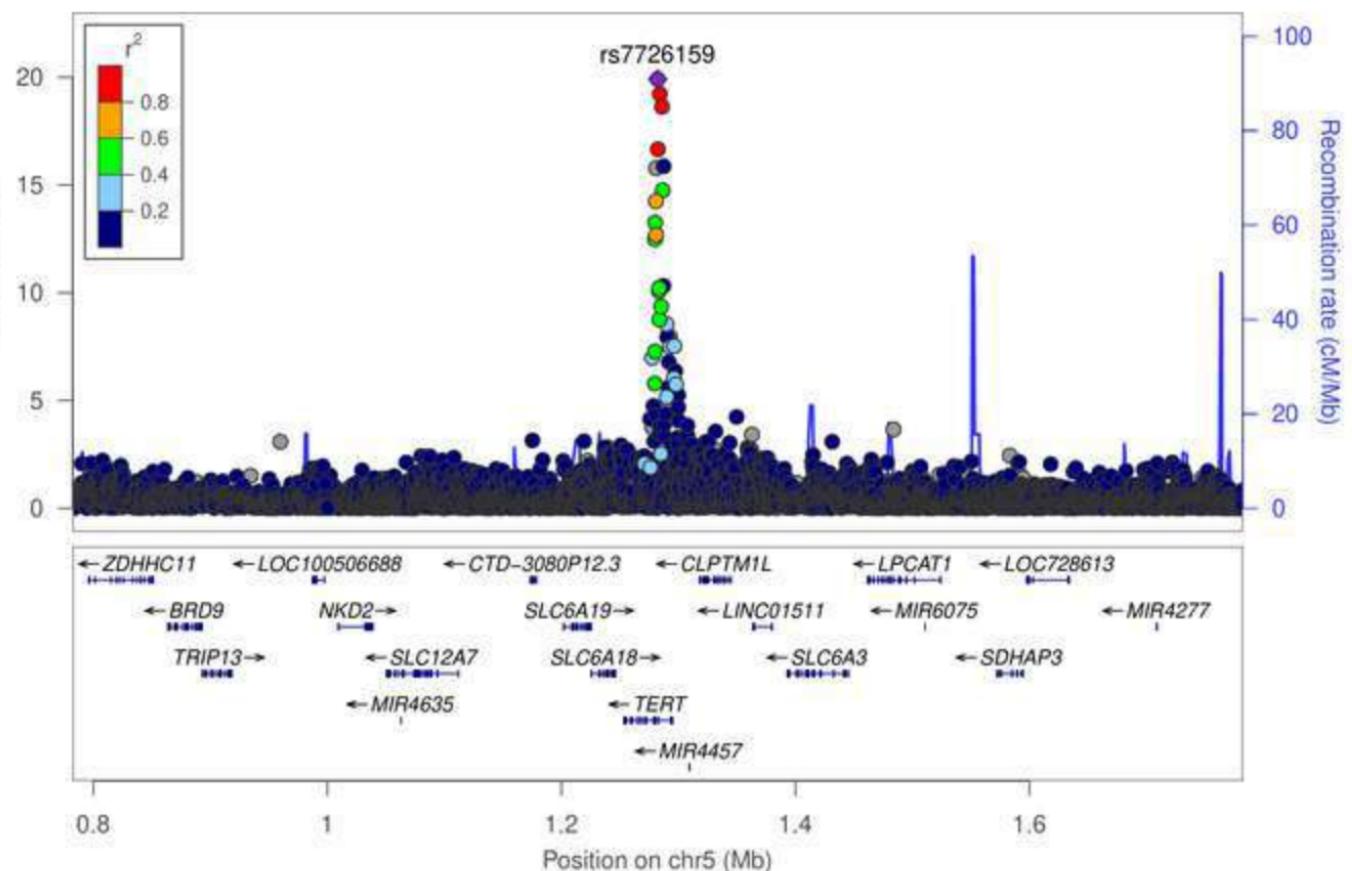
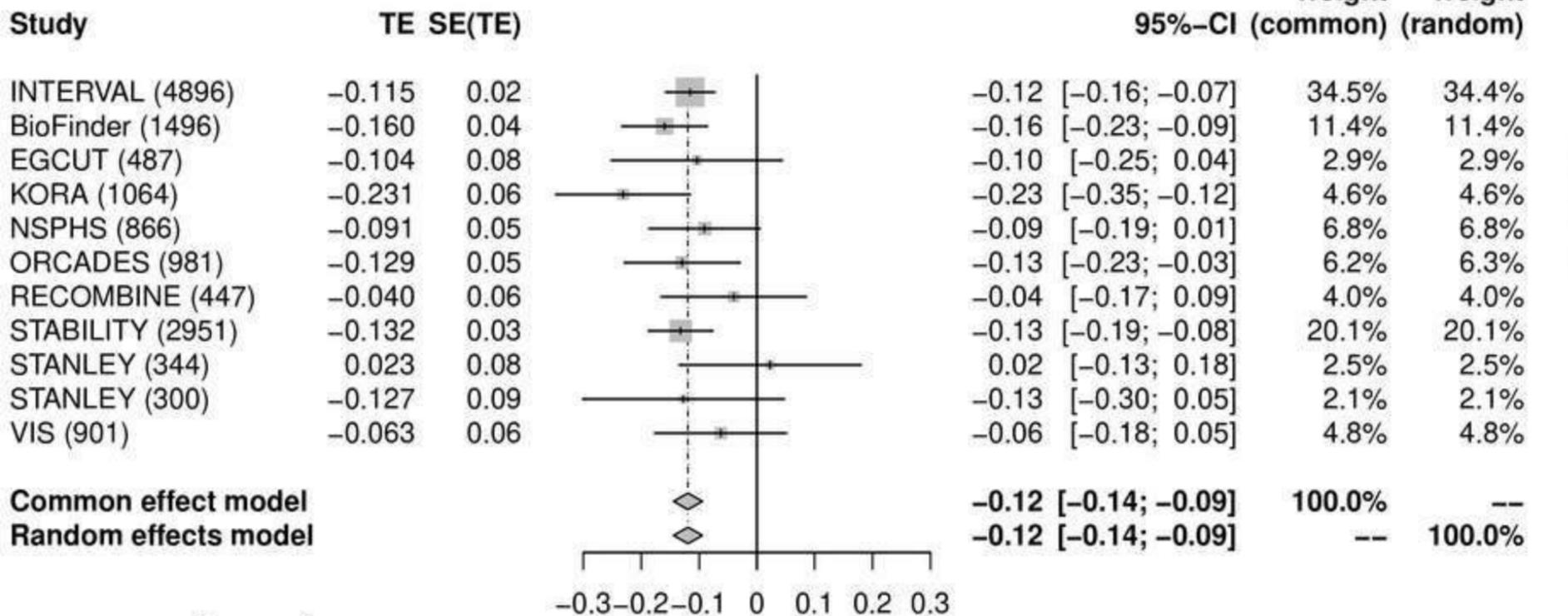


		Weight 95%-CI (common)	Weight (random)
	0.24 [ 0.13; 0.35]	33.2%	33.2%
	0.17 [-0.04; 0.38]	9.0%	9.0%
	0.30 [-0.01; 0.61]	4.1%	4.1%
	0.25 [-0.00; 0.49]	6.6%	6.6%
	0.27 [ 0.02; 0.51]	6.9%	6.9%
	0.22 [-0.02; 0.47]	6.7%	6.7%
	0.12 [-0.30; 0.53]	2.4%	2.4%
	0.22 [ 0.07; 0.37]	19.0%	19.0%
	-0.24 [-0.71; 0.24]	1.8%	1.8%
	0.19 [-0.41; 0.79]	1.1%	1.1%
	0.24 [ 0.03; 0.44]	9.3%	9.3%
Common effect model	<b>0.22 [ 0.16; 0.28]</b>	100.0%	--
Random effects model	<b>0.22 [ 0.16; 0.28]</b>	--	100.0%

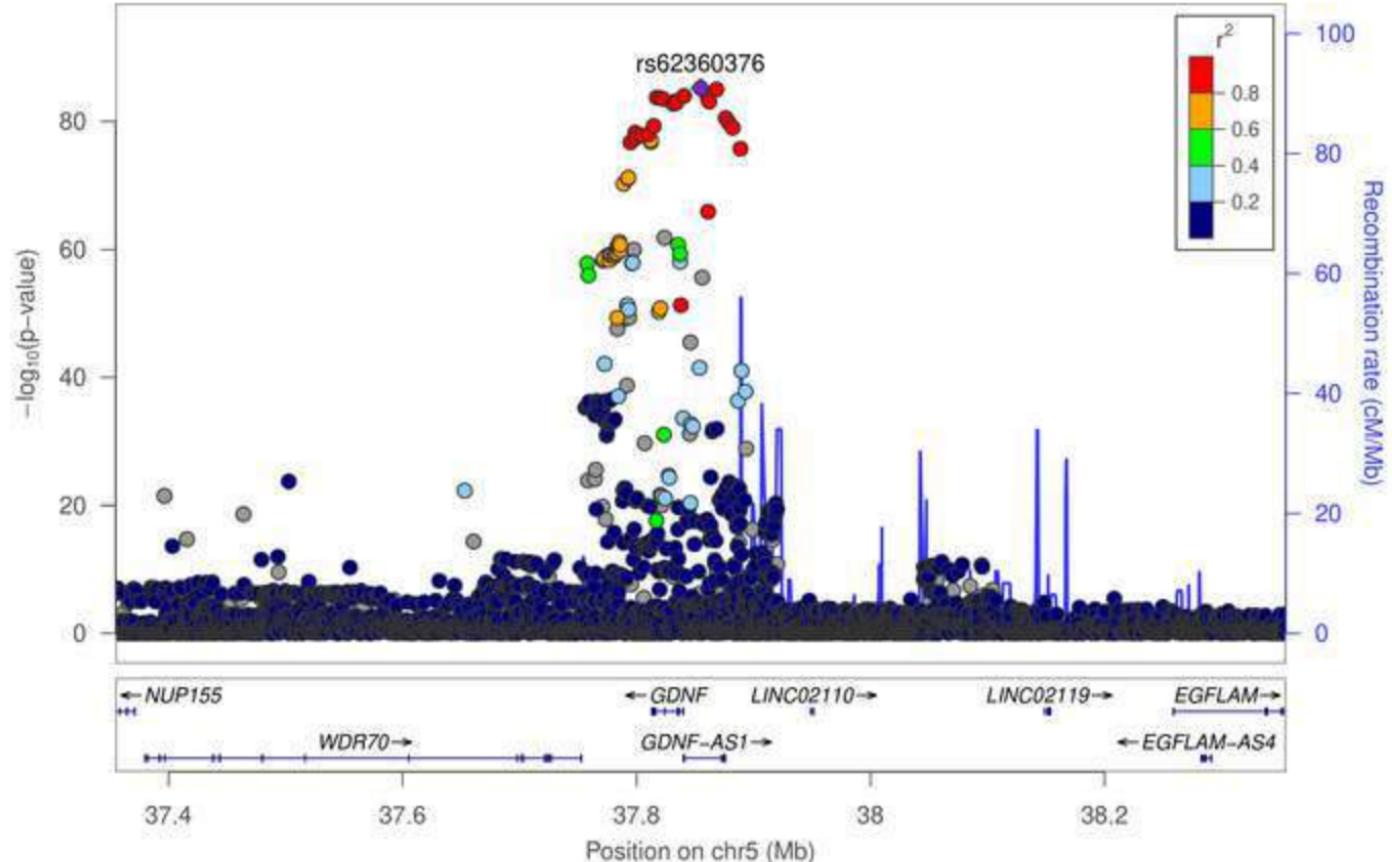
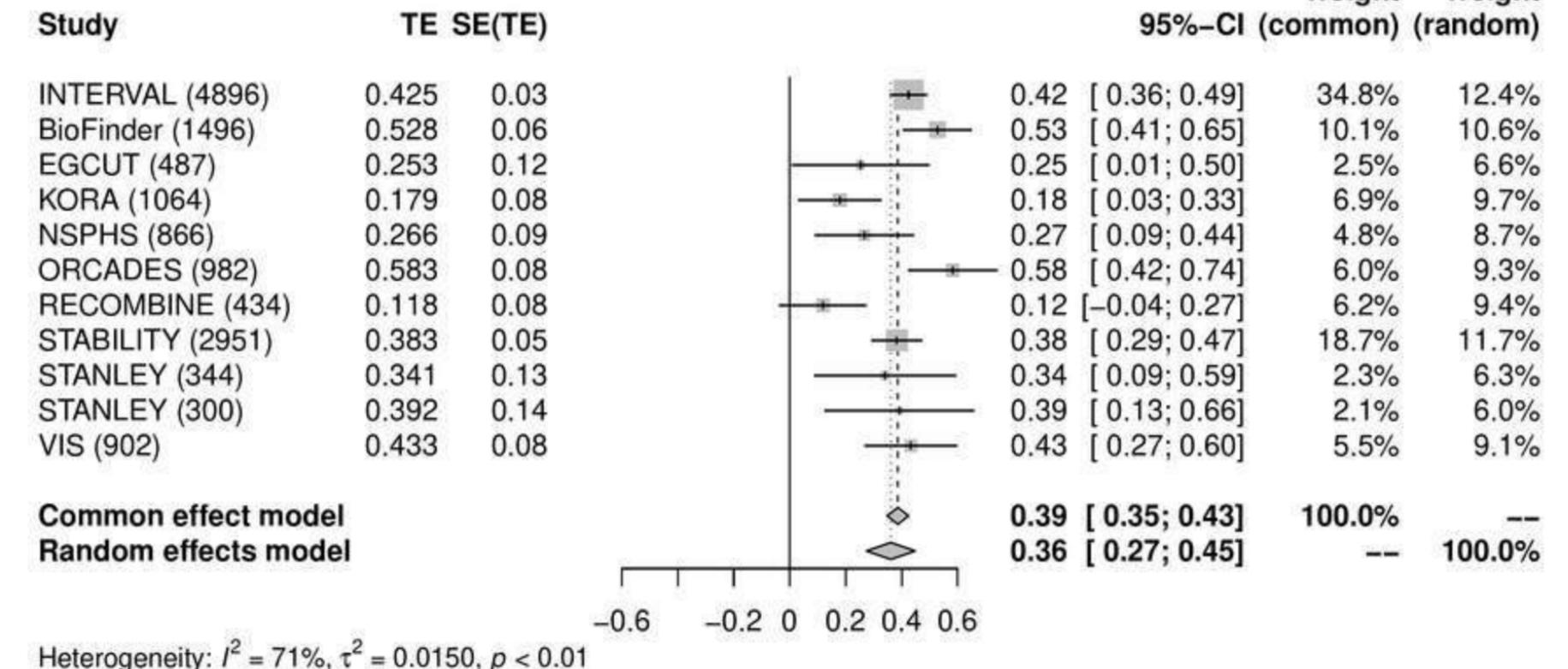
Heterogeneity:  $I^2 = 0\%$ ,  $\tau^2 = 0$ ,  $p = 0.92$



# Flt3L (FLT3LG)-rs7726159

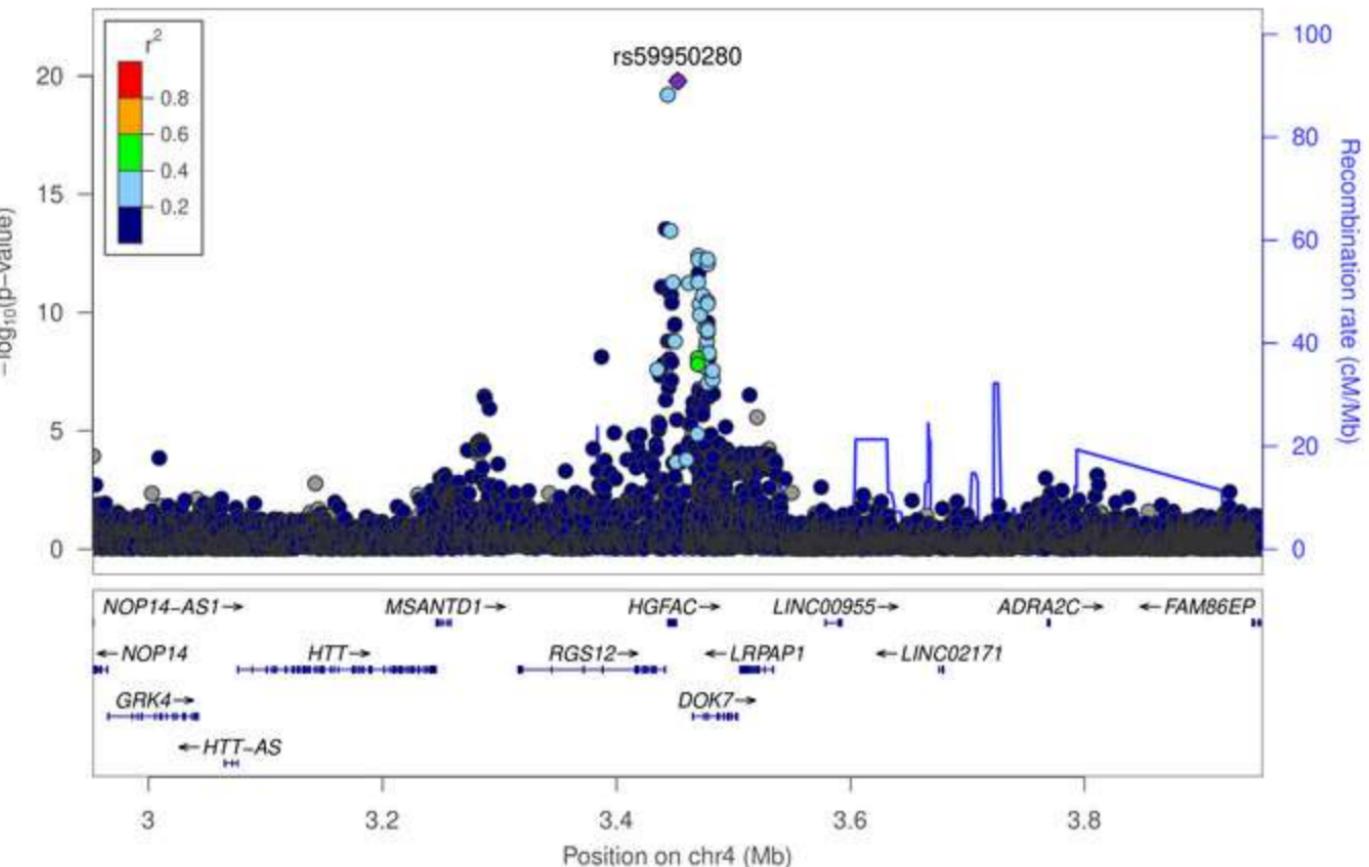
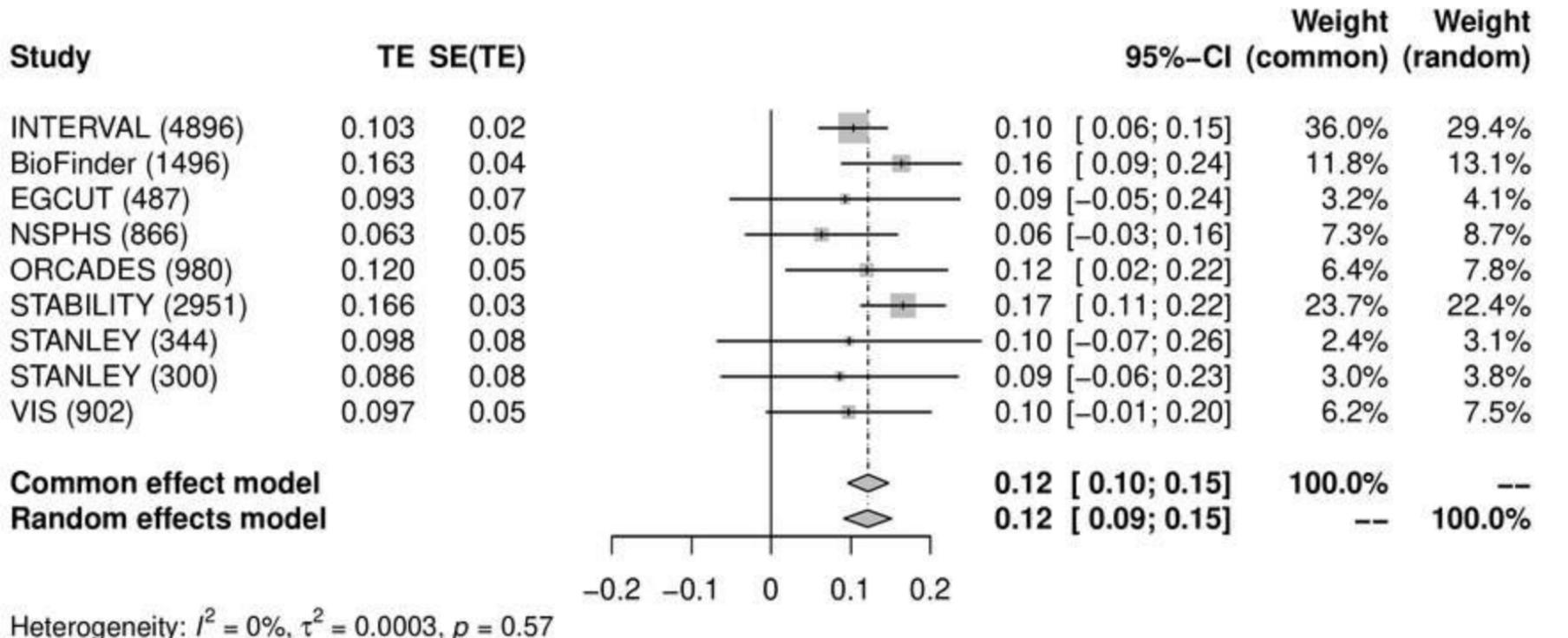


# hGDNF (GDNF)-rs62360376

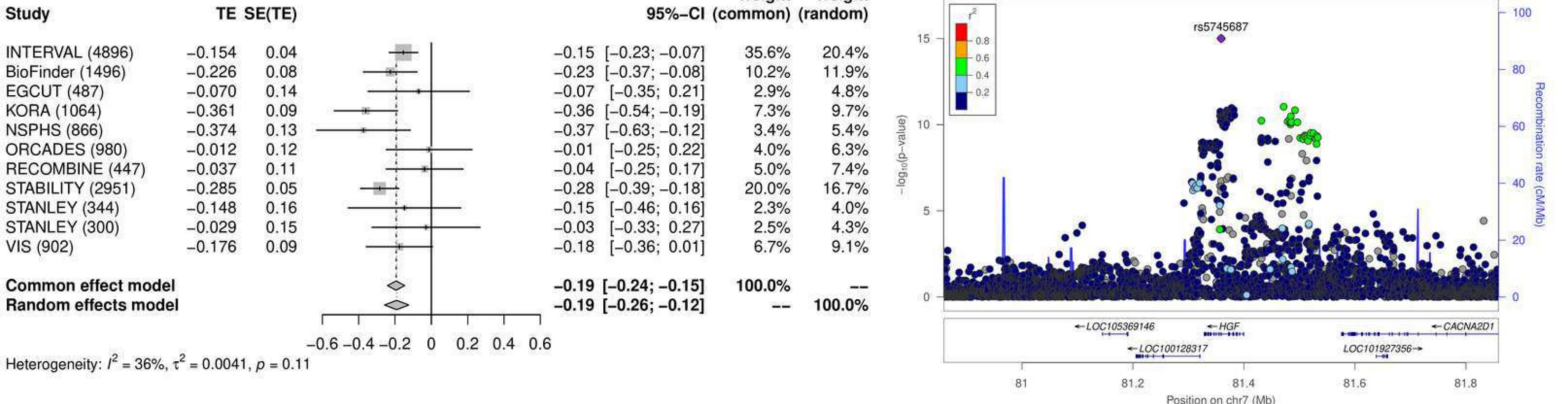


# HGF (HGF)-rs59950280

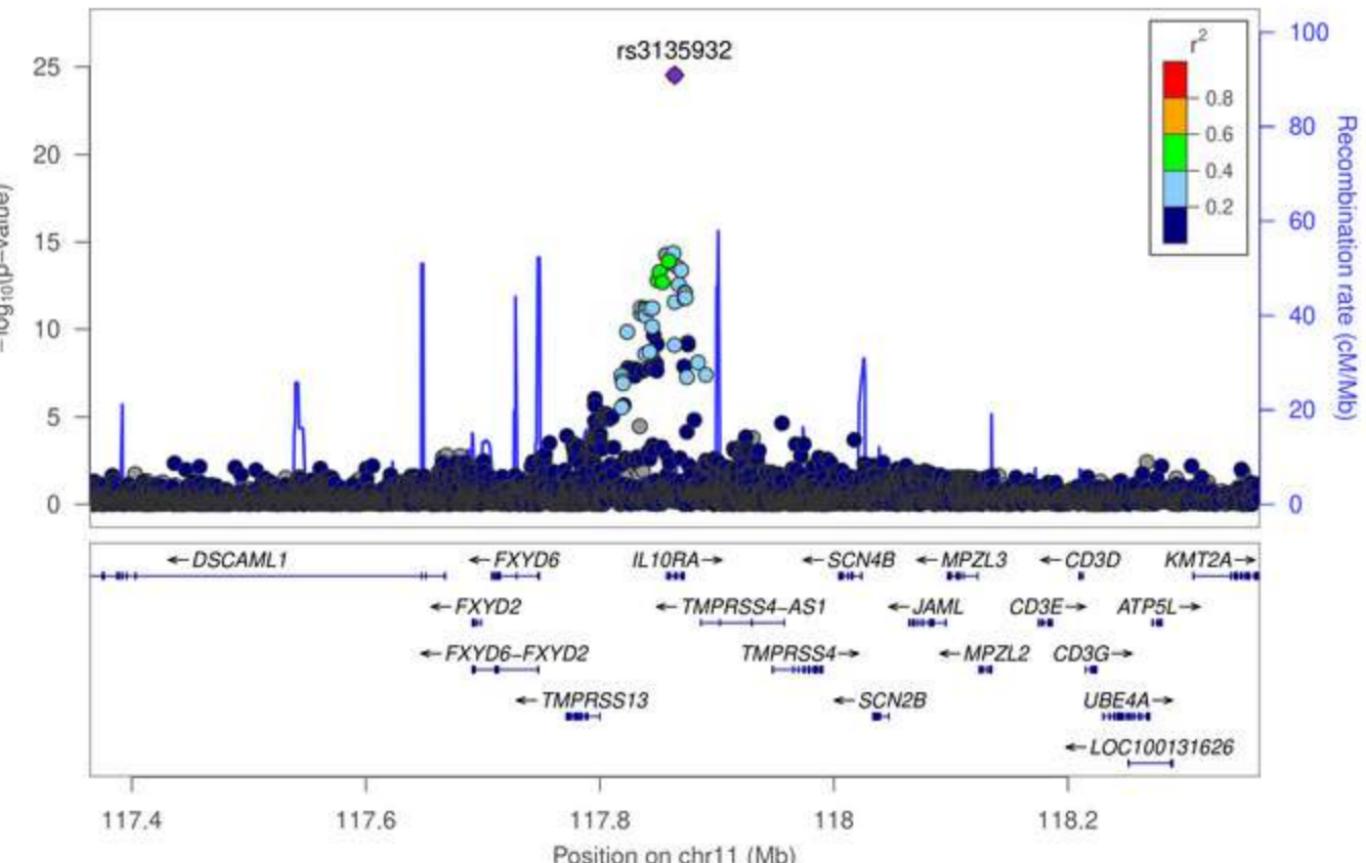
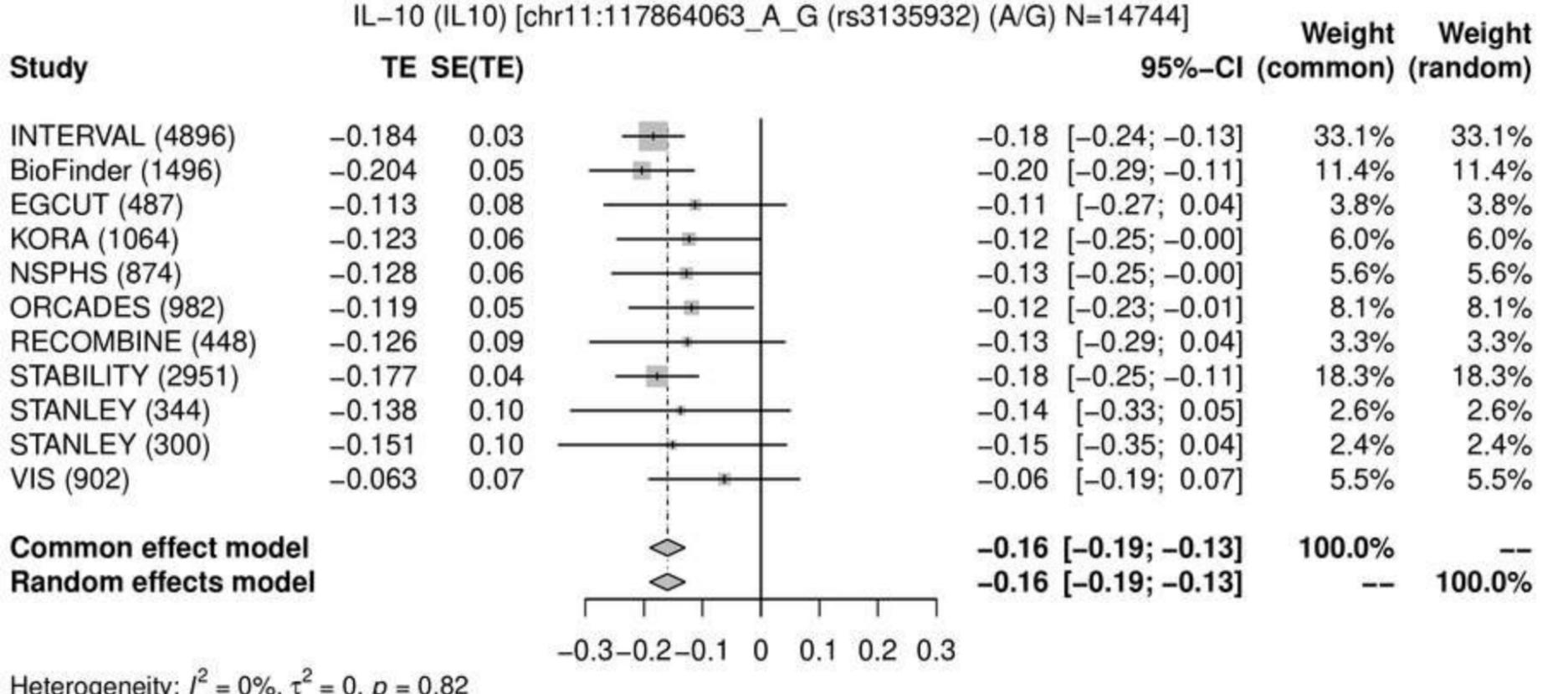
HGF (HGF) [chr4:3452345\_A\_G (rs59950280) (A/G) N=13222]



## HGF (HGF)-rs5745687

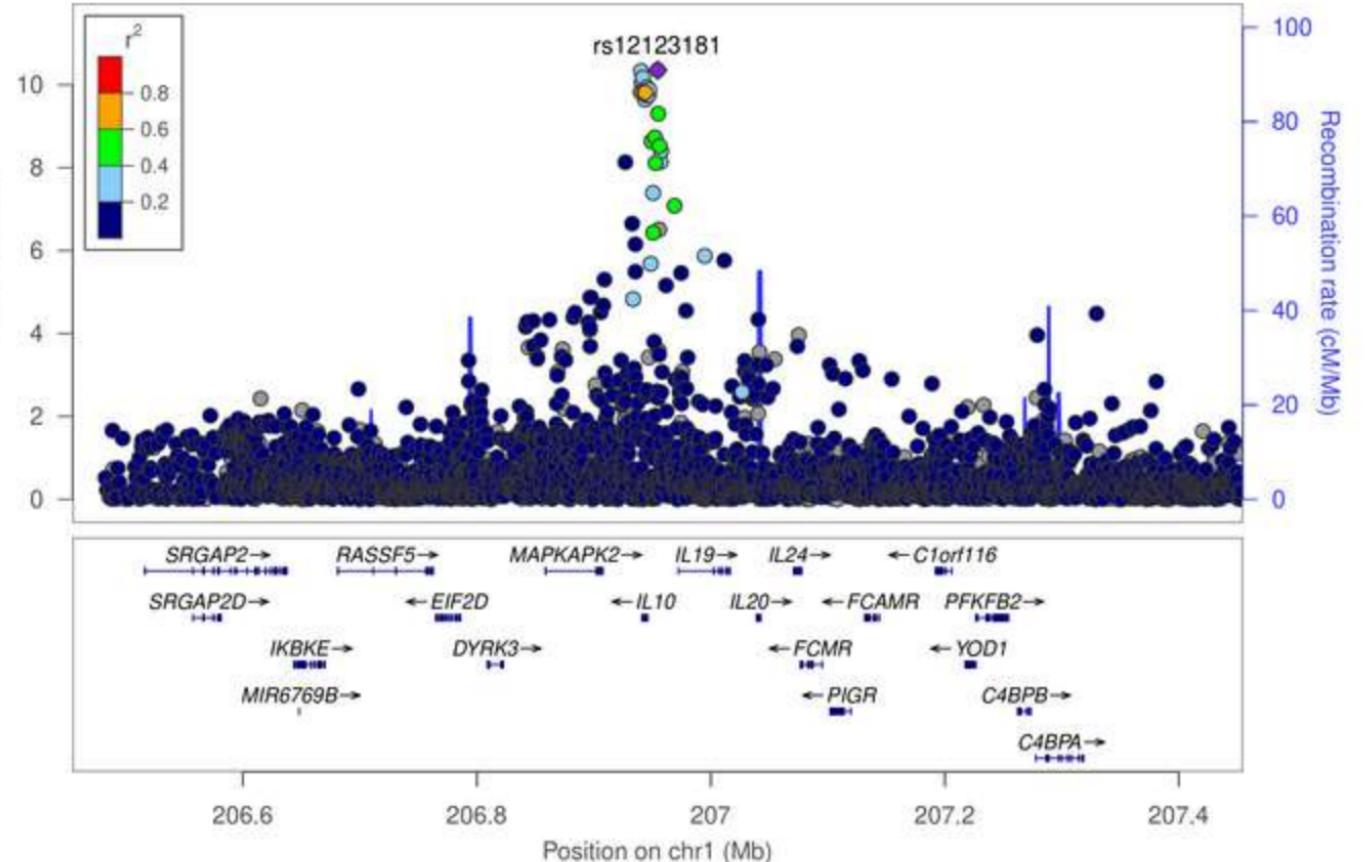
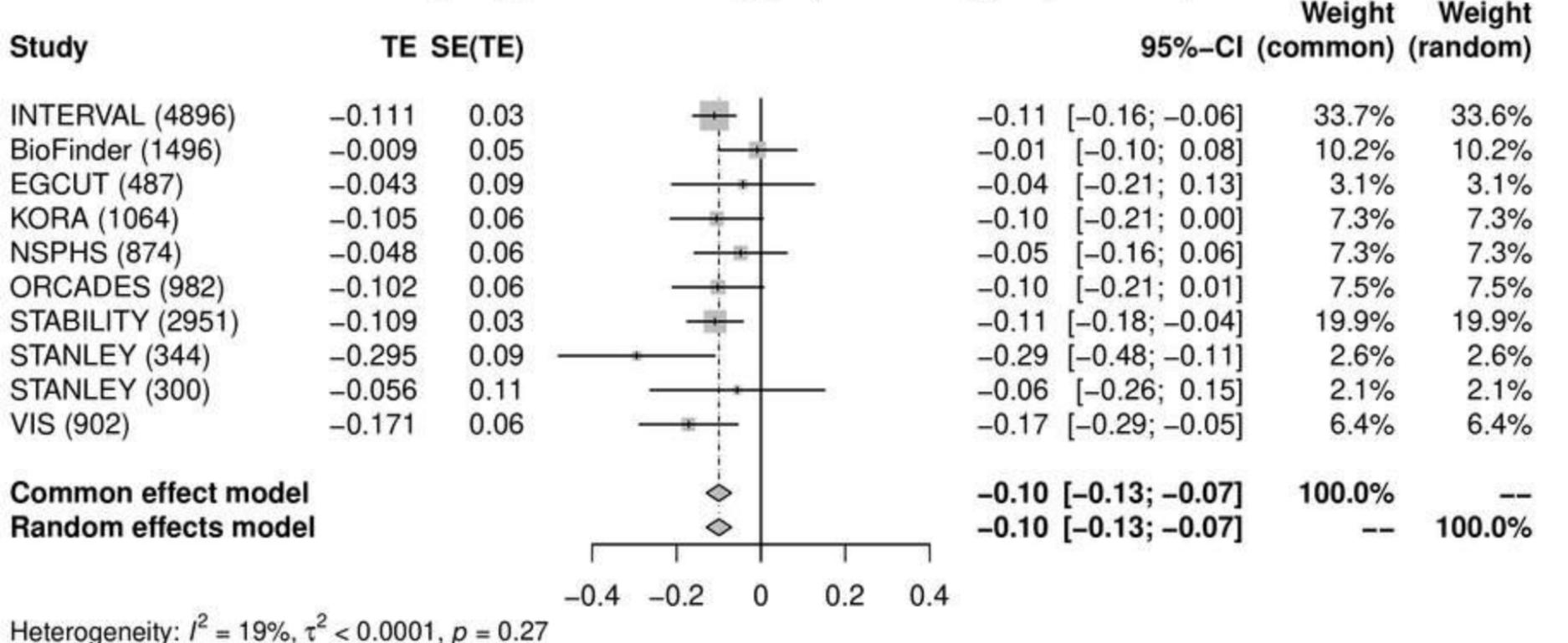


# IL-10 (IL10)-rs3135932



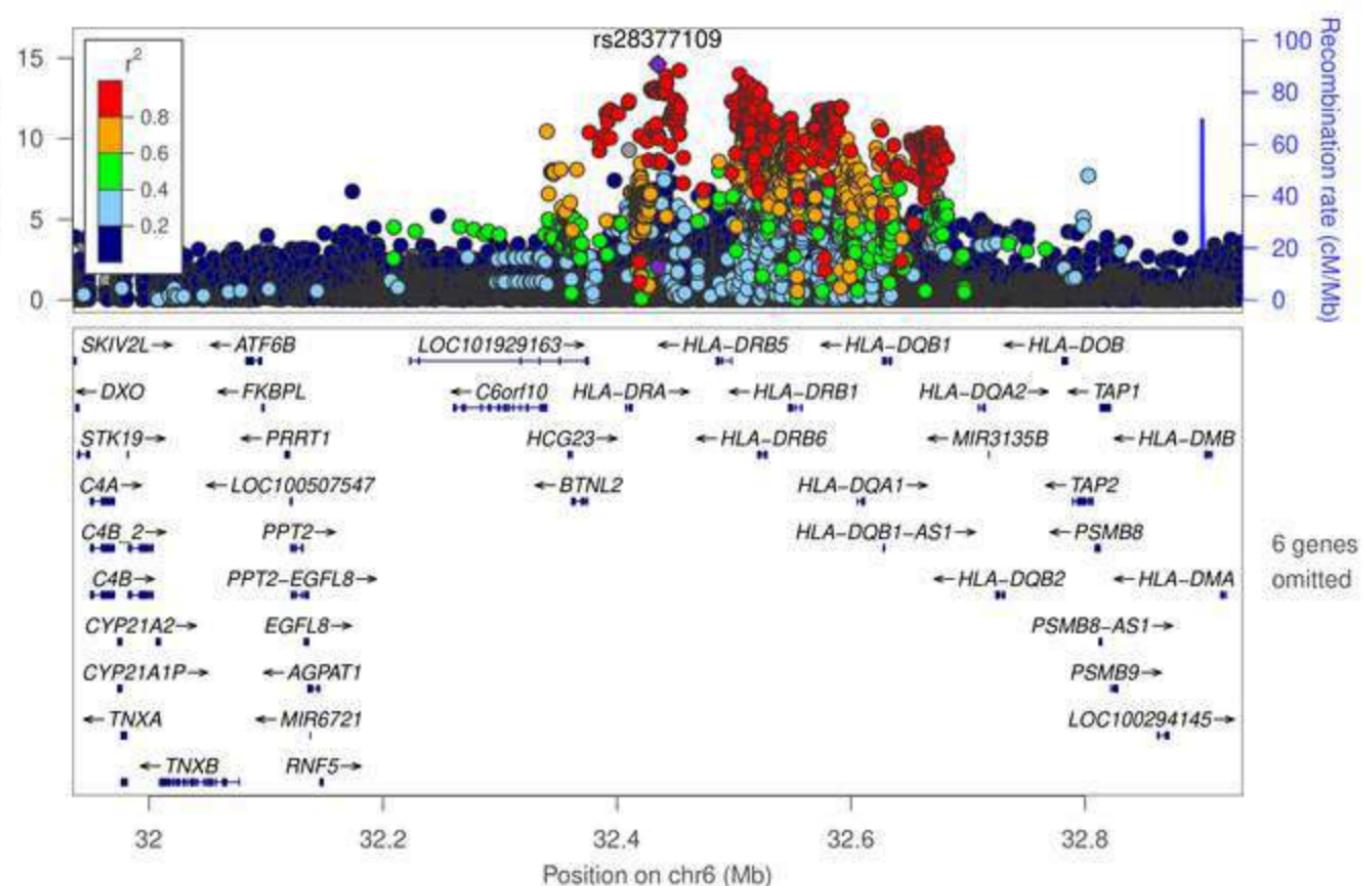
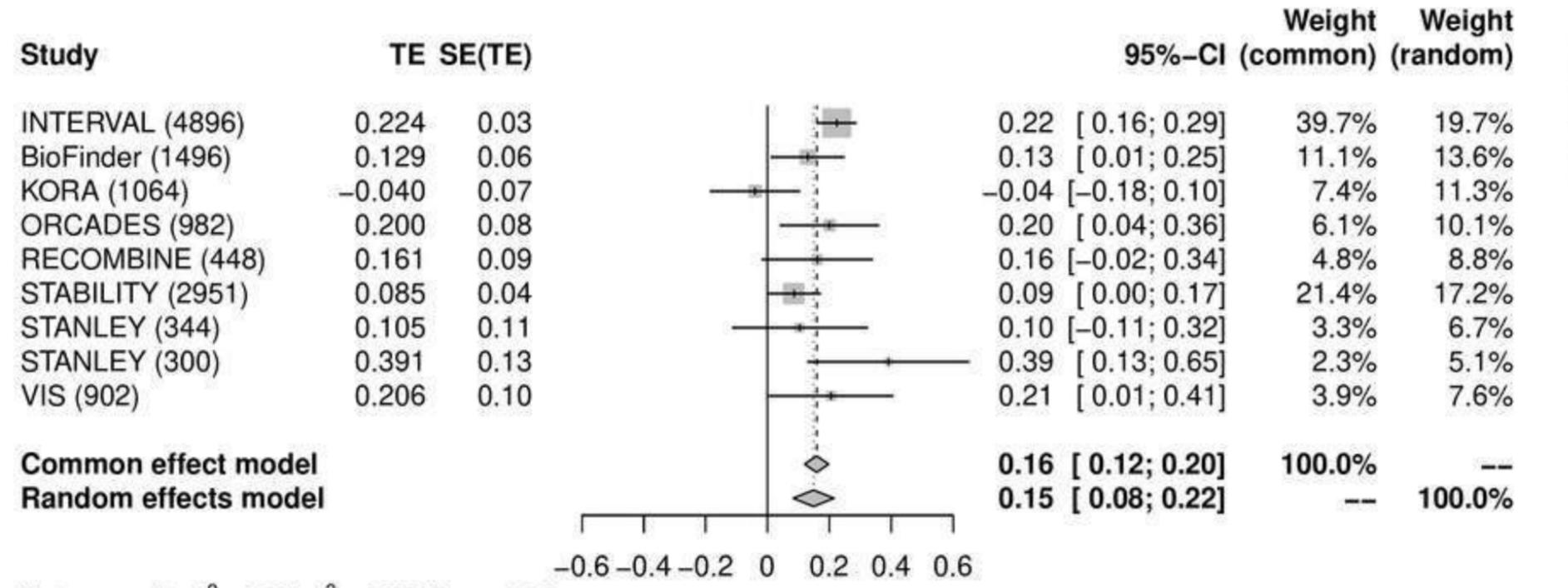
# IL-10 (IL10)-rs12123181

IL-10 (IL10) [chr1:206954566\_A\_G (rs12123181) (A/G) N=14296]



L-10 (IL10)-rs28377109

L-10 (IL10) [chr6:32434716\_A\_C (rs28377109) (A/C) N=13383]



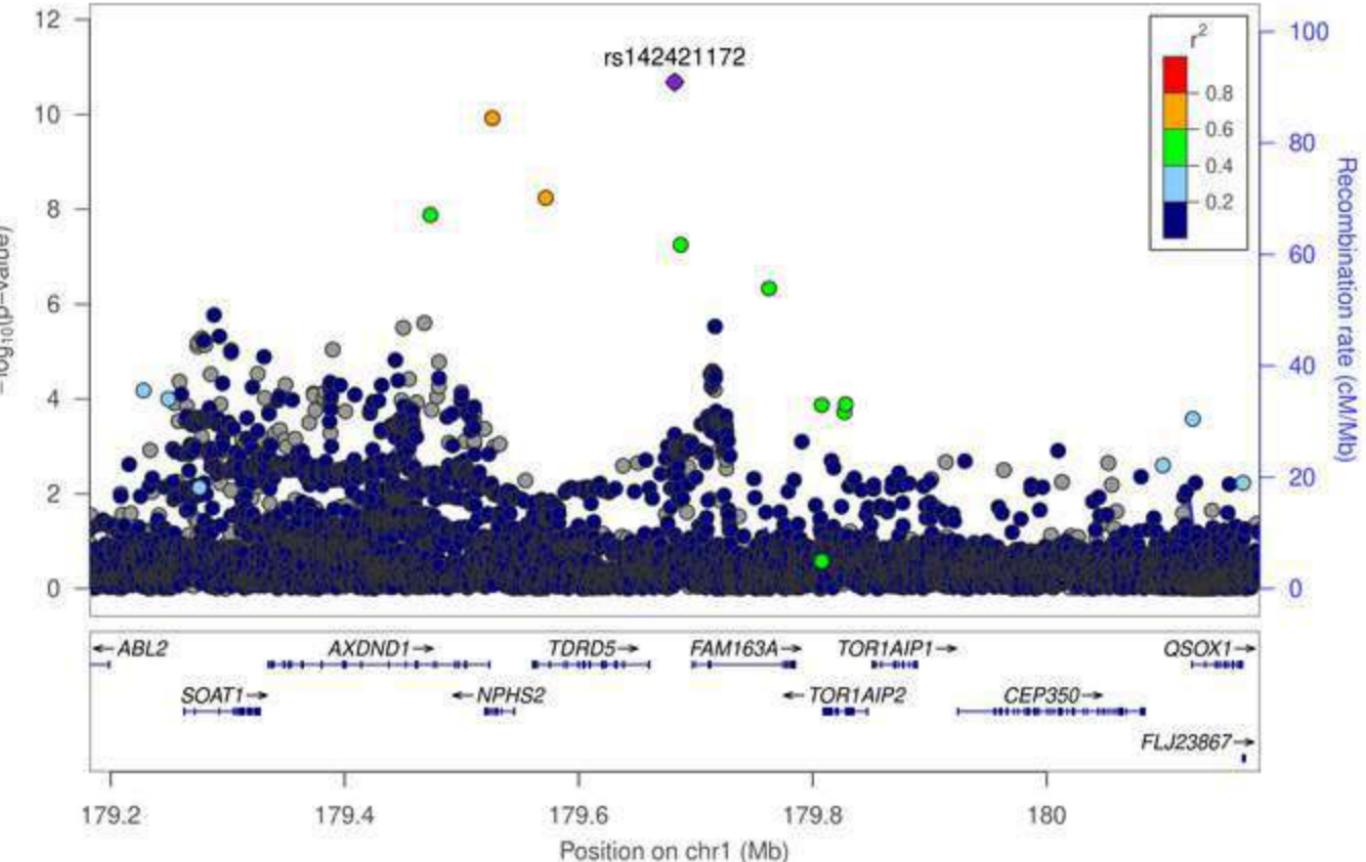
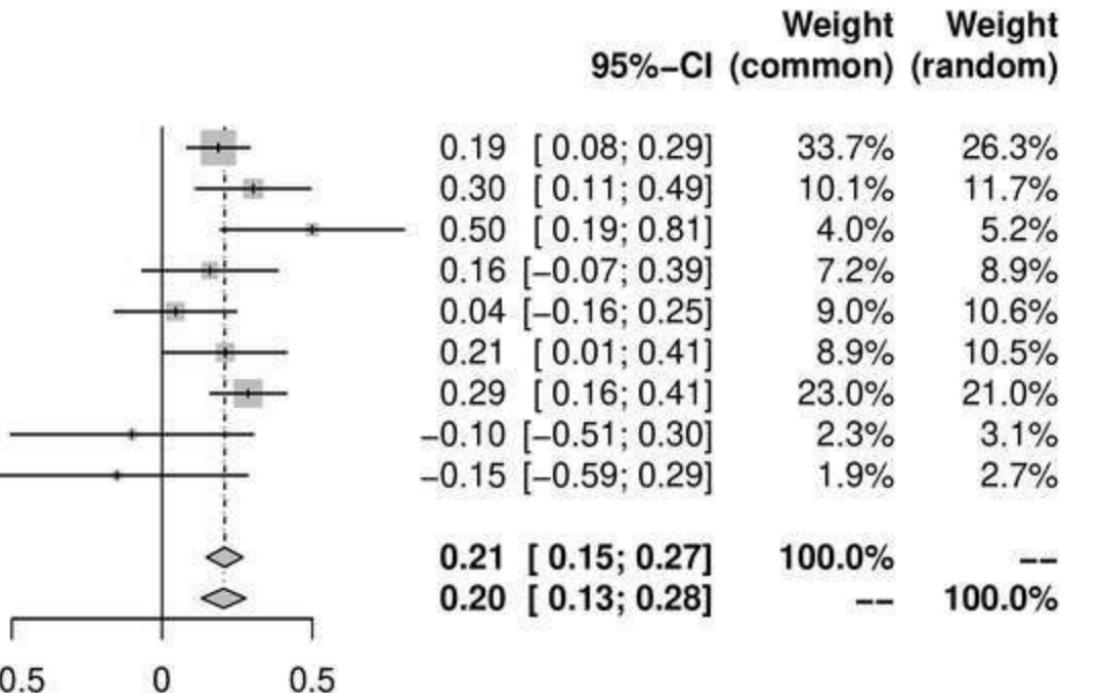
# IL10RB (IL10RB)-rs142421172

IL10RB (IL10RB) [chr1:179682087\_A\_G (rs142421172) (A/G) N=12840]

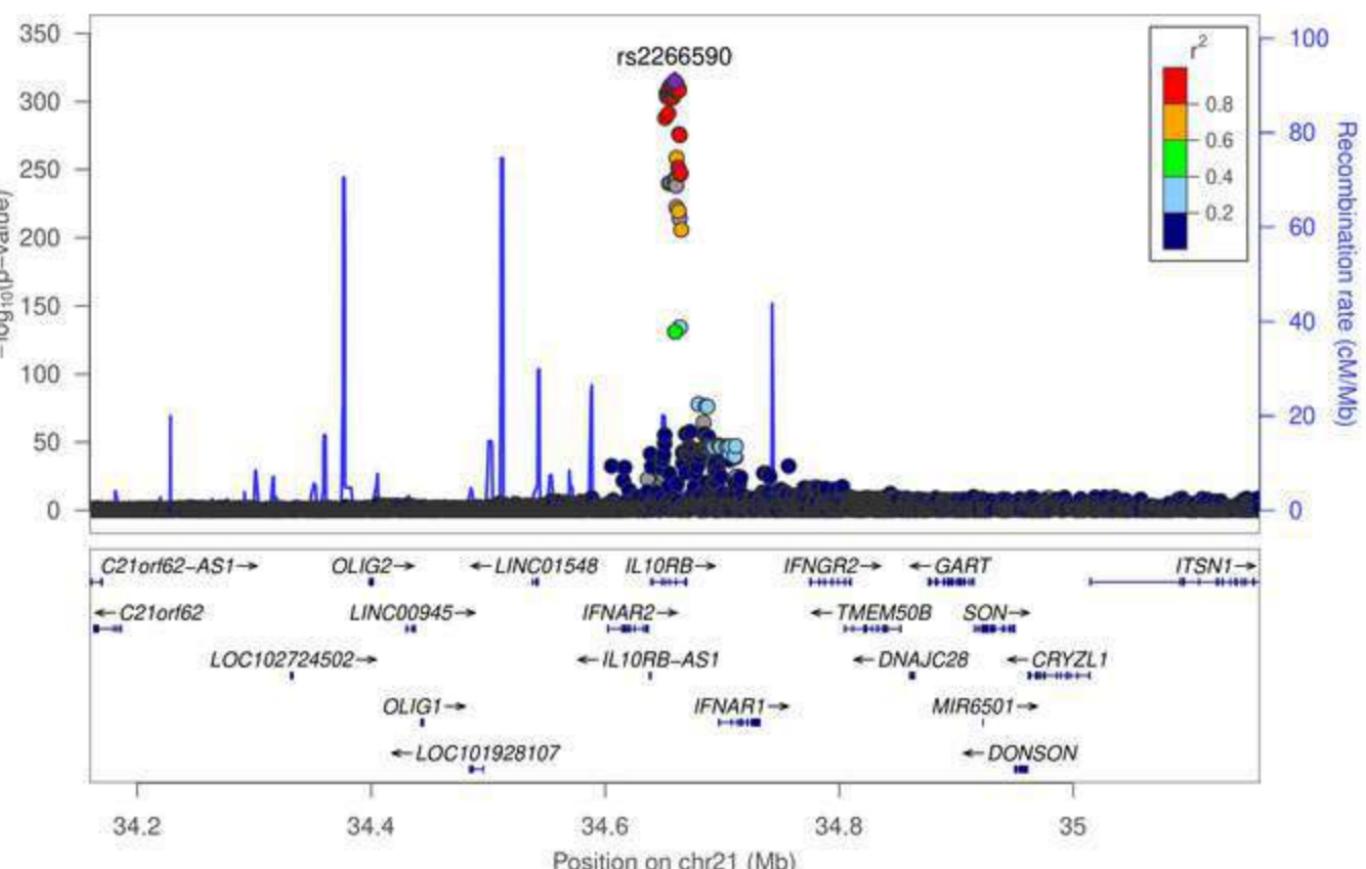
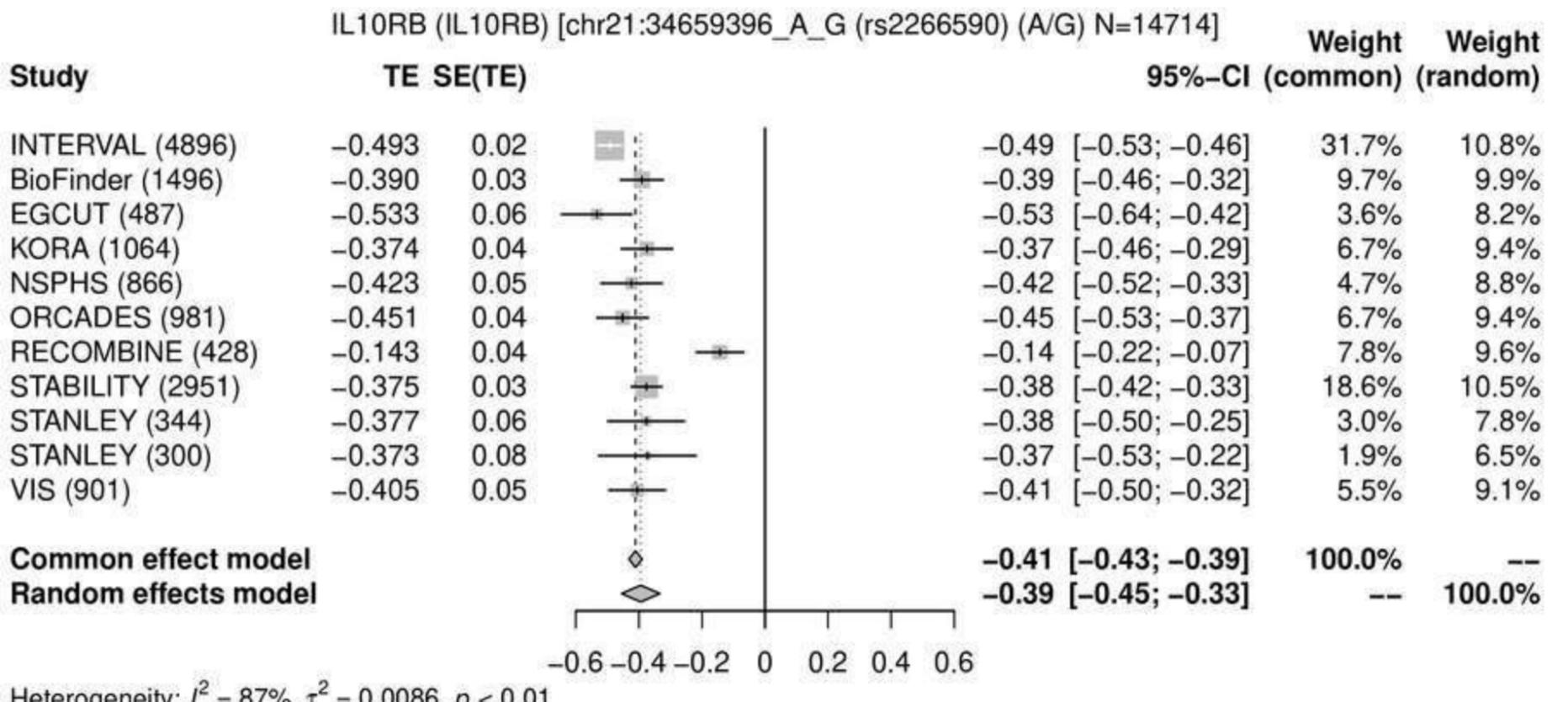
## Study

	TE	SE(TE)
INTERVAL (4896)	0.187	0.05
BioFinder (1496)	0.303	0.10
EGCUT (487)	0.499	0.16
KORA (1064)	0.159	0.12
NSPHS (866)	0.044	0.10
RECOMBINE (436)	0.210	0.10
STABILITY (2951)	0.286	0.06
STANLEY (344)	-0.101	0.21
STANLEY (300)	-0.151	0.22

TE SE(TE)

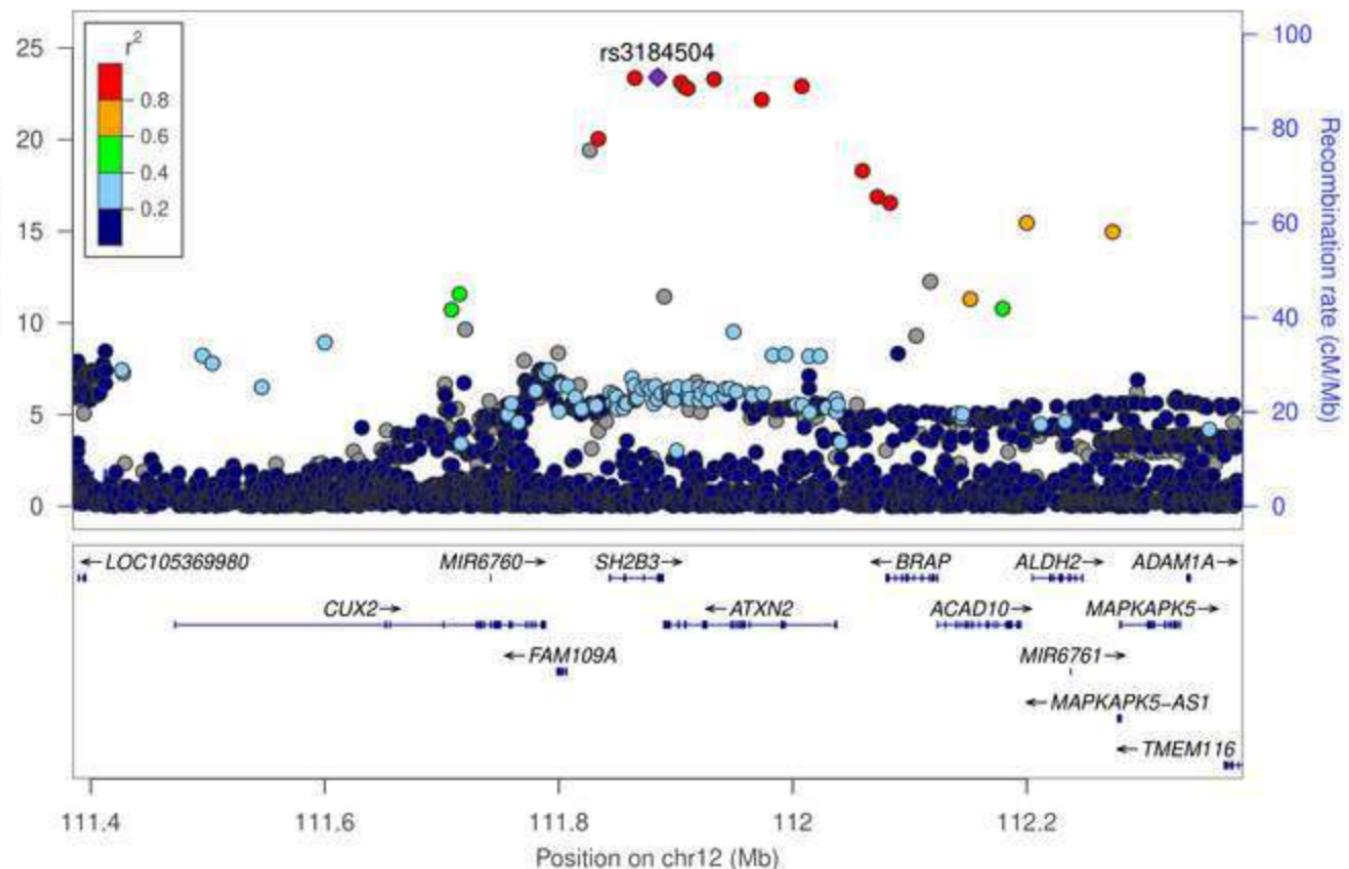
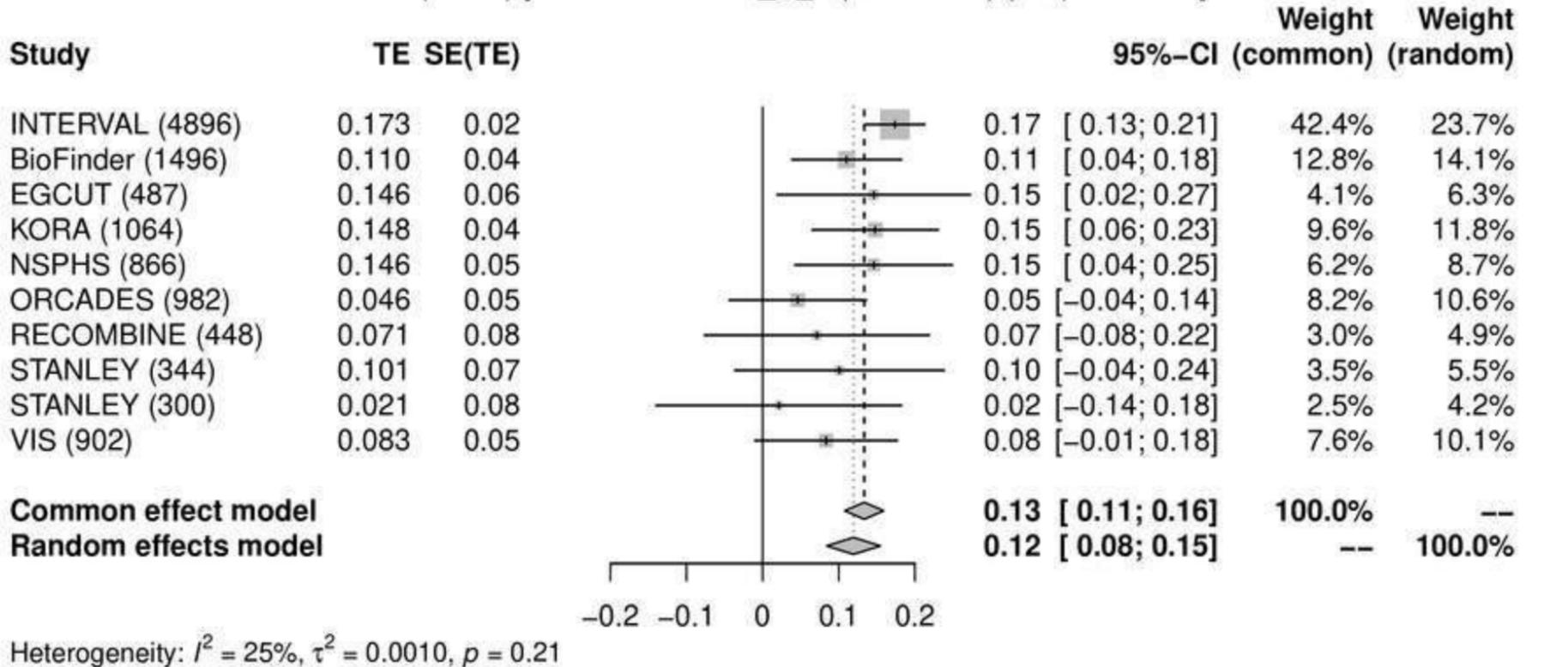


# IL10RB (IL10RB)-rs2266590



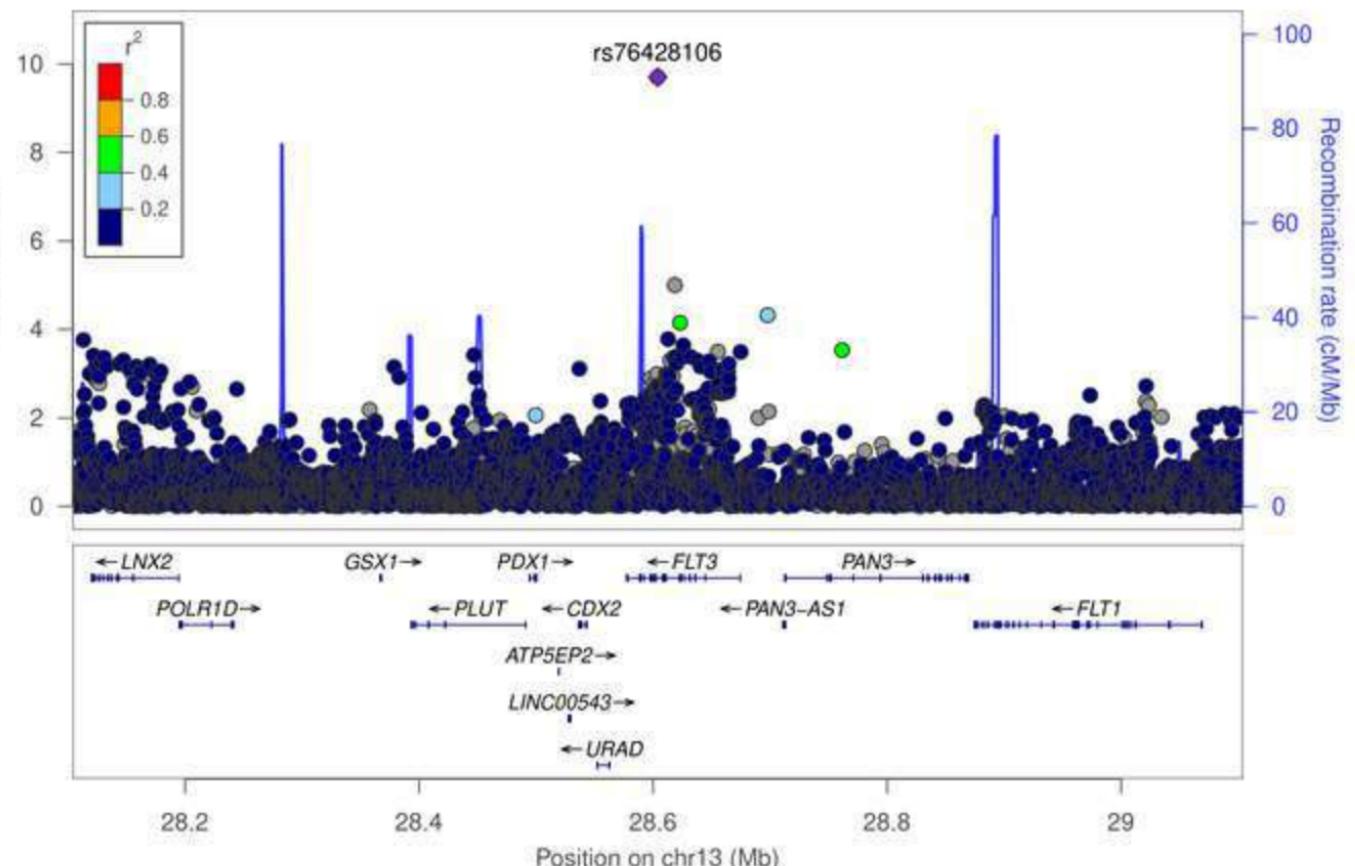
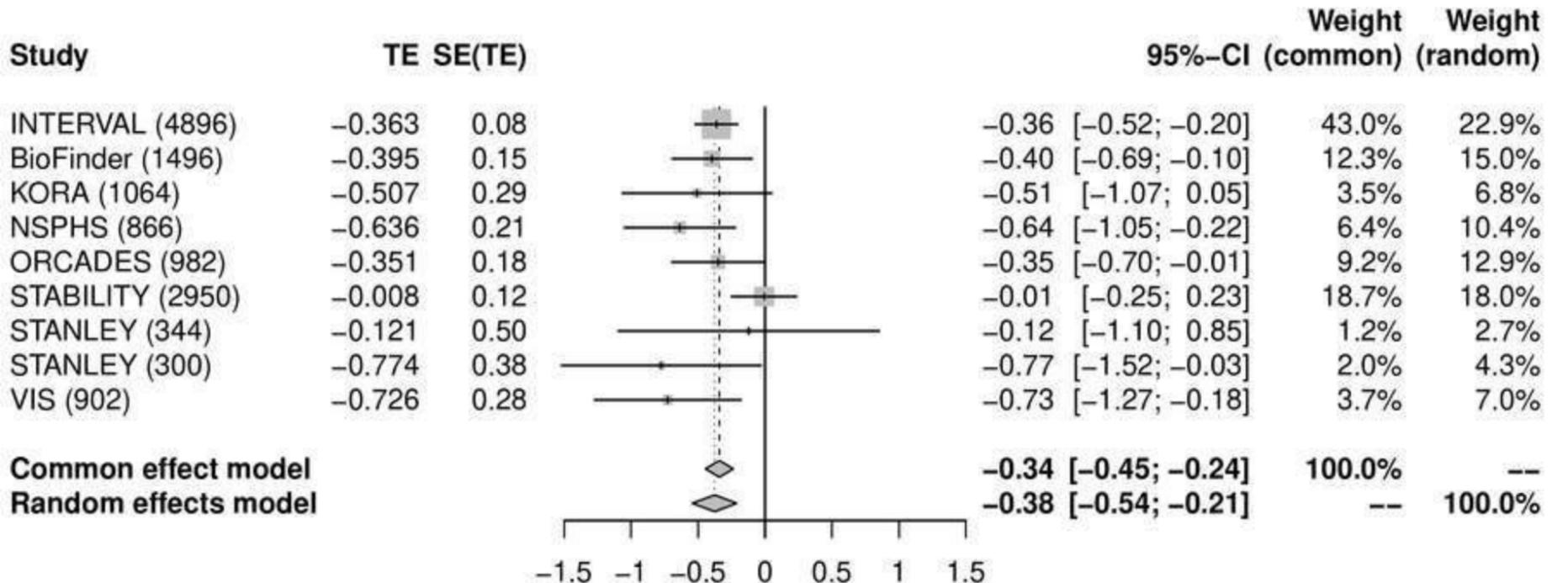
# IL-12B (IL12B)-rs3184504

IL-12B (IL12B) [chr12:111884608\_C\_T (rs3184504) (T/C) N=11785]



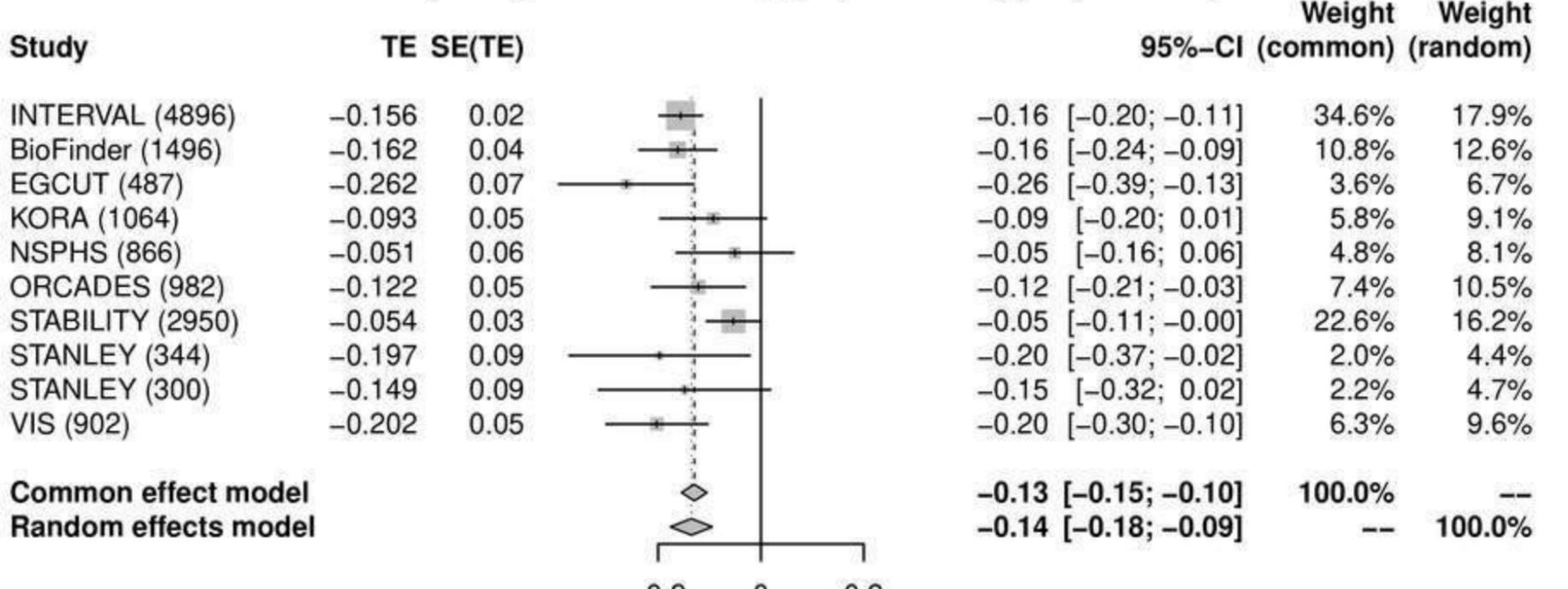
# IL-12B (IL12B)-rs76428106

IL-12B (IL12B) [chr13:28604007\_C\_T (rs76428106) (T/C) N=13800]

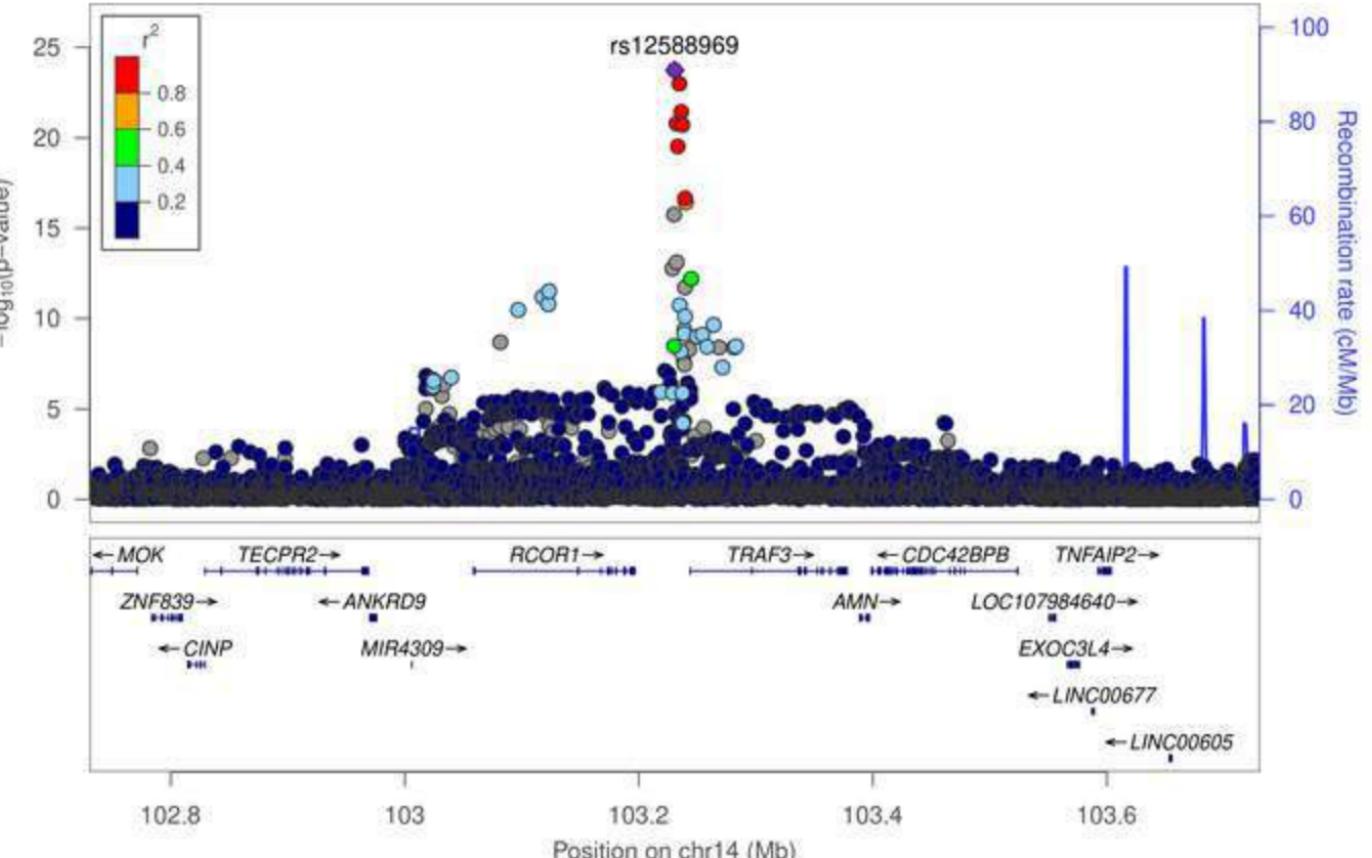


# IL-12B (IL12B)-rs12588969

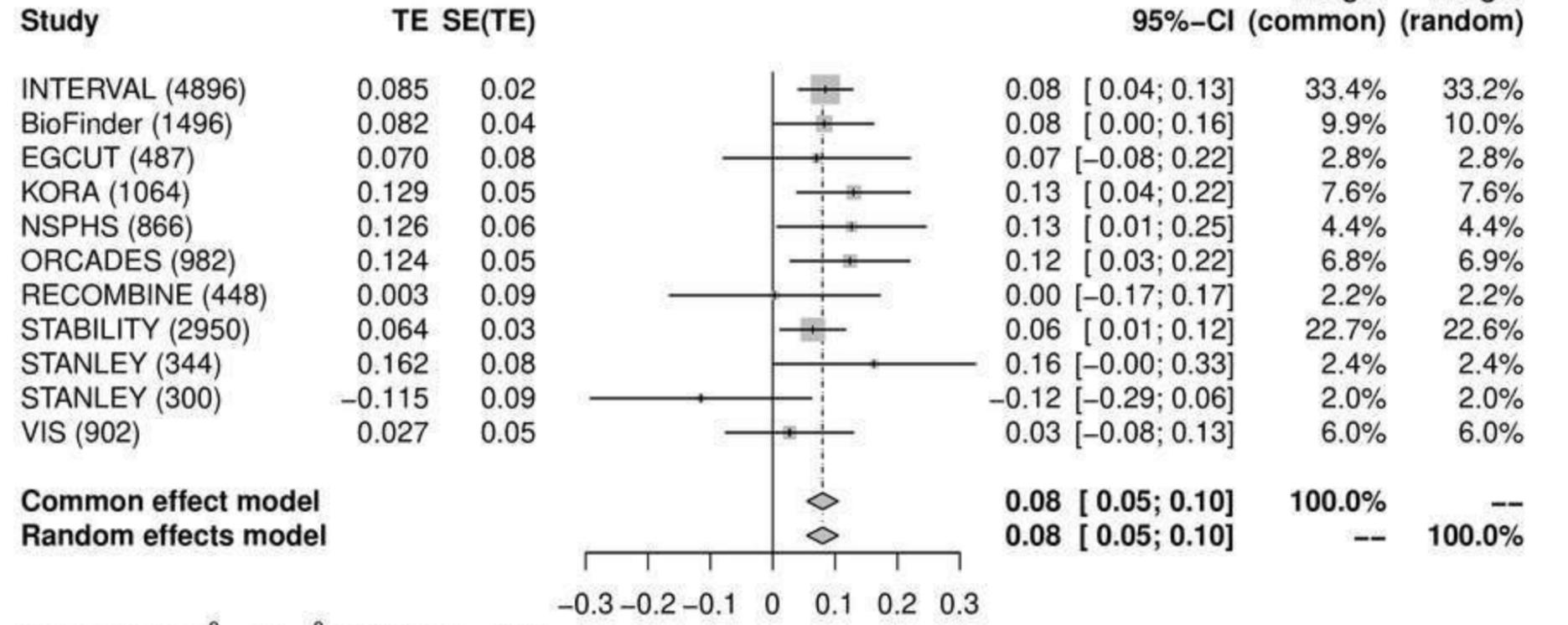
IL-12B (IL12B) [chr14:103230758\_C\_G (rs12588969) (C/G) N=14287]



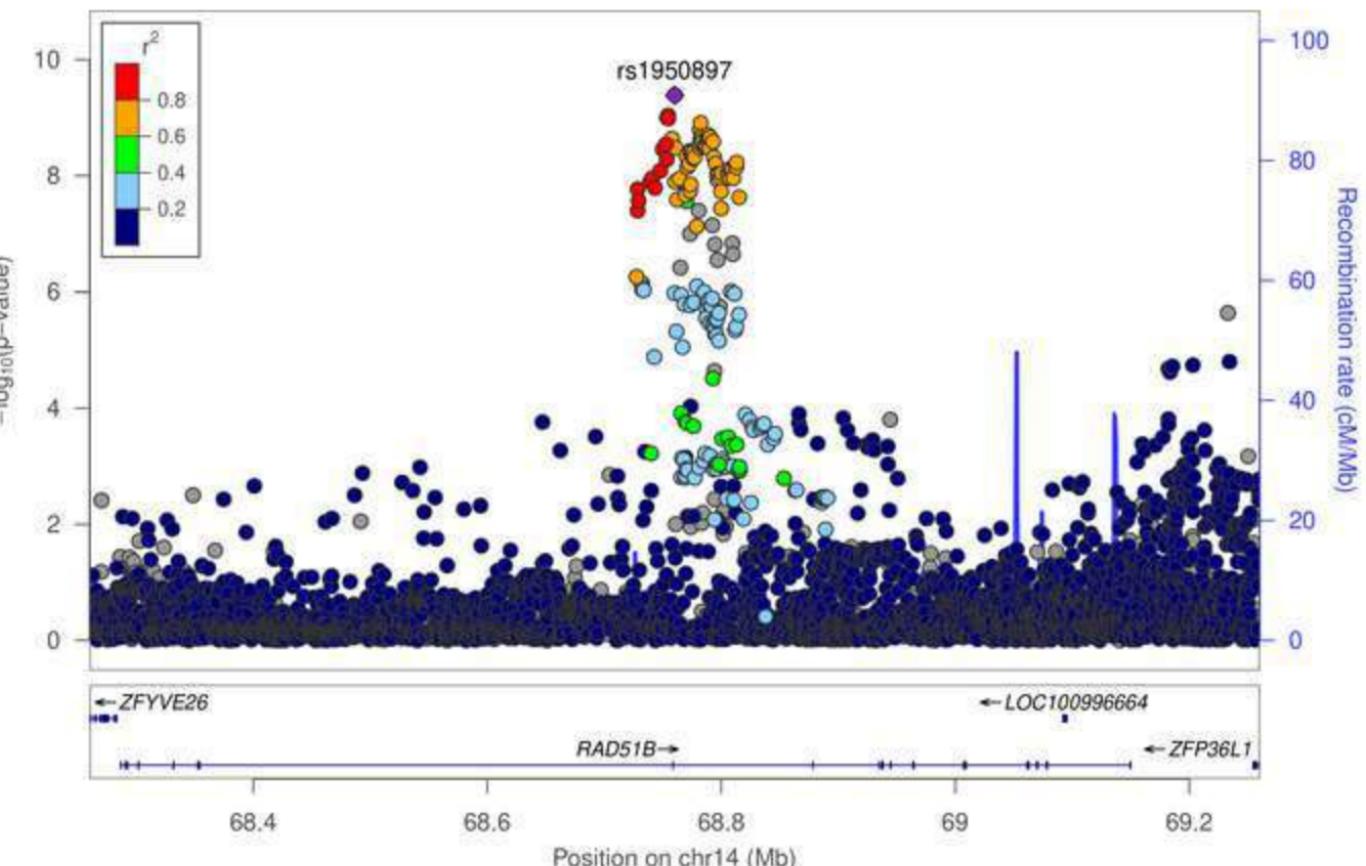
Heterogeneity:  $I^2 = 53\%$ ,  $\tau^2 = 0.0020$ ,  $p = 0.02$



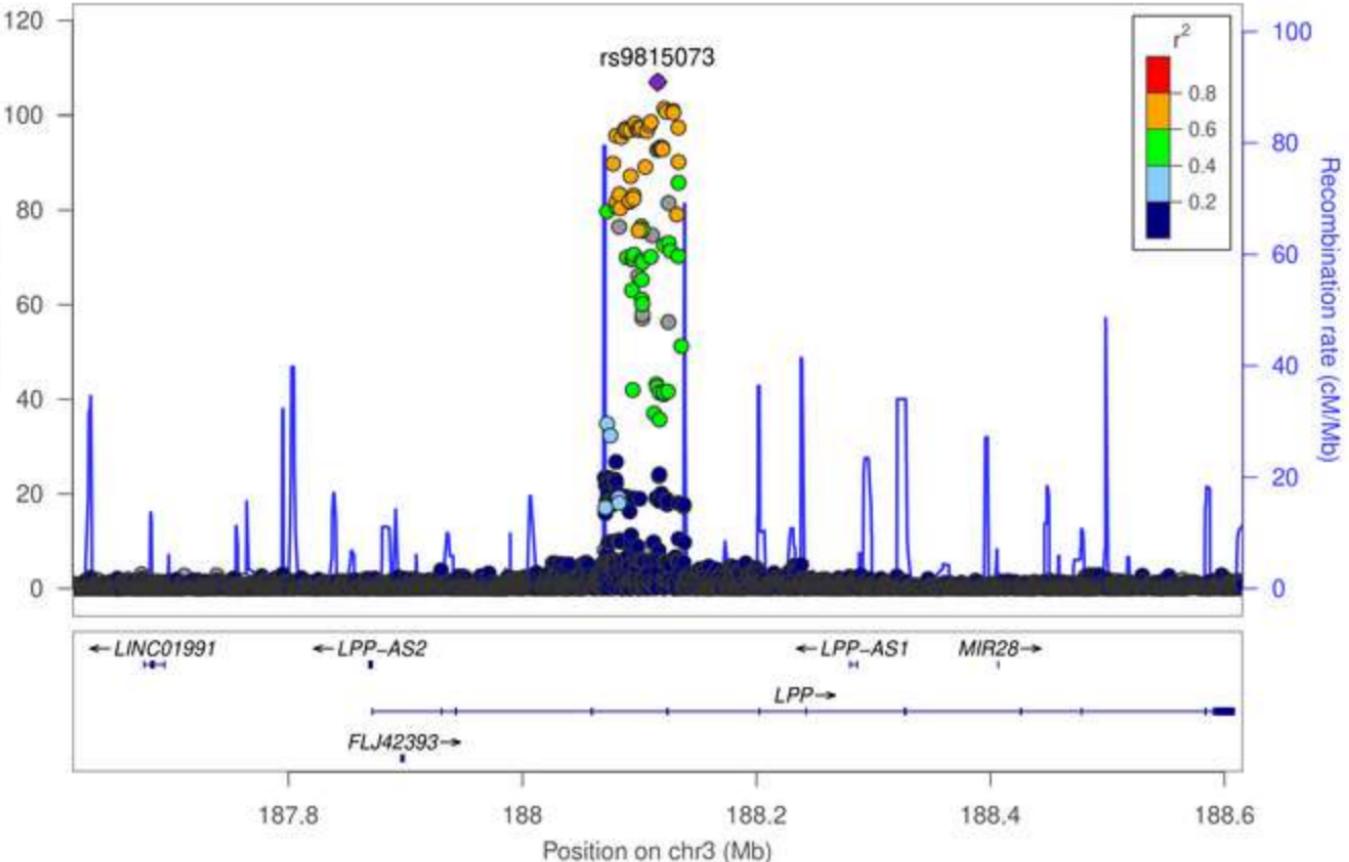
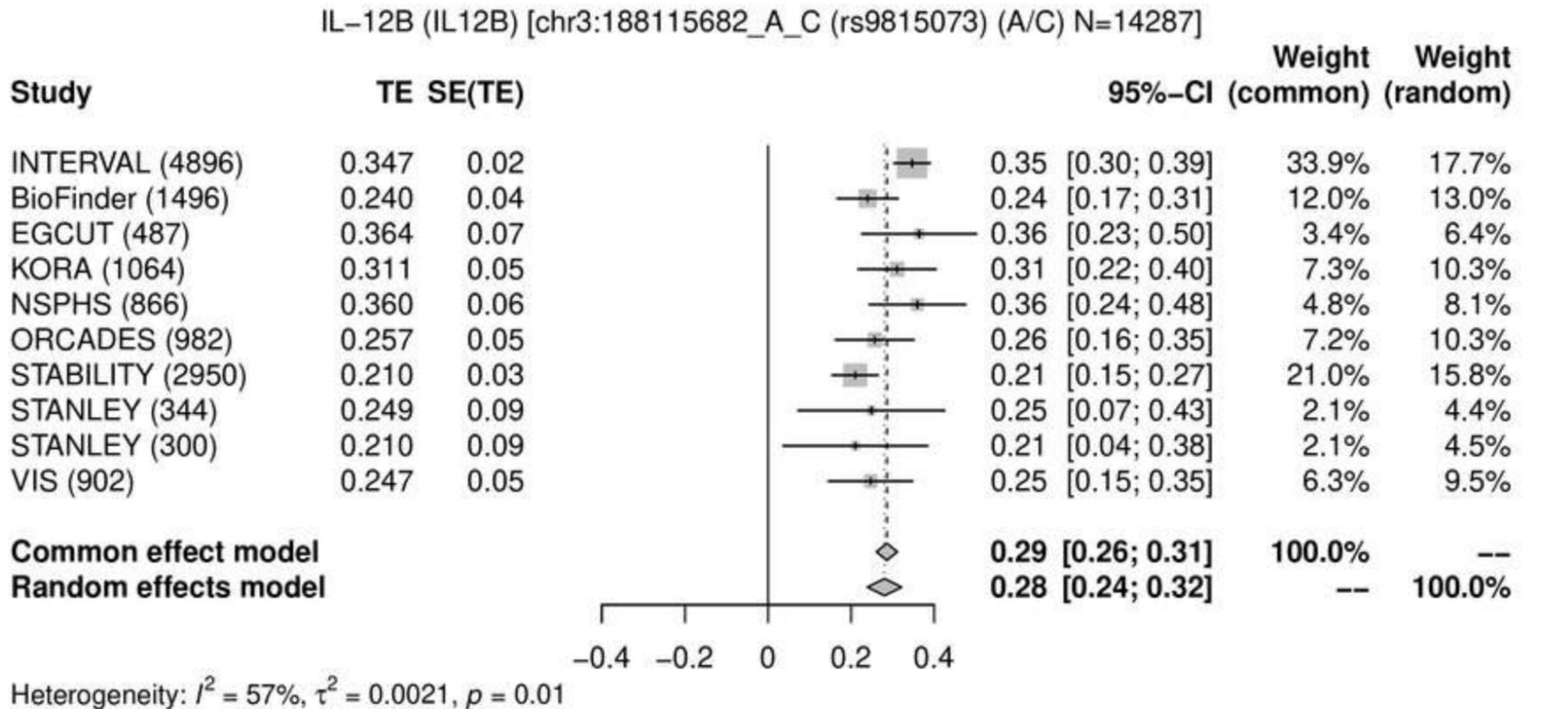
## IL-12B (IL12B) [chr14:68760141\_C\_T (rs1950897) (T/C) N=14735]



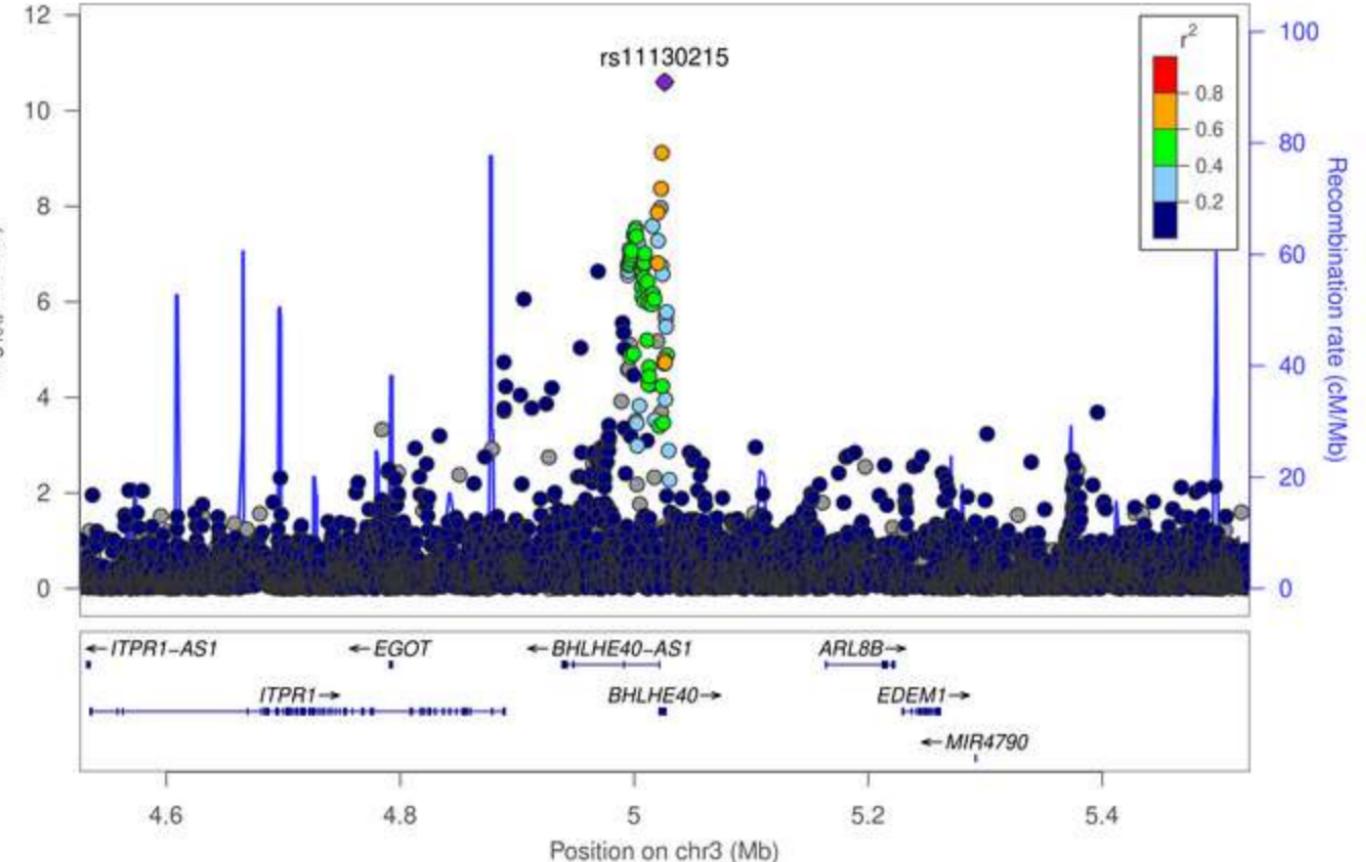
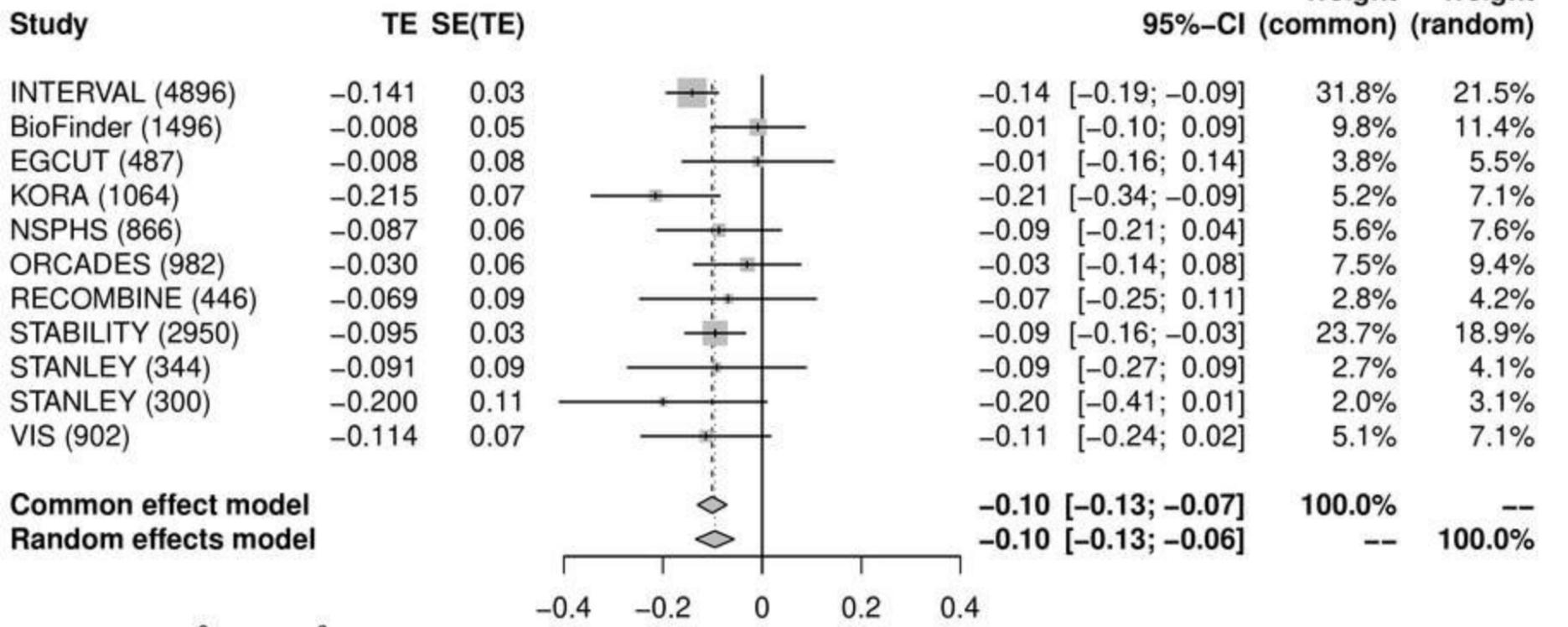
## IL-12B (IL12B)-rs1950897



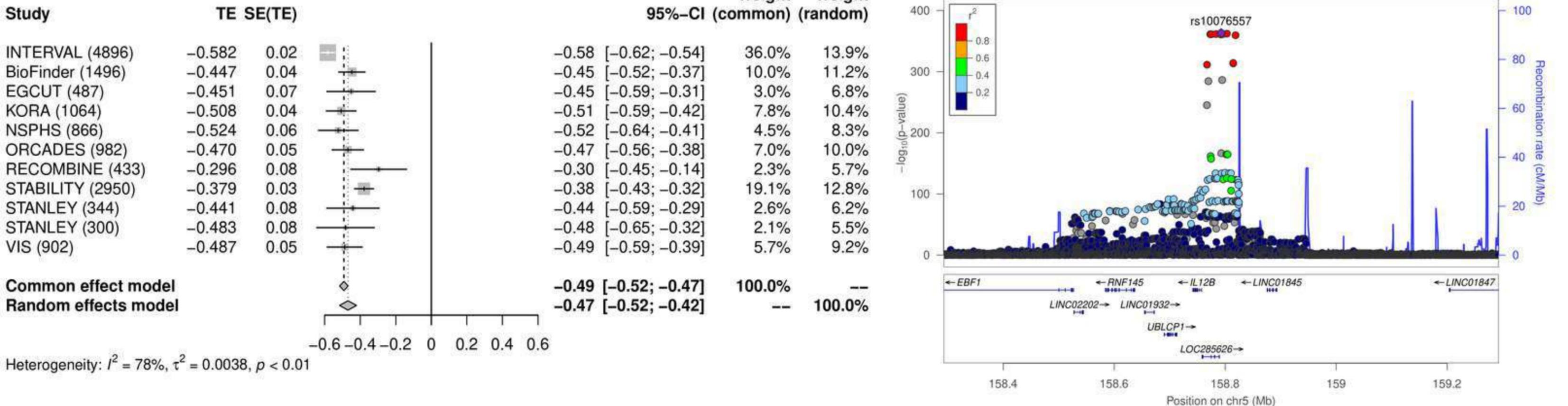
# IL-12B (IL12B)-rs9815073



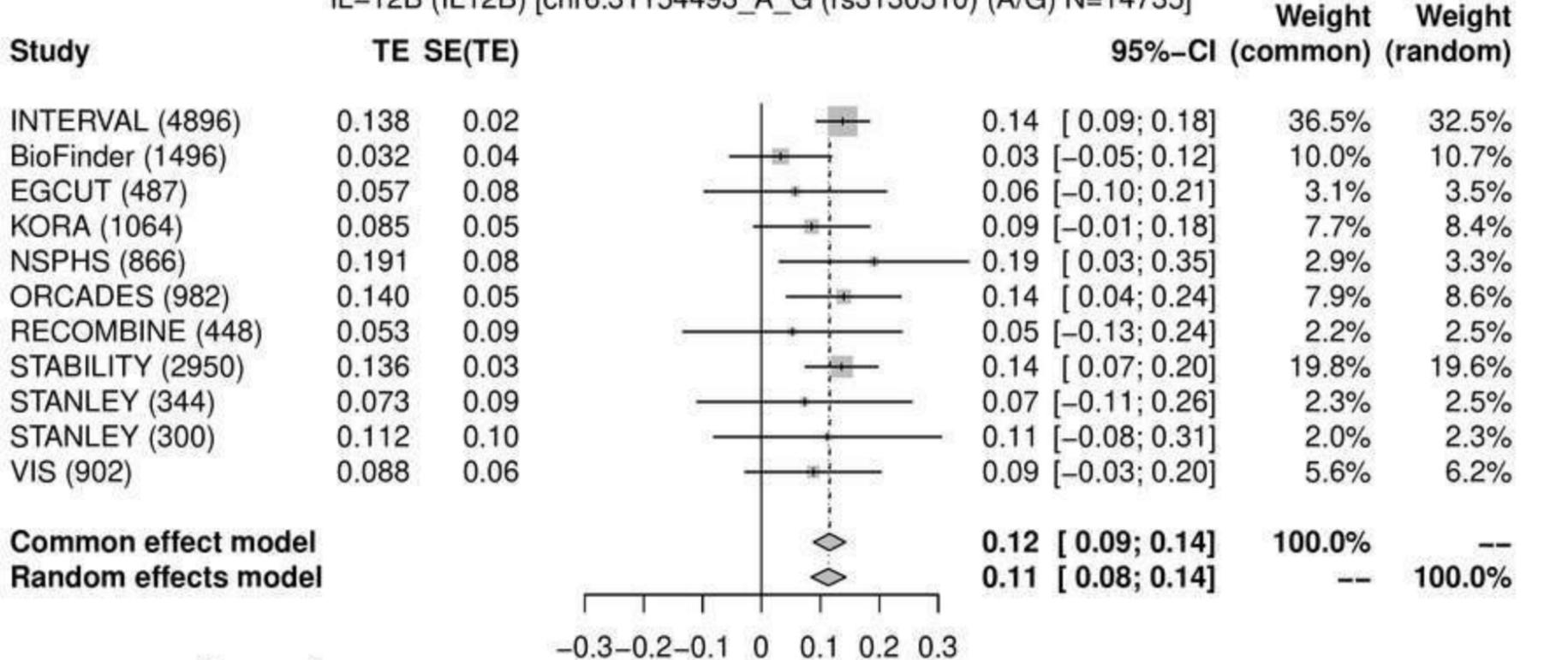
# IL-12B (IL12B)-rs11130215



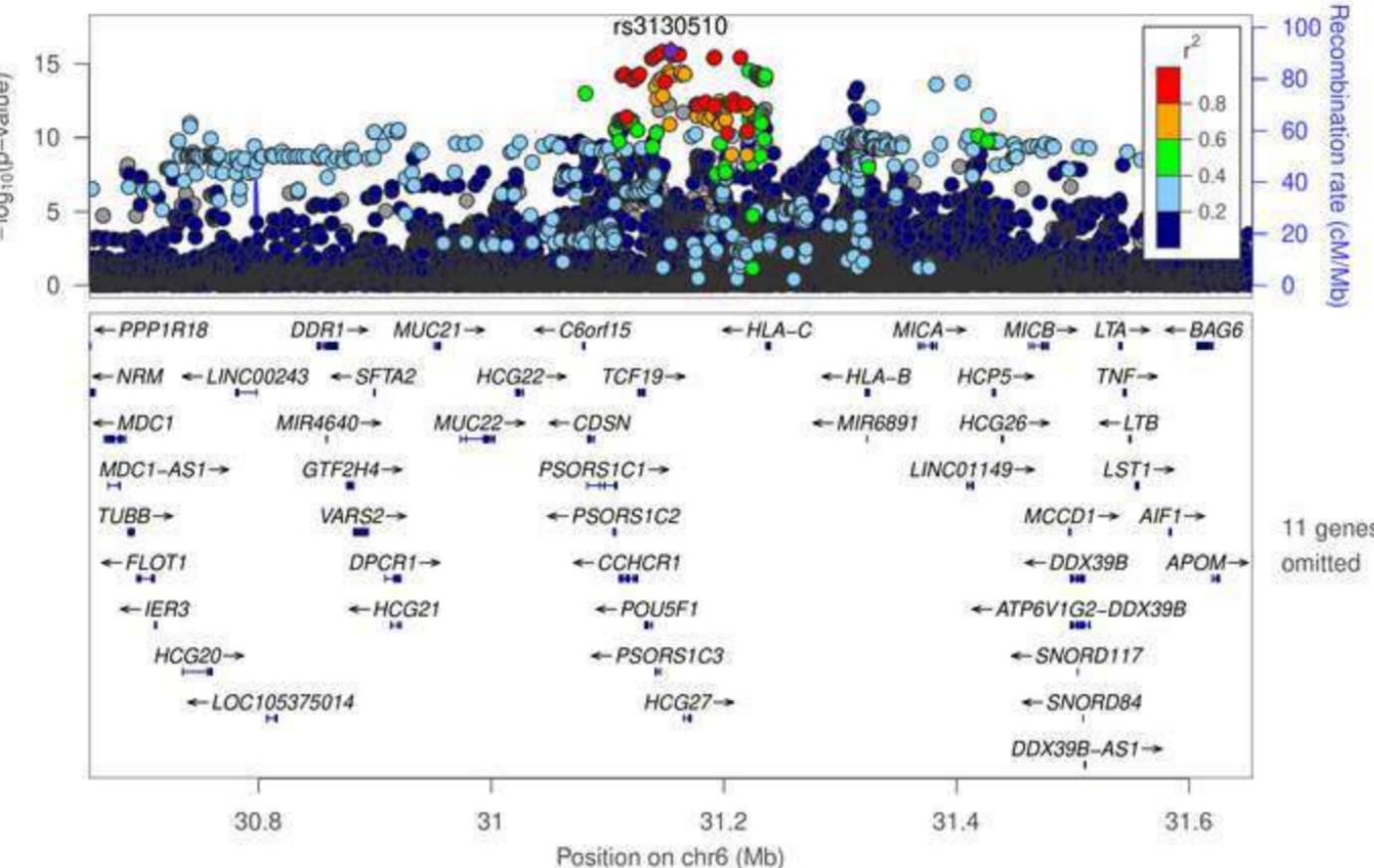
# IL-12B (IL12B)-rs10076557



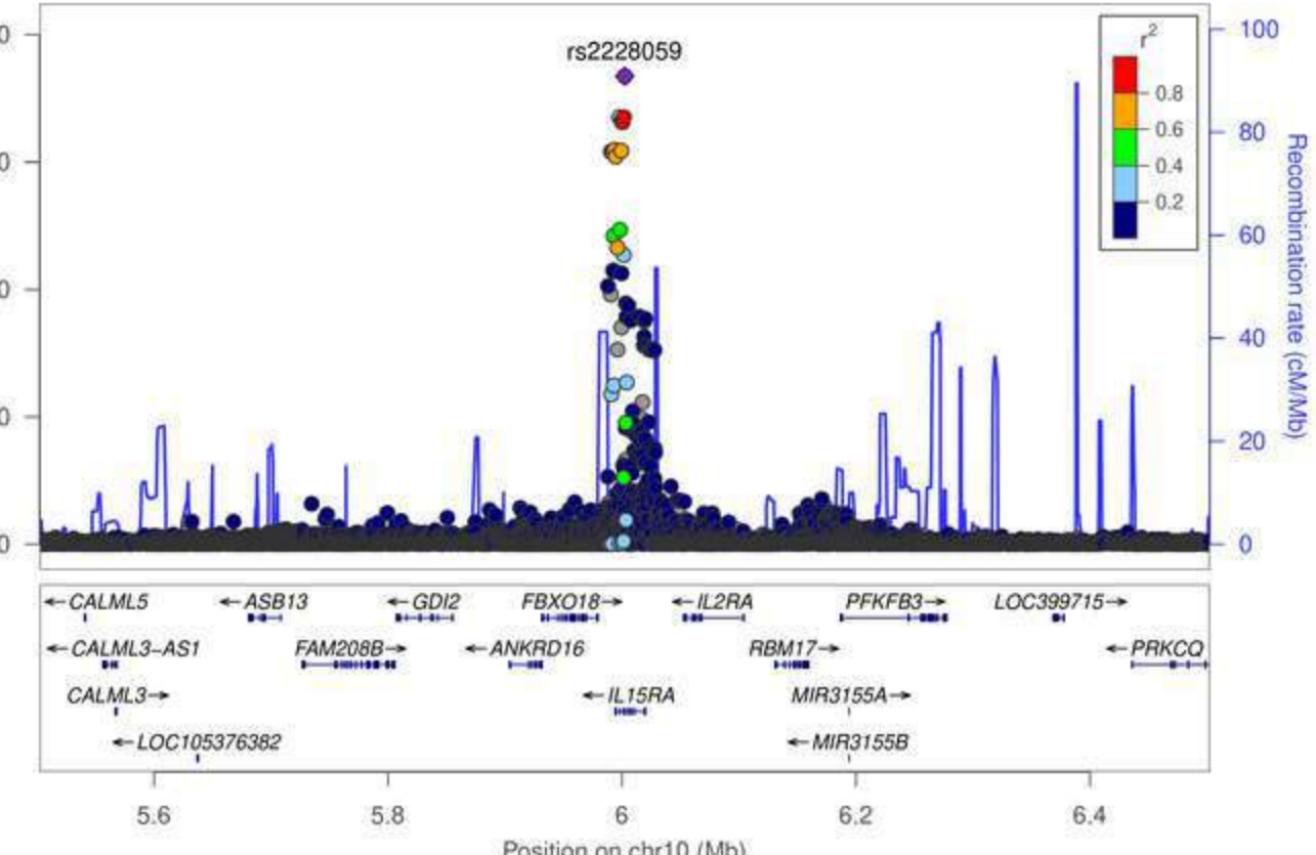
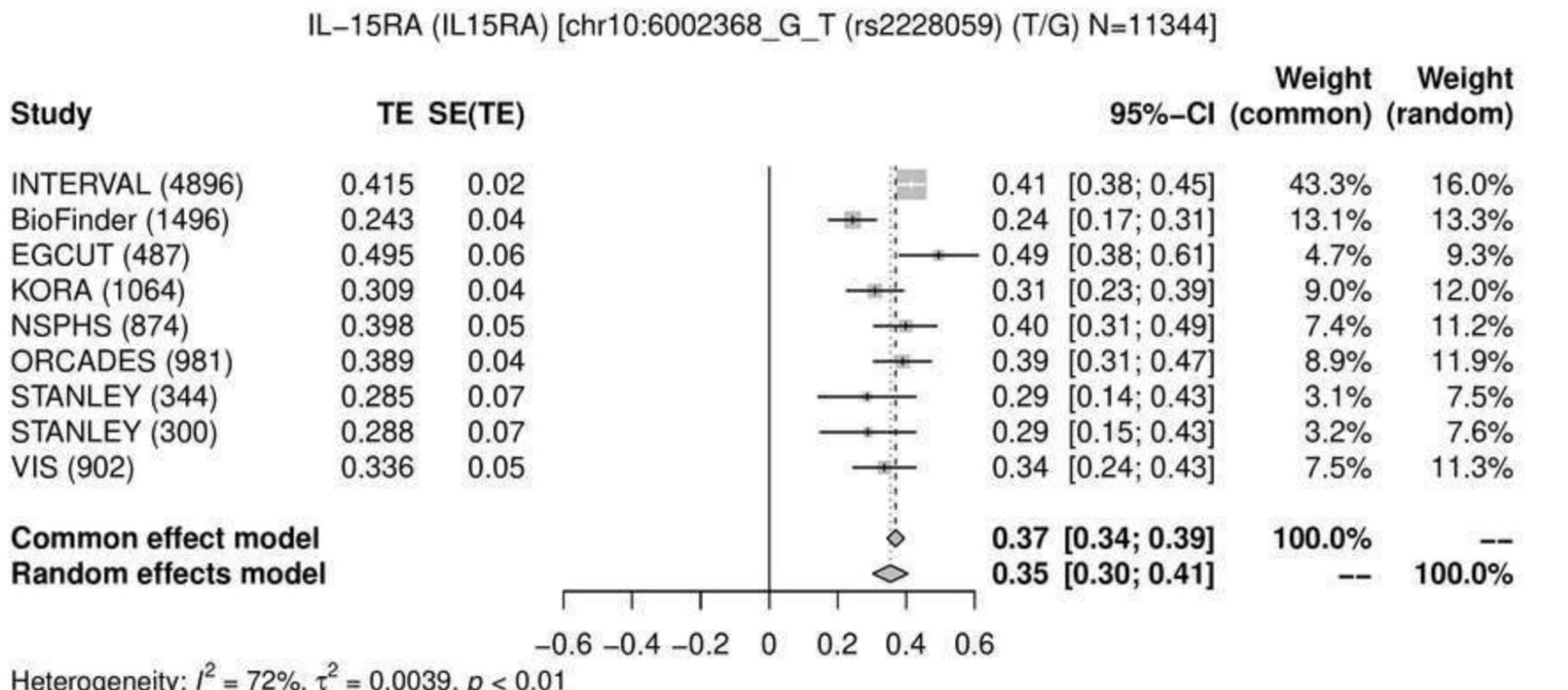
## IL-12B (IL12B) [chr6:31154493\_A\_G (rs3130510) (A/G) N=14735]



## IL-12B (IL12B)-rs3130510

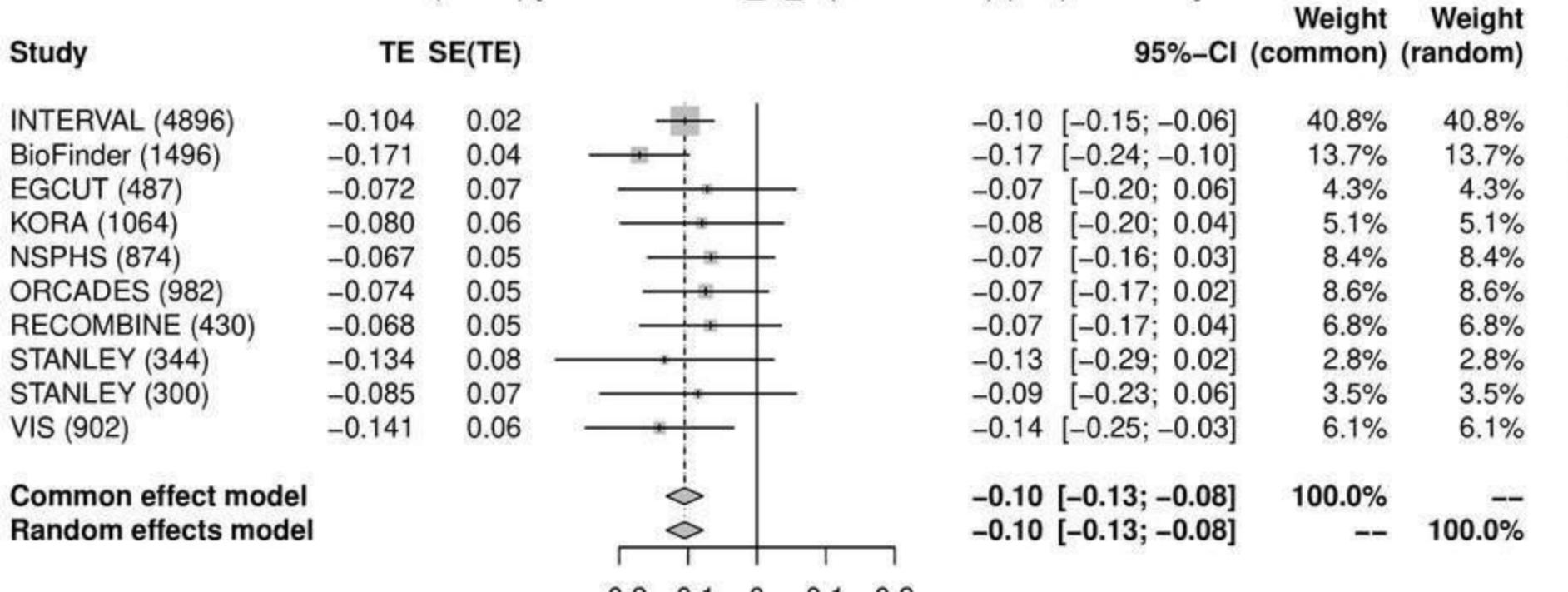


# IL-15RA (IL15RA)-rs2228059

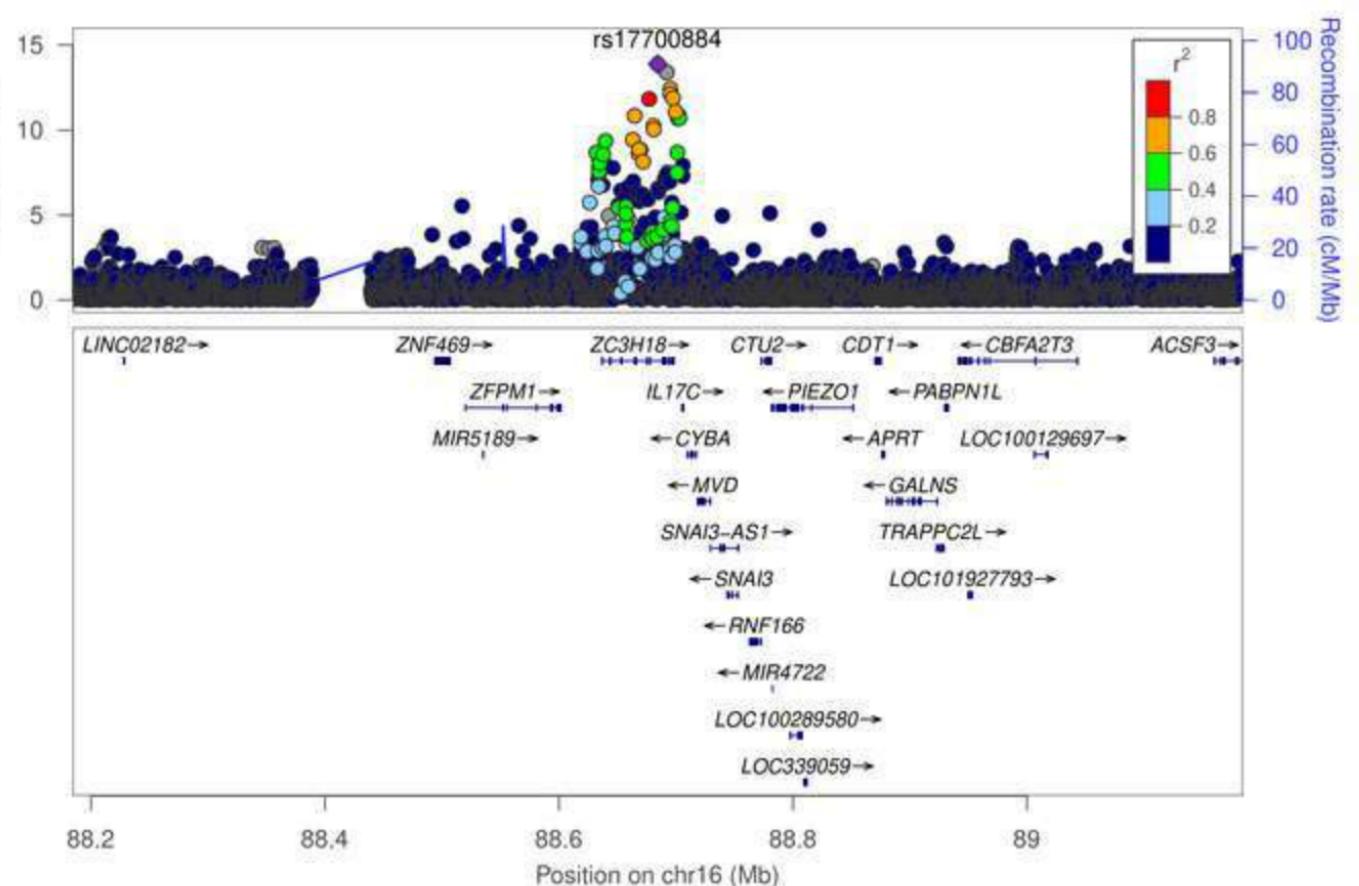


# IL-17C (IL17C)-rs17700884

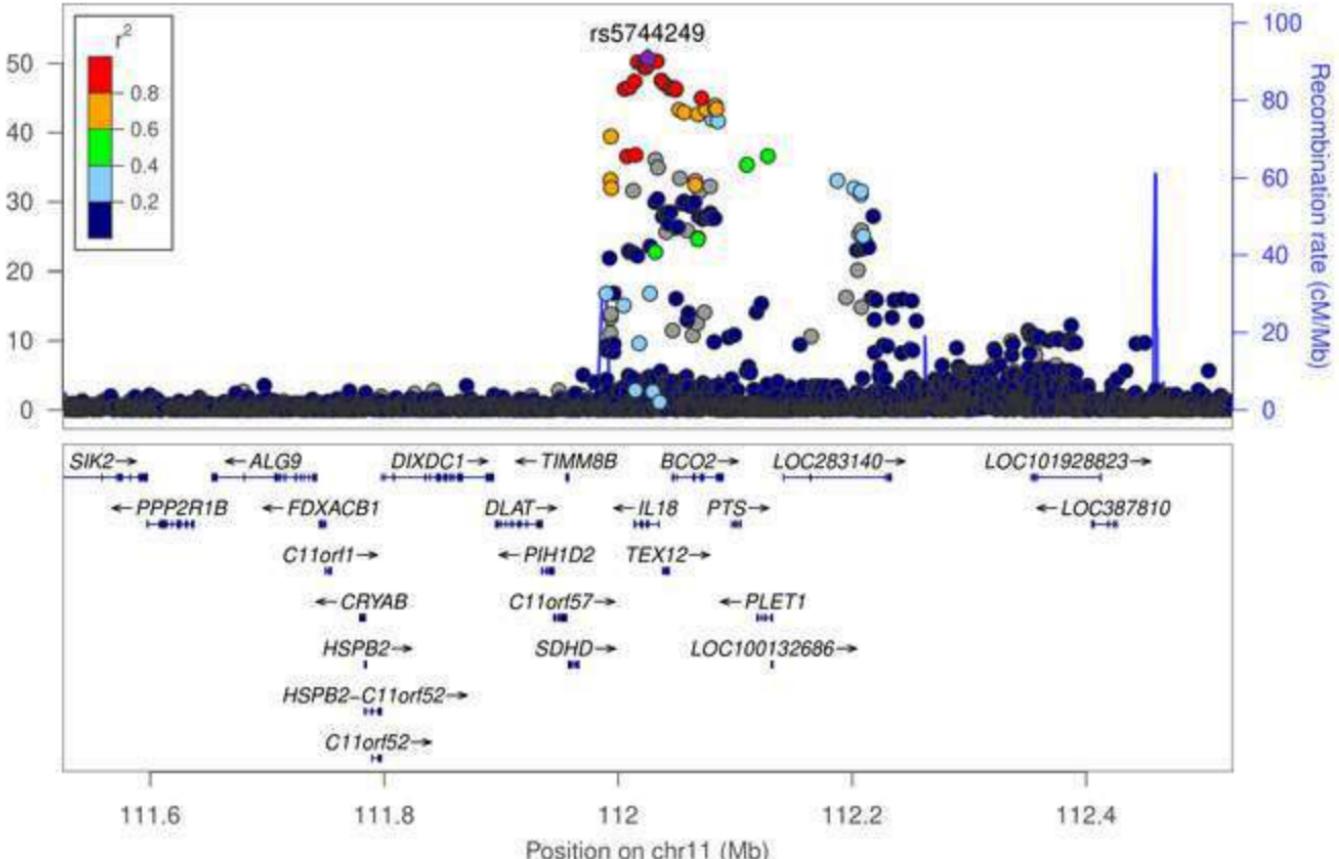
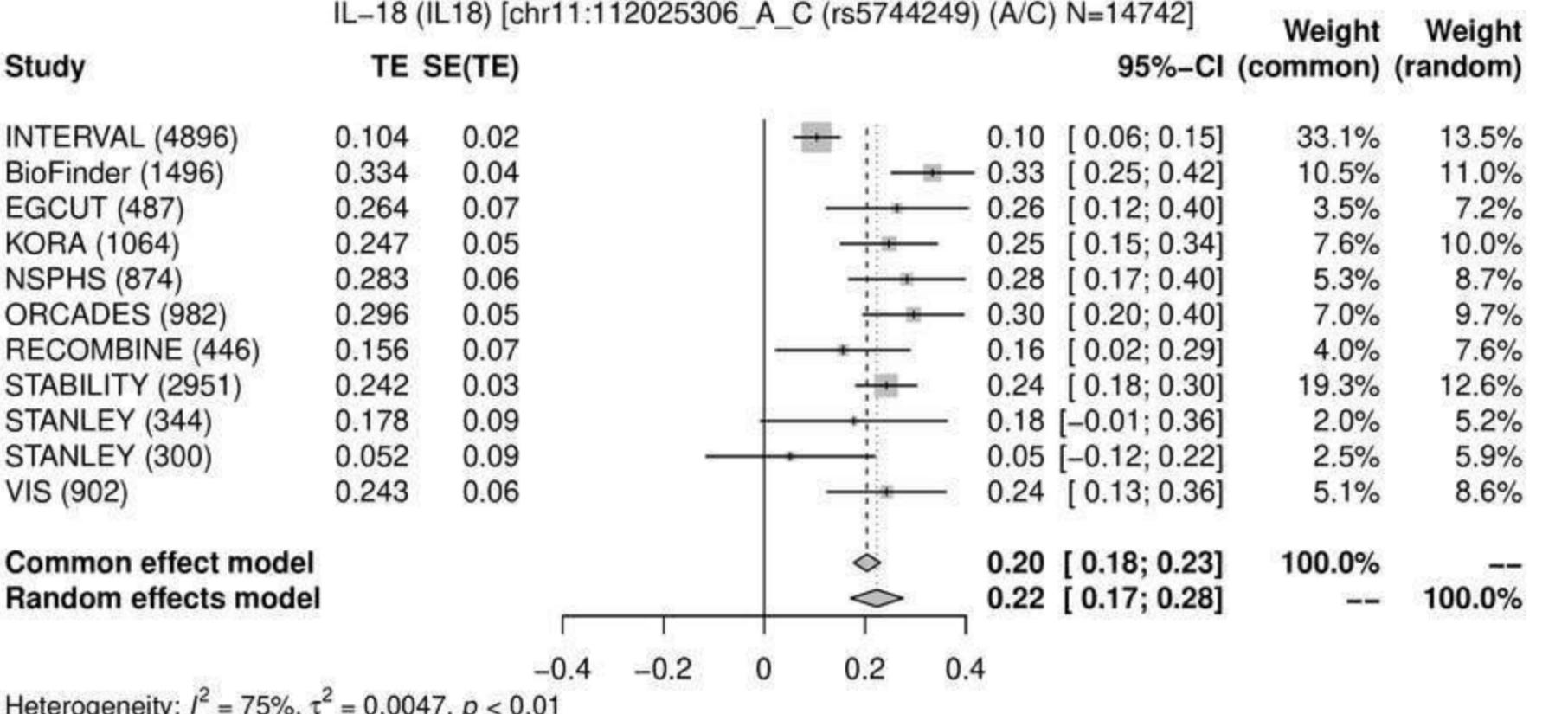
IL-17C (IL17C) [chr16:88684495\_G\_T (rs17700884) (T/G) N=11775]



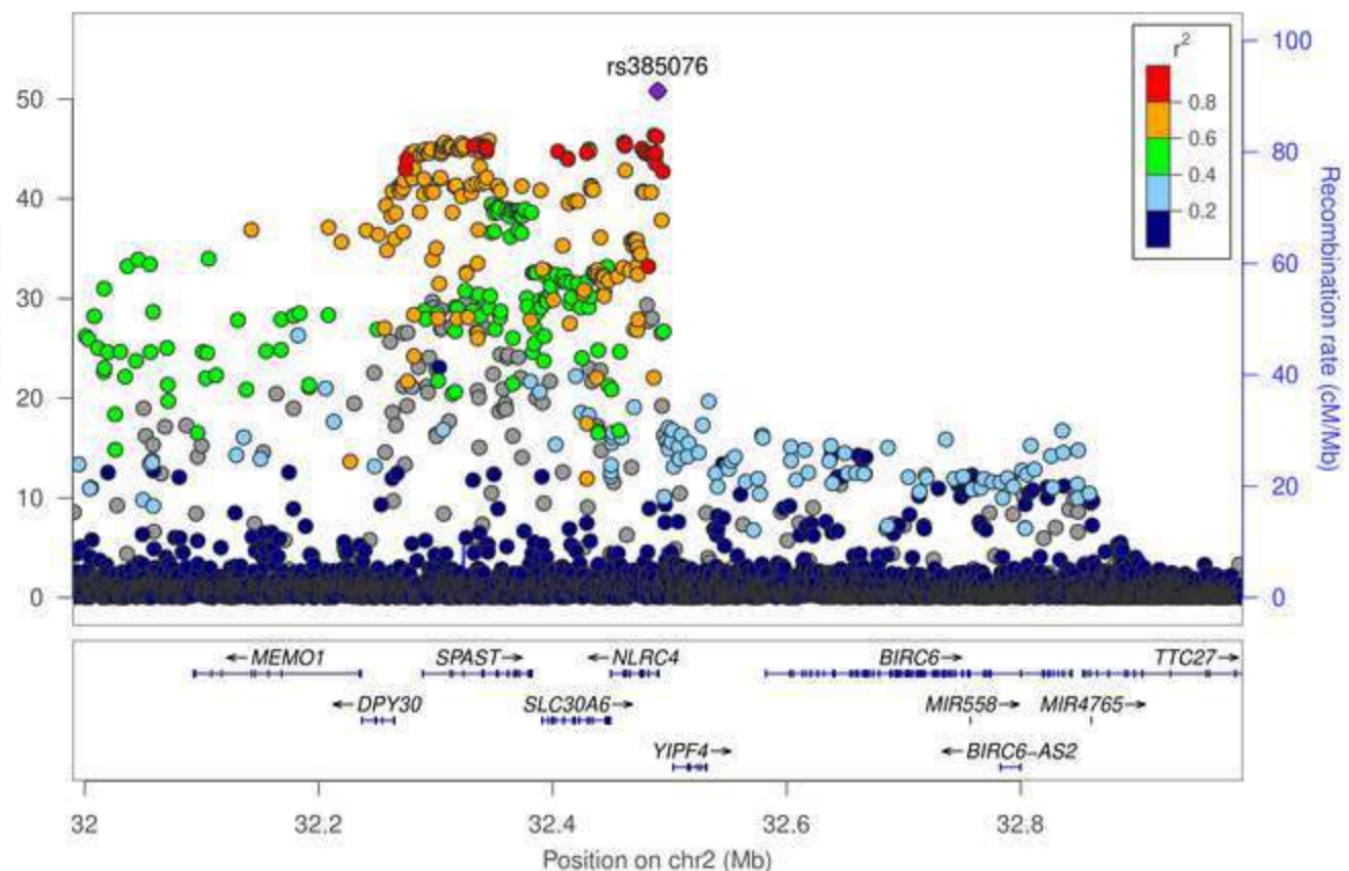
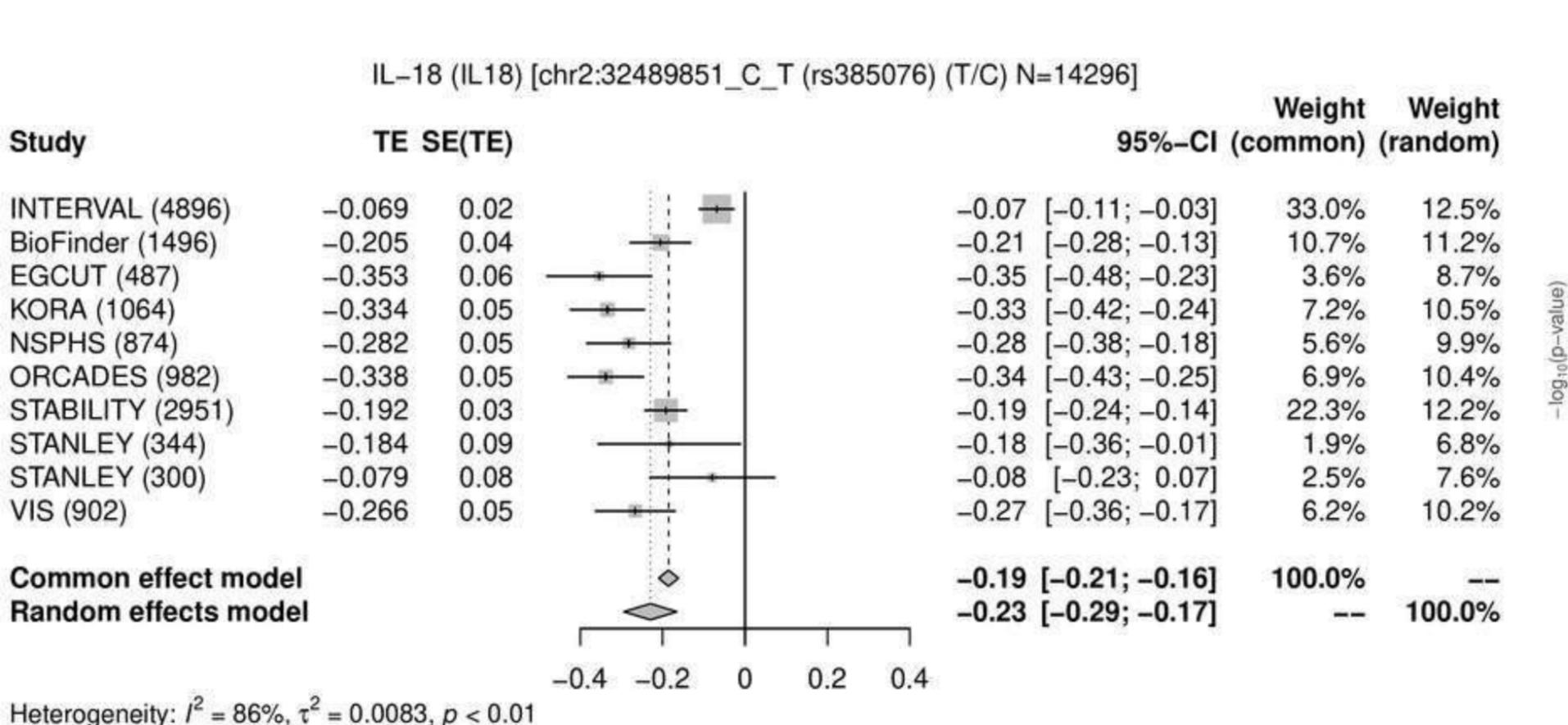
Heterogeneity:  $I^2 = 0\%$ ,  $\tau^2 = 0$ ,  $p = 0.75$



# IL-18 (IL18)-rs5744249

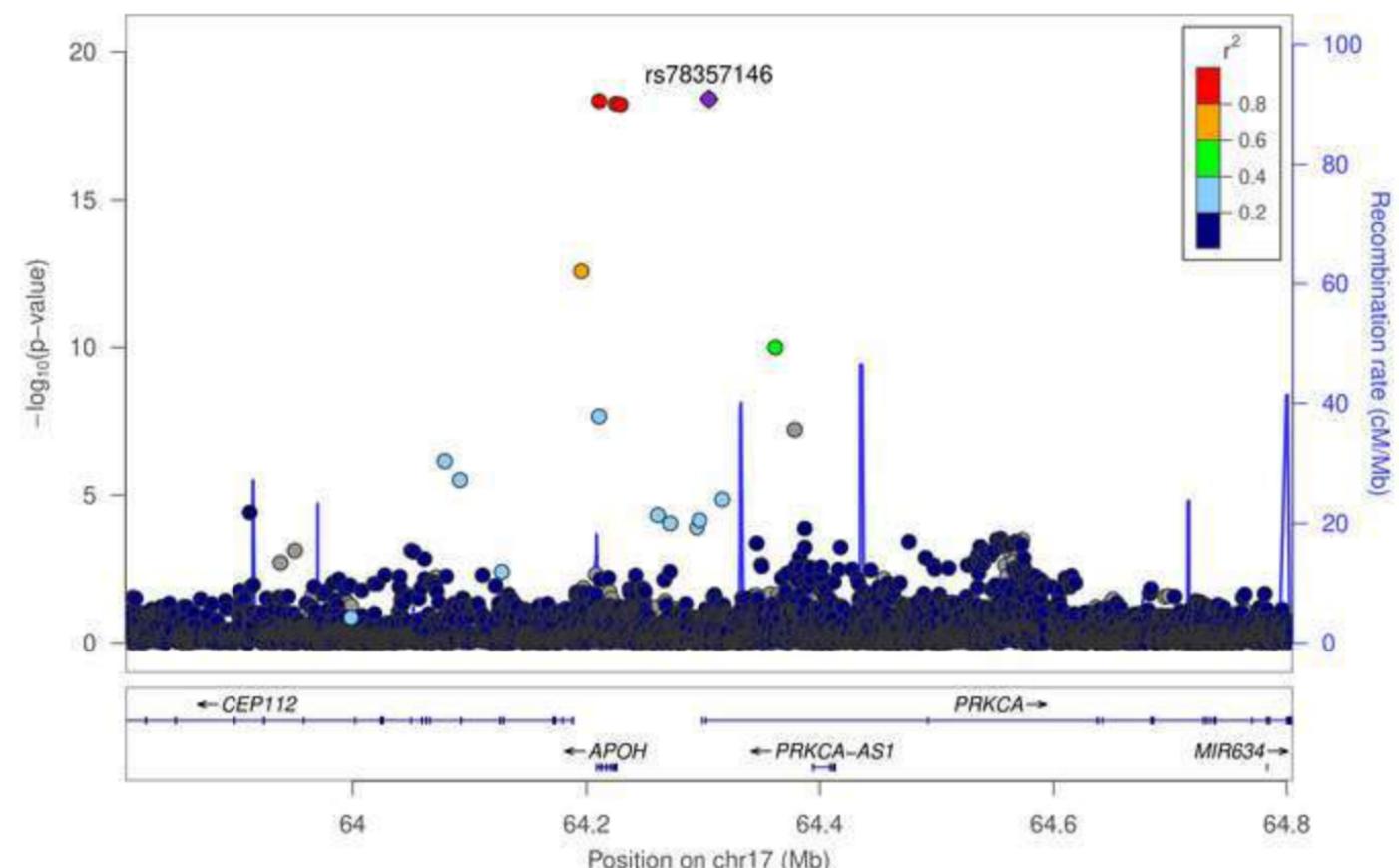
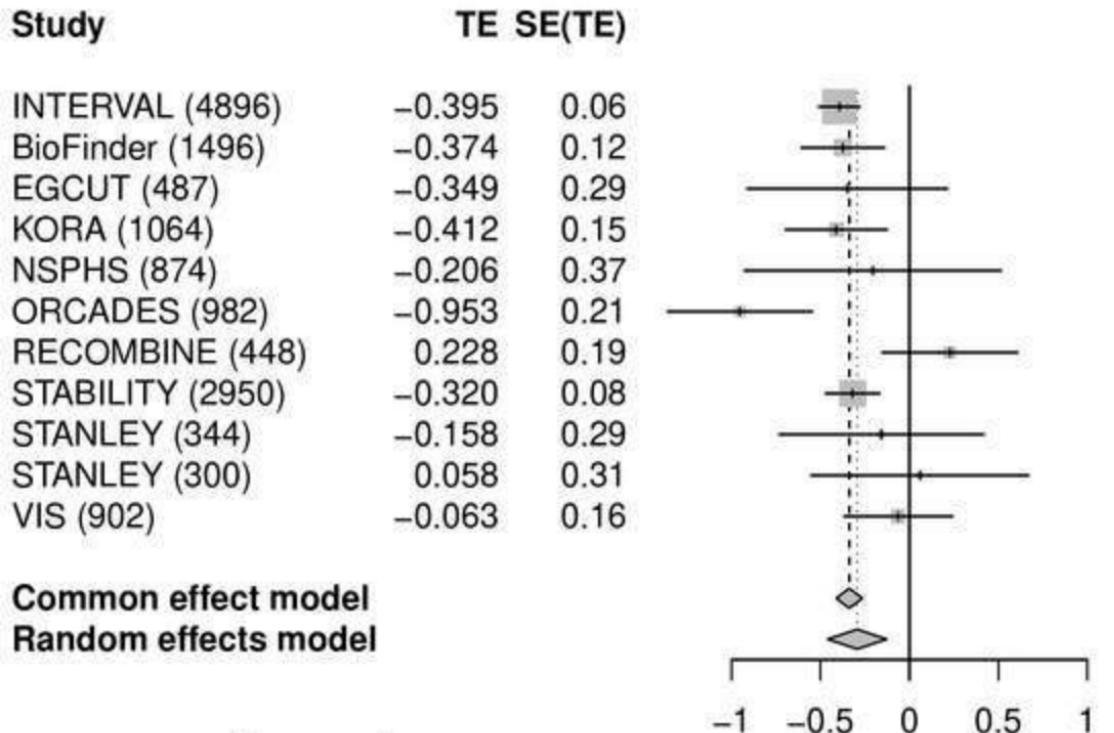


# IL-18 (IL18)-rs385076

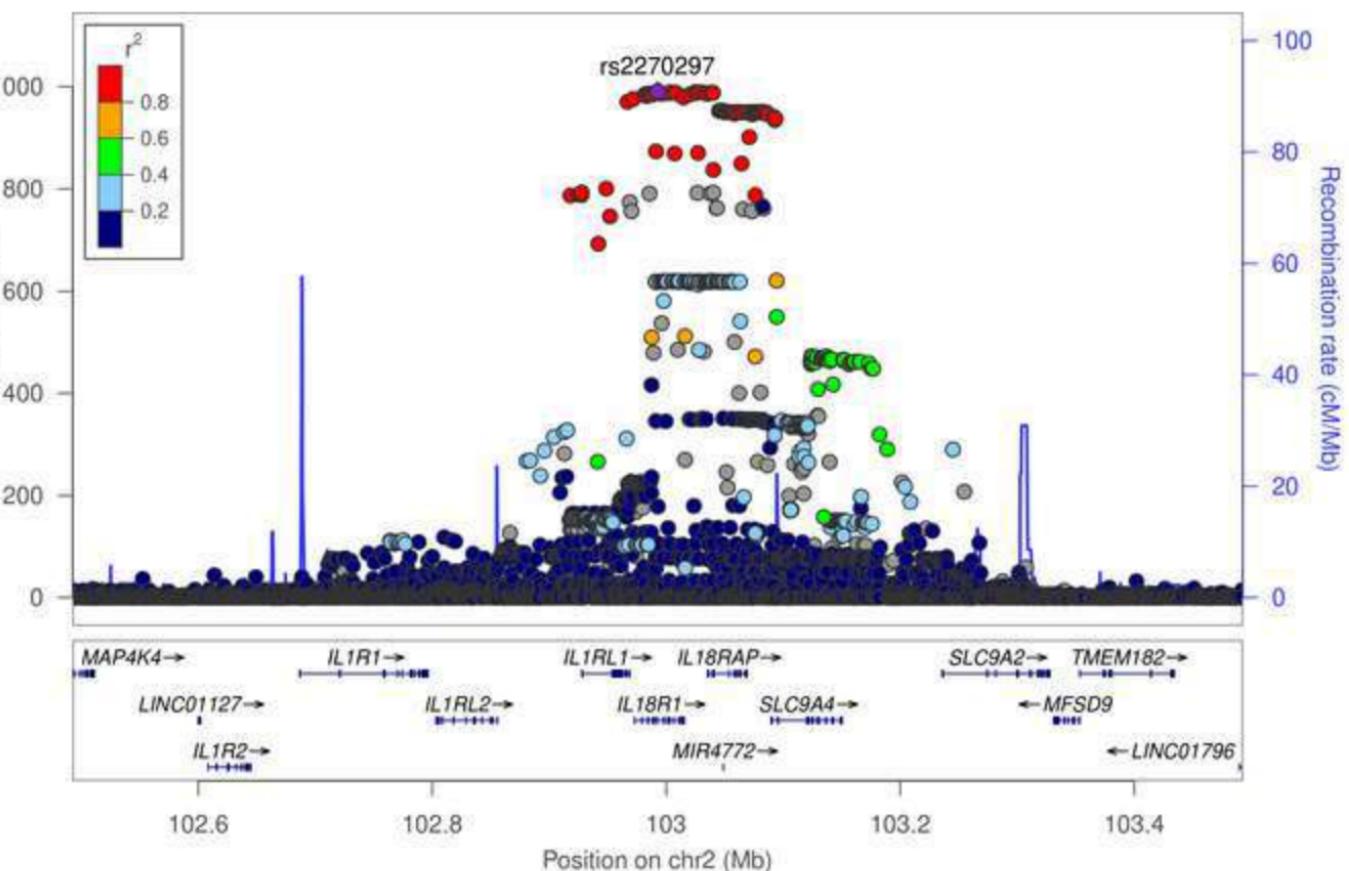
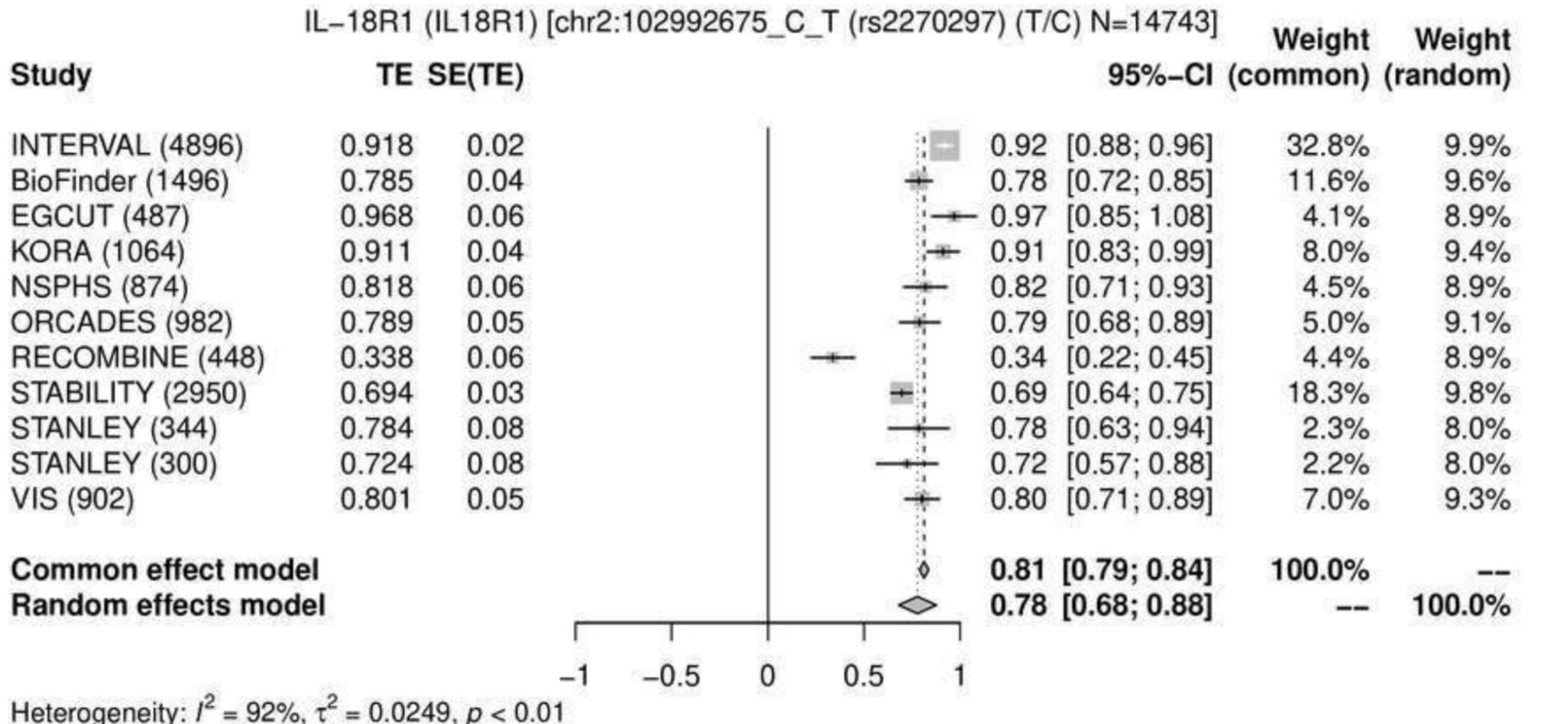


# IL-18R1 (IL18R1)-rs78357146

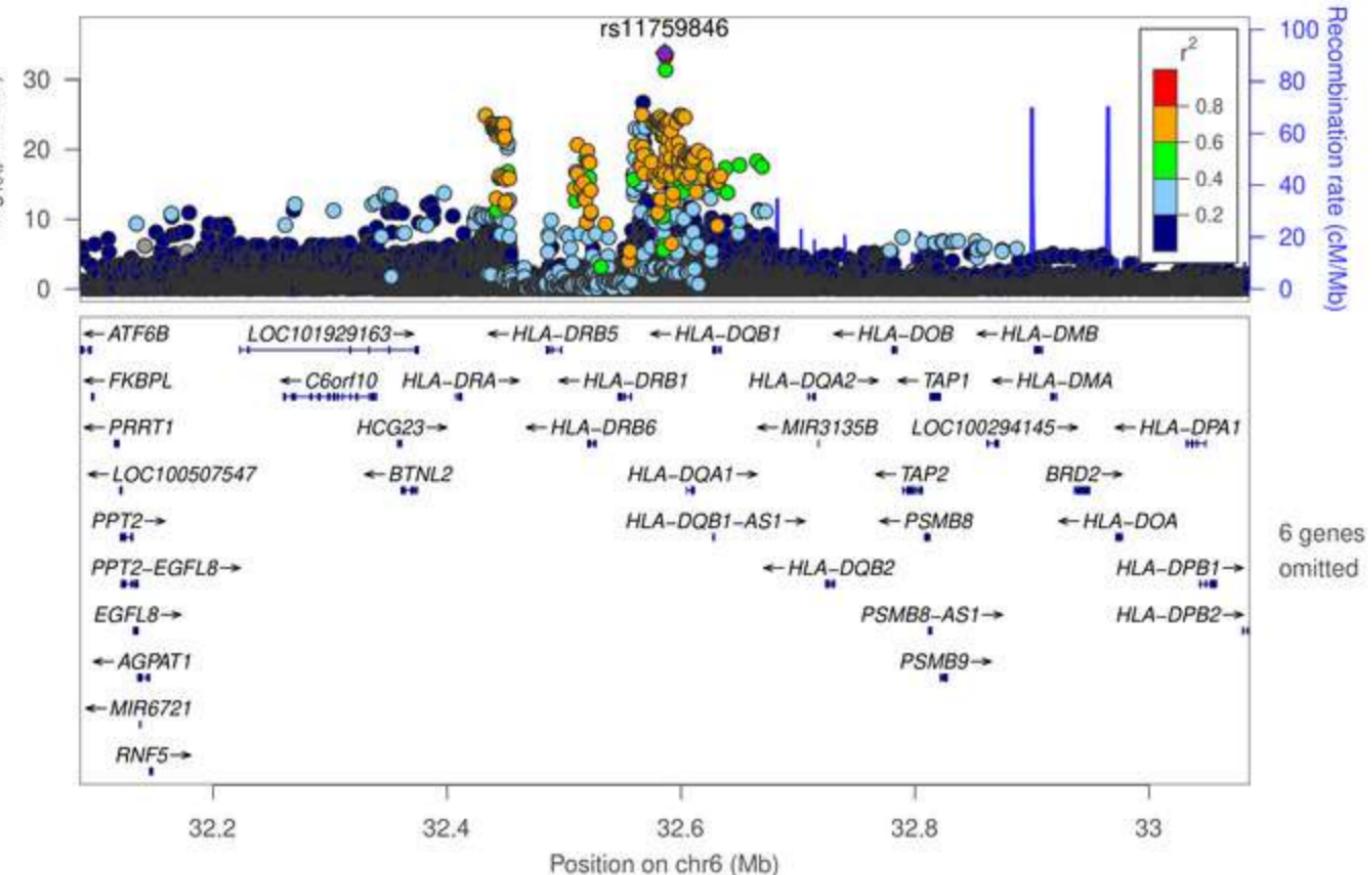
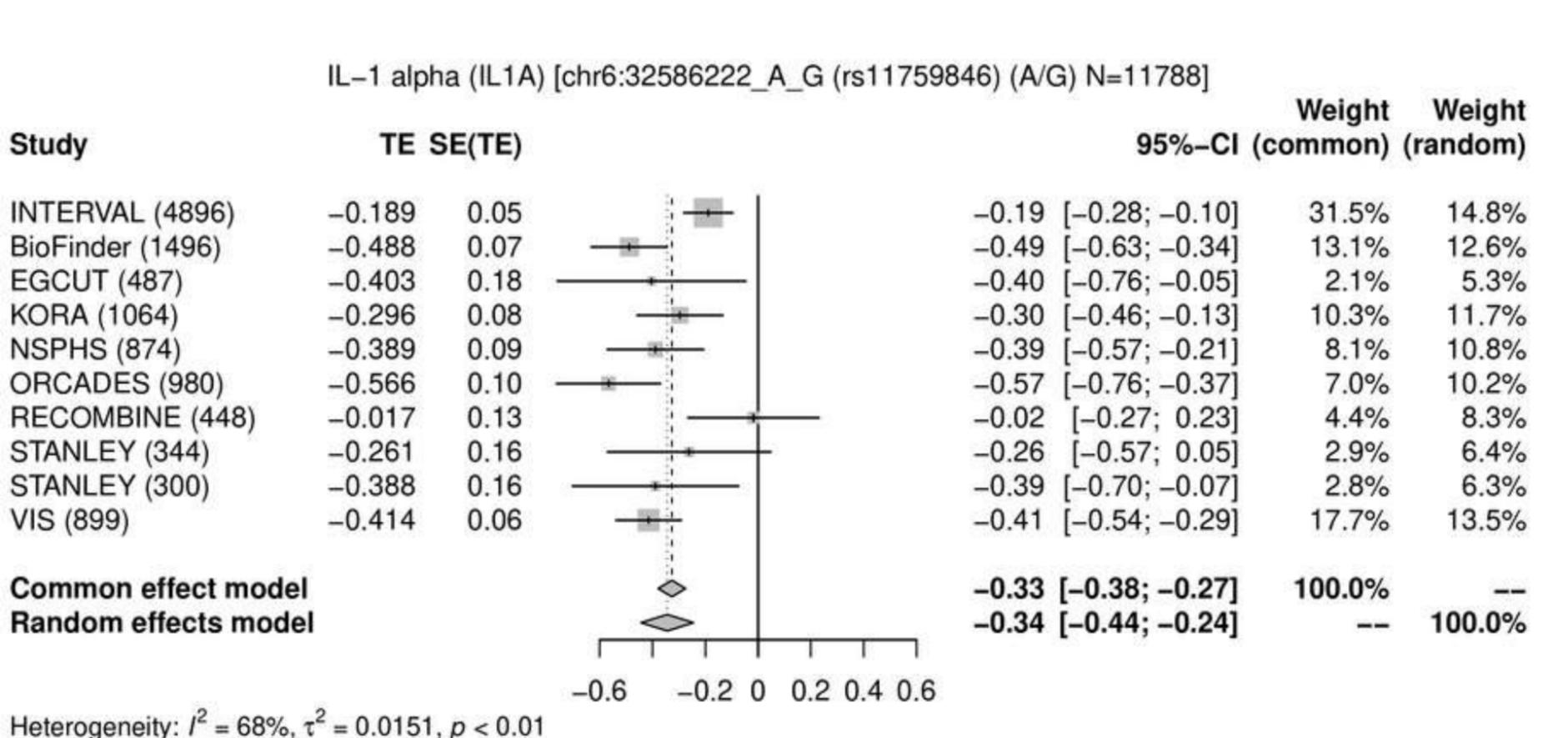
**Study**



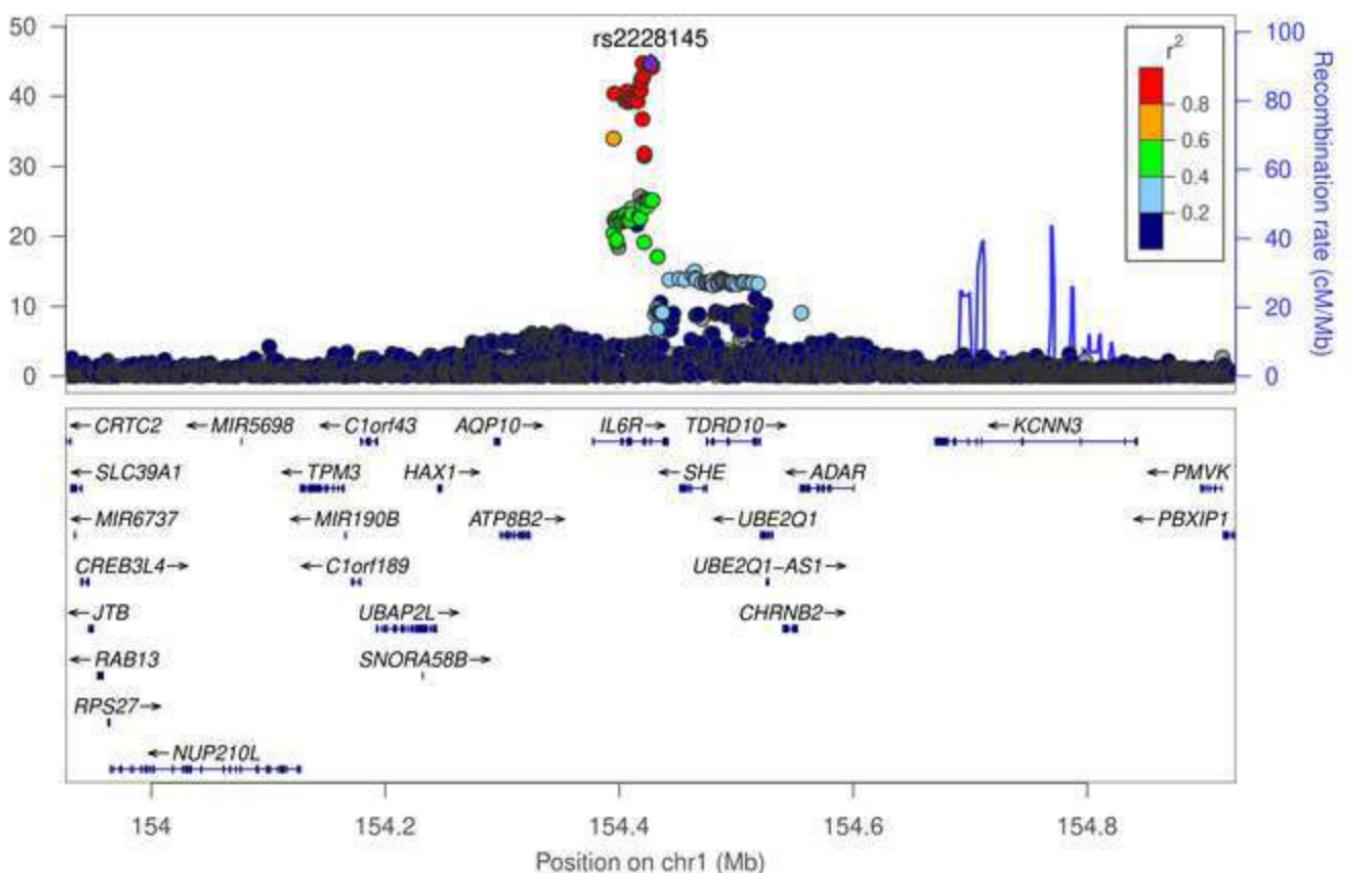
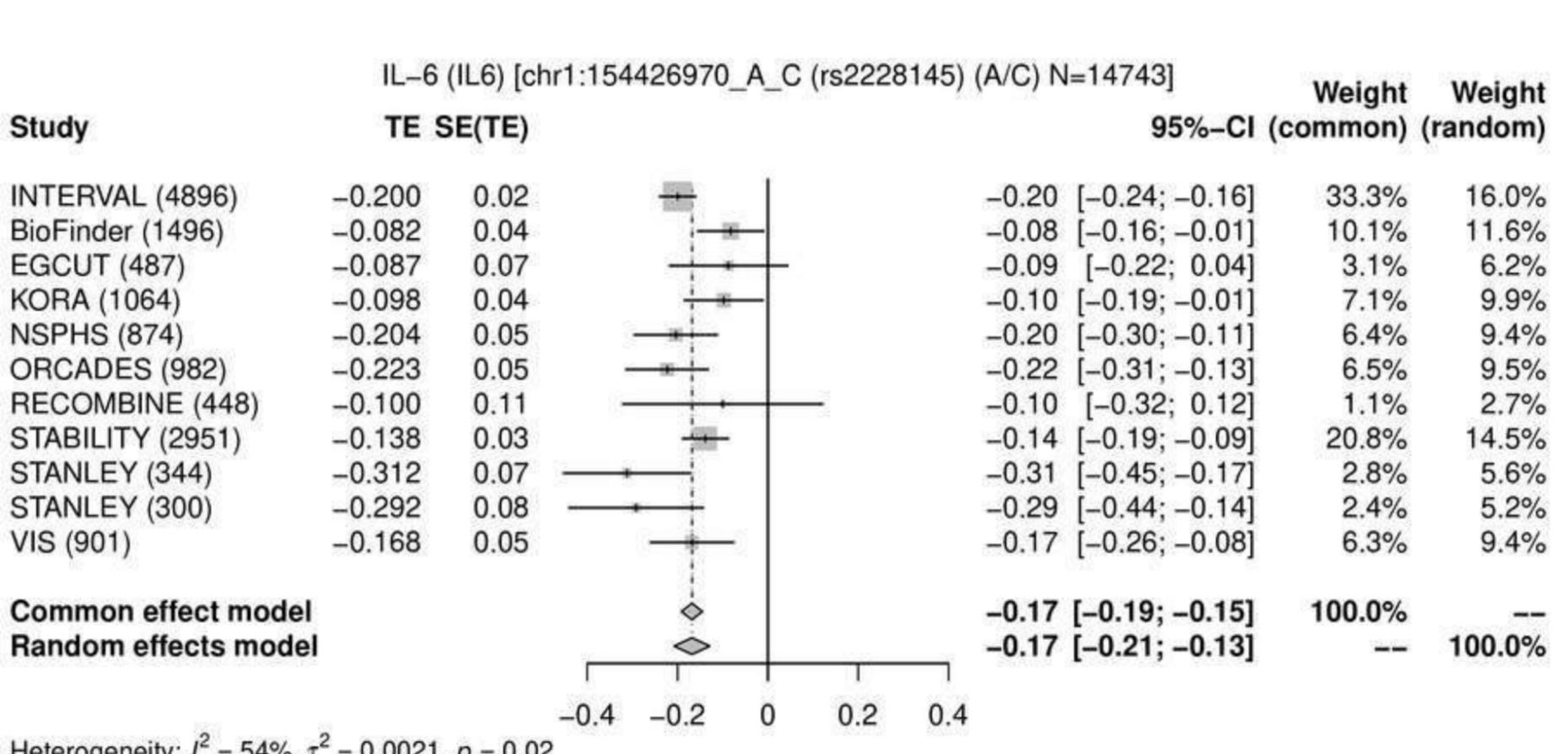
# IL-18R1 (IL18R1)-rs2270297



# IL-1 (alpha)-rs11759846



# IL-6 (IL6)-rs2228145



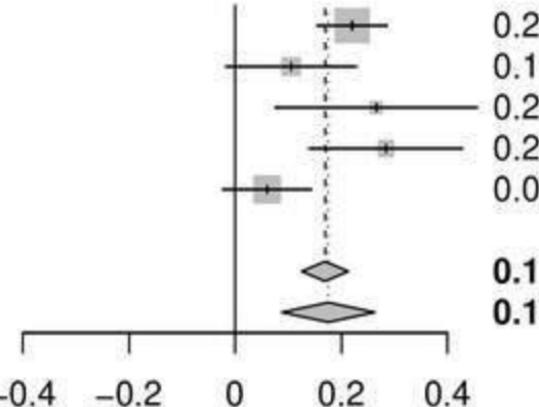
IL-7 (IL7) [chr8:79713766\_A\_G (rs112359206) (A/G) N=10894]

**Study**

INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
STABILITY (2951)

**TE SE(TE)**

0.220 0.03  
0.105 0.06  
0.265 0.10  
0.283 0.07  
0.060 0.04



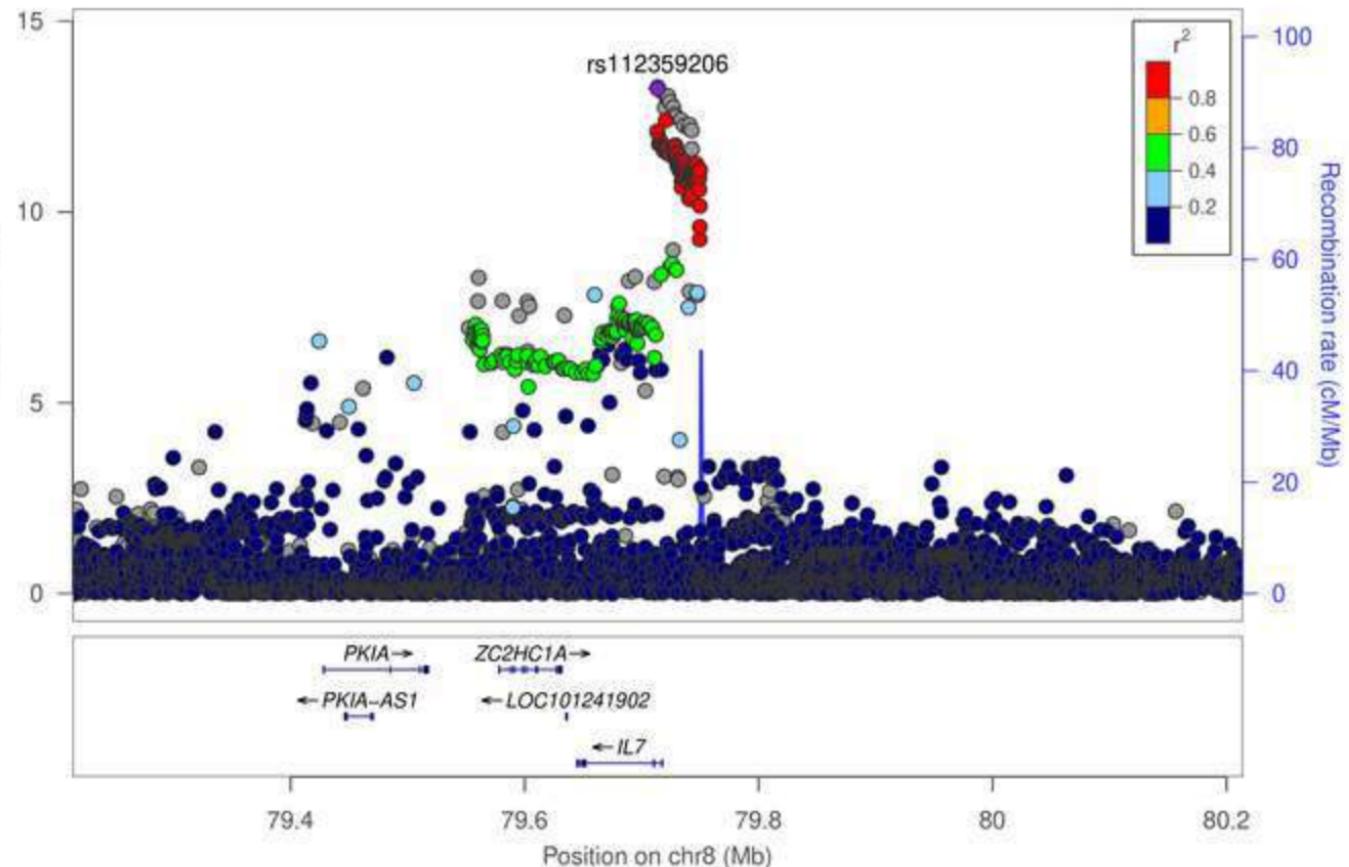
**Weight**  
**95%-CI (common)**  
**Weight**  
**(random)**

44.5% [ 0.15; 0.29]  
12.9% [-0.02; 0.23]  
5.4% [ 0.08; 0.46]  
9.3% [ 0.14; 0.43]  
27.8% [ -0.02; 0.14]  
100.0% [ 0.13; 0.21]  
0.18 [ 0.09; 0.26]  
--  
100.0%

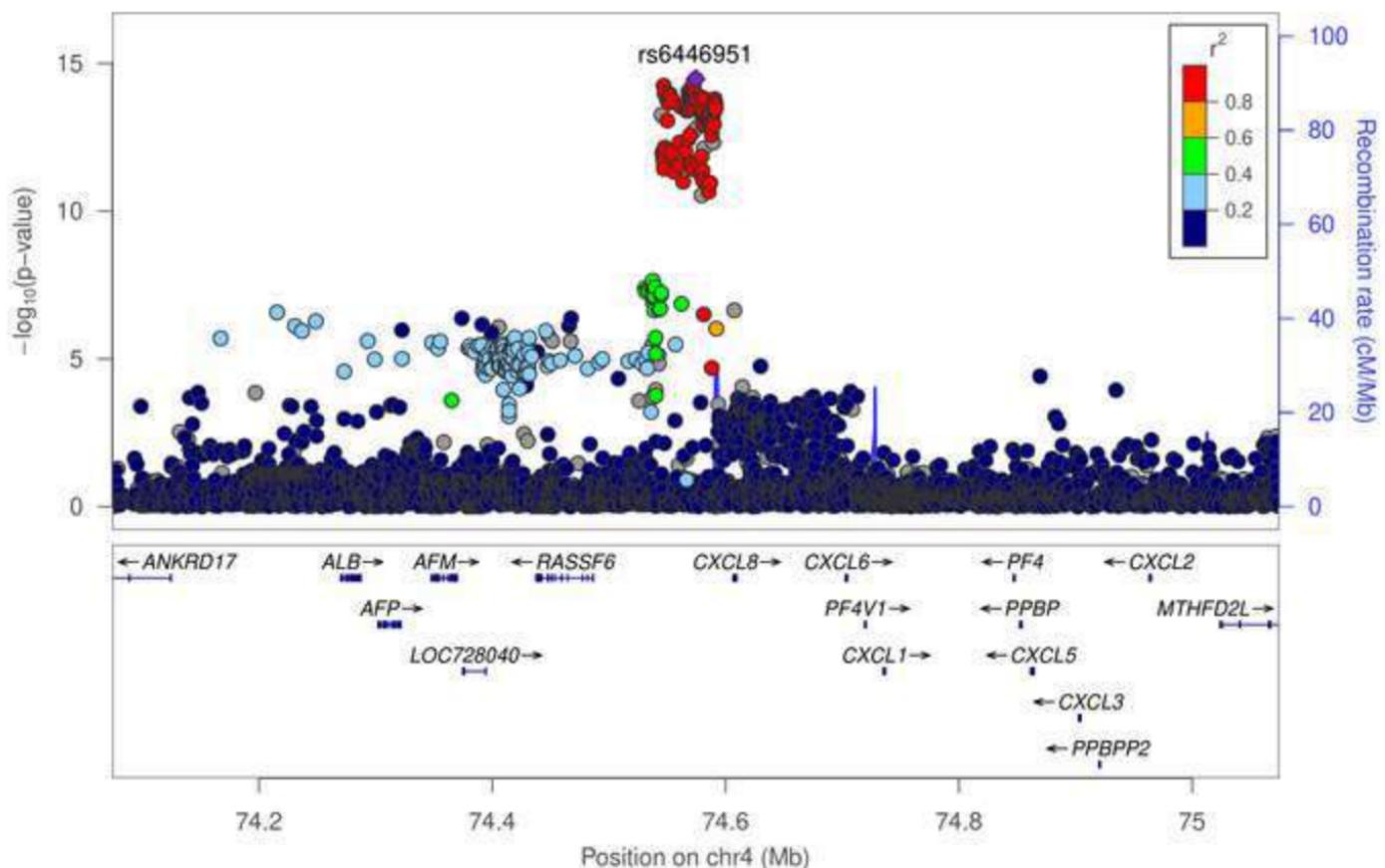
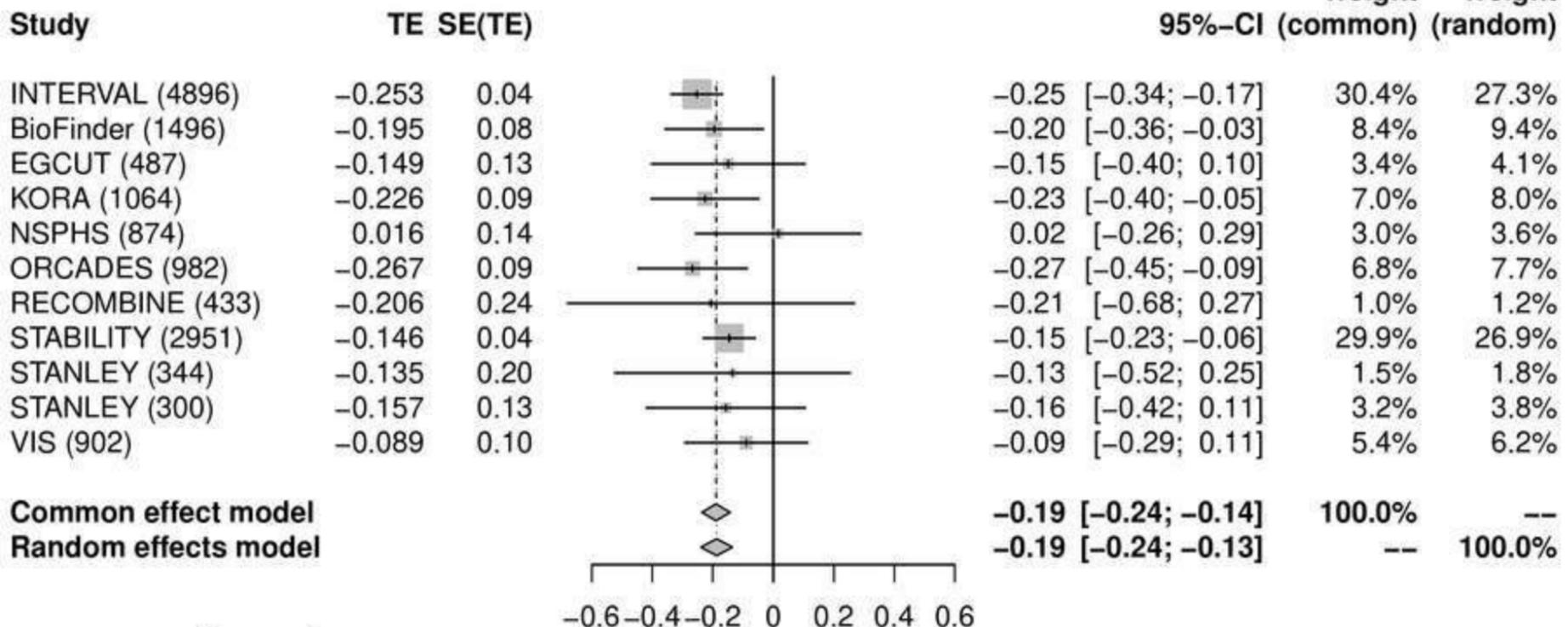
**Common effect model**  
**Random effects model**

Heterogeneity:  $I^2 = 70\%$ ,  $\tau^2 = 0.0064$ ,  $p = 0.01$

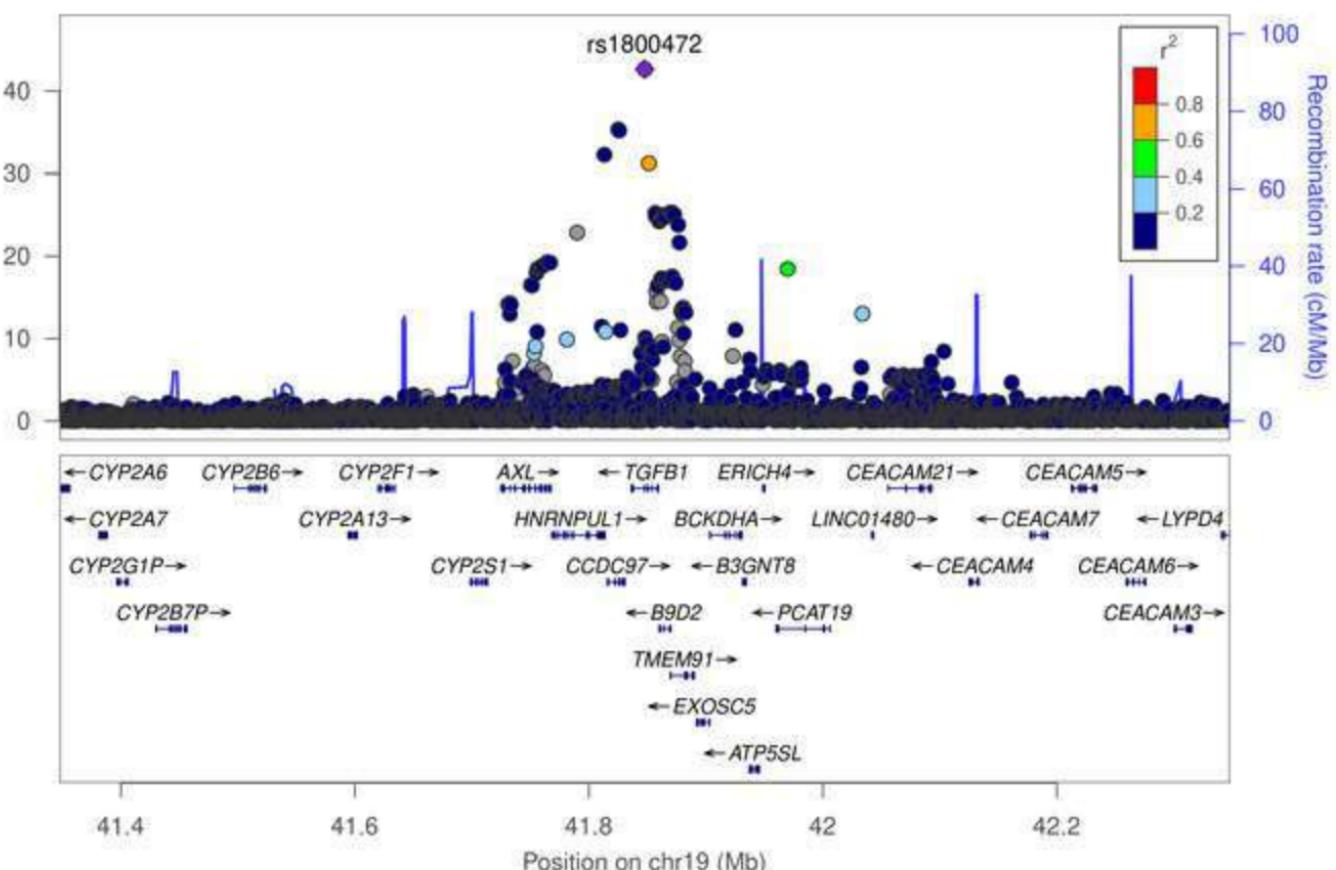
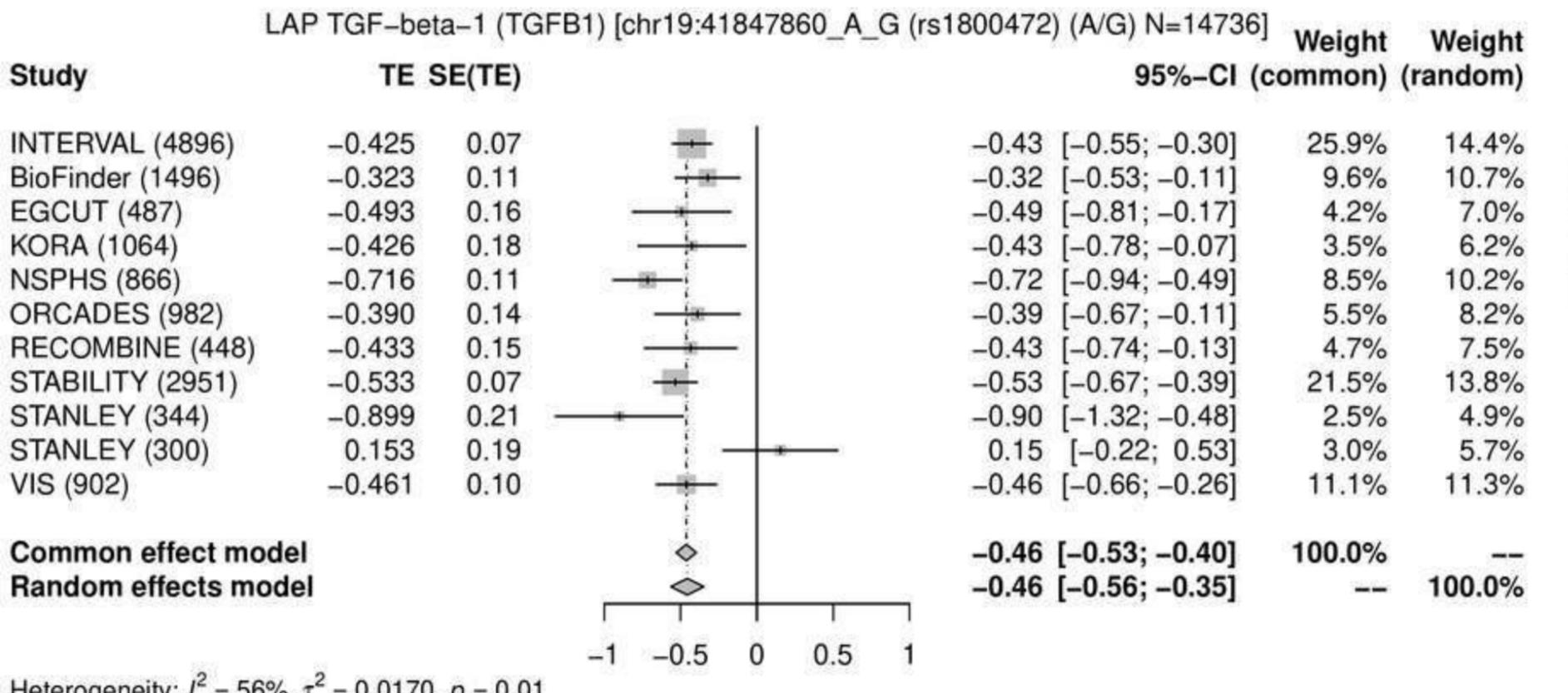
IL-7 (IL7)-rs112359206



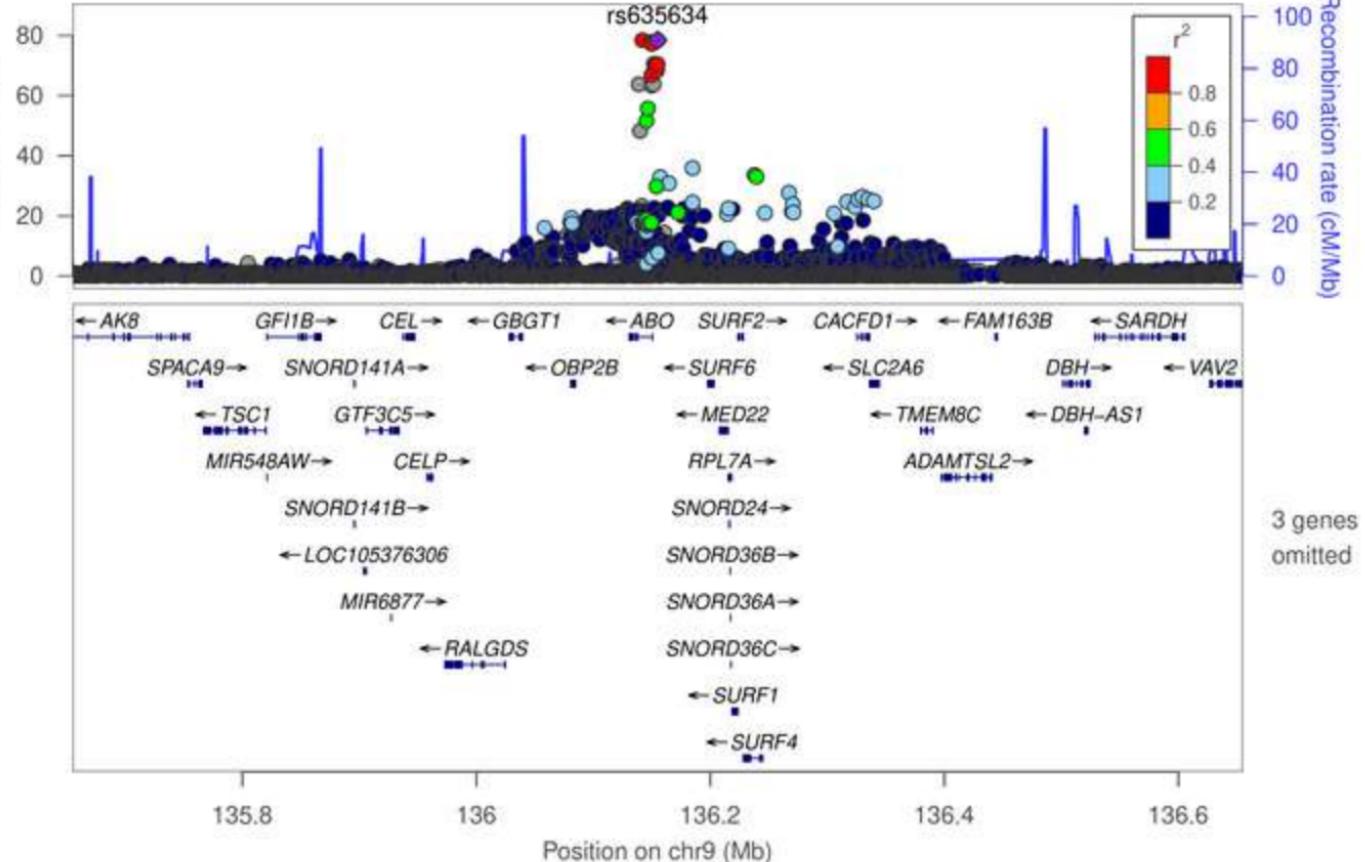
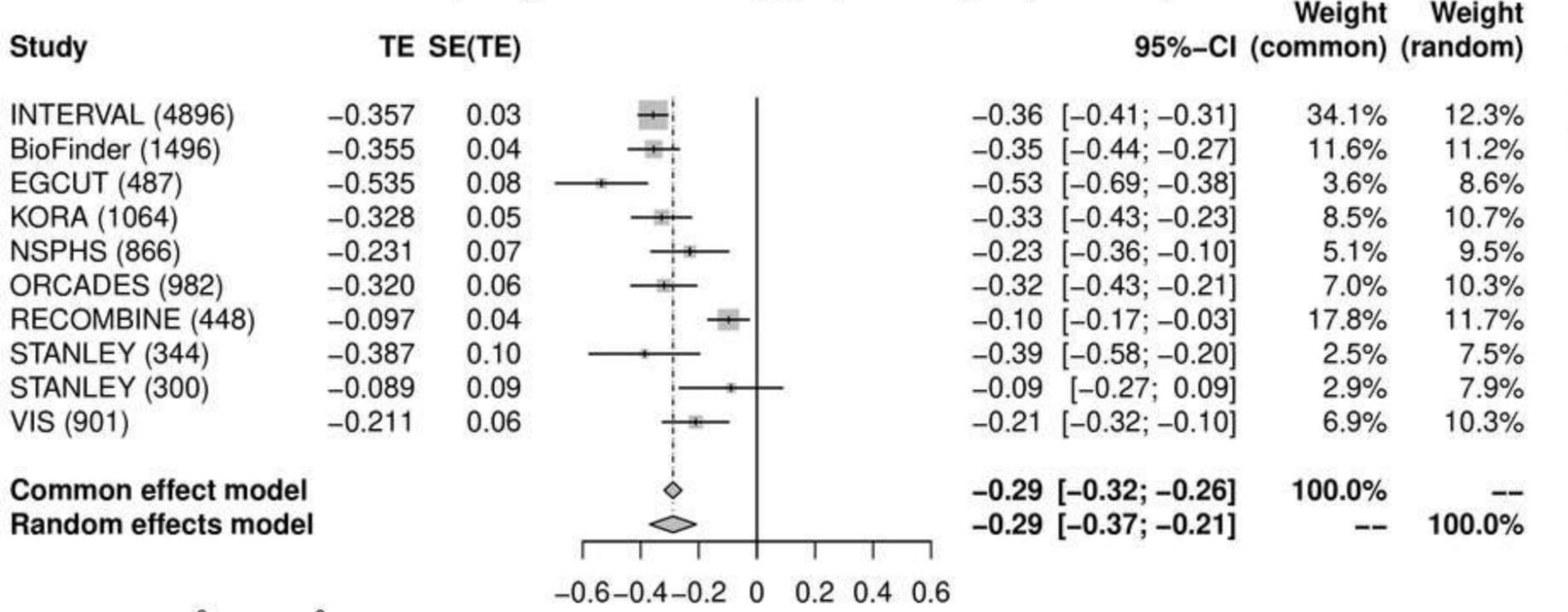
# IL-8 (IL8)-rs6446951



# LAP (TGF-beta-1)-rs1800472



# LIF-R (LIFR)-rs635634



# MCP-1 (CCL2)-rs12075

MCP-1 (CCL2) [chr1:159175354\_A\_G (rs12075) (A/G) N=14730]

## Study

	TE	SE(TE)
INTERVAL (4896)	0.182	0.02
BioFinder (1496)	0.070	0.04
EGCUT (487)	0.110	0.07
KORA (1064)	0.756	0.04
NSPHS (866)	0.087	0.05
ORCADES (981)	-0.055	0.05
RECOMBINE (445)	0.335	0.06
STABILITY (2951)	0.021	0.02
STANLEY (344)	0.360	0.07
STANLEY (300)	0.311	0.07
VIS (900)	0.001	0.05

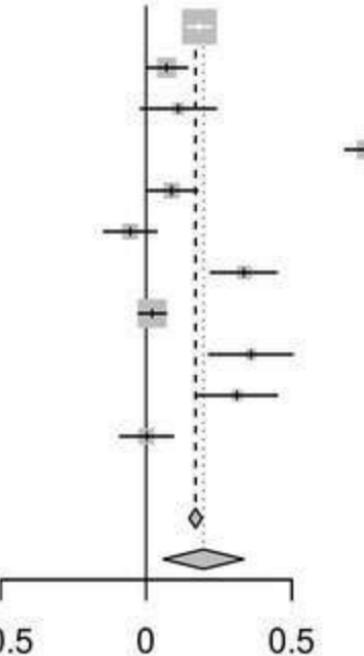
TE SE(TE)

Weight  
95%-CI (common)  
(random)

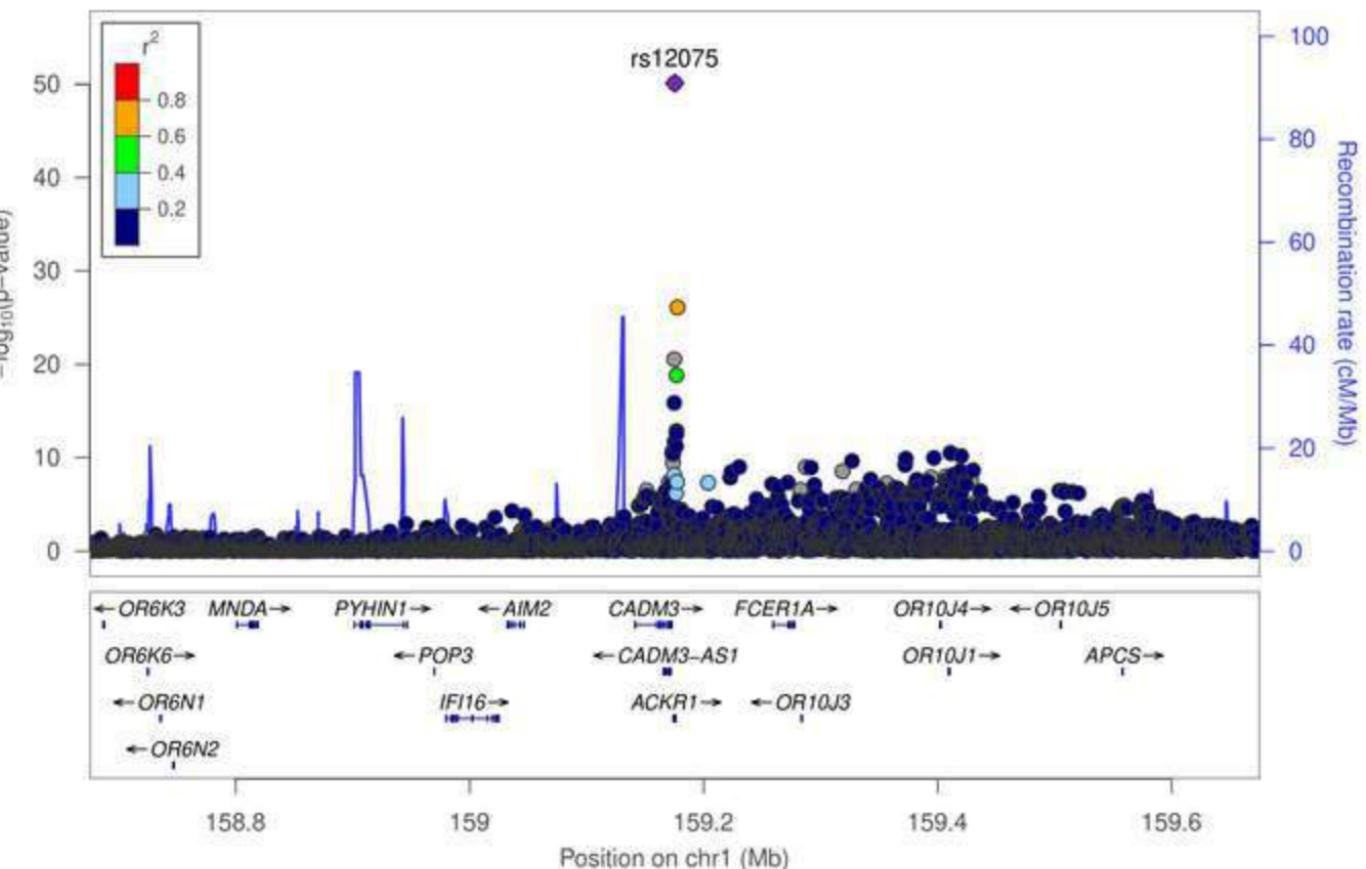
0.18	[ 0.14; 0.22]	31.0%	9.5%
0.07	[ -0.00; 0.14]	9.4%	9.3%
0.11	[ -0.02; 0.24]	2.9%	8.8%
0.76	[ 0.68; 0.83]	8.9%	9.3%
0.09	[ -0.00; 0.18]	6.2%	9.2%
-0.05	[ -0.15; 0.04]	5.9%	9.2%
0.33	[ 0.22; 0.45]	3.8%	9.0%
0.02	[ -0.03; 0.07]	21.2%	9.4%
0.36	[ 0.22; 0.50]	2.4%	8.6%
0.31	[ 0.17; 0.45]	2.5%	8.7%
0.00	[ -0.09; 0.09]	5.8%	9.1%

0.17 [ 0.15; 0.19]  
0.20 [ 0.06; 0.34]

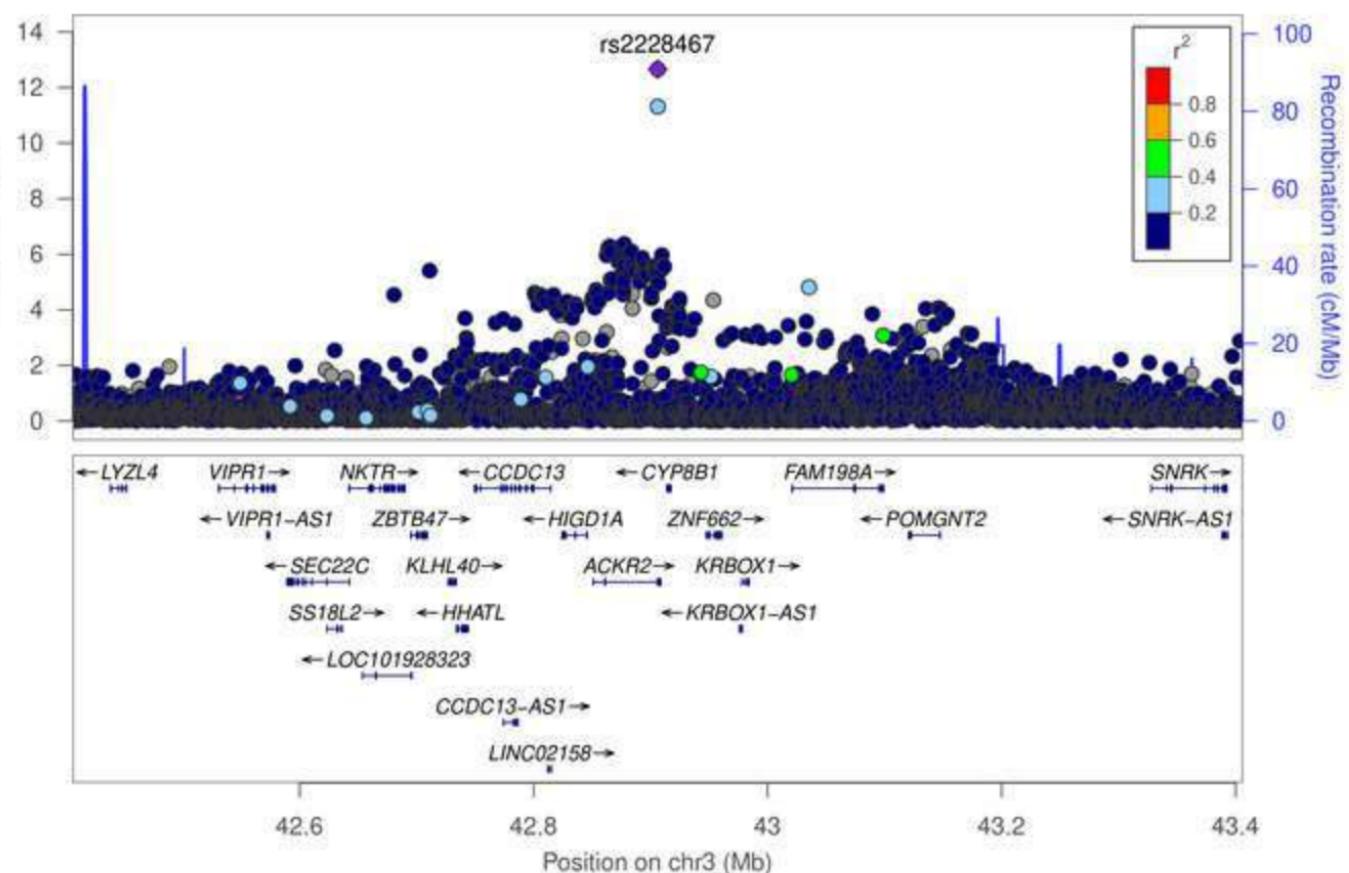
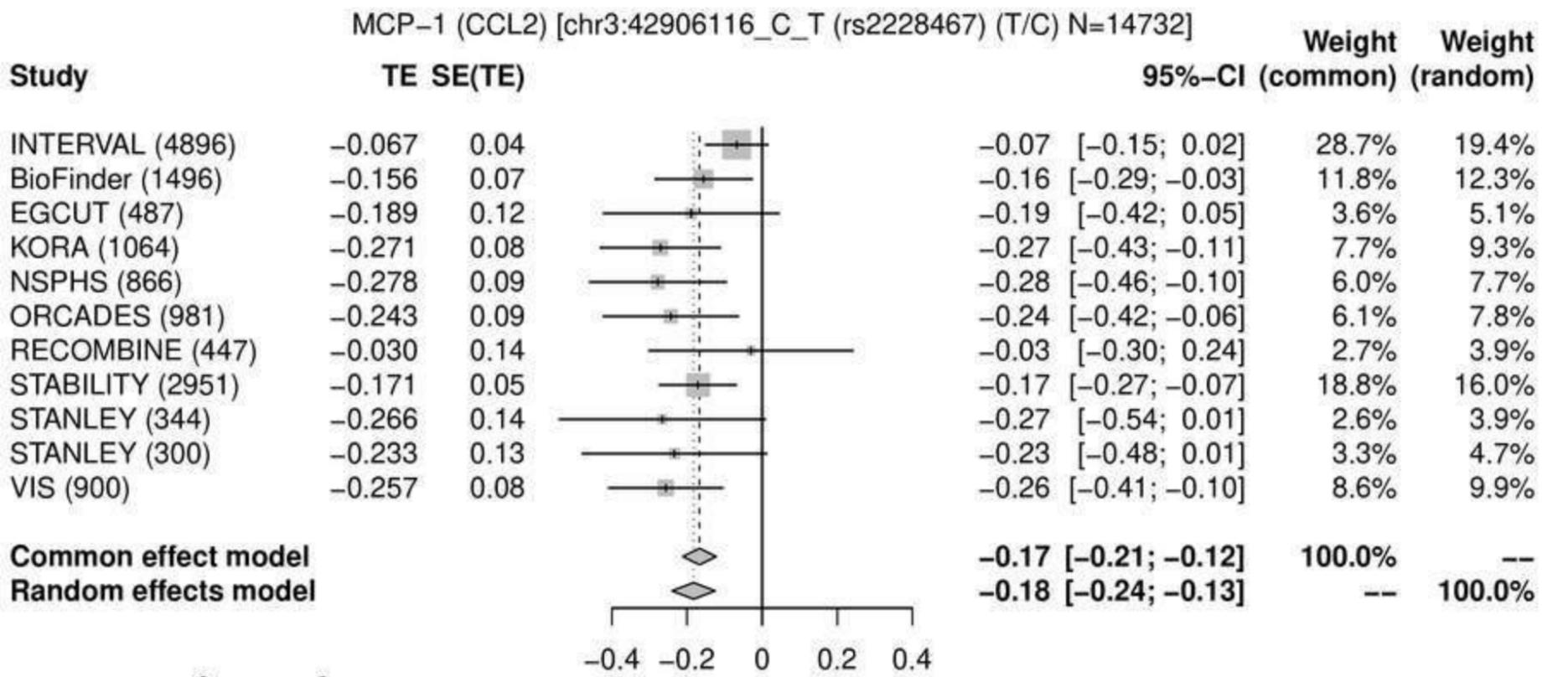
100.0% -- 100.0%



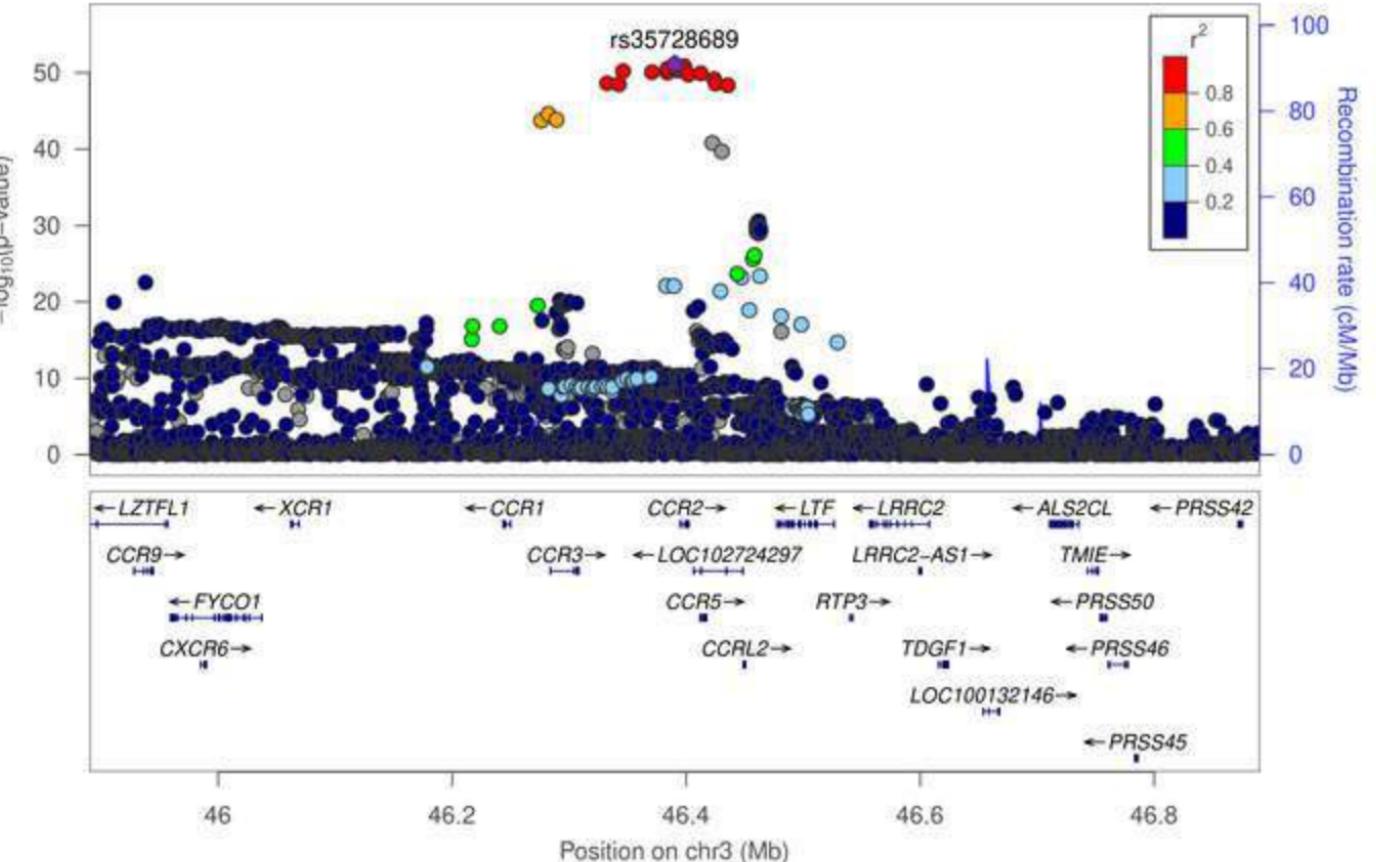
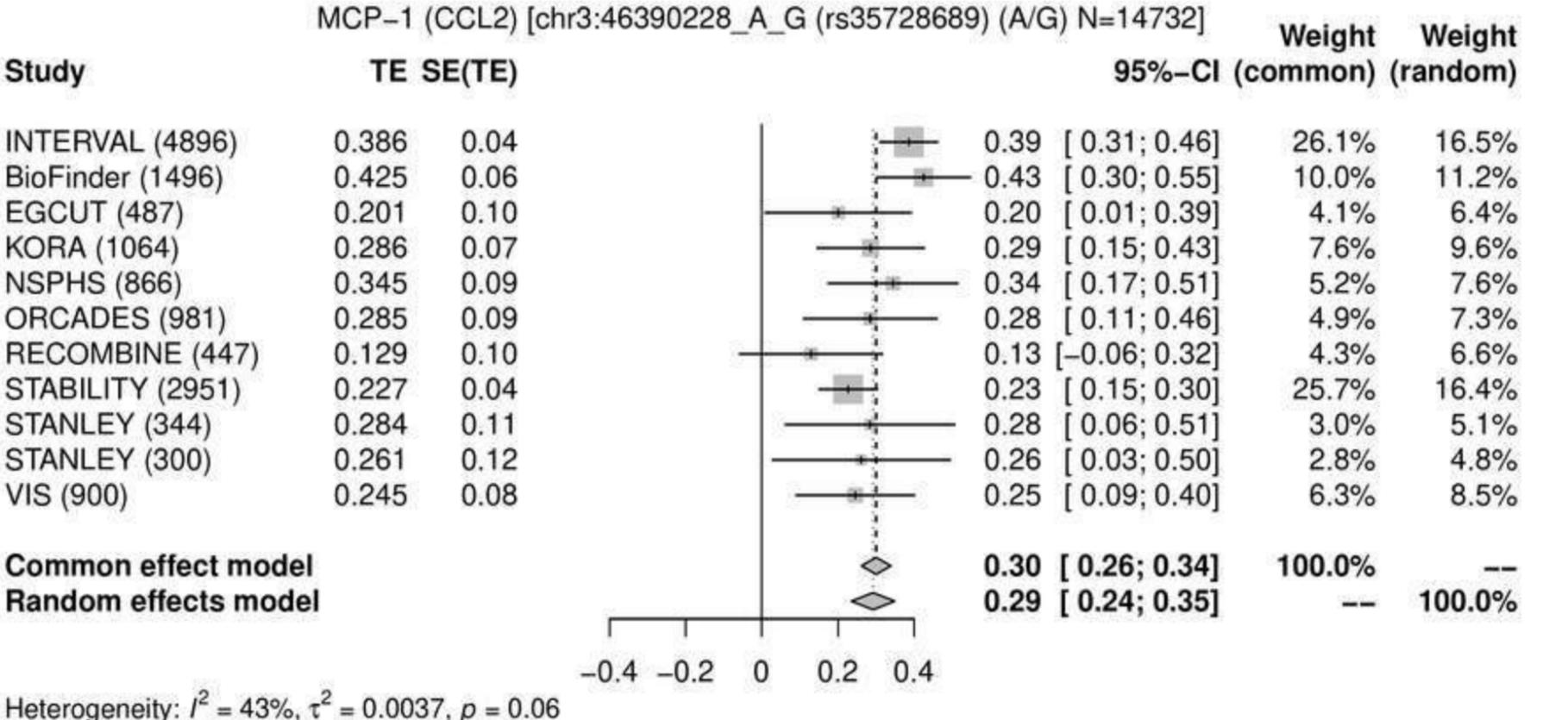
Heterogeneity:  $I^2 = 97\%$ ,  $\tau^2 = 0.0528$ ,  $p < 0.01$



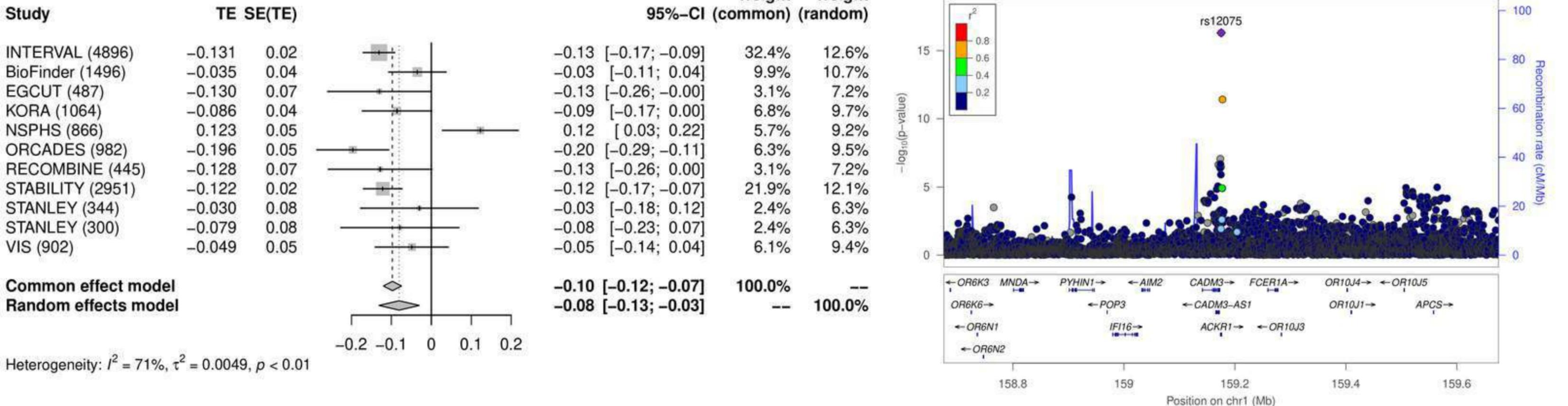
# MCP-1 (CCL2)-rs2228467



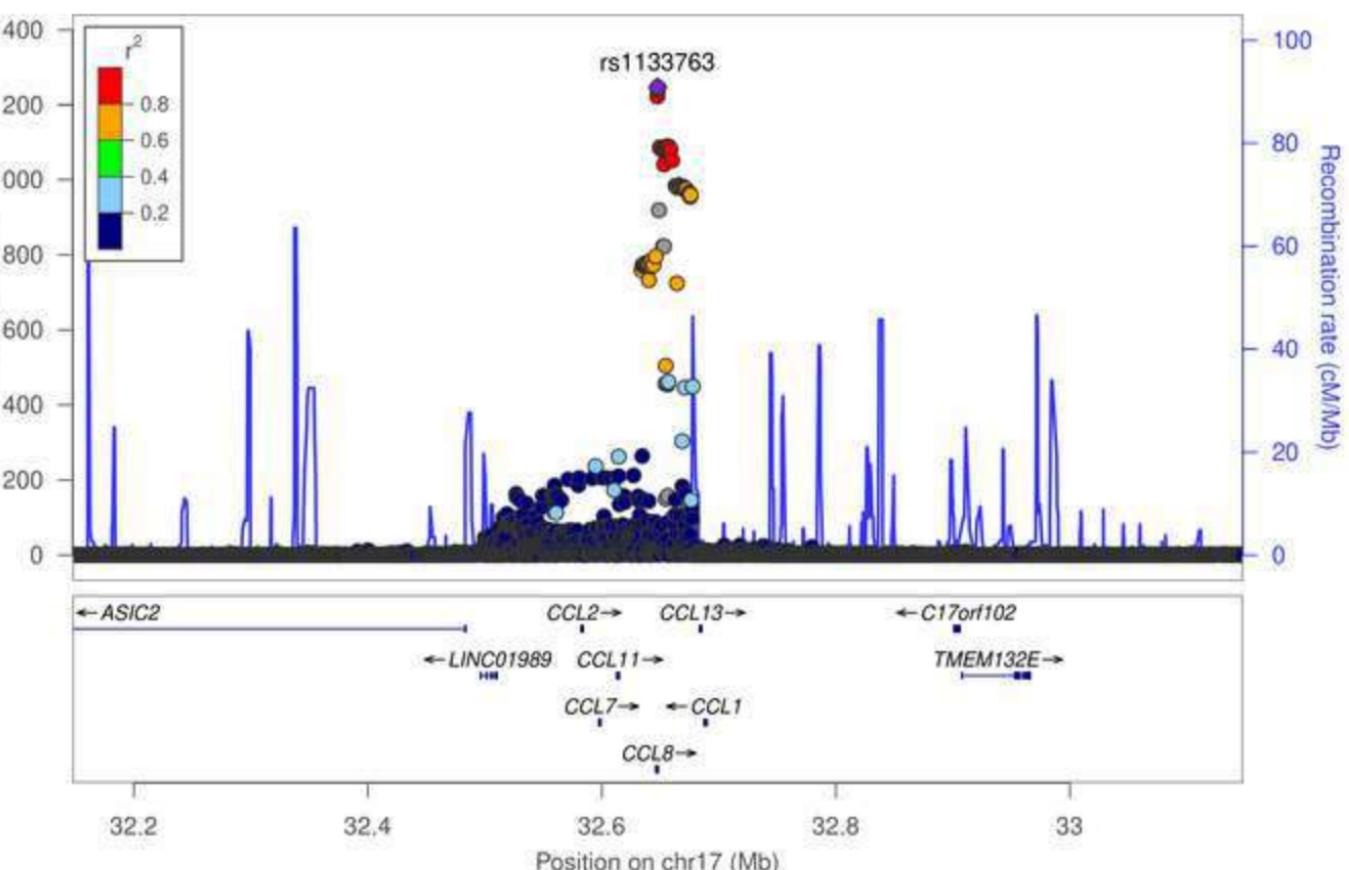
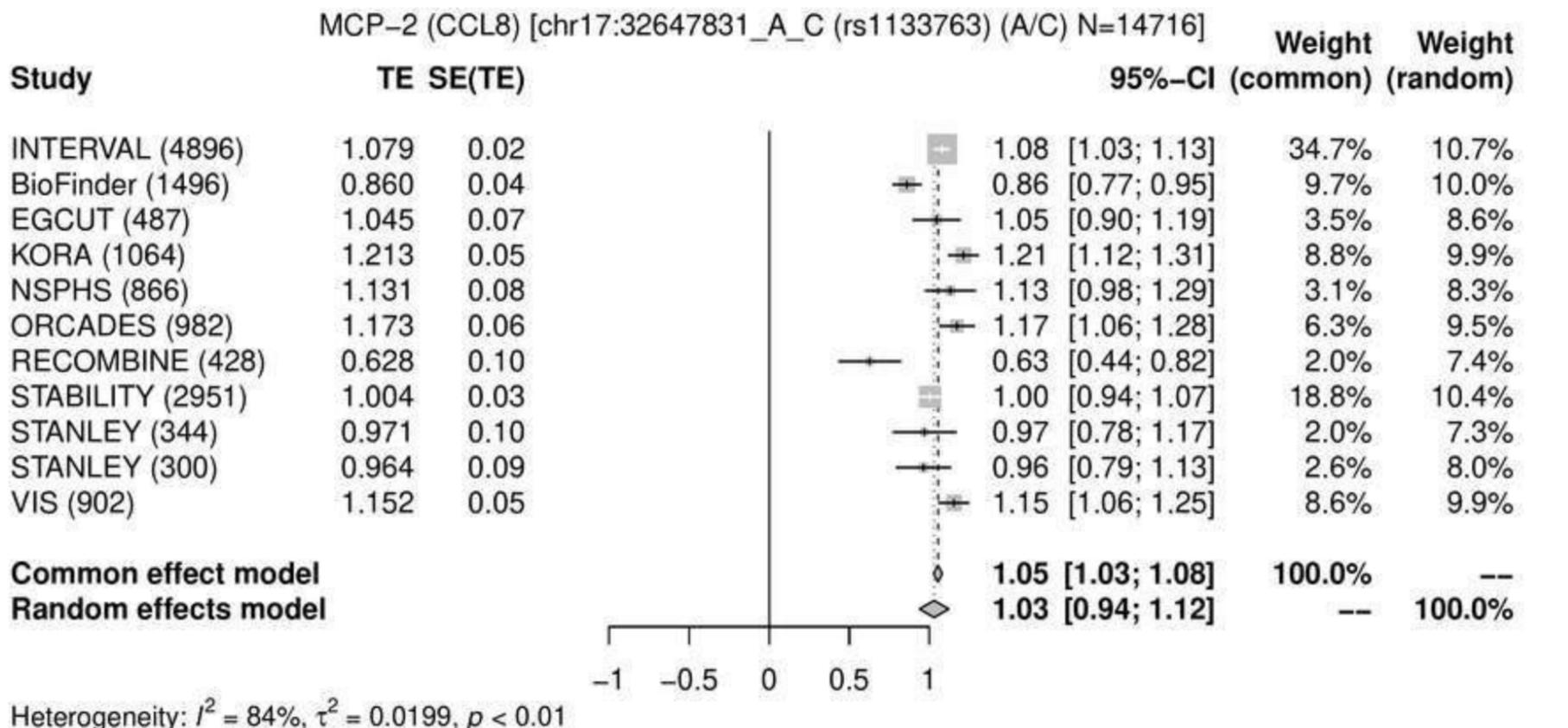
# MCP-1 (CCL2)-rs35728689



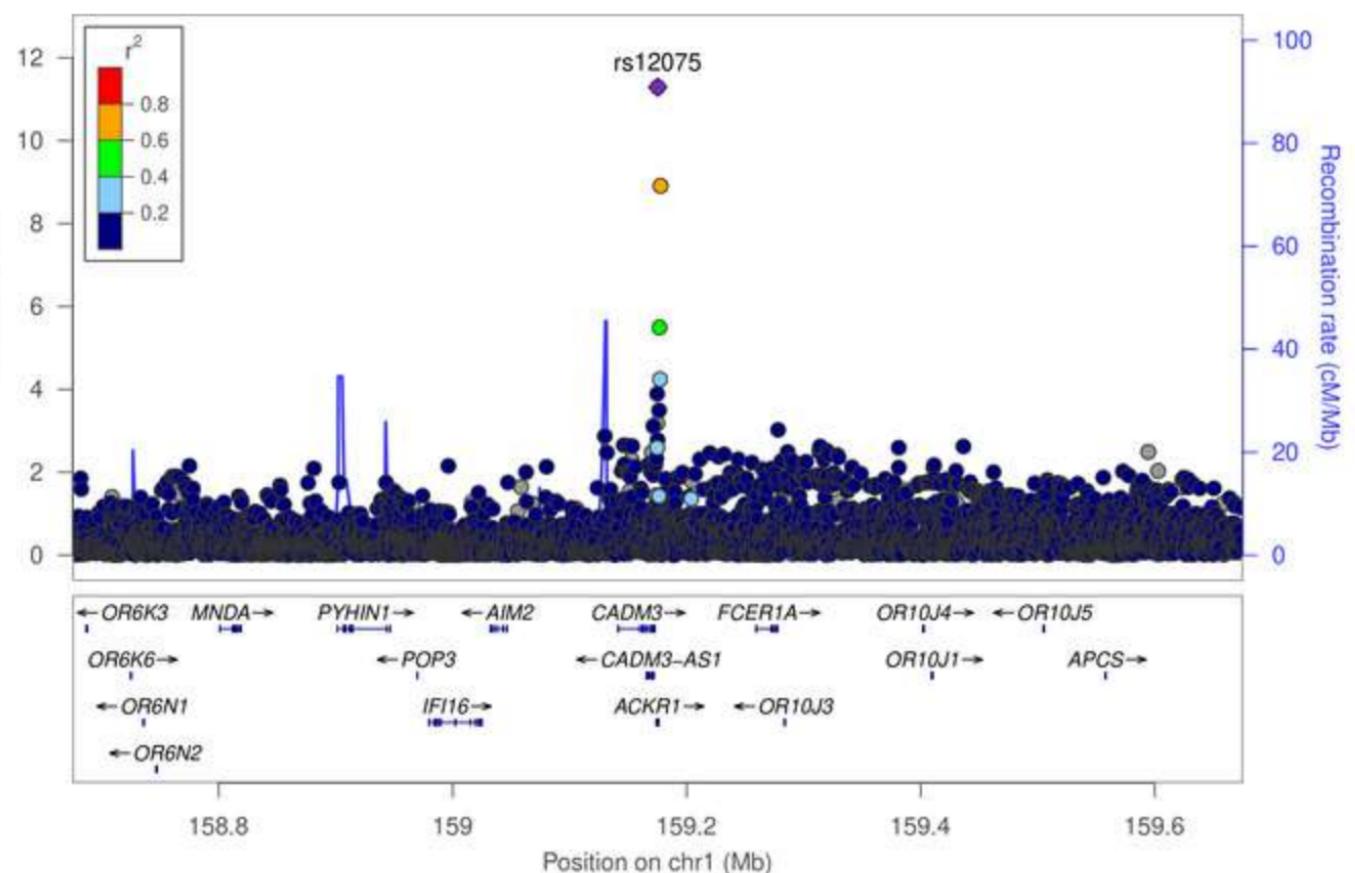
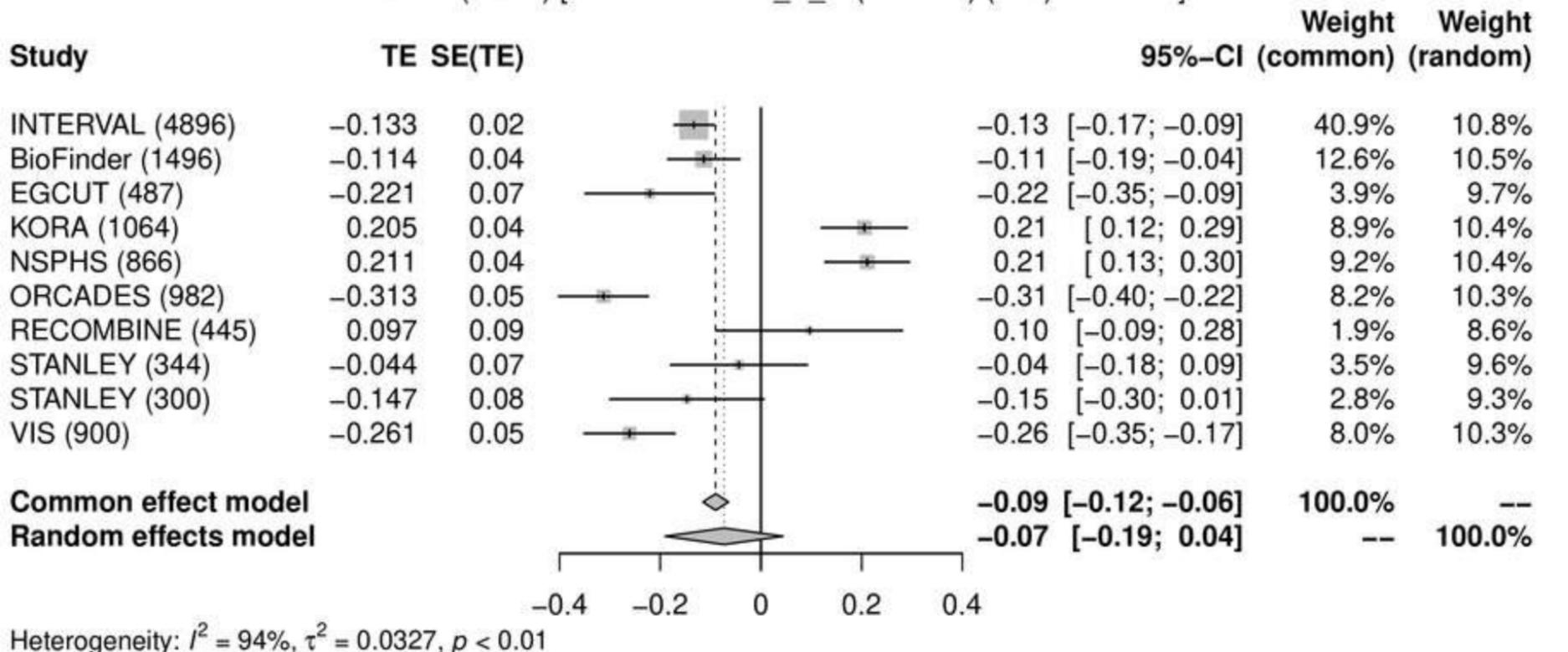
# MCP-2 (CCL8)-rs12075



# MCP-2 (CCL8)-rs1133763

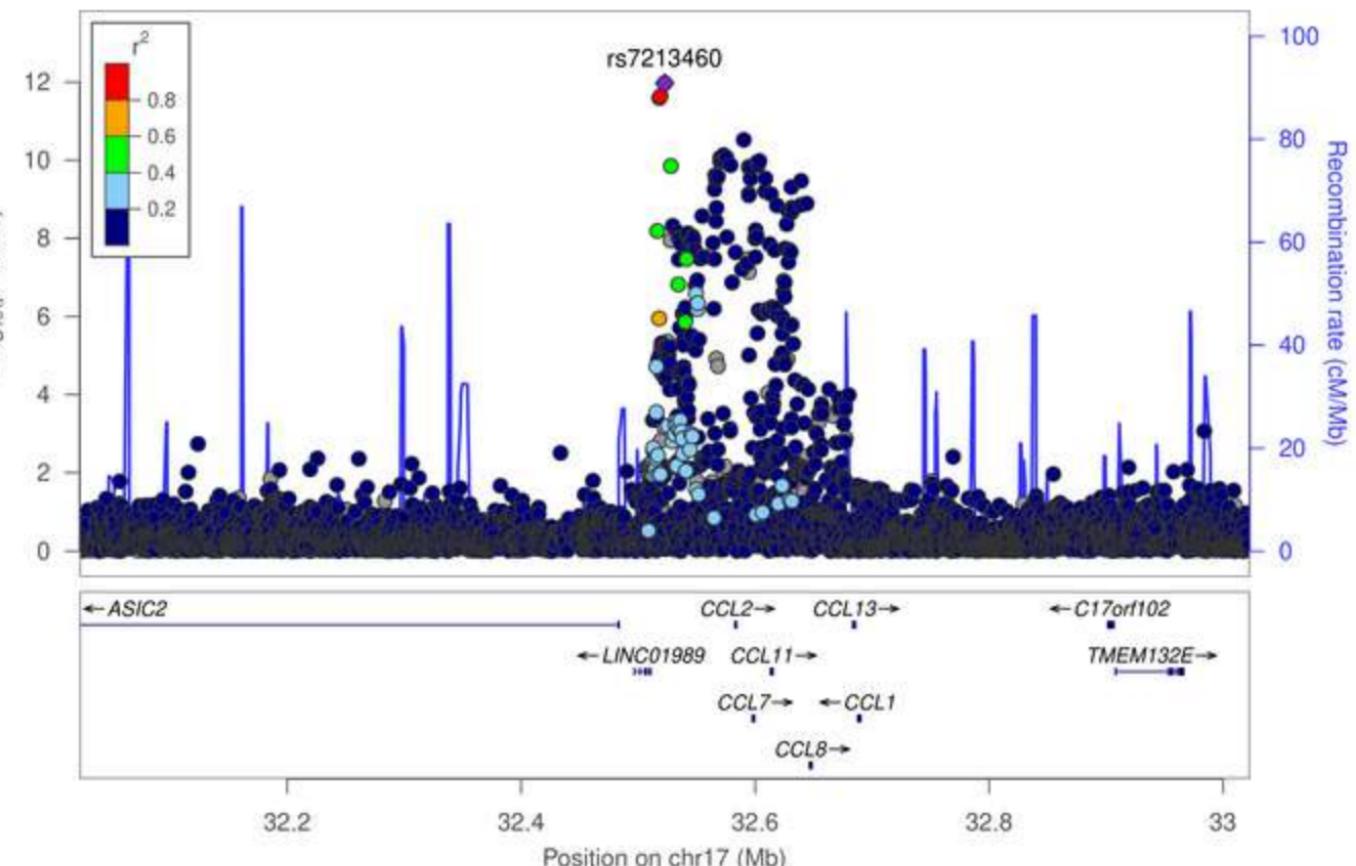
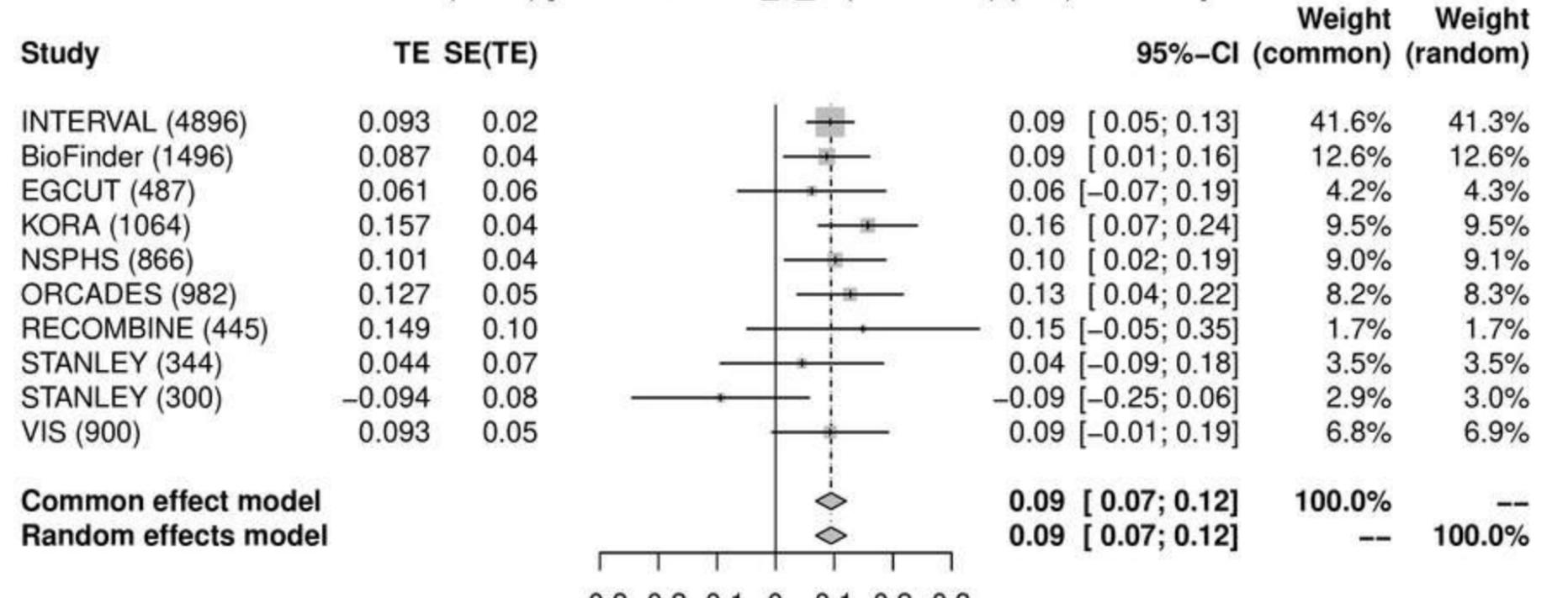


# MCP-3 (CCL7)-rs12075



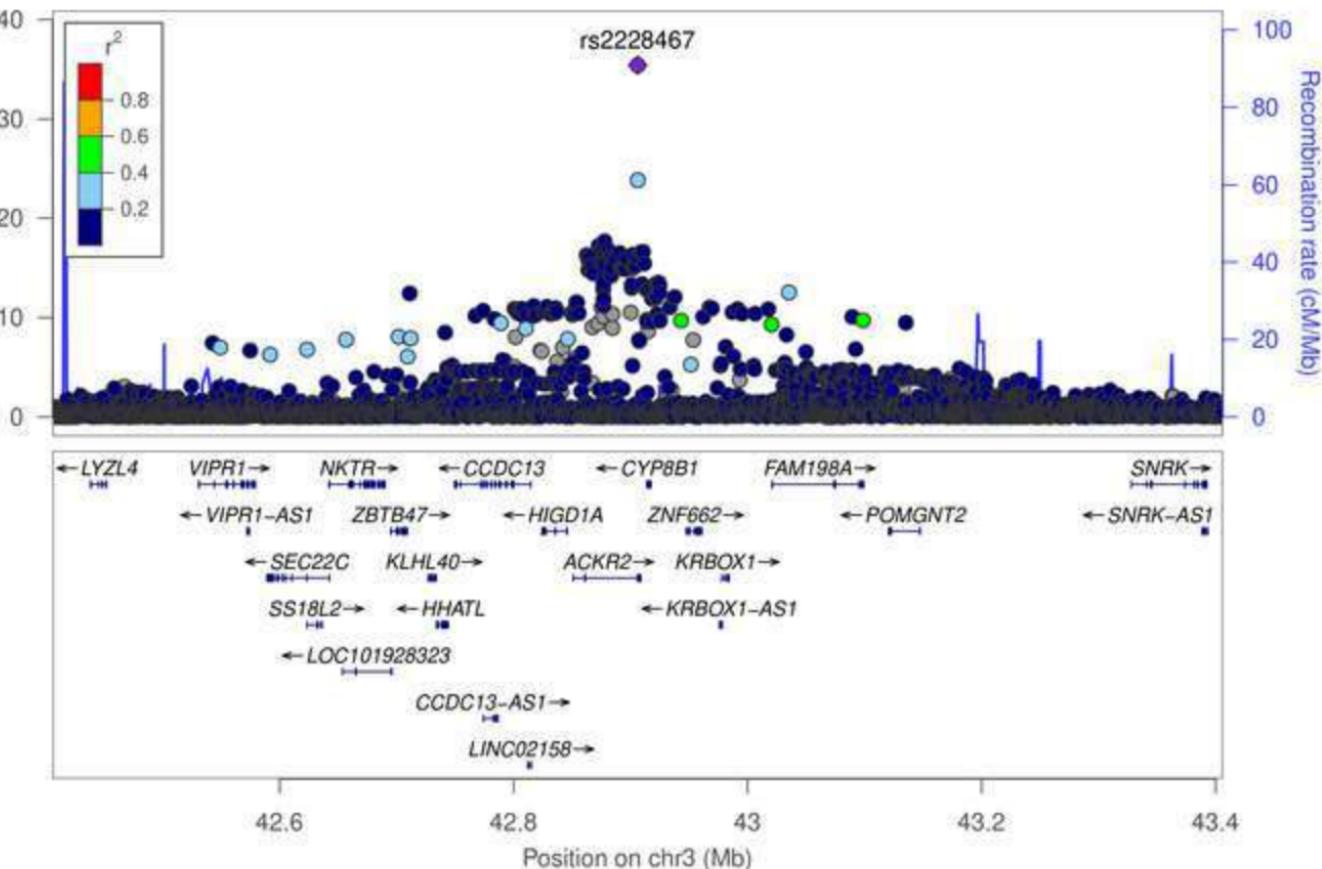
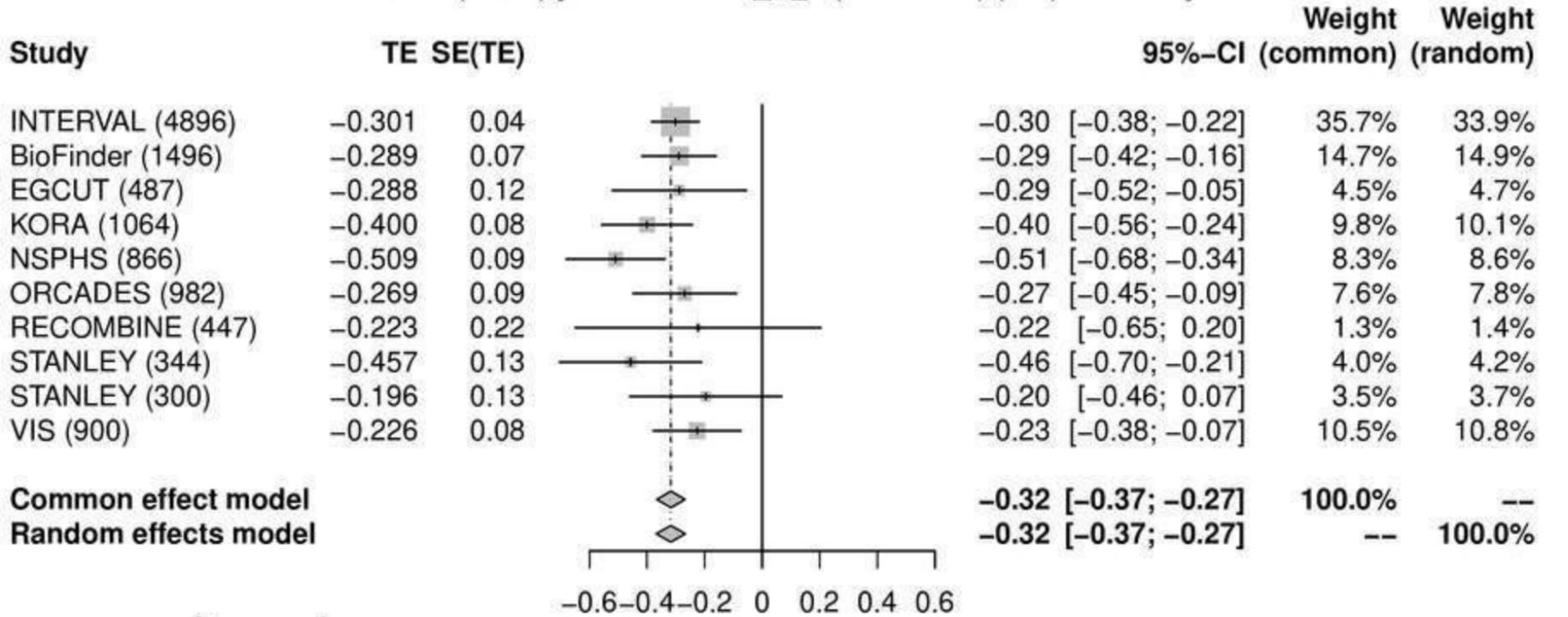
# MCP-3 (CCL7)-rs7213460

MCP-3 (CCL7) [chr17:32522613\_A\_G (rs7213460) (A/G) N=11780]



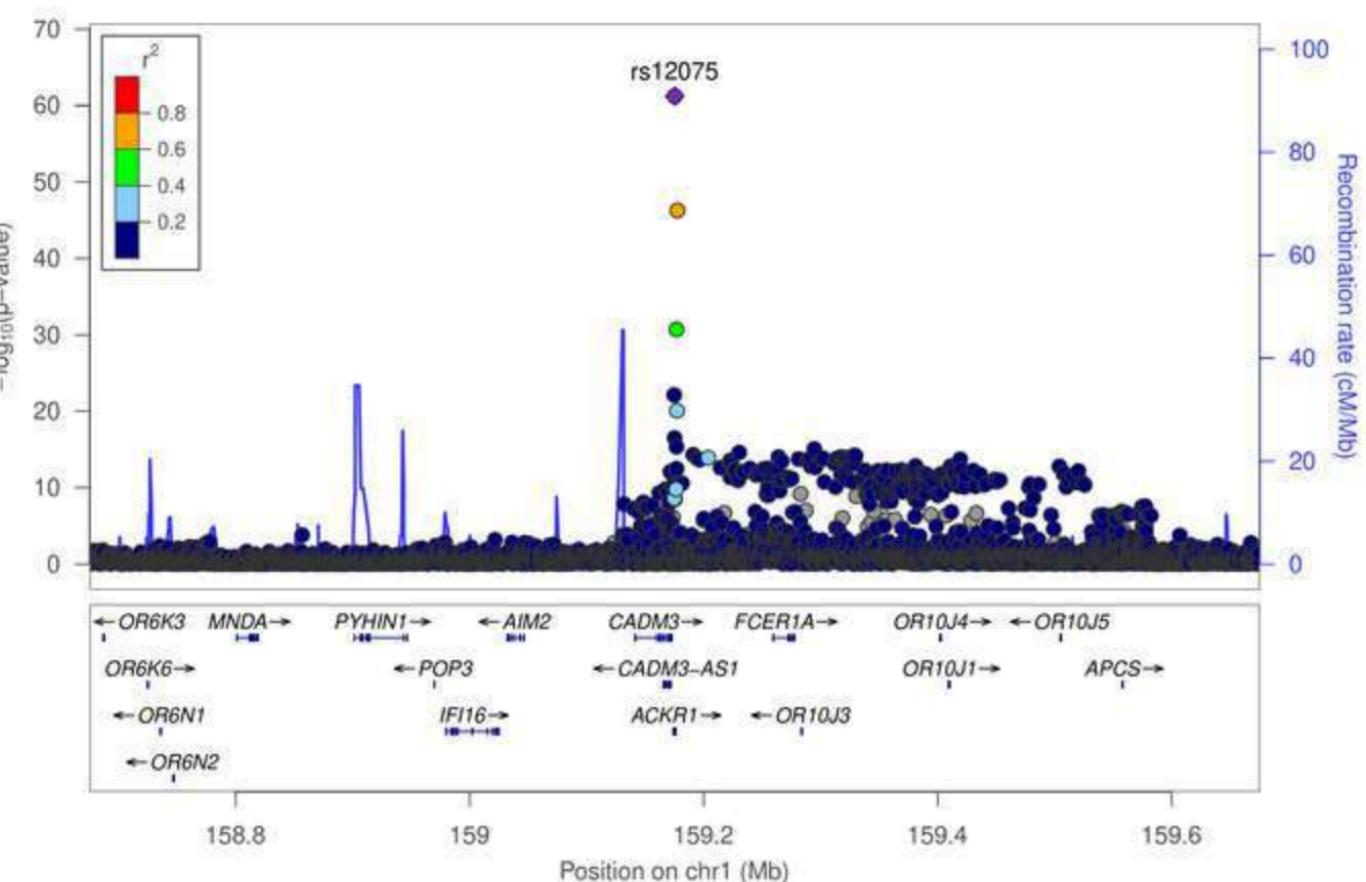
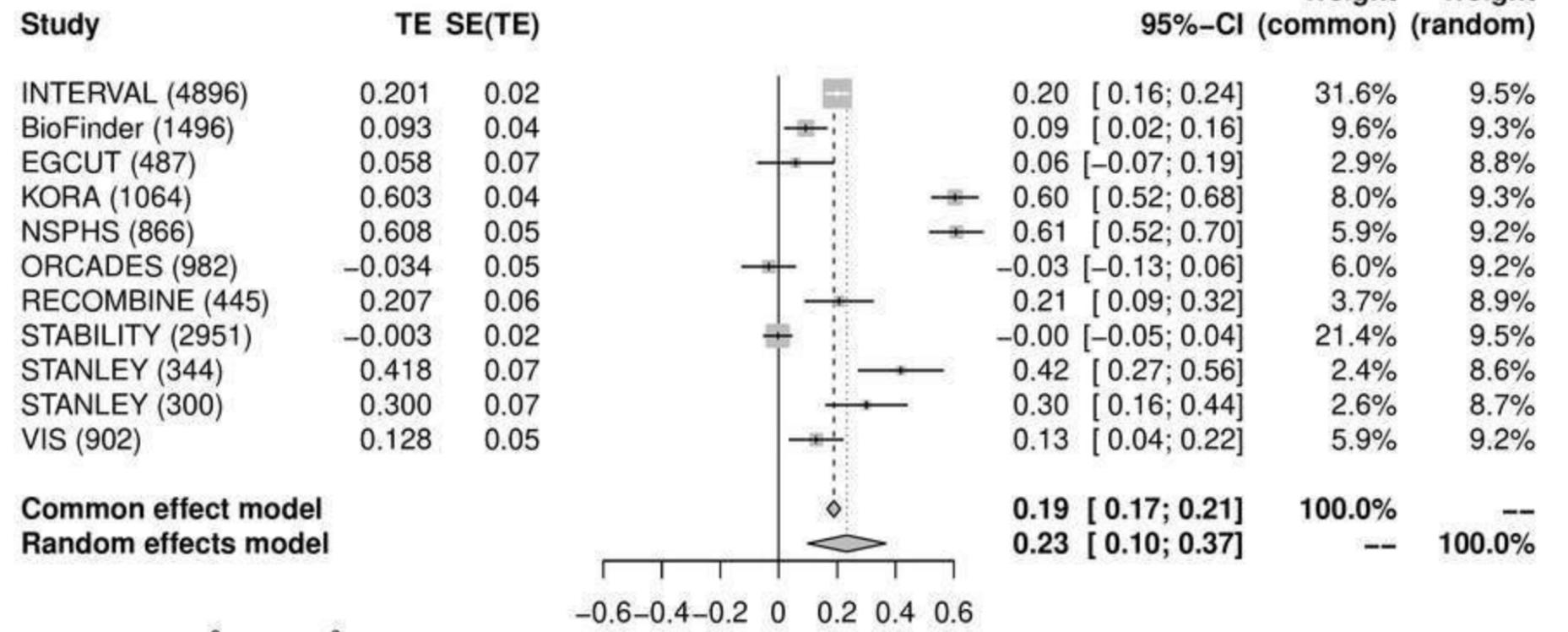
# MCP-3 (CCL7)-rs2228467

MCP-3 (CCL7) [chr3:42906116\_C\_T (rs2228467) (T/C) N=11782]



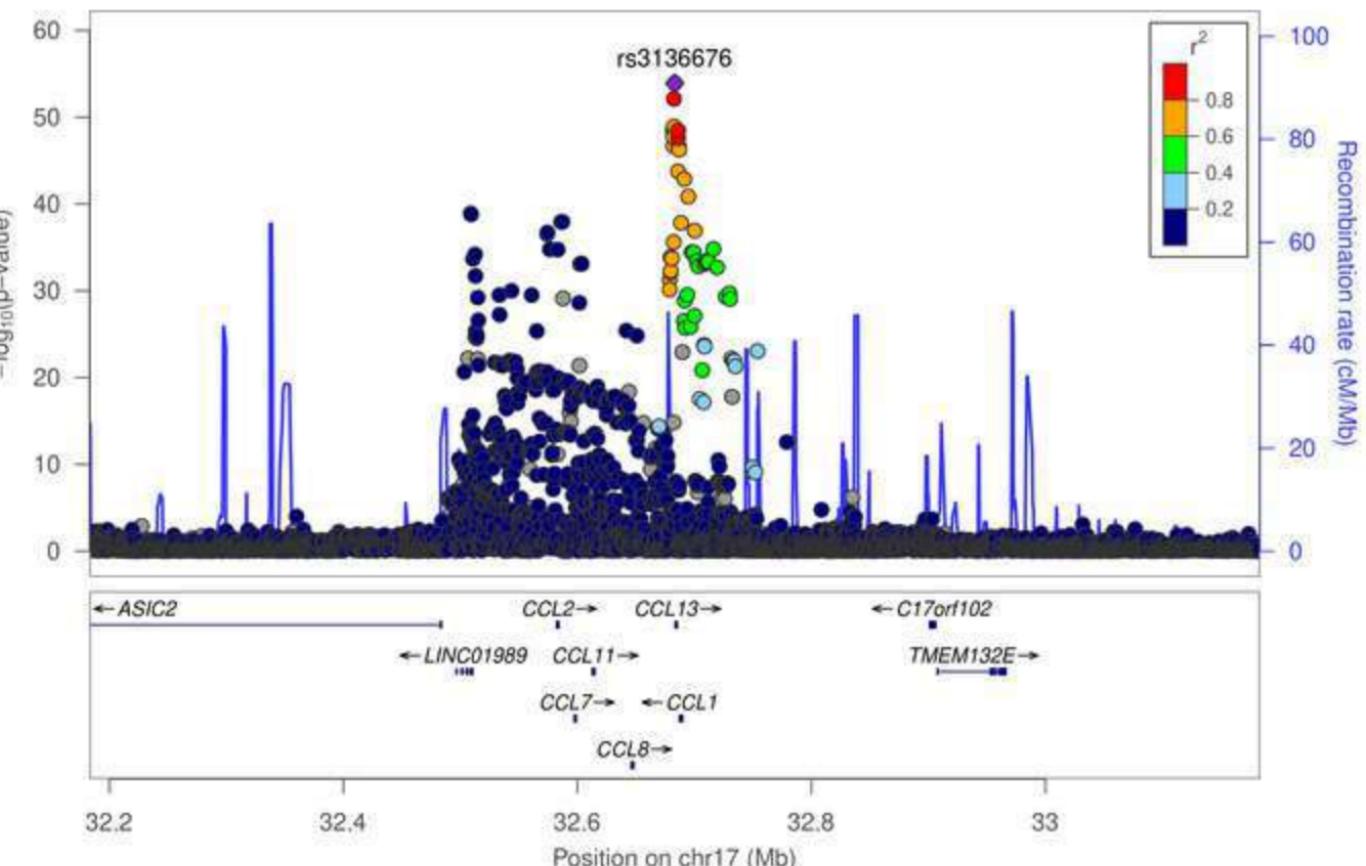
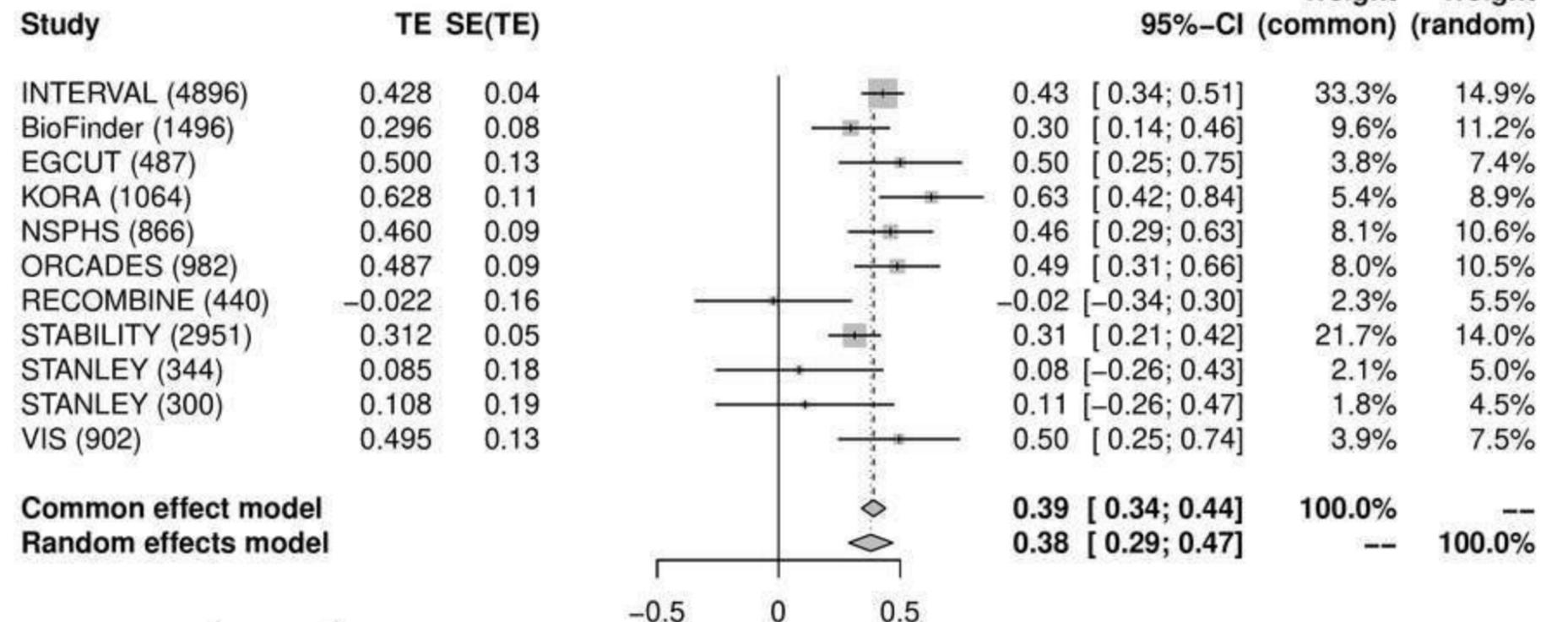
# MCP-4 (CCL13)-rs12075

MCP-4 (CCL13) [chr1:159175354\_A\_G (rs12075) (A/G) N=14733]



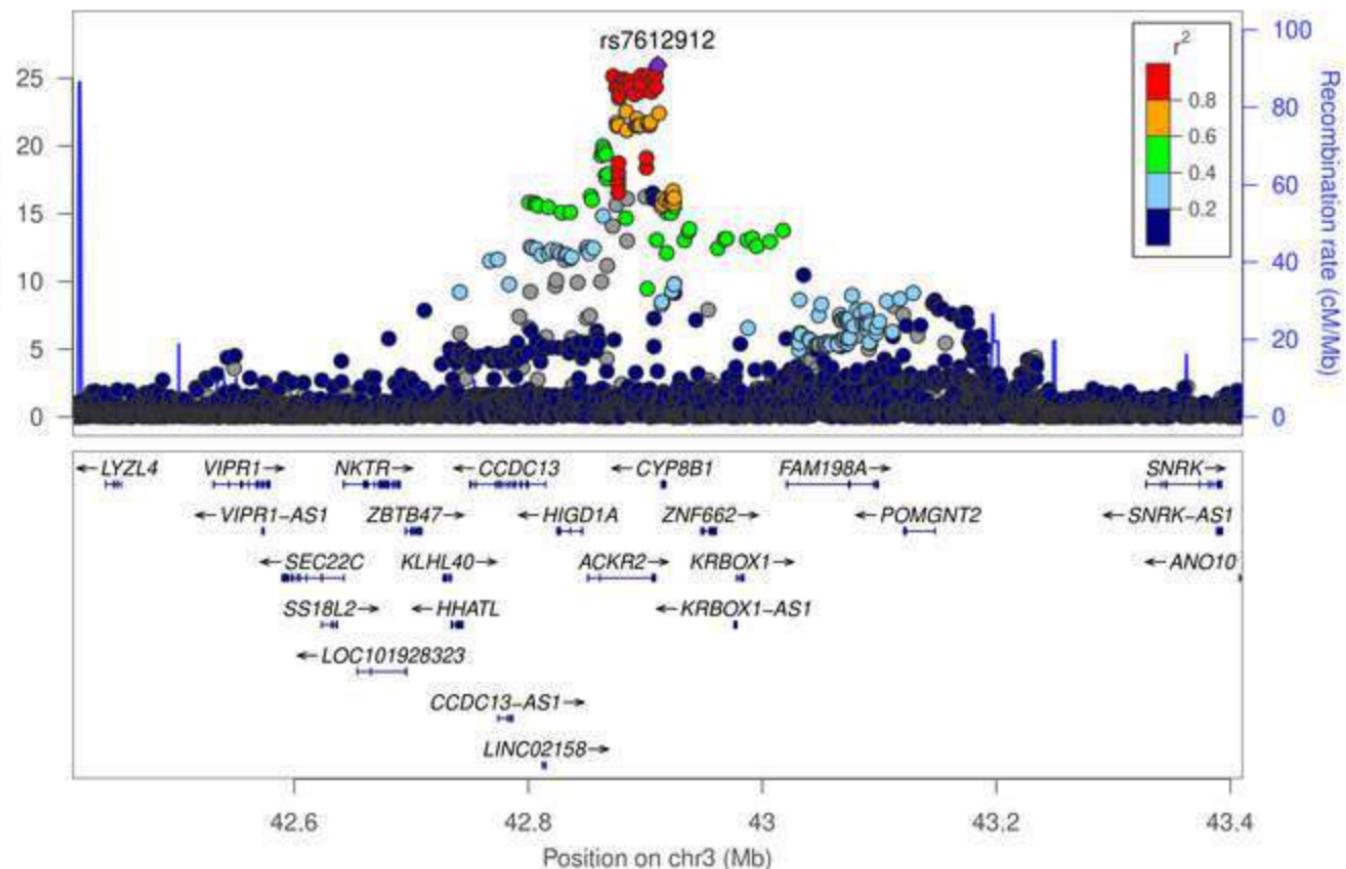
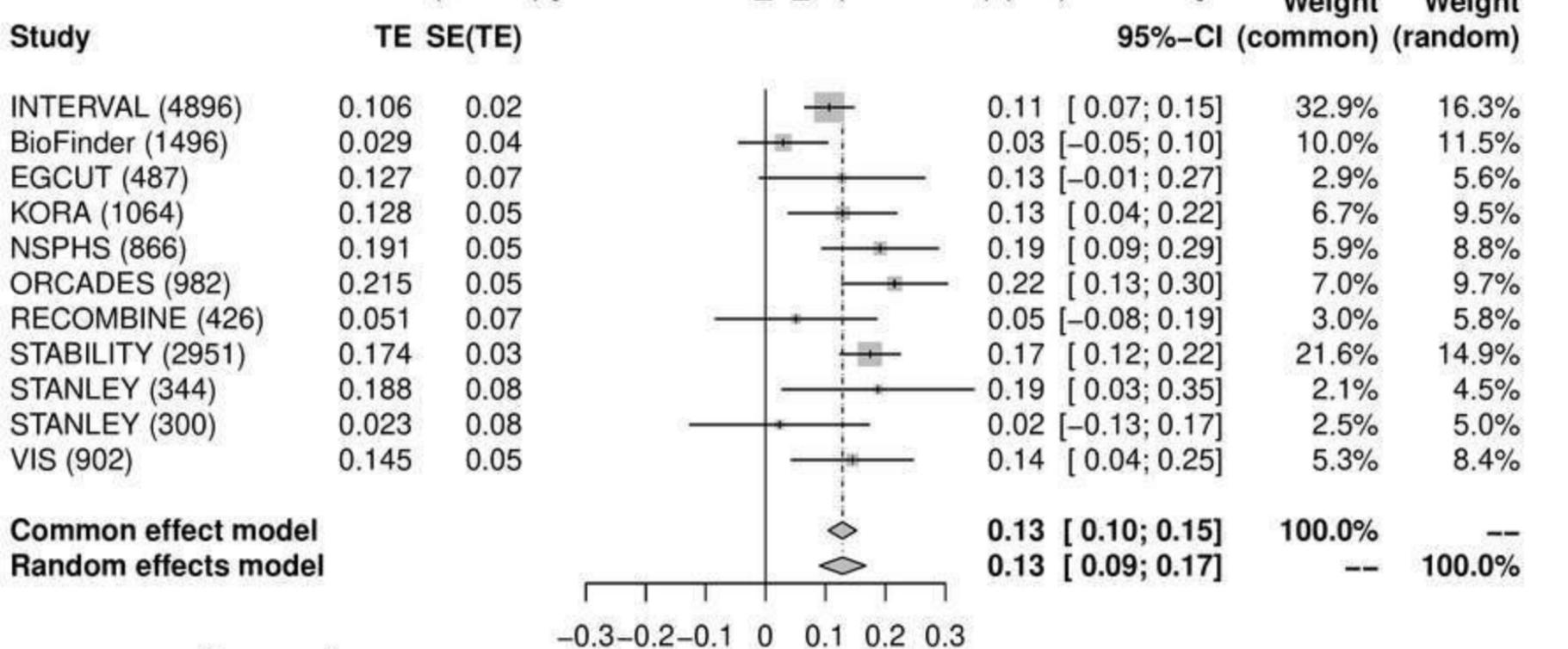
# MCP-4 (CCL13)-rs3136676

MCP-4 (CCL13) [chr17:32683289\_A\_G (rs3136676) (A/G) N=14728]



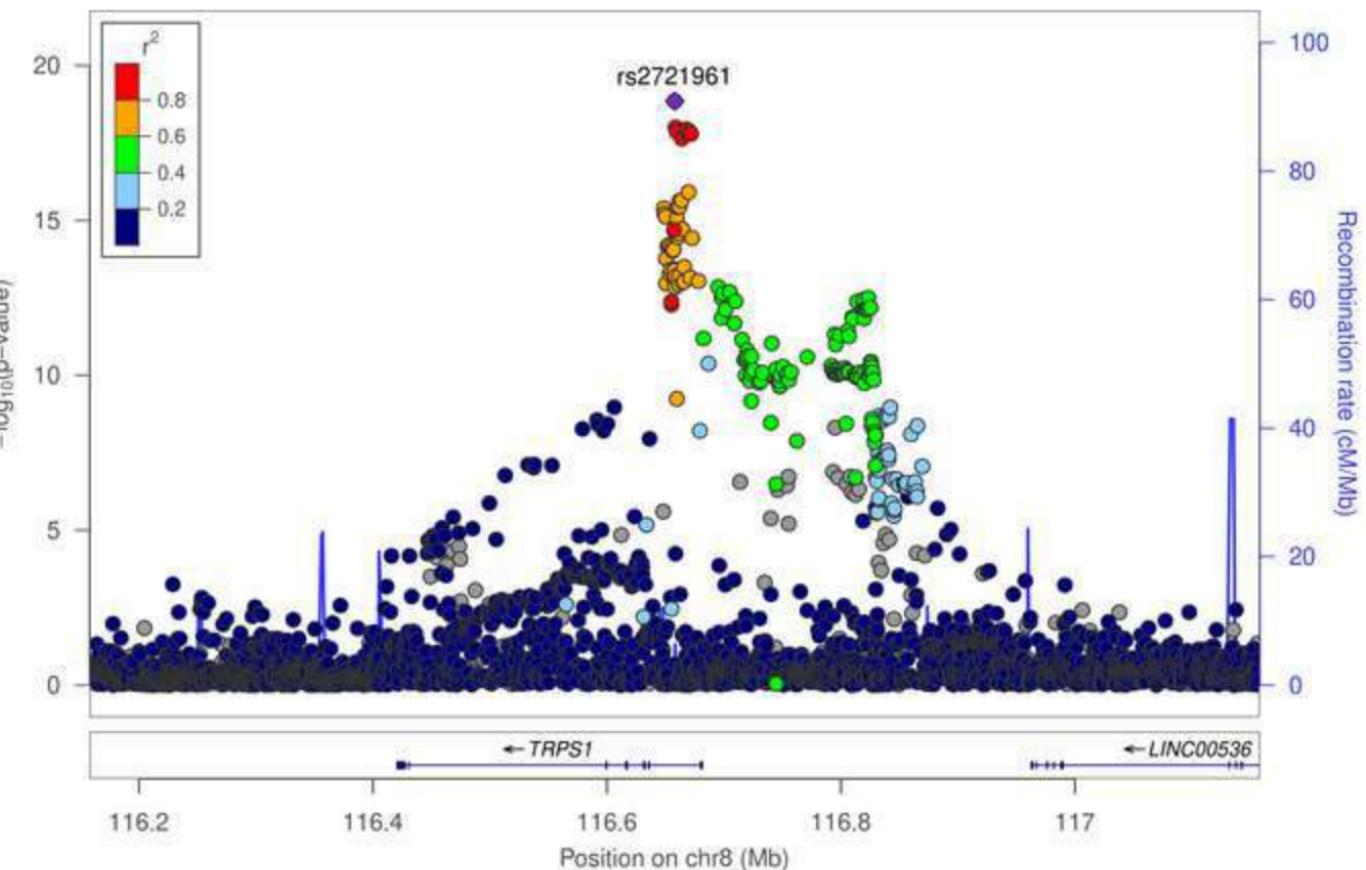
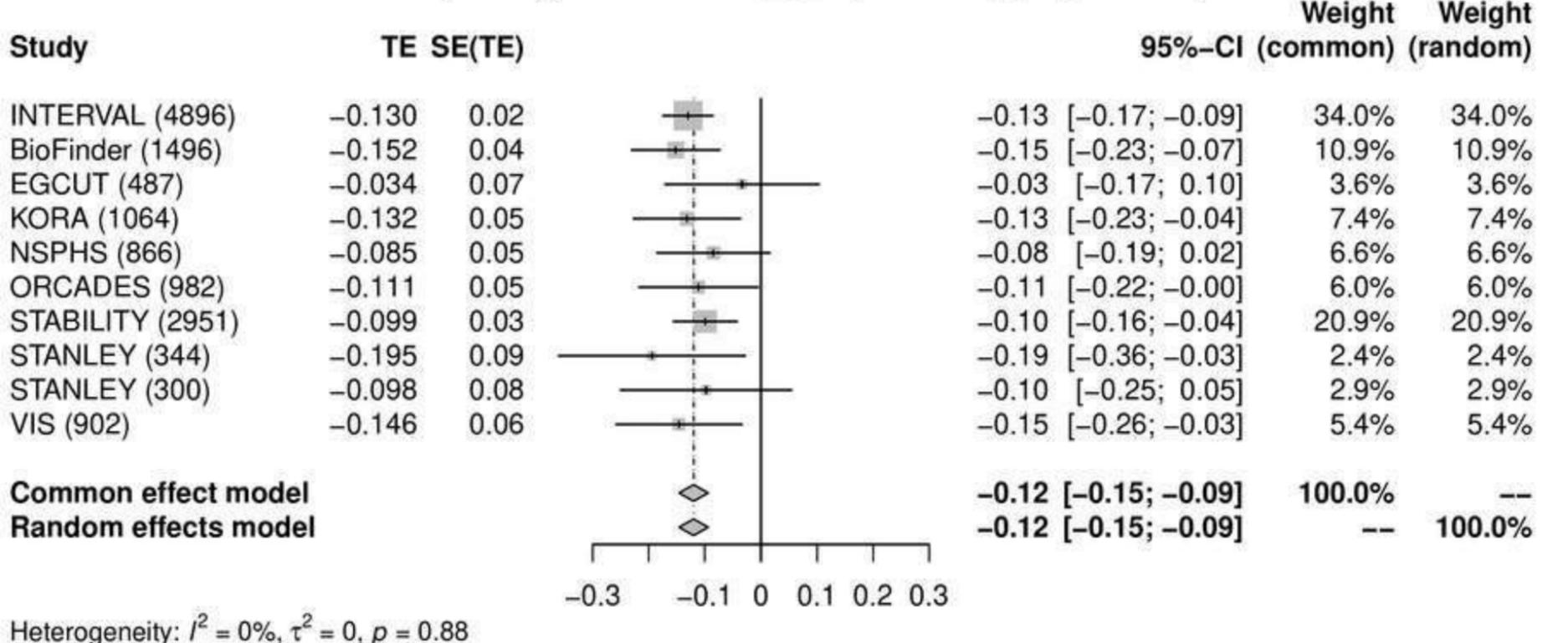
# MCP-4 (CCL13)-rs7612912

MCP-4 (CCL13) [chr3:42910621\_C\_T (rs7612912) (T/C) N=14714]



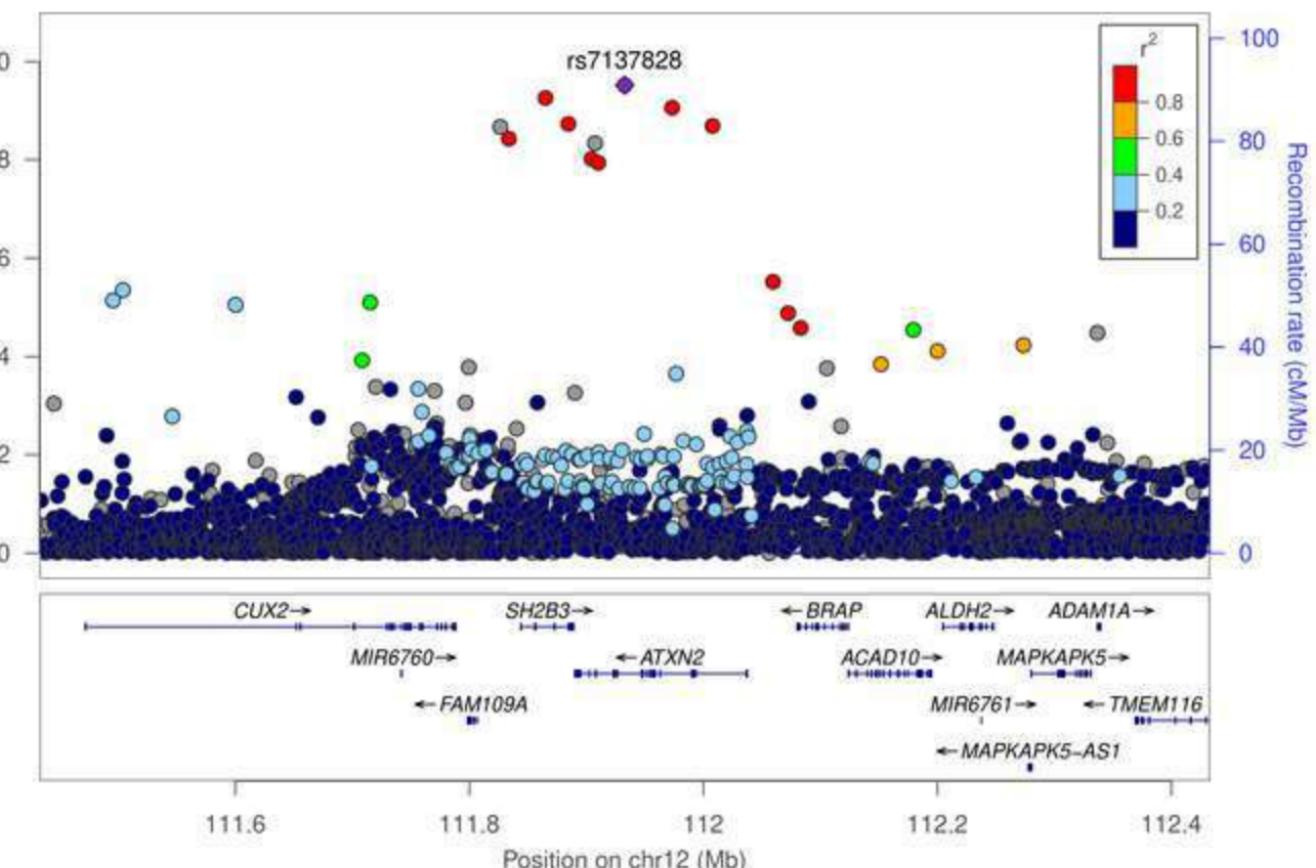
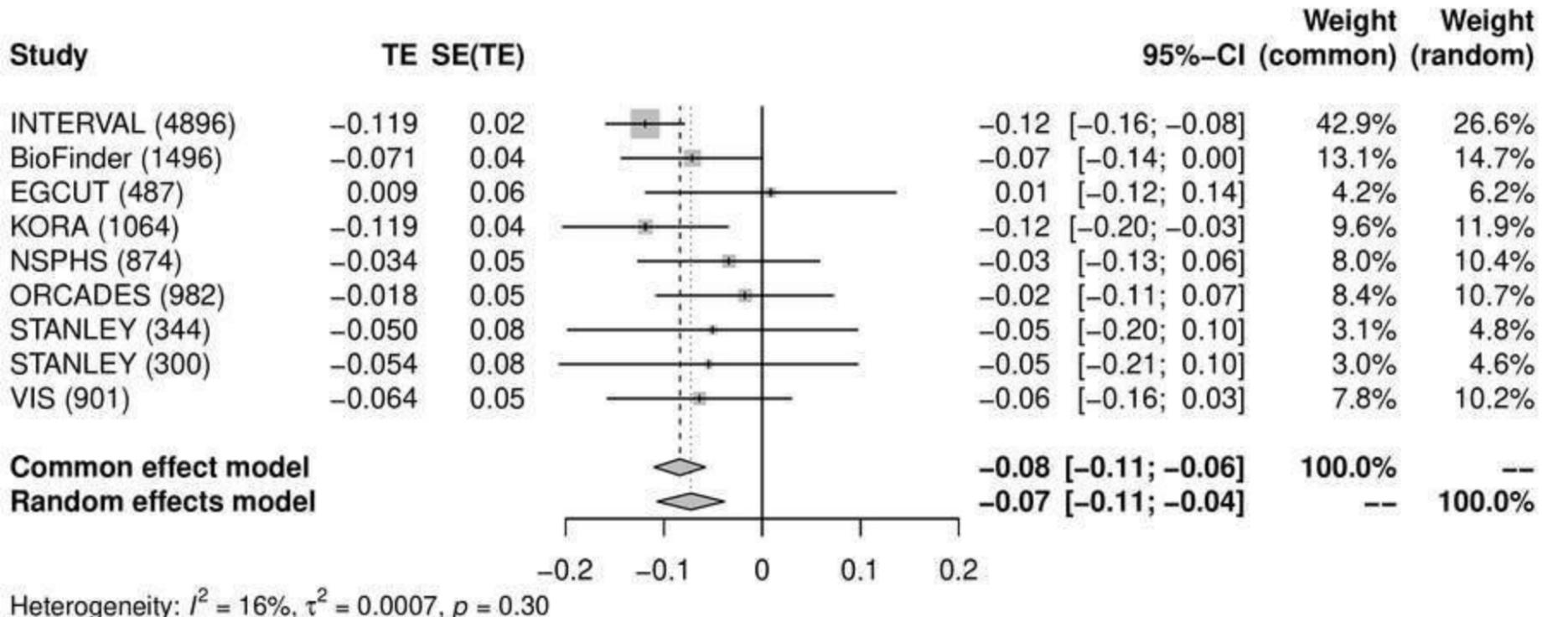
# MCP-4 (CCL13)-rs2721961

MCP-4 (CCL13) [chr8:116657911\_G\_T (rs2721961) (T/G) N=14288]



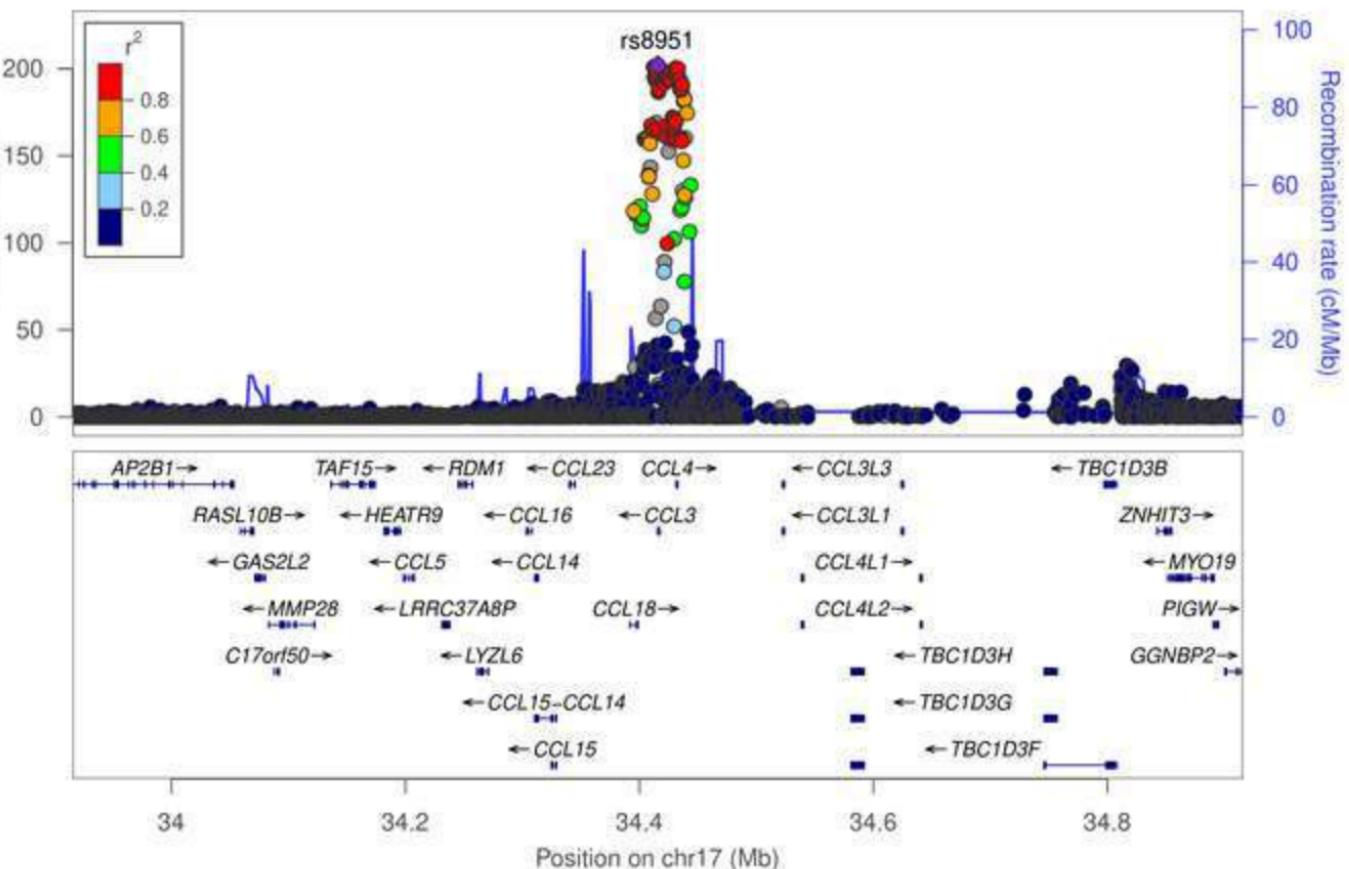
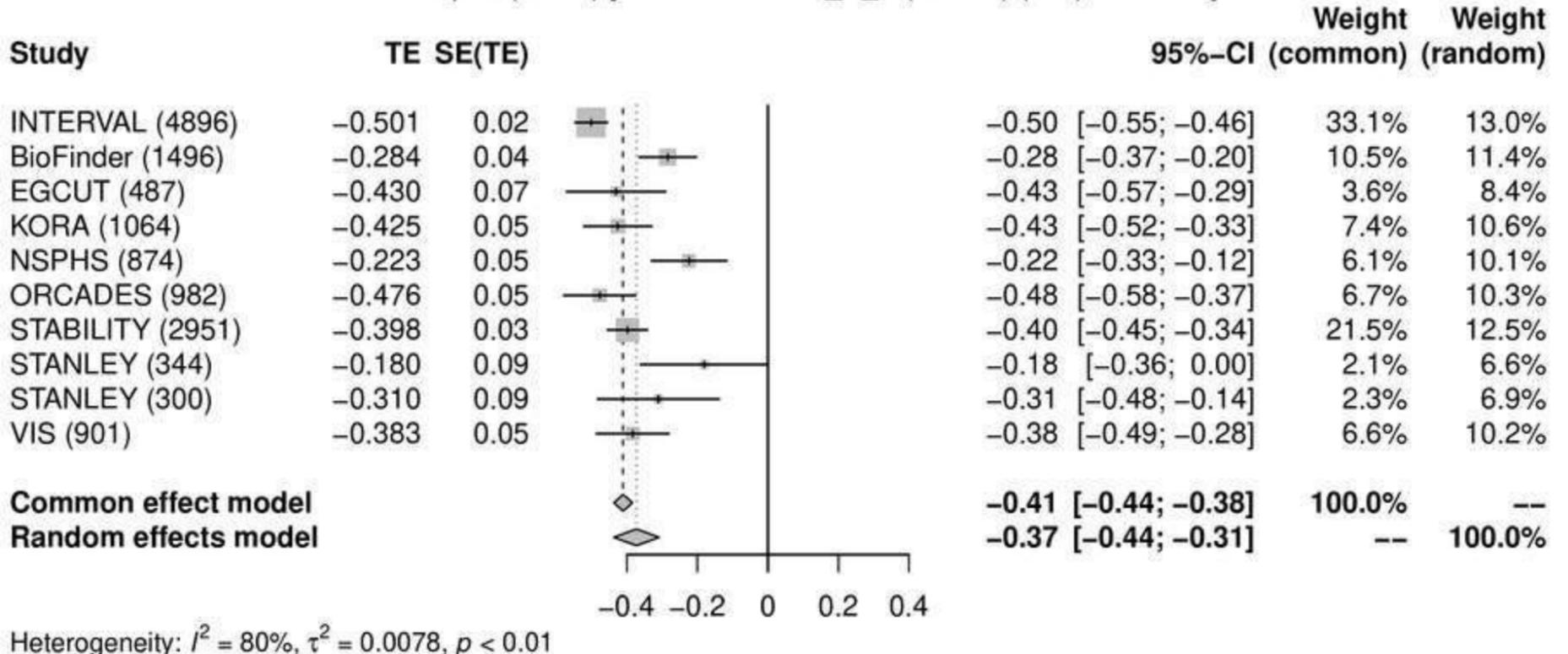
# MIP-1 (alpha)-rs7137828

MIP-1 alpha (CCL3) [chr12:111932800\_C\_T (rs7137828) (T/C) N=11344]



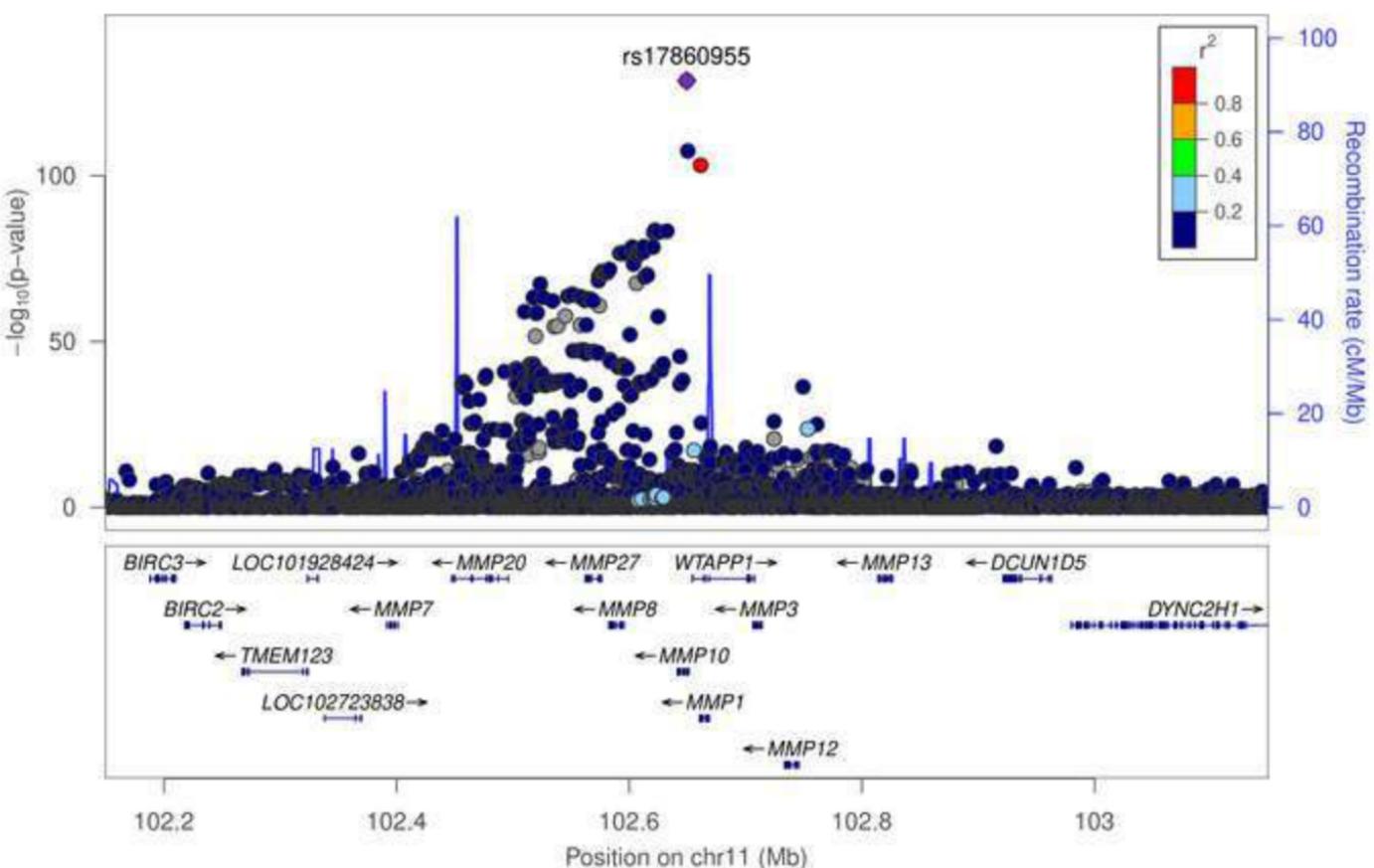
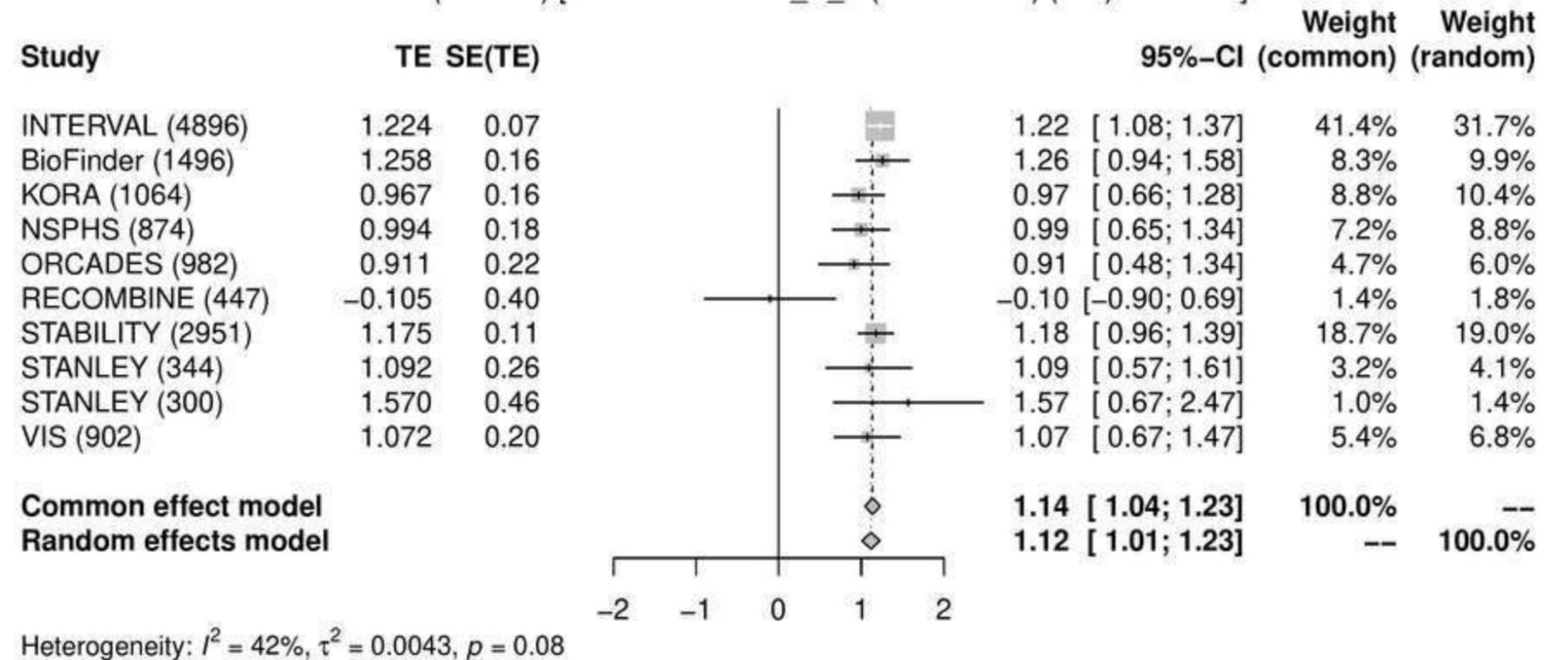
# MIP-1 (alpha)-rs8951

MIP-1 alpha (CCL3) [chr17:34415720\_C\_T (rs8951) (T/C) N=14295]

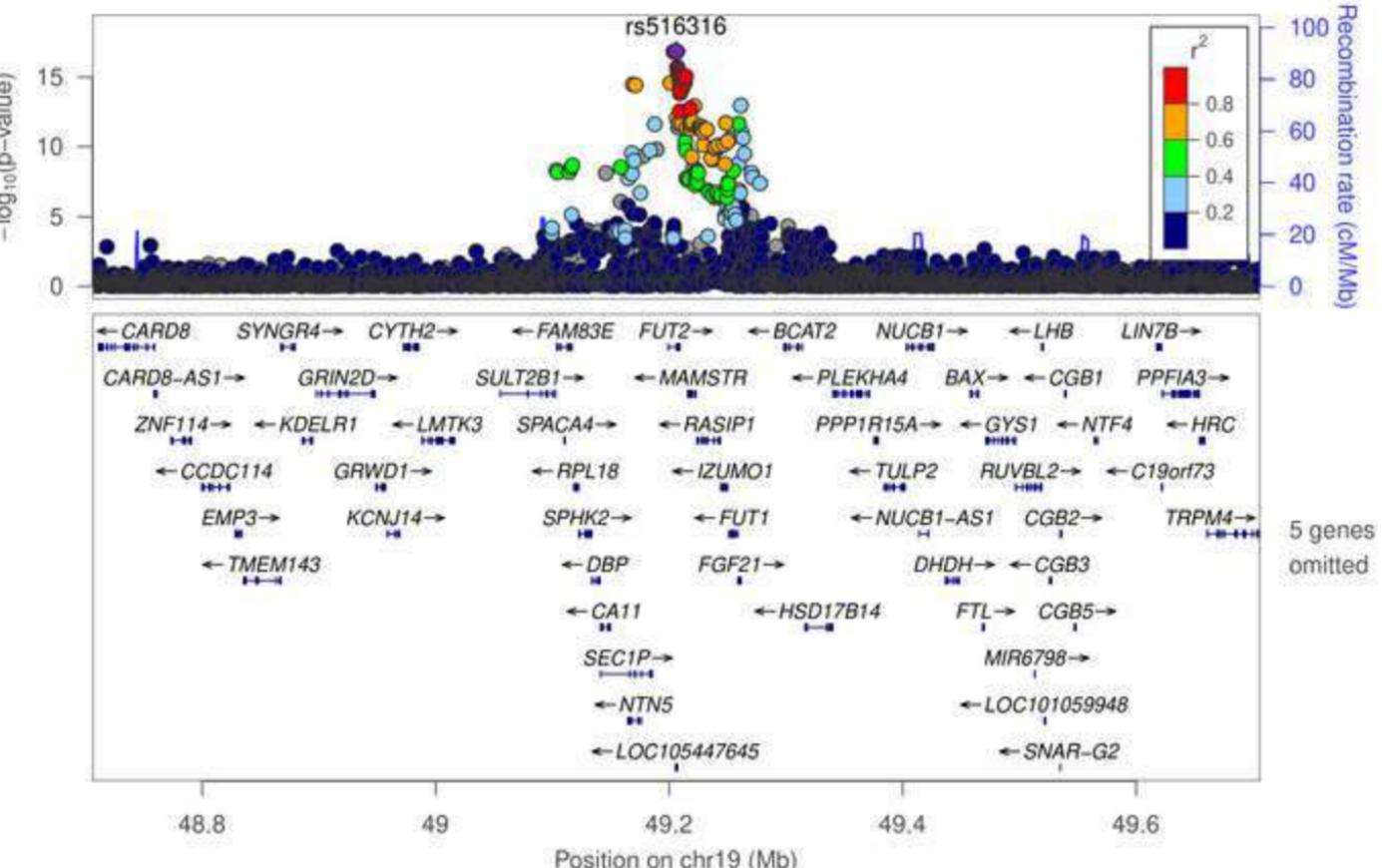
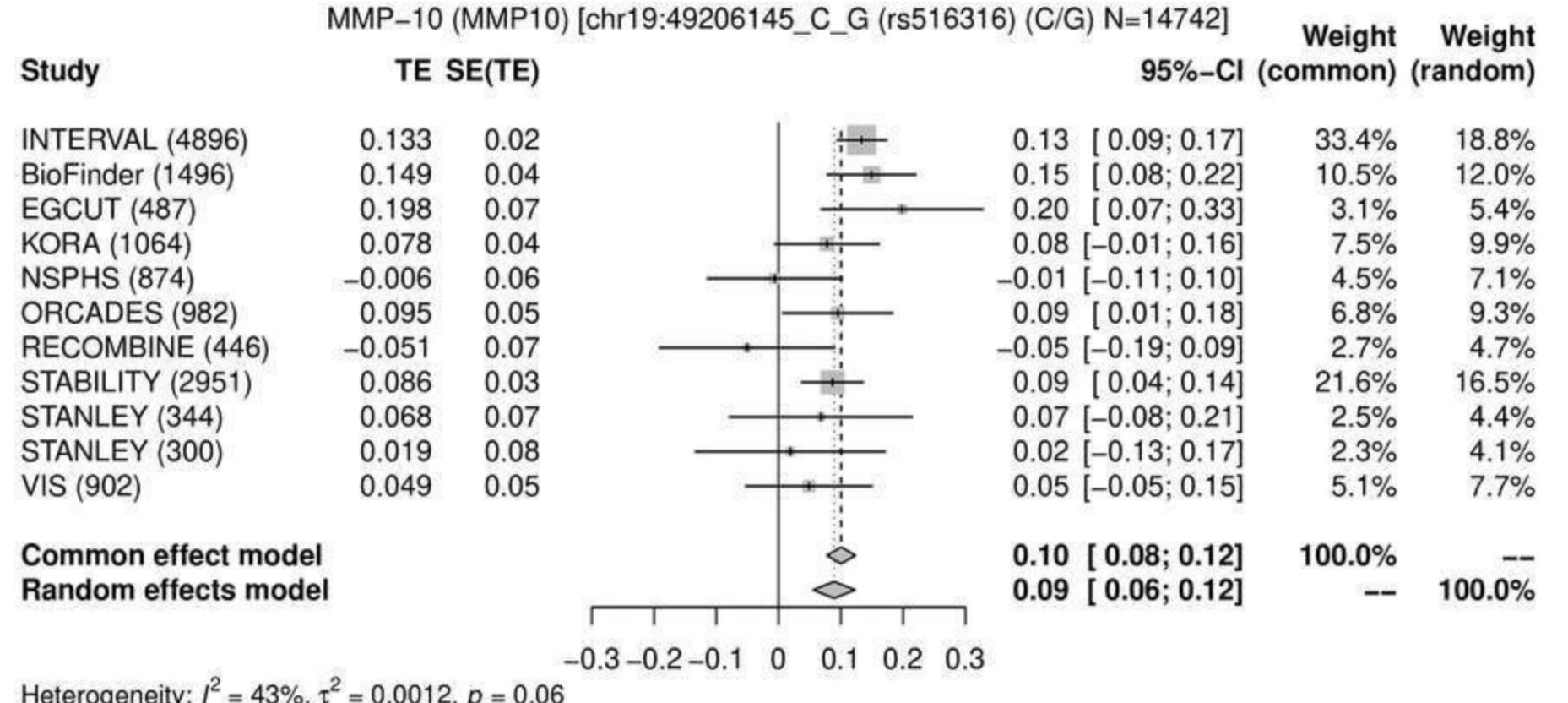


# MMP-10 (MMP10)-rs17860955

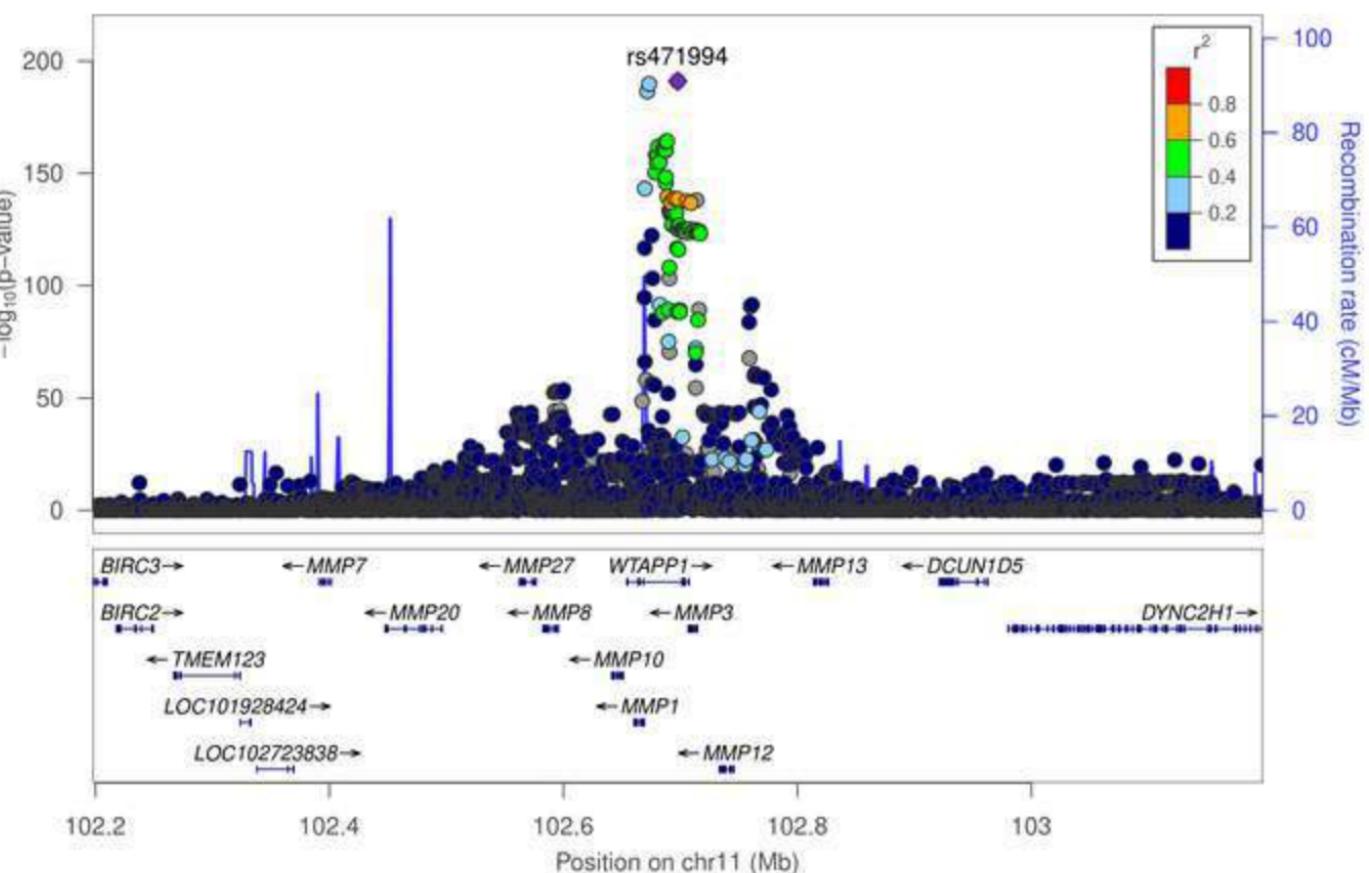
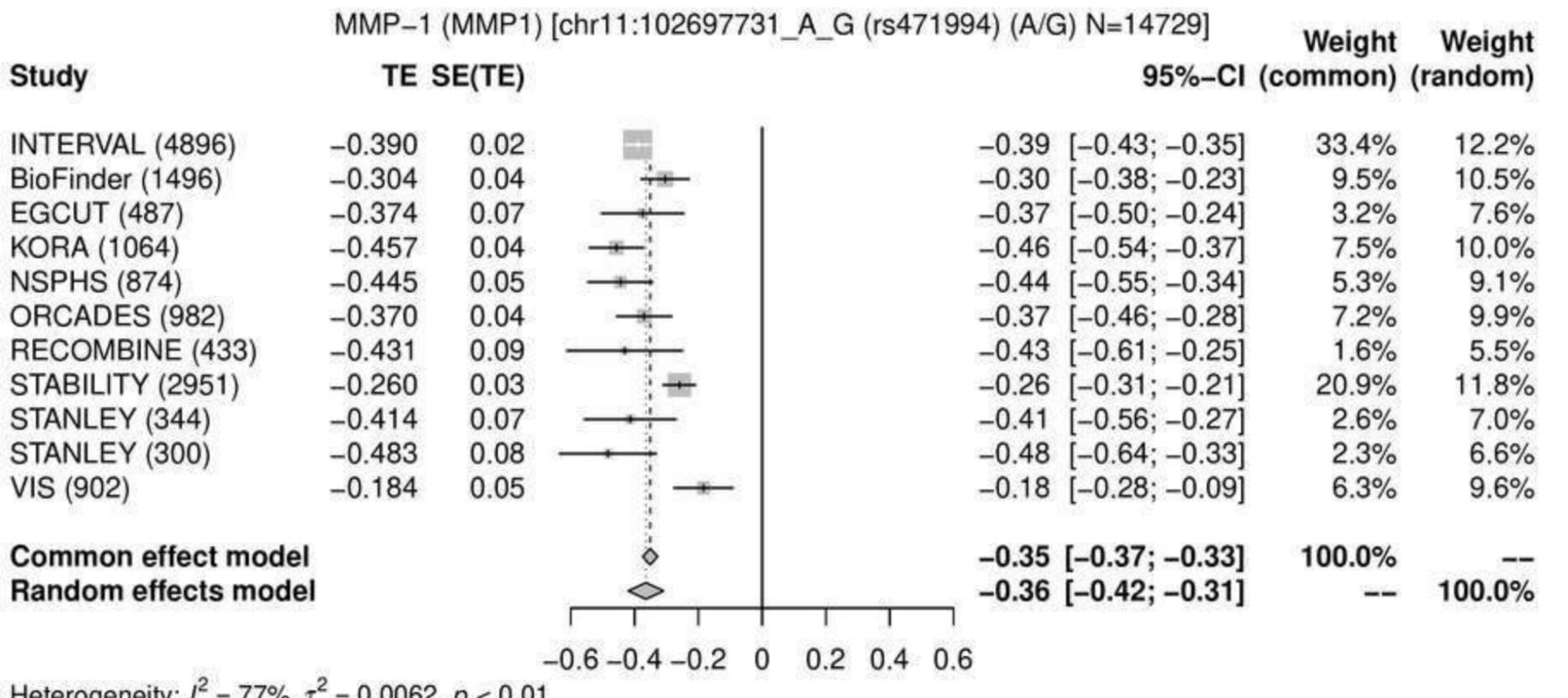
MMP-10 (MMP10) [chr11:102649482\_C\_T (rs17860955) (T/C) N=14256]



# MMP-10 (MMP10)-rs516316

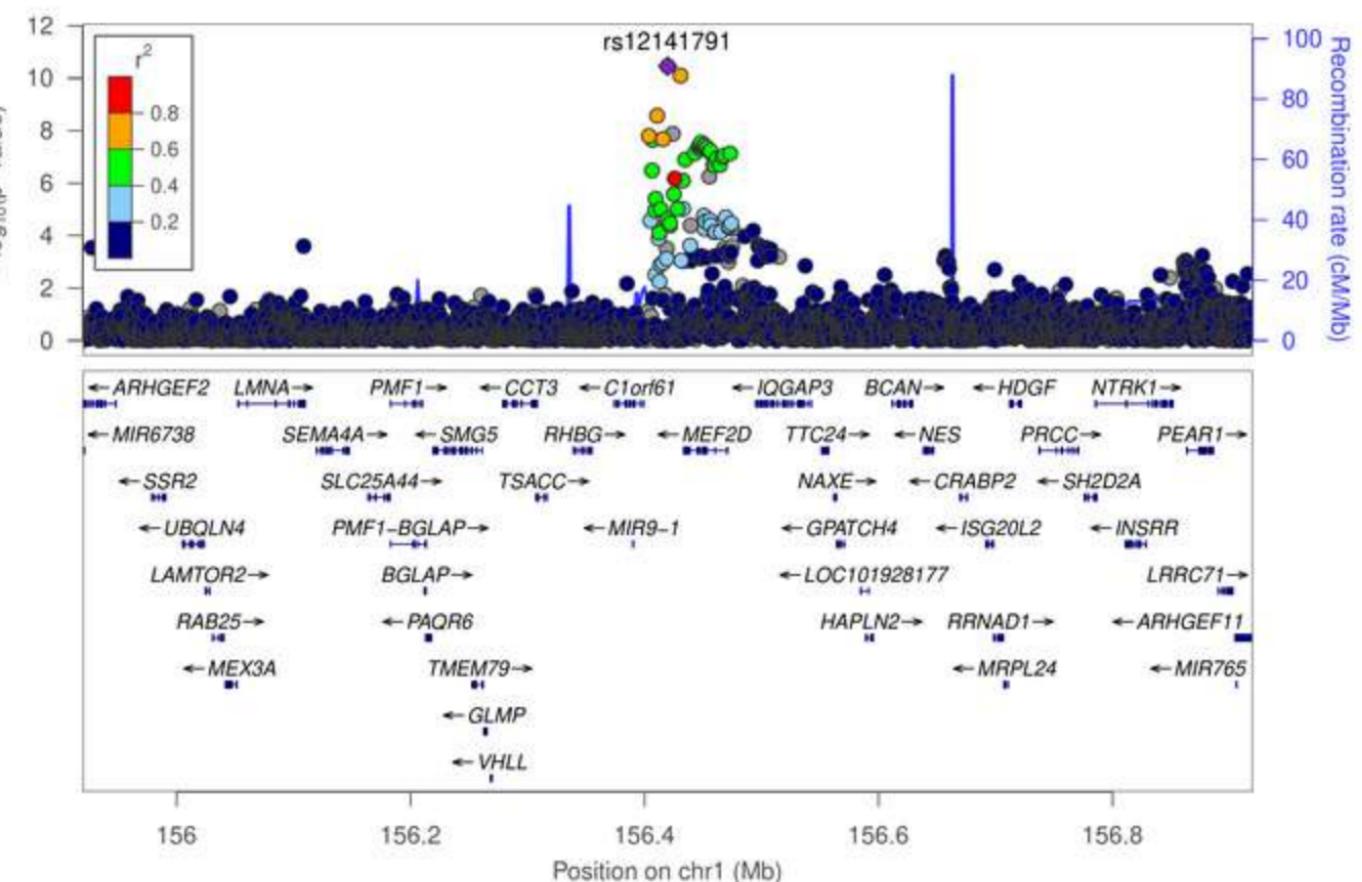
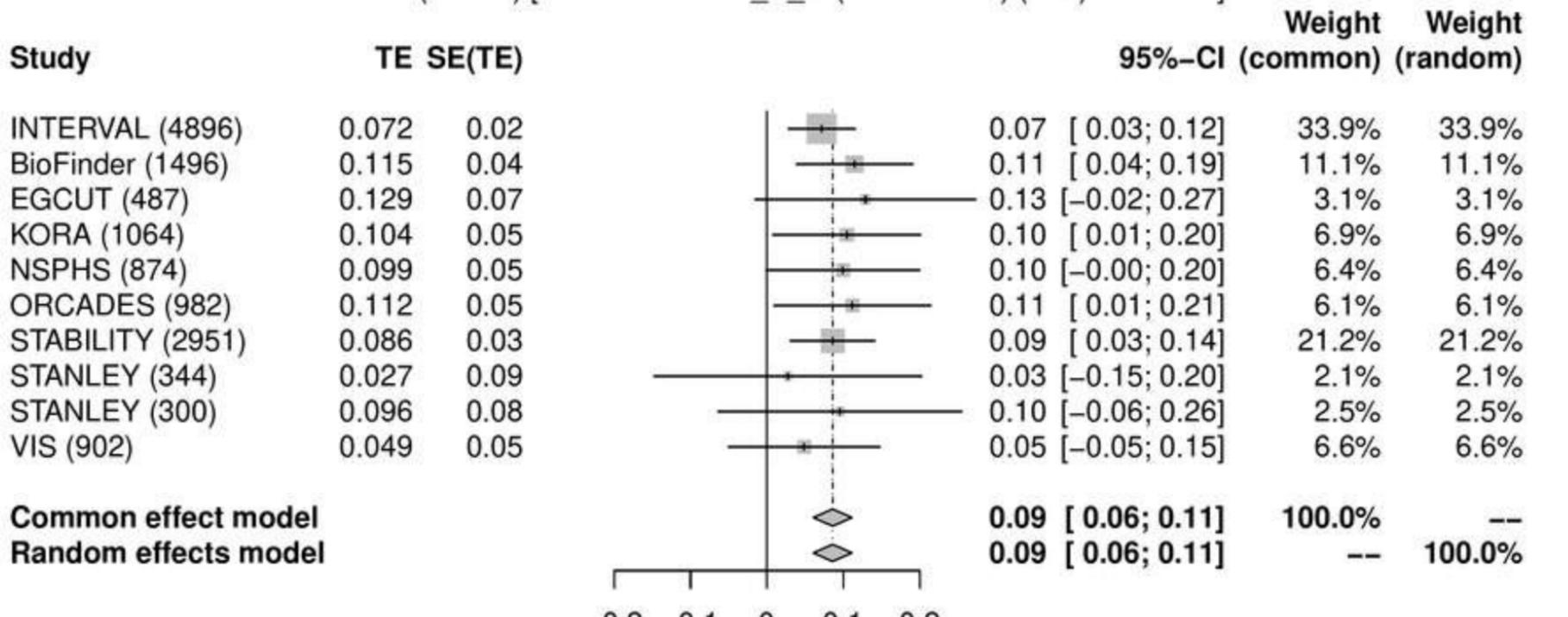


# MMP-1 (MMP1)-rs471994



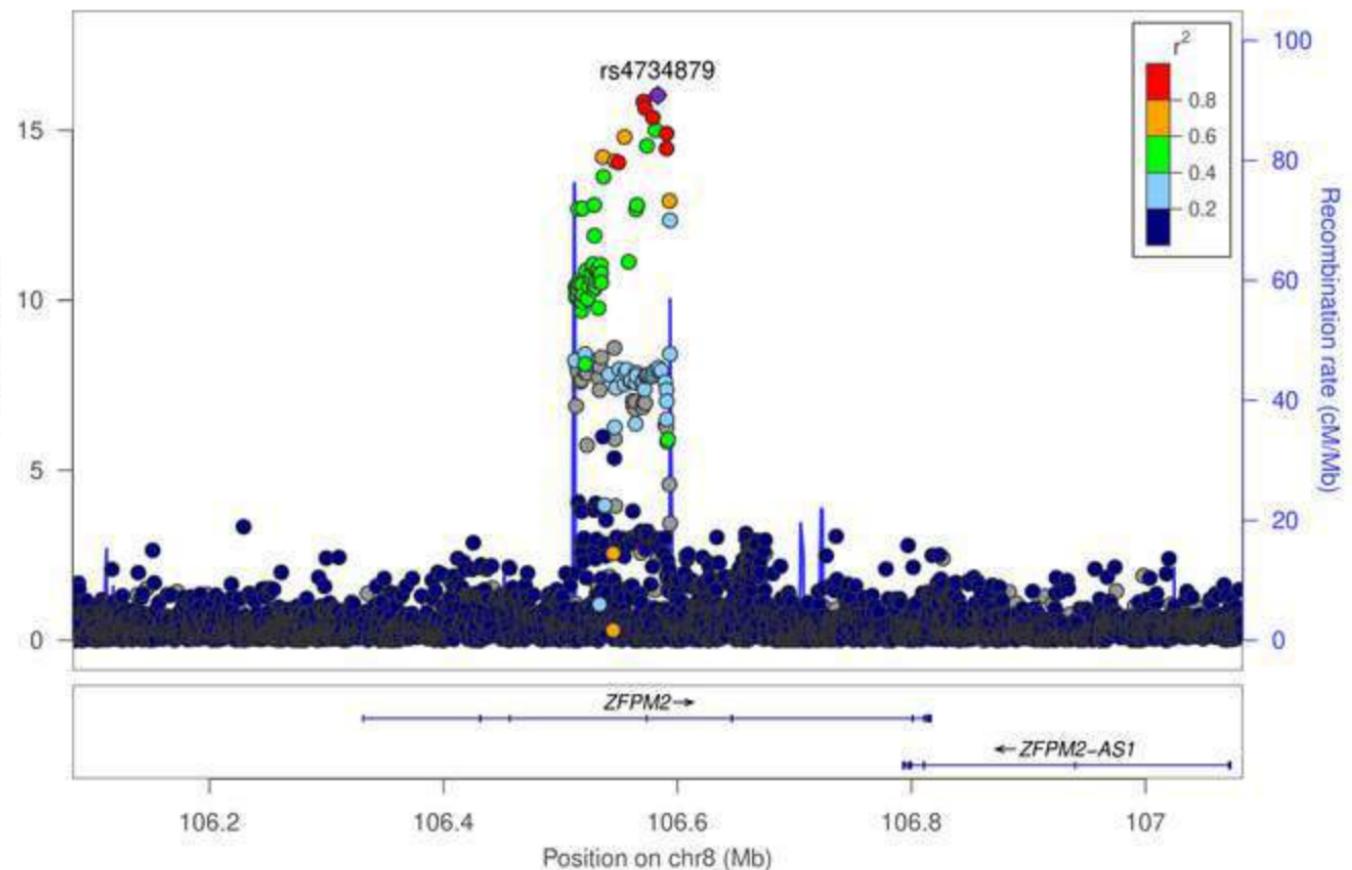
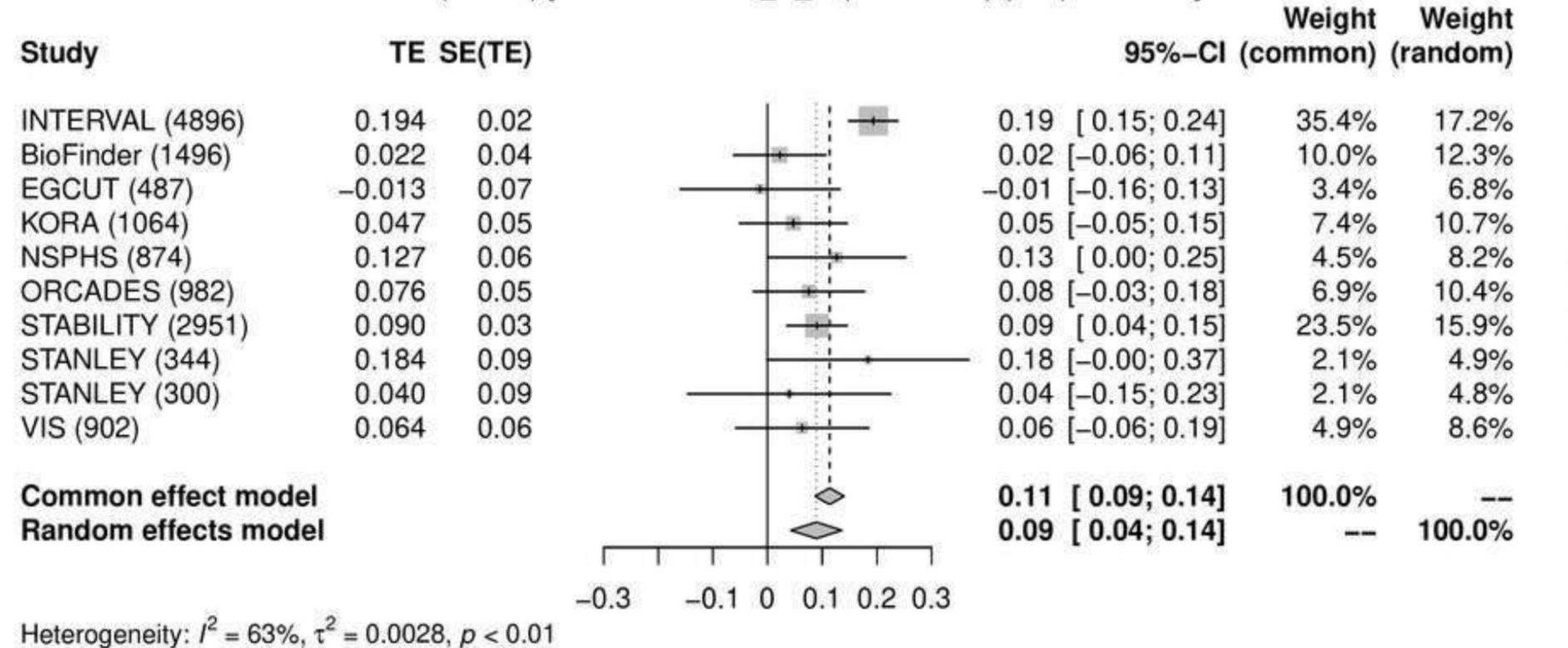
# MMP-1 (MMP1)-rs12141791

MMP-1 (MMP1) [chr1:156419786\_A\_G (rs12141791) (A/G) N=14296]

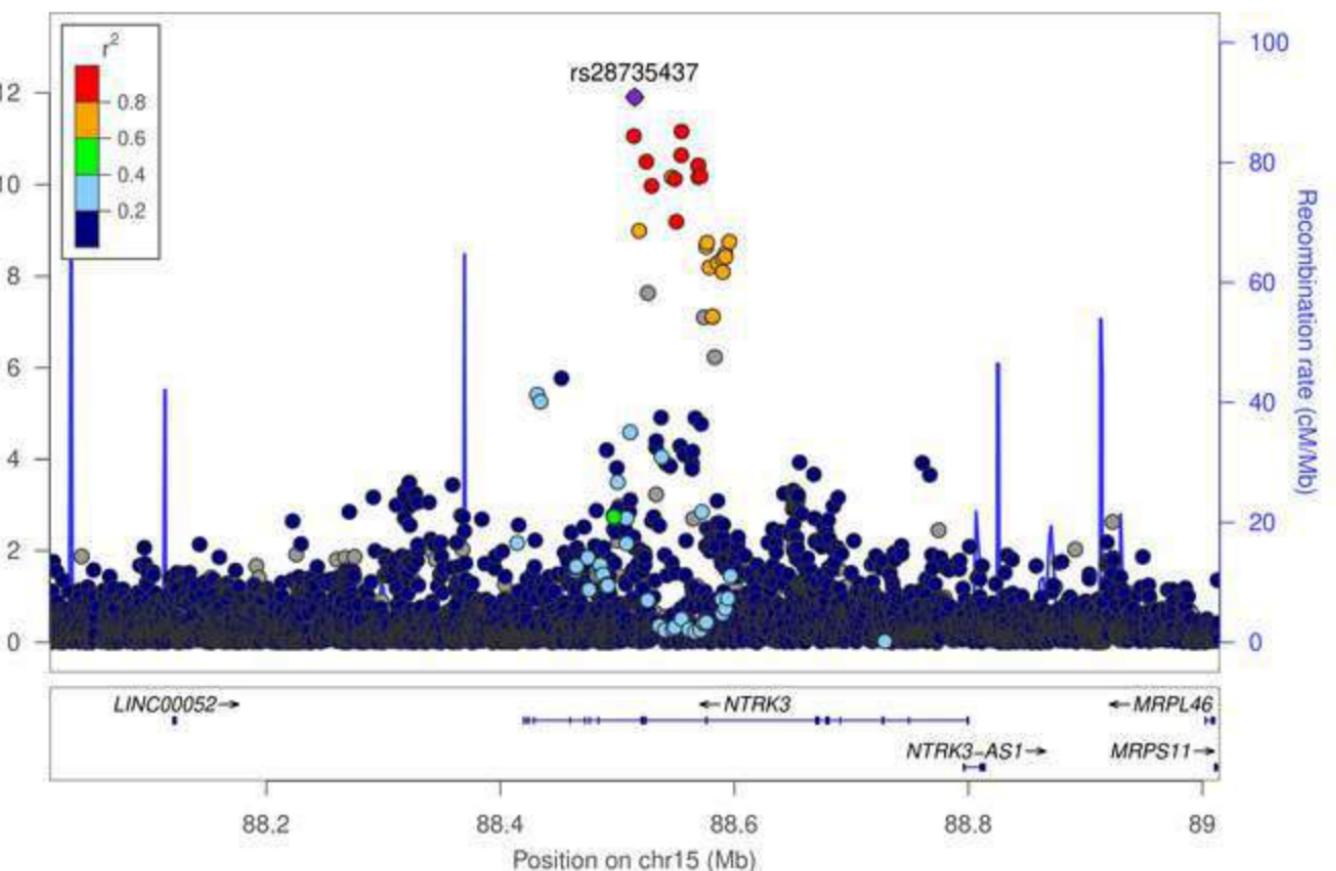
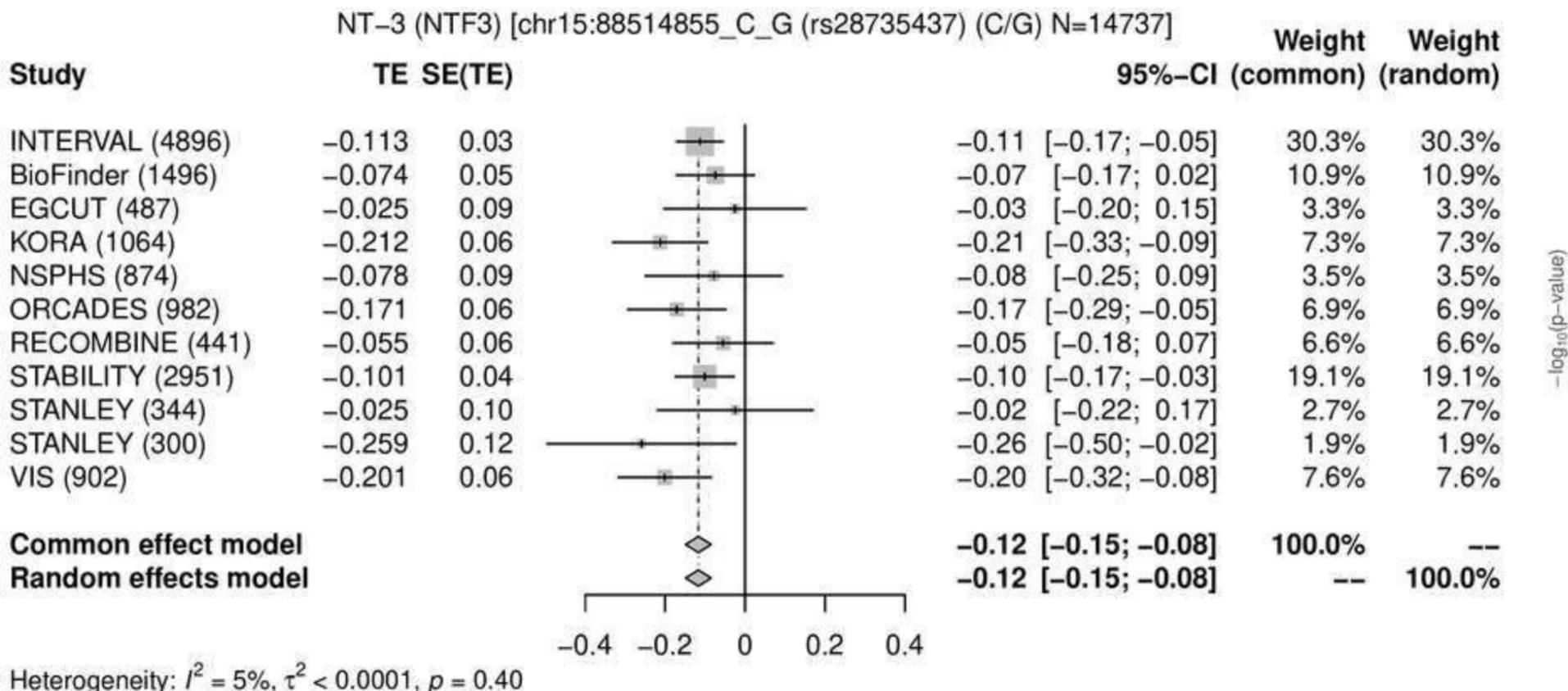


# MMP-1 (MMP1)-rs4734879

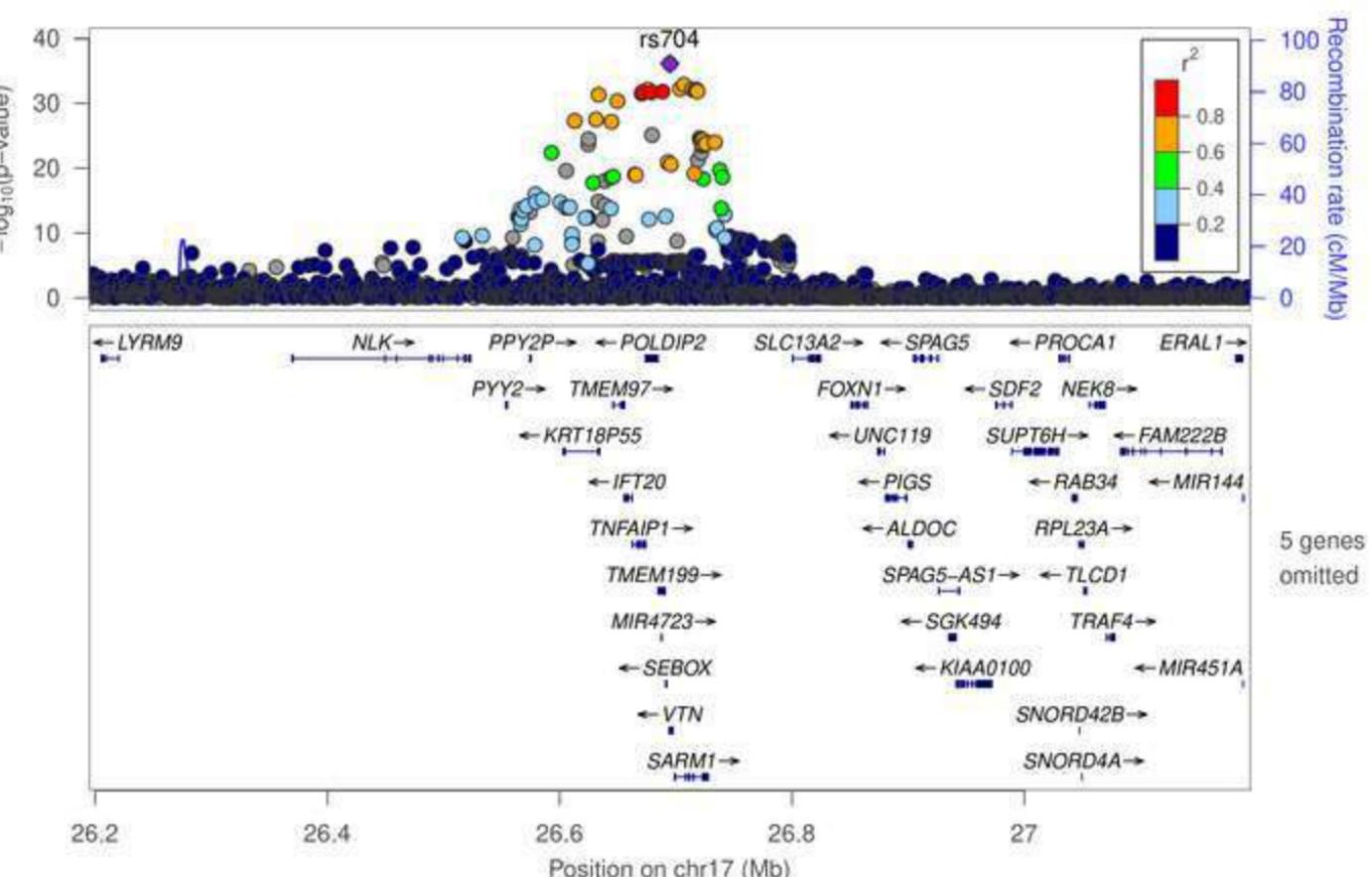
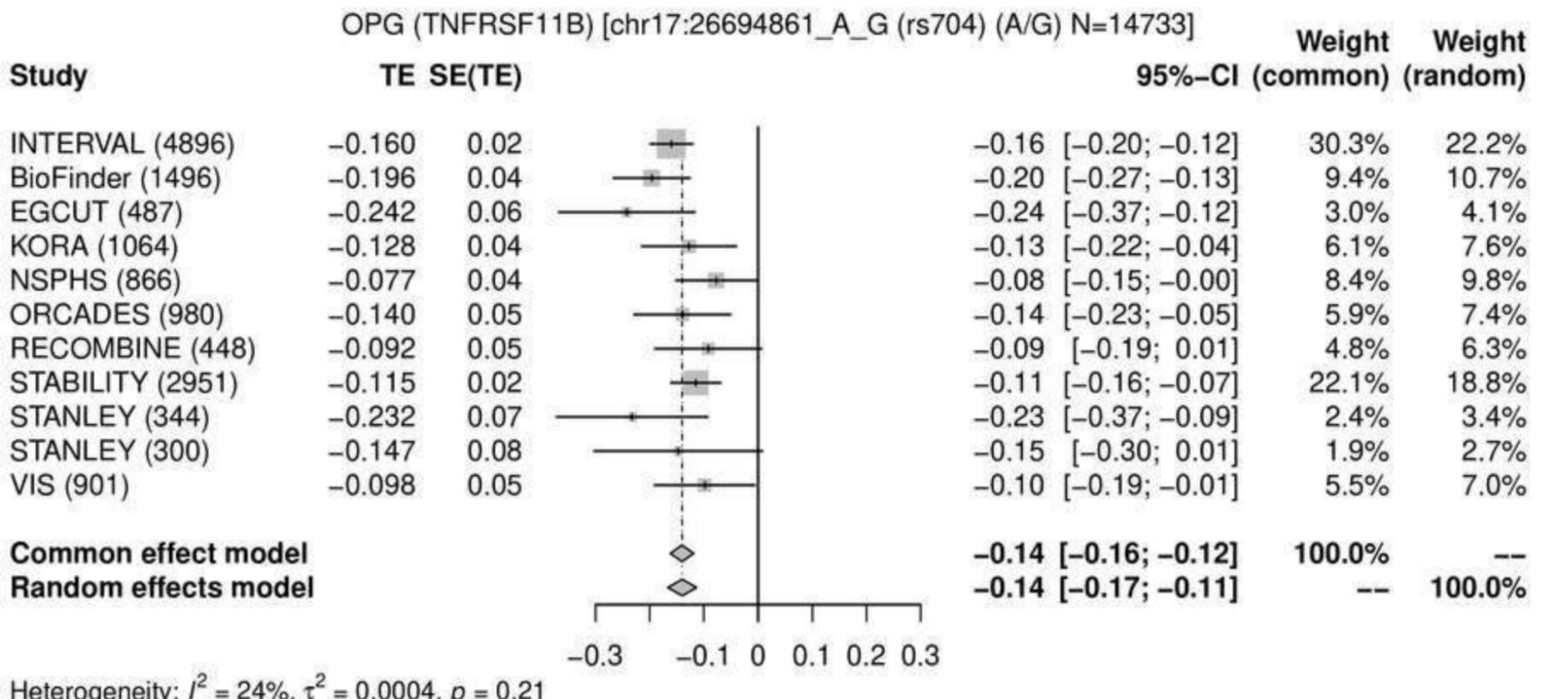
MMP-1 (MMP1) [chr8:106583124\_A\_G (rs4734879) (A/G) N=14296]



# NT-3 (NTF3)-rs28735437

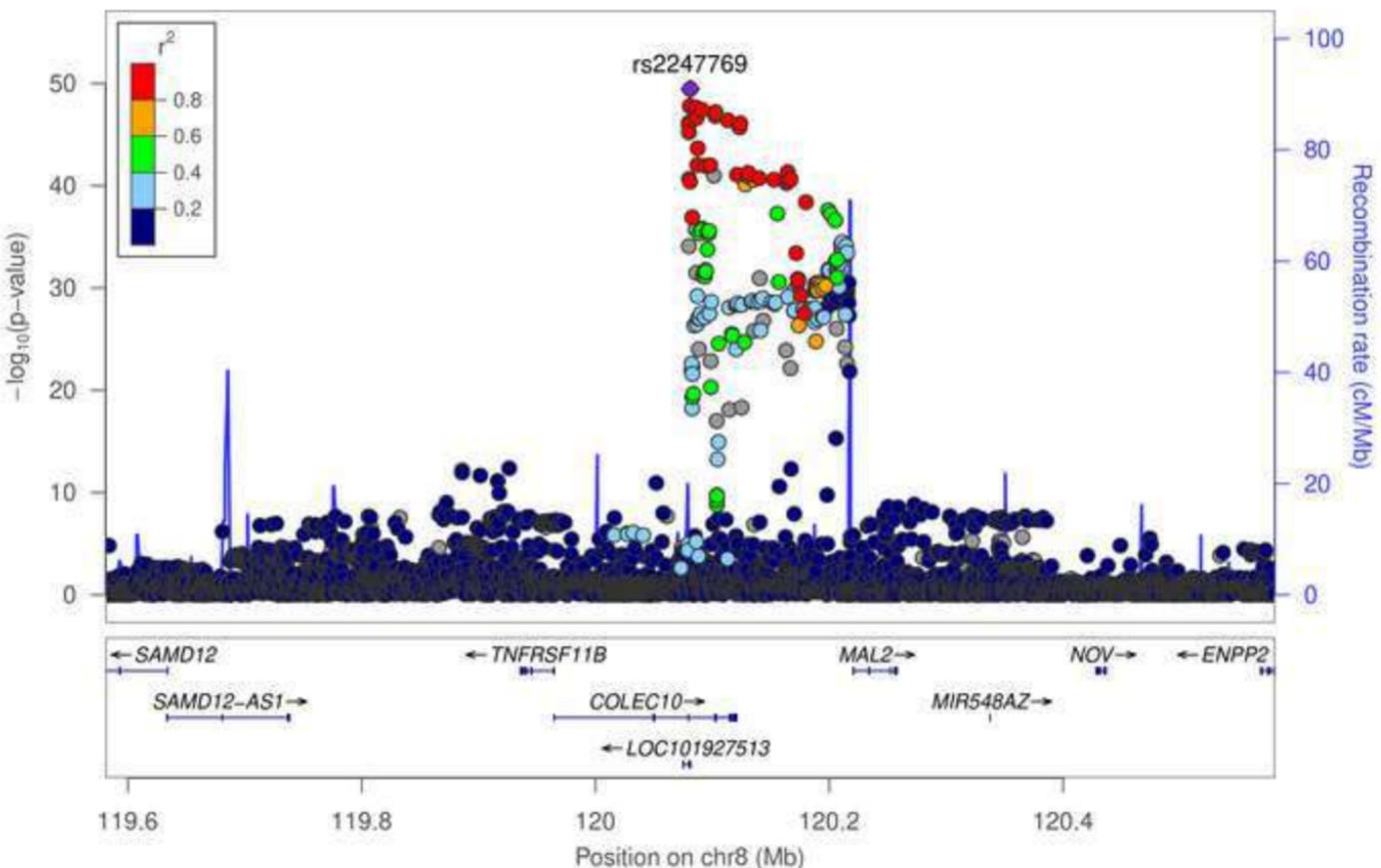
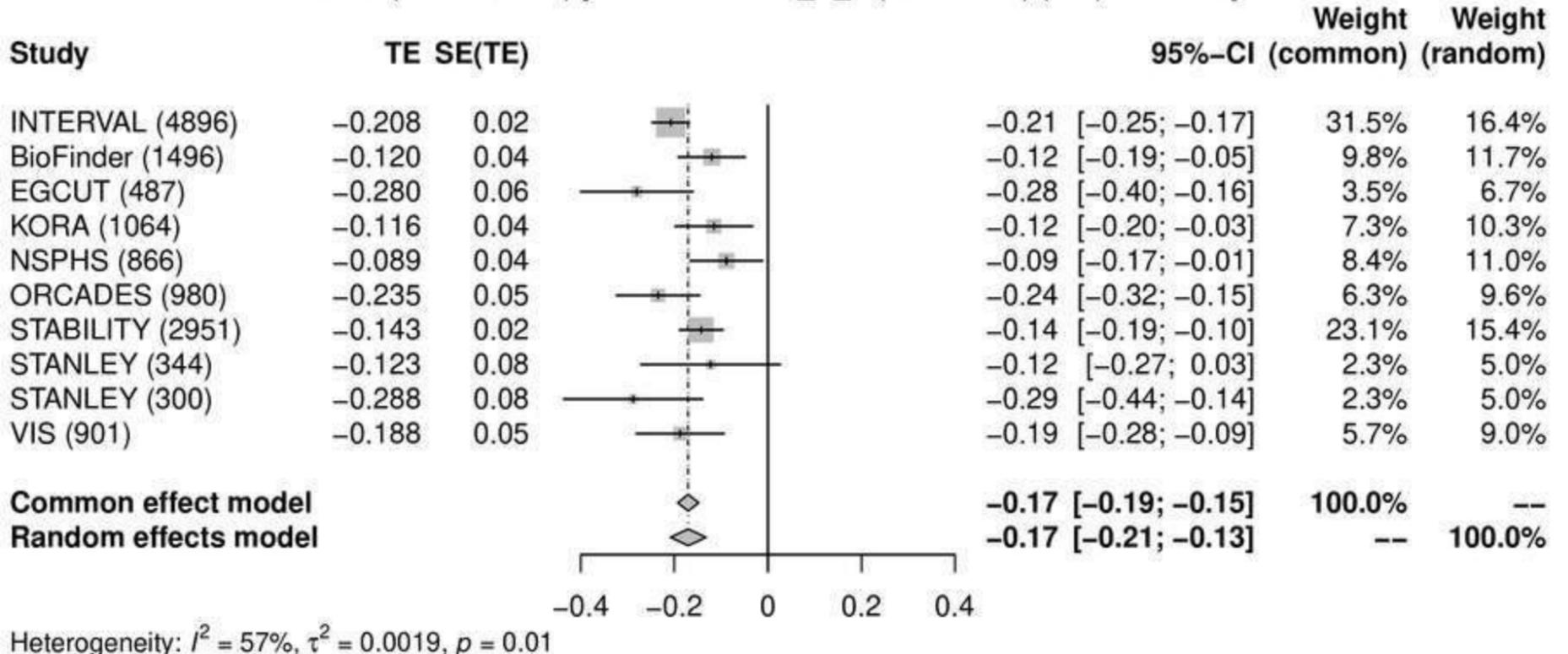


# OPG (TNFRSF11B)-rs704



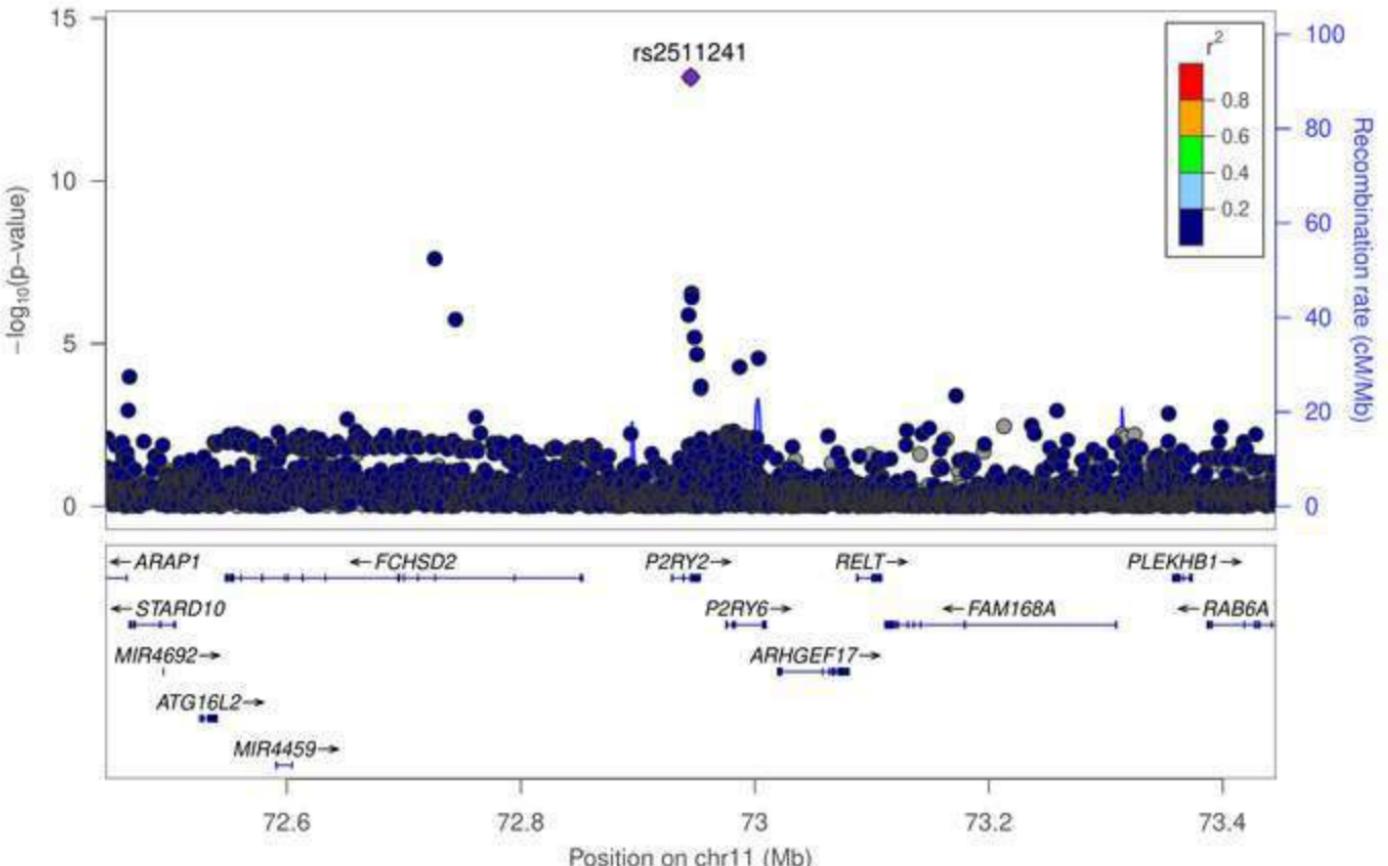
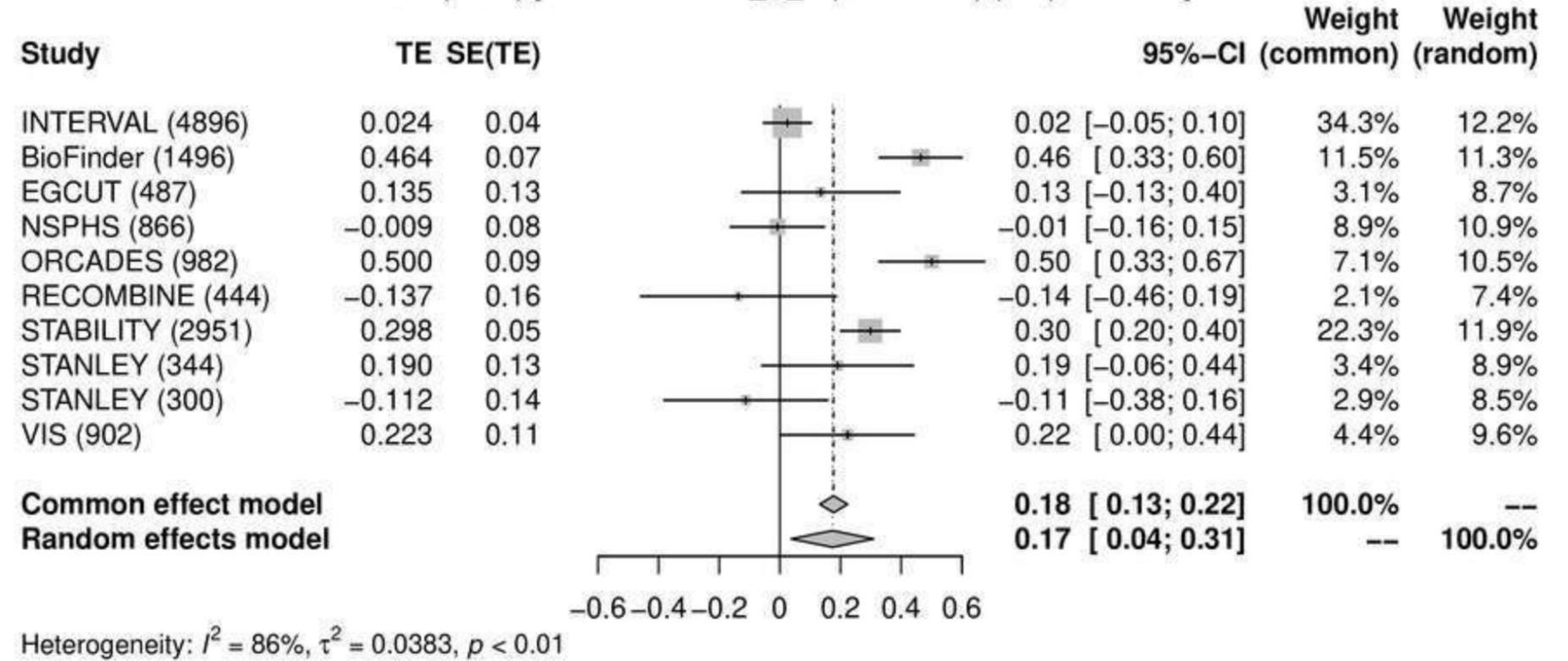
# OPG (TNFRSF11B)-rs2247769

OPG (TNFRSF11B) [chr8:120081031\_C\_T (rs2247769) (T/C) N=14285]

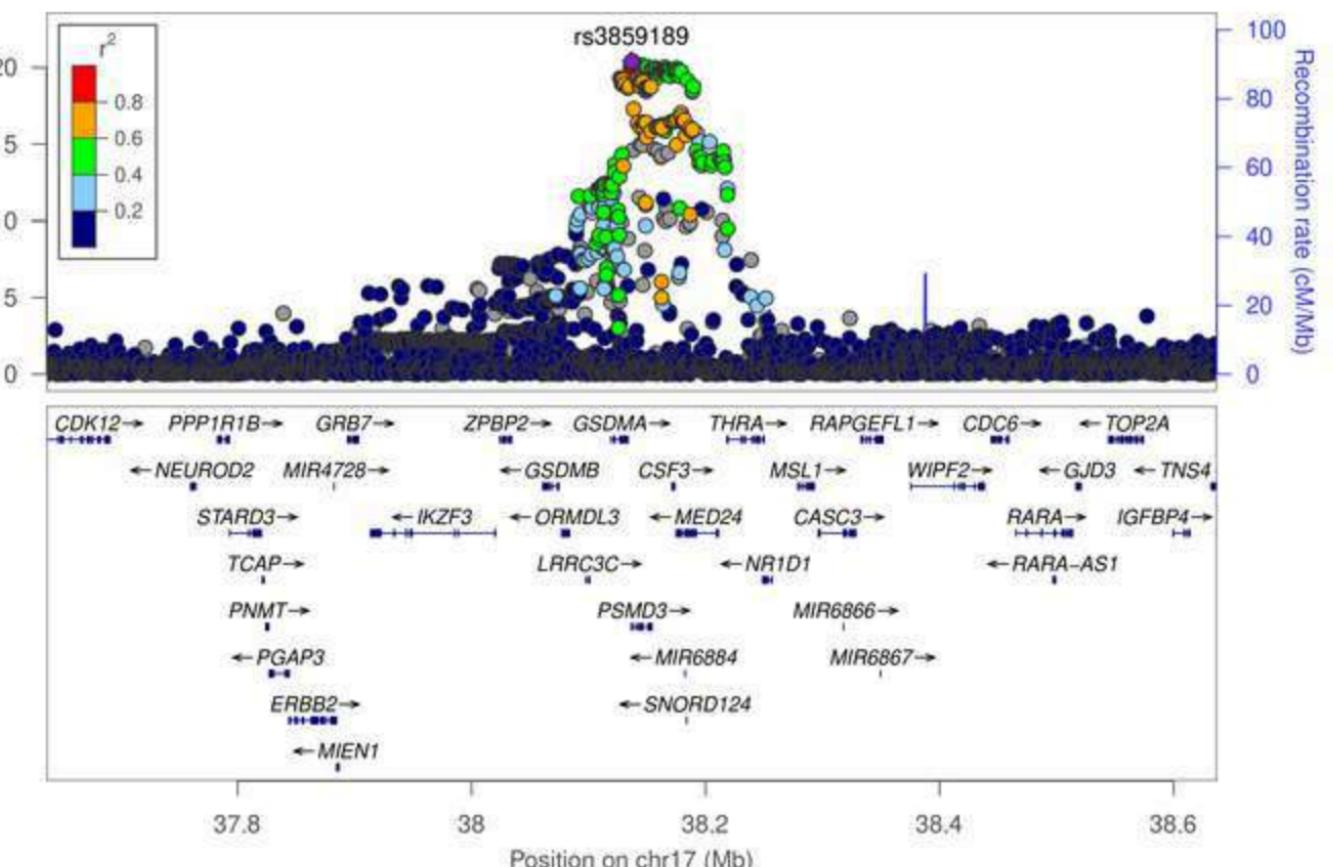
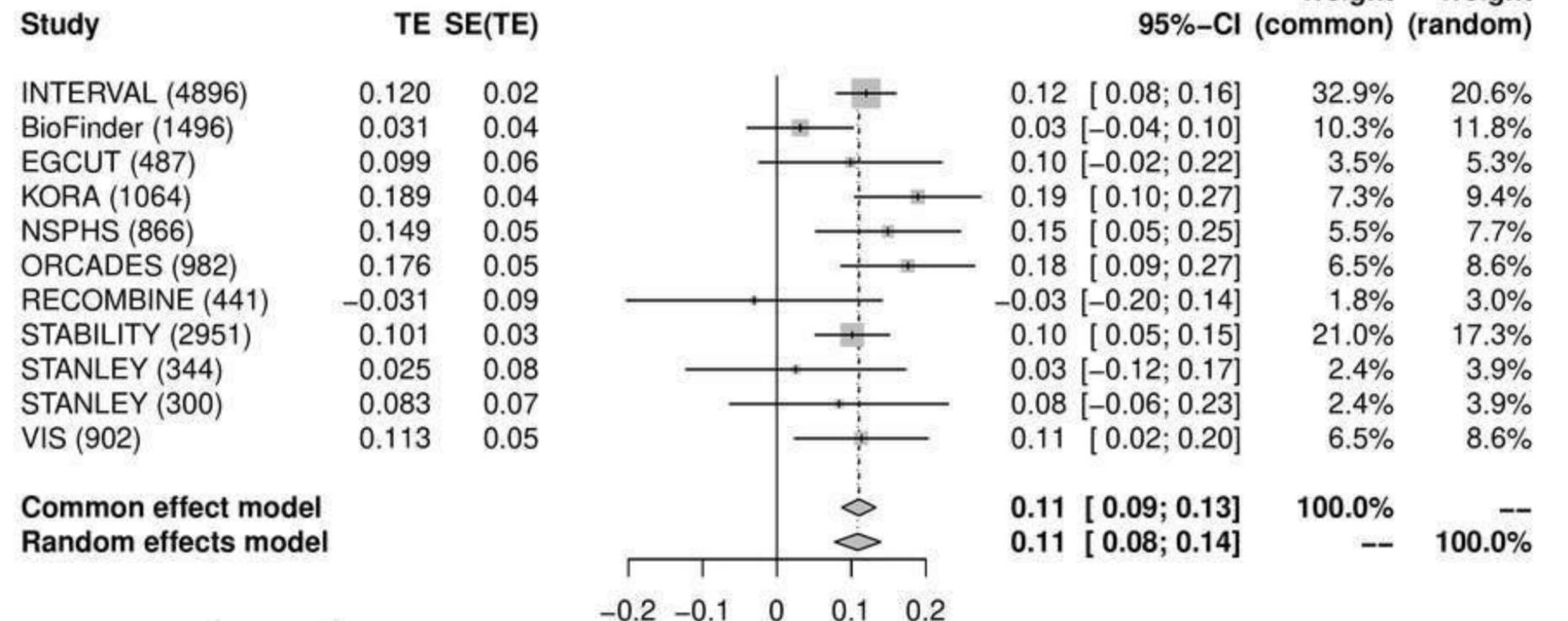


# OSM (OSM)-rs2511241

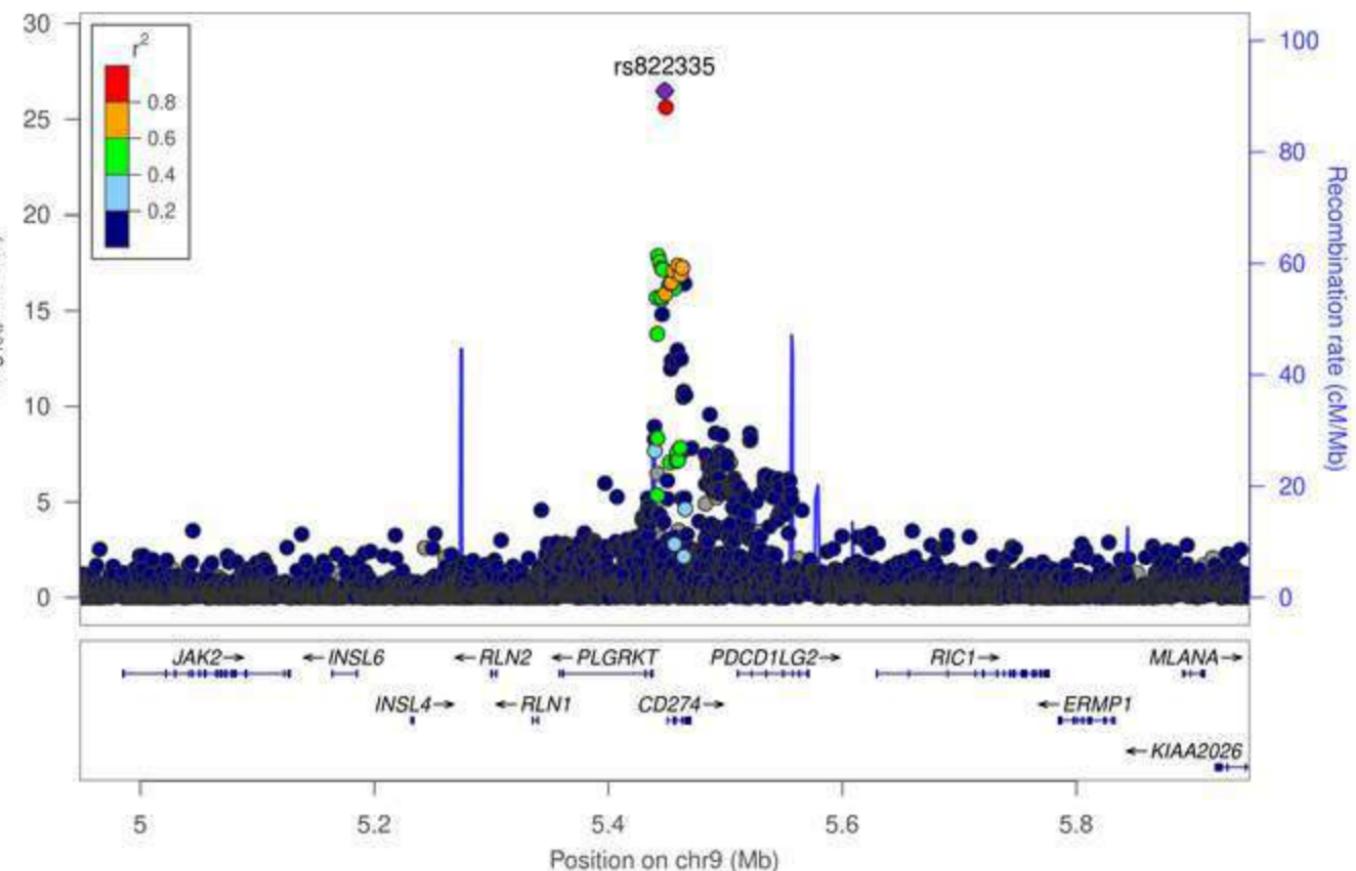
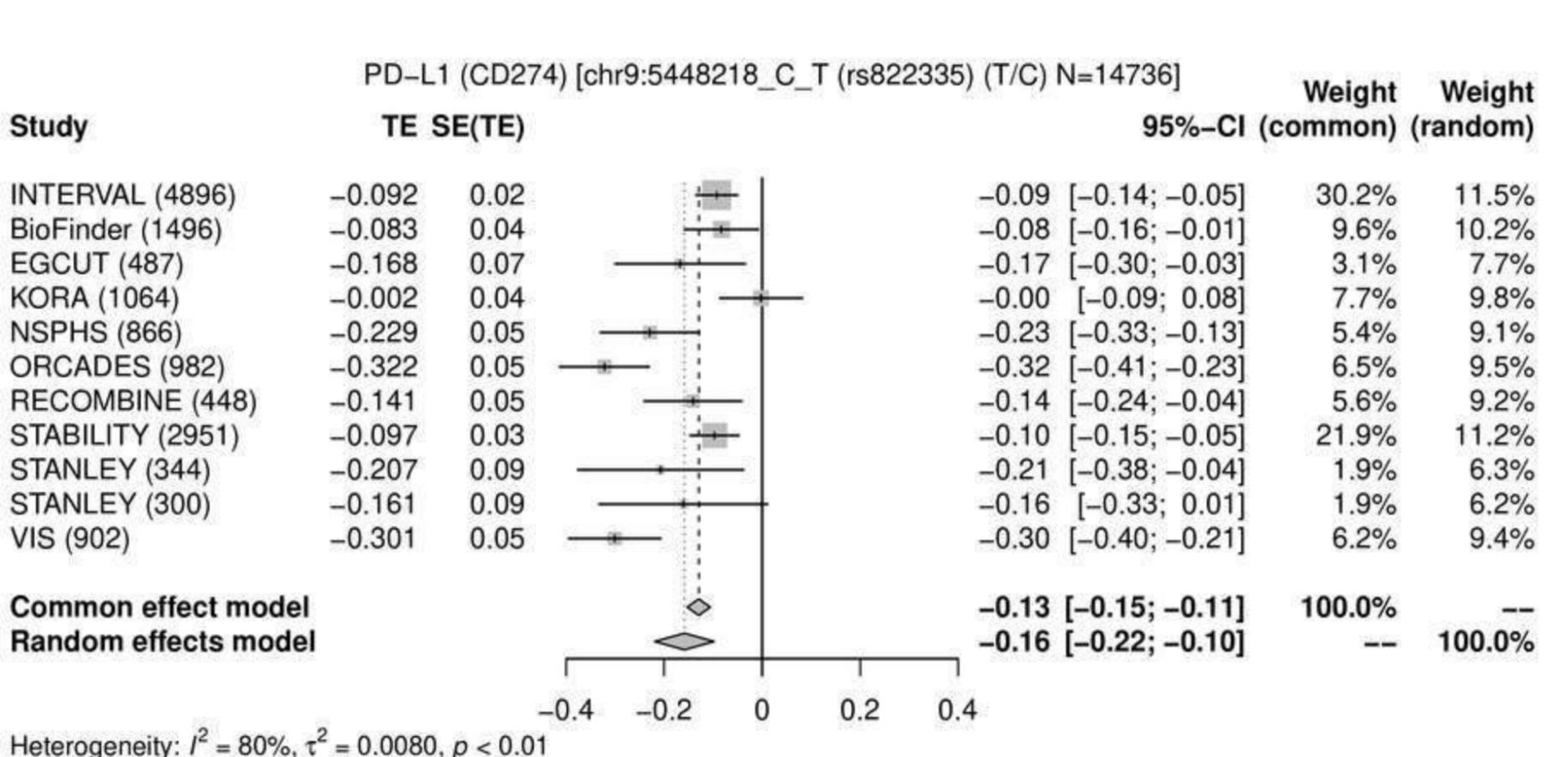
OSM (OSM) [chr11:72945341\_C\_T (rs2511241) (T/C) N=13668]



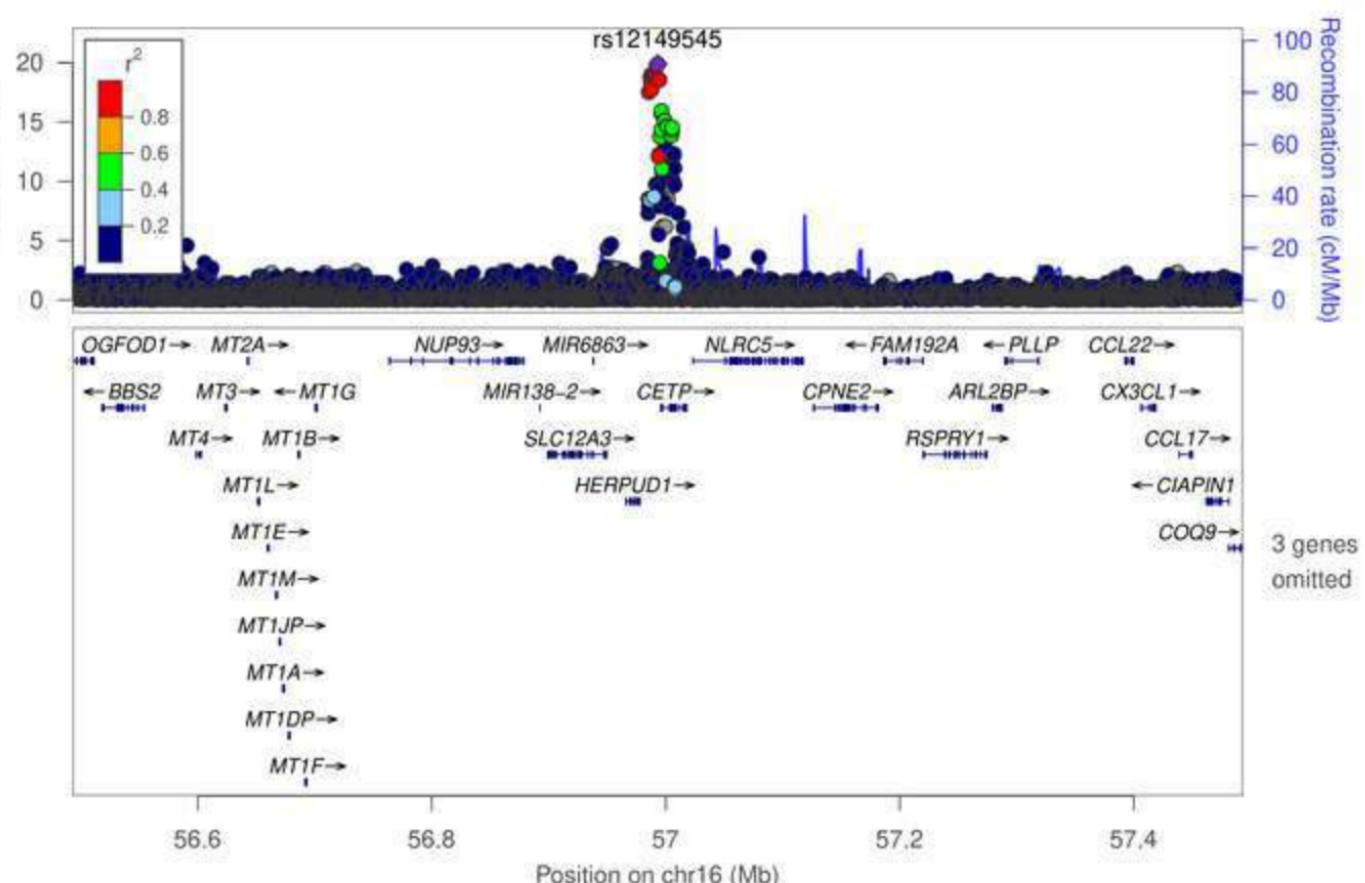
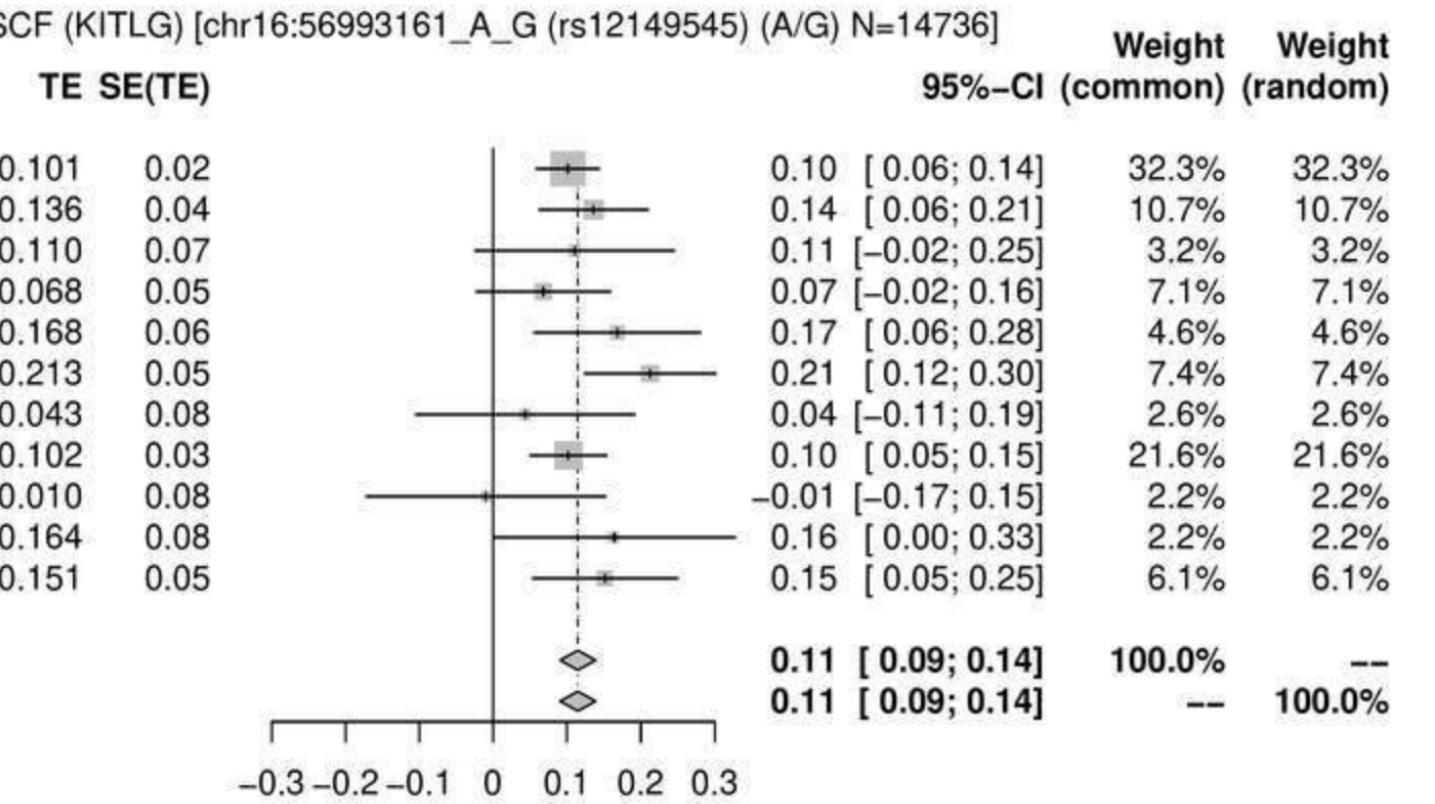
# OSM (OSM)-rs3859189



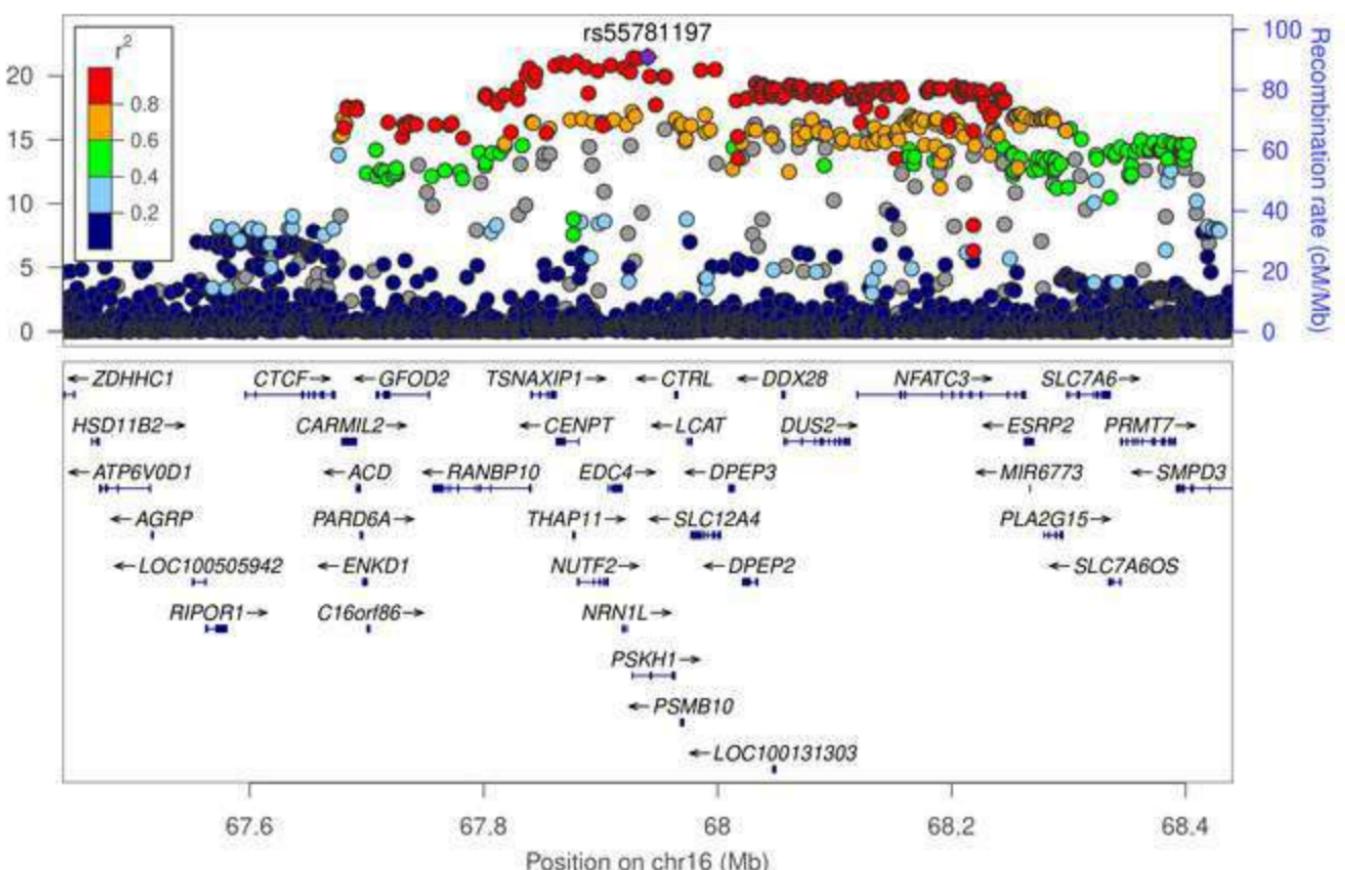
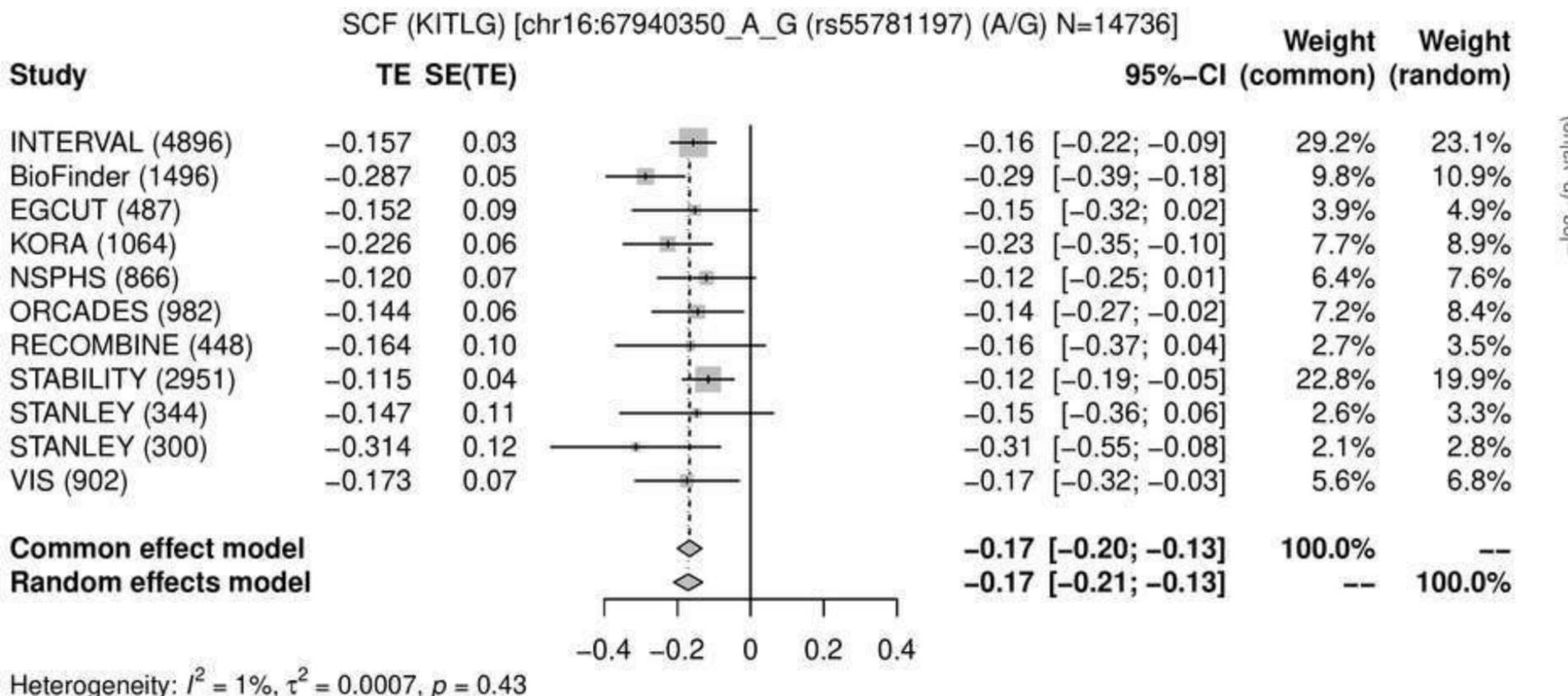
# PD-L1 (CD274)-rs822335



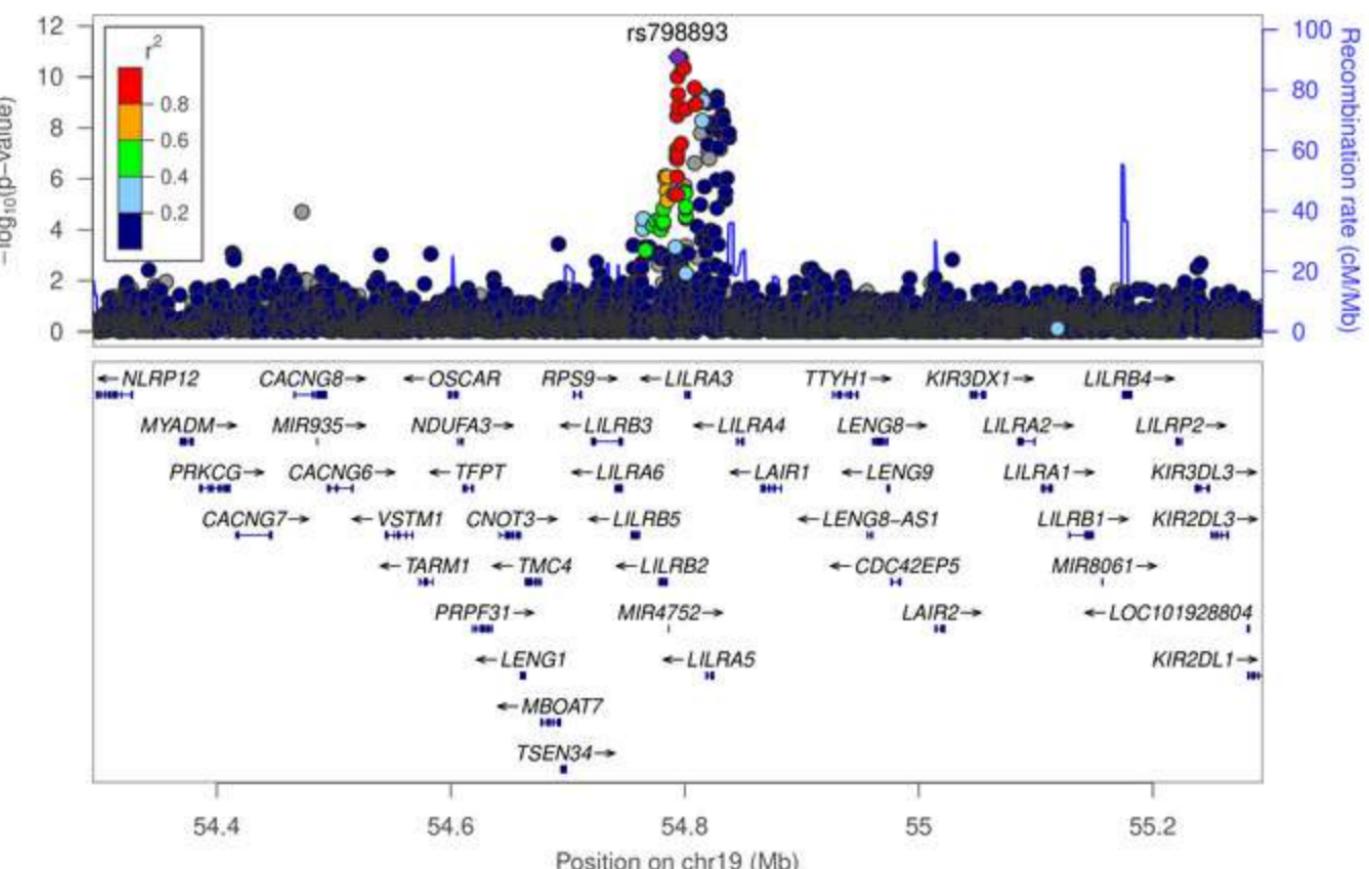
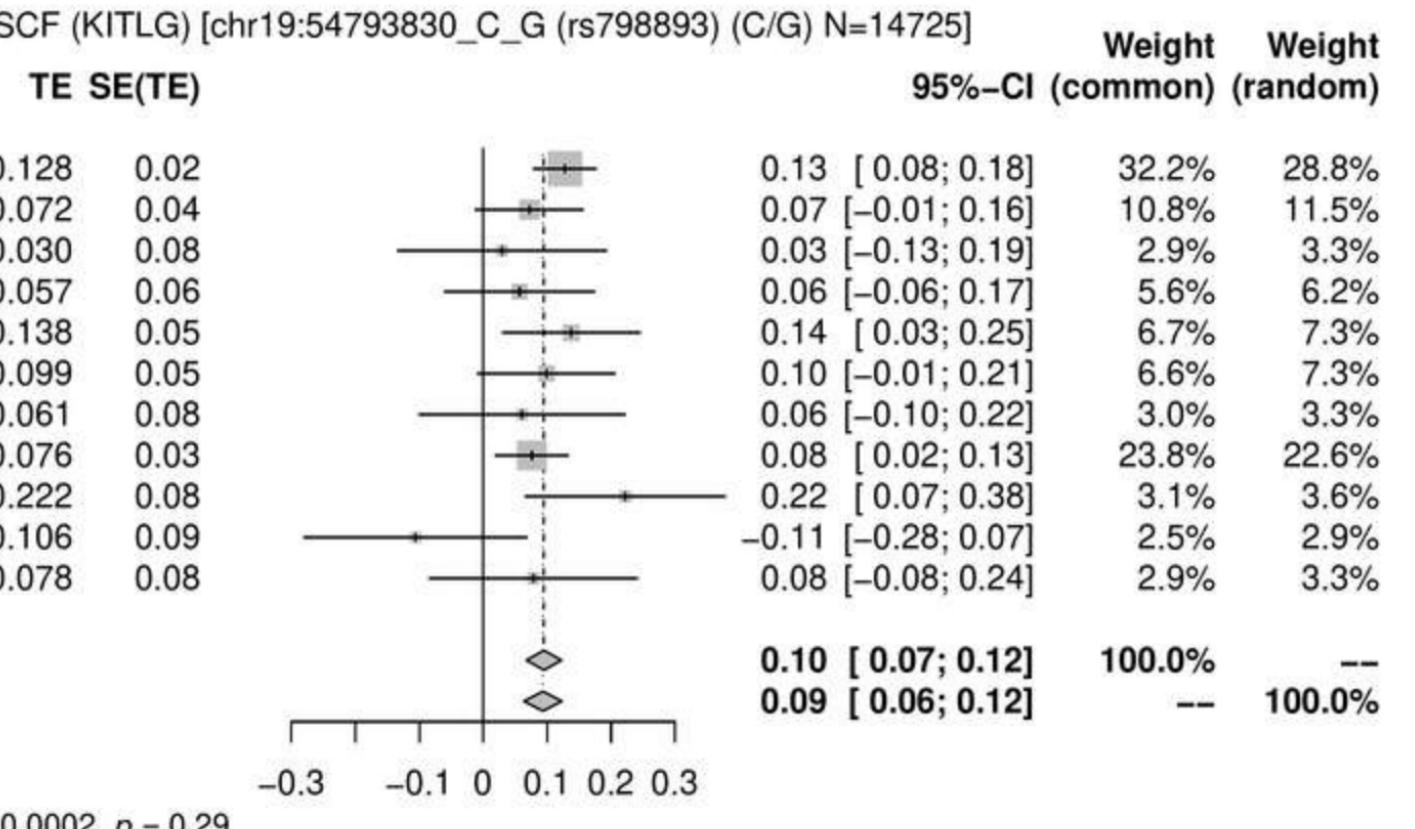
# SCF (KITLG)-rs12149545



# SCF (KITLG)-rs55781197

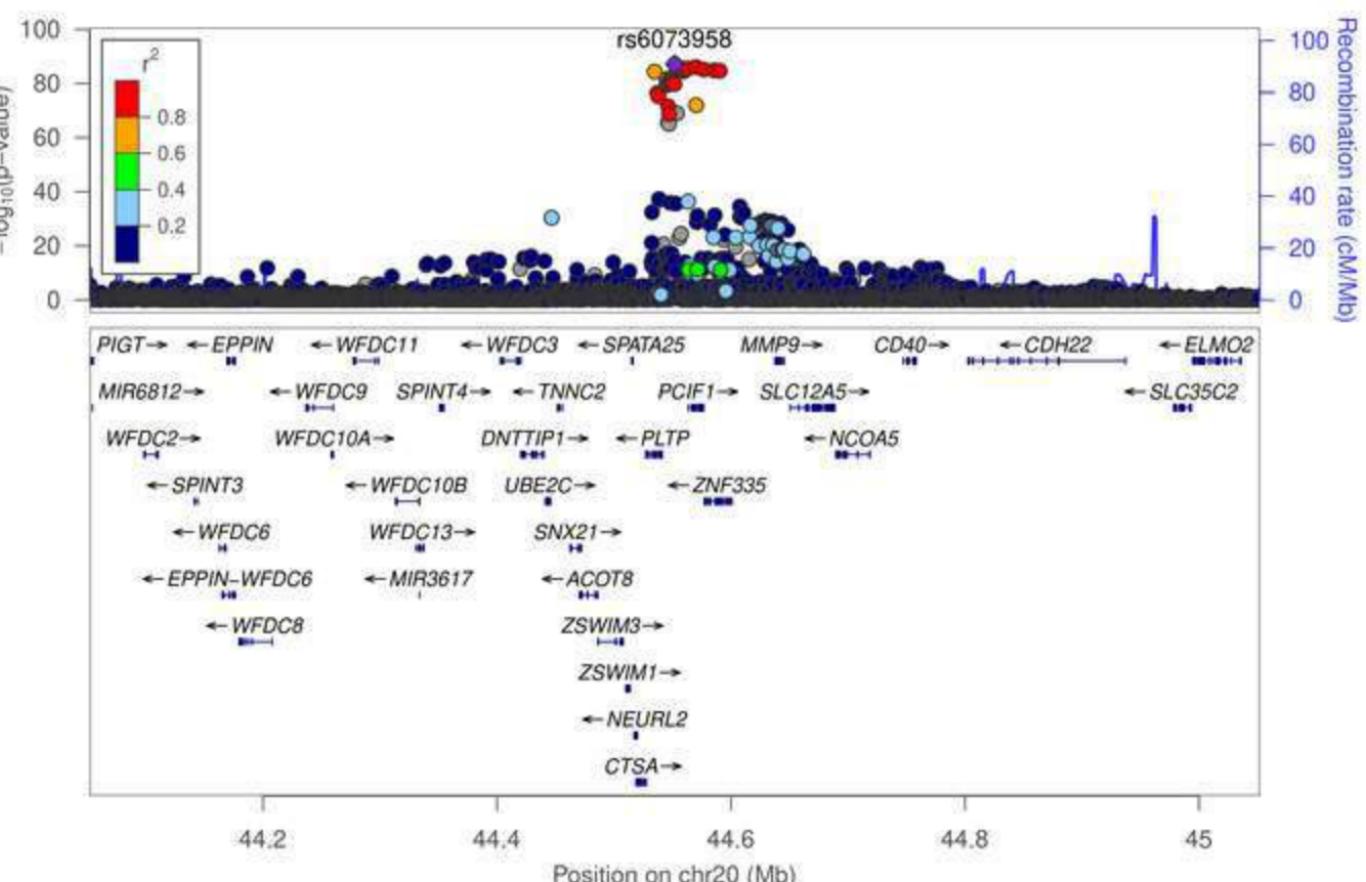
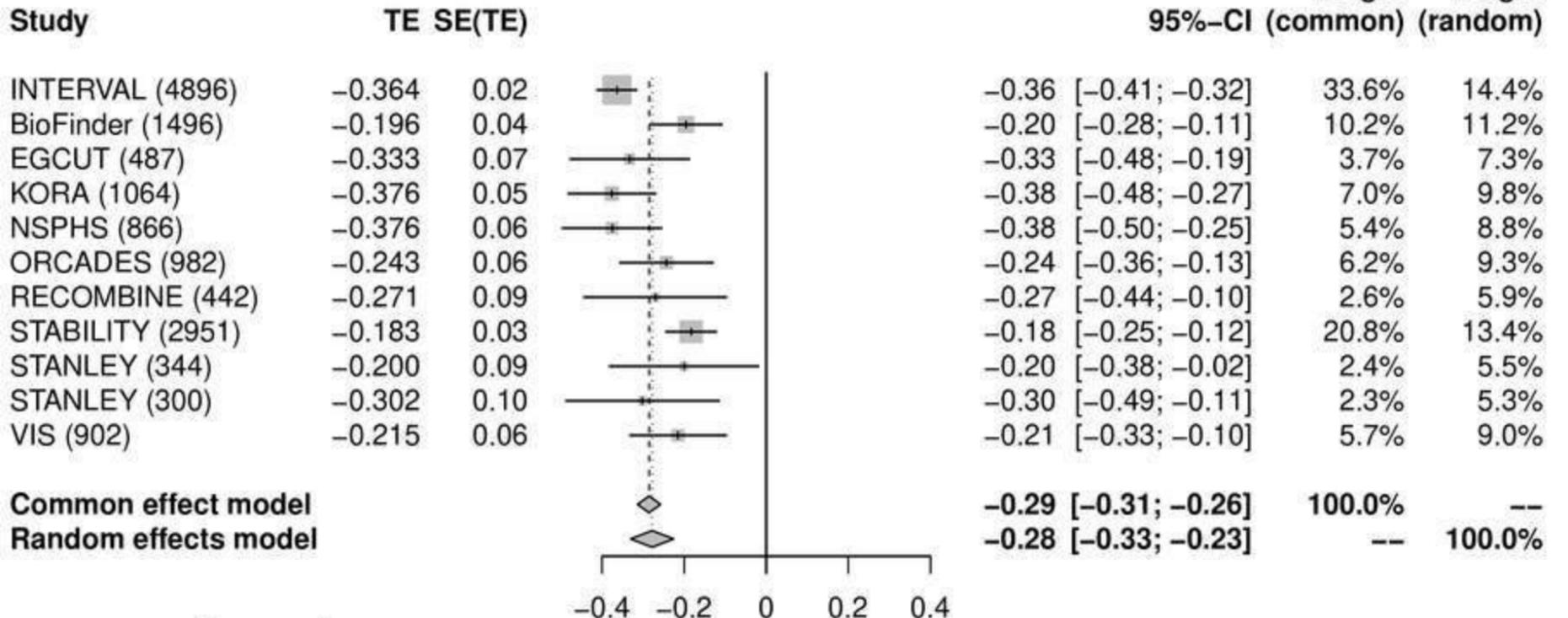


# SCF (KITLG)-rs798893



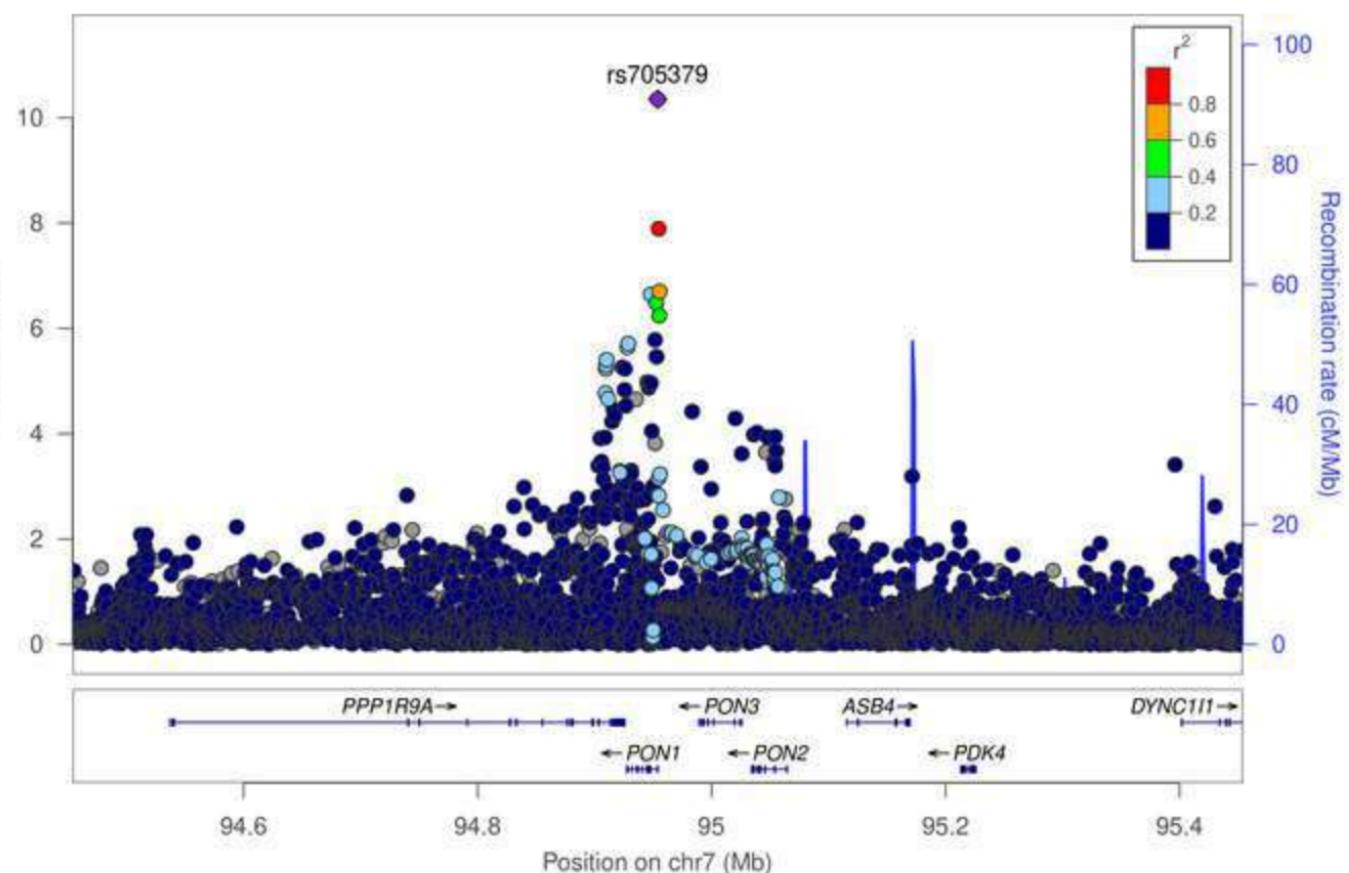
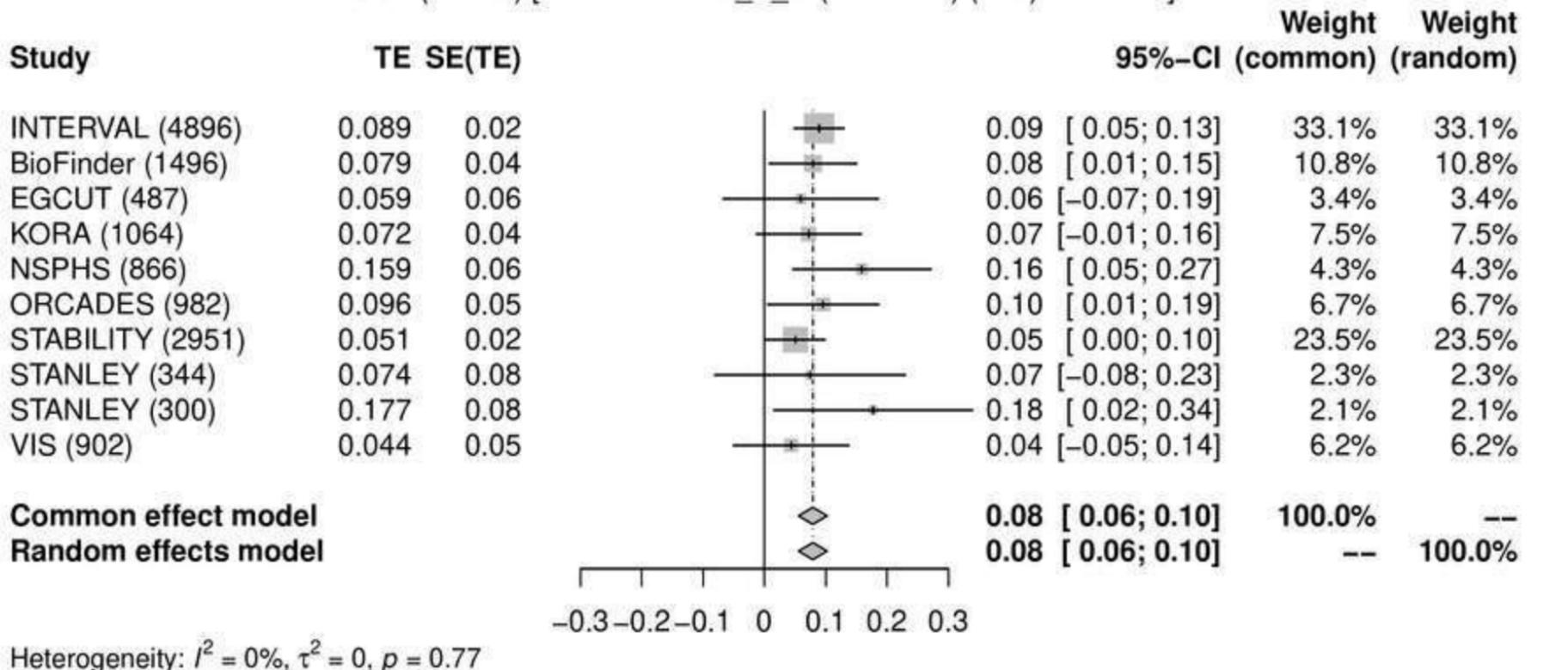
# SCF (KITLG)-rs6073958

## Study

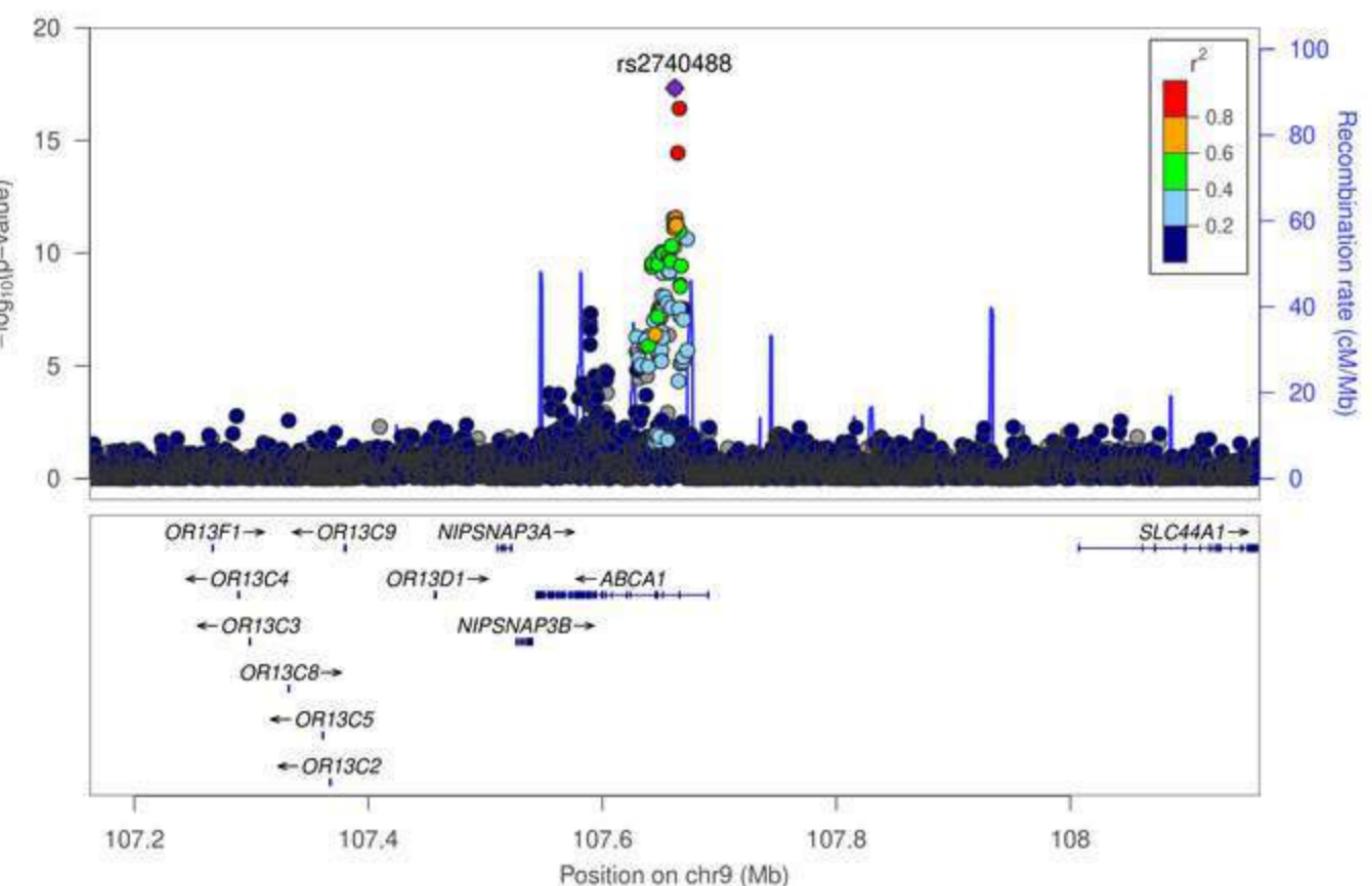
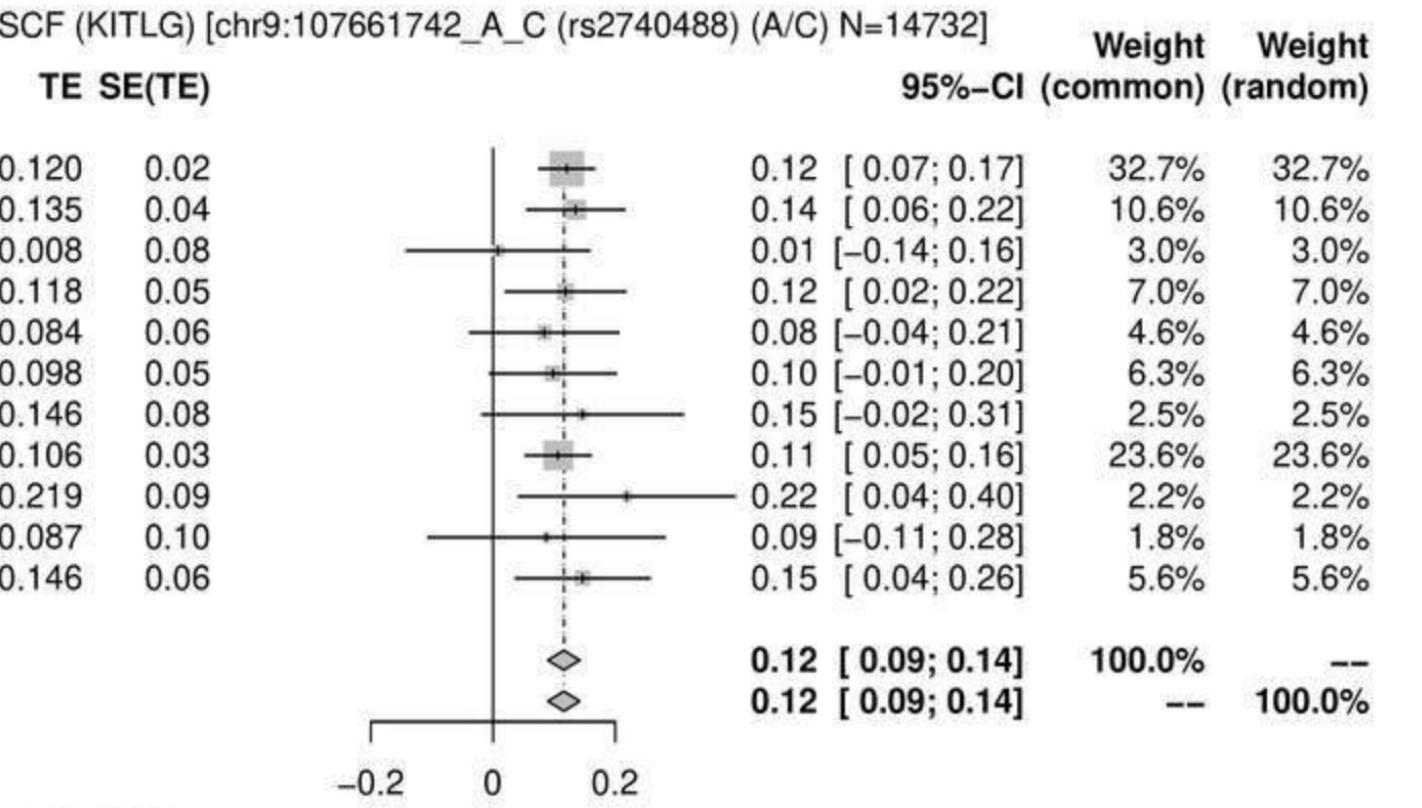


# SCF (KITLG)-rs705379

SCF (KITLG) [chr7:94953895\_A\_G (rs705379) (A/G) N=14288]

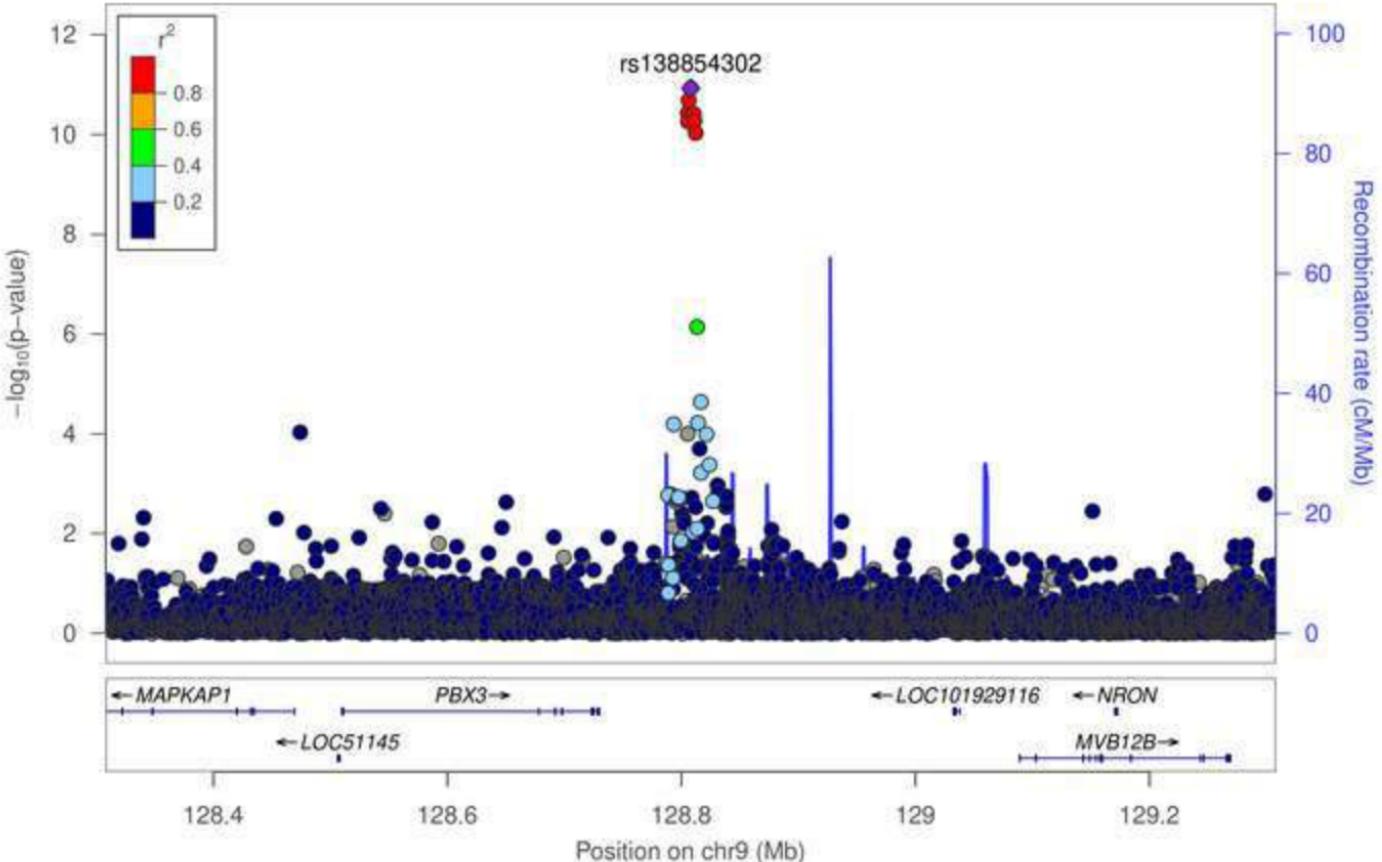
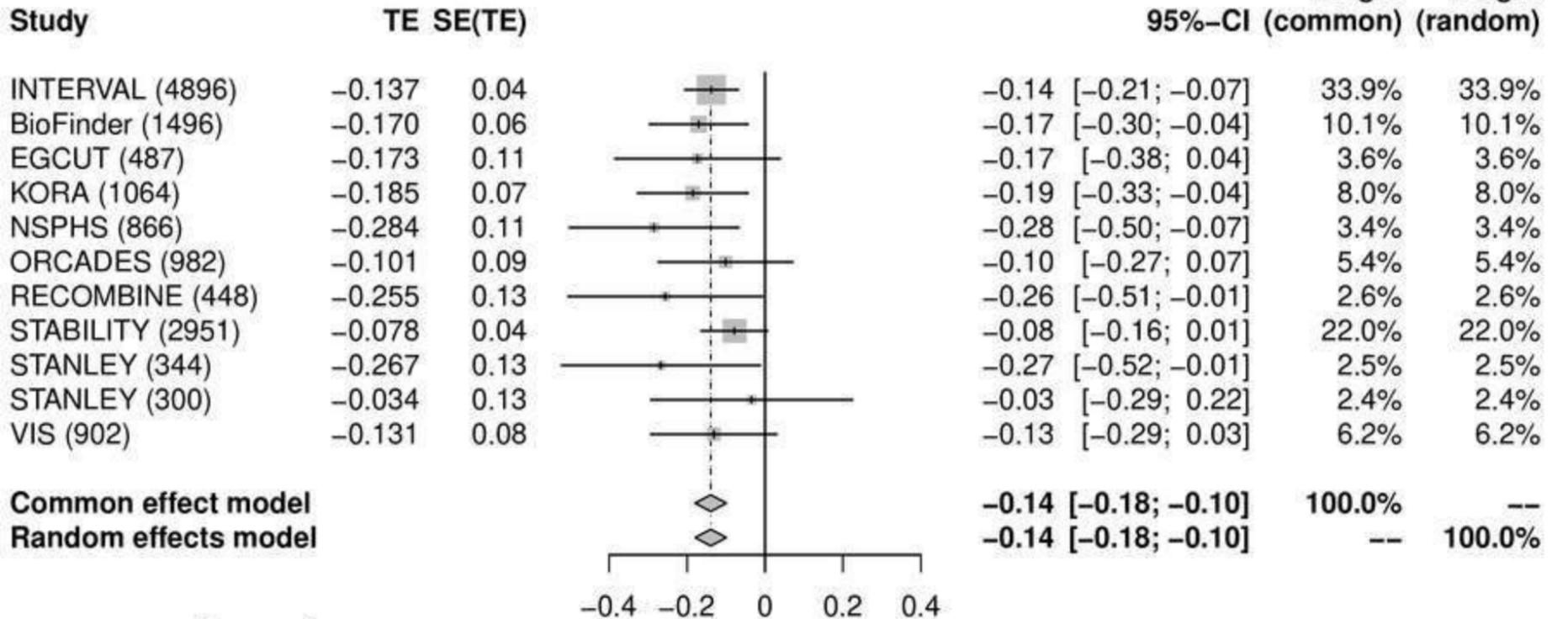


# SCF (KITLG)-rs2740488

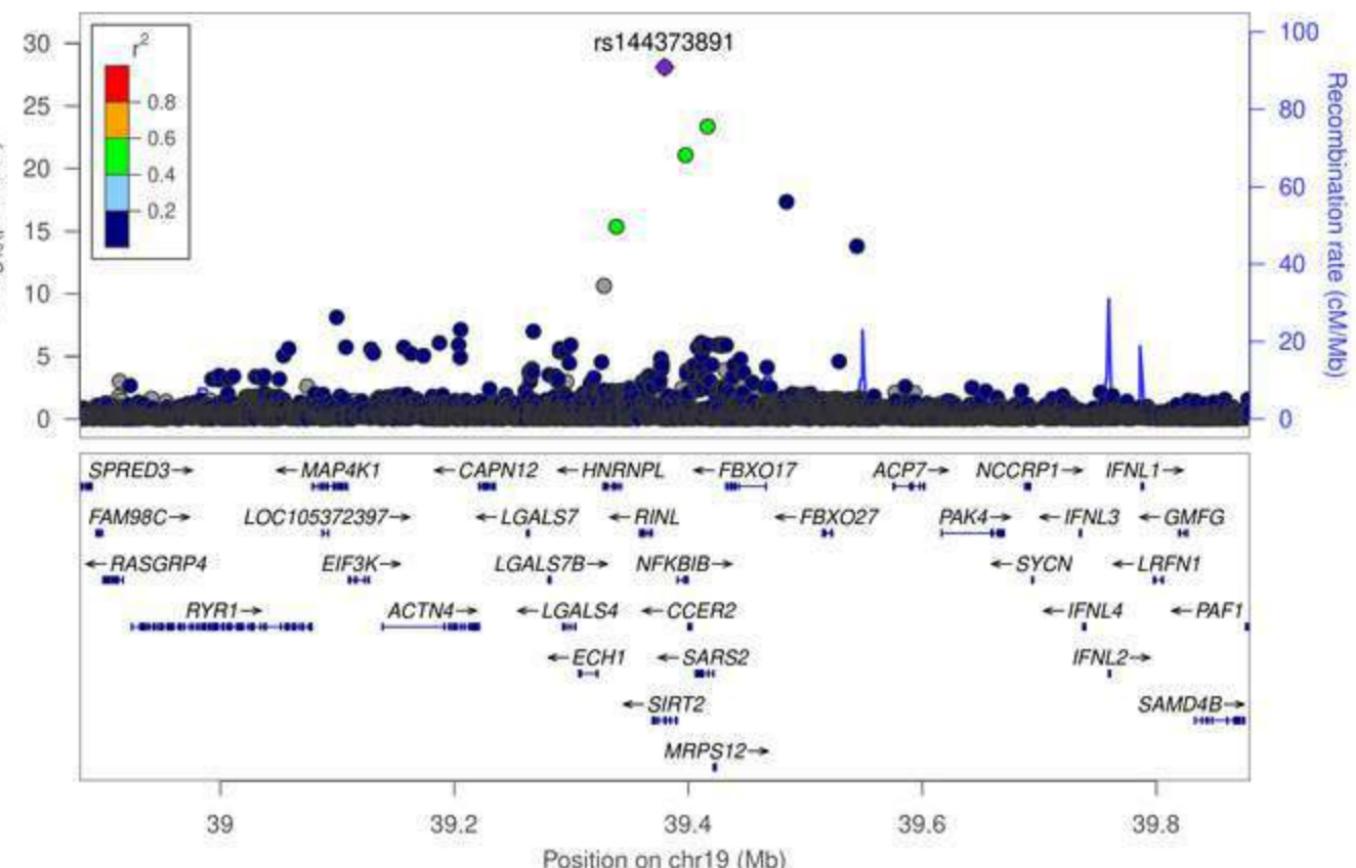
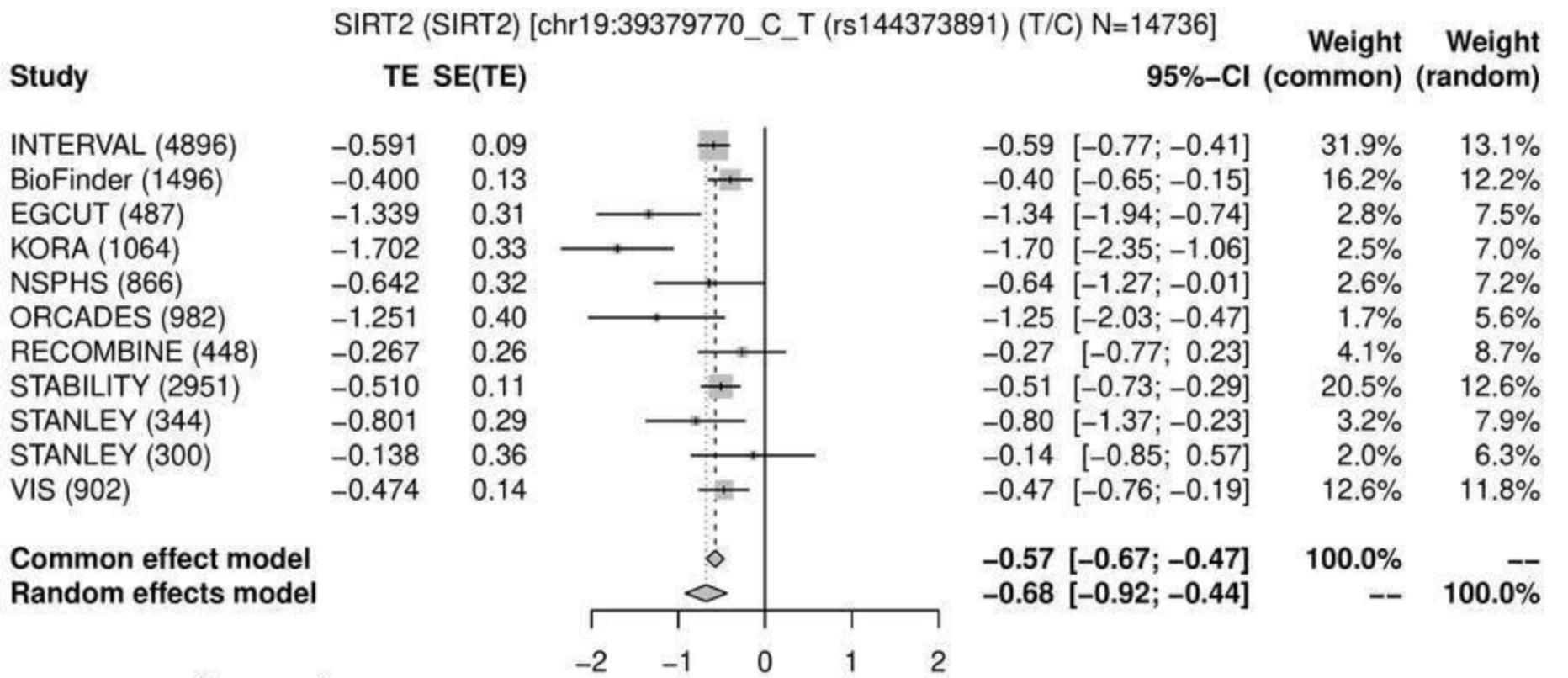


# SCF (KITLG)-rs138854302

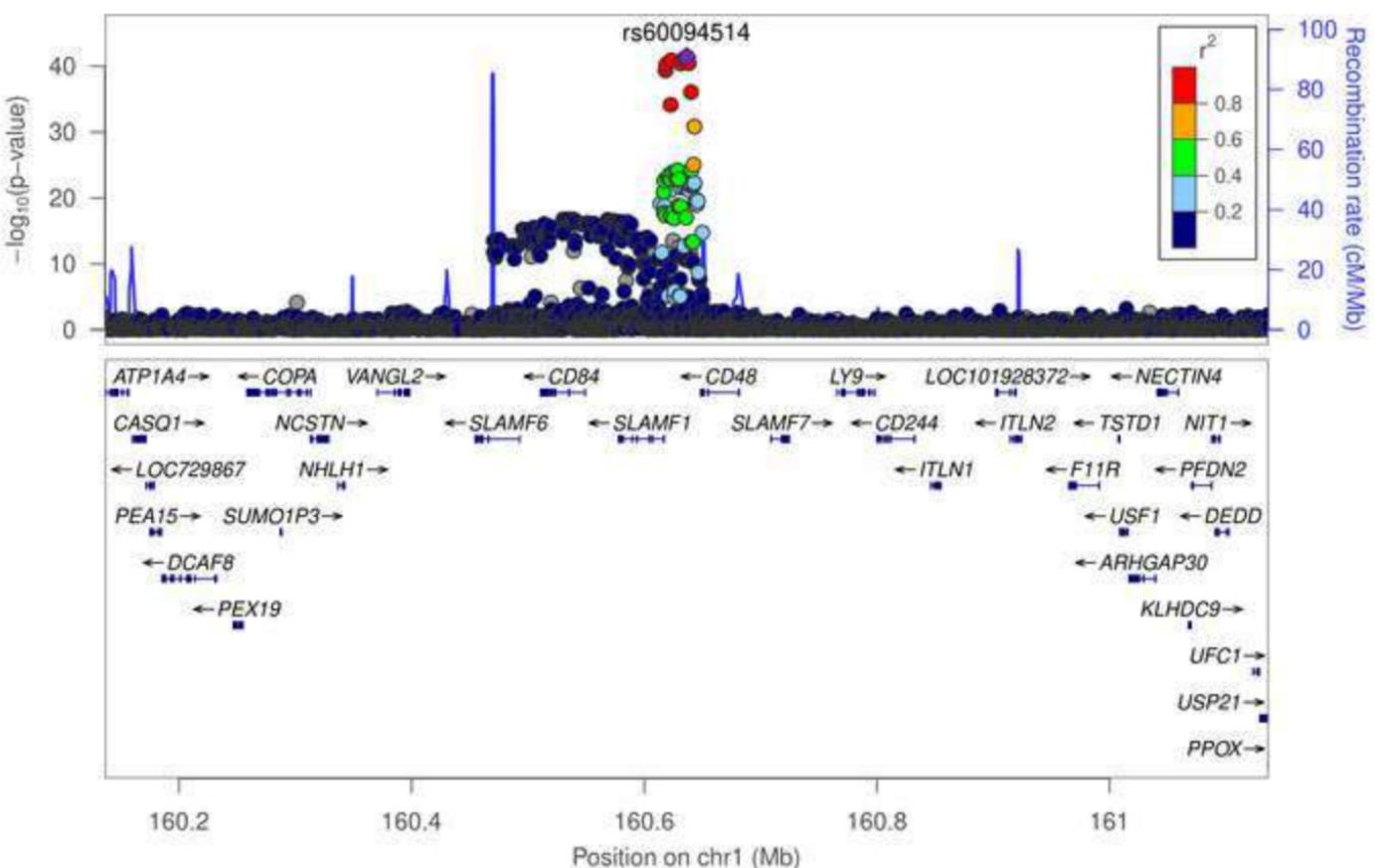
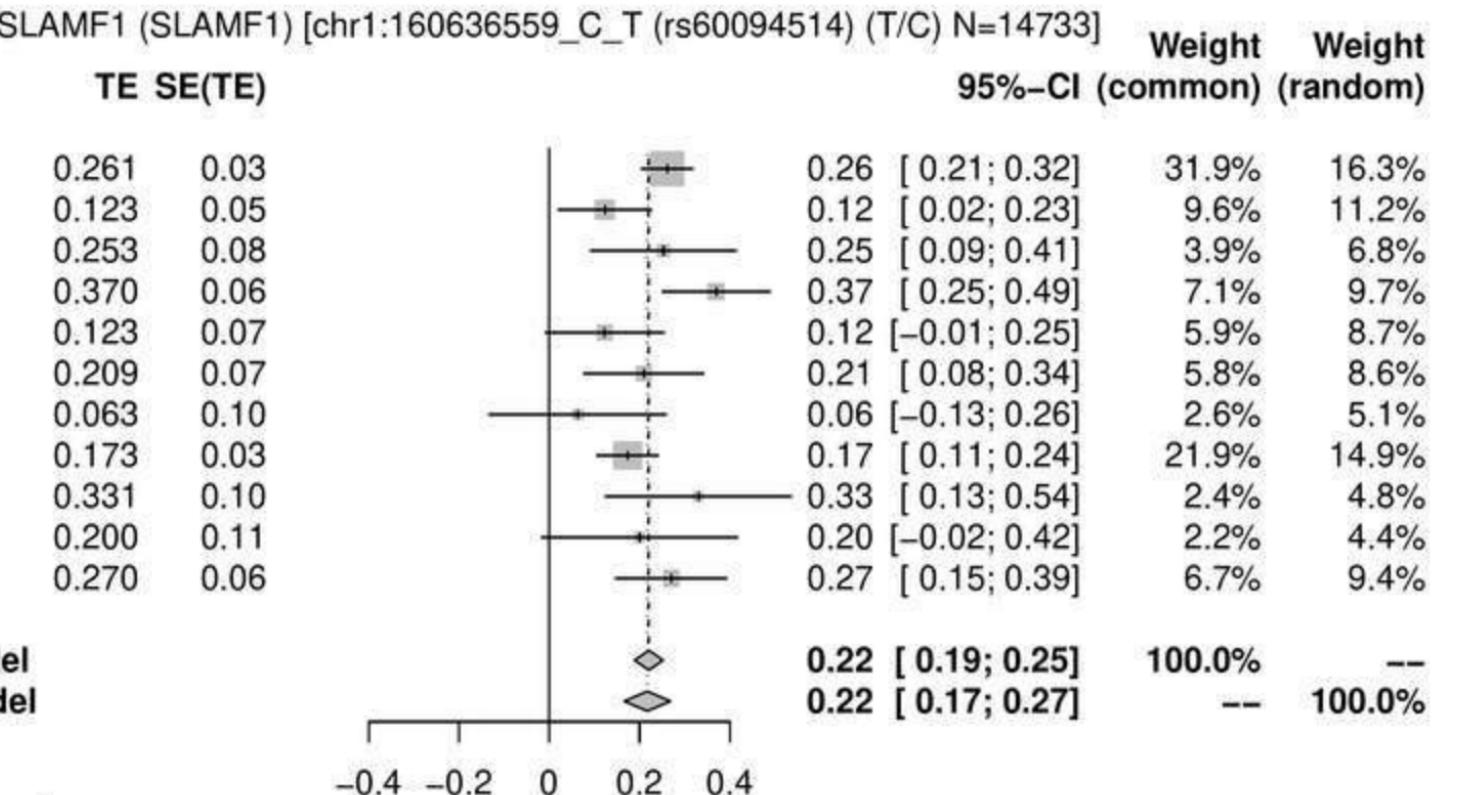
**Study**



# SIRT2 (SIRT2)-rs144373891

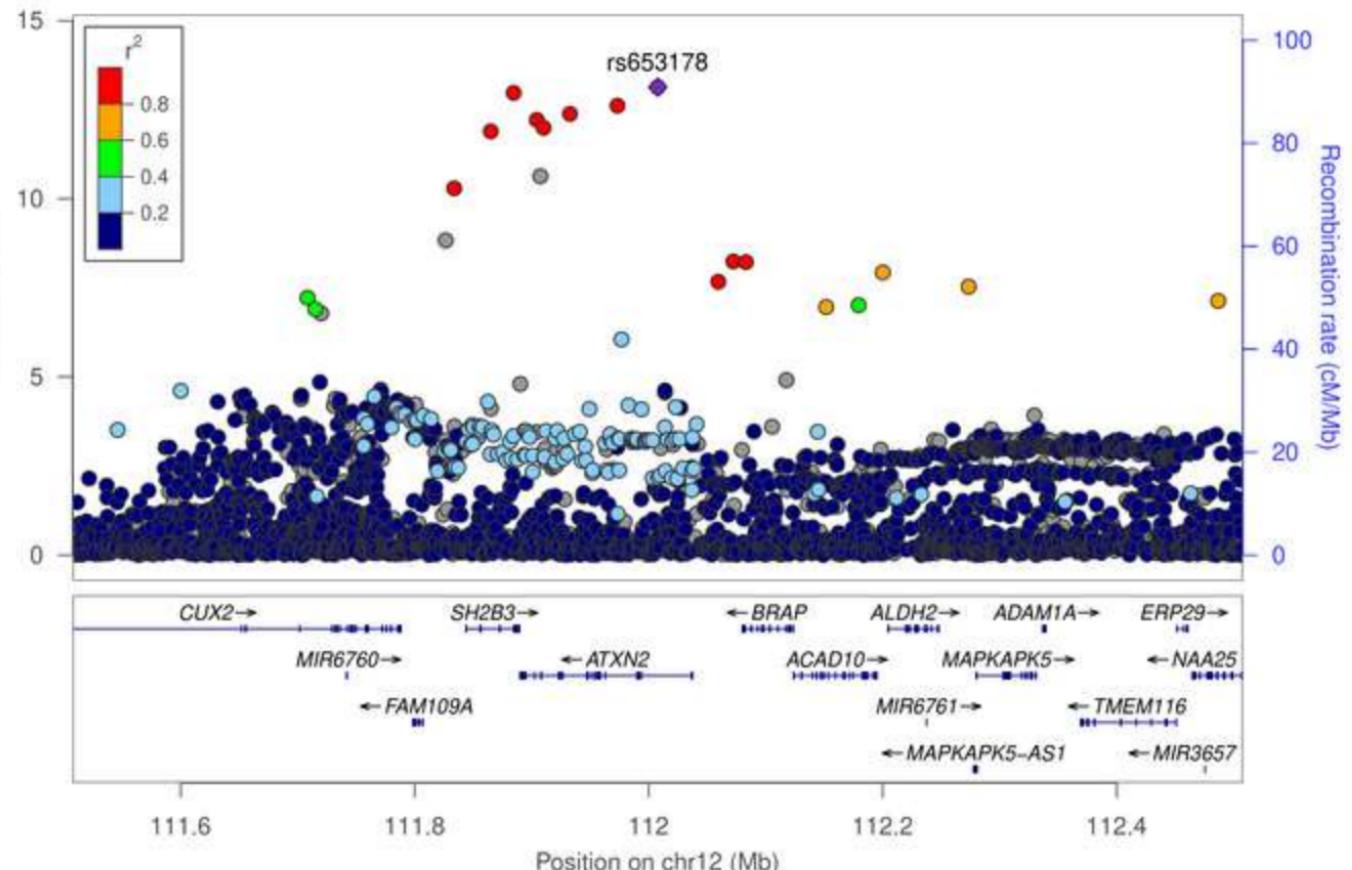
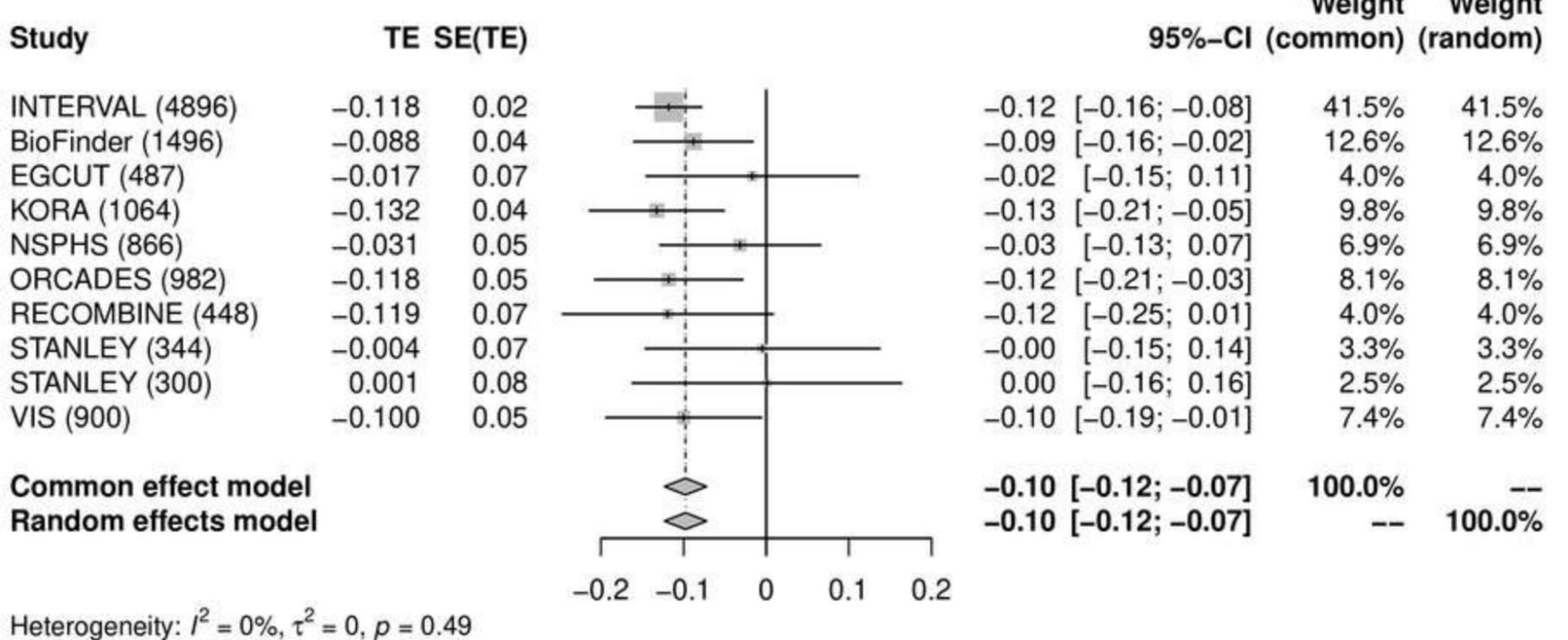


# SLAMF1 (SLAMF1)-rs60094514

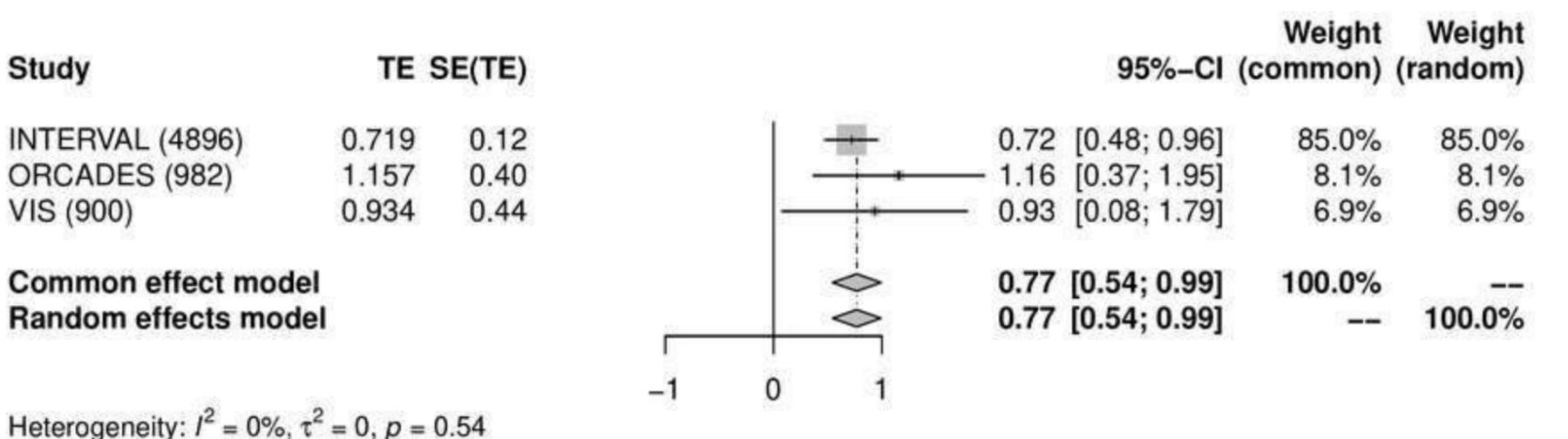


# SLAMF1 (SLAMF1)-rs653178

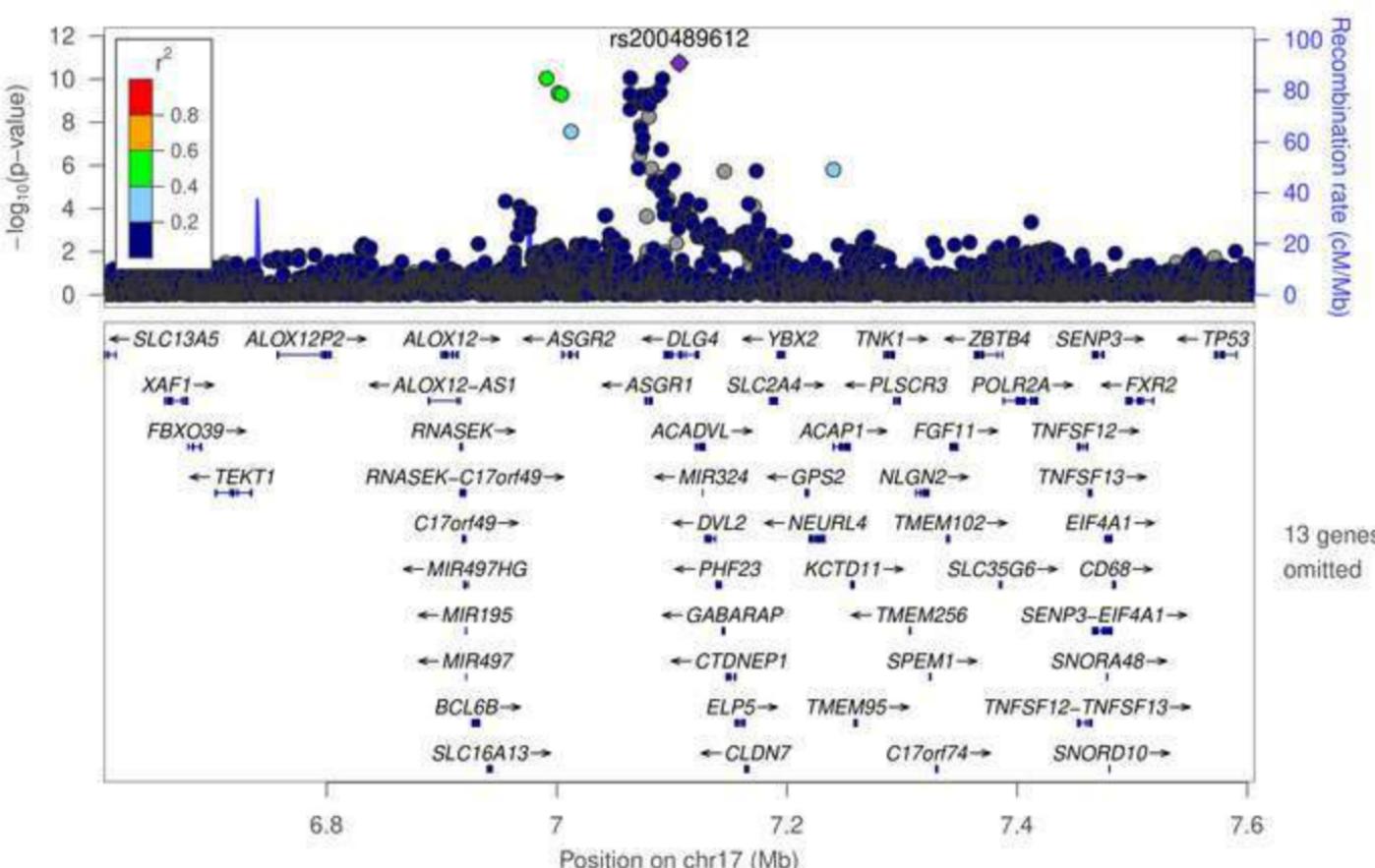
SLAMF1 (SLAMF1) [chr12:112007756\_C\_T (rs653178) (T/C) N=11783]



SLAMF1 (SLAMF1) [chr17:7106378\_A\_G (rs200489612) (A/G) N=6778]

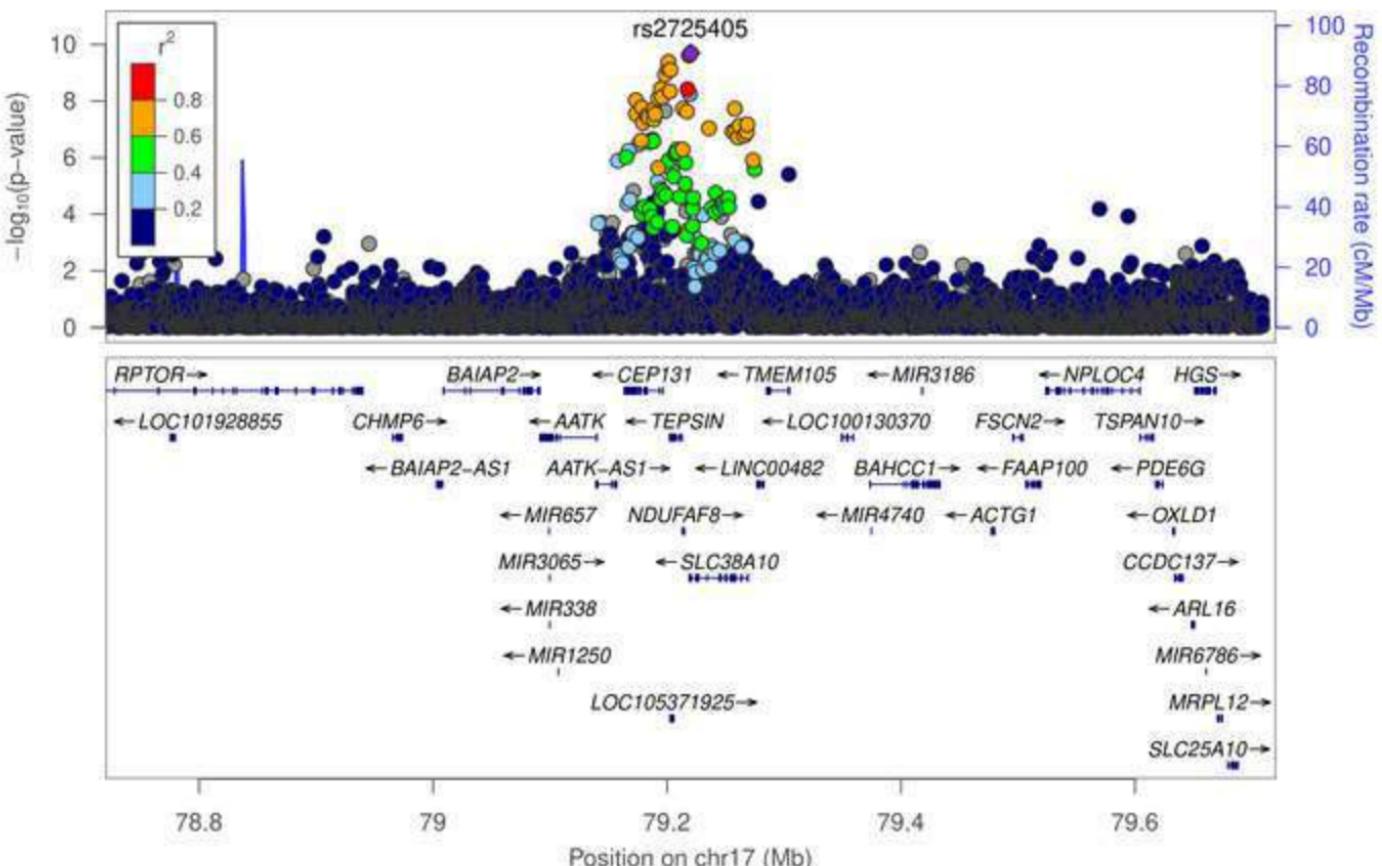
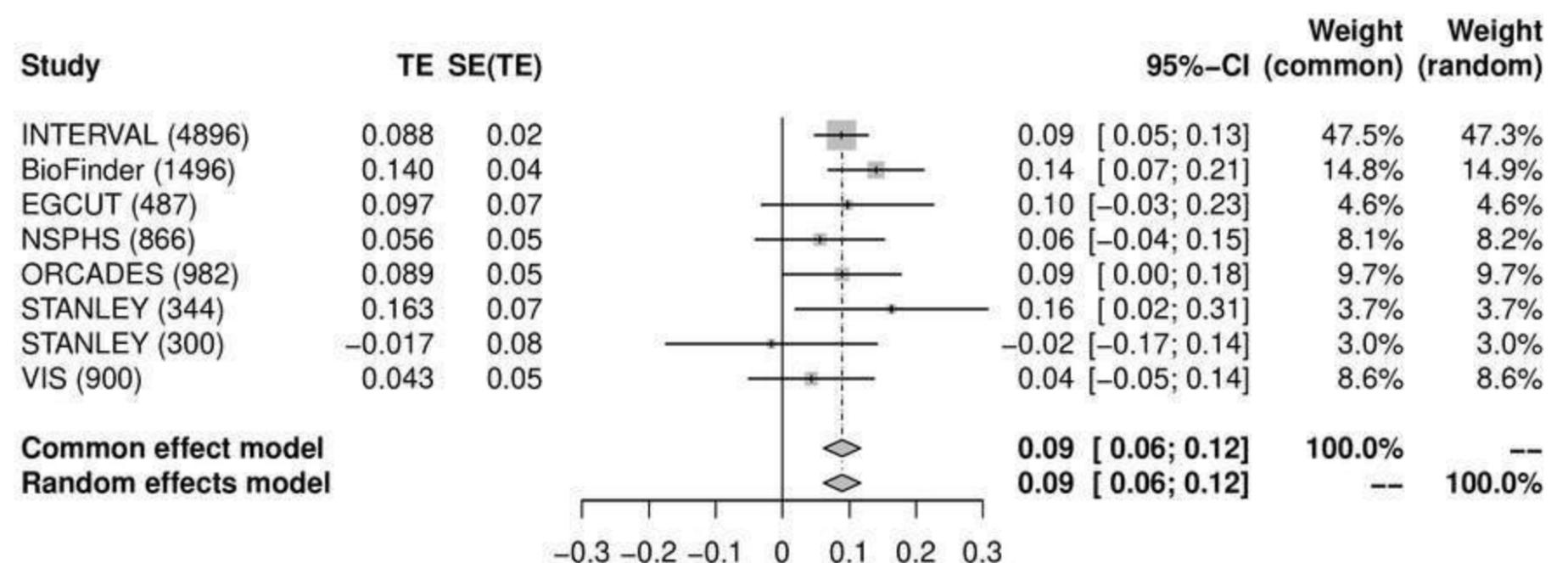


SLAMF1 (SLAMF1)-rs200489612



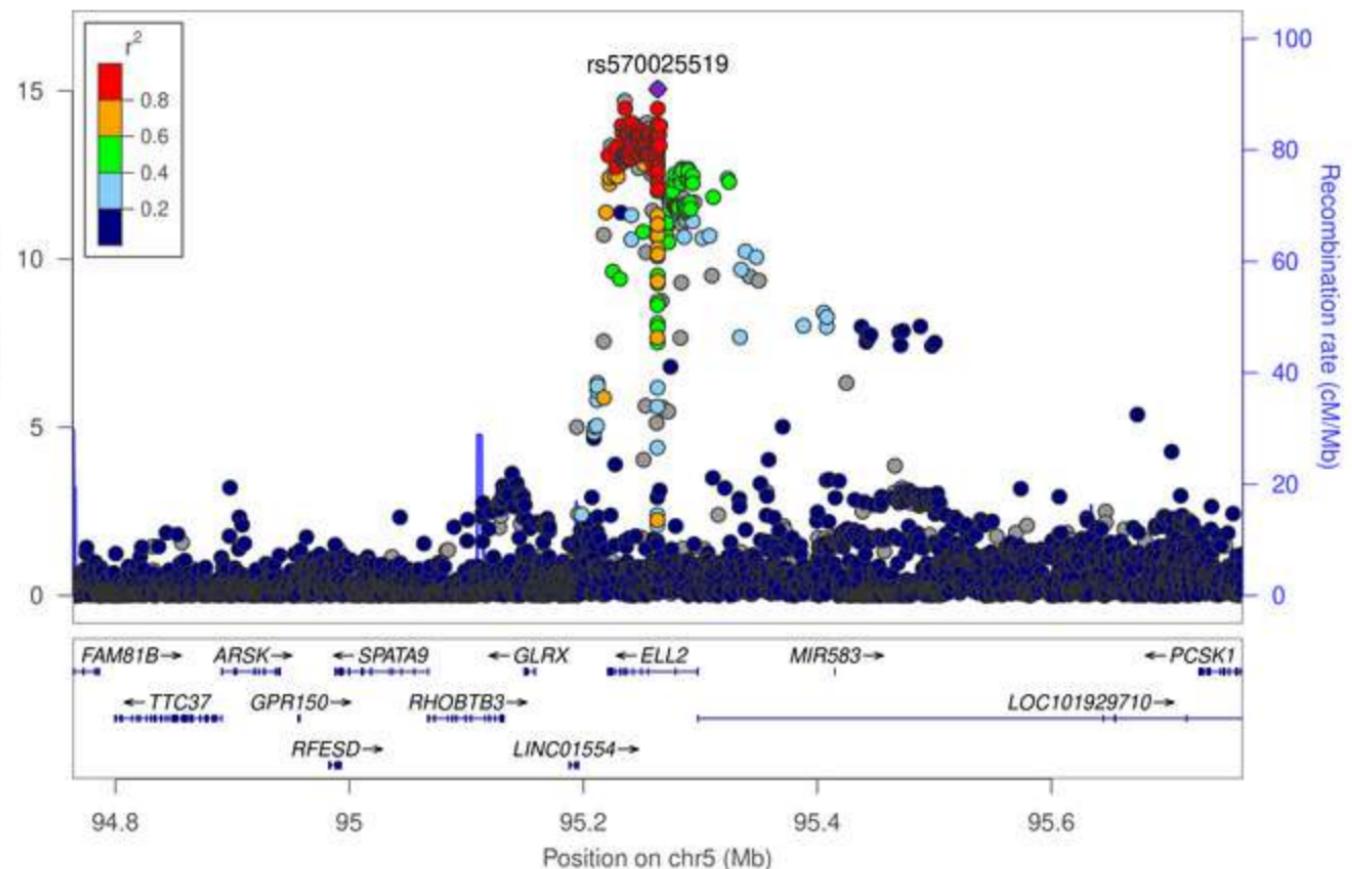
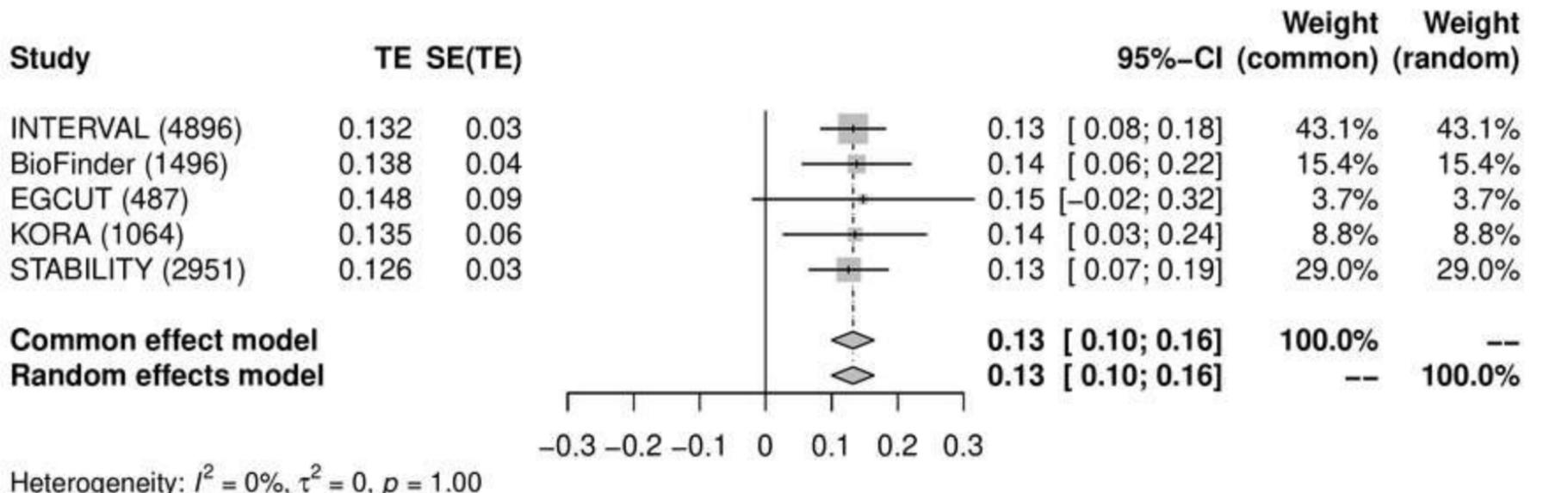
# SLAMF1 (SLAMF1)-rs2725405

SLAMF1 (SLAMF1) [chr17:79220224\_C\_G (rs2725405) (C/G) N=10271]



# SLAMF1 (SLAMF1)-rs570025519

SLAMF1 (SLAMF1) [chr5:95263427\_A\_G (rs570025519) (A/G) N=10894]



# ST1A1 (SULT1A1)-rs149278

ST1A1 (SULT1A1) [chr16:28561581\_C\_T (rs149278) (T/C) N=11345]

## Study

INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
NSPHS (874)  
ORCADES (982)  
STANLEY (344)  
STANLEY (300)  
VIS (902)

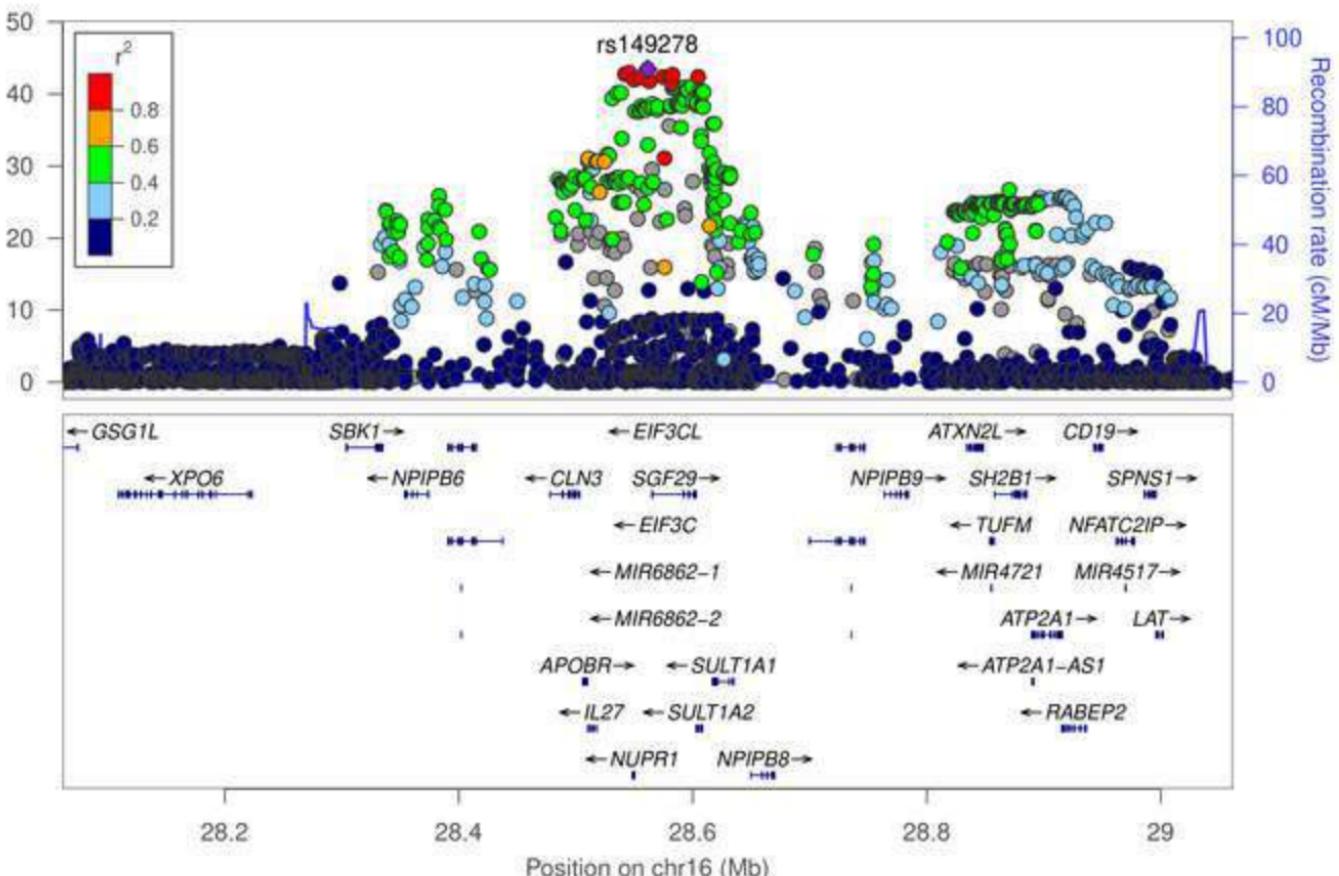
TE SE(TE)

Weight  
95%-CI (common)  
Weight  
(random)

	TE	SE(TE)	95%-CI (common)	Weight (common)	Weight (random)
INTERVAL (4896)	-0.118	0.02	-0.12 [-0.16; -0.08]	42.7%	15.8%
BioFinder (1496)	-0.253	0.04	-0.25 [-0.32; -0.18]	13.7%	13.4%
EGCUT (487)	-0.333	0.06	-0.33 [-0.45; -0.21]	4.7%	9.4%
KORA (1064)	-0.332	0.05	-0.33 [-0.42; -0.24]	8.4%	11.7%
NSPHS (874)	-0.273	0.05	-0.27 [-0.37; -0.17]	7.2%	11.1%
ORCADES (982)	-0.167	0.05	-0.17 [-0.26; -0.08]	8.8%	11.9%
STANLEY (344)	-0.193	0.08	-0.19 [-0.35; -0.04]	2.9%	7.3%
STANLEY (300)	-0.139	0.08	-0.14 [-0.29; 0.01]	3.1%	7.6%
VIS (902)	-0.180	0.05	-0.18 [-0.27; -0.09]	8.4%	11.7%
<b>Common effect model</b>			<b>-0.19 [-0.21; -0.16]</b>	<b>100.0%</b>	--
<b>Random effects model</b>			<b>-0.22 [-0.27; -0.16]</b>	--	<b>100.0%</b>



Heterogeneity:  $I^2 = 76\%$ ,  $\tau^2 = 0.0046$ ,  $p < 0.01$



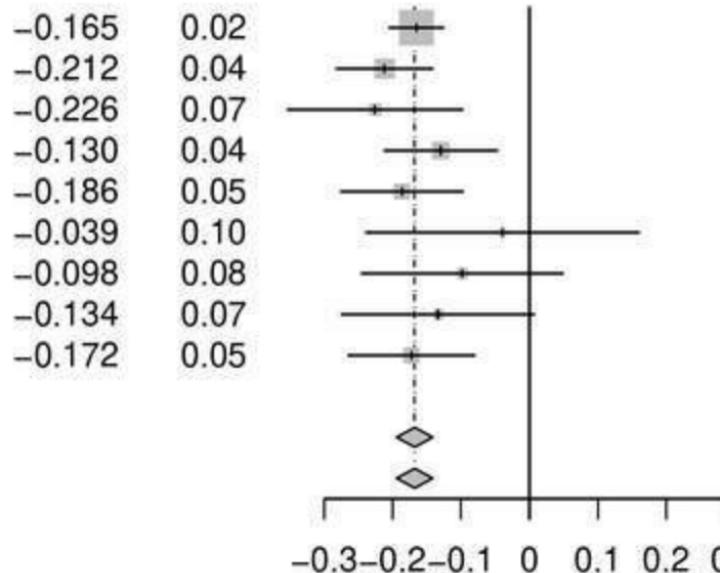
# ST1A1 (SULT1A1)-rs66530140

ST1A1 (SULT1A1) [chr4:187161211\_C\_T (rs66530140) (T/C) N=10913]

## Study

INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
ORCADES (982)  
RECOMBINE (442)  
STANLEY (344)  
STANLEY (300)  
VIS (902)

**TE SE(TE)**

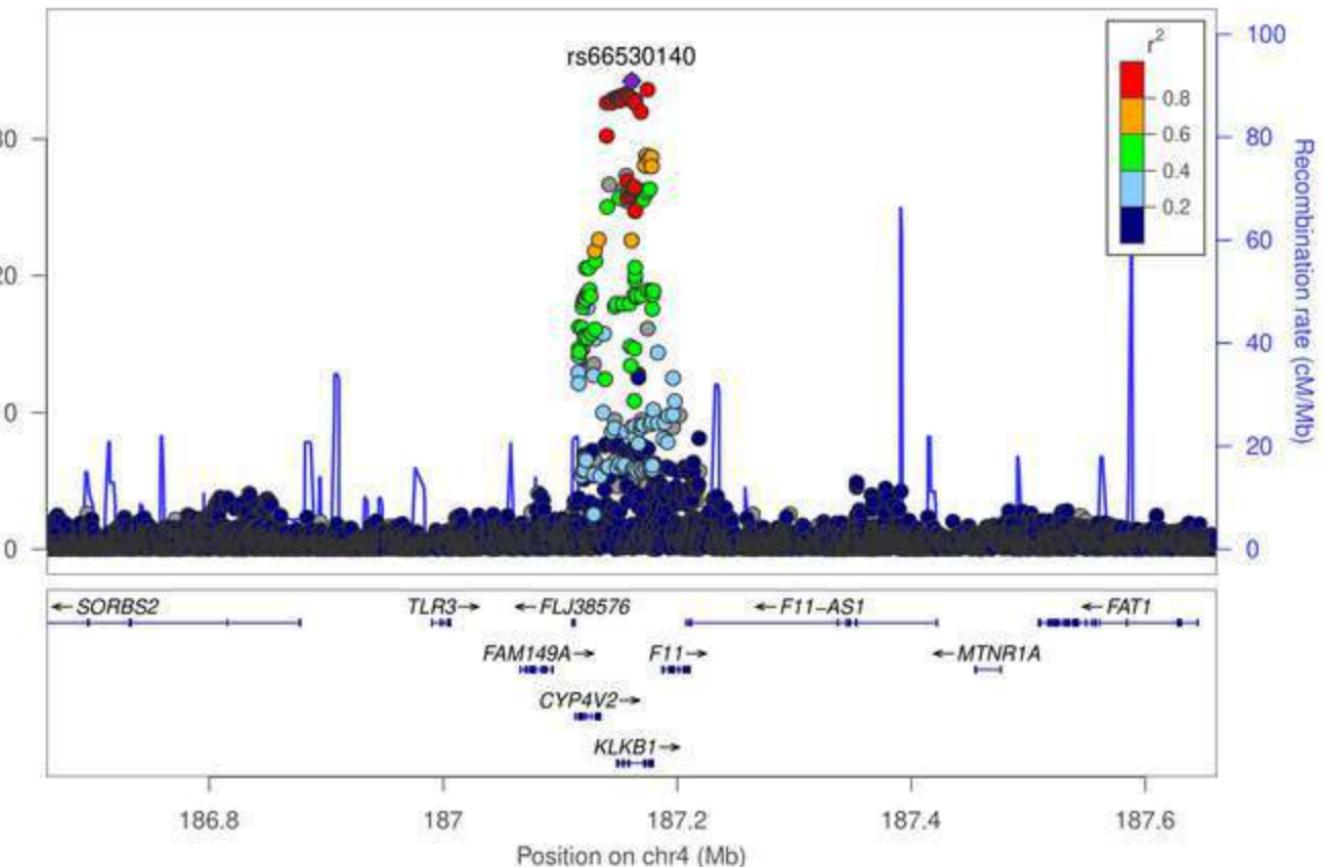


**Weight  
95%-CI (common) (random)**

	Weight 95%-CI (common) (random)	
-0.17 [-0.20; -0.13]	45.1%	45.1%
-0.21 [-0.28; -0.14]	14.4%	14.4%
-0.23 [-0.35; -0.10]	4.3%	4.3%
-0.13 [-0.21; -0.05]	10.4%	10.4%
-0.19 [-0.28; -0.10]	8.9%	8.9%
-0.04 [-0.24; 0.16]	1.8%	1.8%
-0.10 [-0.25; 0.05]	3.3%	3.3%
-0.13 [-0.27; 0.01]	3.6%	3.6%
-0.17 [-0.27; -0.08]	8.3%	8.3%

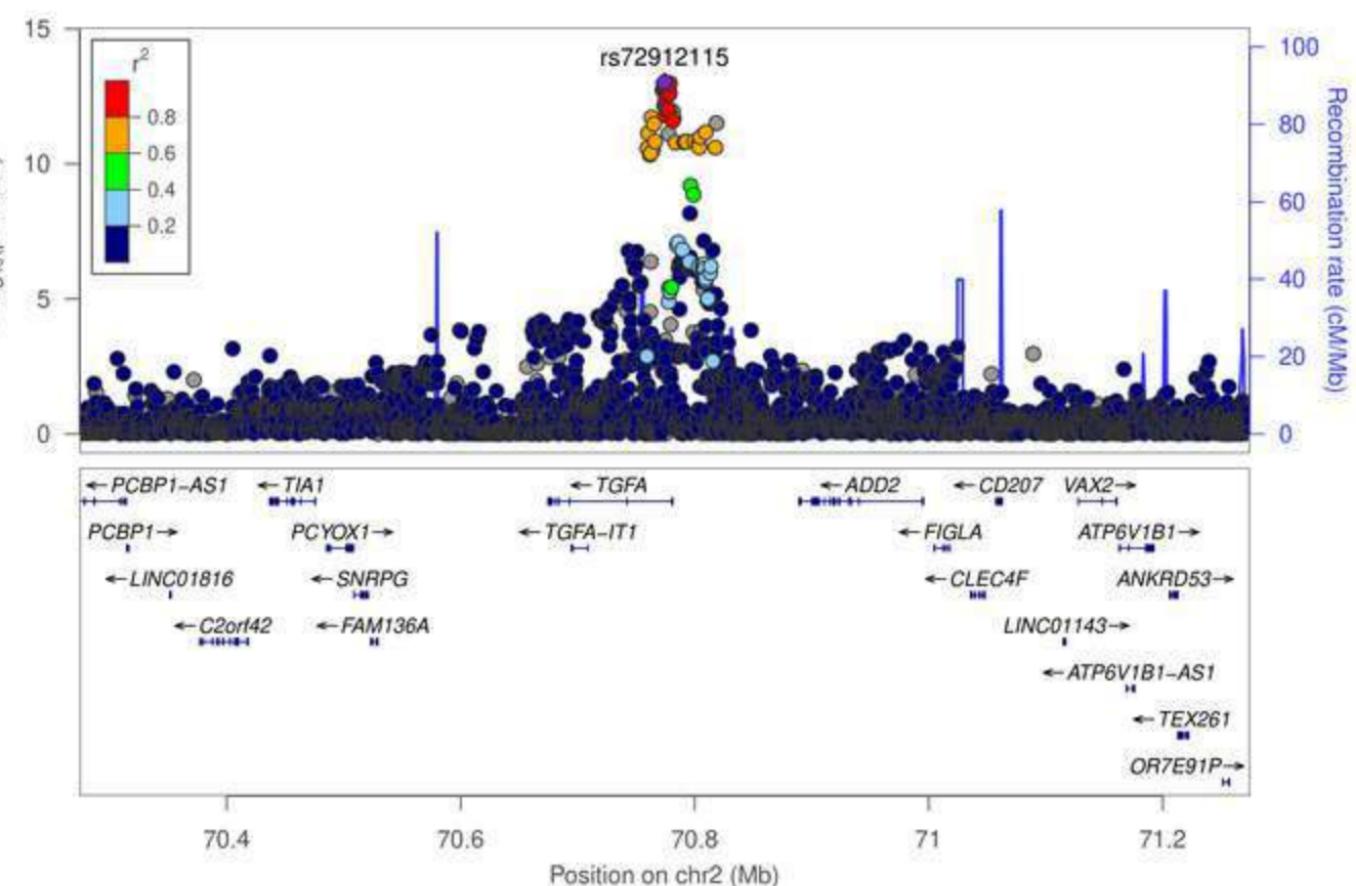
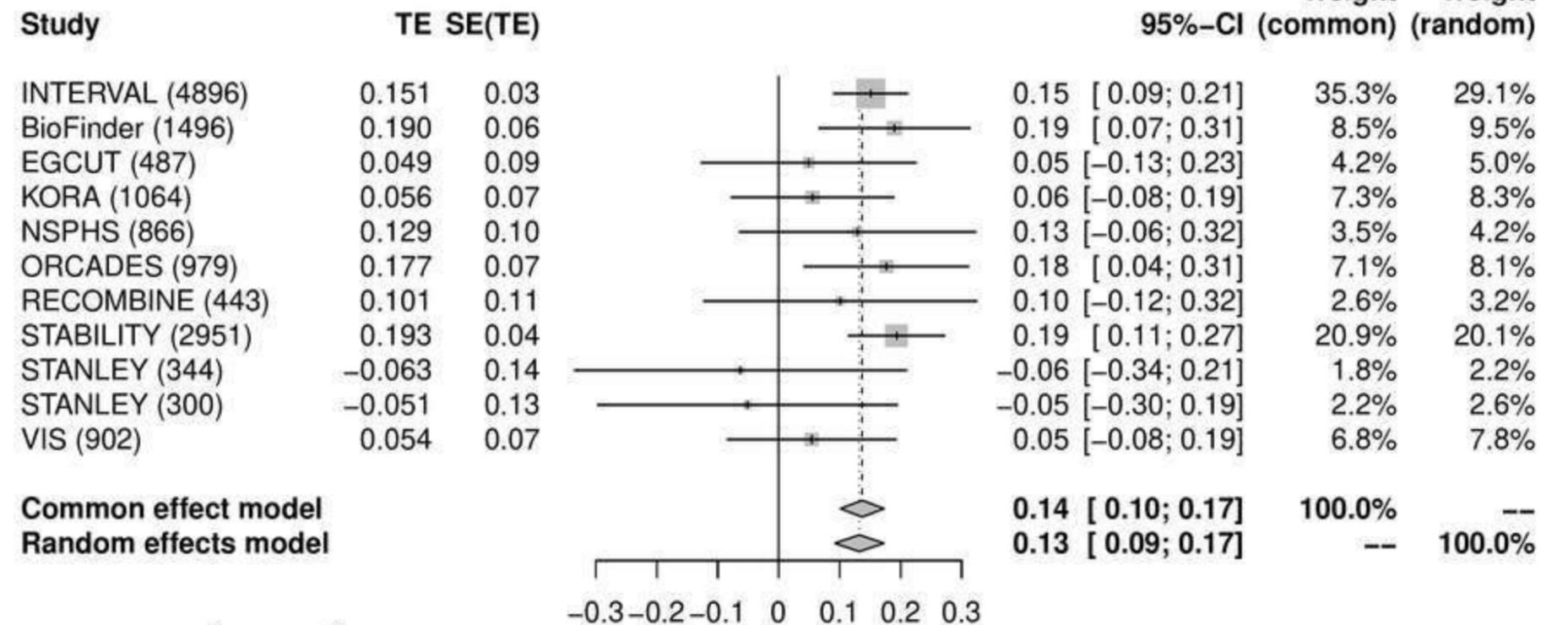
**Common effect model  
Random effects model**

Heterogeneity:  $I^2 = 0\%$ ,  $\tau^2 = 0$ ,  $p = 0.65$



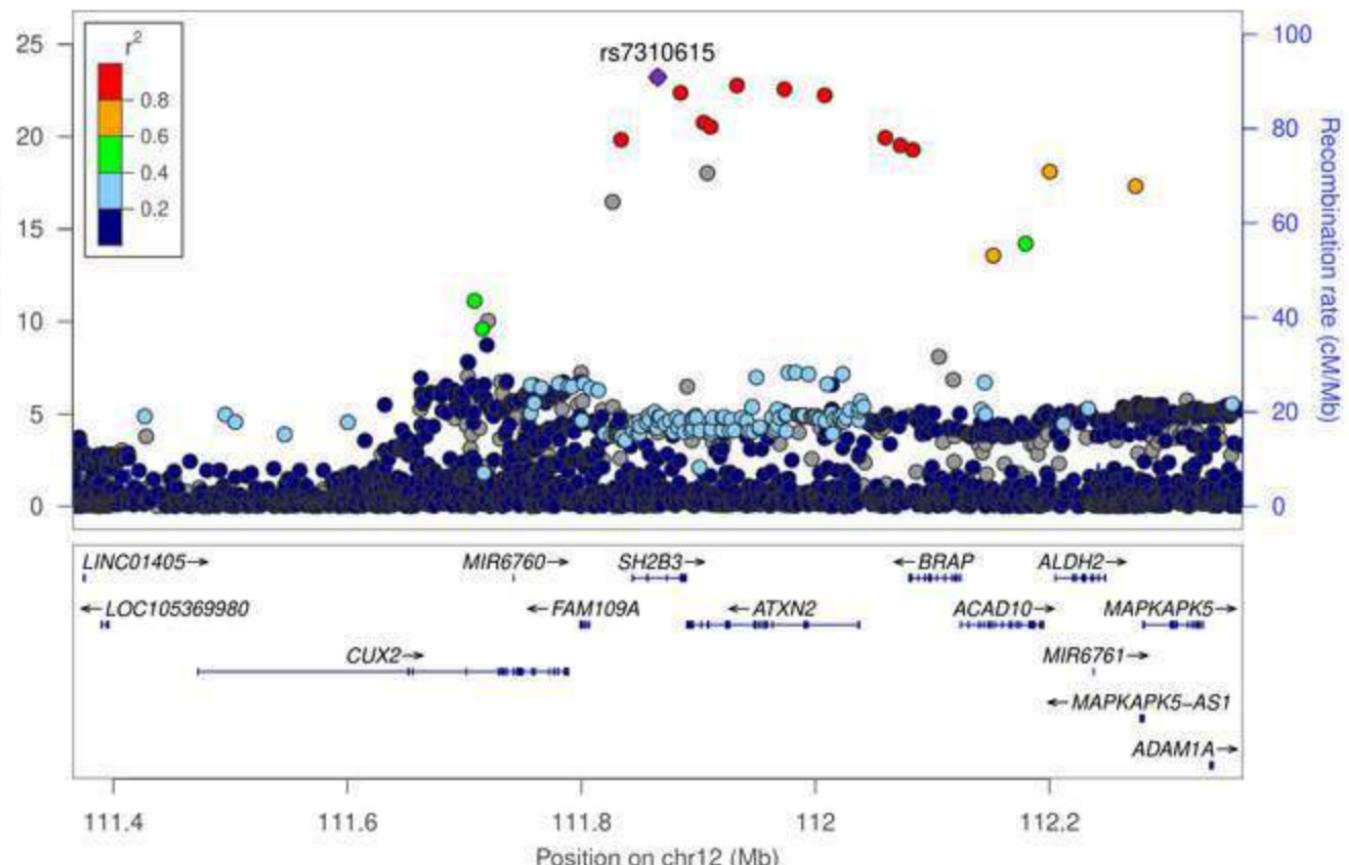
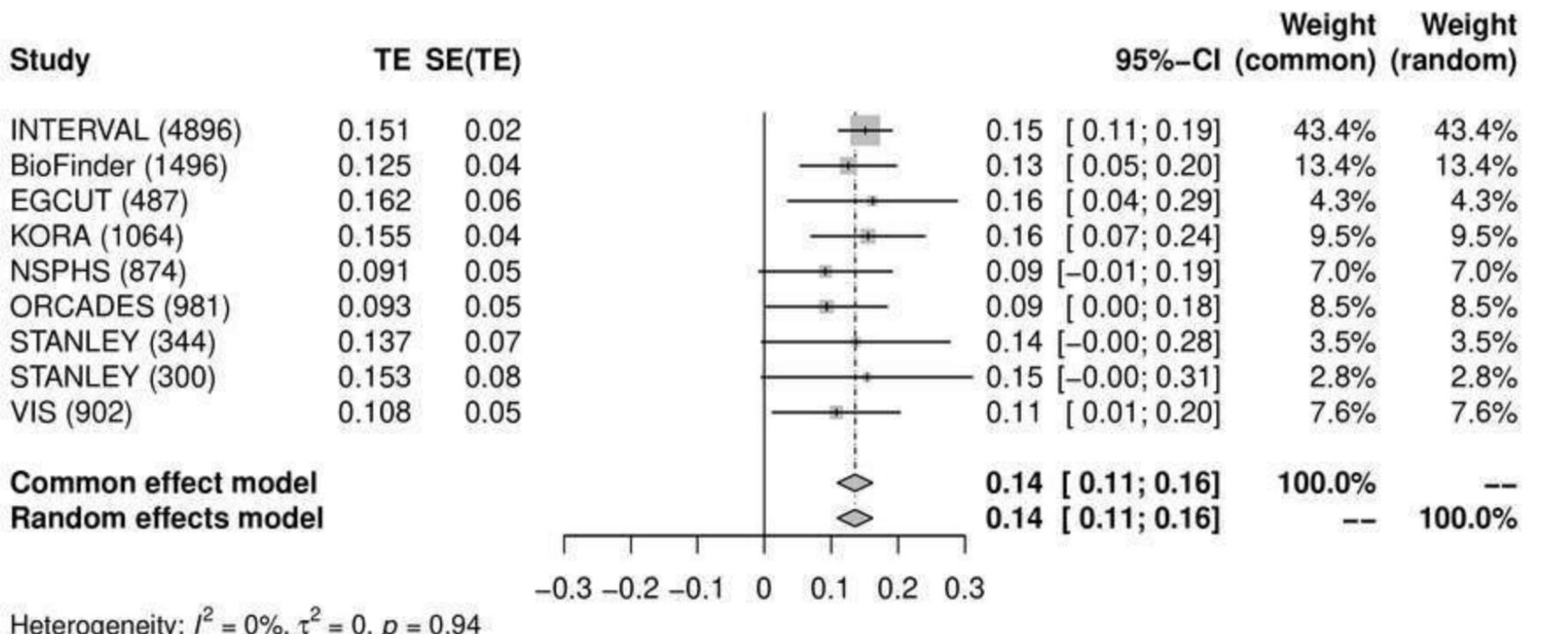
# TGF-alpha (TGFA)-rs72912115

TGF-alpha (TGFA) [chr2:70774295\_A\_T (rs72912115) (A/T) N=14728]



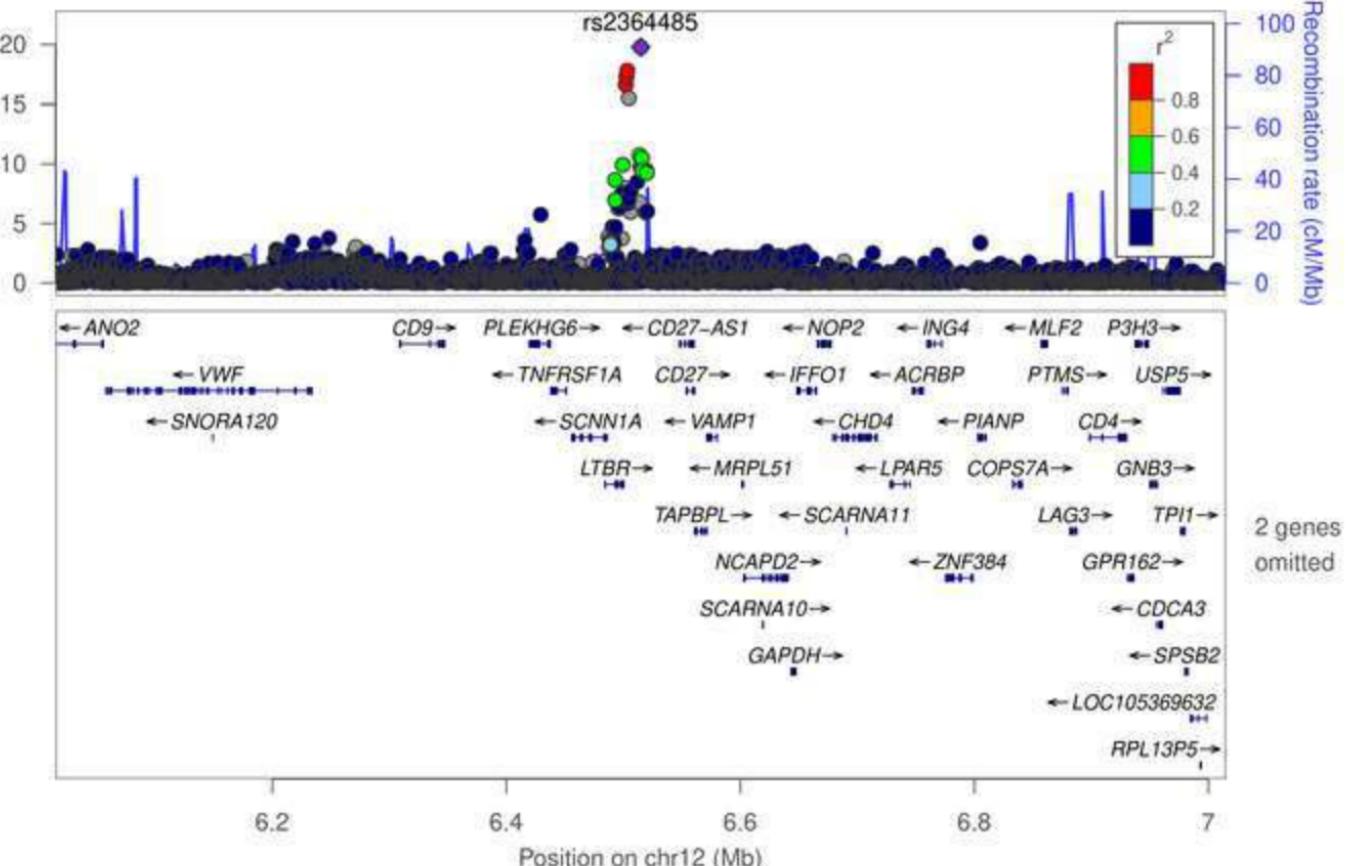
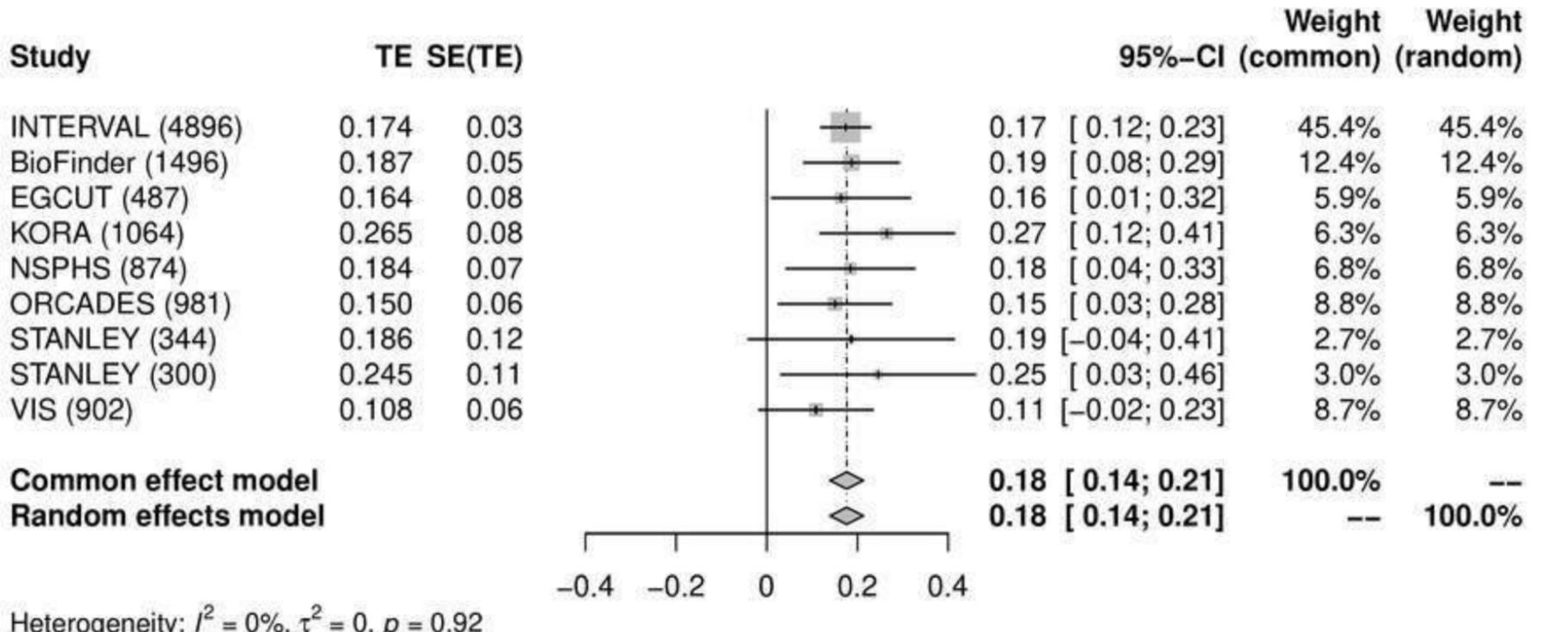
# TNFB (LTA)-rs7310615

TNFB (LTA) [chr12:111865049\_C\_G (rs7310615) (C/G) N=11344]

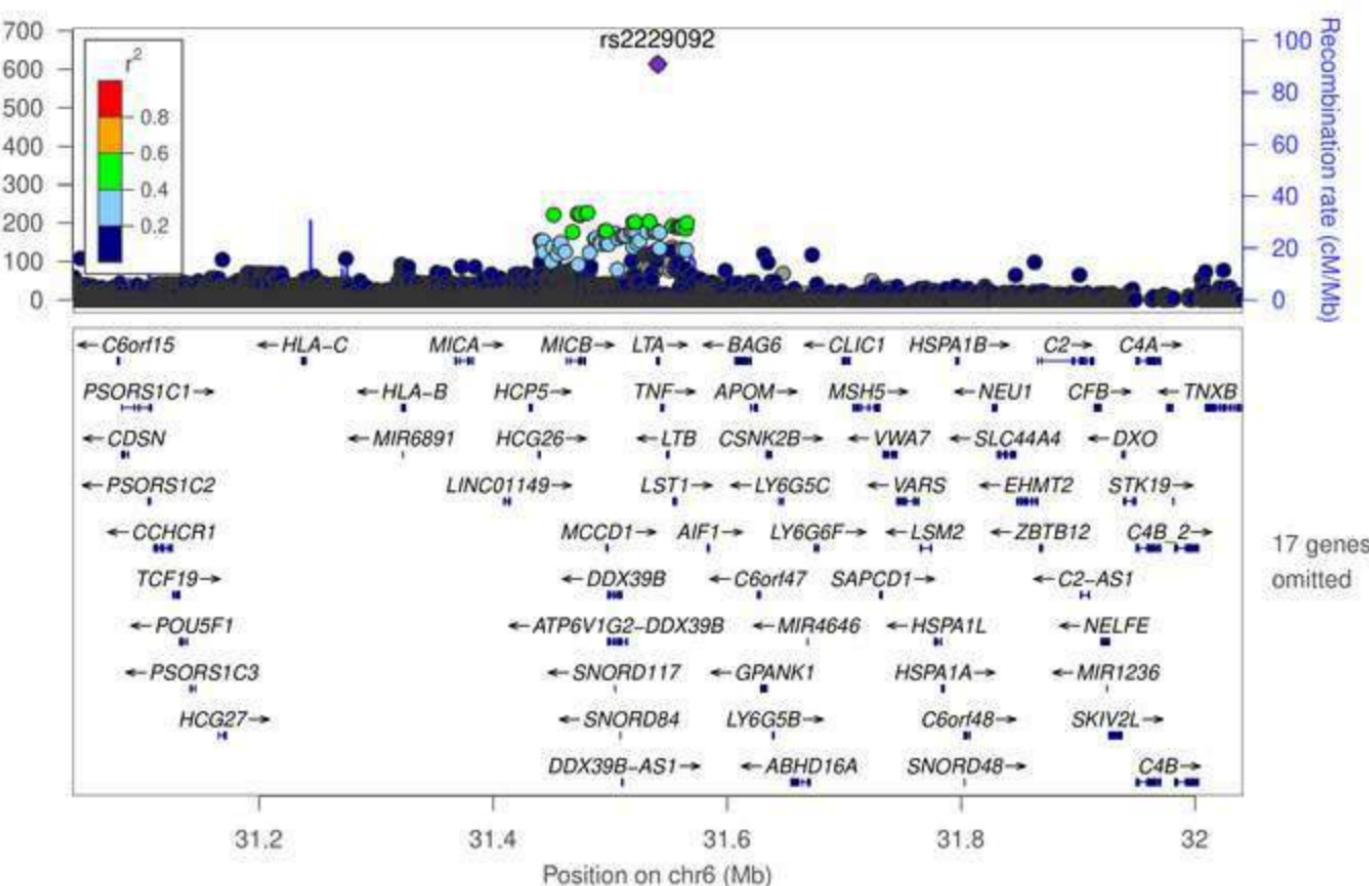
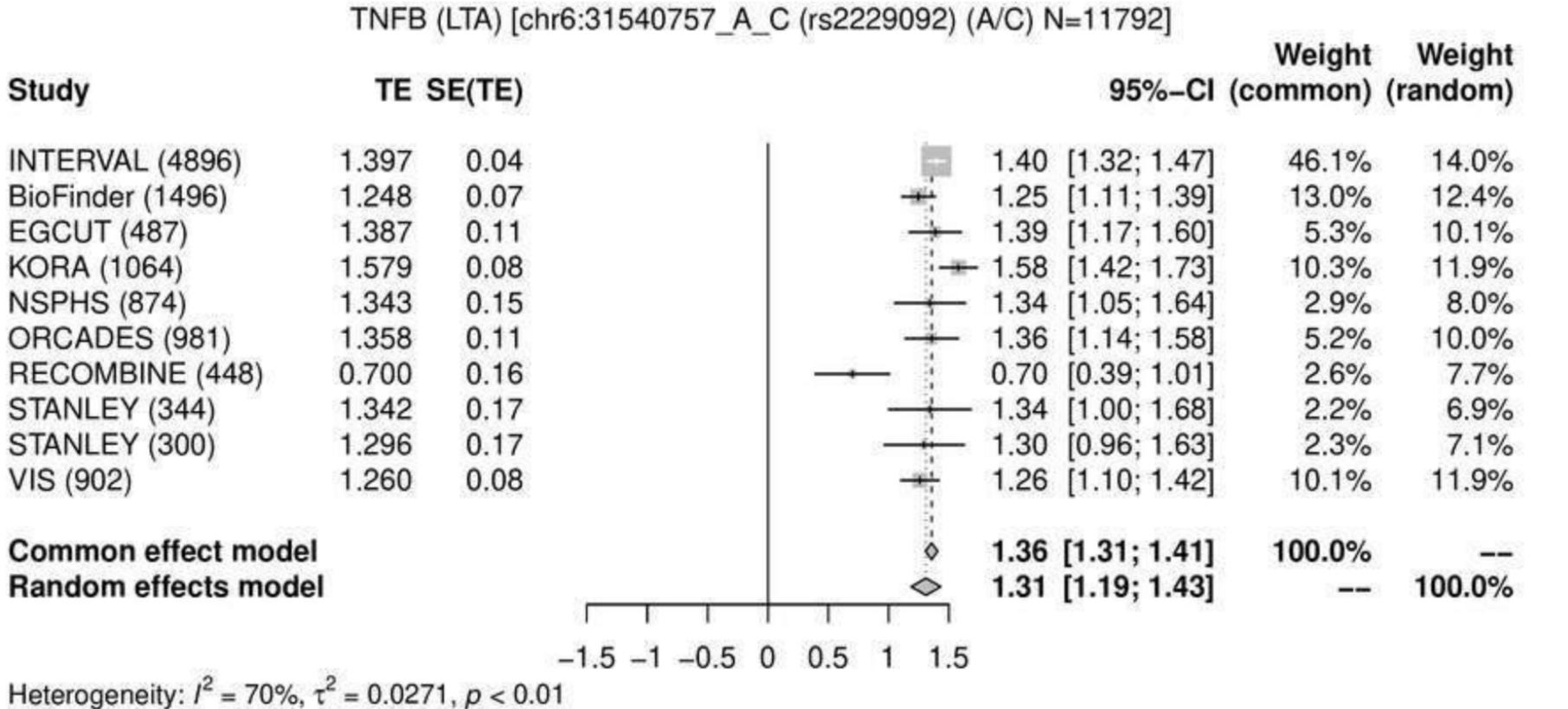


# TNFB (LTA)-rs2364485

TNFB (LTA) [chr12:6514963\_A\_C (rs2364485) (A/C) N=11344]

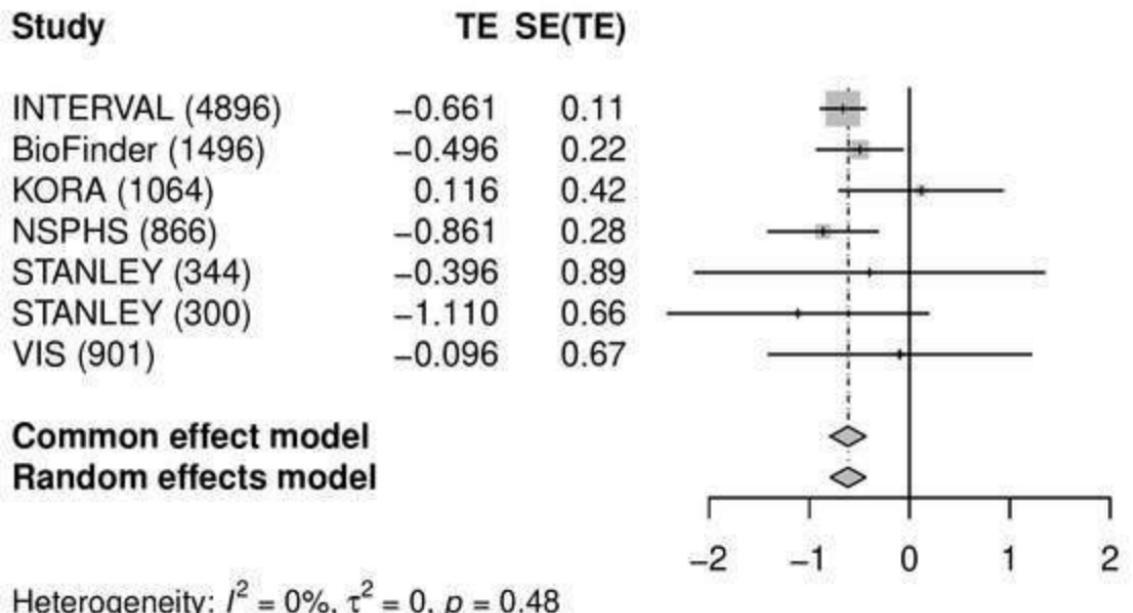


# TNFB (LTA)-rs2229092

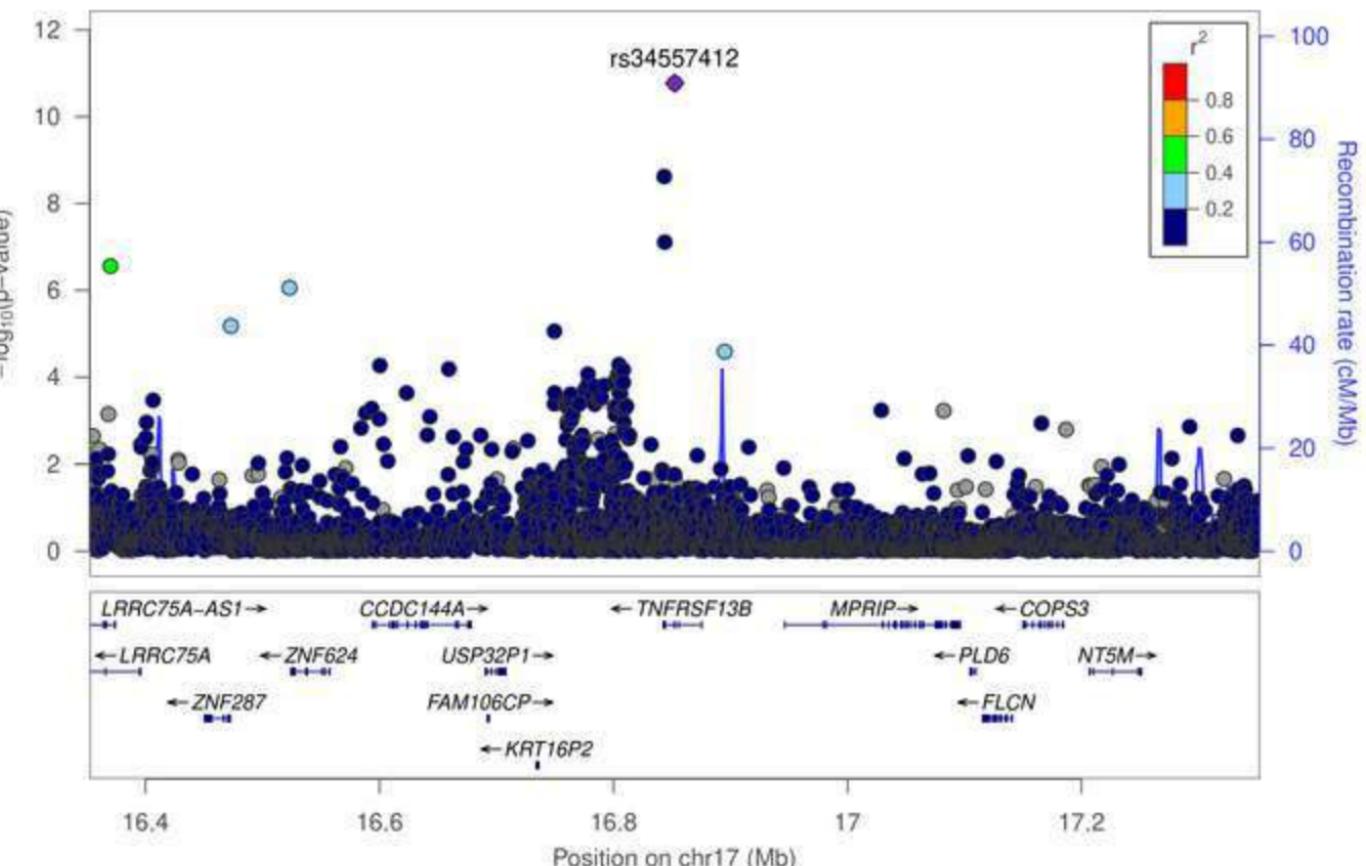


# TNFRSF9 (TNFRSF9)-rs34557412

TNFRSF9 (TNFRSF9) [chr17:16852187\_A\_G (rs34557412) (A/G) N=9867]

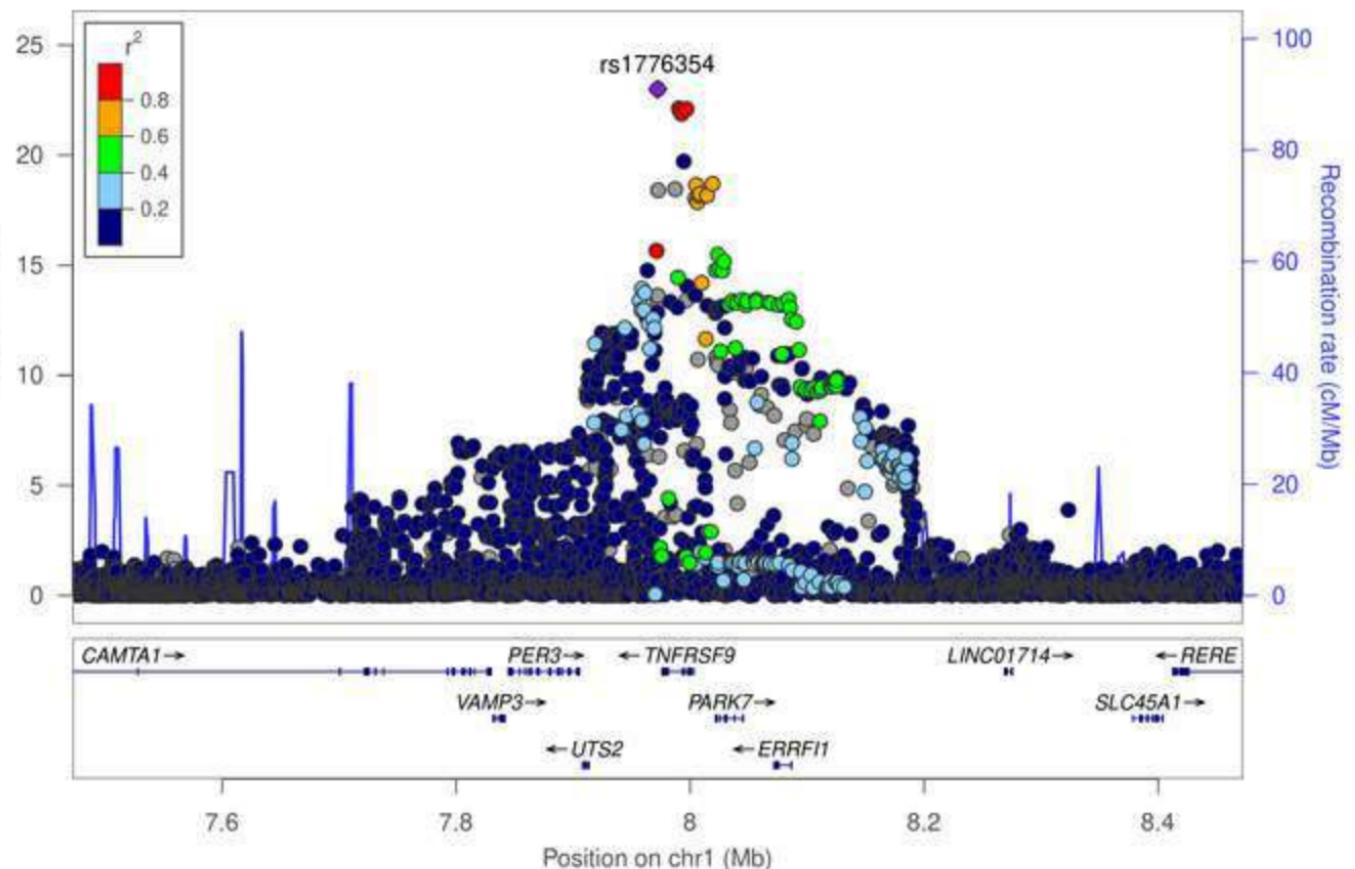
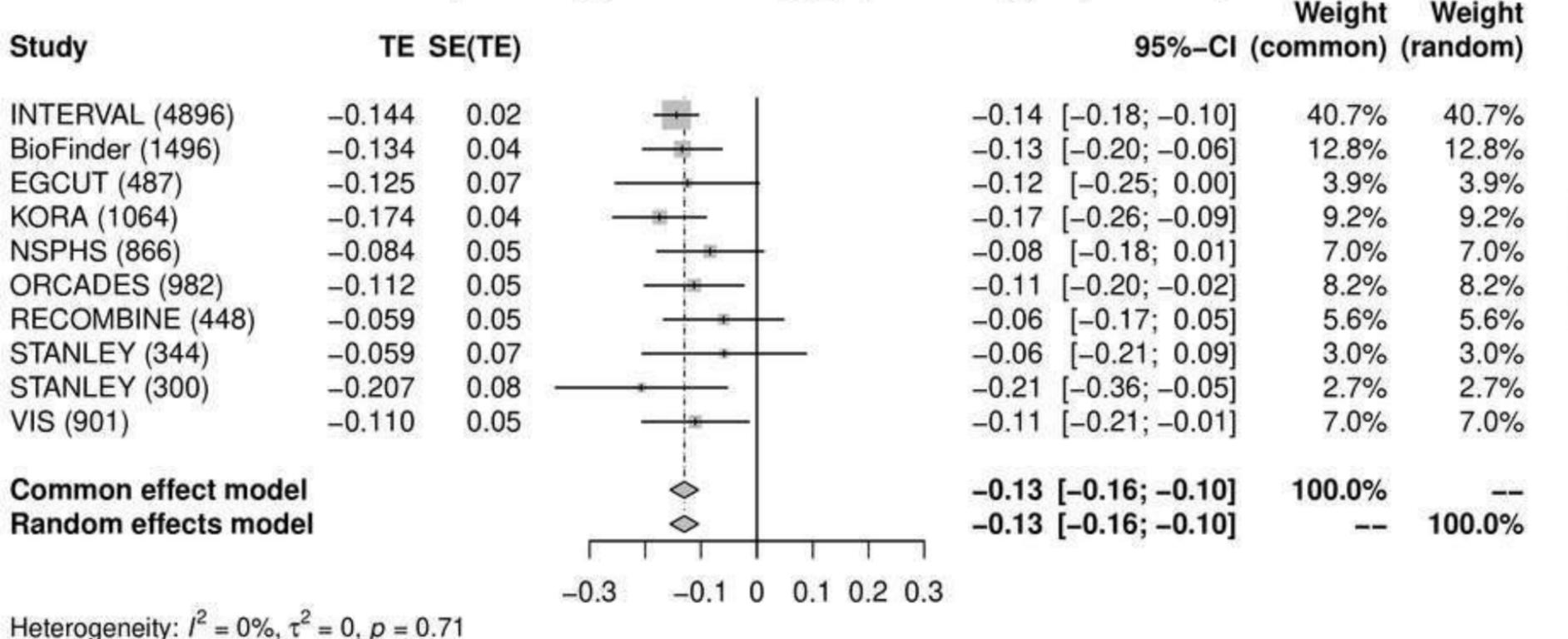


	Weight	Weight
	95%-CI (common)	(random)
-0.66 [-0.89; -0.44]	62.7%	62.7%
-0.50 [-0.93; -0.07]	17.2%	17.2%
0.12 [-0.70; 0.93]	4.7%	4.7%
-0.86 [-1.41; -0.31]	10.6%	10.6%
-0.40 [-2.14; 1.35]	1.0%	1.0%
-1.11 [-2.41; 0.19]	1.9%	1.9%
-0.10 [-1.41; 1.21]	1.9%	1.9%
<b>-0.61 [-0.79; -0.43]</b>	<b>100.0%</b>	--
<b>-0.61 [-0.79; -0.43]</b>	--	<b>100.0%</b>



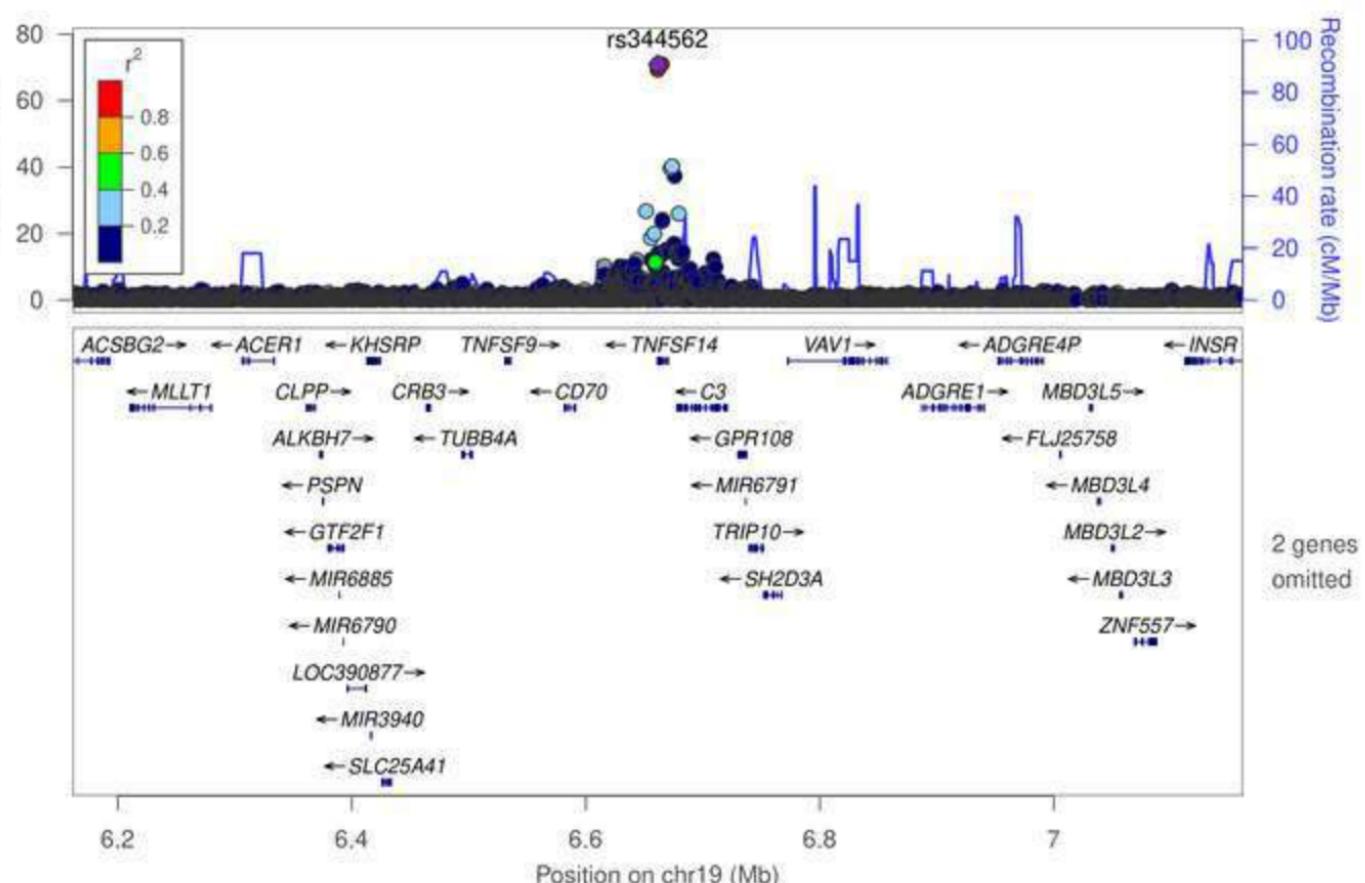
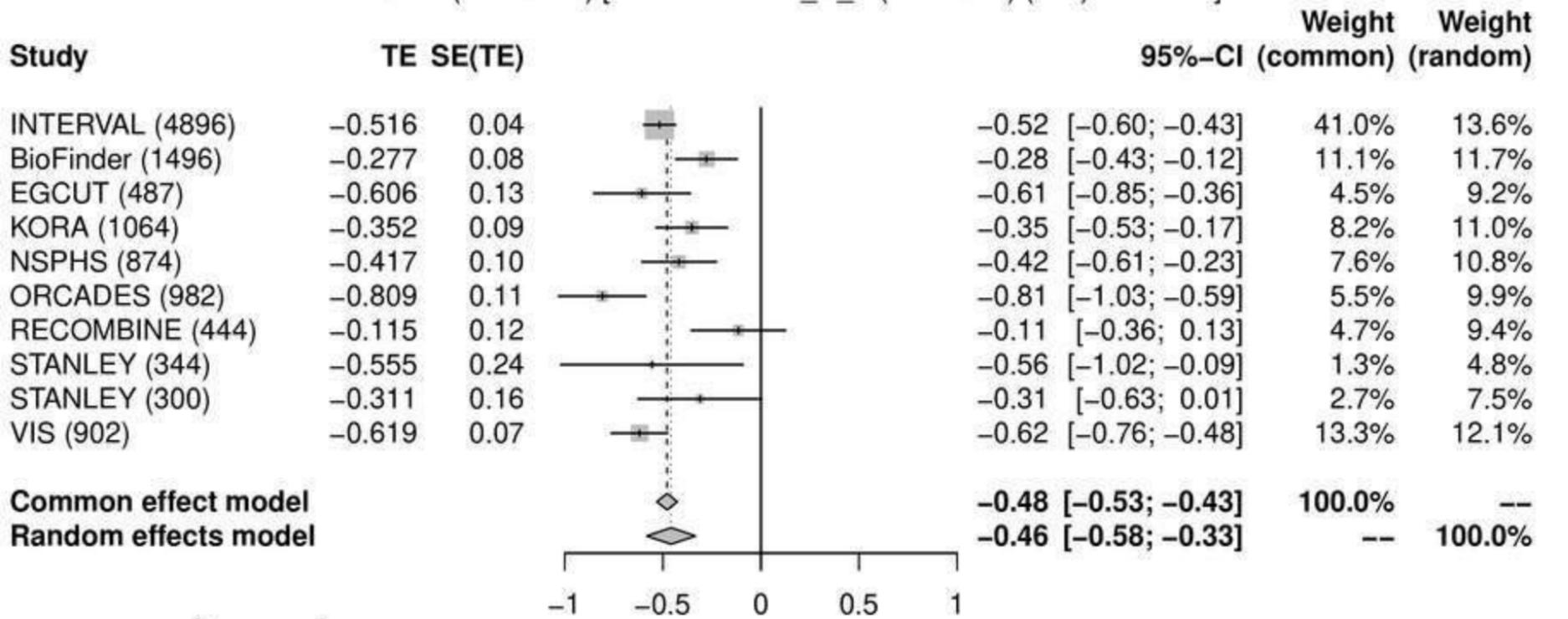
# TNFRSF9 (TNFRSF9)-rs1776354

TNFRSF9 (TNFRSF9) [chr1:7972201\_A\_G (rs1776354) (A/G) N=11784]



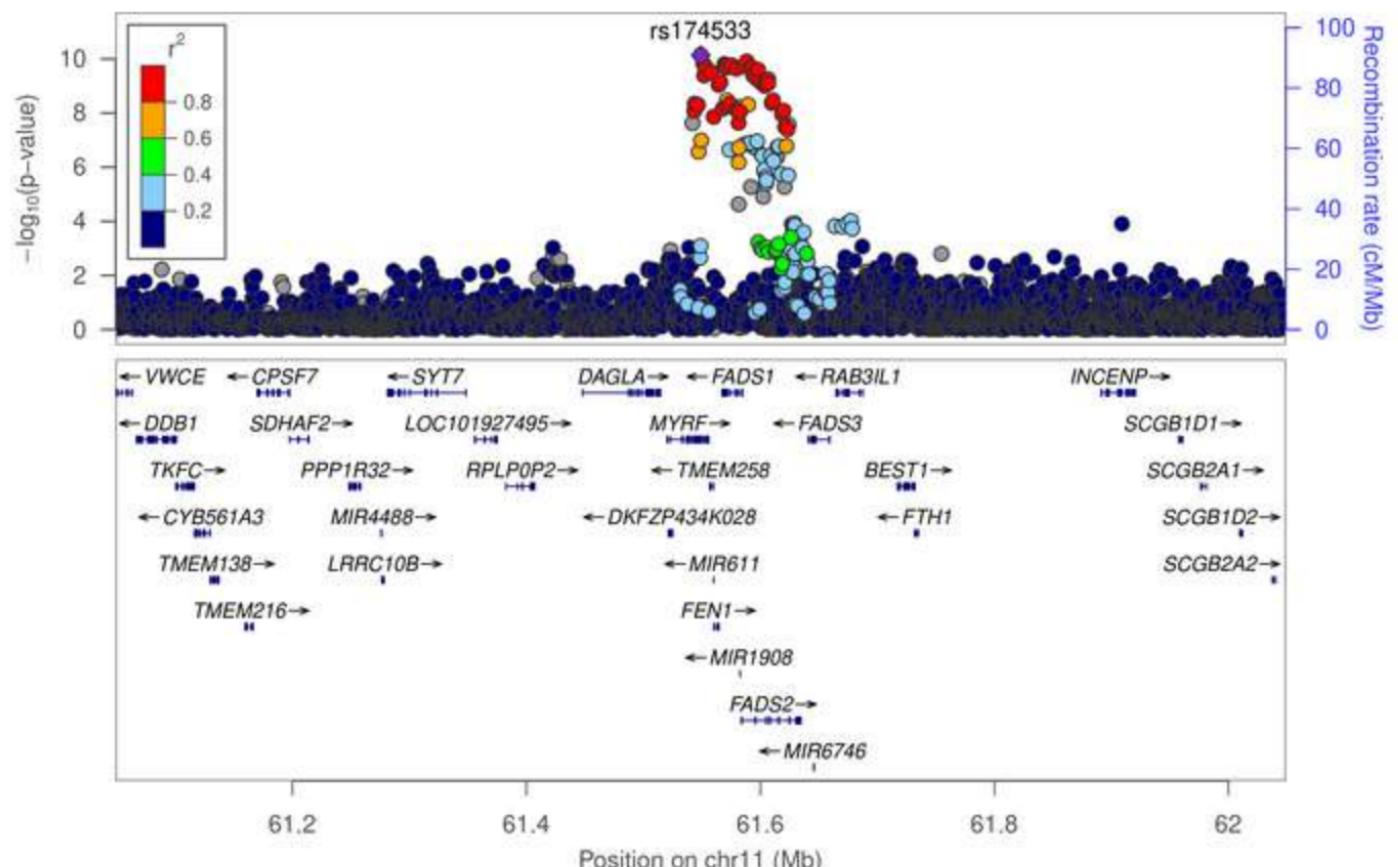
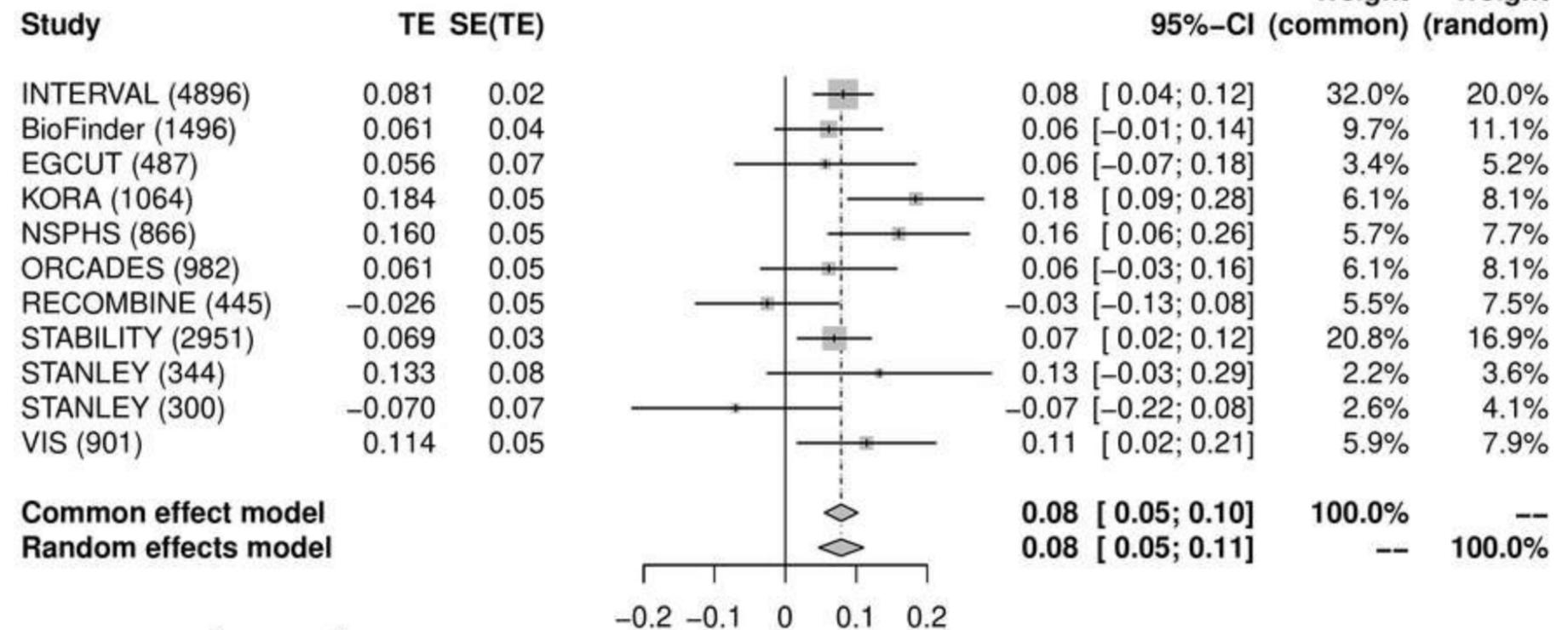
# TNFSF14 (TNFSF14)-rs344562

TNFSF14 (TNFSF14) [chr19:6661549\_C\_T (rs344562) (T/C) N=11789]

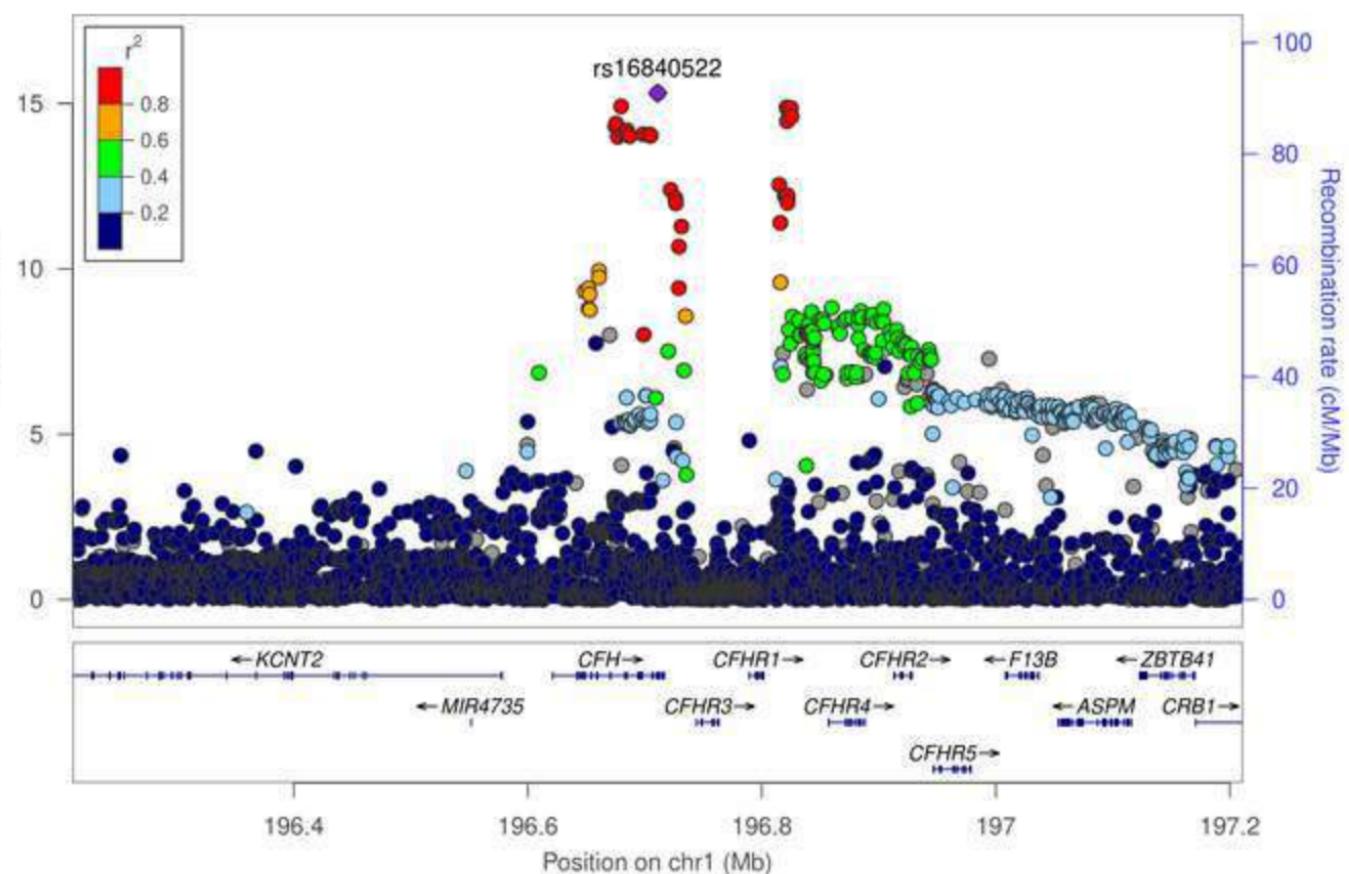
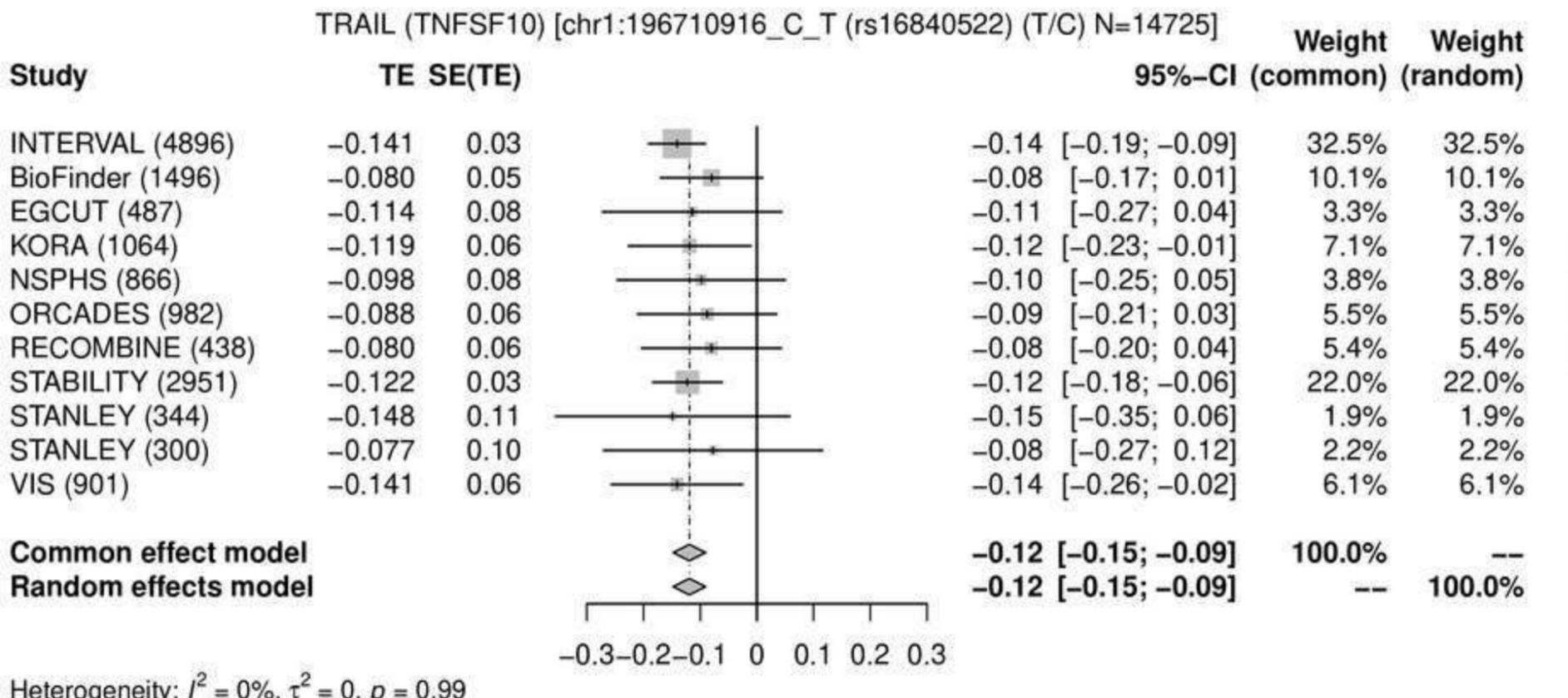


# TRAIL (TNFSF10)-rs174533

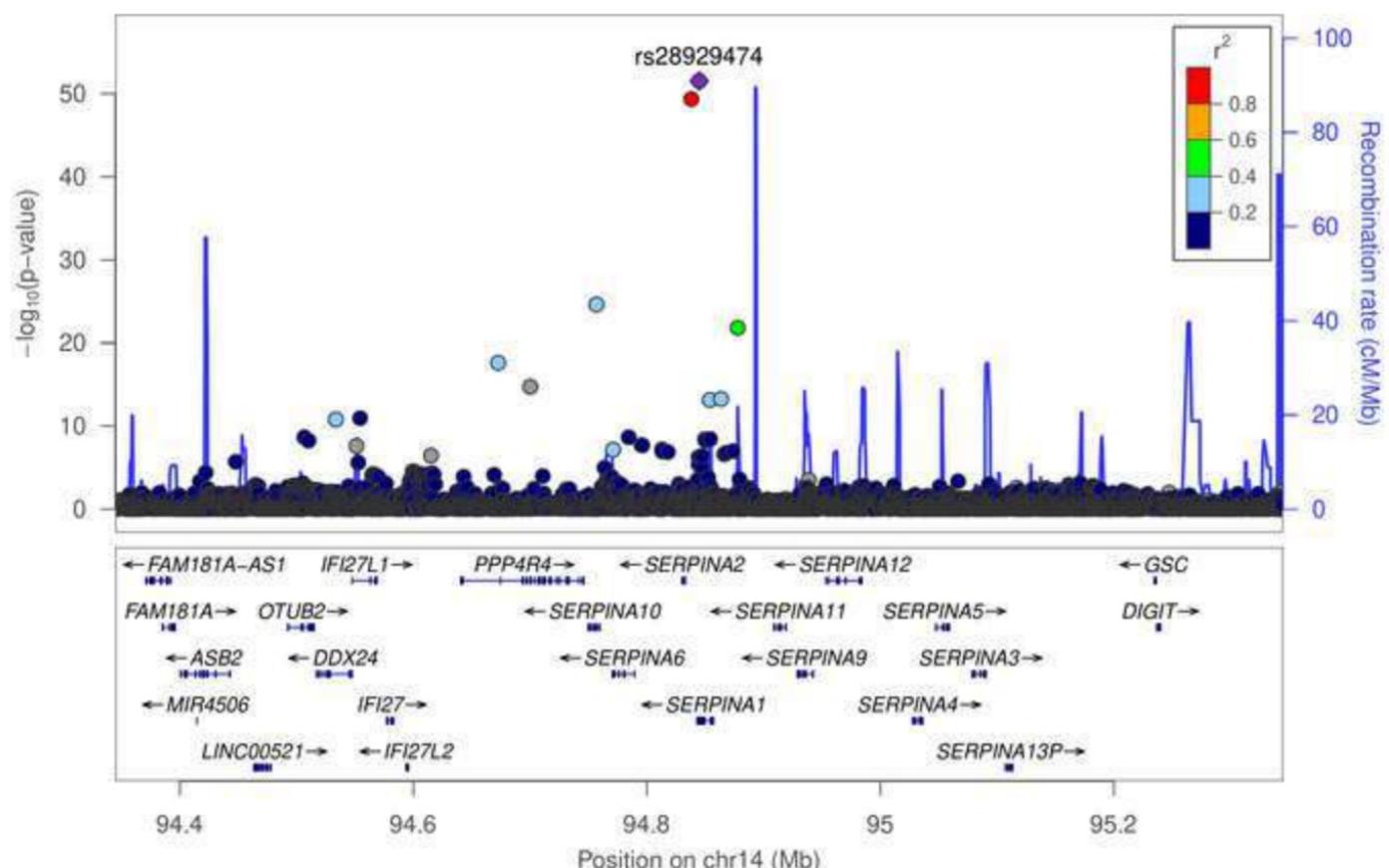
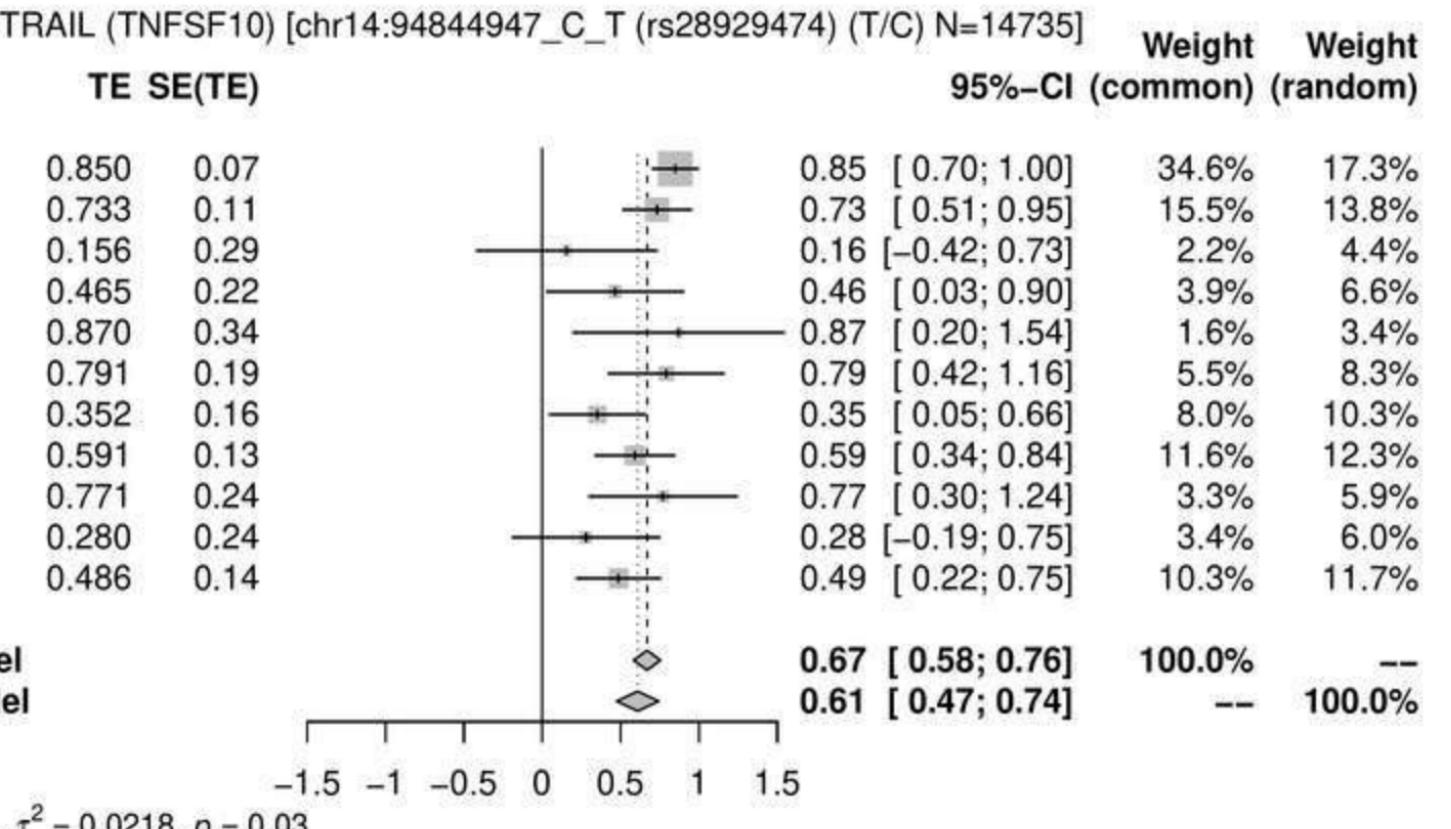
TRAIL (TNFSF10) [chr11:61549025\_A\_G (rs174533) (A/G) N=14732]



# TRAIL (TNFSF10)-rs16840522



# TRAIL (TNFSF10)-rs28929474



# TRAIL (TNFSF10)-rs8178824

TRAIL (TNFSF10) [chr17:64224775\_C\_T (rs8178824) (T/C) N=14735]

## Study

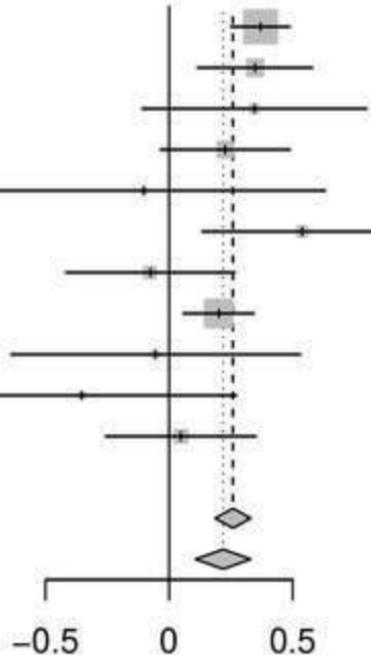
INTERVAL (4896)  
BioFinder (1496)  
EGCUT (487)  
KORA (1064)  
NSPHS (866)  
ORCADES (982)  
RECOMBINE (448)  
STABILITY (2951)  
STANLEY (344)  
STANLEY (300)  
VIS (901)

TE SE(TE)

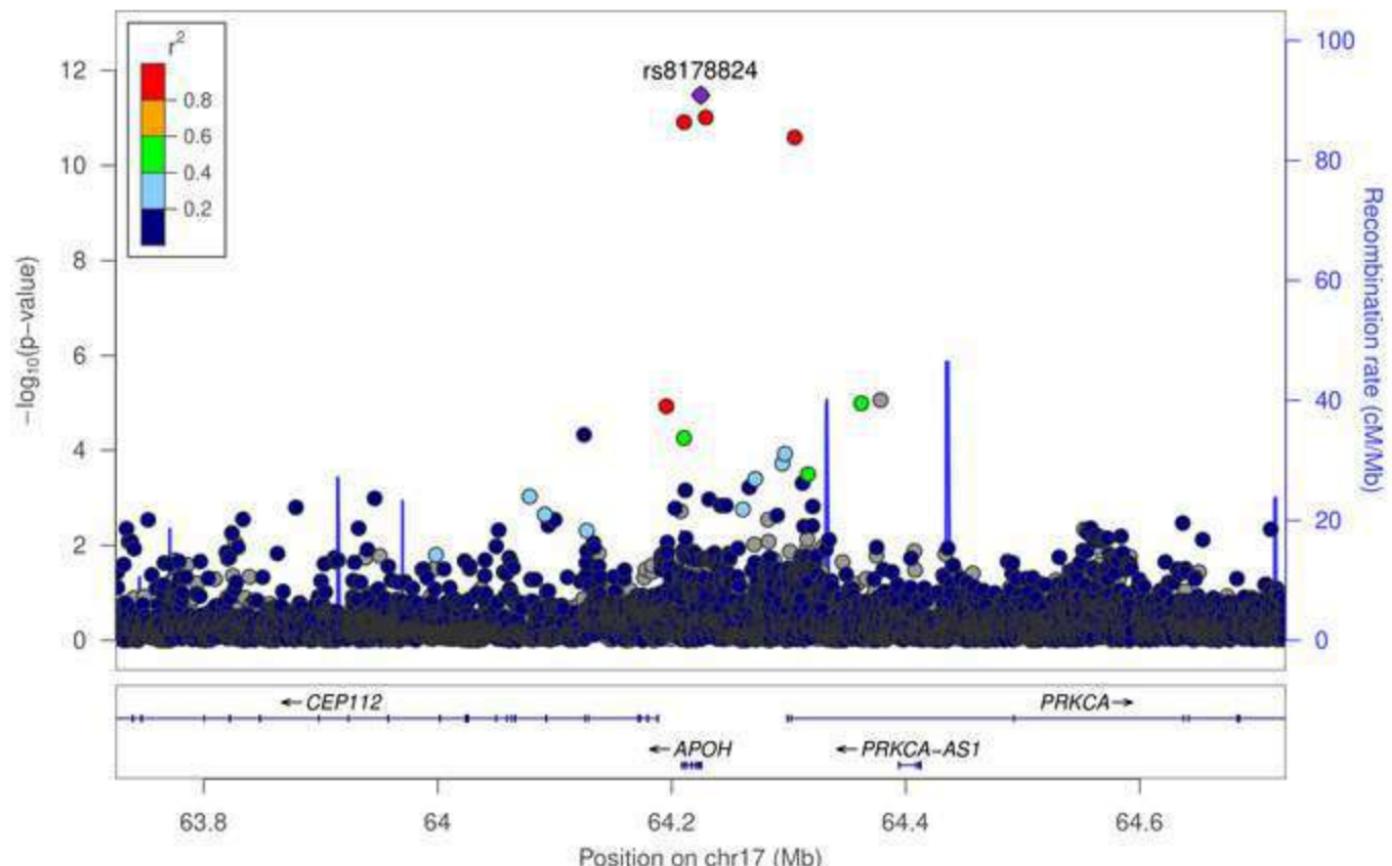
	TE	SE(TE)
INTERVAL (4896)	0.369	0.06
BioFinder (1496)	0.347	0.12
EGCUT (487)	0.344	0.23
KORA (1064)	0.226	0.13
NSPHS (866)	-0.104	0.37
ORCADES (982)	0.537	0.21
RECOMBINE (448)	-0.076	0.17
STABILITY (2951)	0.200	0.07
STANLEY (344)	-0.055	0.30
STANLEY (300)	-0.353	0.32
VIS (901)	0.047	0.15

Weight  
95%-CI (common) (random)

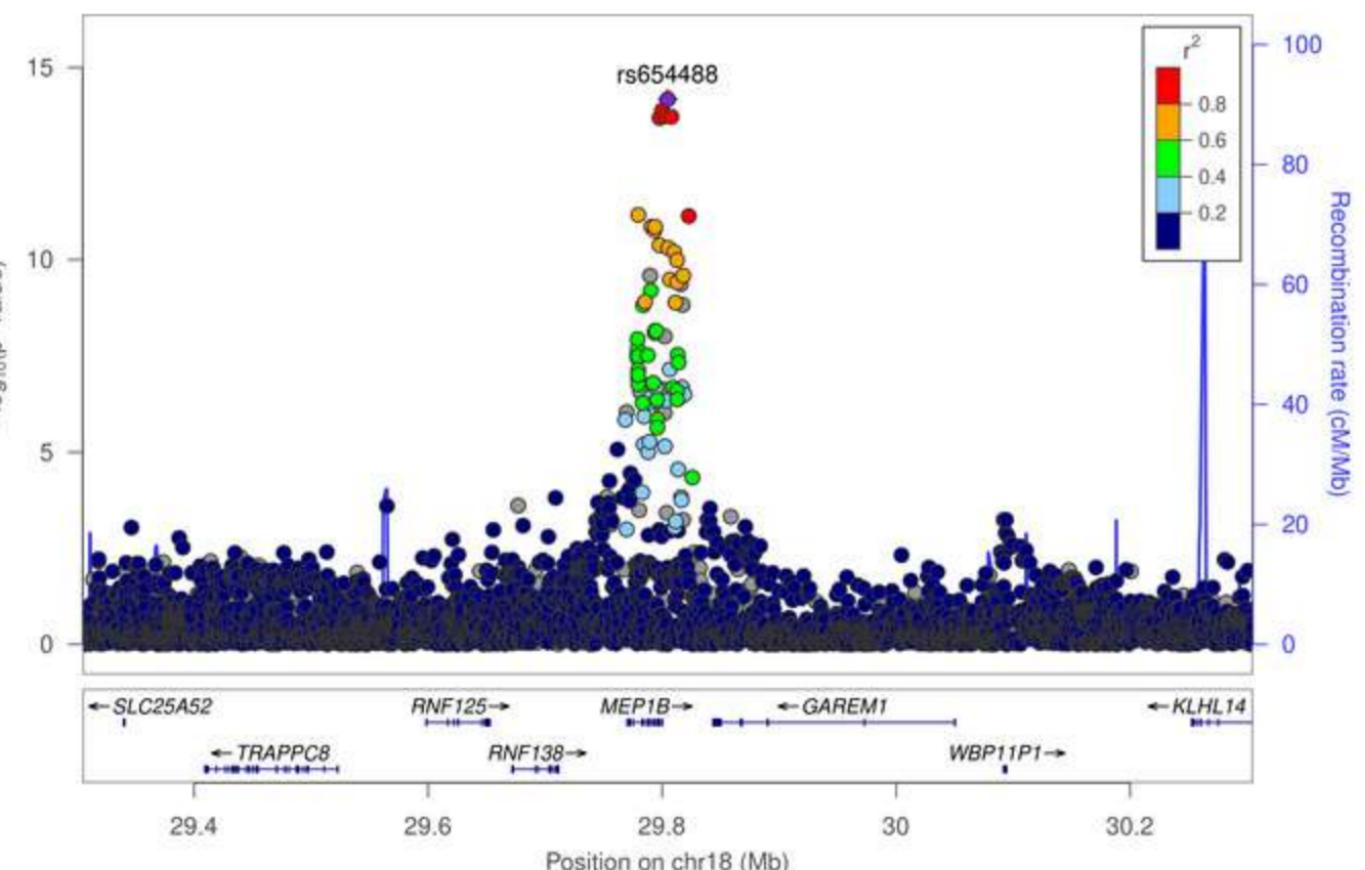
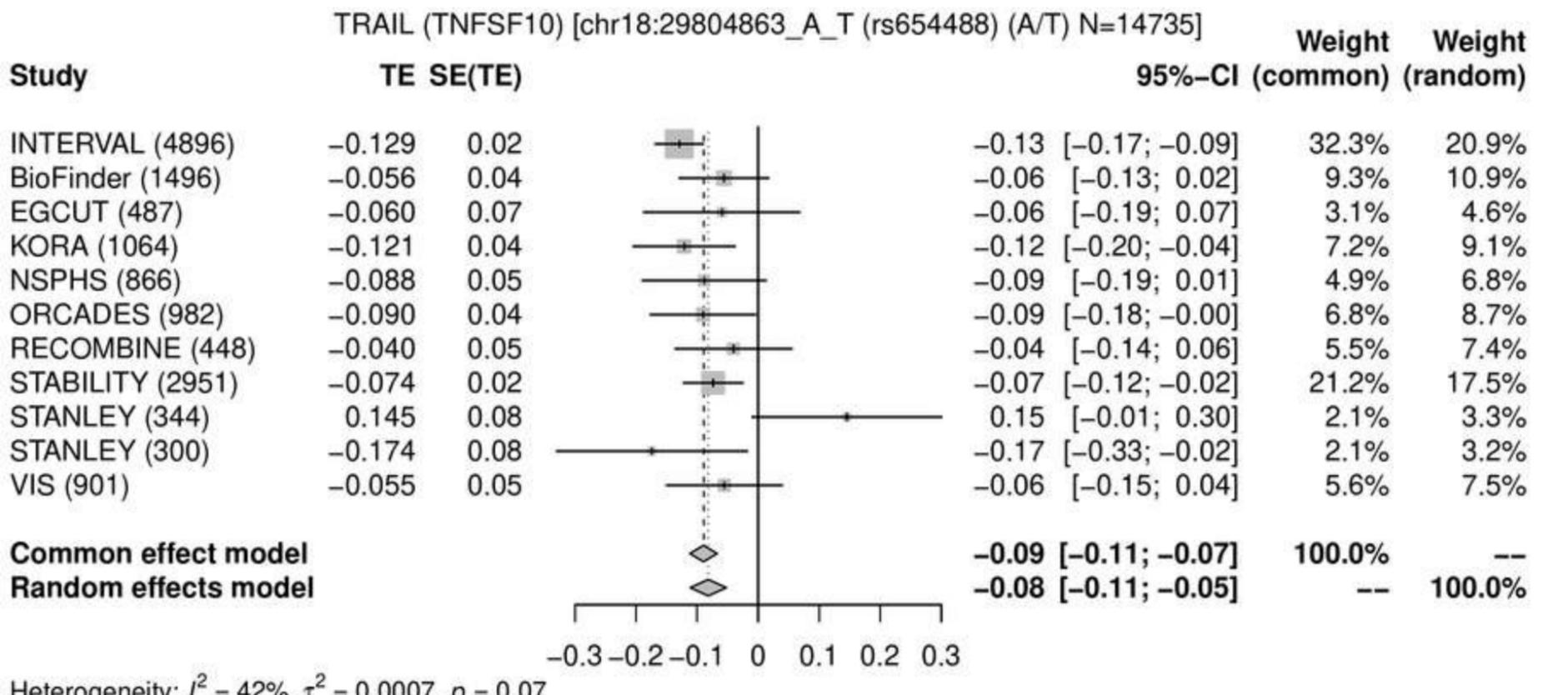
	95%-CI (common)	(random)
	0.37 [ 0.25; 0.49]	37.0% 21.0%
	0.35 [ 0.11; 0.58]	9.7% 12.6%
	0.34 [-0.11; 0.80]	2.5% 5.0%
	0.23 [-0.04; 0.49]	7.7% 11.0%
	-0.10 [-0.84; 0.63]	1.0% 2.2%
	0.54 [ 0.13; 0.94]	3.2% 6.0%
	-0.08 [-0.42; 0.27]	4.5% 7.8%
	0.20 [ 0.06; 0.34]	25.9% 19.1%
	-0.06 [-0.64; 0.53]	1.5% 3.3%
	-0.35 [-0.98; 0.27]	1.3% 2.9%
	0.05 [-0.26; 0.35]	5.7% 9.1%
<b>Common effect model</b>	<b>0.26 [ 0.18; 0.33]</b>	<b>100.0%</b>
<b>Random effects model</b>	<b>0.22 [ 0.11; 0.33]</b>	<b>--</b>
		<b>100.0%</b>



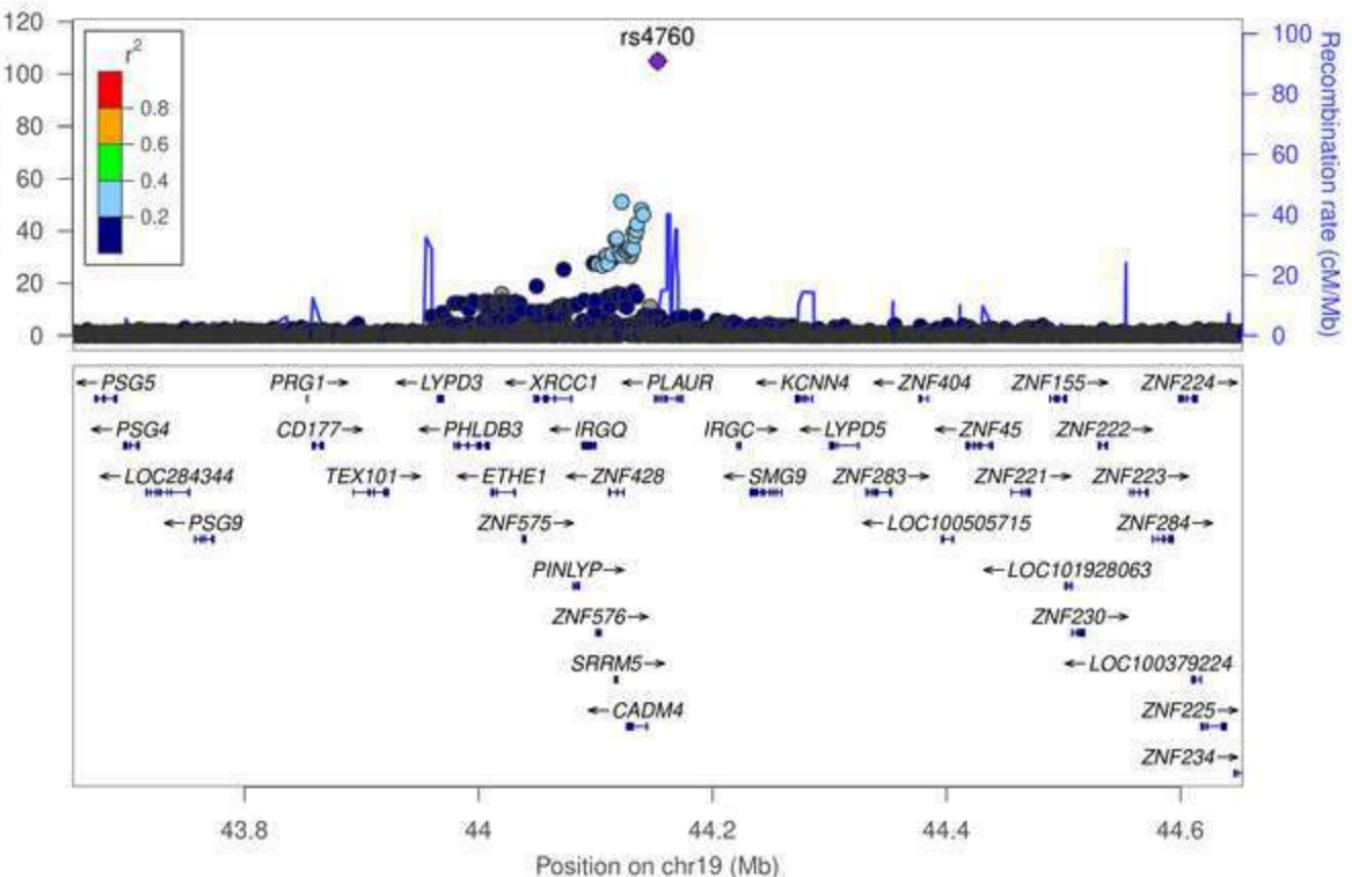
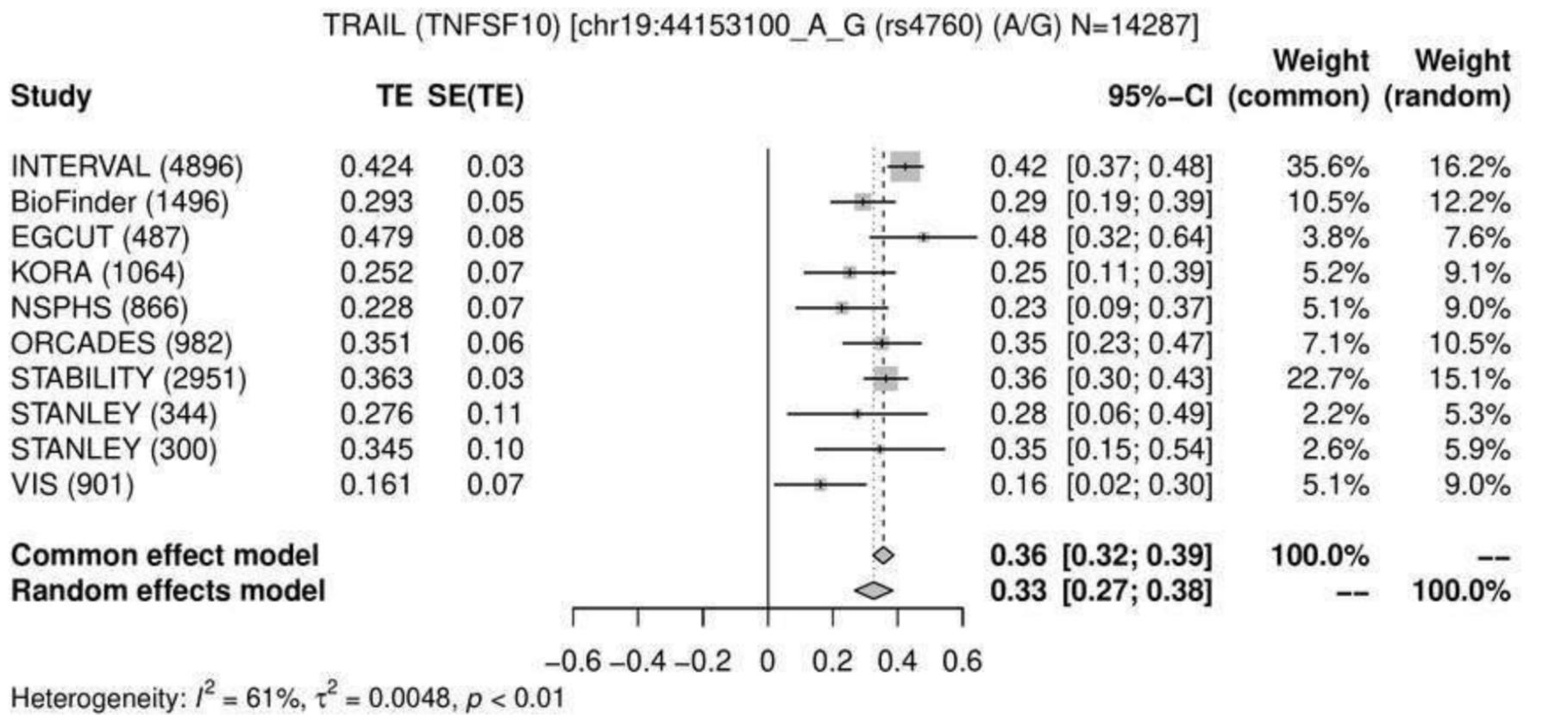
Heterogeneity:  $I^2 = 44\%$ ,  $\tau^2 = 0.0120$ ,  $p = 0.06$



# TRAIL (TNFSF10)-rs654488



# TRAIL (TNFSF10)-rs4760



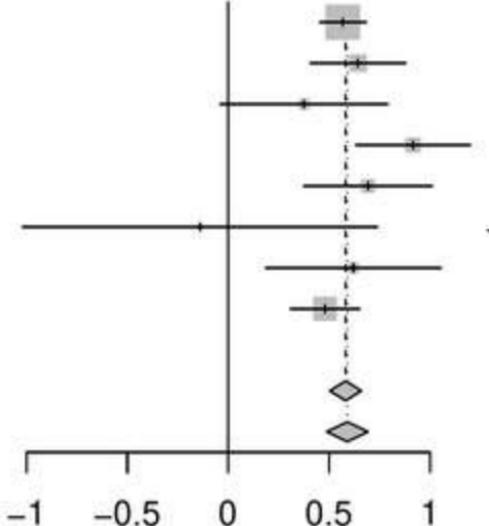
# TRAIL (TNFSF10)-rs574044675

TRAIL (TNFSF10) [chr3:172274232\_A\_C (rs574044675) (A/C) N=13173]

## Study

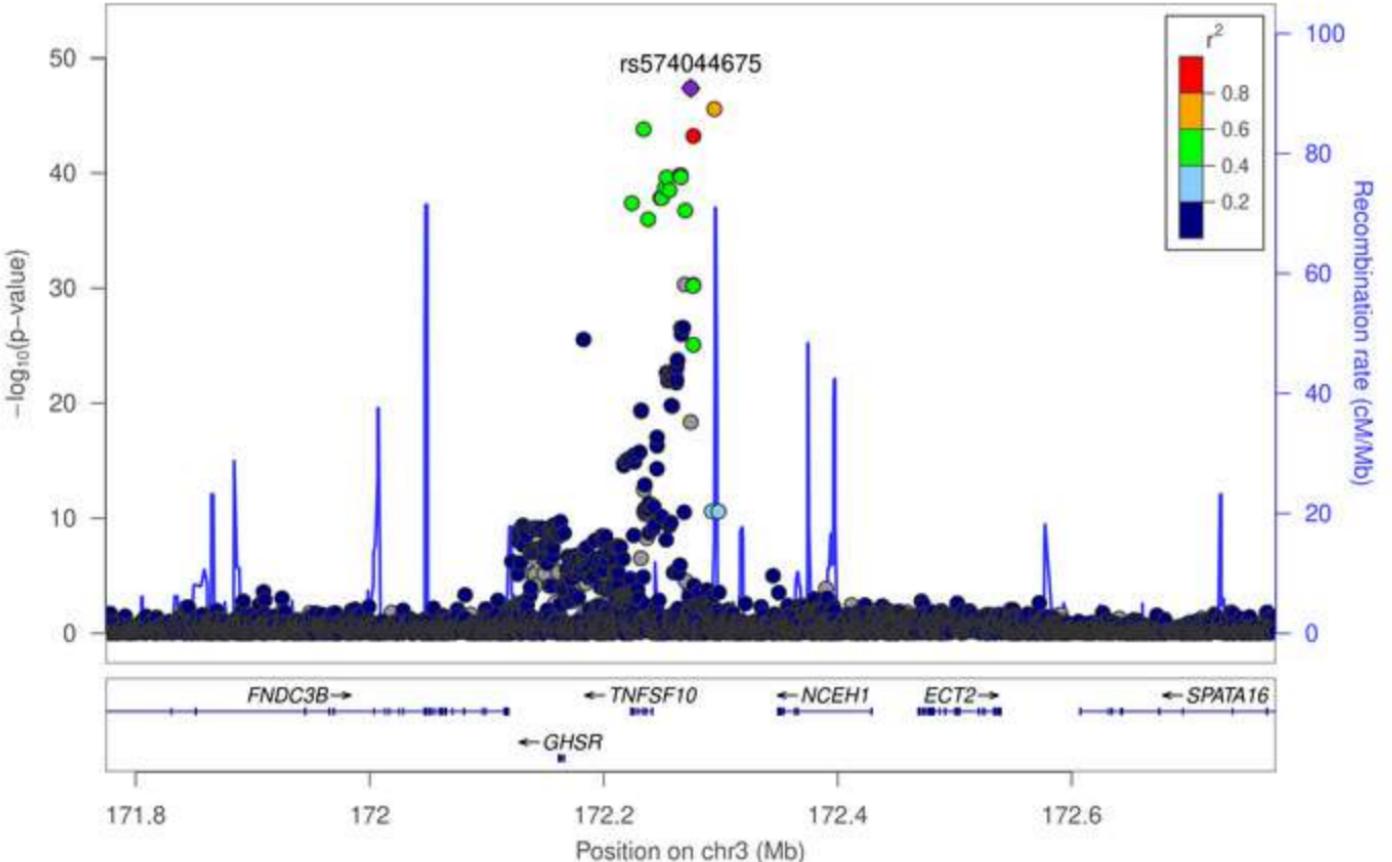
	TE	SE(TE)
INTERVAL (4896)	0.569	0.06
BioFinder (1496)	0.644	0.12
EGCUT (487)	0.376	0.21
KORA (1064)	0.916	0.14
NSPHS (866)	0.693	0.16
ORCADES (982)	-0.140	0.45
RECOMBINE (431)	0.620	0.22
STABILITY (2951)	0.480	0.09

TE SE(TE)



	Weight 95%-CI (common)	Weight (random)
INTERVAL (4896)	46.8% [ 0.45; 0.68]	32.7%
BioFinder (1496)	11.0% [ 0.41; 0.88]	14.1%
EGCUT (487)	3.6% [-0.04; 0.79]	5.5%
KORA (1064)	7.6% [ 0.63; 1.20]	10.7%
NSPHS (866)	6.1% [ 0.38; 1.01]	8.8%
ORCADES (982)	0.8% [-1.02; 0.74]	1.3%
RECOMBINE (431)	3.3% [ 0.19; 1.05]	5.1%
STABILITY (2951)	20.9% [ 0.31; 0.65]	21.8%
<b>Common effect model</b>	<b>0.58 [ 0.50; 0.66]</b>	--
<b>Random effects model</b>	<b>0.59 [ 0.49; 0.69]</b>	<b>--</b>

Heterogeneity:  $I^2 = 37\%, \tau^2 = 0.0050, p = 0.14$



# TRAIL (TNFSF10)-rs5030044

TRAIL (TNFSF10) [chr3:186449122\_A\_G (rs5030044) (A/G) N=14287]

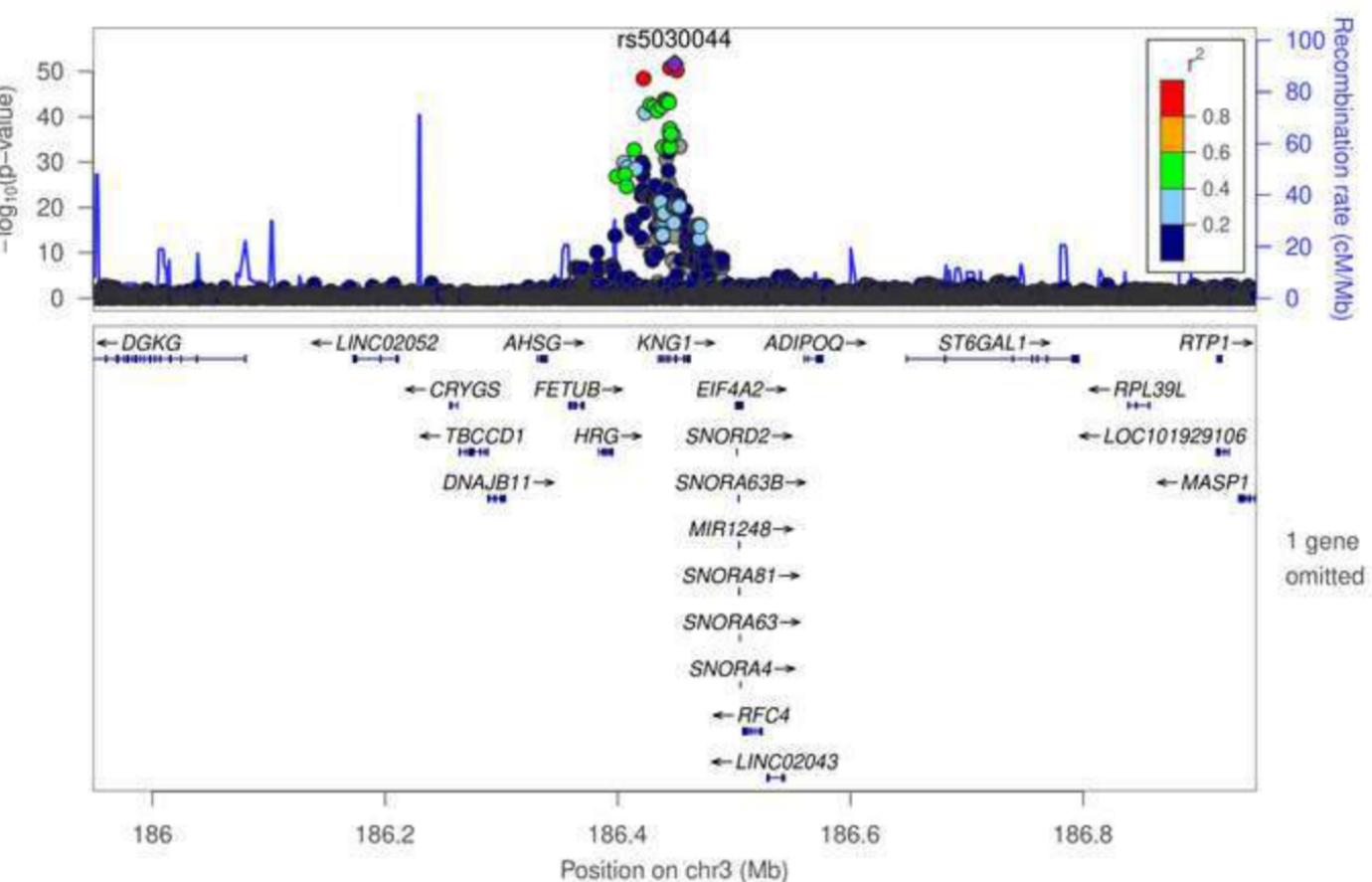
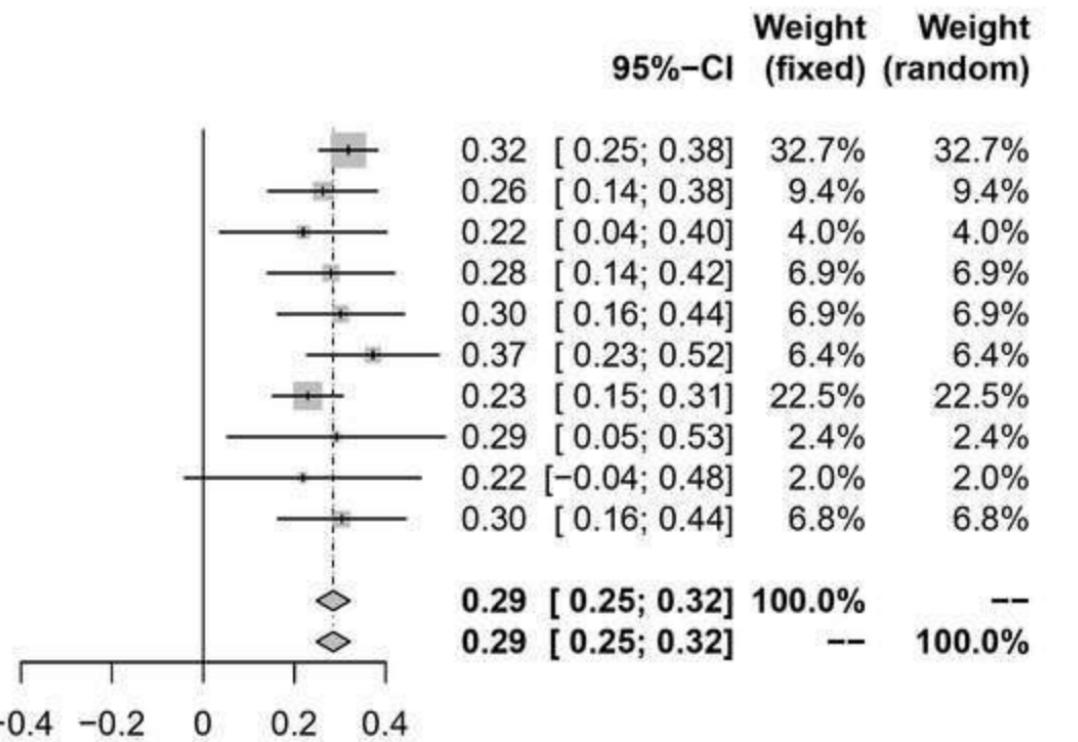
## Study

	TE	seTE
INTERVAL (4896)	0.32	0.0327
BioFinder (1496)	0.26	0.0611
EGCUT (487)	0.22	0.0935
KORA (1064)	0.28	0.0711
NSPHS (866)	0.30	0.0710
ORCADES (982)	0.37	0.0738
STABILITY (2951)	0.23	0.0394
STANLEY (344)	0.29	0.1219
STANLEY (300)	0.22	0.1322
VIS (901)	0.30	0.0717

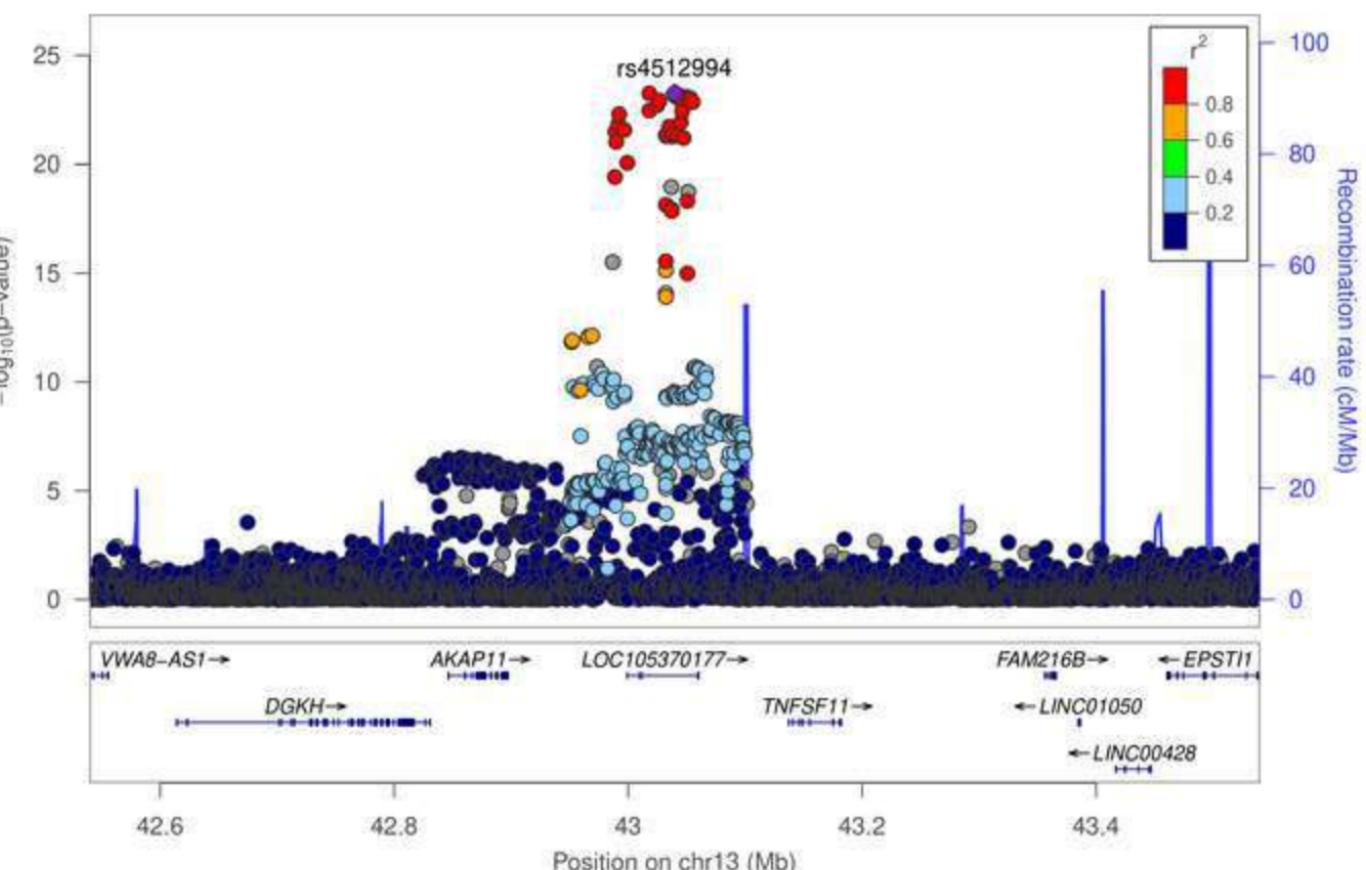
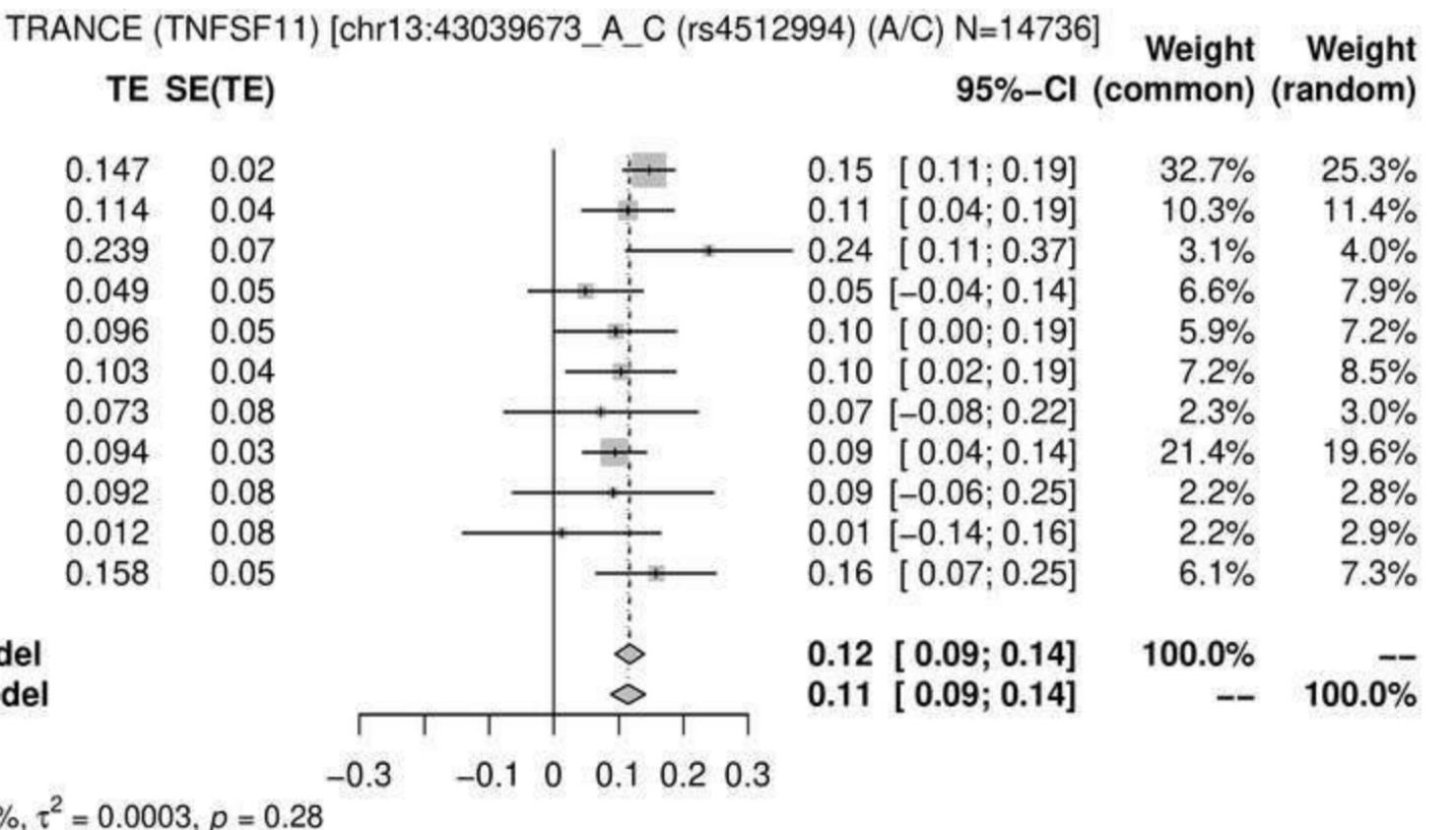
## Fixed effect model

## Random effects model

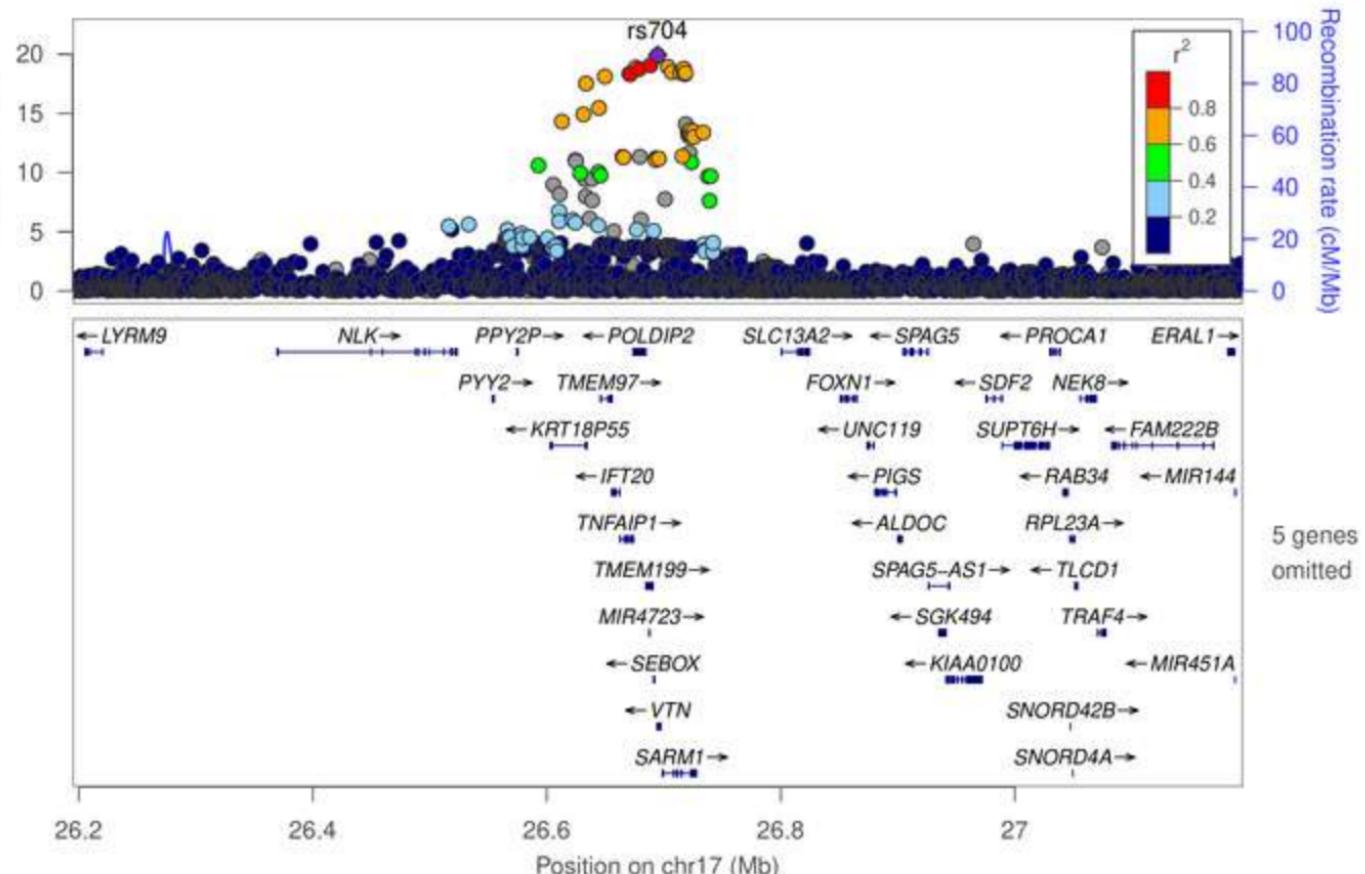
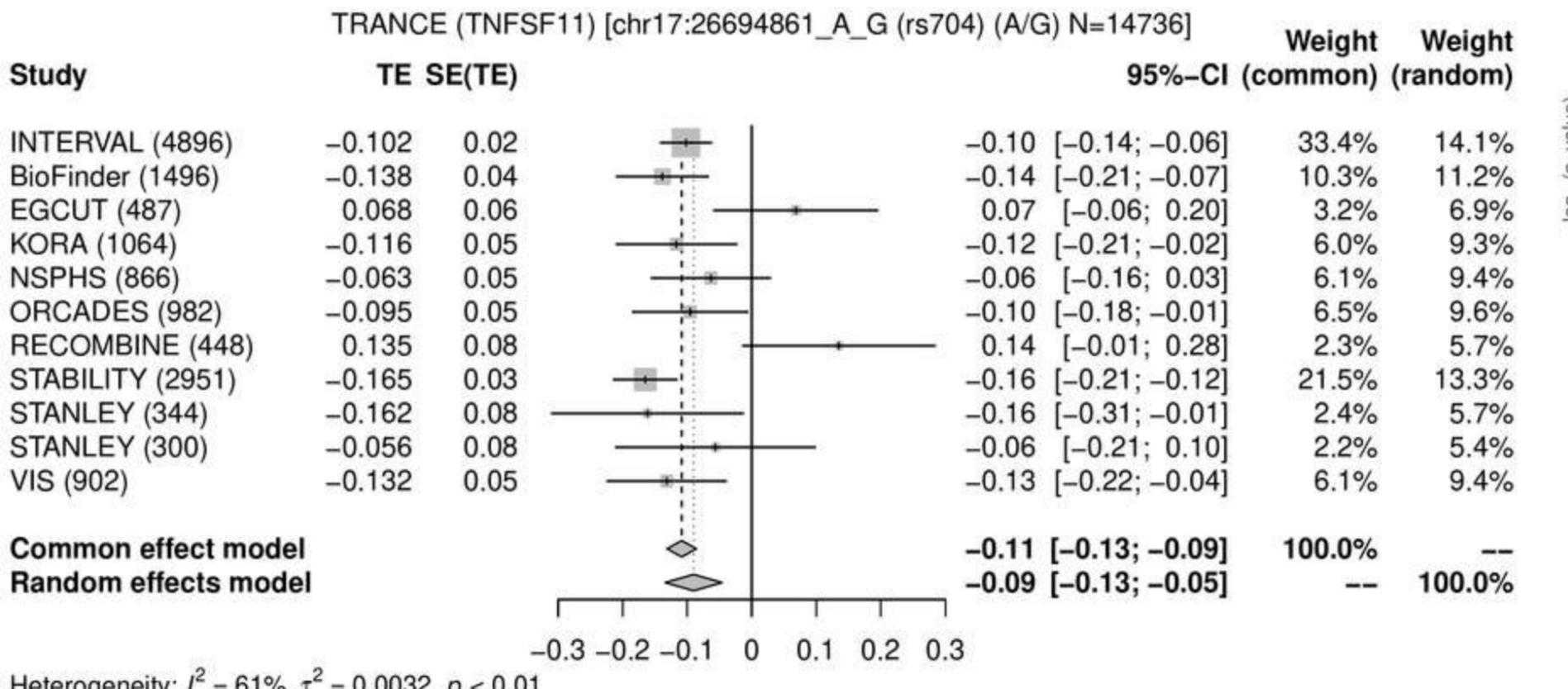
Heterogeneity:  $I^2 = 0\%$ ,  $\tau^2 = 0$ ,  $p = 0.79$



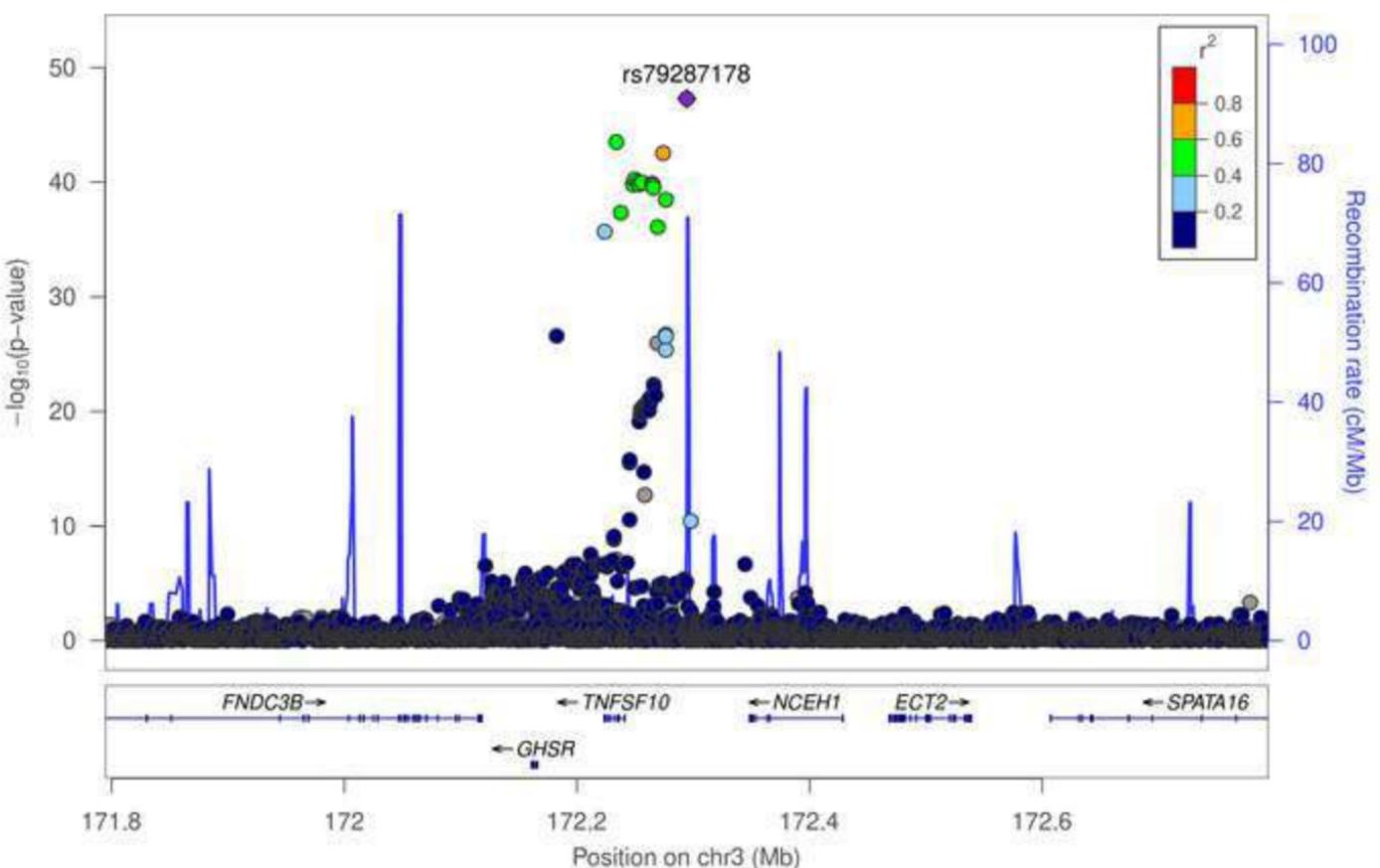
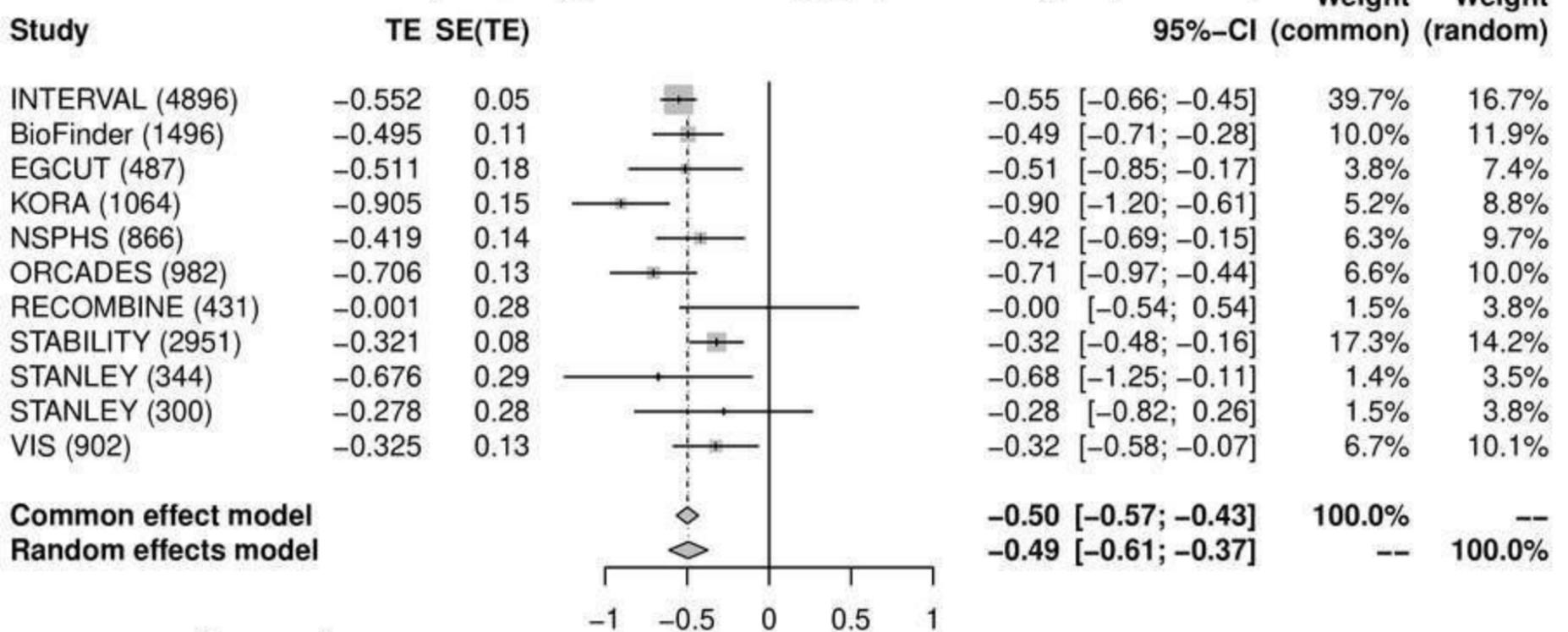
# TRANCE (TNFSF11)-rs4512994



# TRANCE (TNFSF11)-rs704

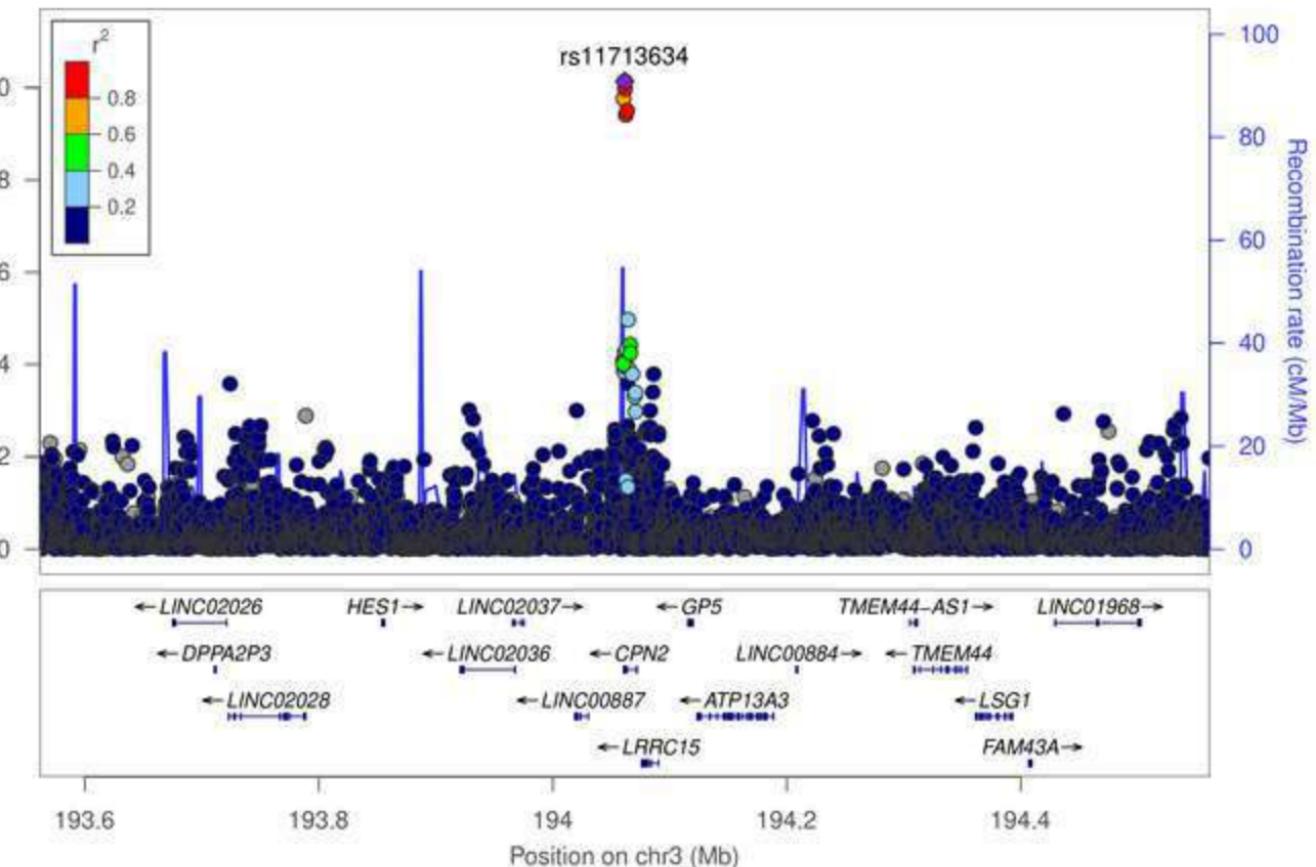
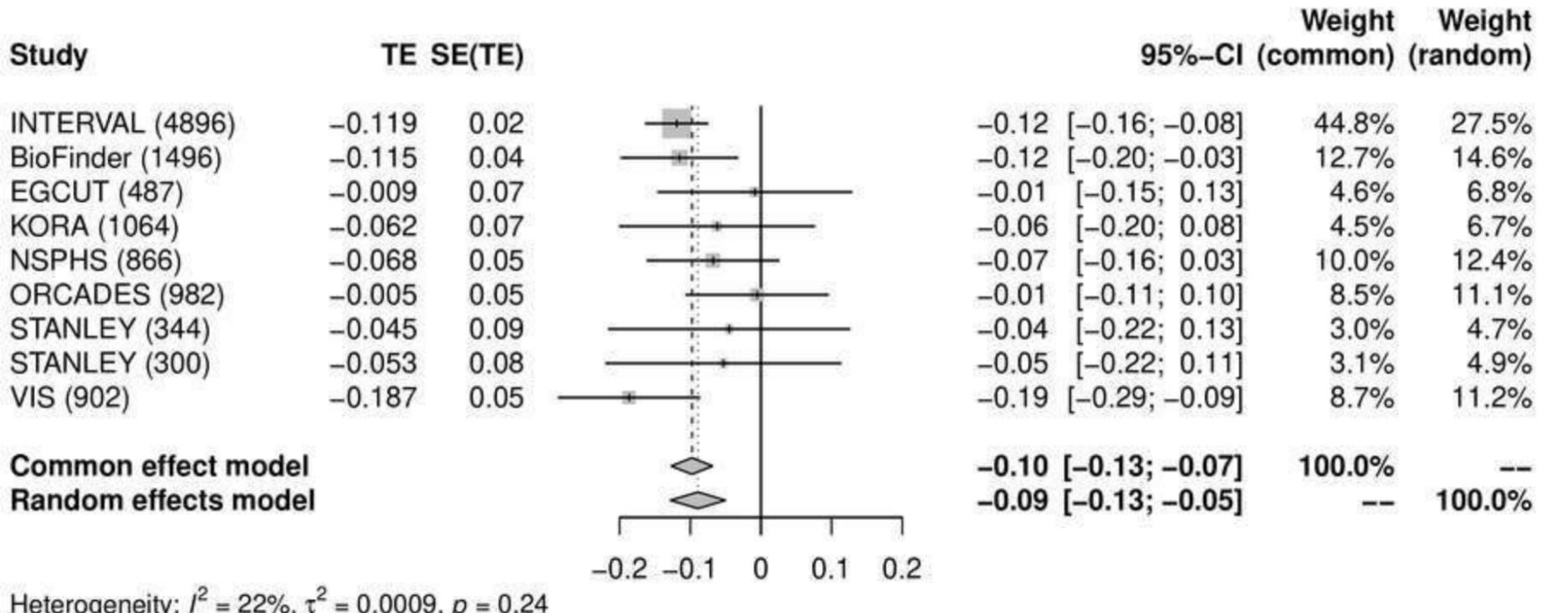


# TRANCE (TNFSF11)-rs79287178

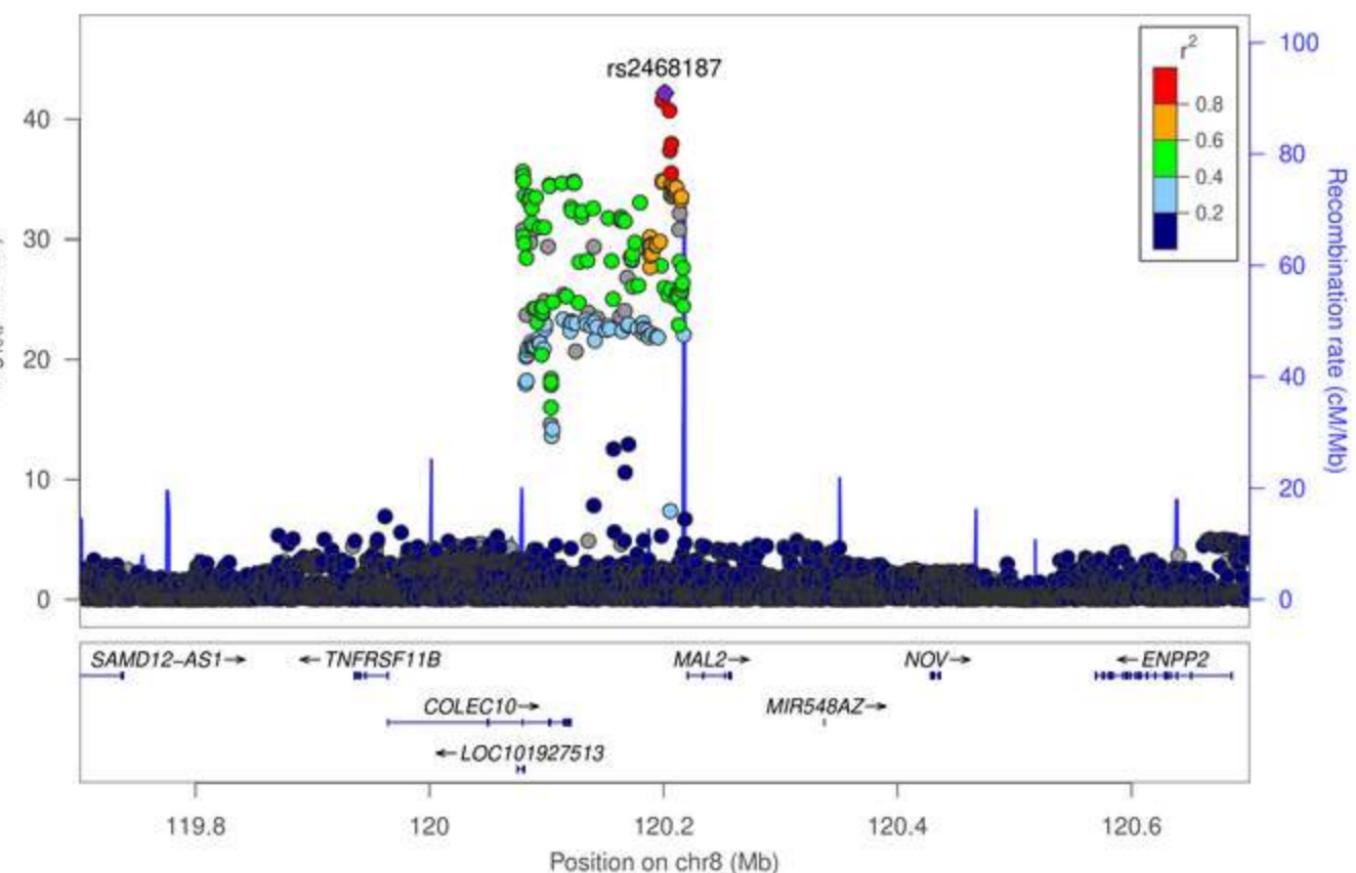
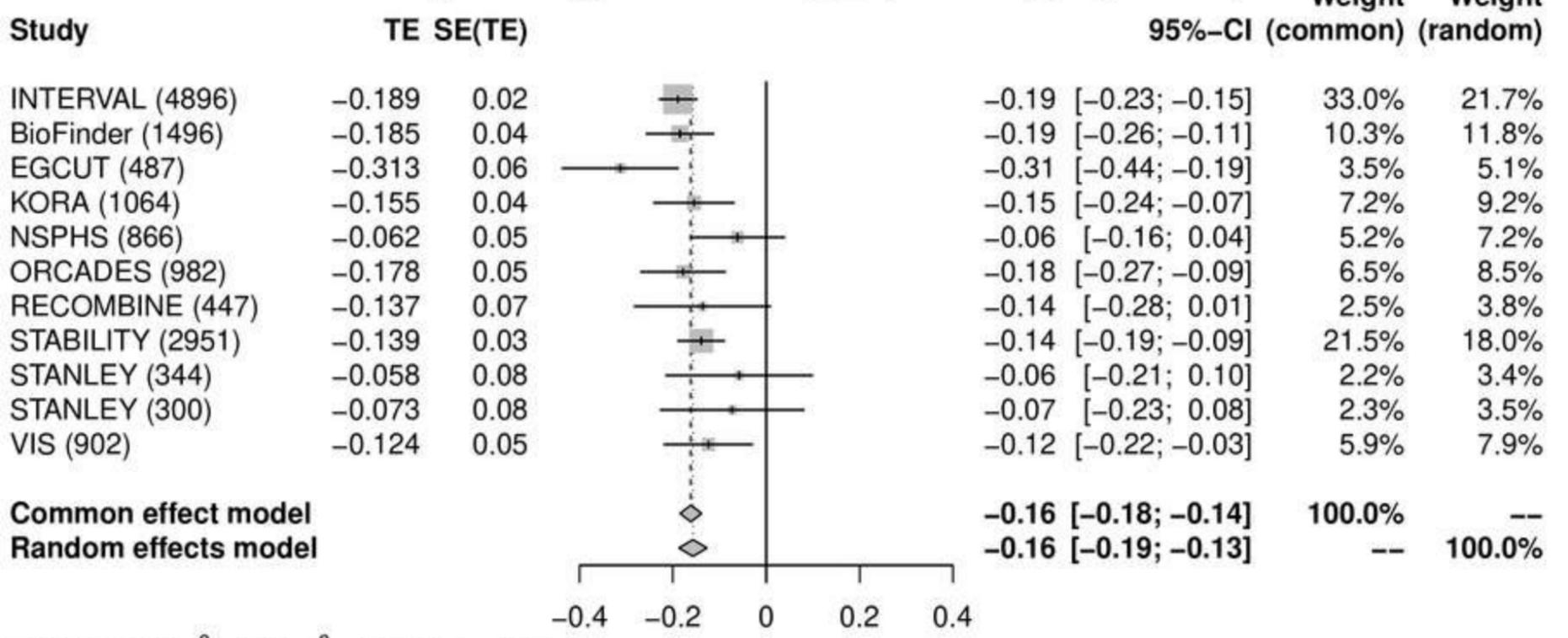


## TRANCE (TNFSF11)-rs11713634

TRANCE (TNFSF11) [chr3:194061578\_A\_G (rs11713634) (A/G) N=11337]

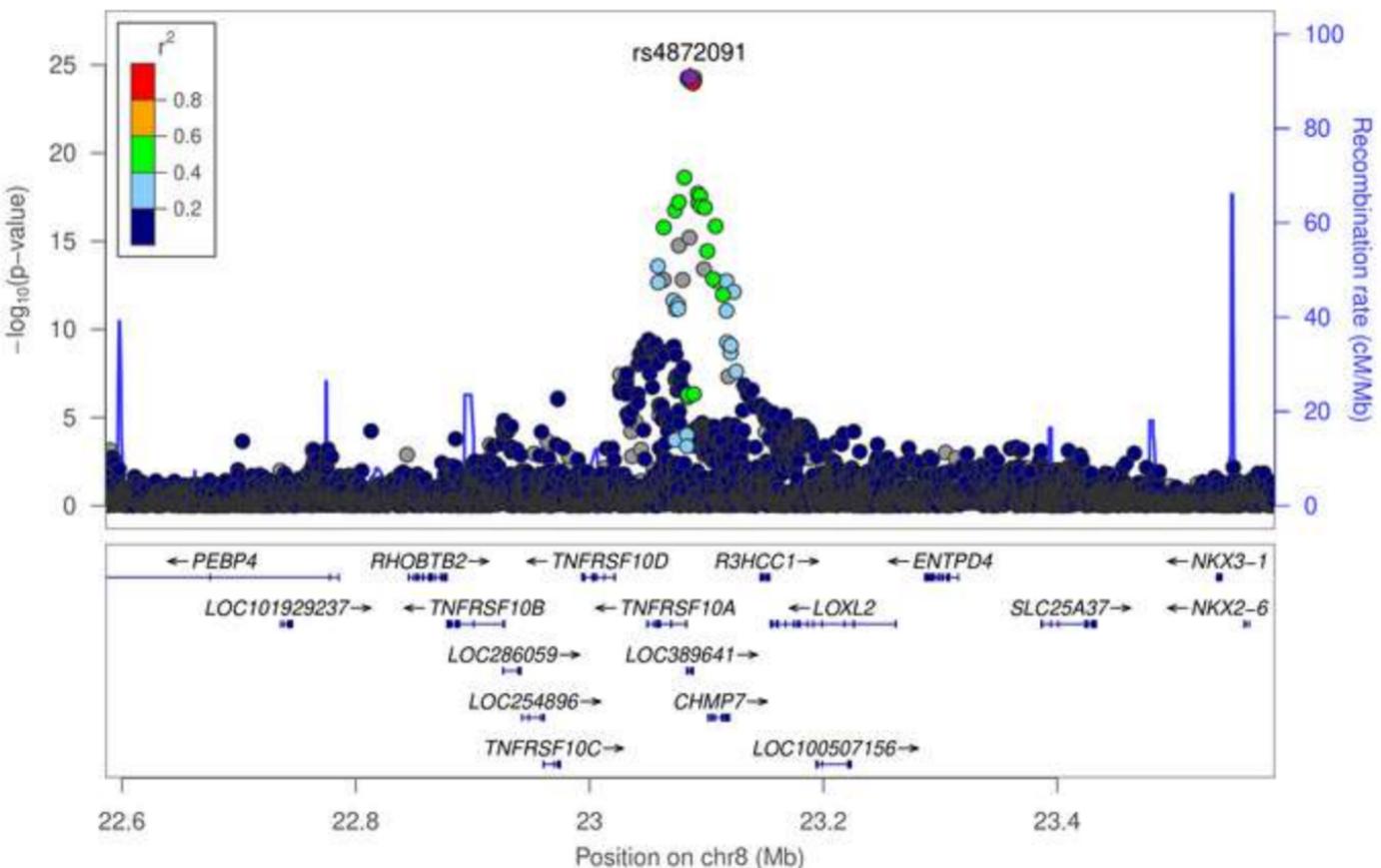
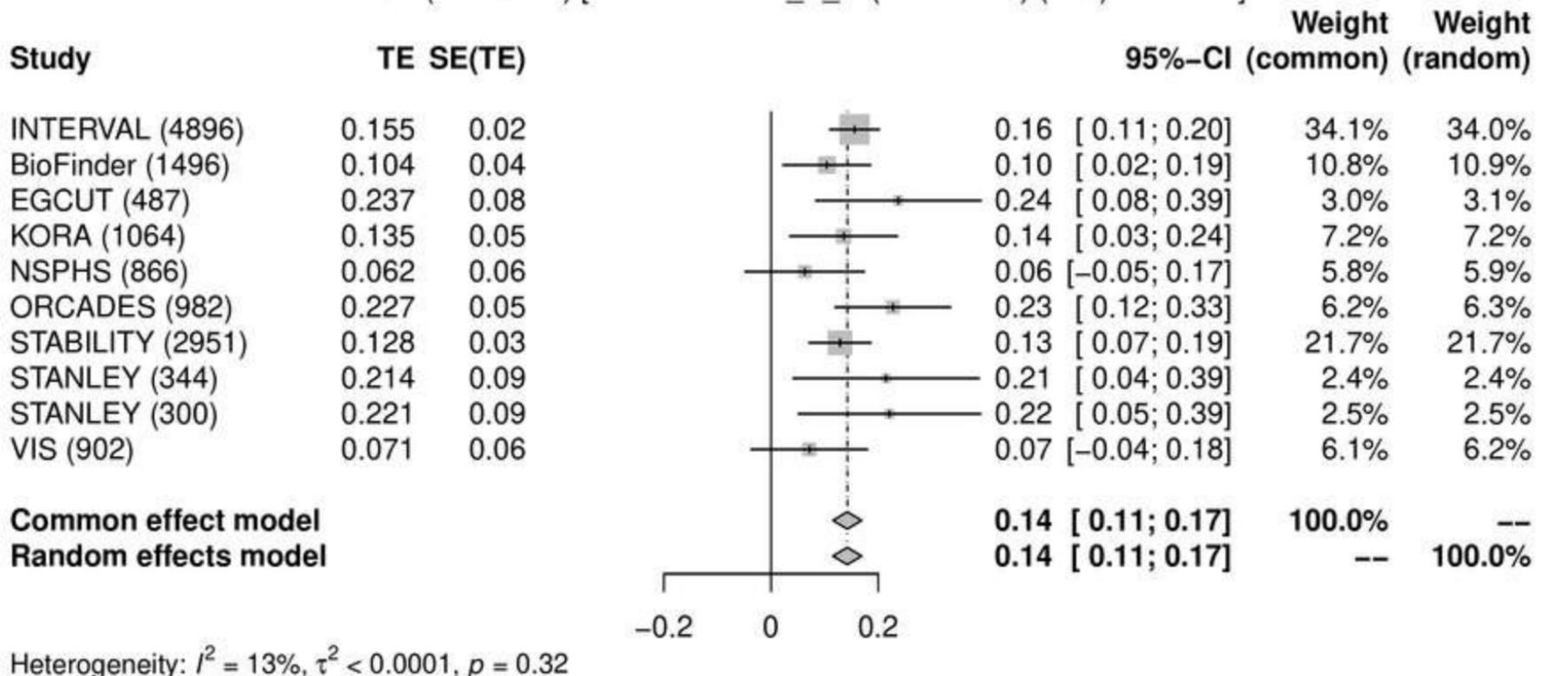


# TRANCE (TNFSF11)-rs2468187

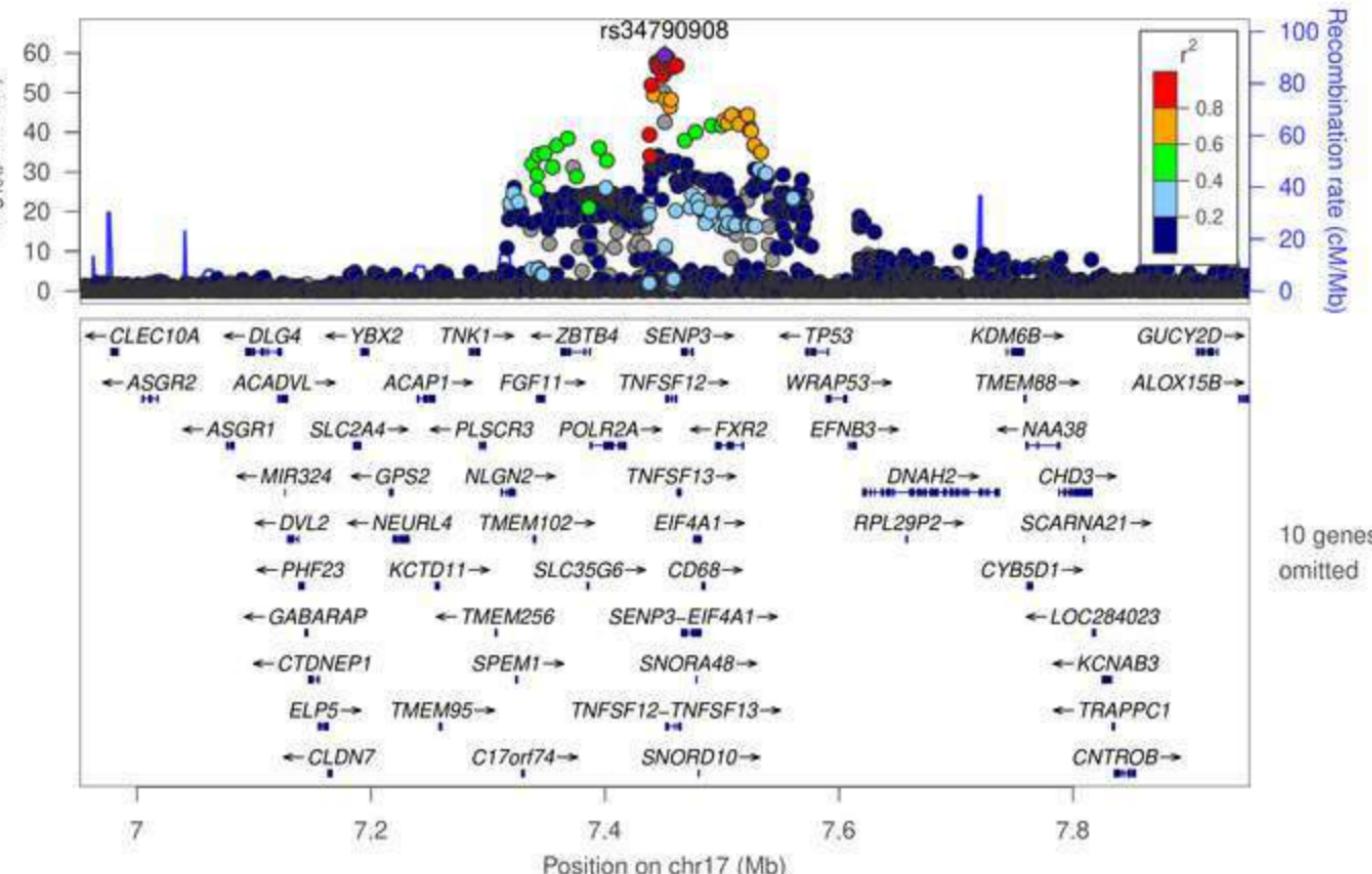
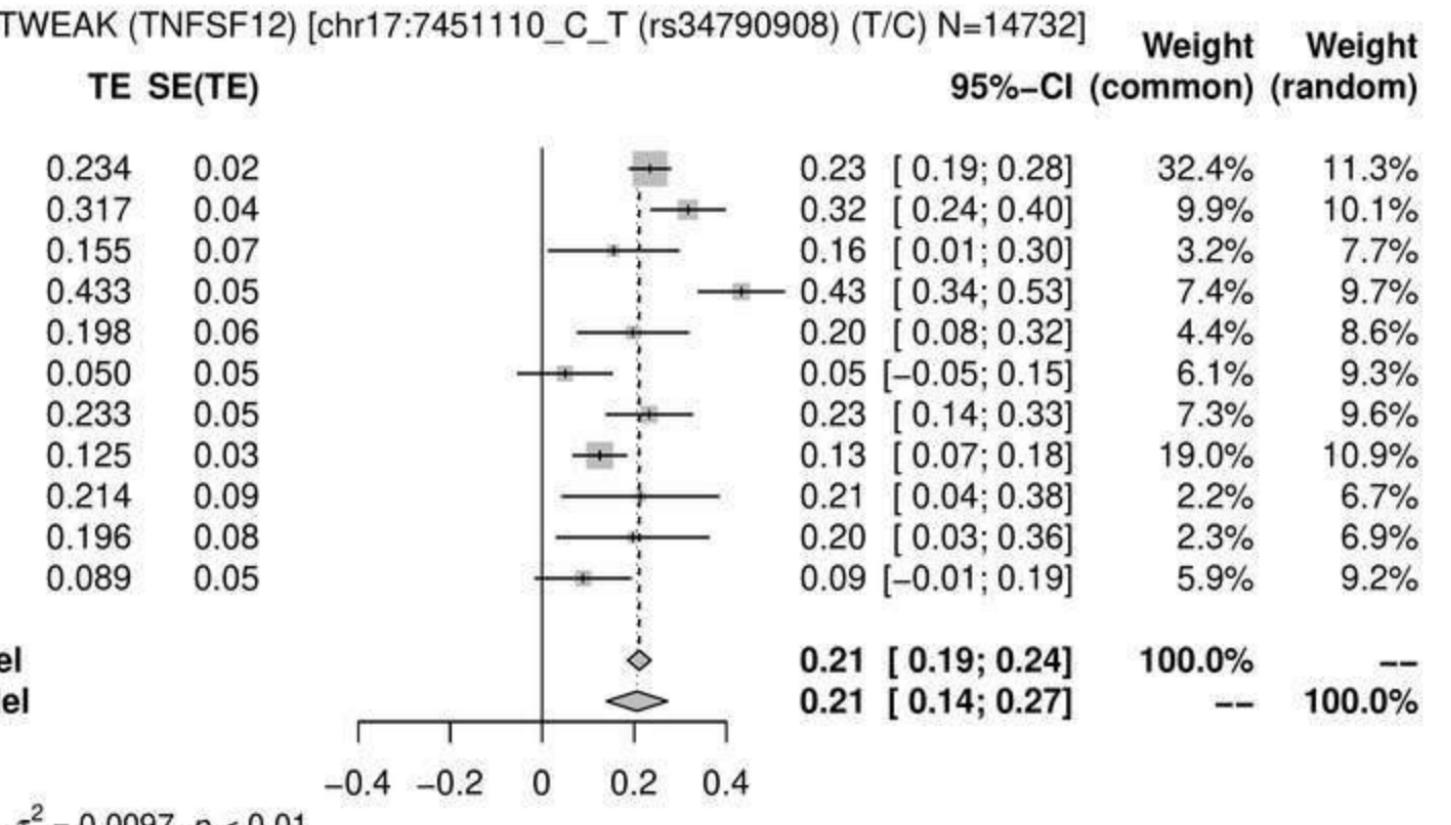


# TRANCE (TNFSF11)-rs4872091

TRANCE (TNFSF11) [chr8:23085868\_A\_G (rs4872091) (A/G) N=14288]

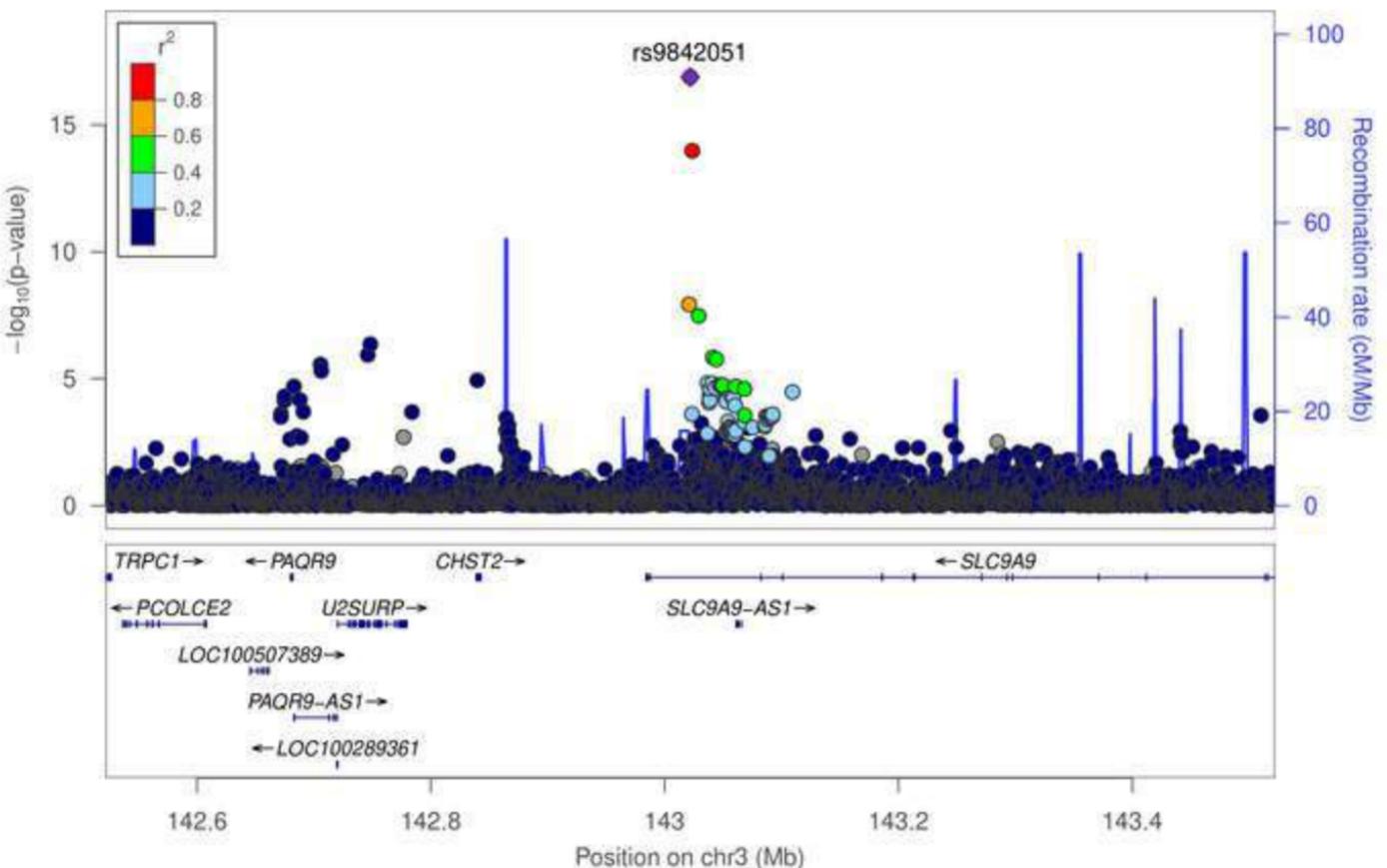
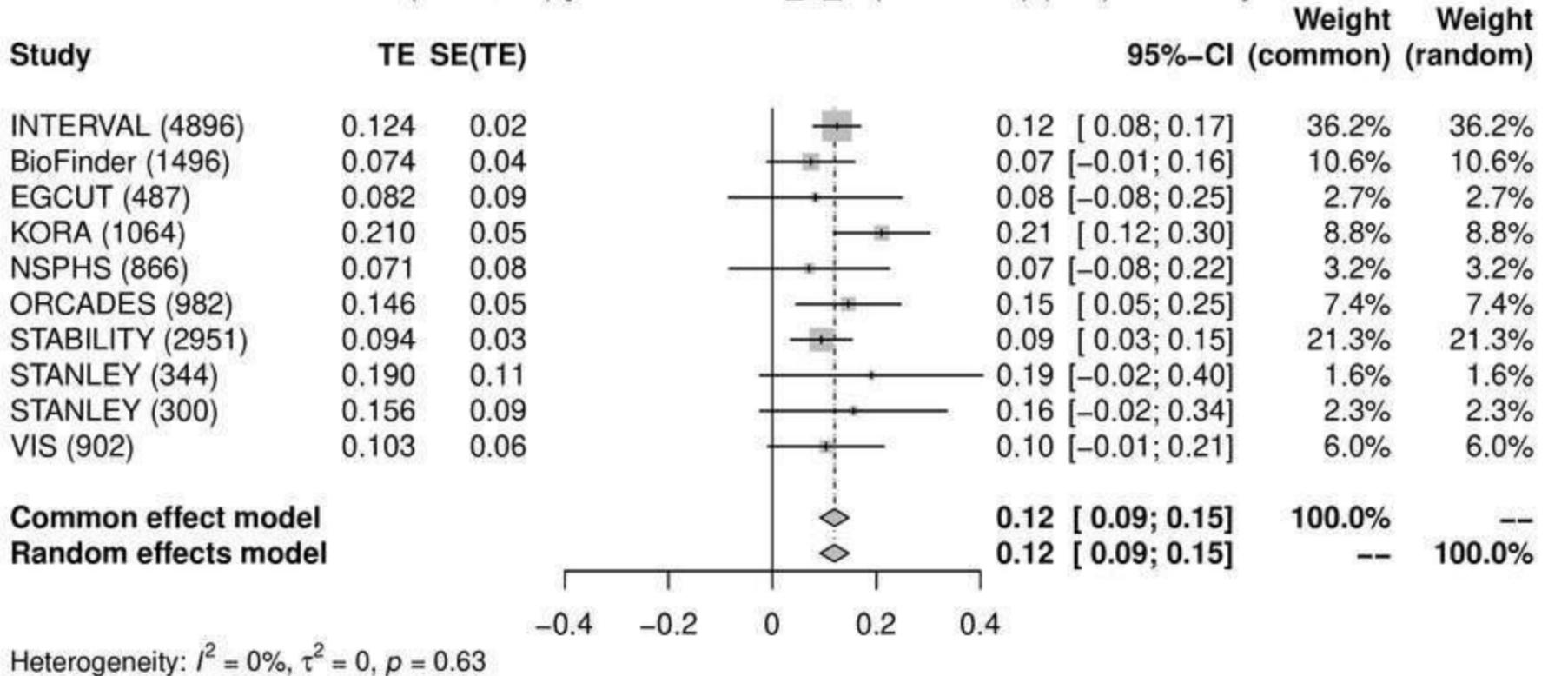


# TWEAK (TNFSF12)-rs34790908



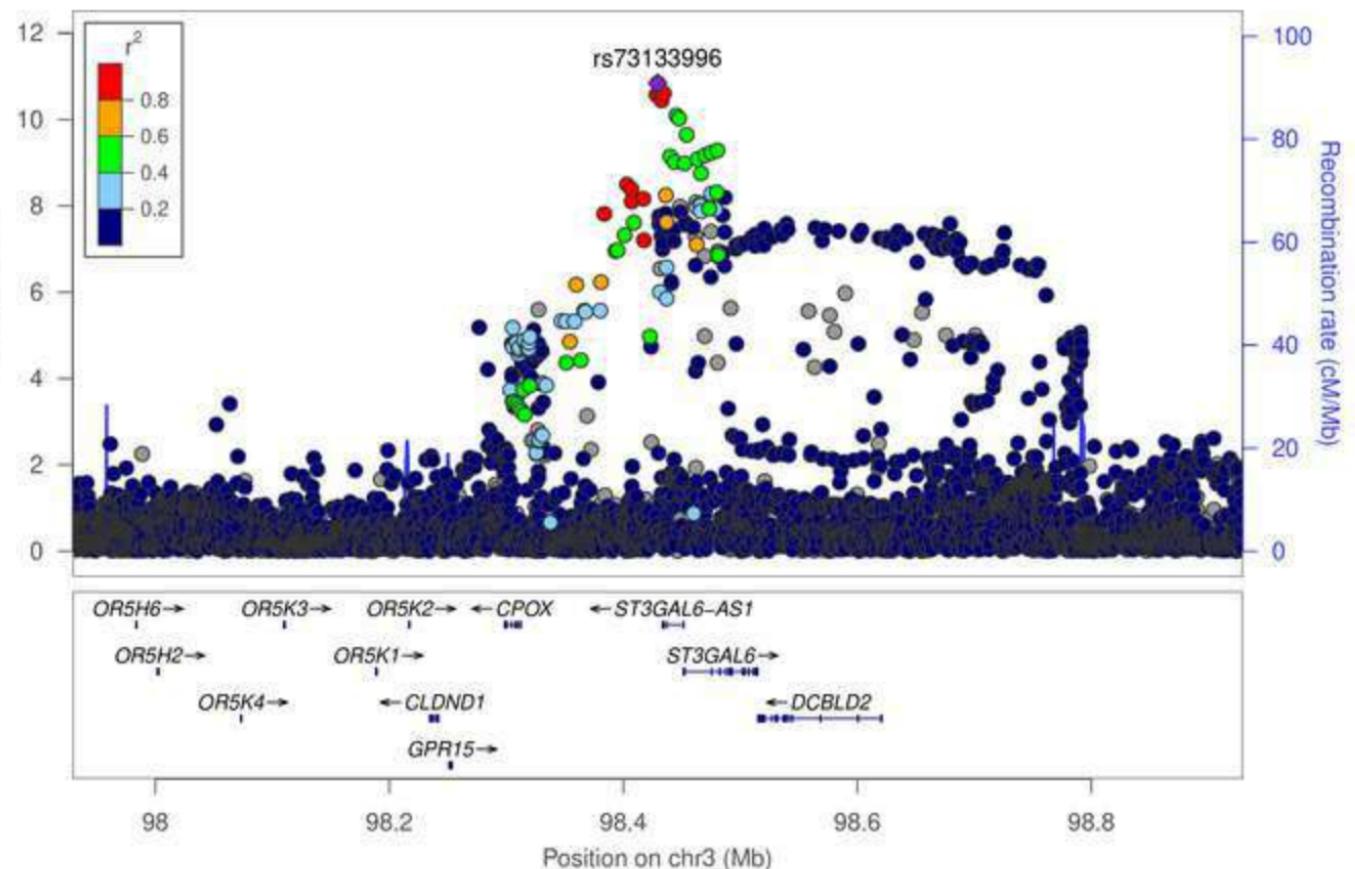
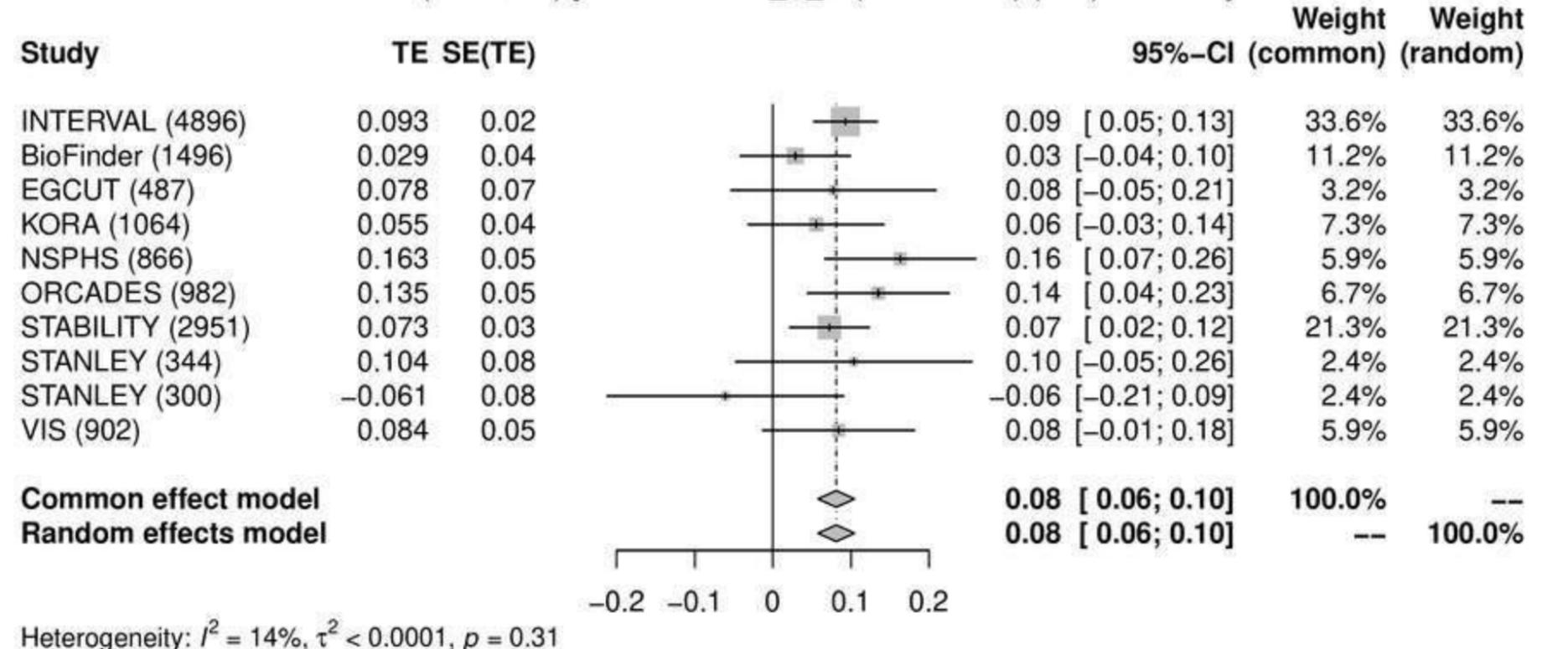
# TWEAK (TNFSF12)-rs9842051

TWEAK (TNFSF12) [chr3:143021856\_C\_G (rs9842051) (C/G) N=14288]



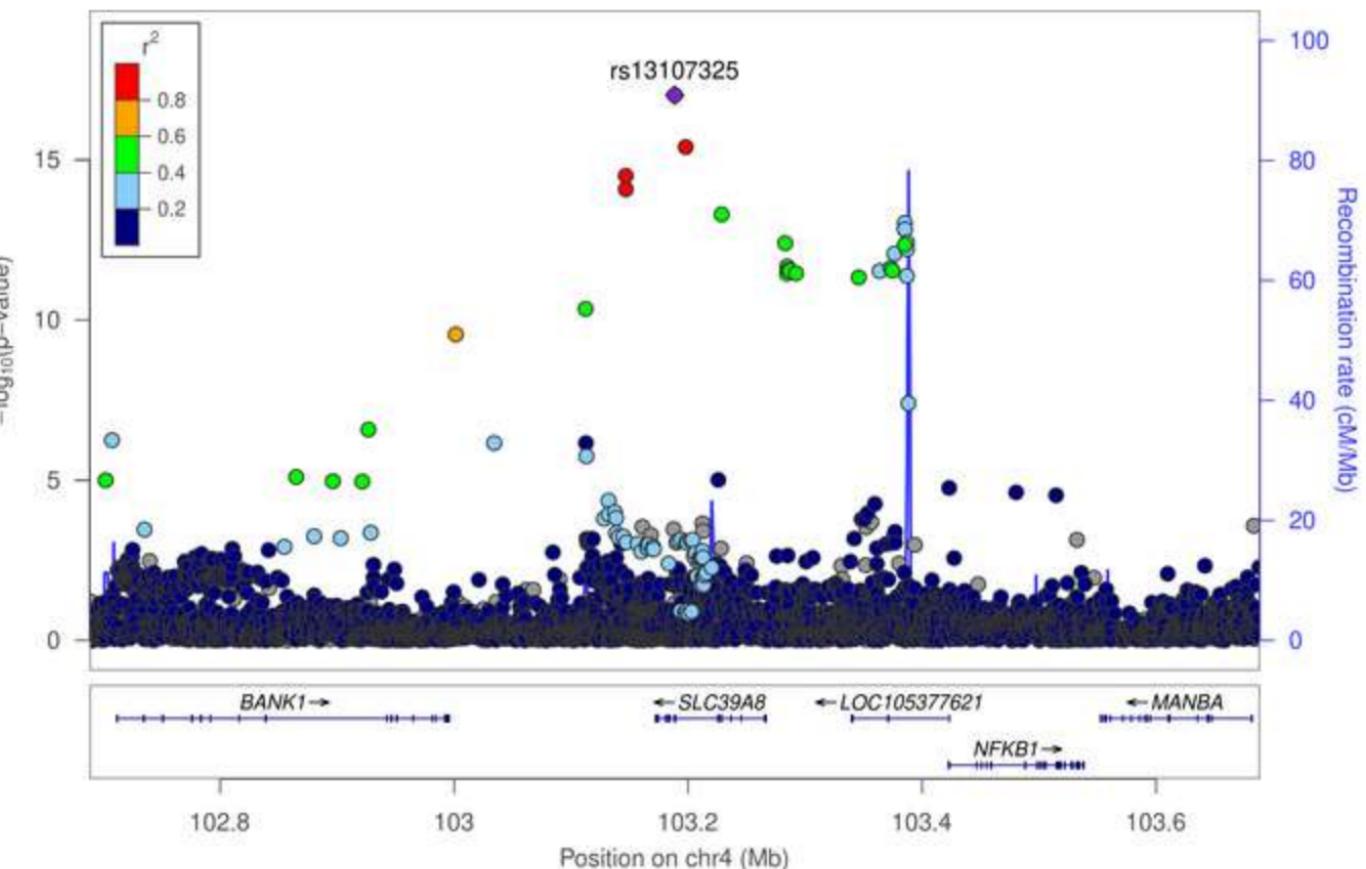
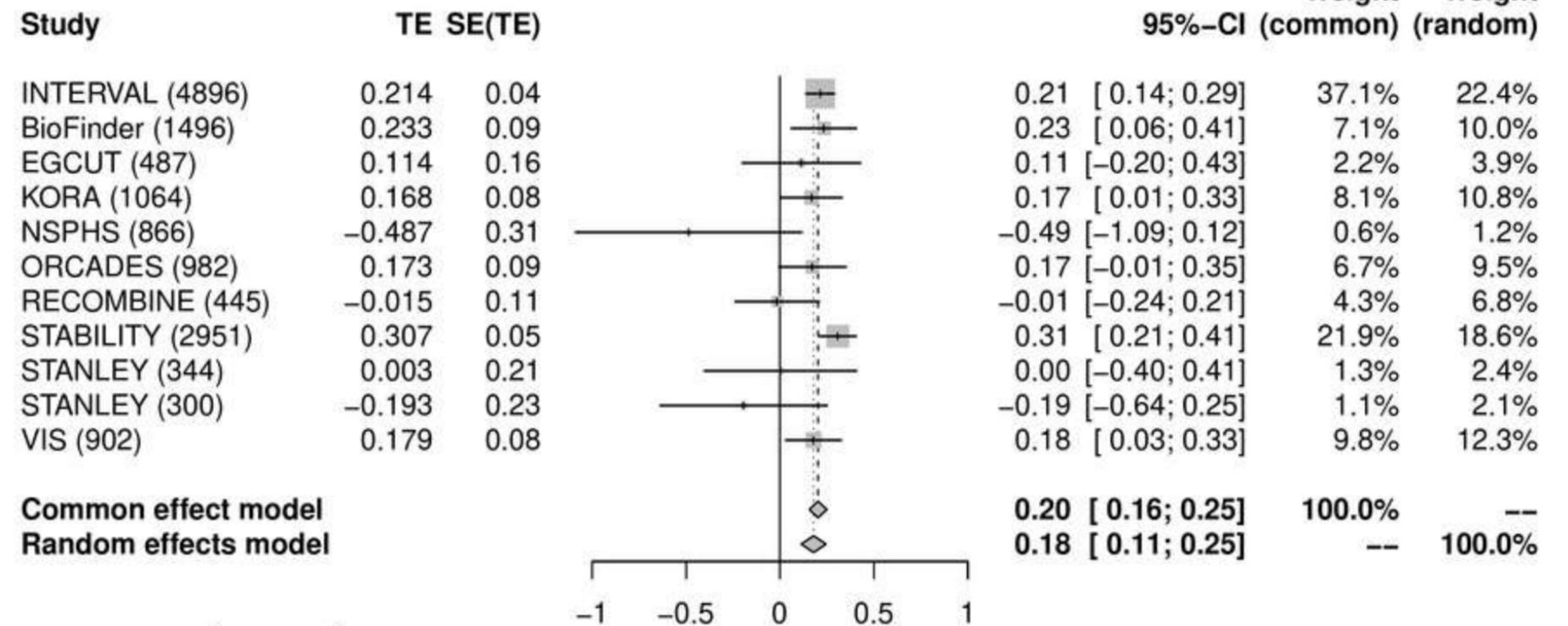
# TWEAK (TNFSF12)-rs73133996

TWEAK (TNFSF12) [chr3:98429219\_C\_G (rs73133996) (C/G) N=14288]



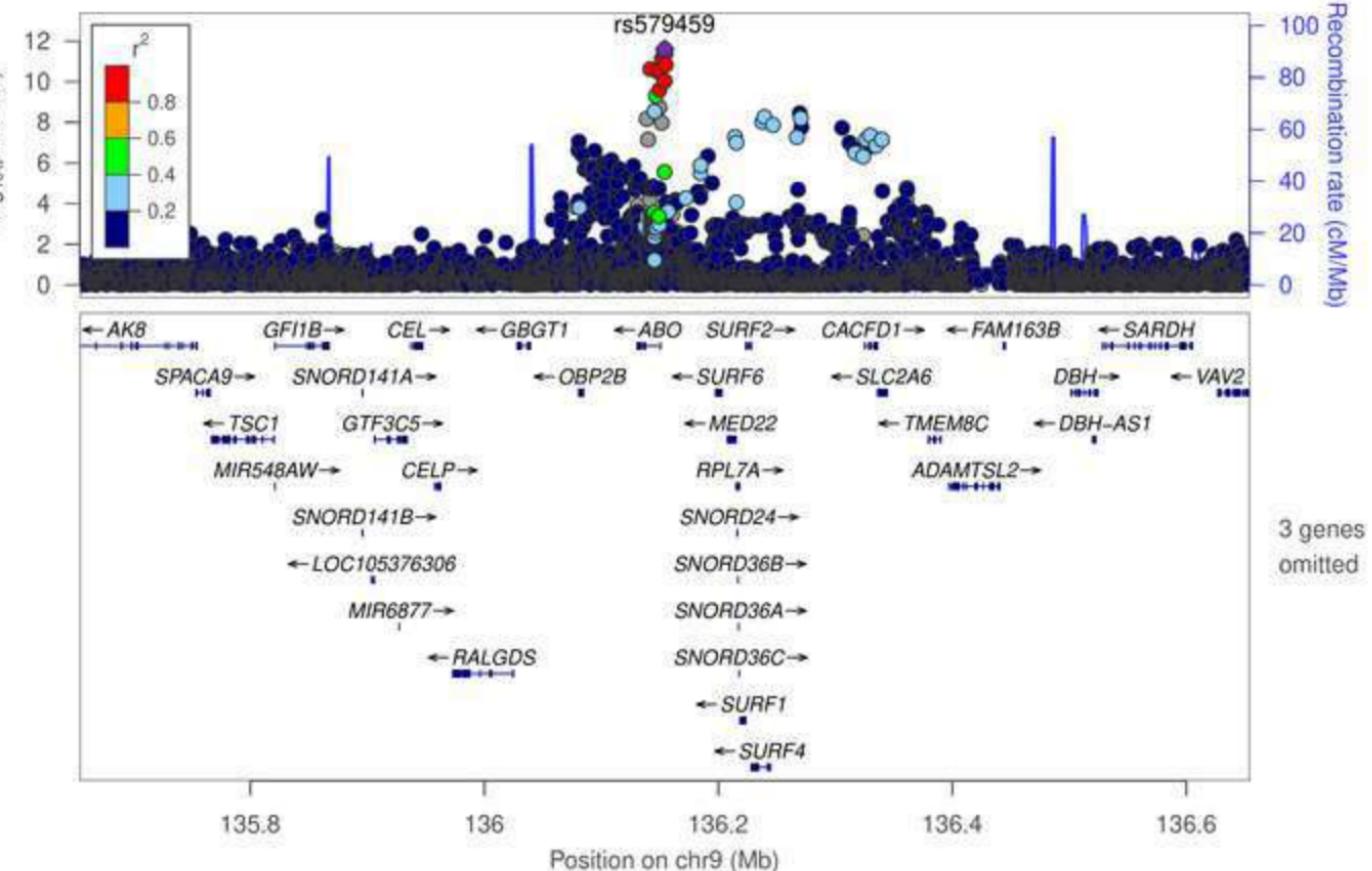
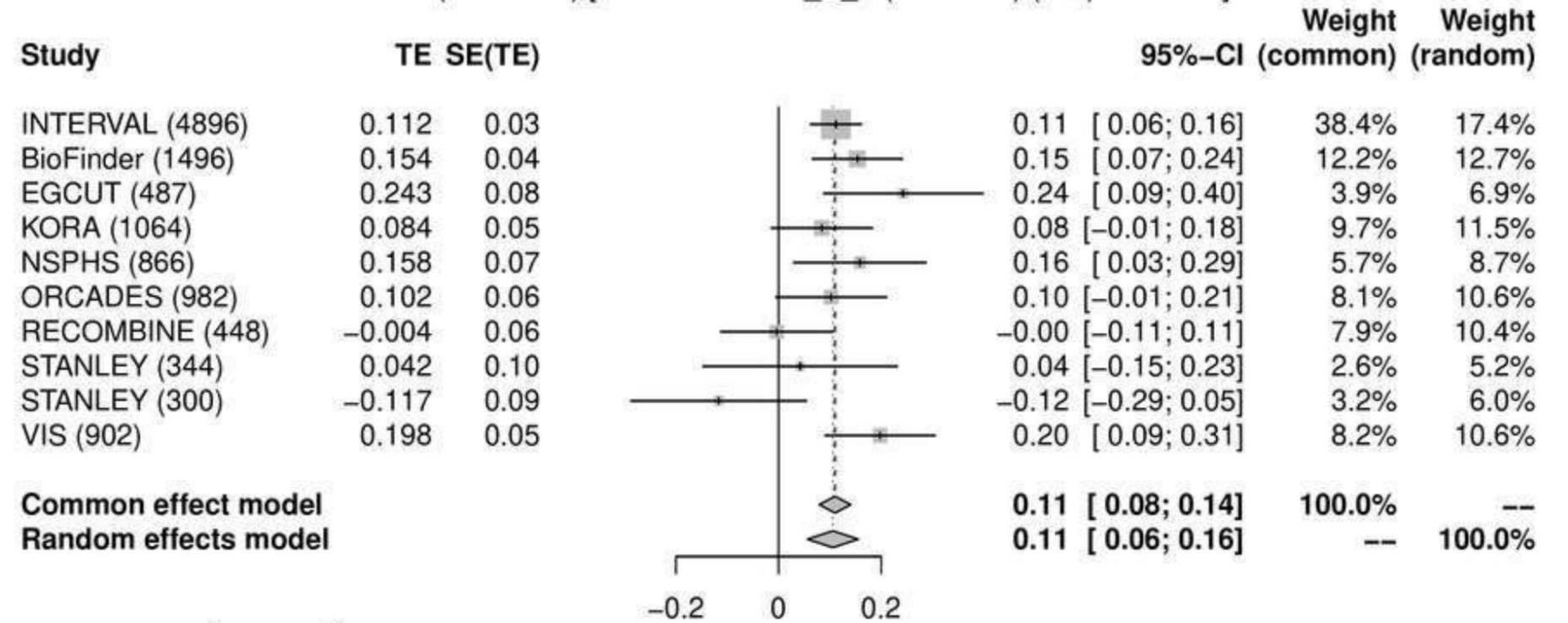
# TWEAK (TNFSF12)-rs13107325

TWEAK (TNFSF12) [chr4:103188709\_C\_T (rs13107325) (T/C) N=14733]

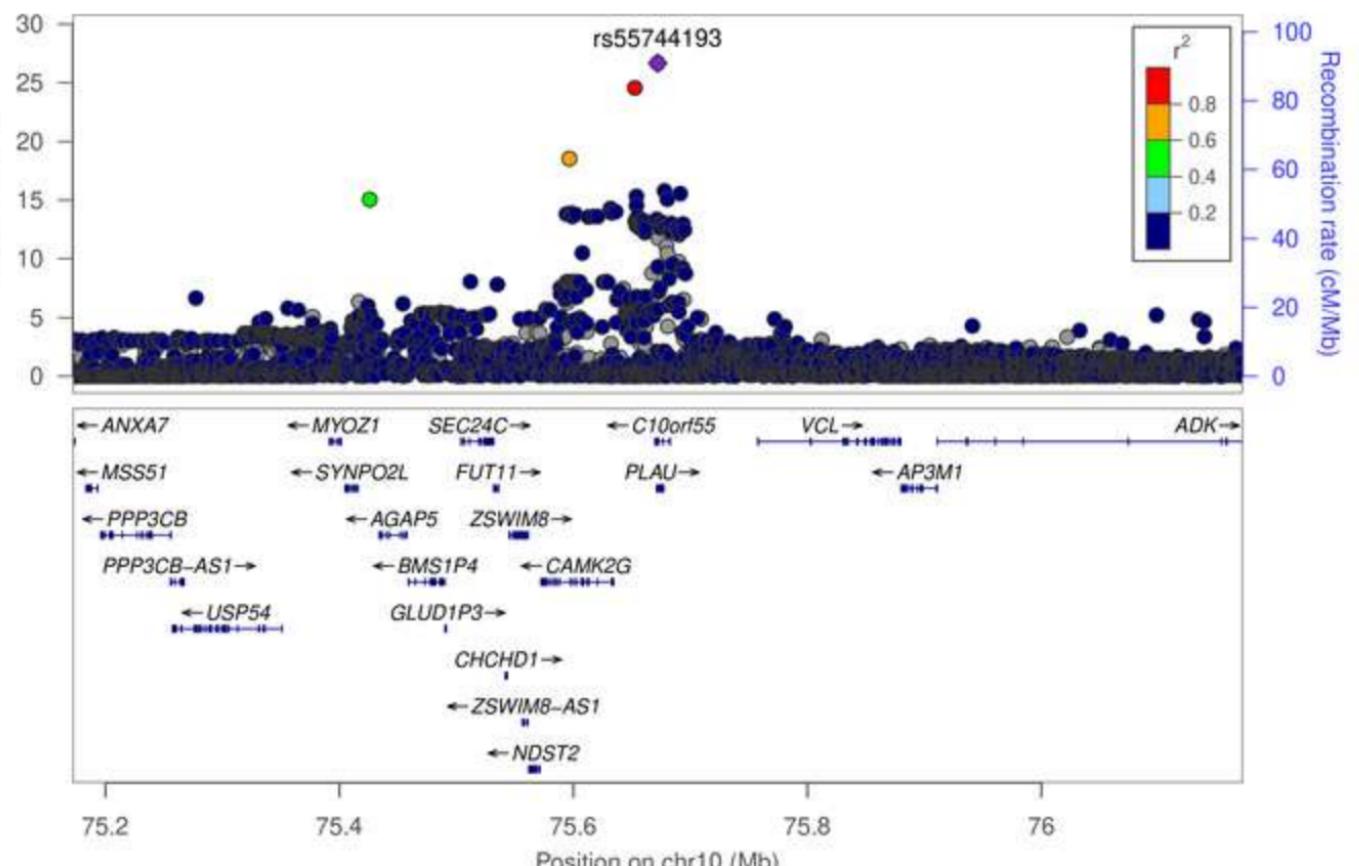
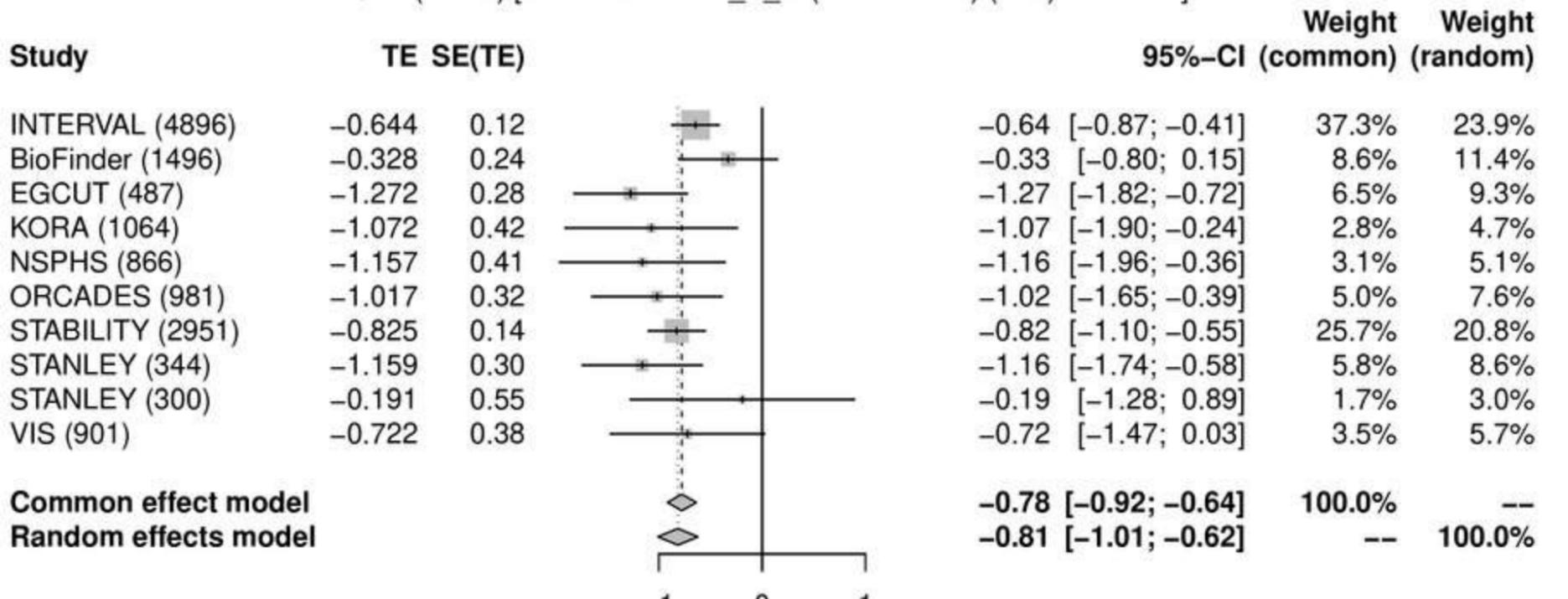


# TWEAK (TNFSF12)-rs579459

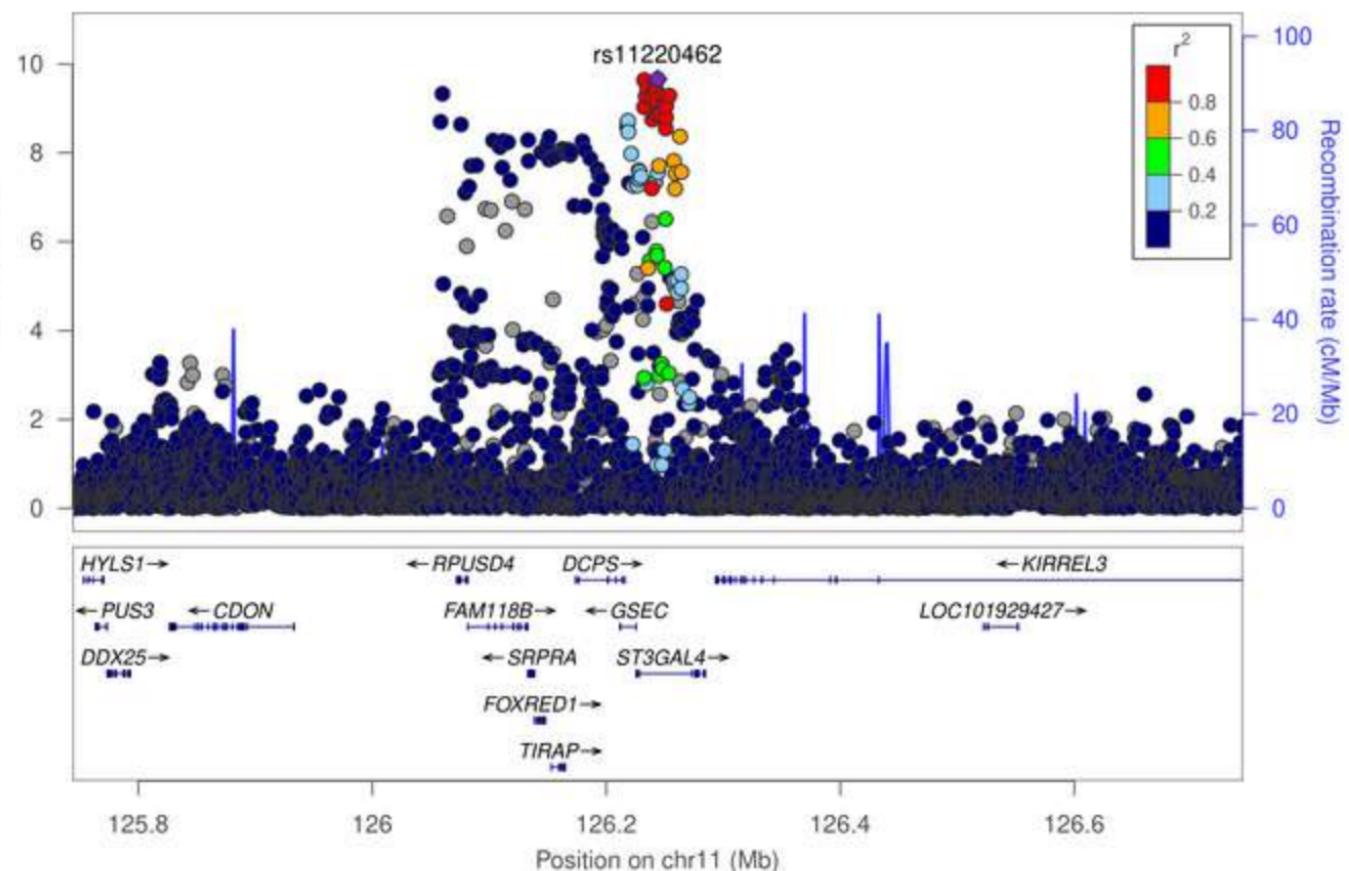
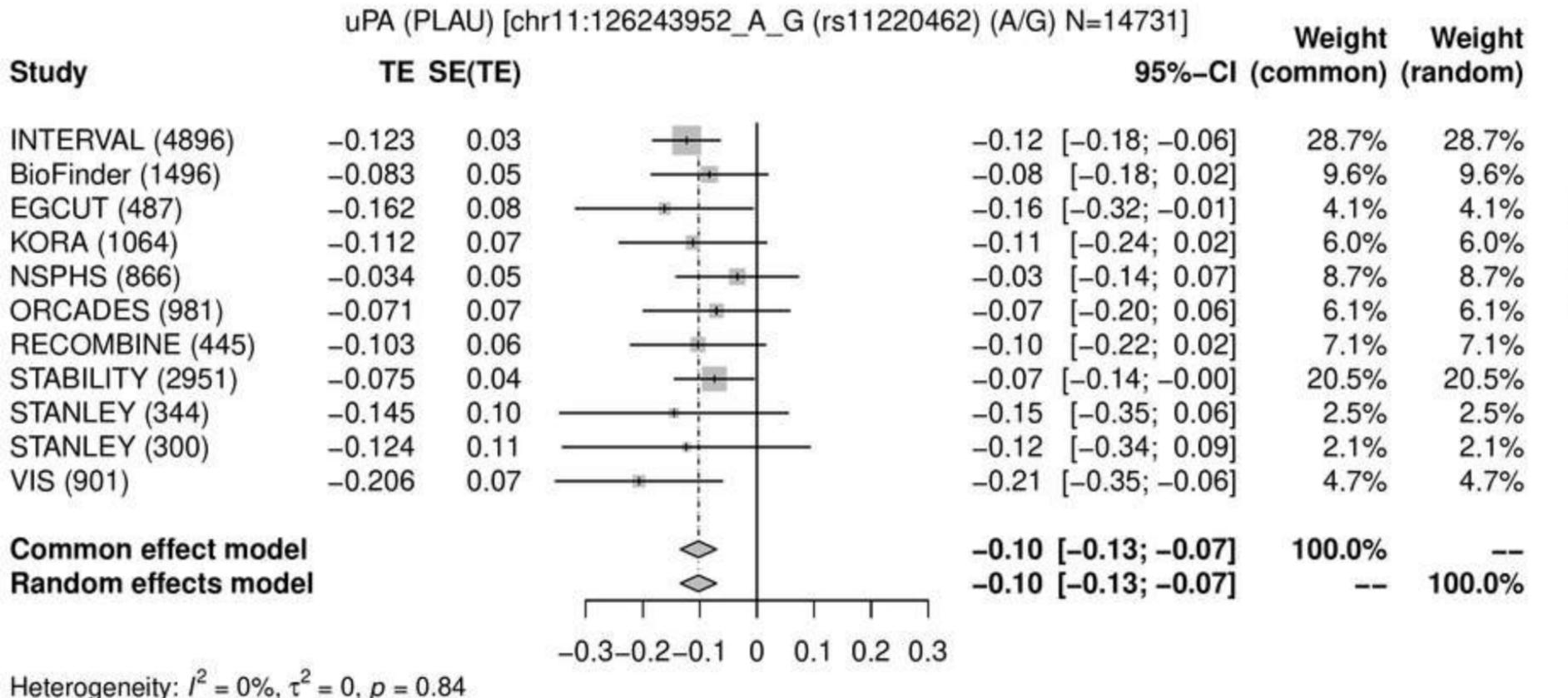
TWEAK (TNFSF12) [chr9:136154168\_C\_T (rs579459) (T/C) N=11785]

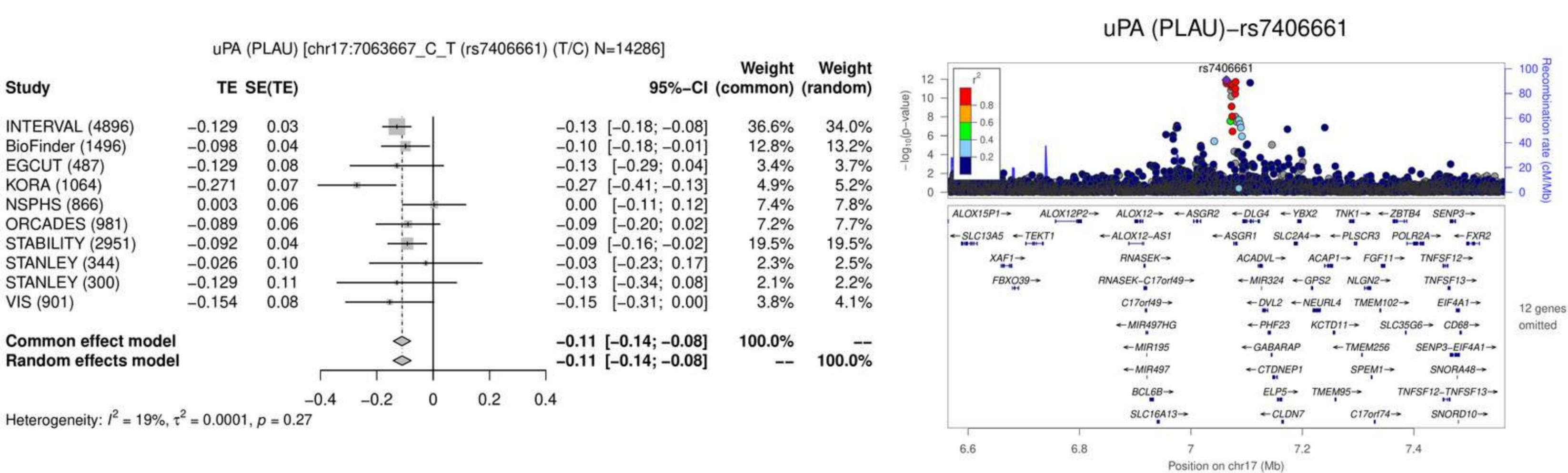


# uPA (PLAU)-rs55744193

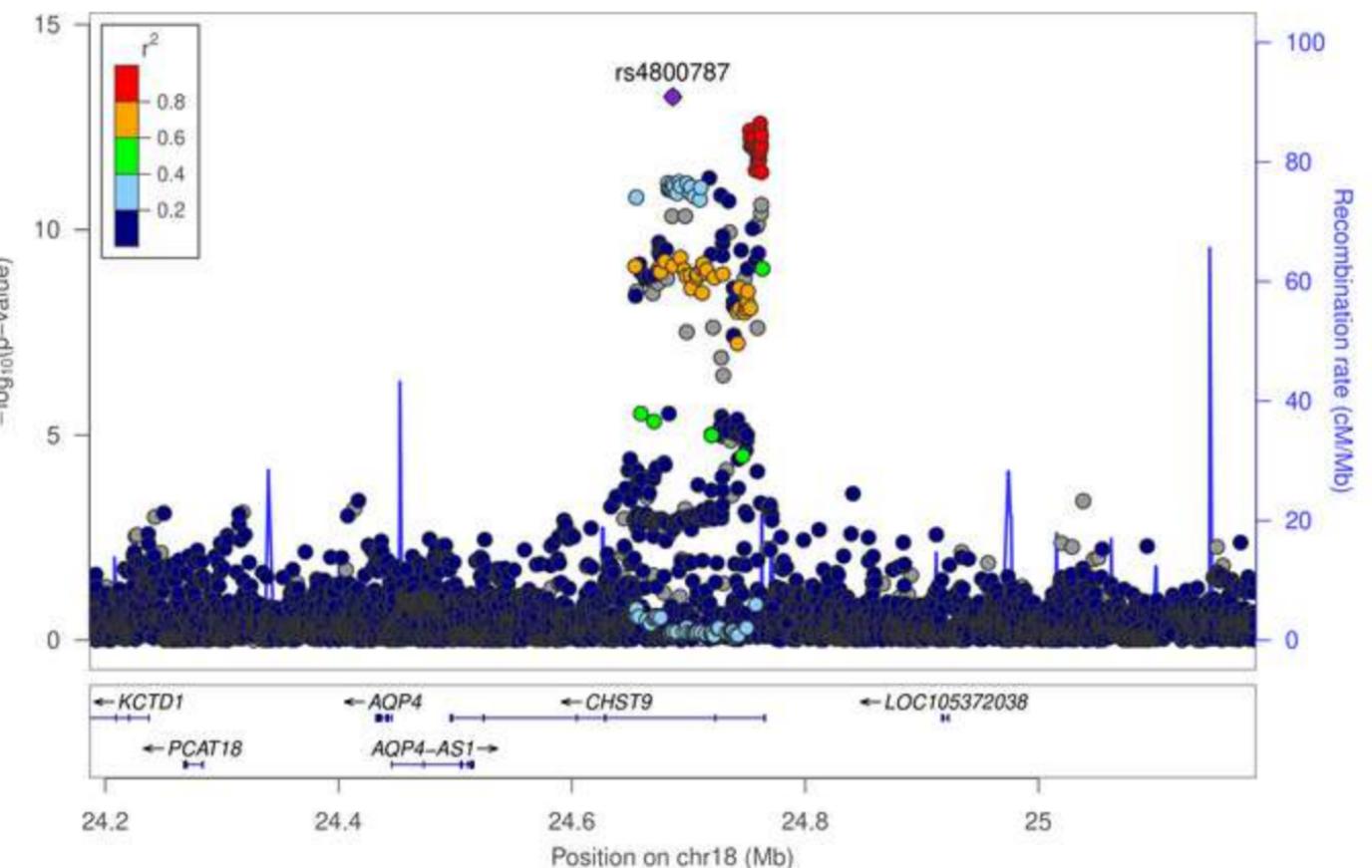
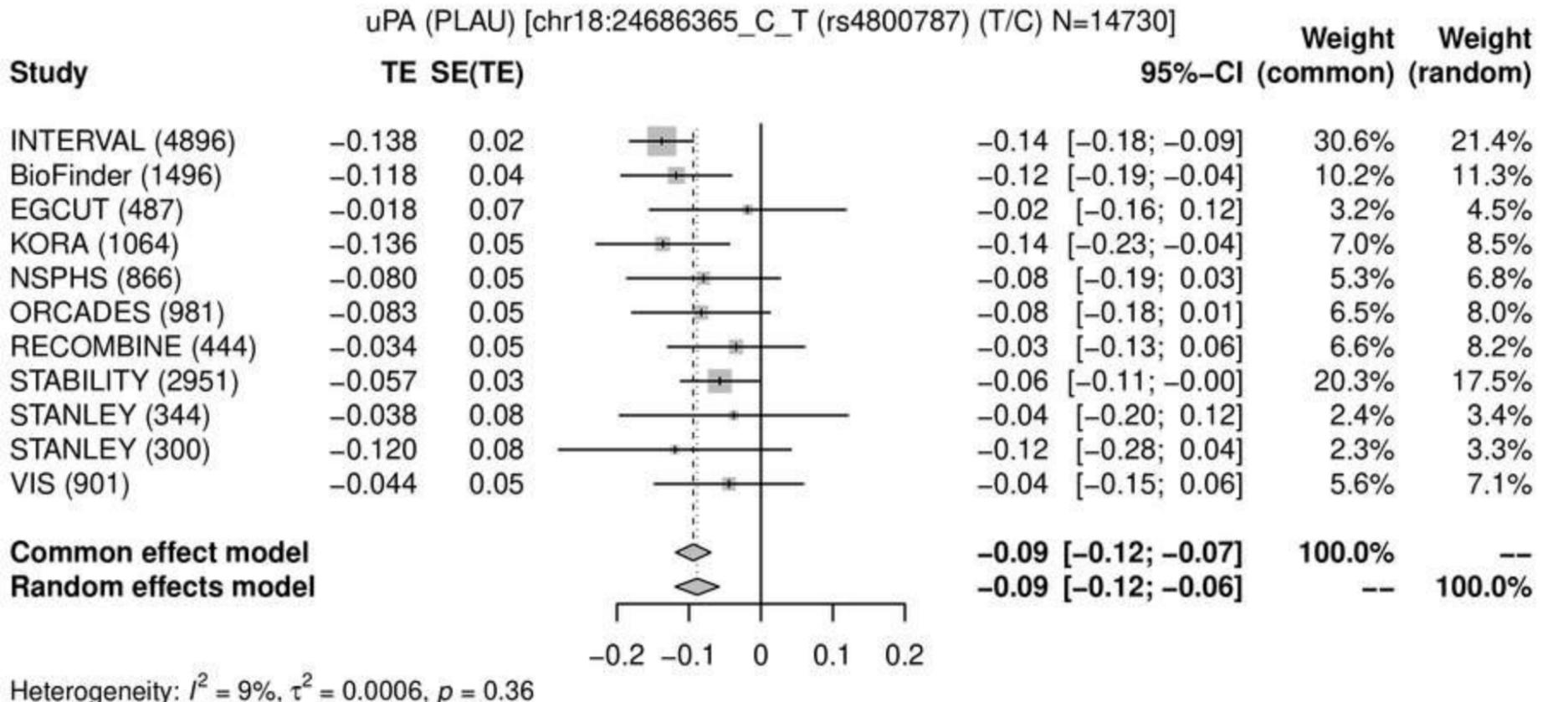


## uPA (PLAU)-rs11220462

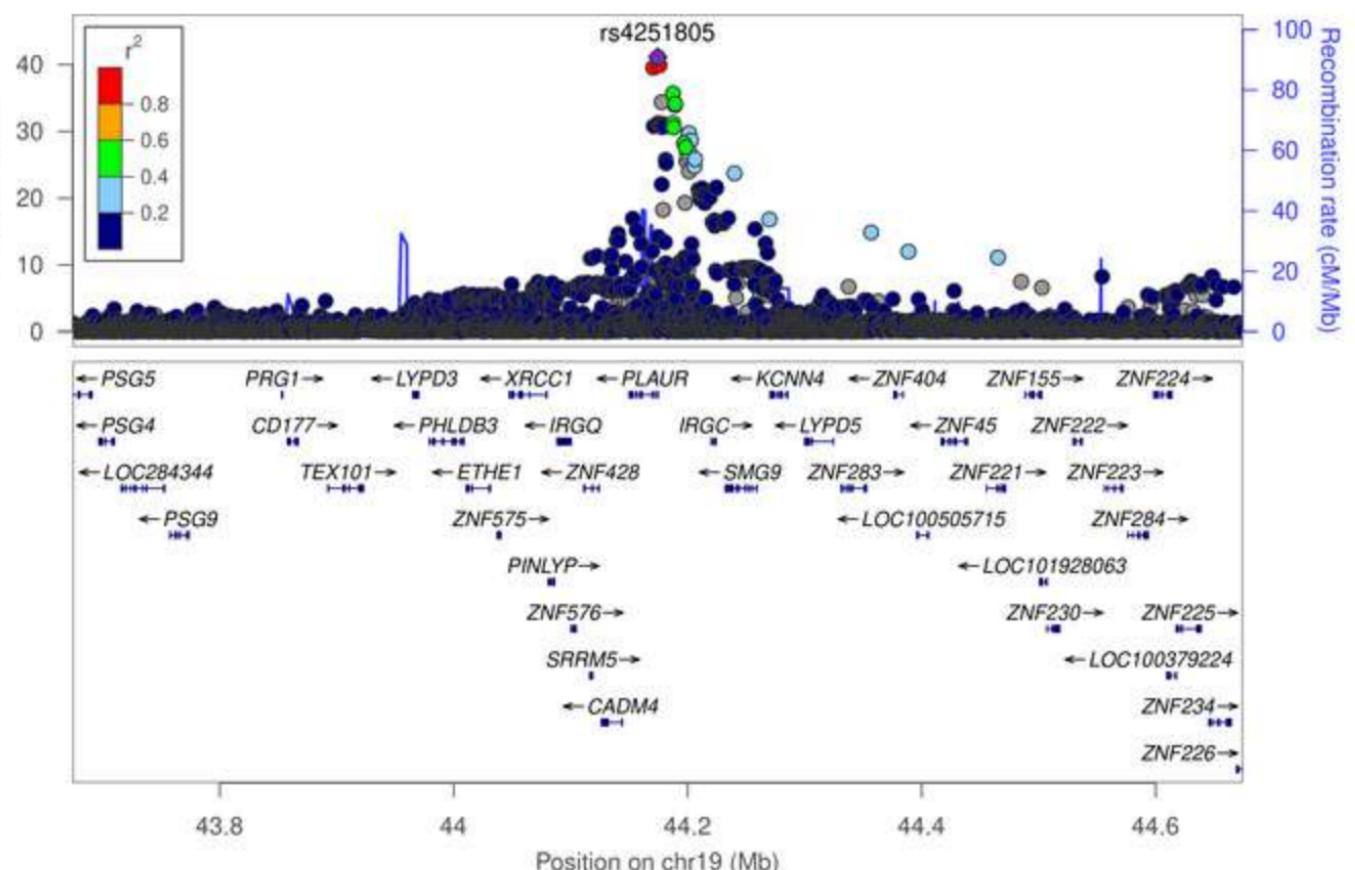
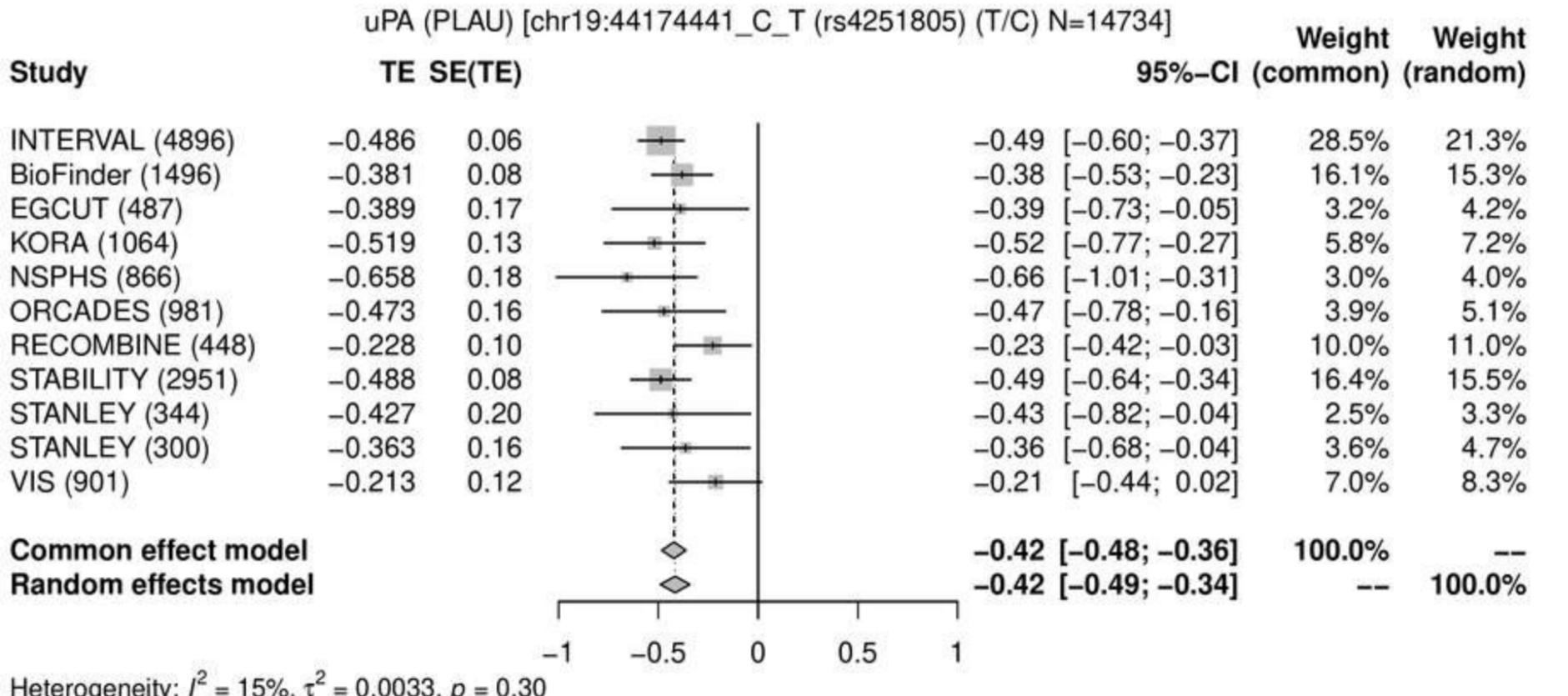




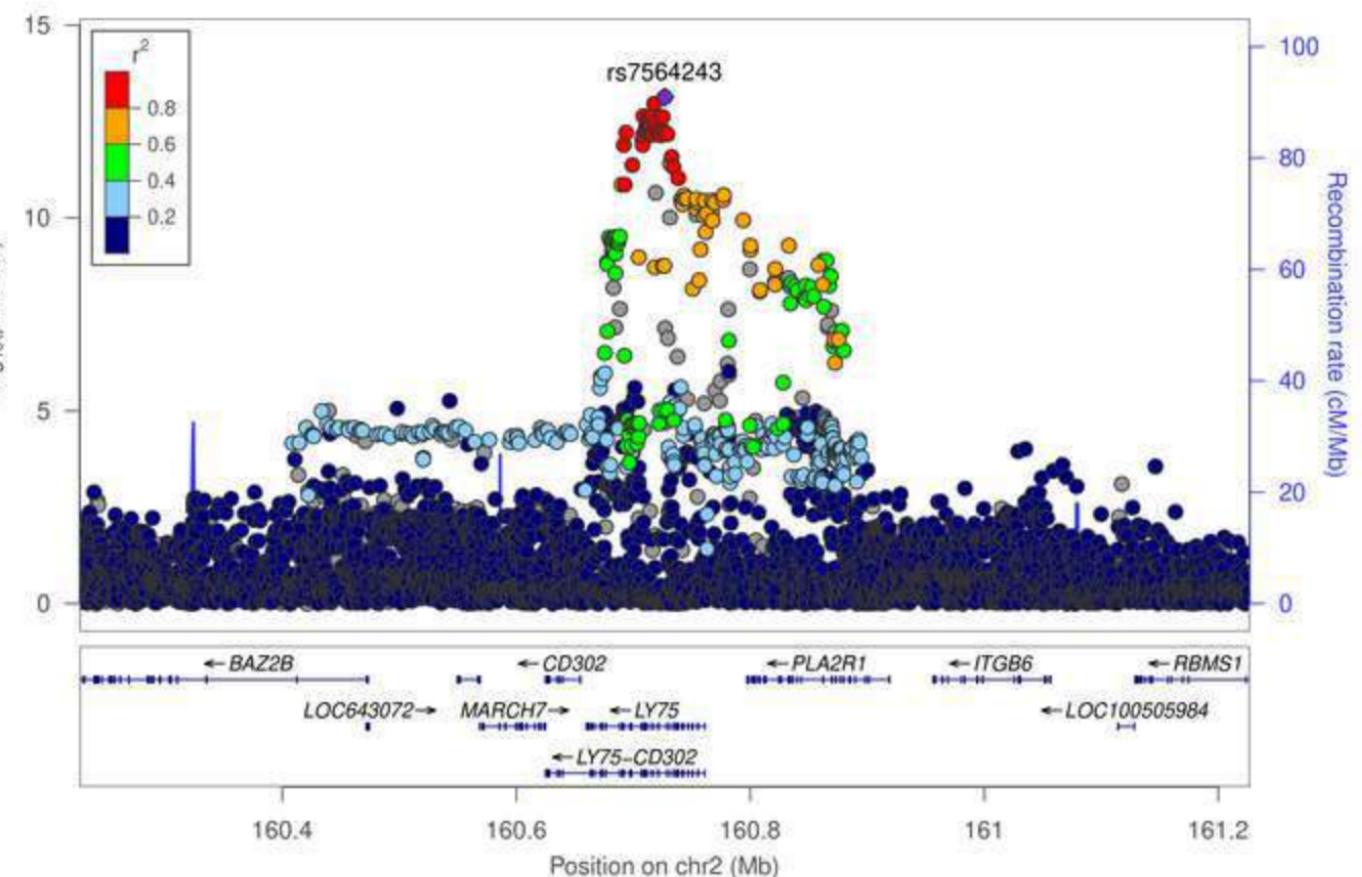
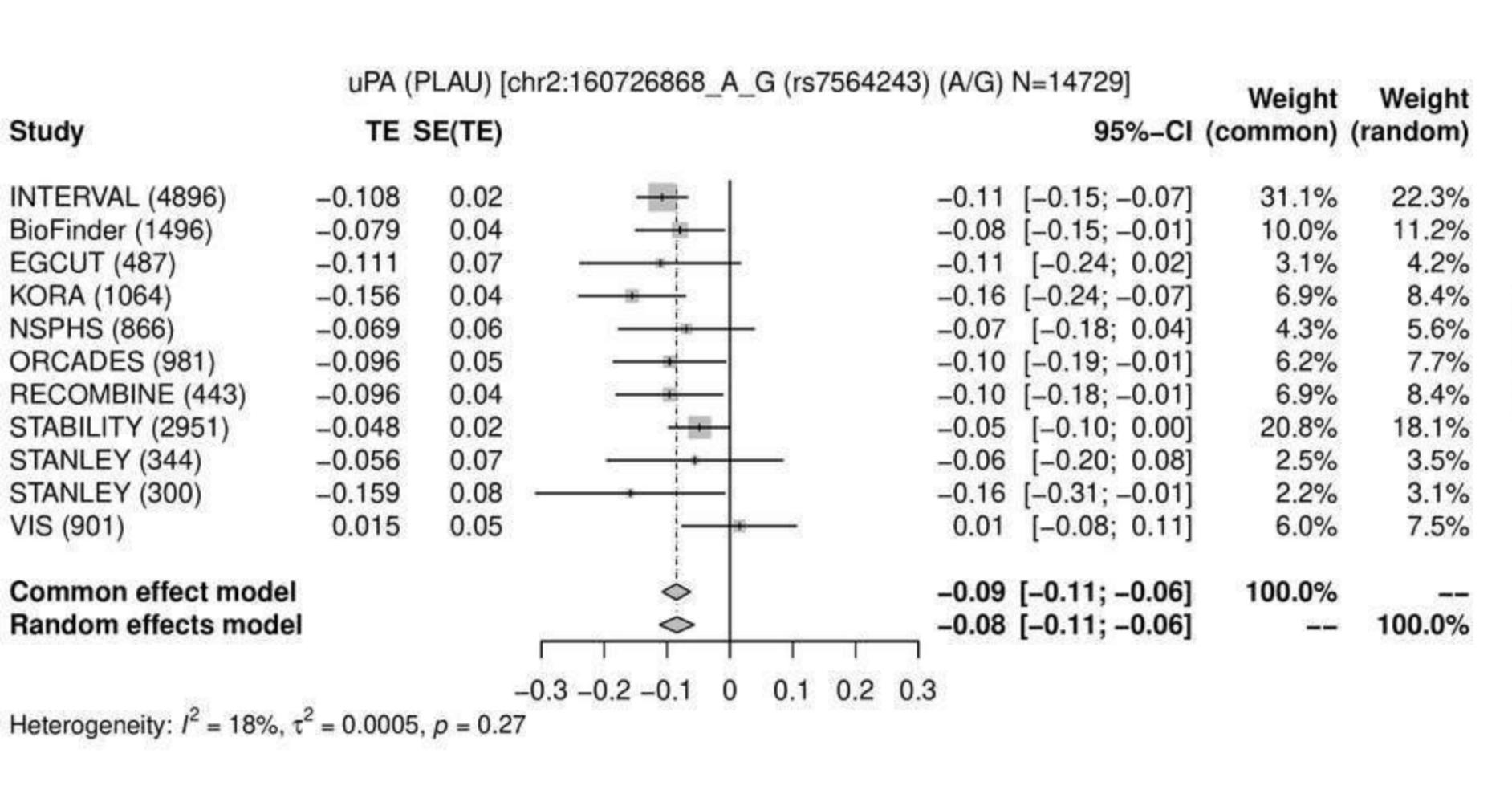
# uPA (PLAU)-rs4800787



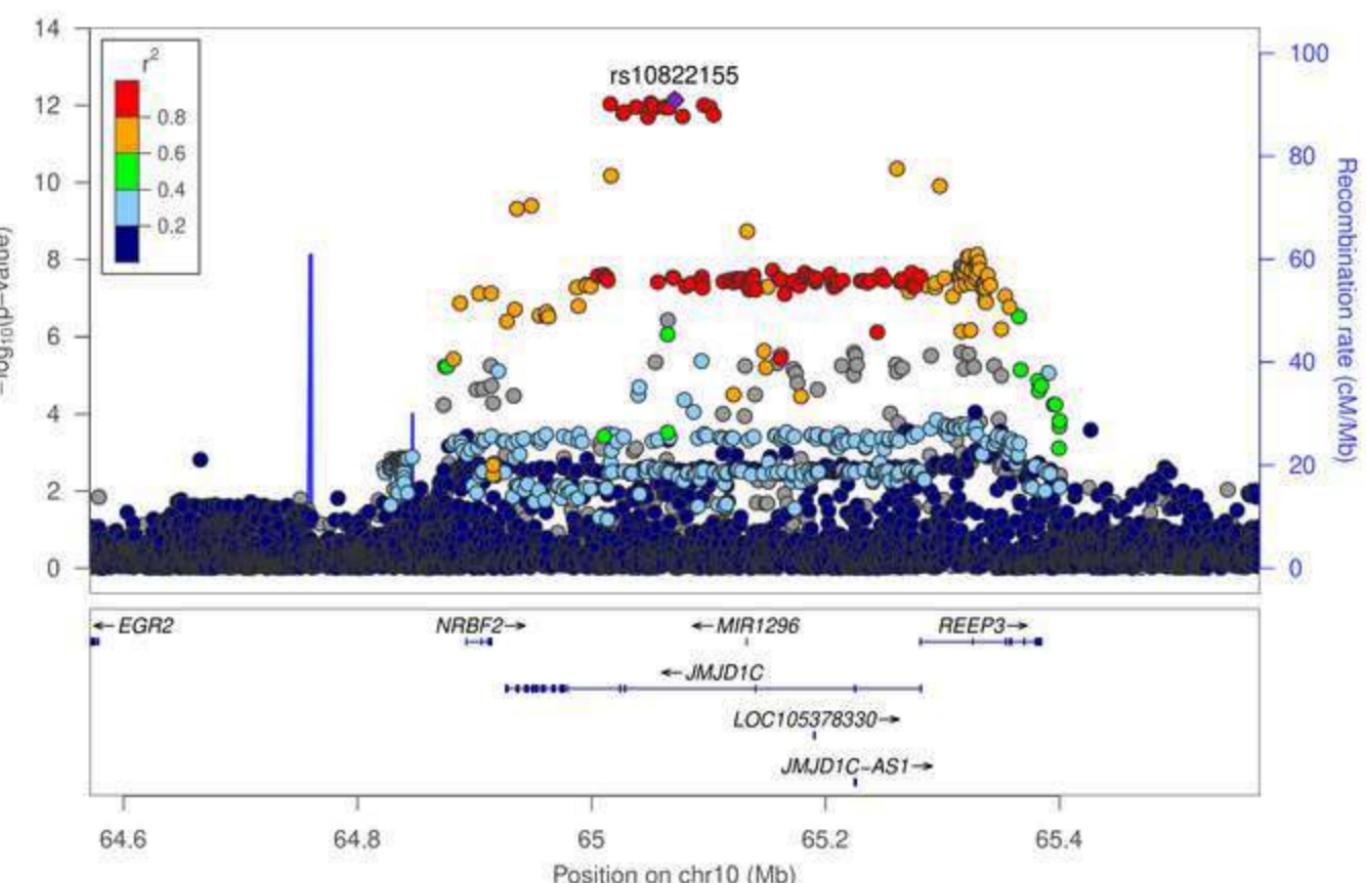
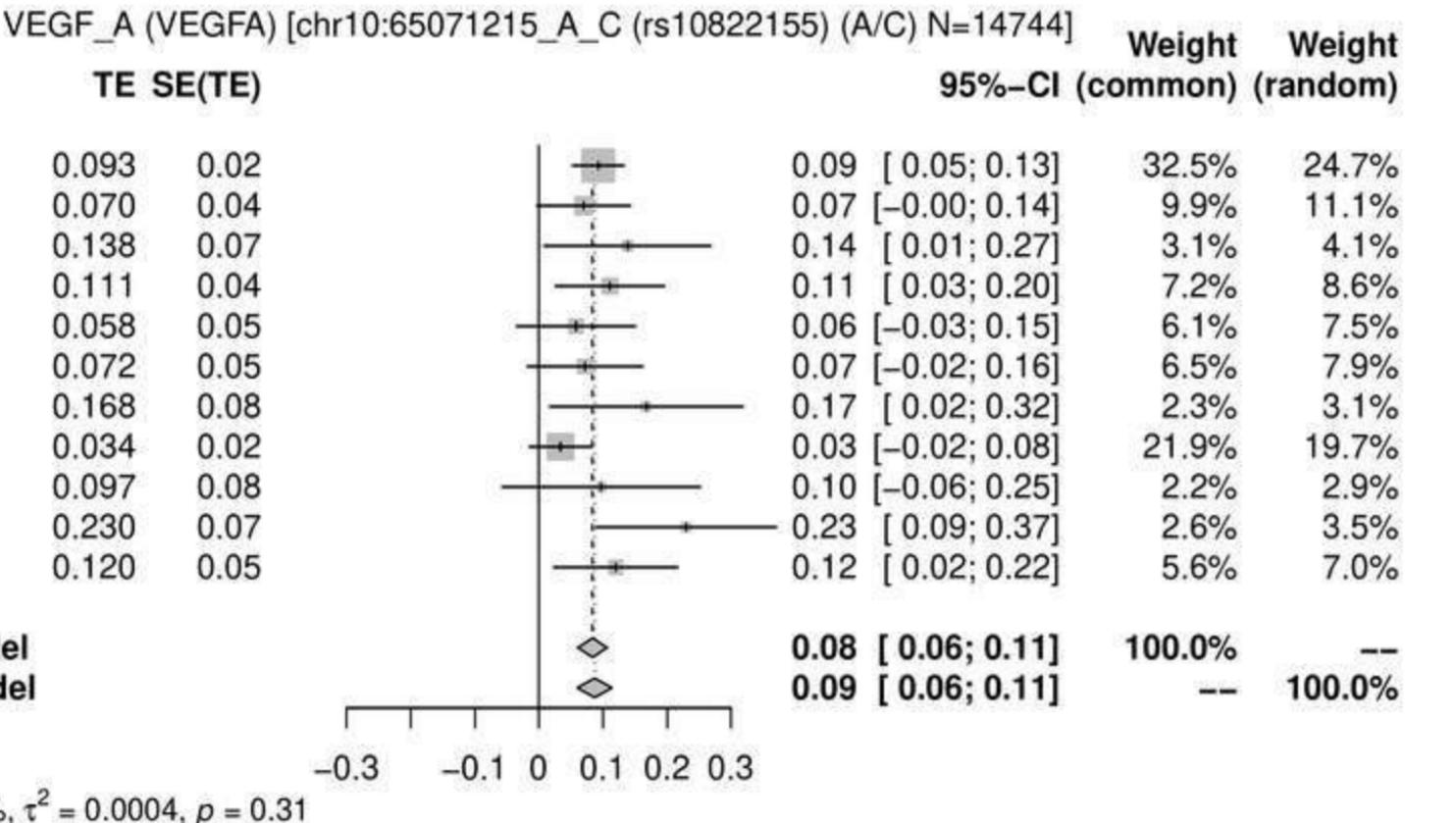
# uPA (PLAU)-rs4251805



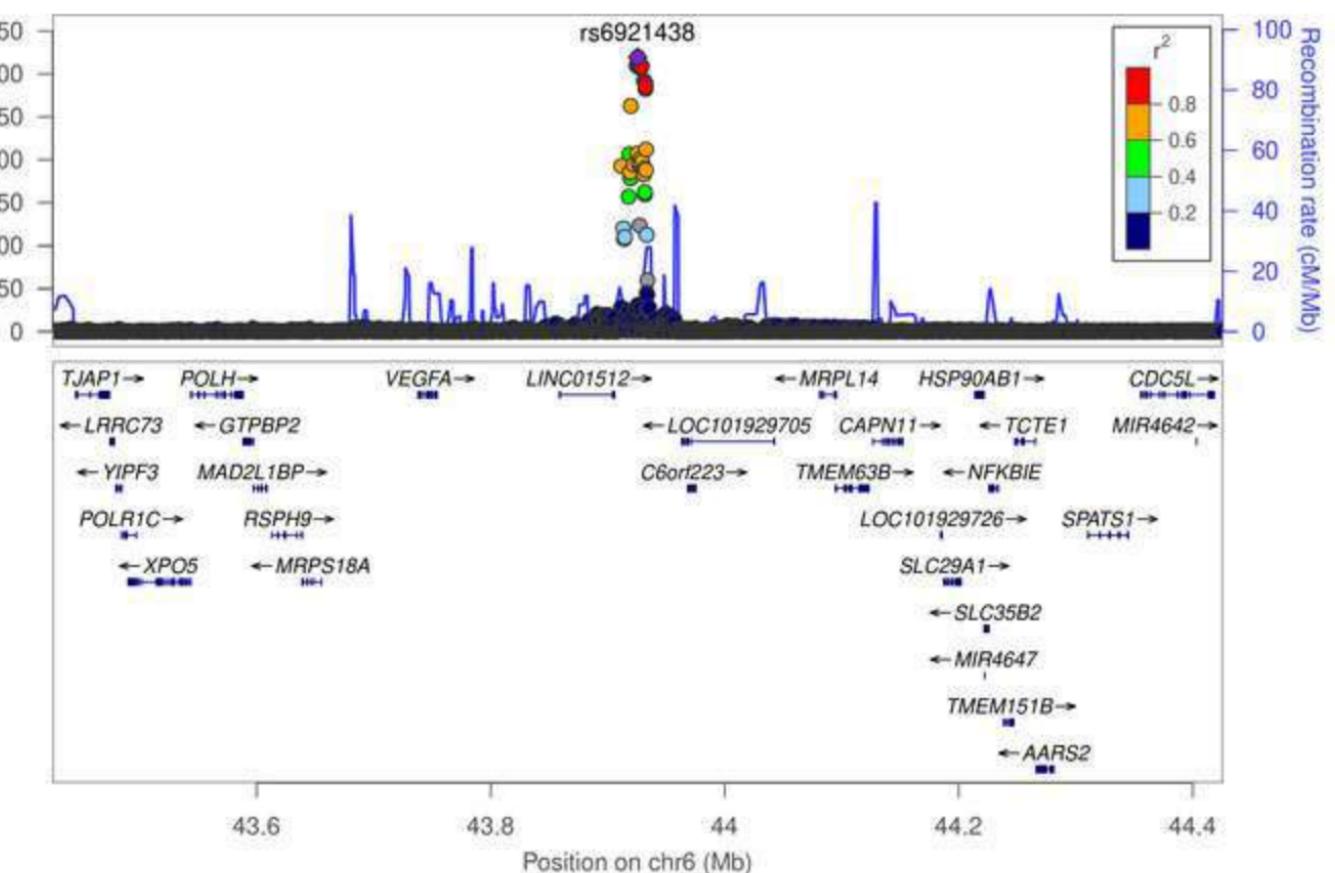
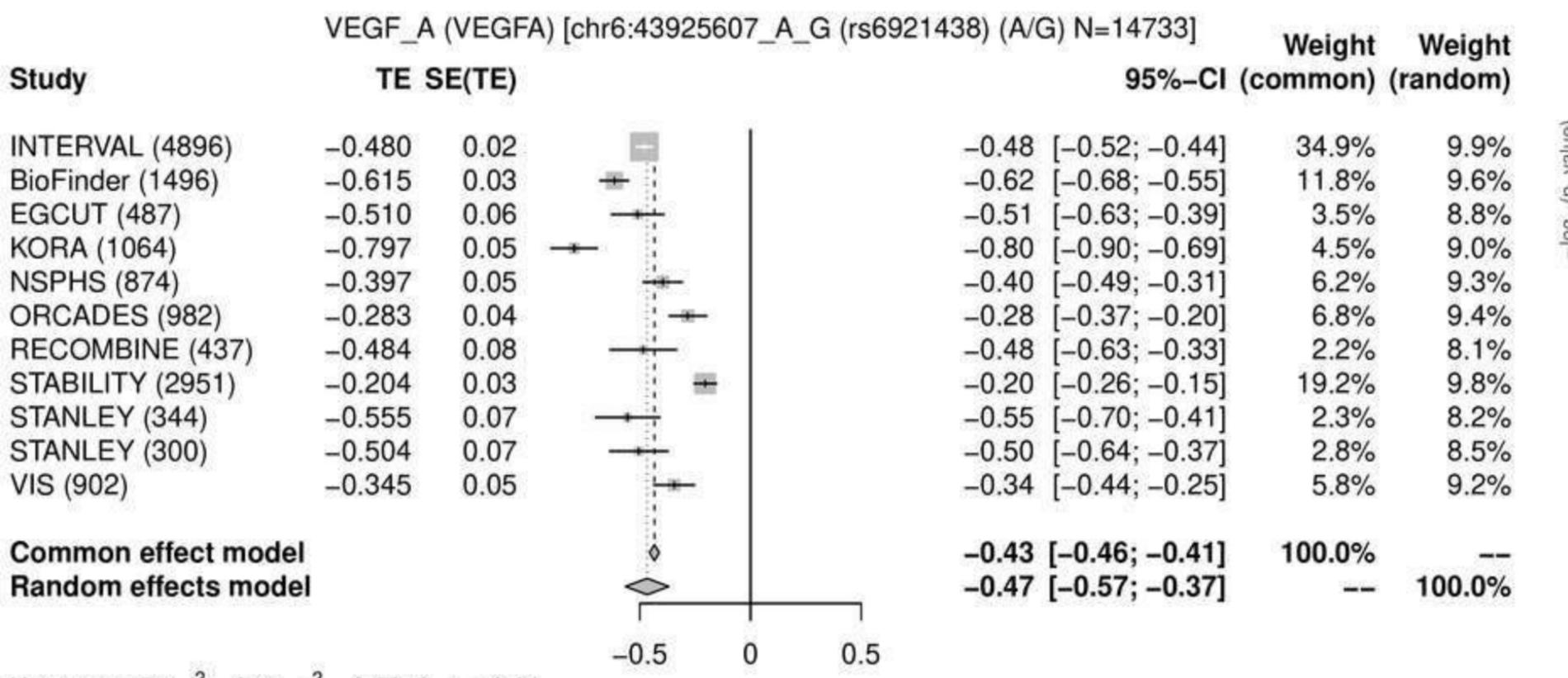
# uPA (PLAU)-rs7564243



# VEGF\_A (VEGFA)-rs10822155

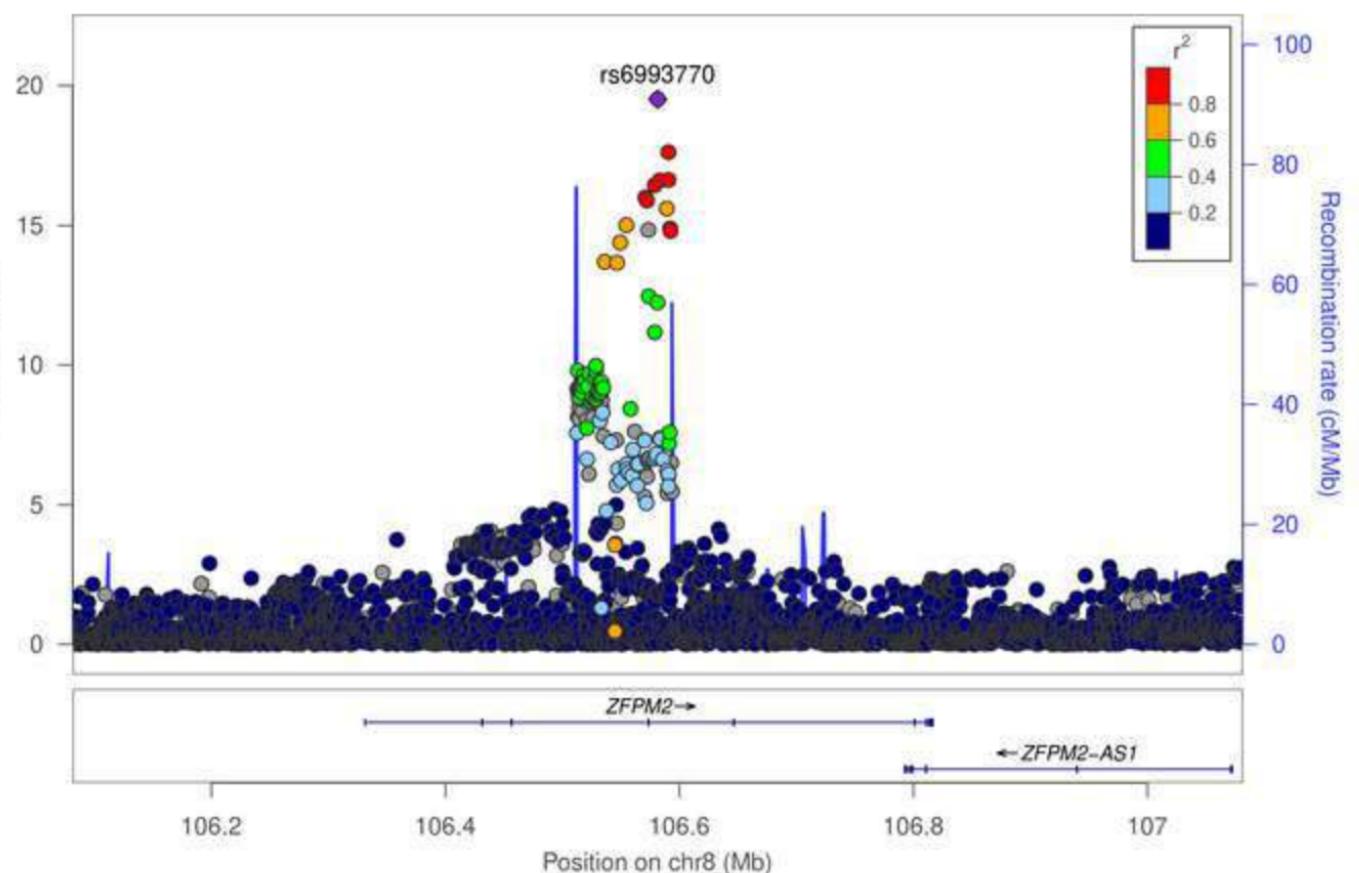
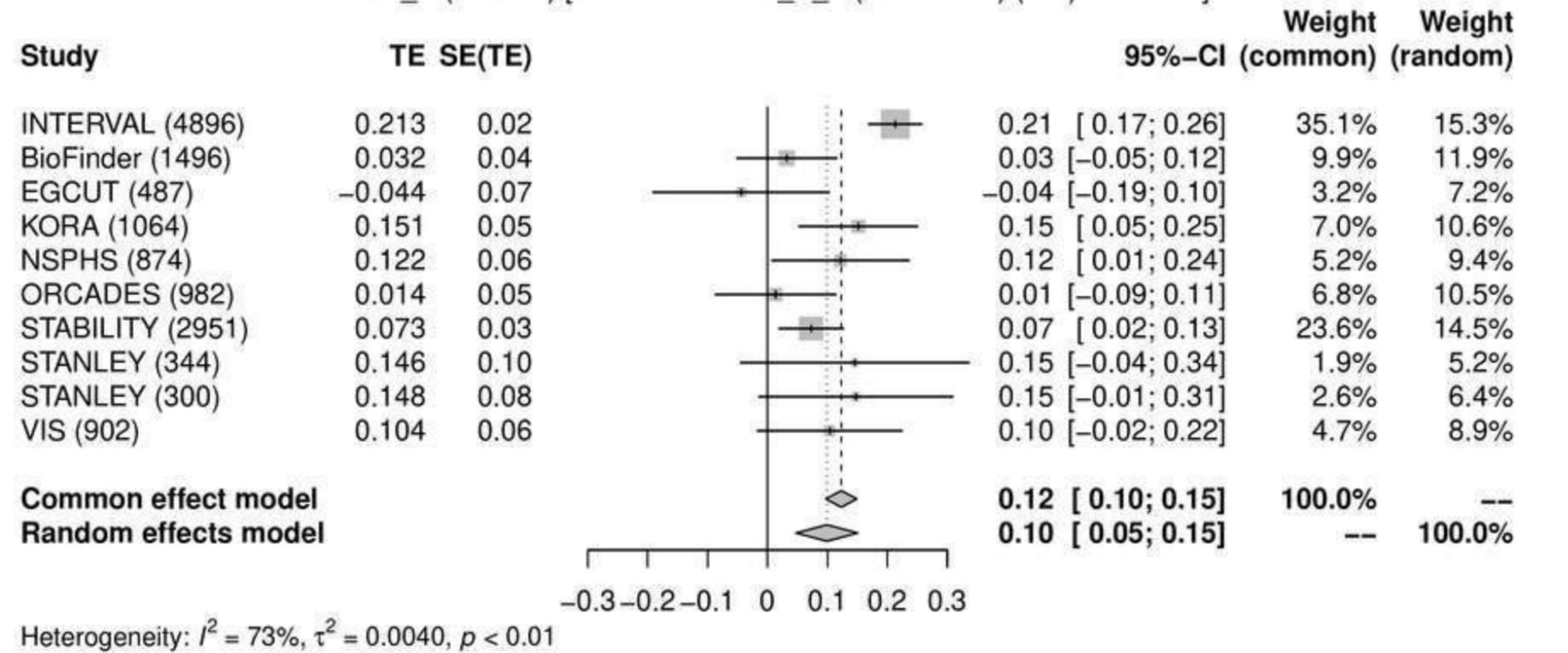


# VEGF\_A (VEGFA)-rs6921438



# VEGF\_A (VEGFA)-rs6993770

VEGF\_A (VEGFA) [chr8:106581528\_A\_T (rs6993770) (A/T) N=14296]



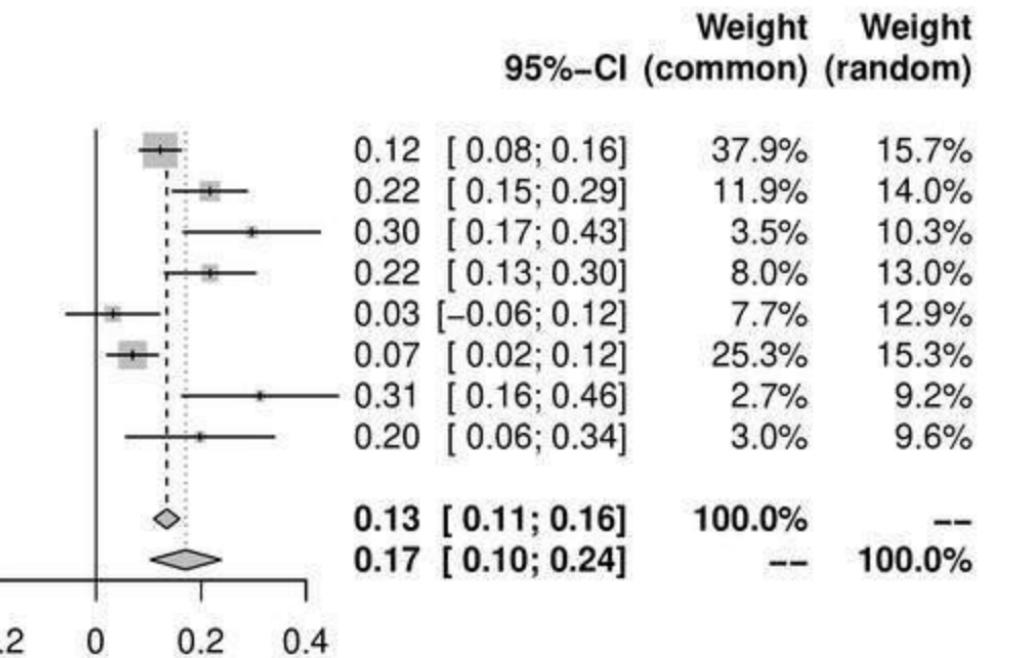
# VEGF\_A (VEGFA)-rs6475938

VEGF\_A (VEGFA) [chr9:2687795\_A\_T (rs6475938) (A/T) N=12412]

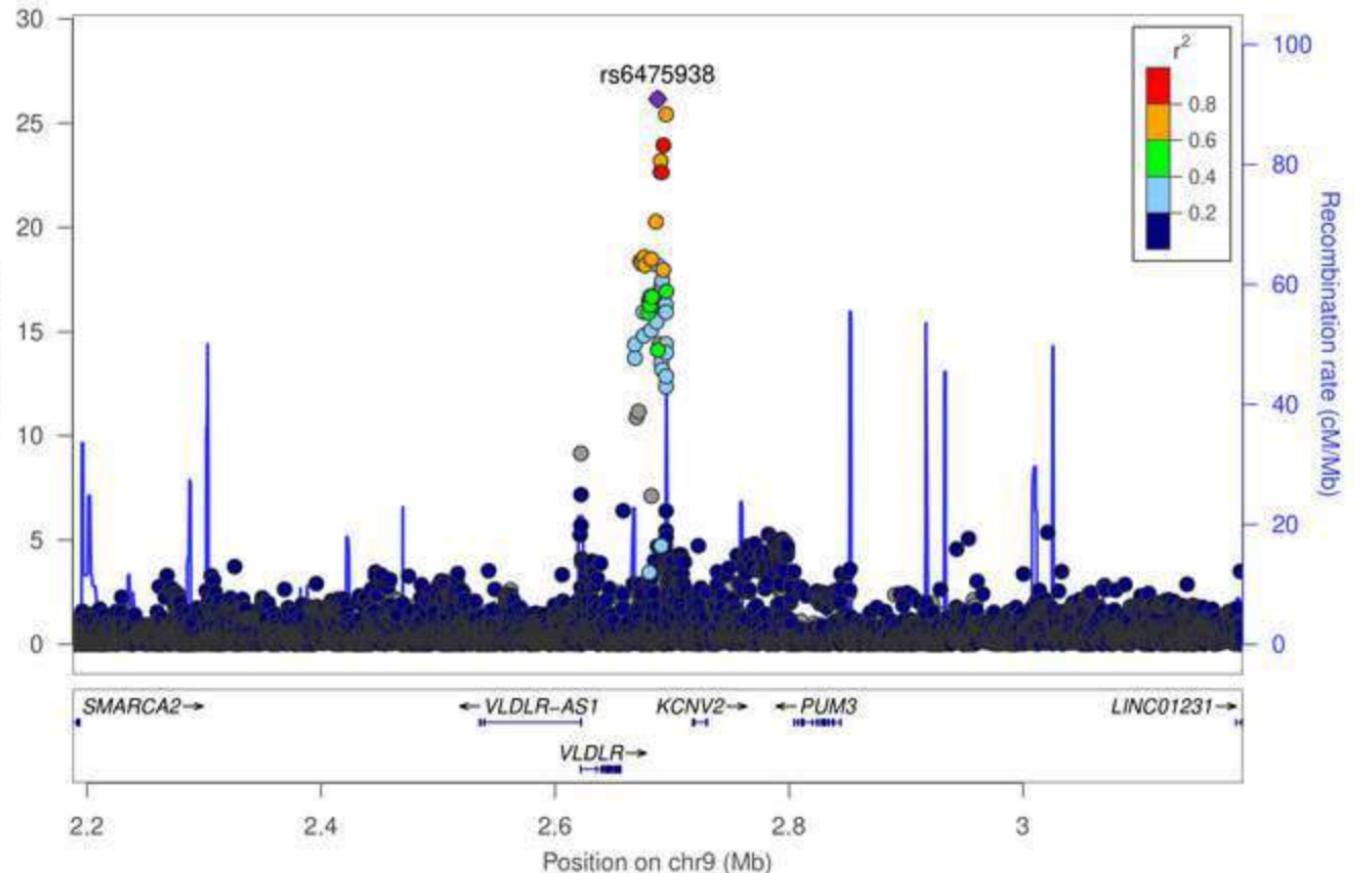
## Study

	TE	SE(TE)
INTERVAL (4896)	0.122	0.02
BioFinder (1496)	0.217	0.04
EGCUT (487)	0.296	0.07
KORA (1064)	0.217	0.04
NSPHS (874)	0.032	0.05
STABILITY (2951)	0.069	0.02
STANLEY (344)	0.312	0.08
STANLEY (300)	0.198	0.07

TE SE(TE)

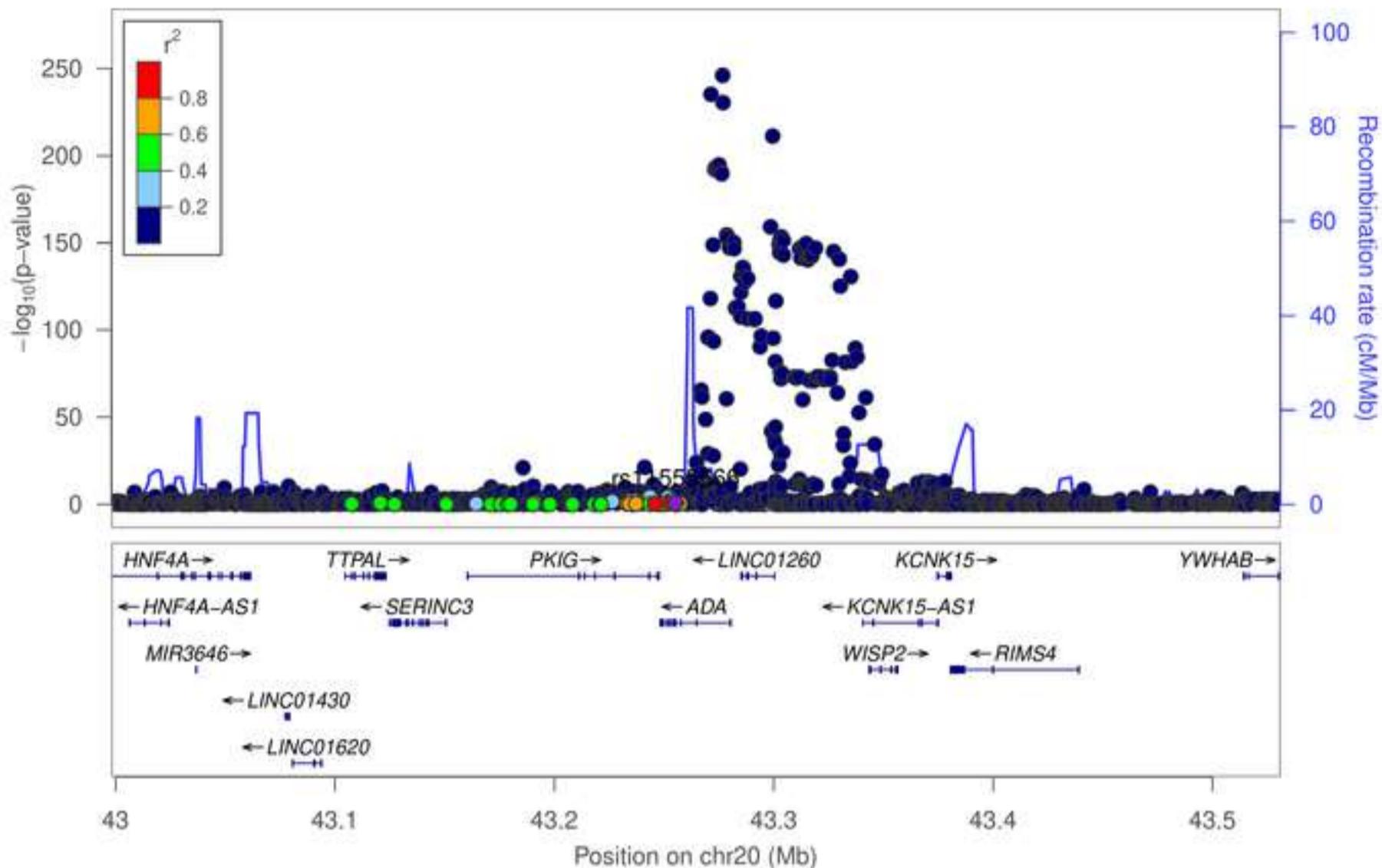


Heterogeneity:  $I^2 = 79\%, \tau^2 = 0.0072, p < 0.01$

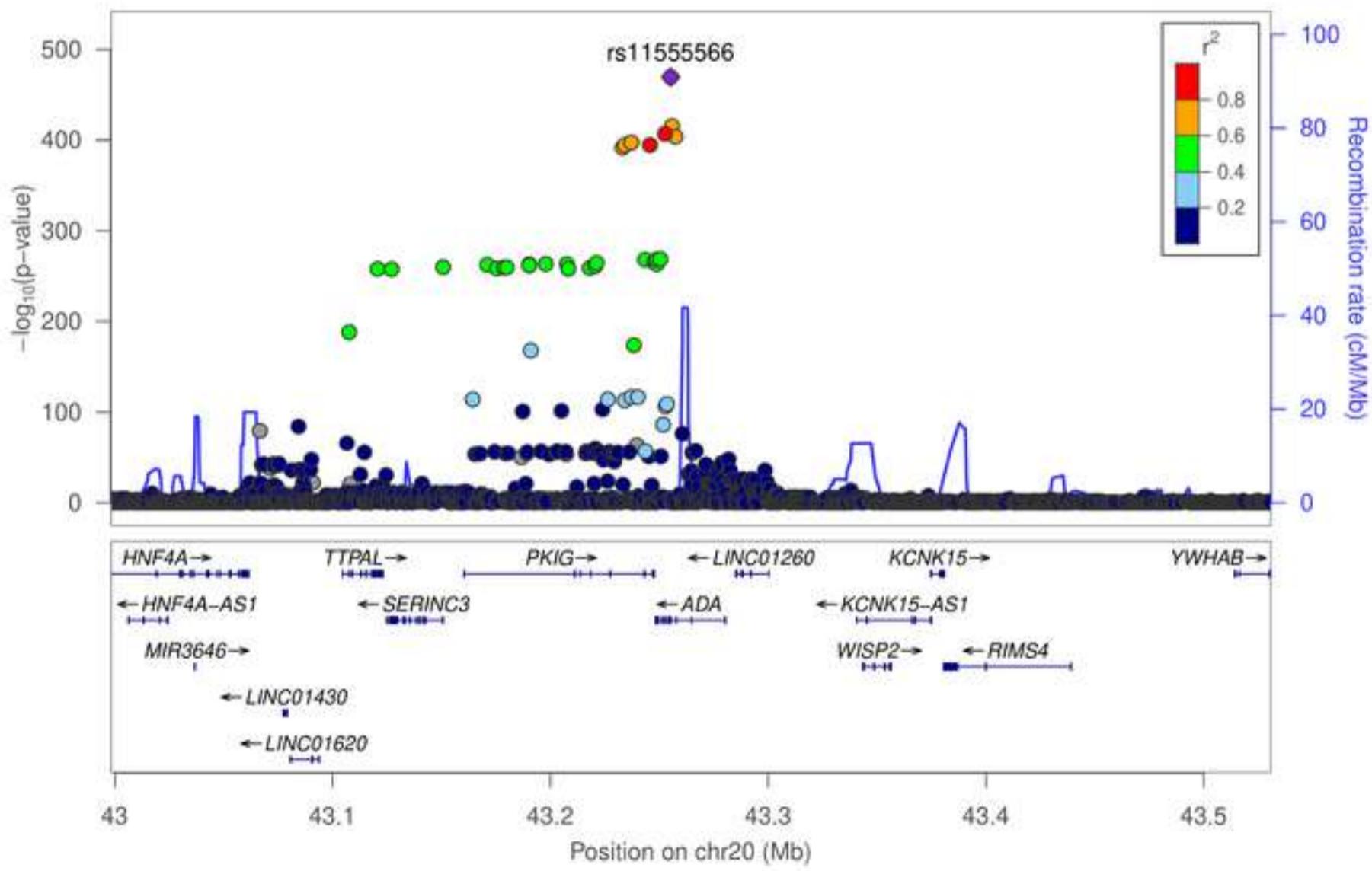


**Supplementary Figure 3.** Regional association plots comparing plasma *cis*-pQTLs and blood *cis*-eQTLs for the gene encoding the corresponding protein. ‘LocusZoom’ regional association plots comparing the plasma *cis*-pQTL signals (lower panel) with the eQTL signals for the encoding gene in whole blood from the eQTLGen data (upper panel). The sentinel variant for the pQTL is coloured in purple. LD ( $r^2$ ) to the sentinel pQTL is indicated by the colour key. Two-sided  $P$ -values are from meta-analysis of linear regression estimates.

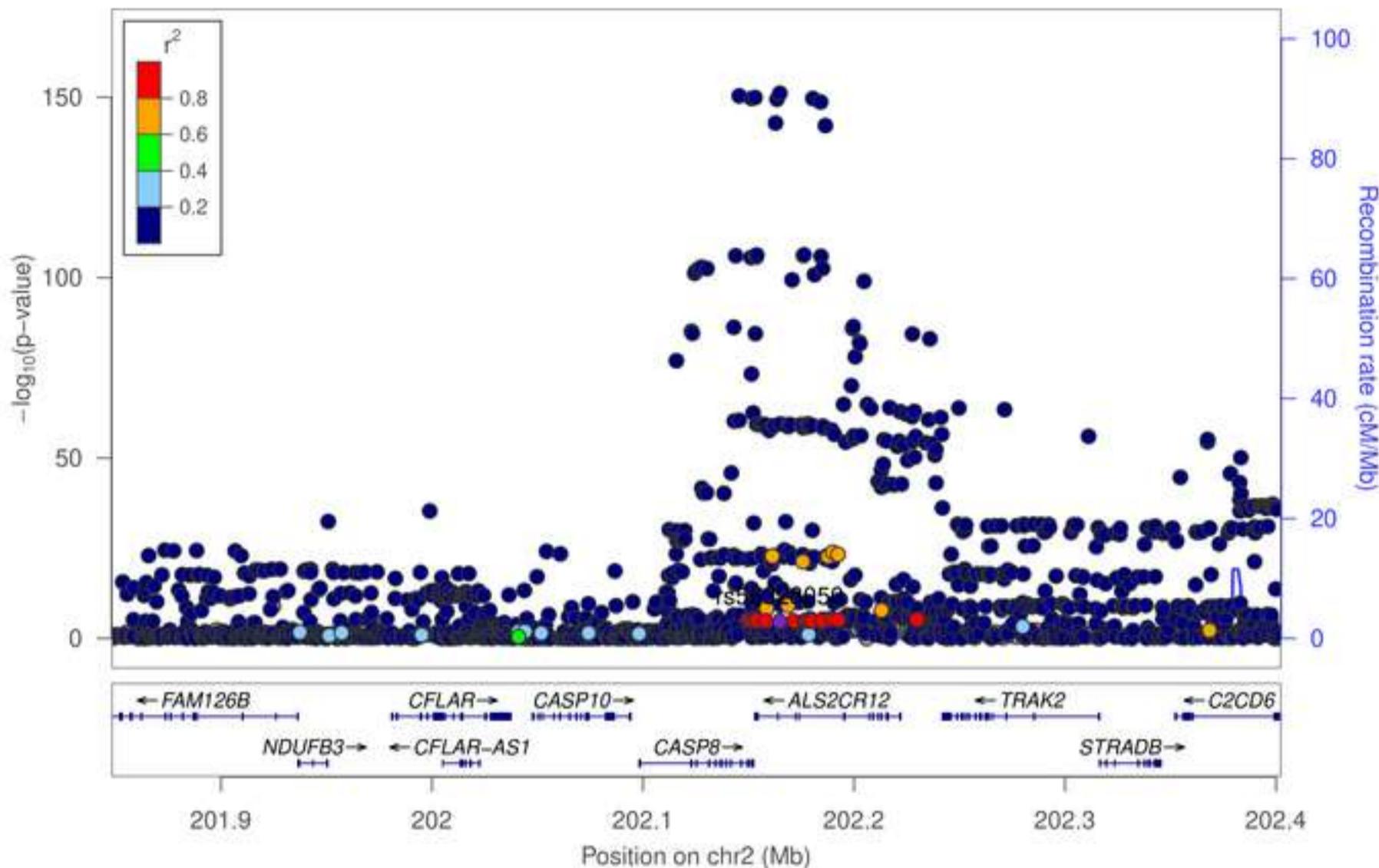
# eQTLGen: ADA (ADA)-rs11555566



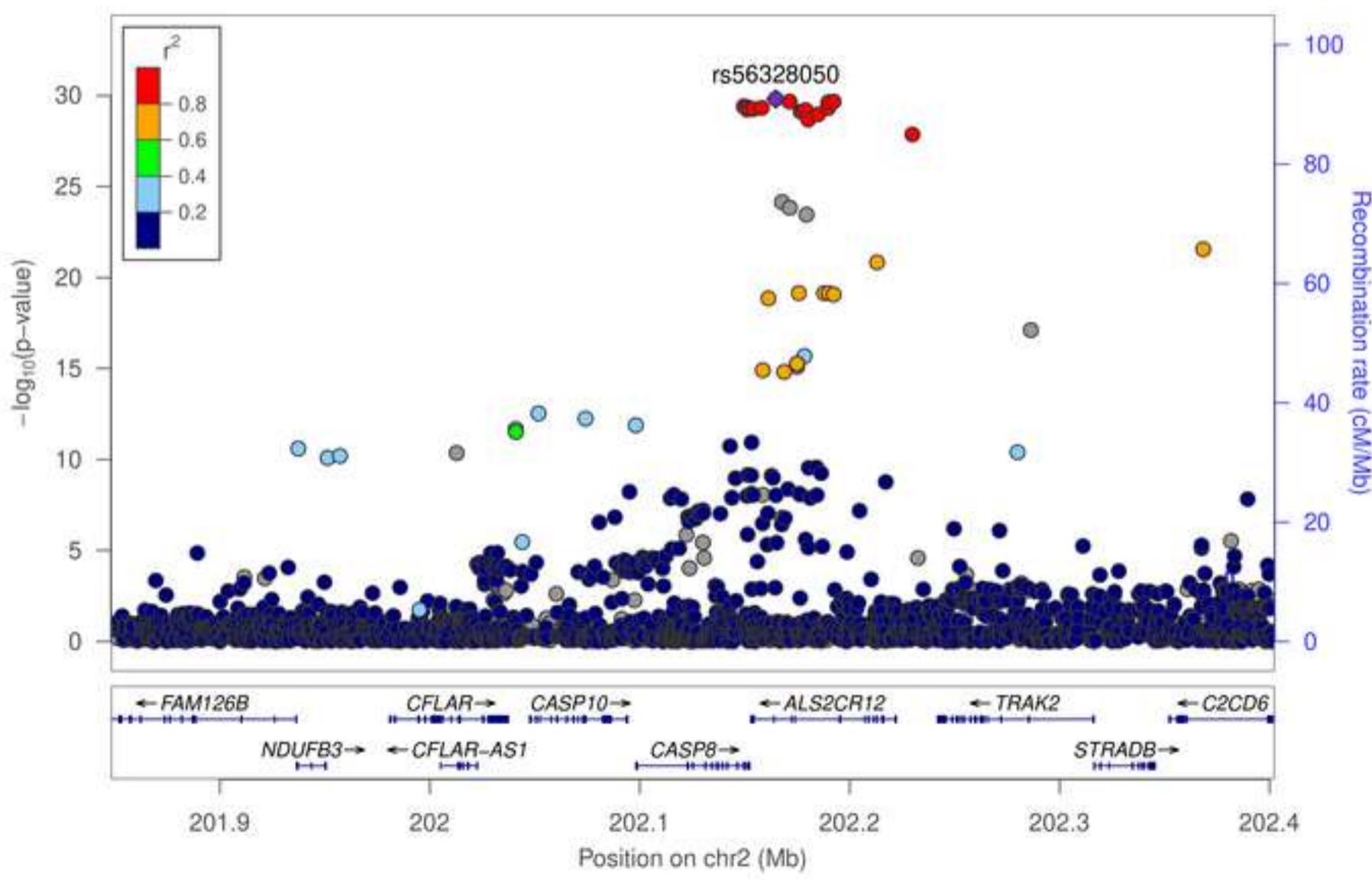
# SCALLOP: ADA (ADA)-rs11555566



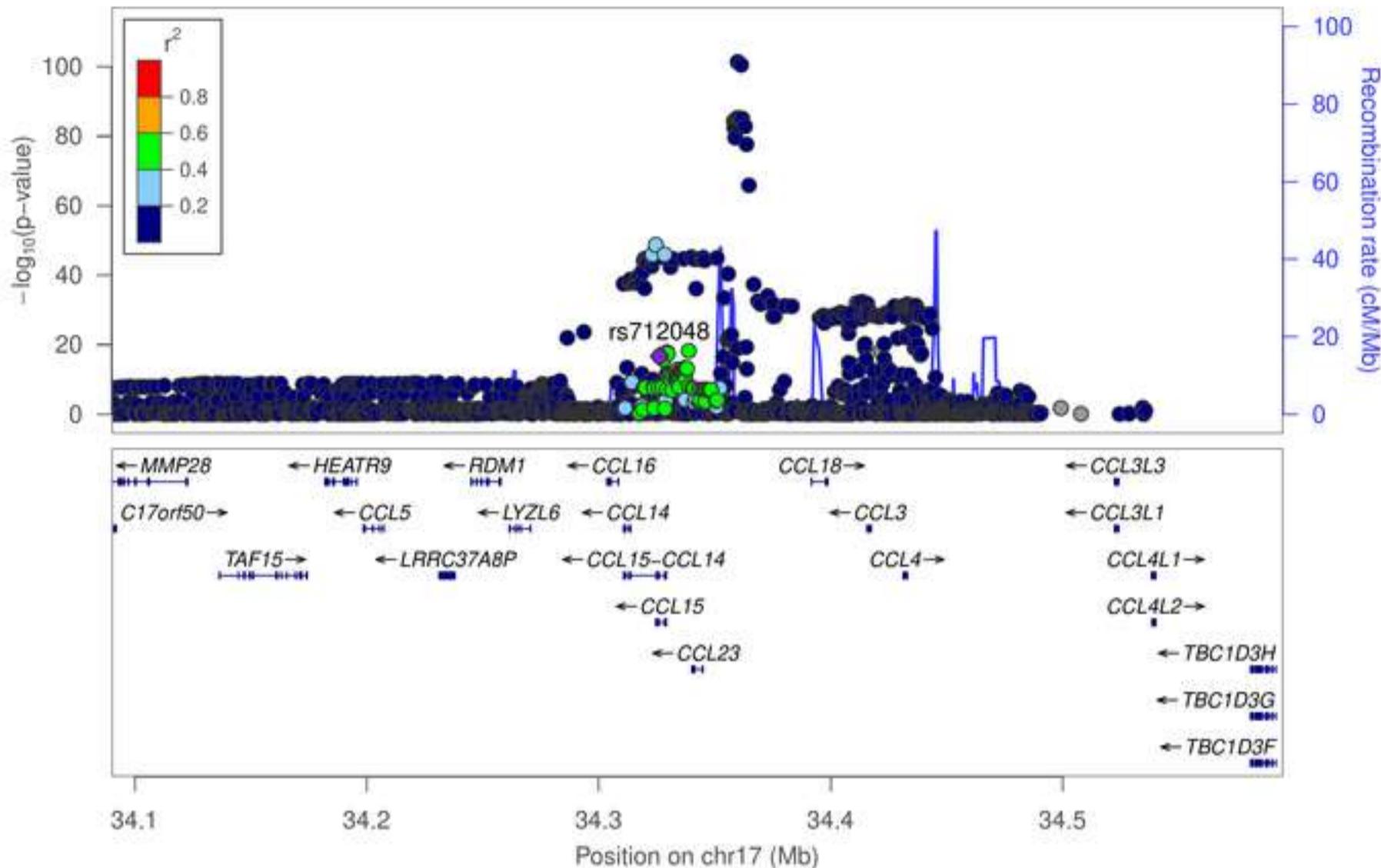
# eQTLGen: CASP-8 (CASP8)-rs56328050



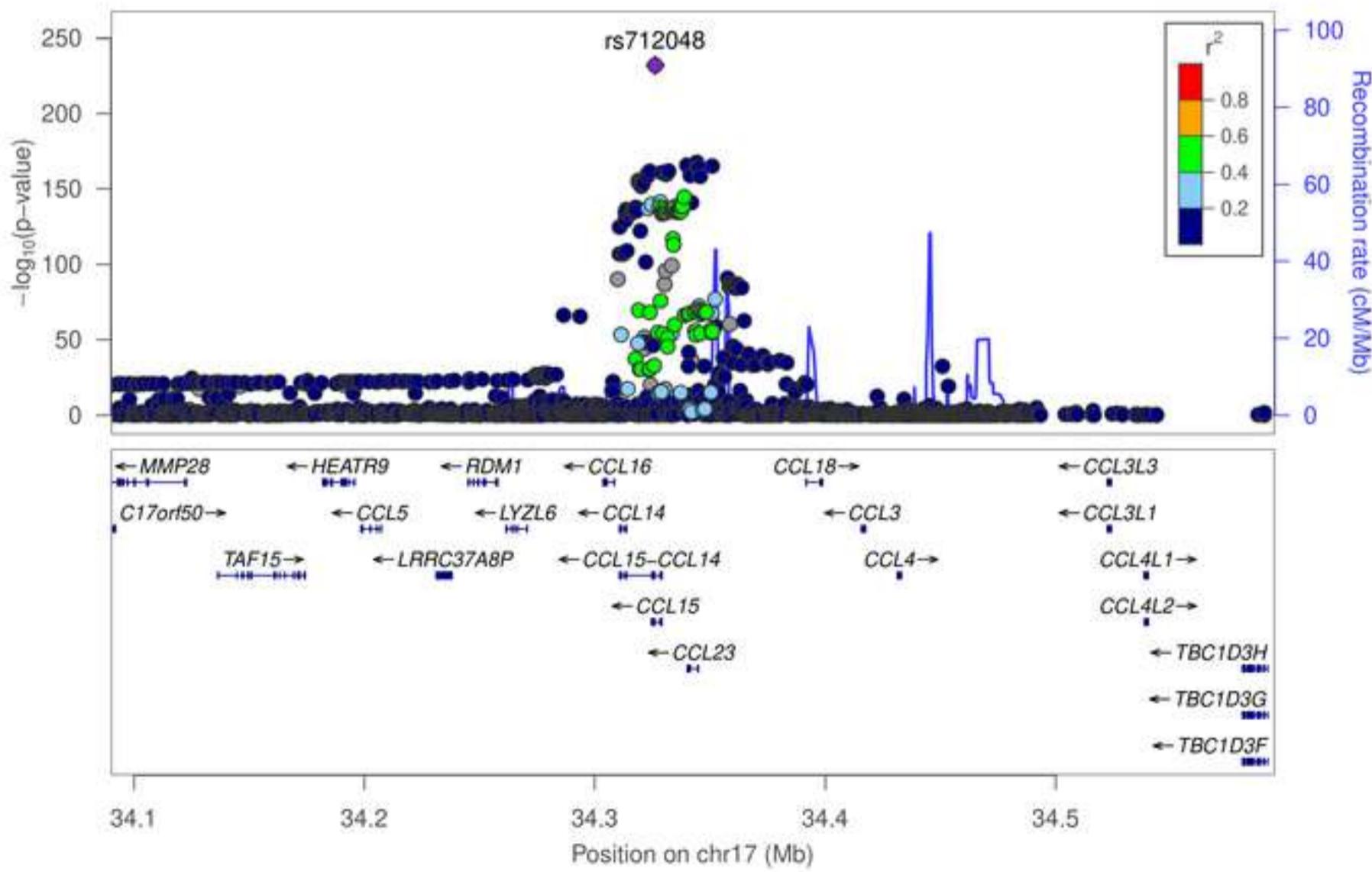
# SCALLOP: CASP-8 (CASP8)-rs56328050



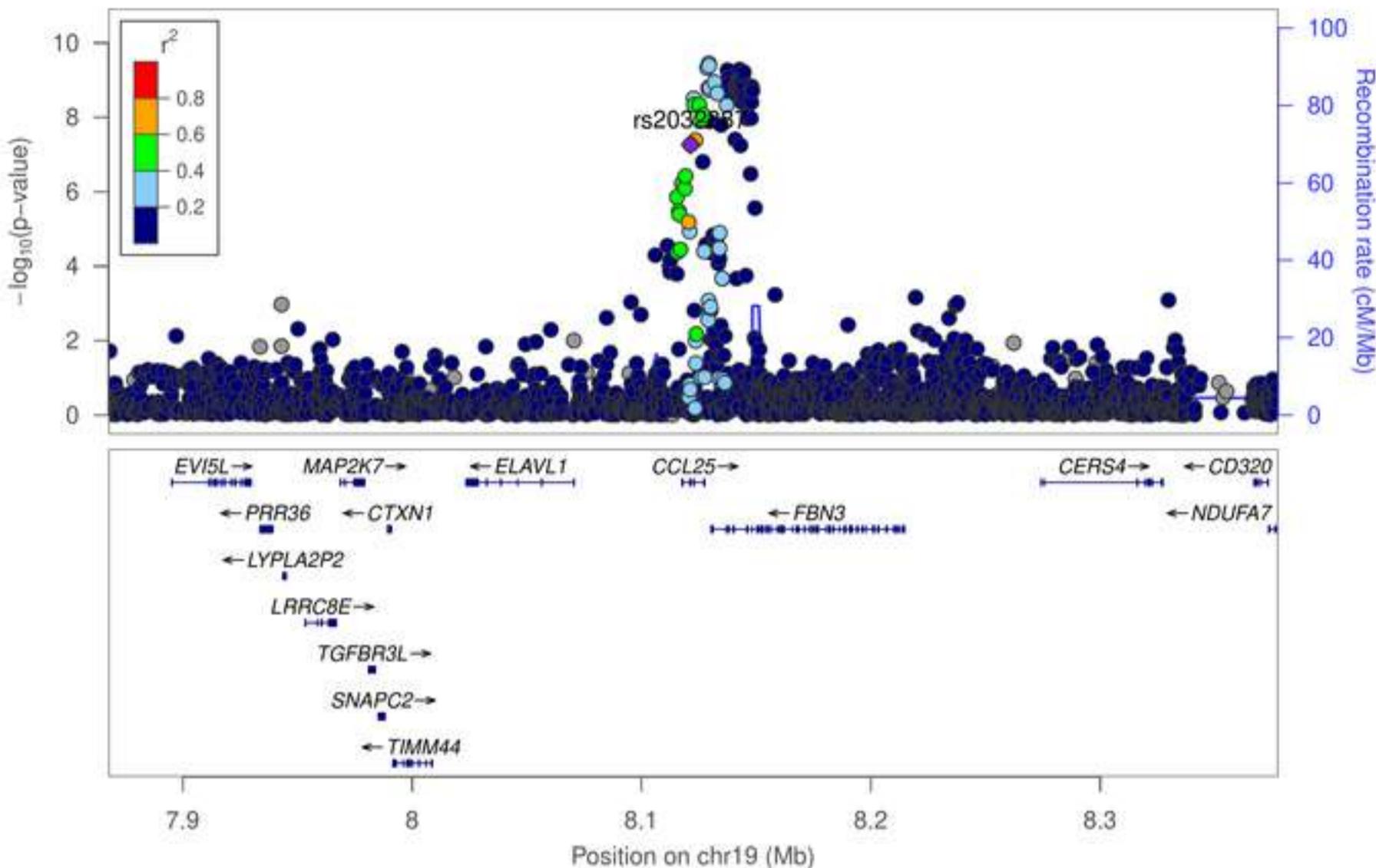
## eQTLGen: CCL23 (CCL23)-rs712048



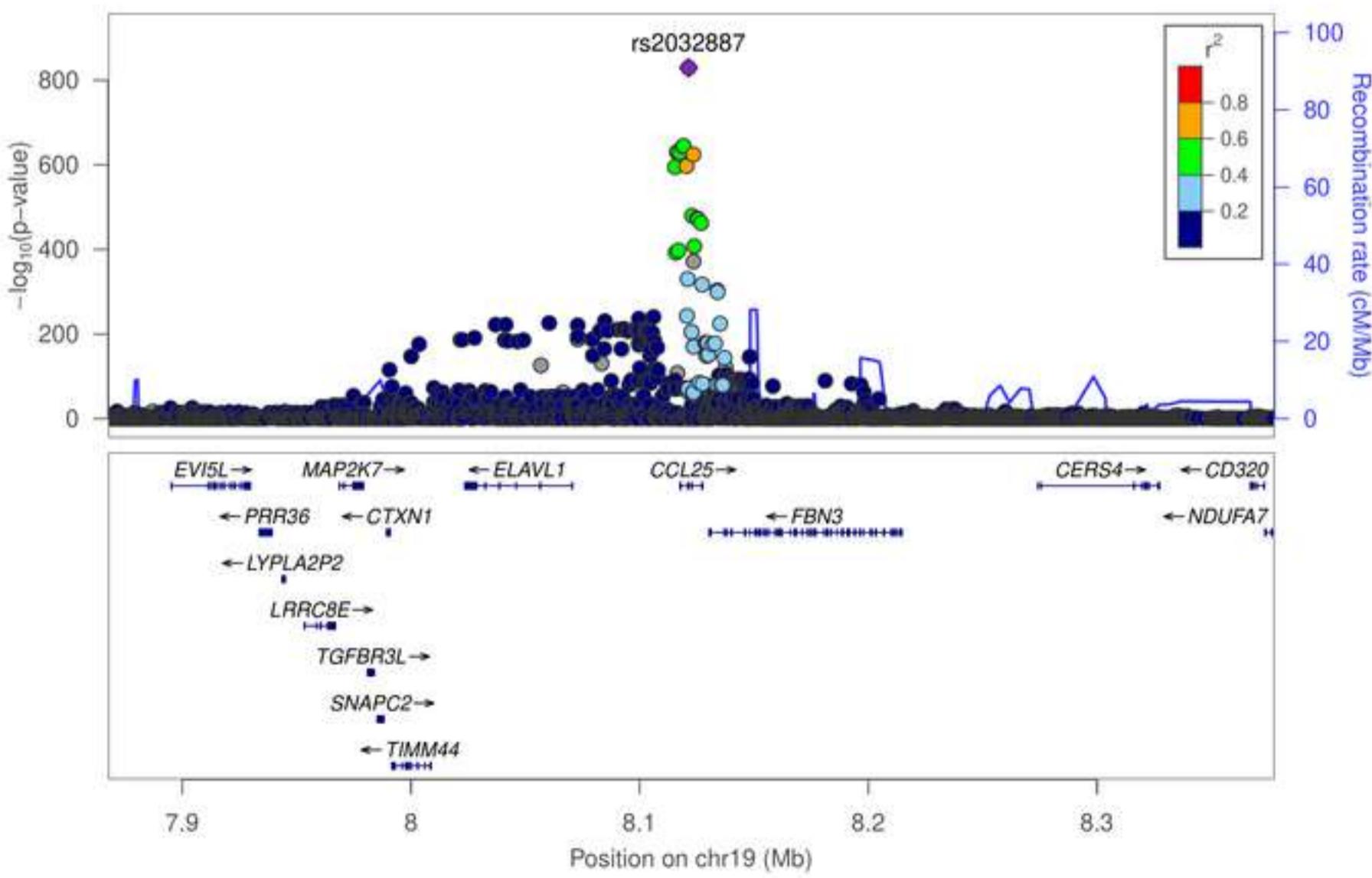
## SCALLOP: CCL23 (CCL23)-rs712048



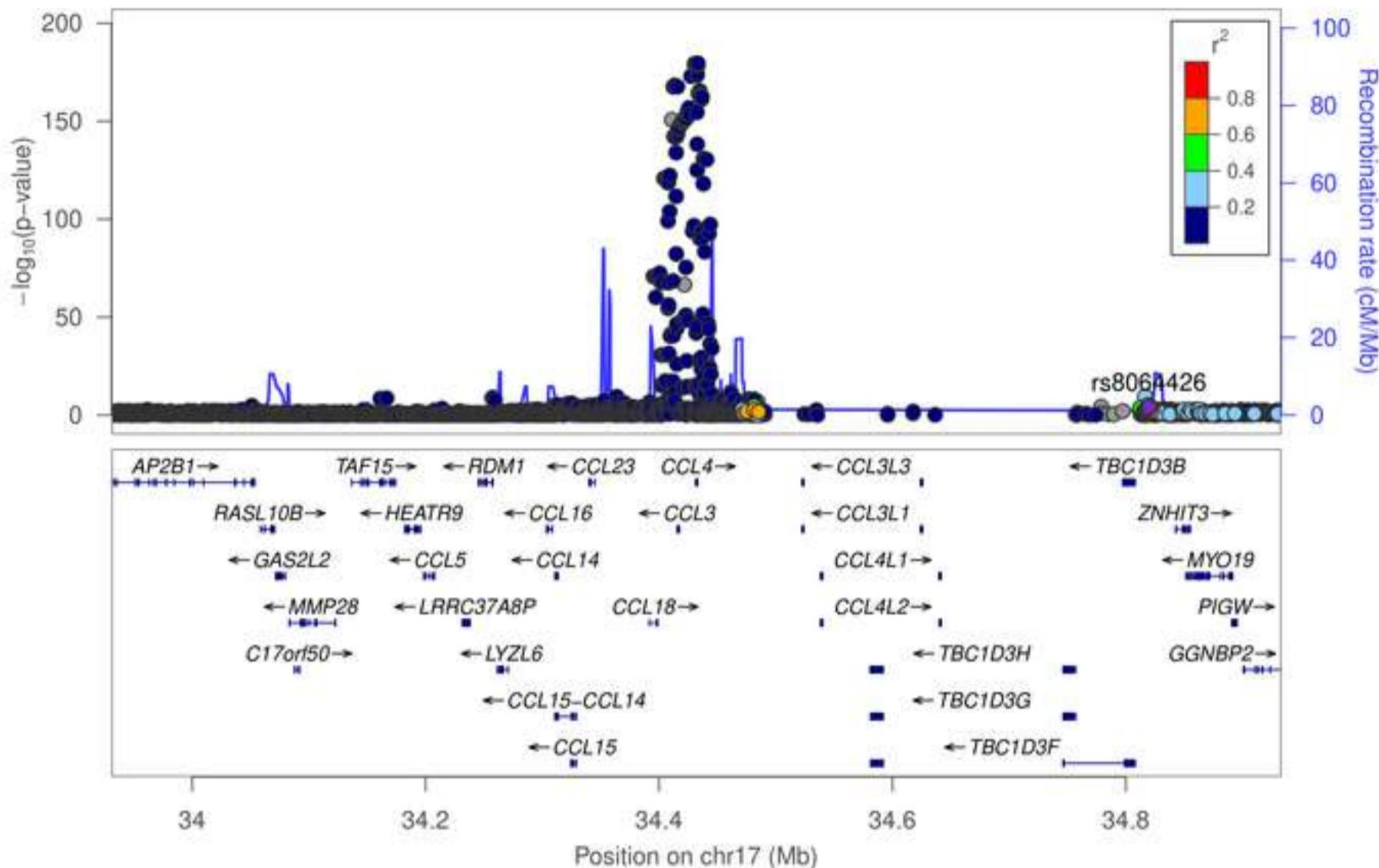
# eQTLGen: CCL25 (CCL25)-rs2032887



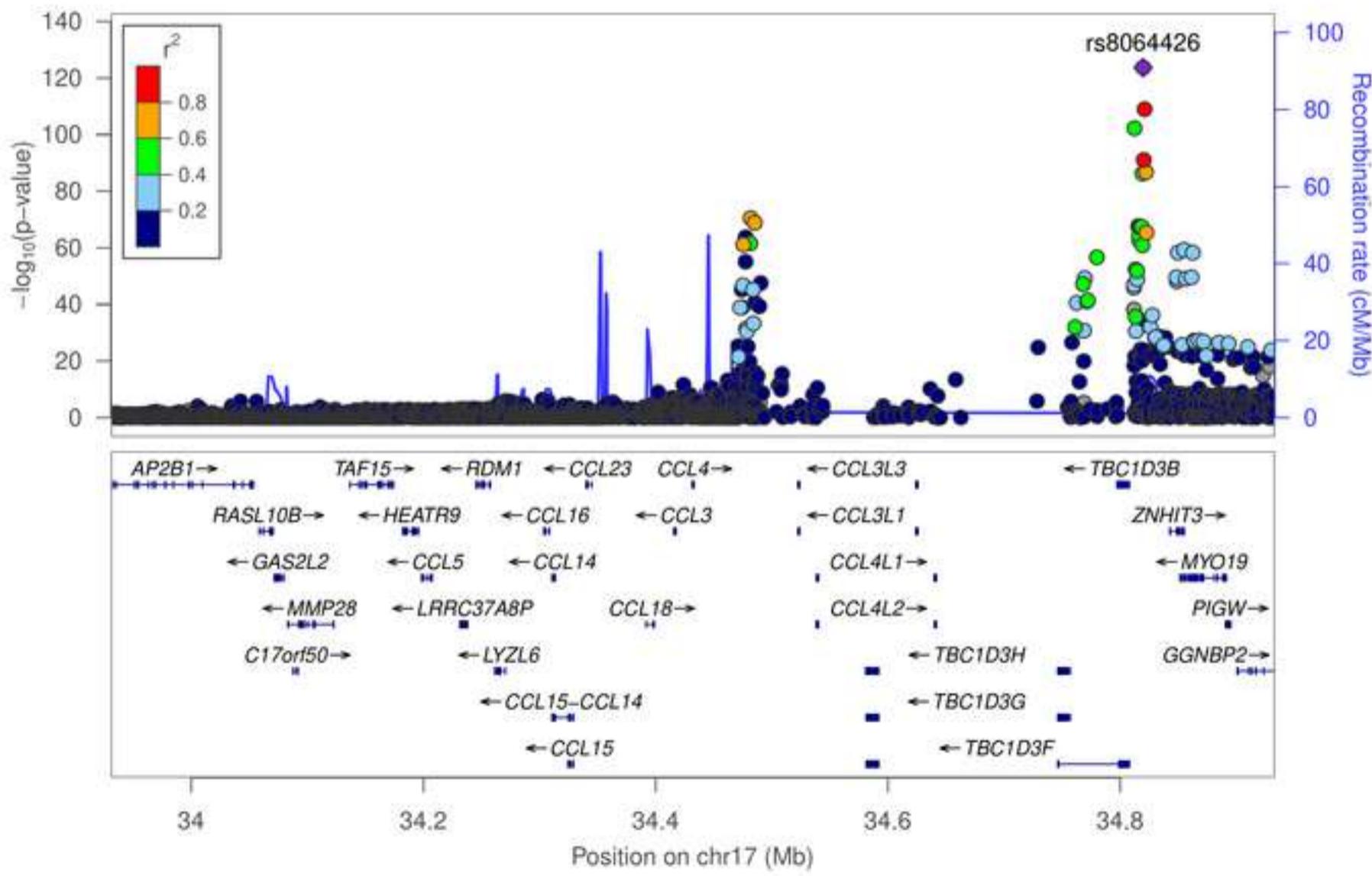
# SCALLOP: CCL25 (CCL25)-rs2032887



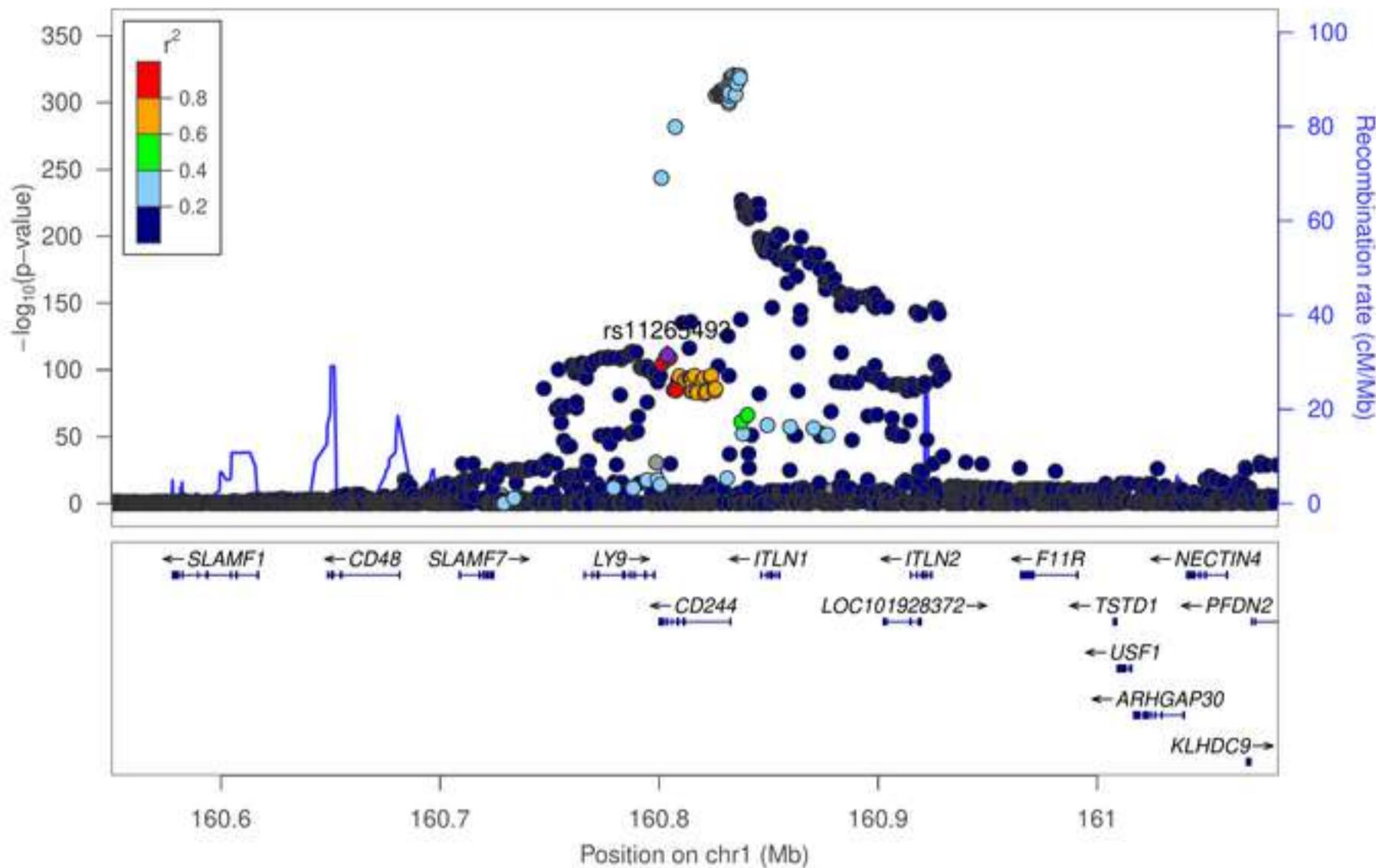
# eQTLGen: CCL4 (CCL4)-rs8064426



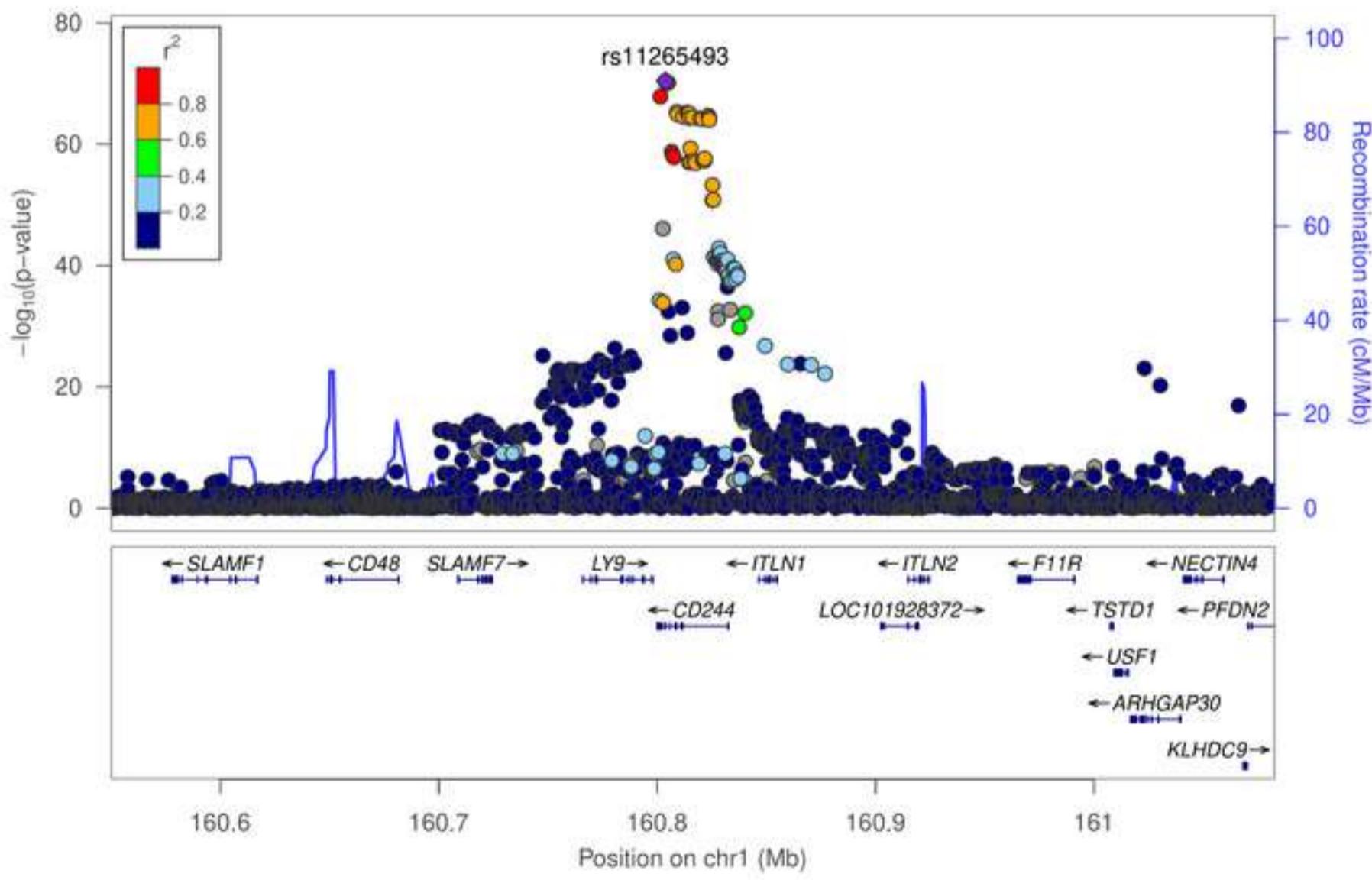
# SCALLOP: CCL4 (CCL4)-rs8064426



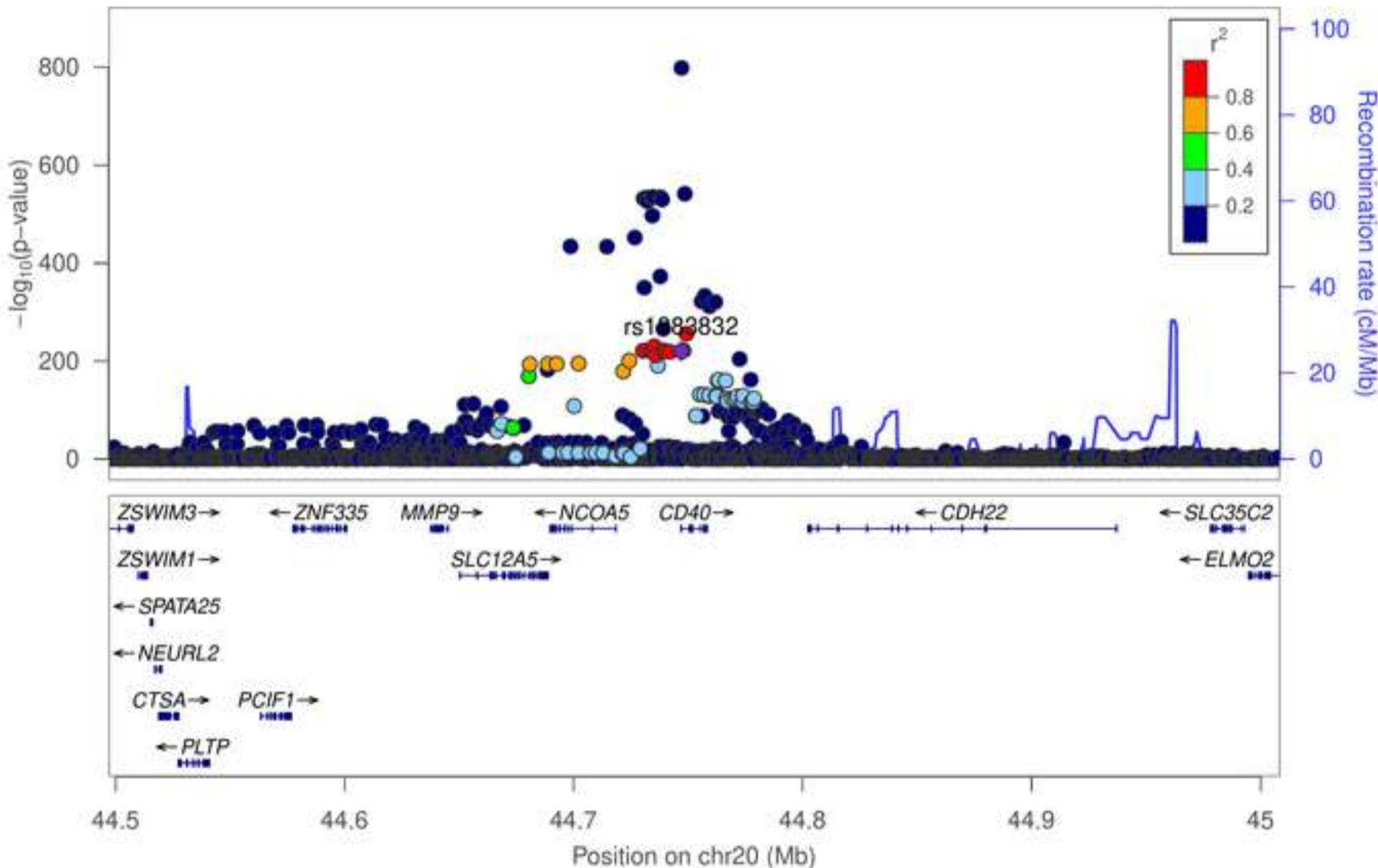
## eQTLGen: CD244 (CD244)-rs11265493



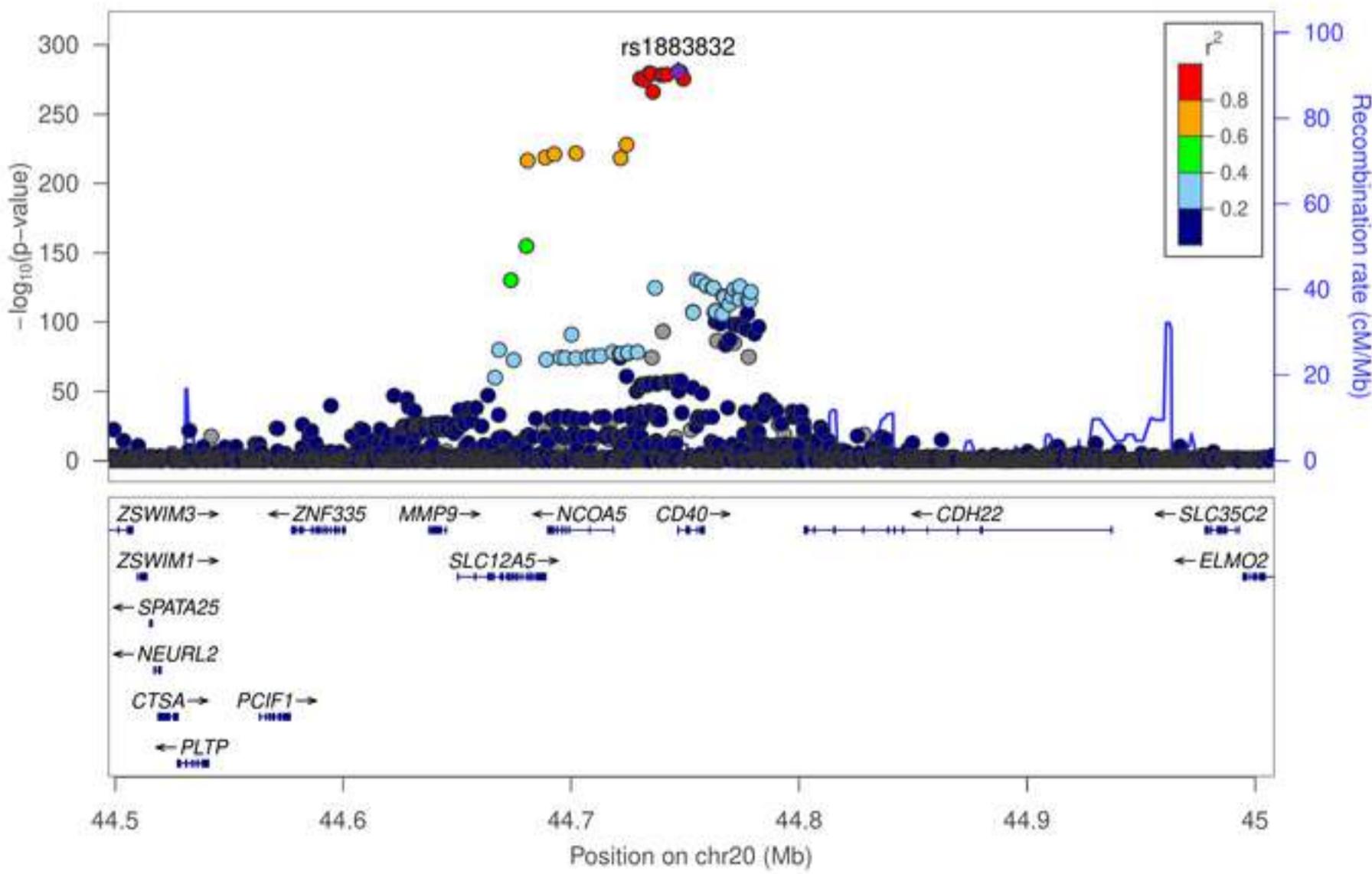
## SCALLOP: CD244 (CD244)-rs11265493



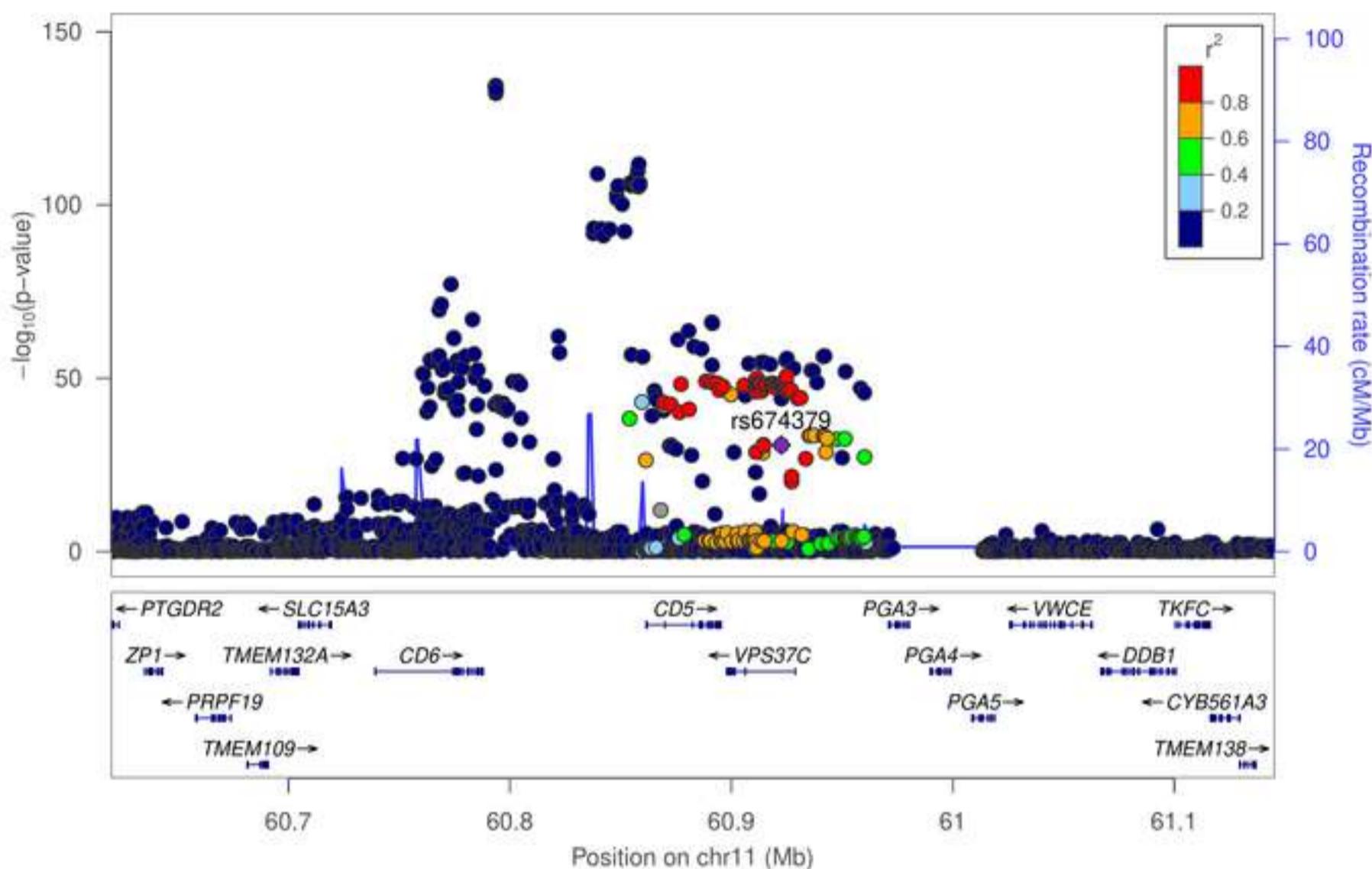
# eQTLGen: CD40 (CD40)-rs1883832



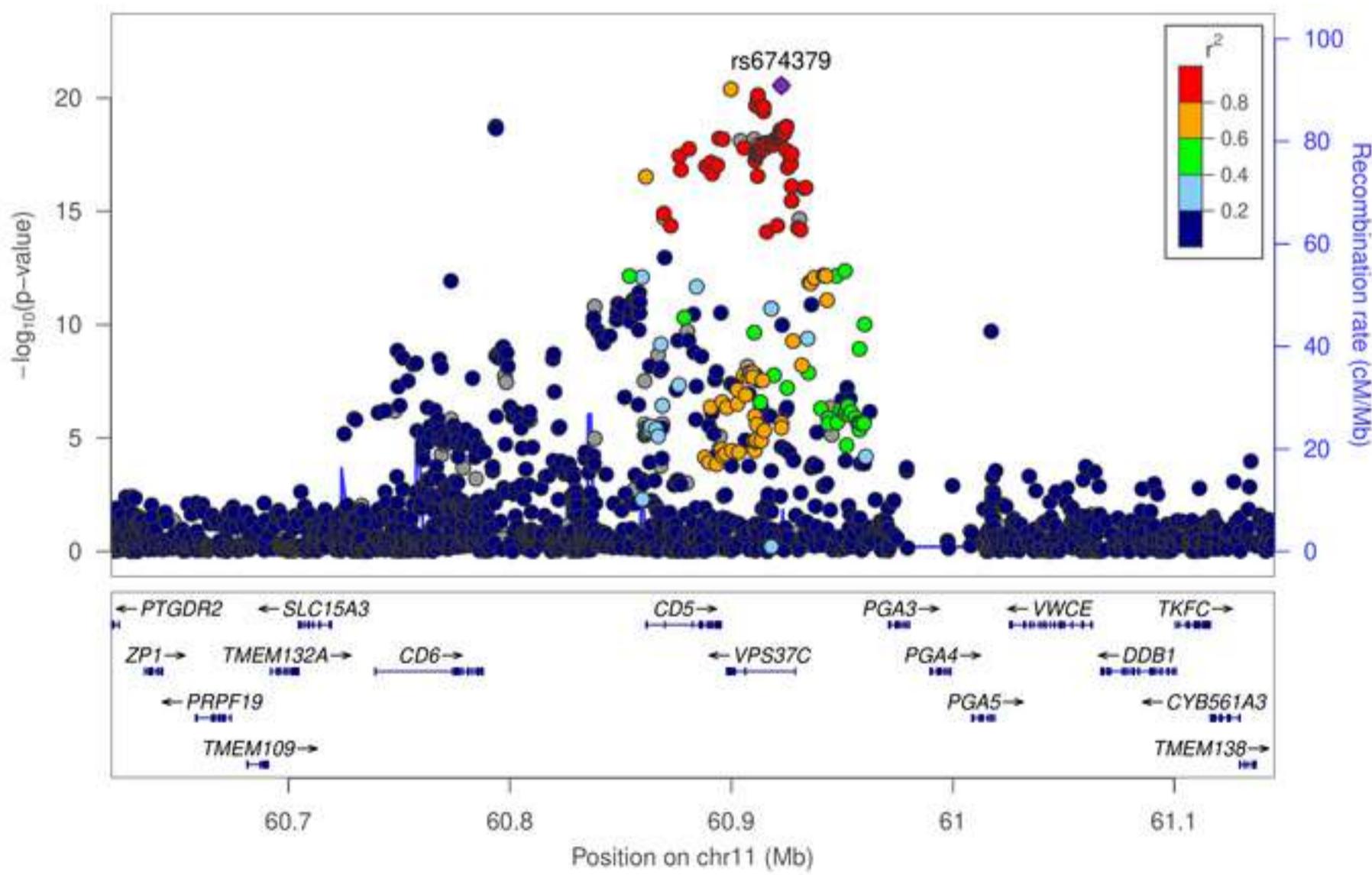
# SCALLOP: CD40 (CD40)-rs1883832



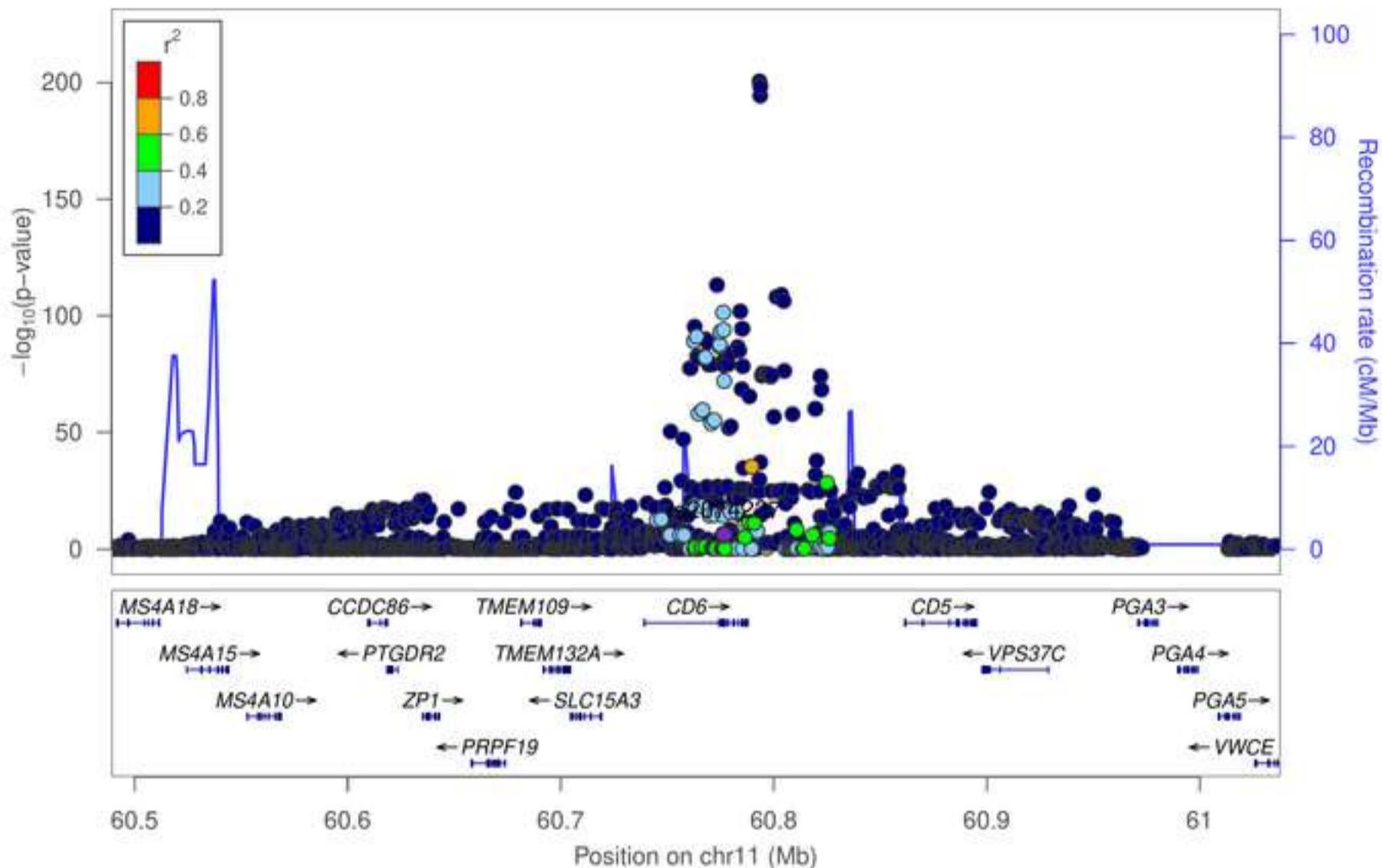
# eQTLGen: CD5 (CD5)-rs674379



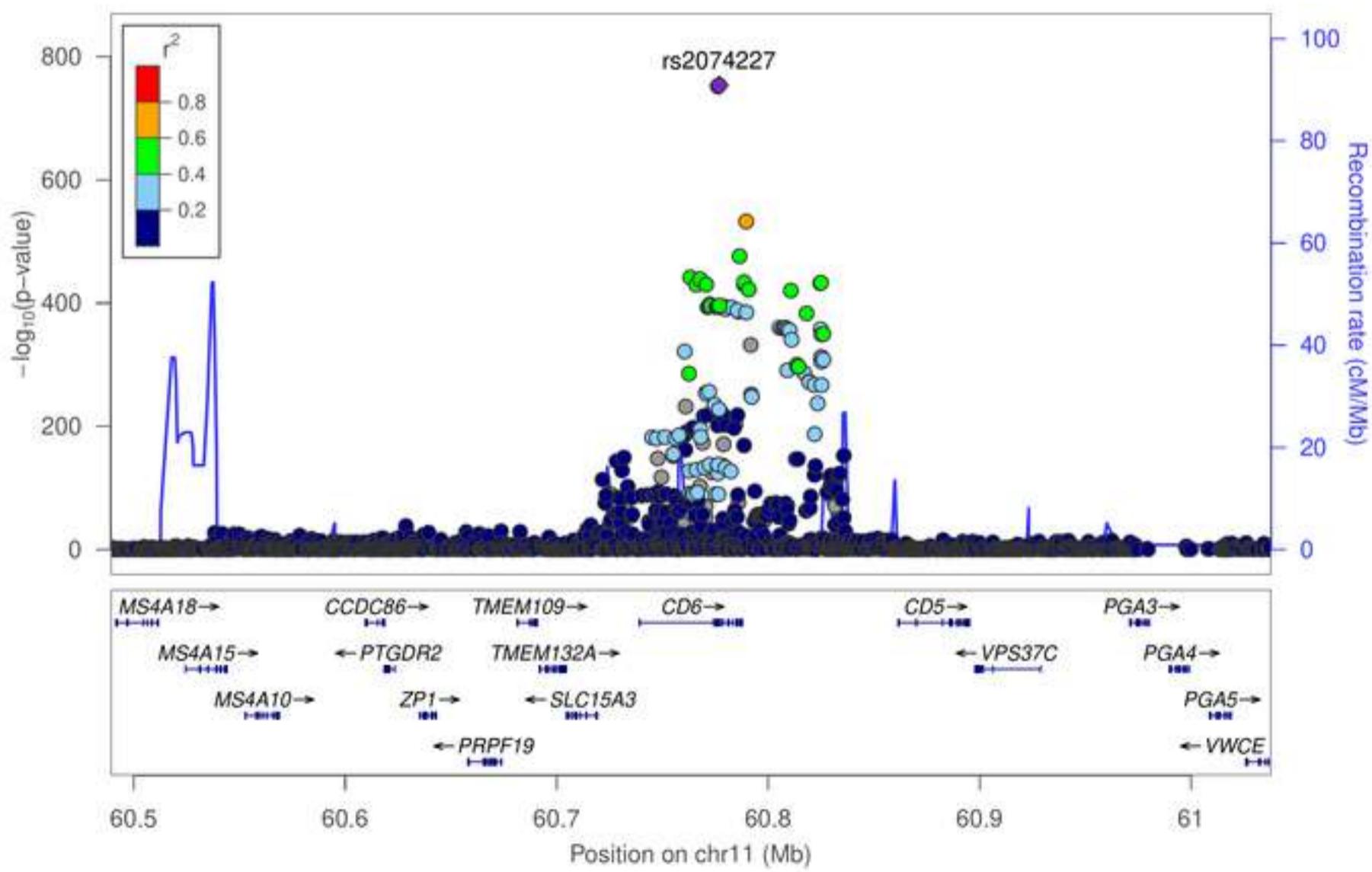
# SCALLOP: CD5 (CD5)-rs674379



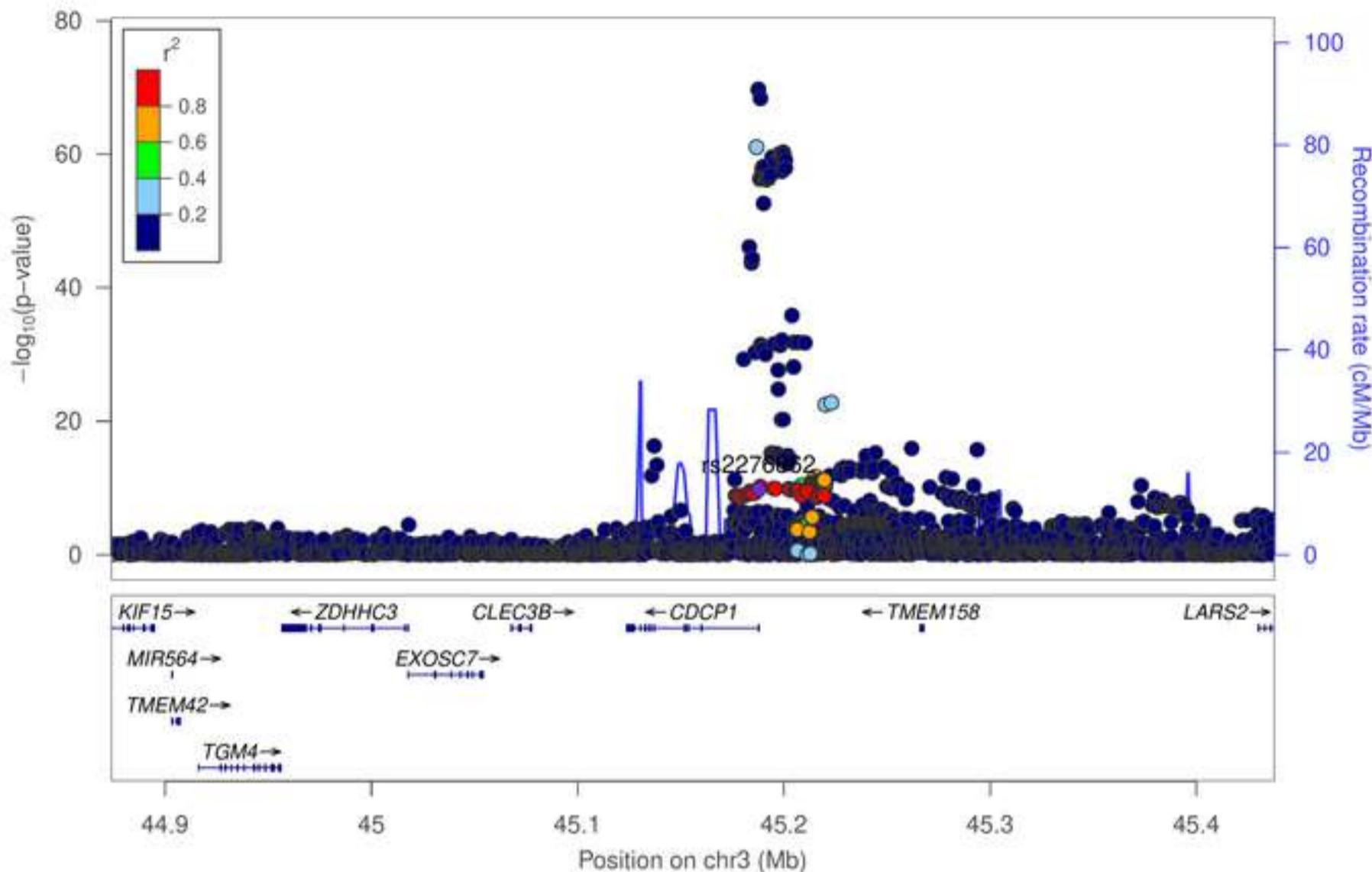
# eQTLGen: CD6 (CD6)-rs2074227



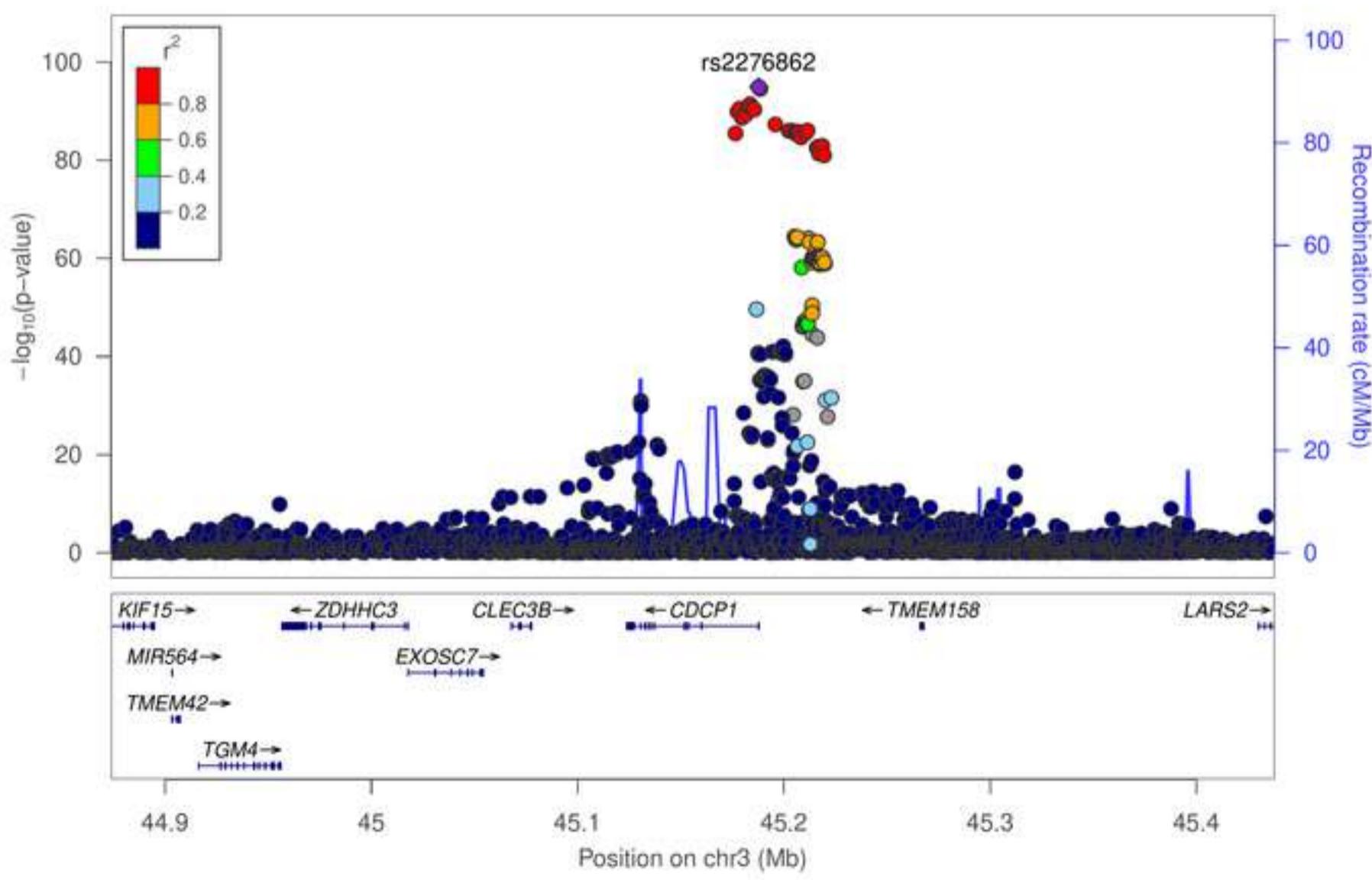
# SCALLOP: CD6 (CD6)-rs2074227



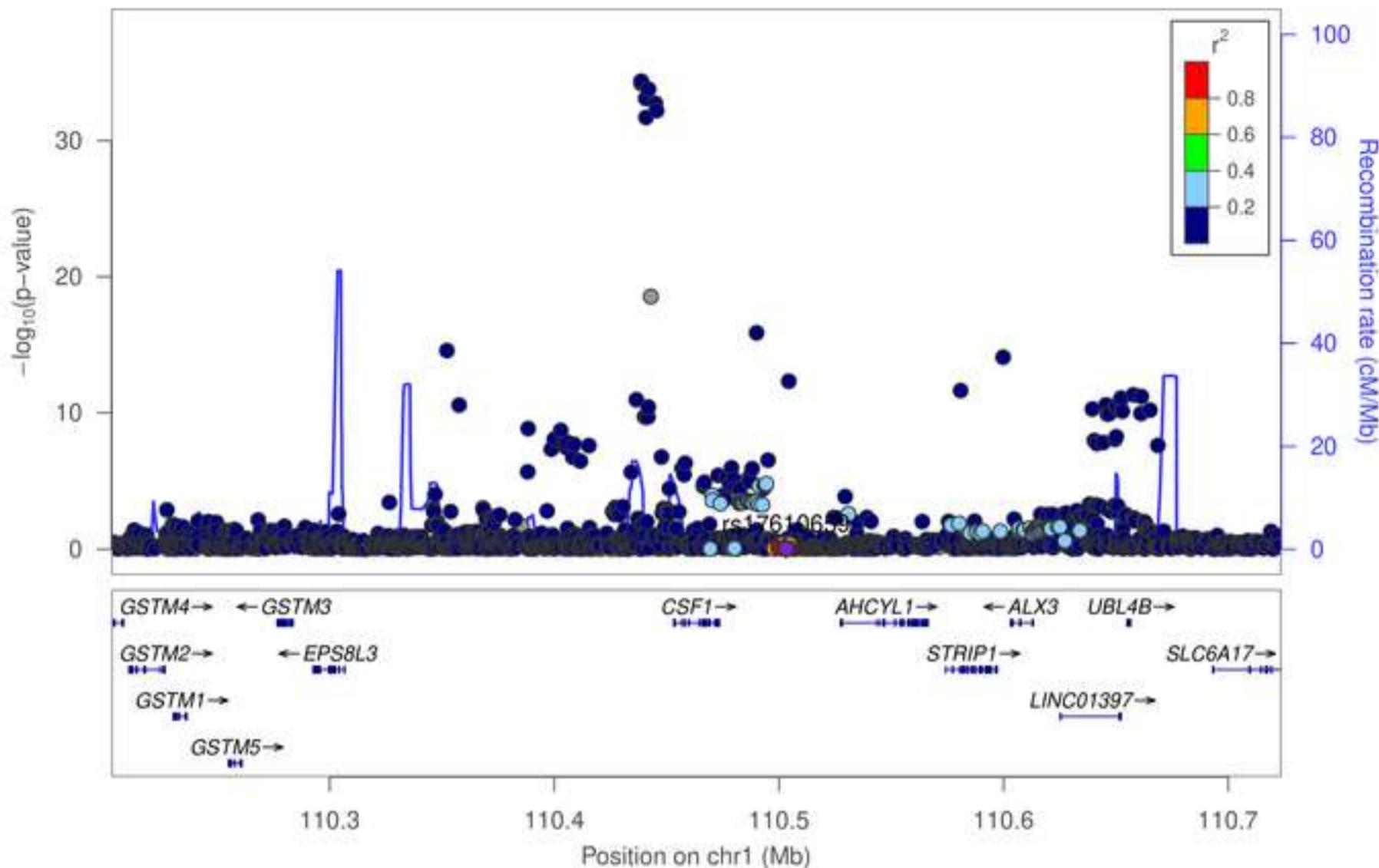
## eQTLGen: CDCP1 (CDCP1)-rs2276862



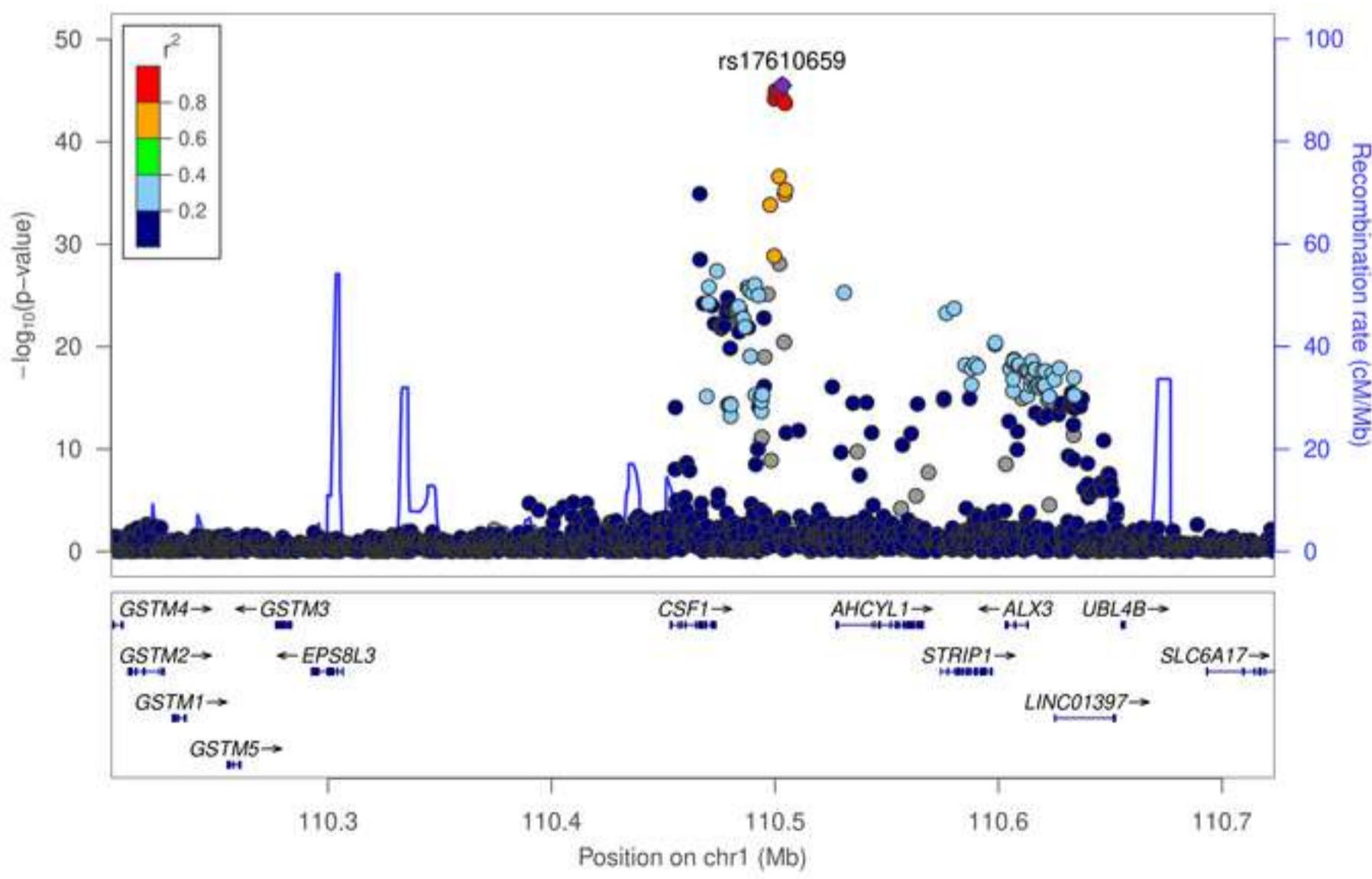
## SCALLOP: CDCP1 (CDCP1)-rs2276862



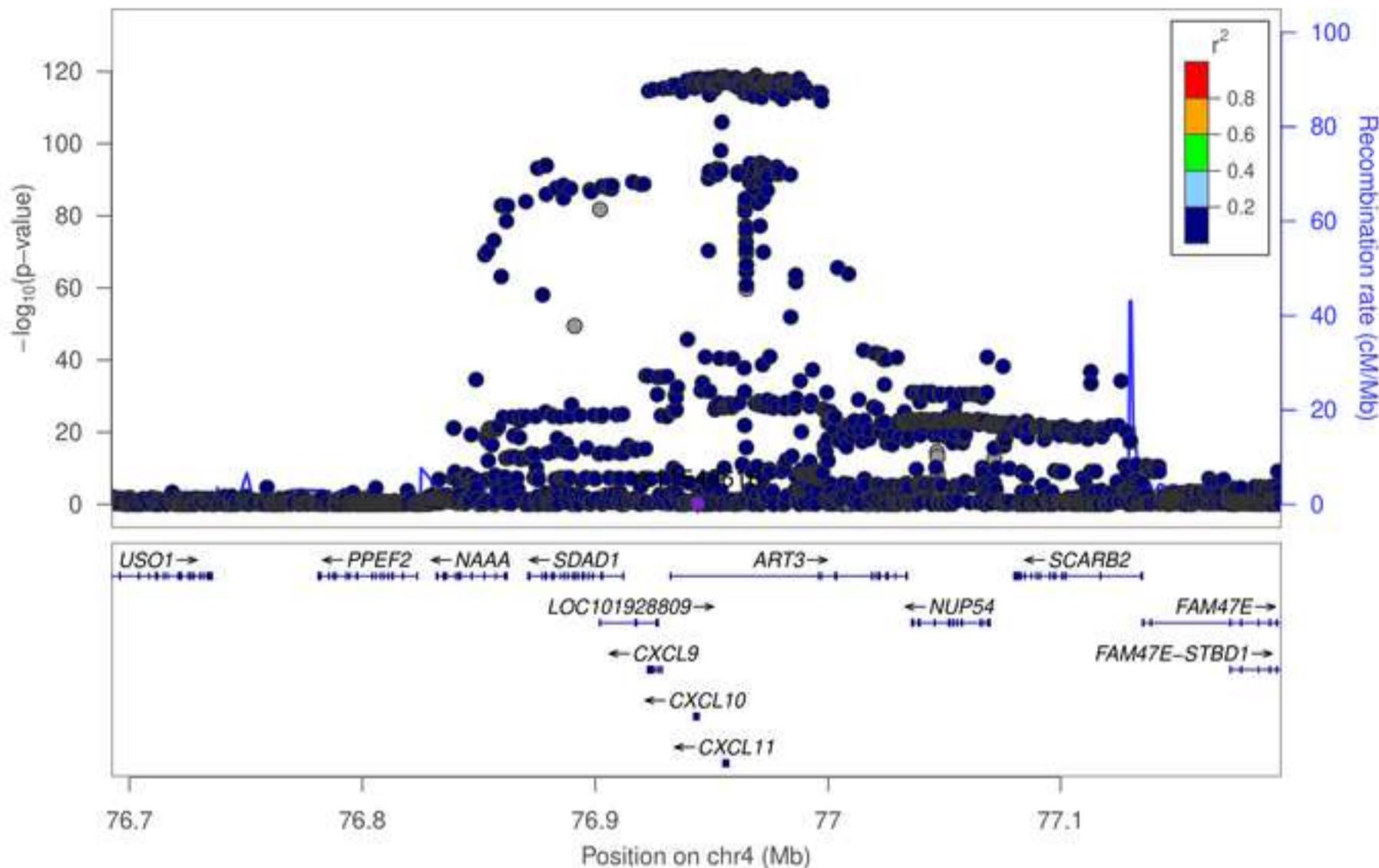
# eQTLGen: CSF-1 (CSF1)-rs17610659



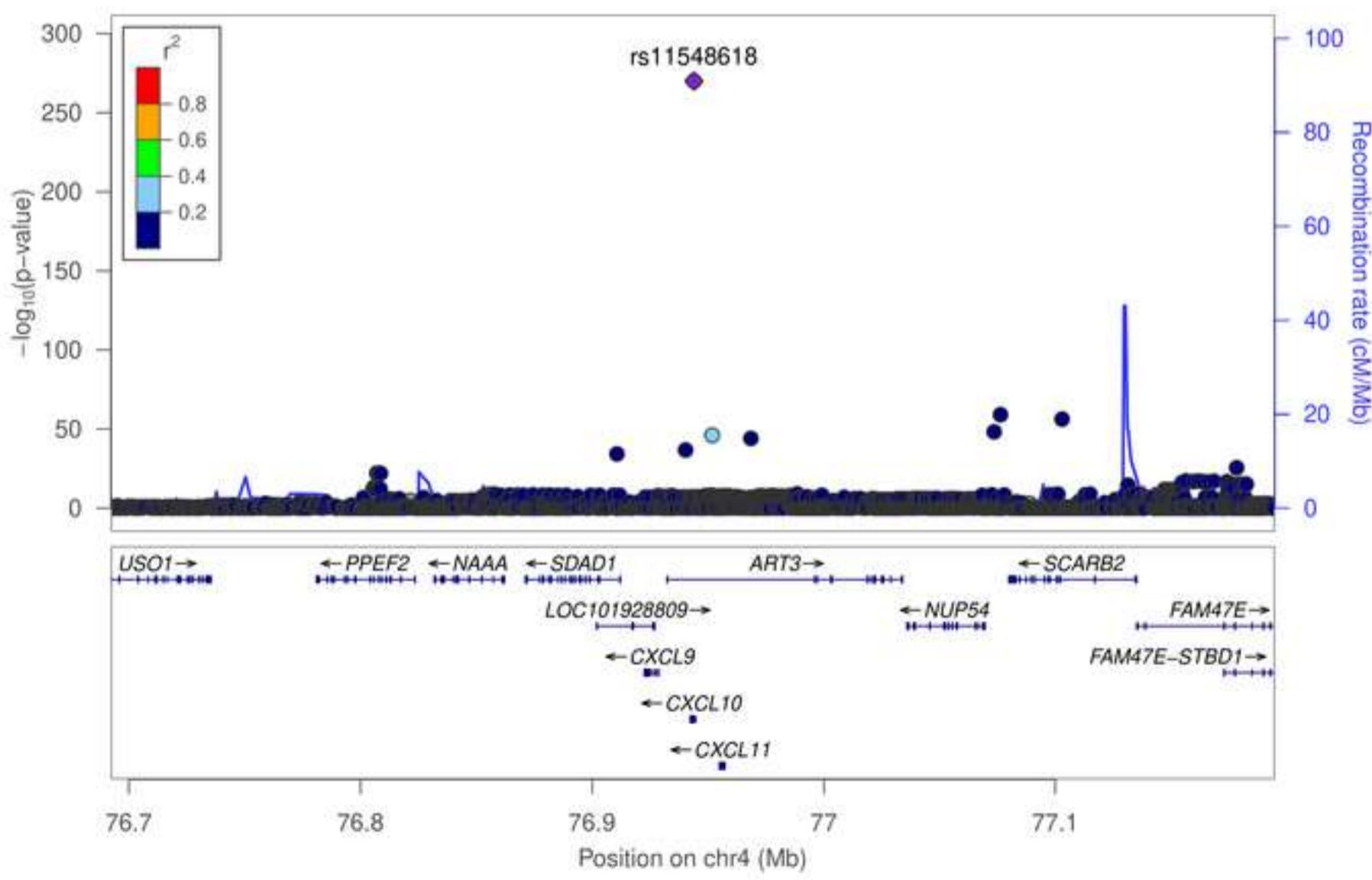
# SCALLOP: CSF-1 (CSF1)-rs17610659



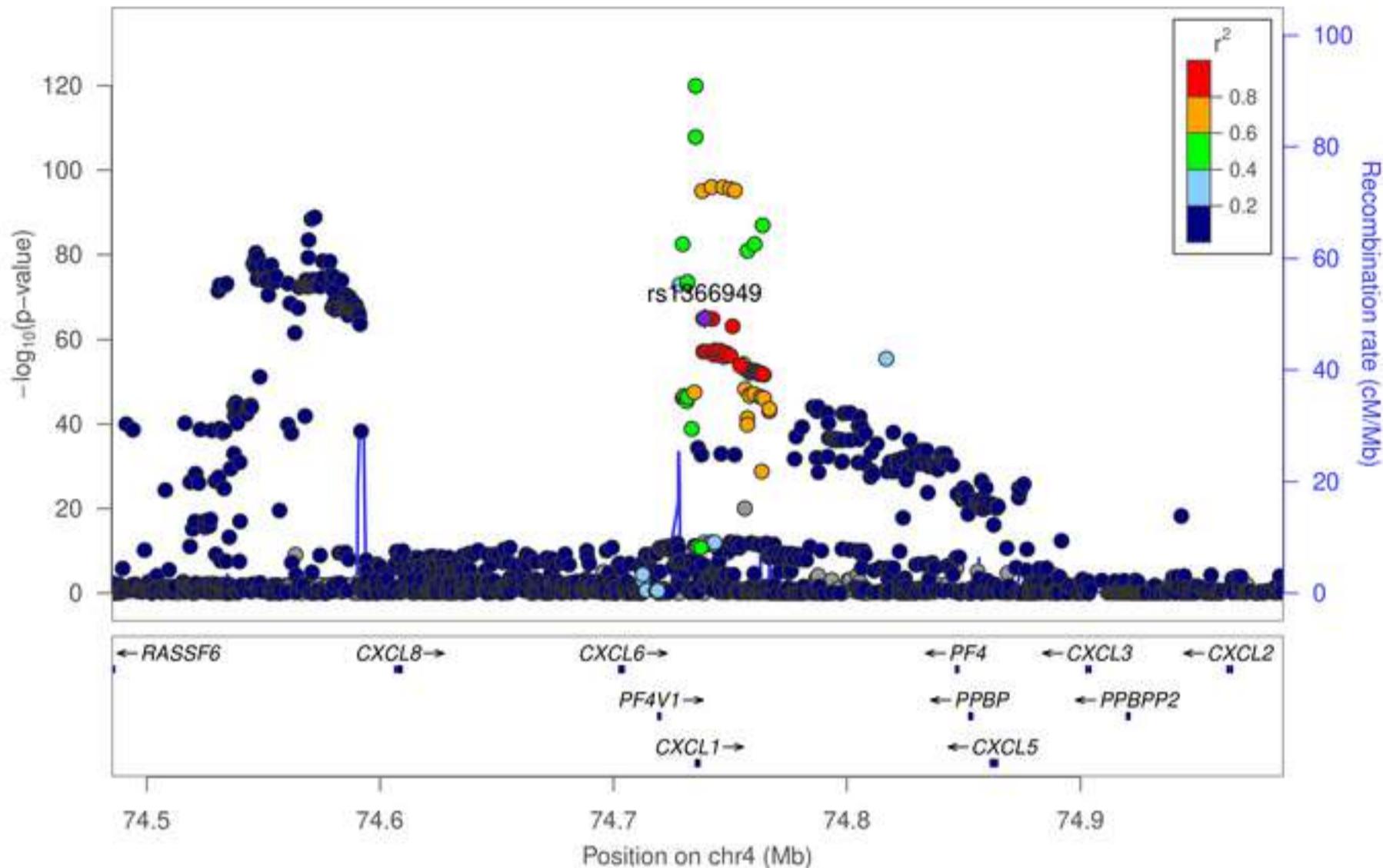
# eQTLGen: CXCL10 (CXCL10)-rs11548618



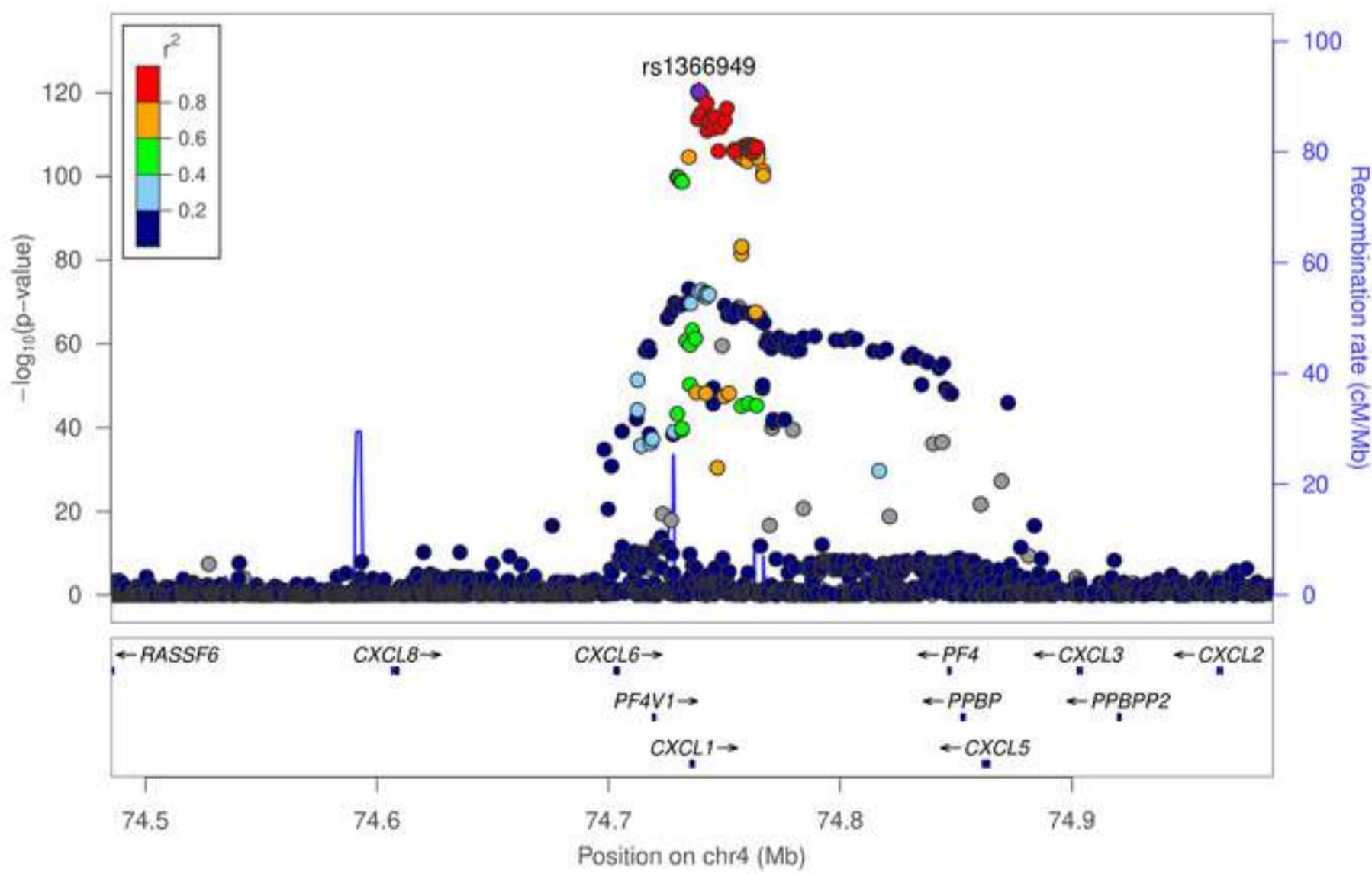
# SCALLOP: CXCL10 (CXCL10)-rs11548618



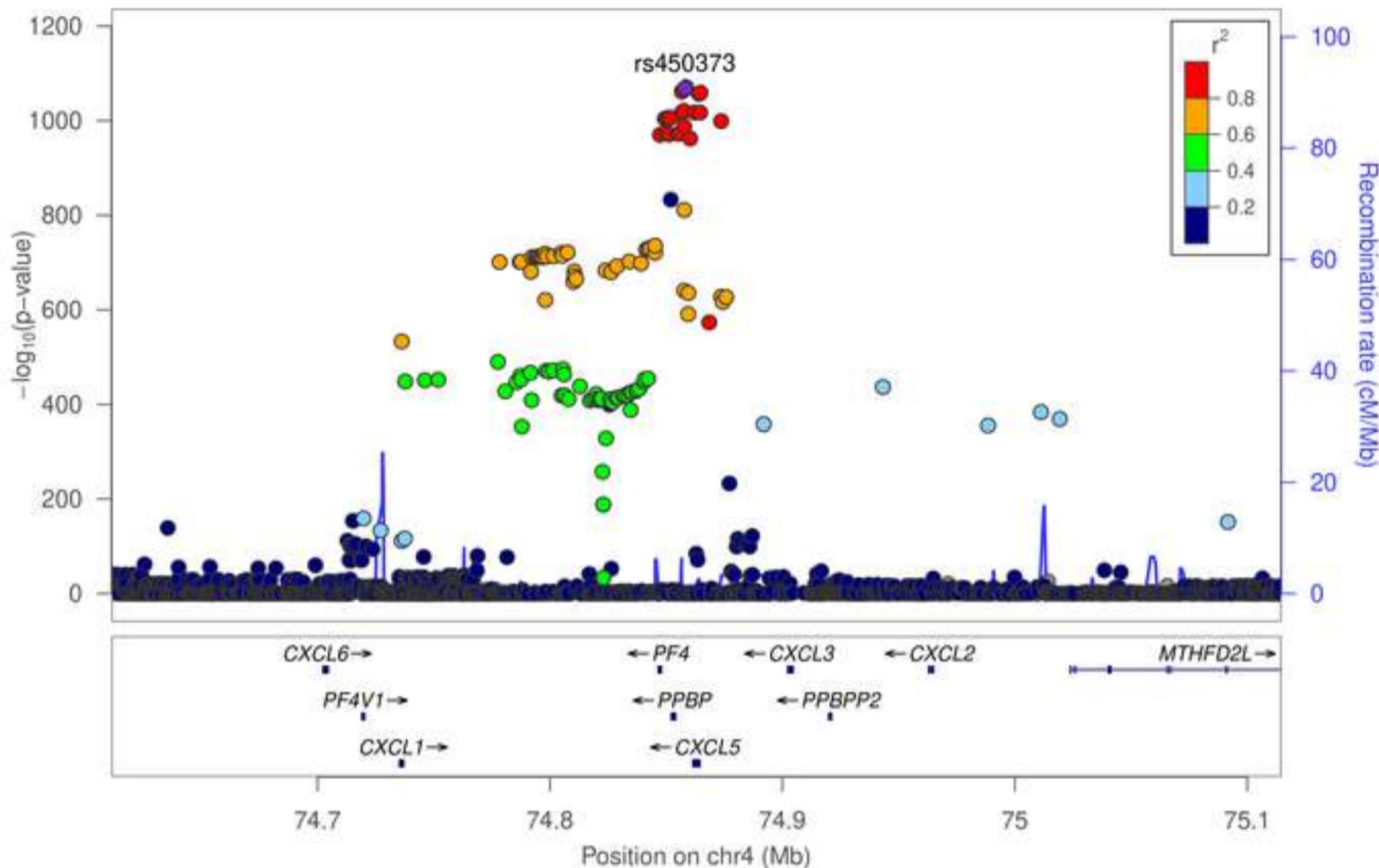
# eQTLGen: CXCL1 (CXCL1)-rs1366949



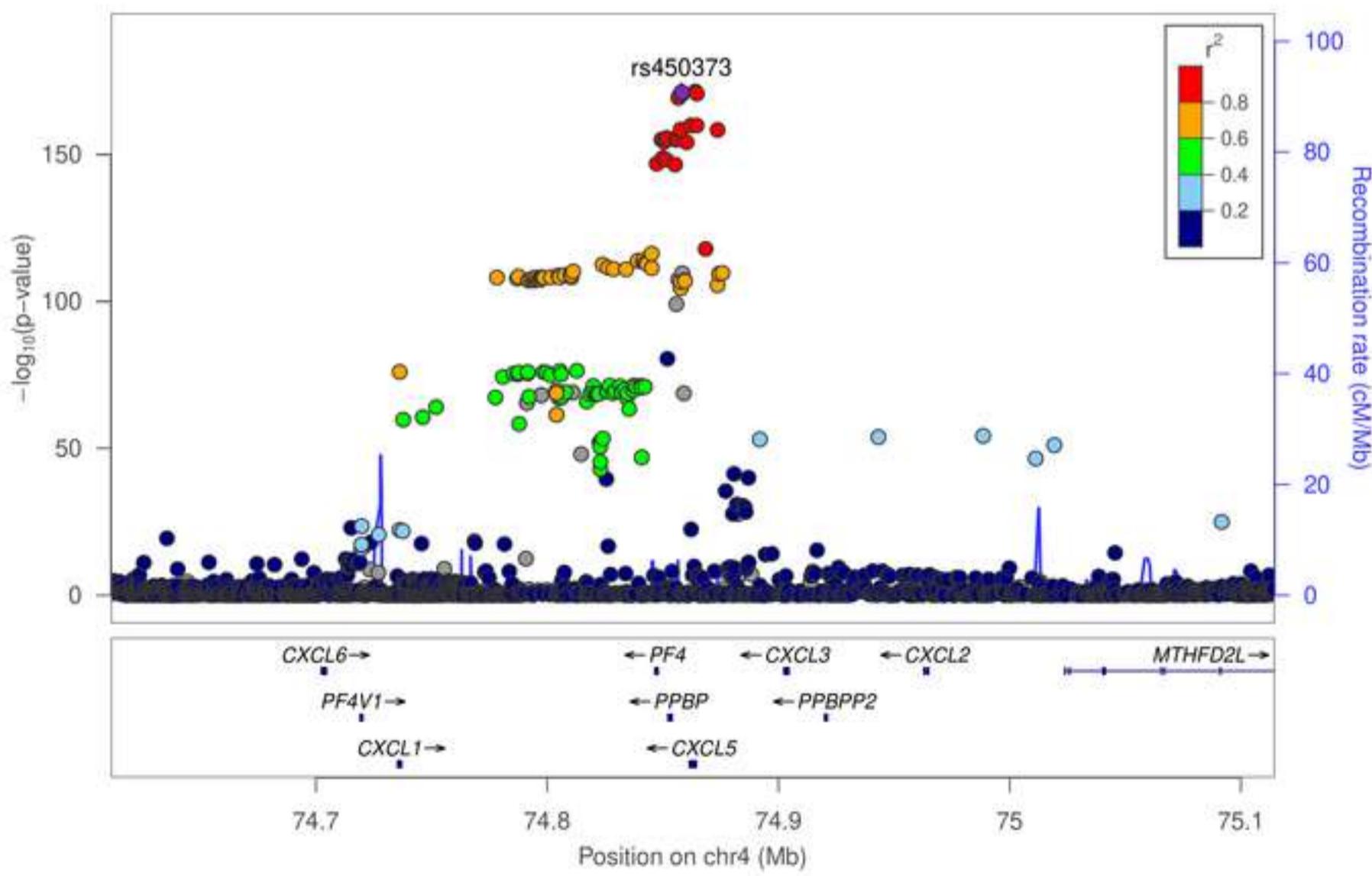
# SCALLOP: CXCL1 (CXCL1)-rs1366949



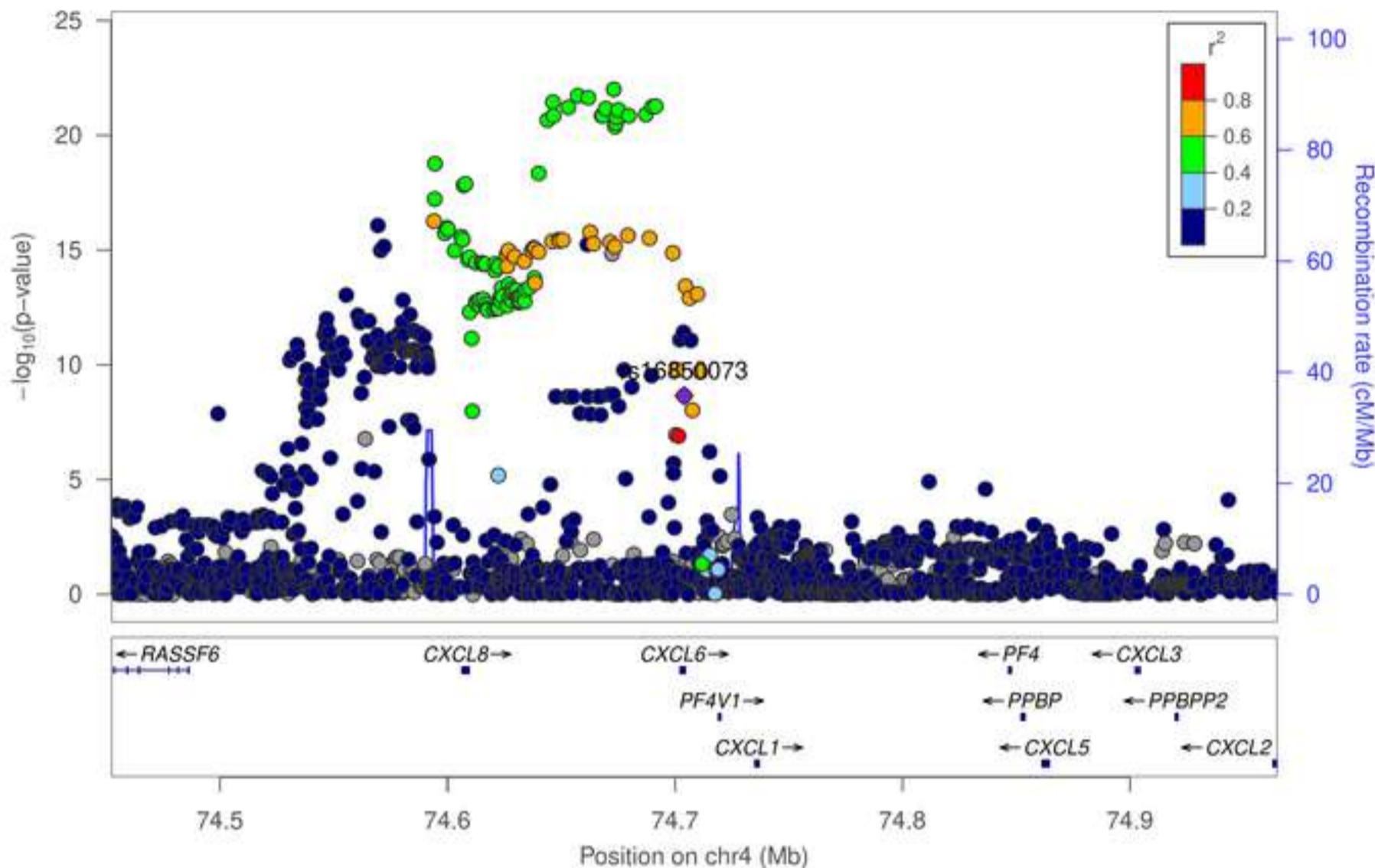
## eQTLGen: CXCL5 (CXCL5)-rs450373



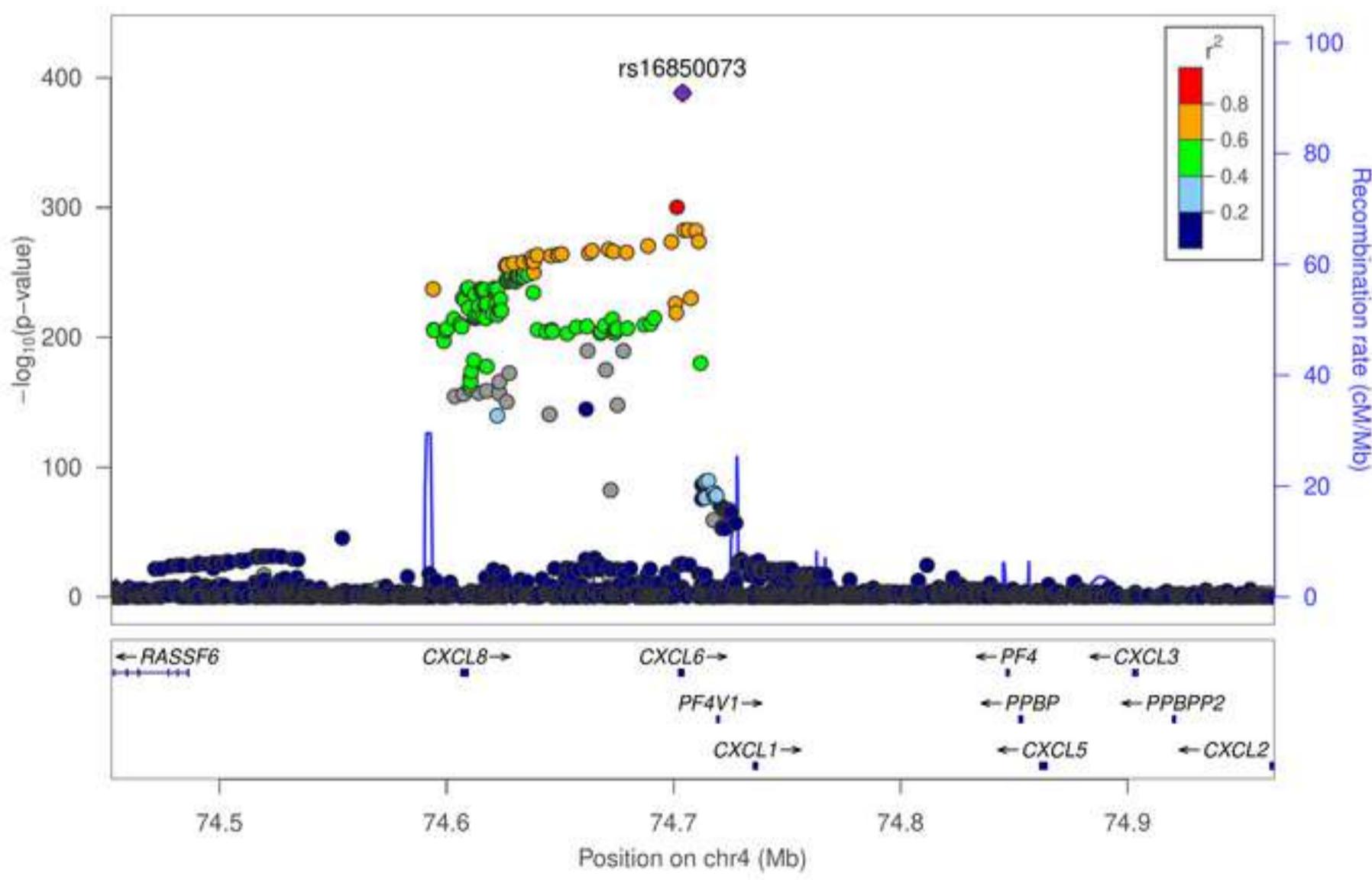
## SCALLOP: CXCL5 (CXCL5)-rs450373



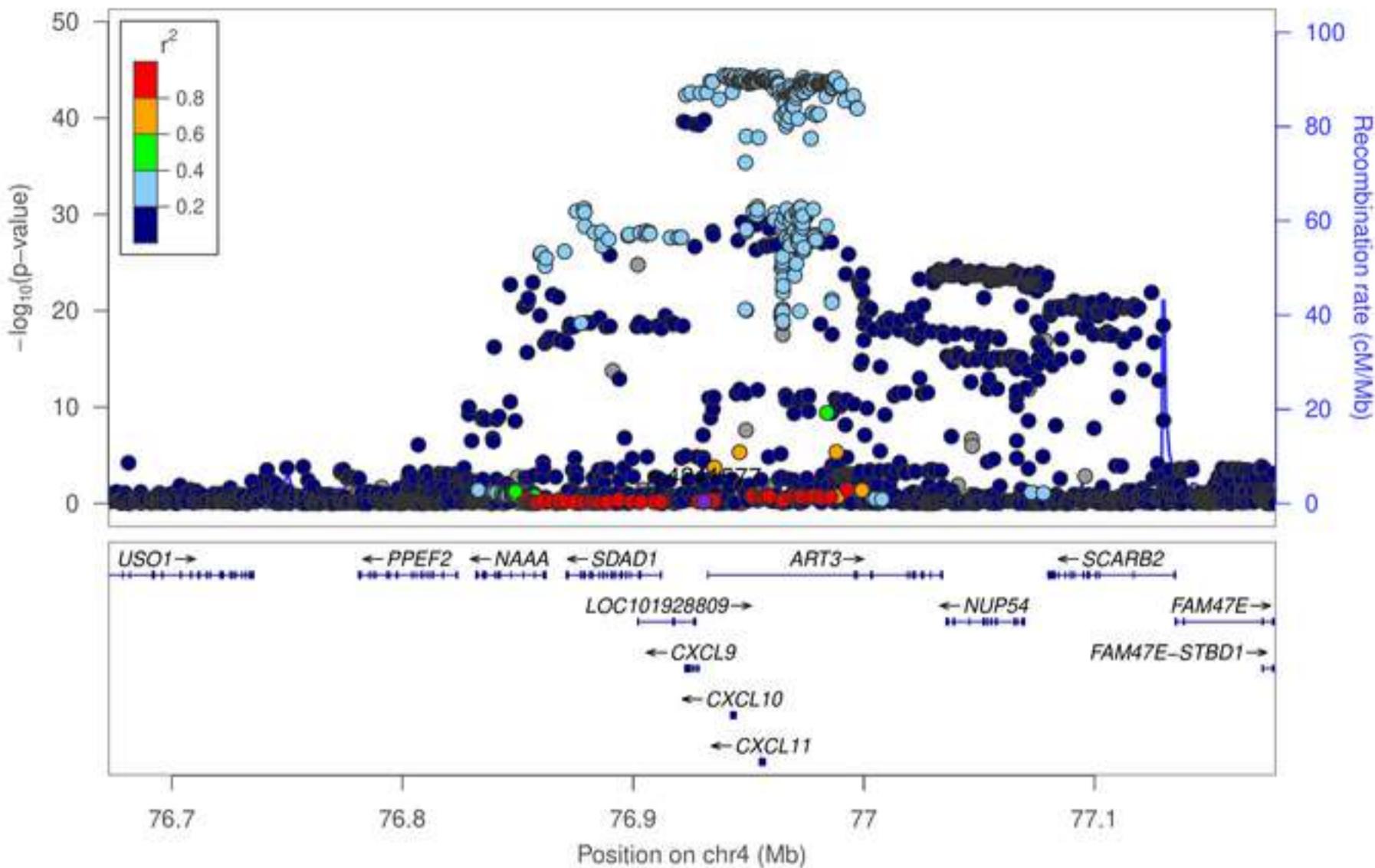
# eQTLGen: CXCL6 (CXCL6)-rs16850073



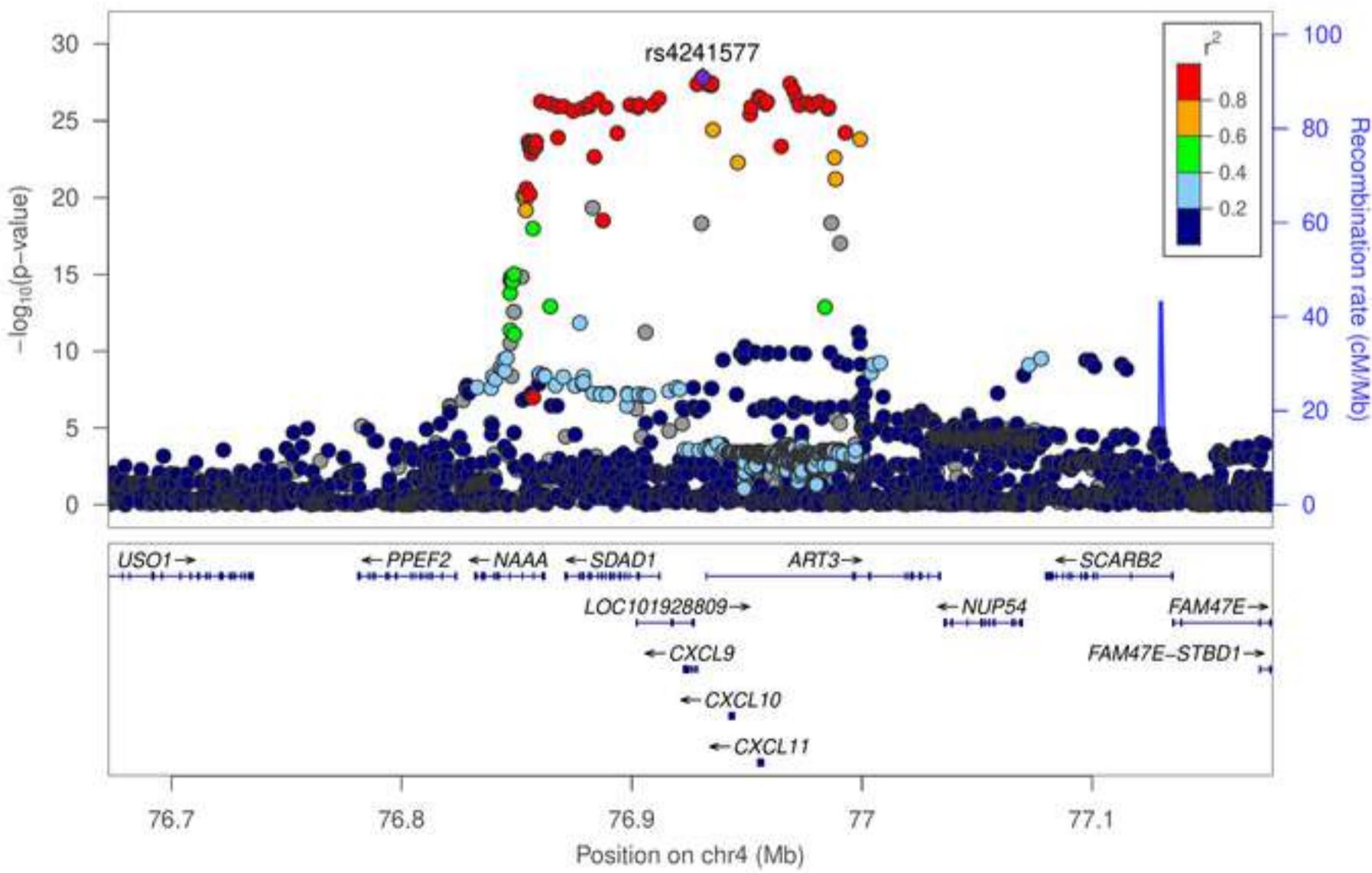
# SCALLOP: CXCL6 (CXCL6)-rs16850073



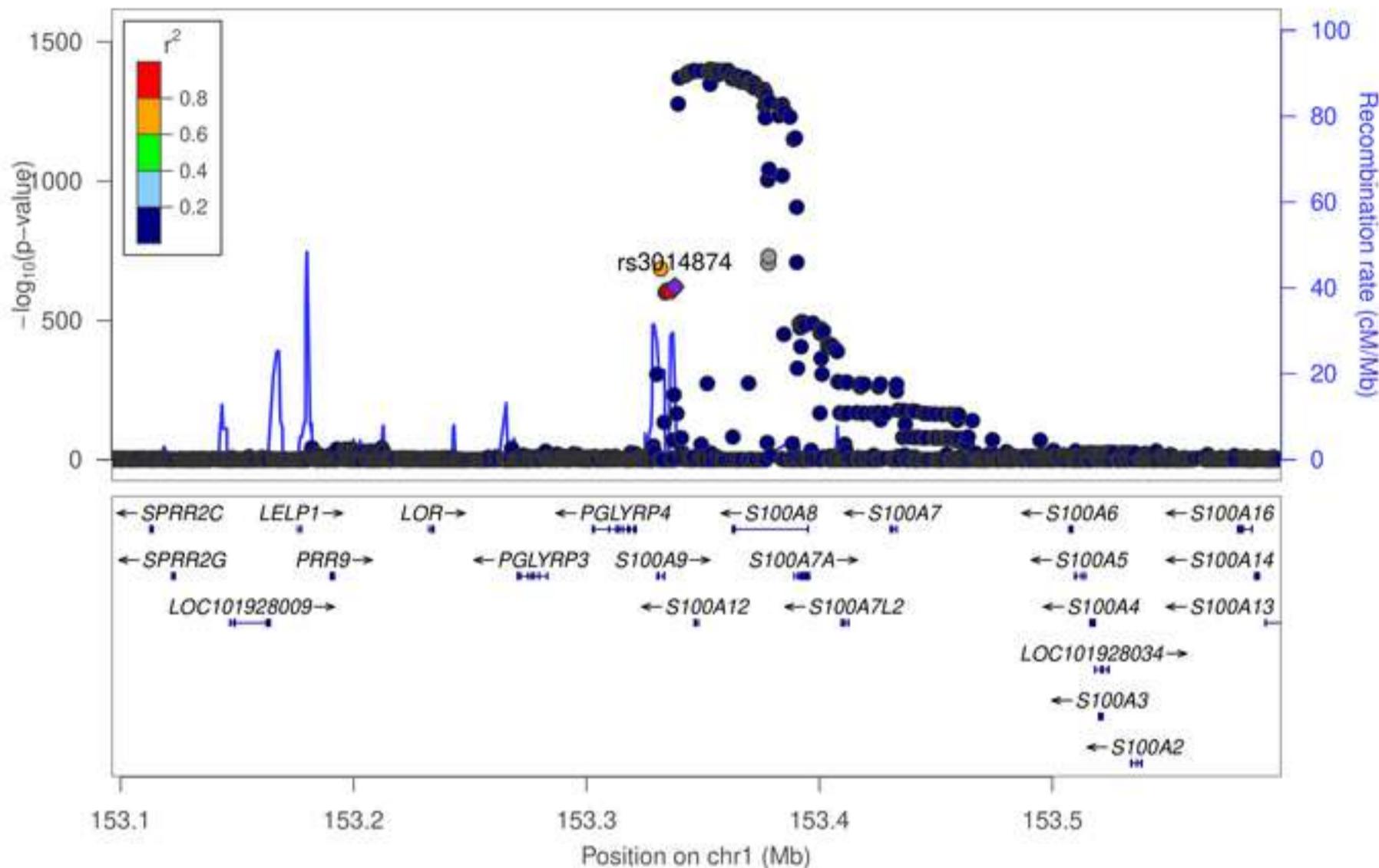
# eQTLGen: CXCL9 (CXCL9)-rs4241577



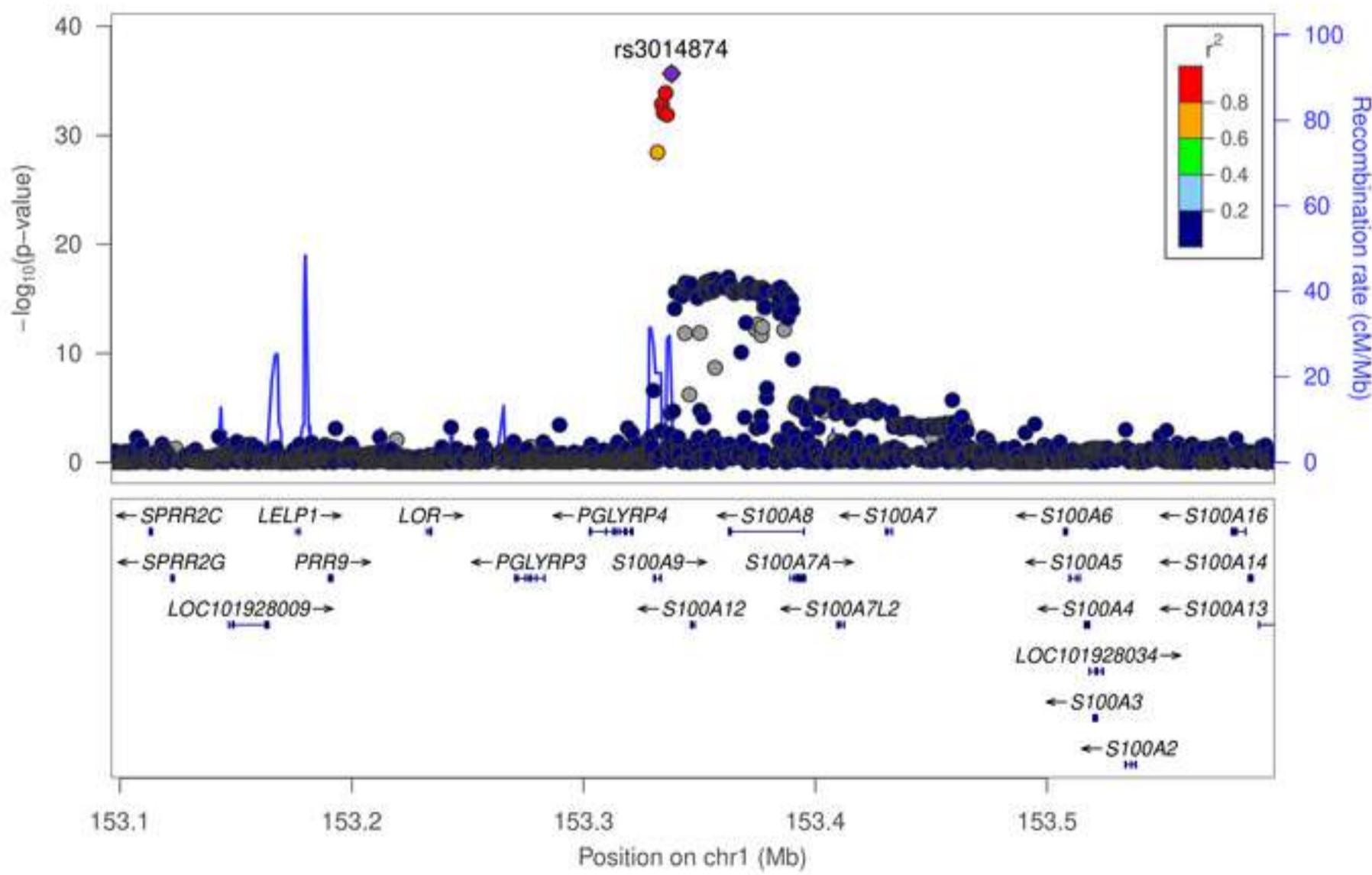
# SCALLOP: CXCL9 (CXCL9)-rs4241577



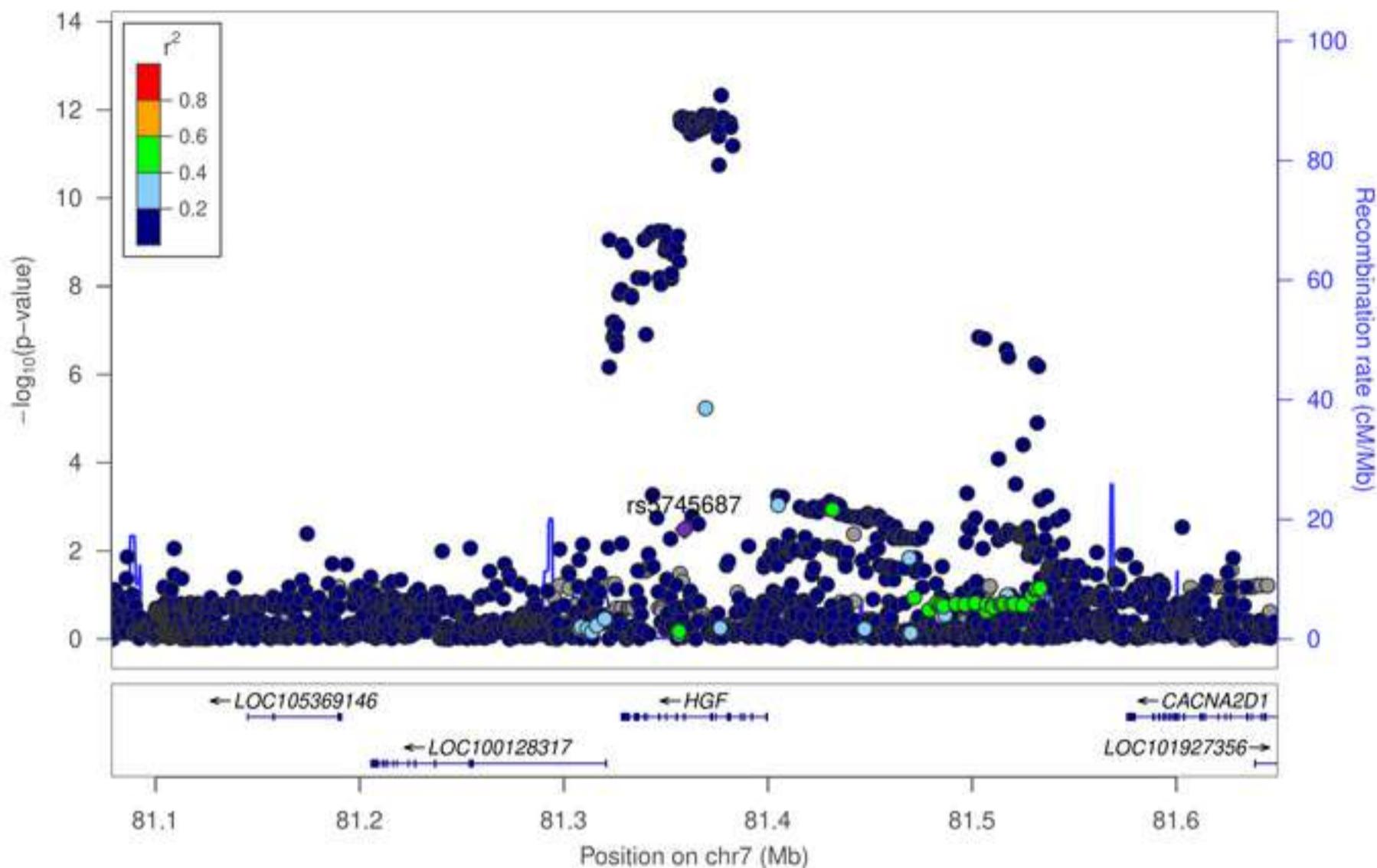
# eQTLGen: EN-RAGE (S100A12)-rs3014874



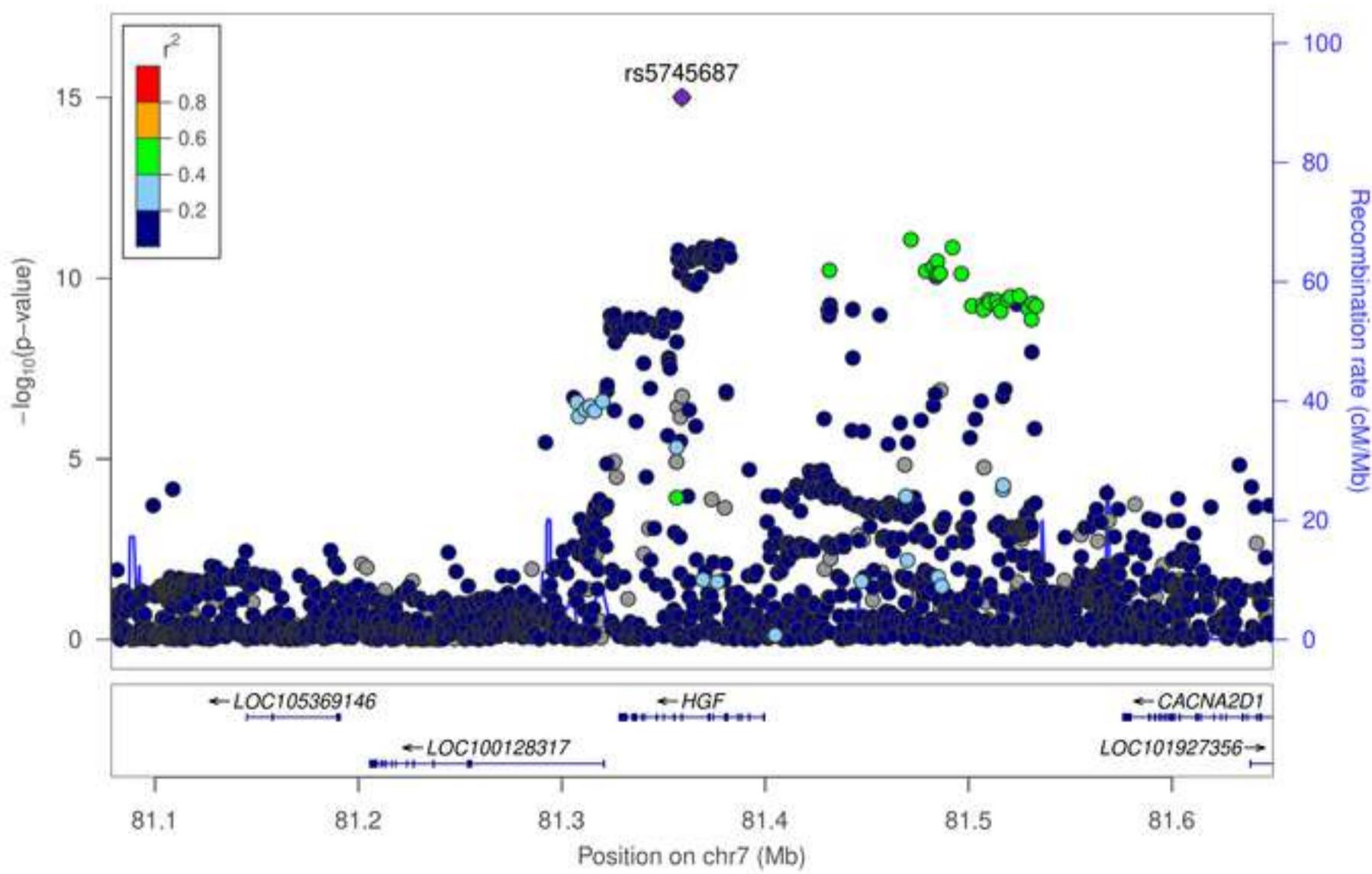
# SCALLOP: EN-RAGE (S100A12)-rs3014874



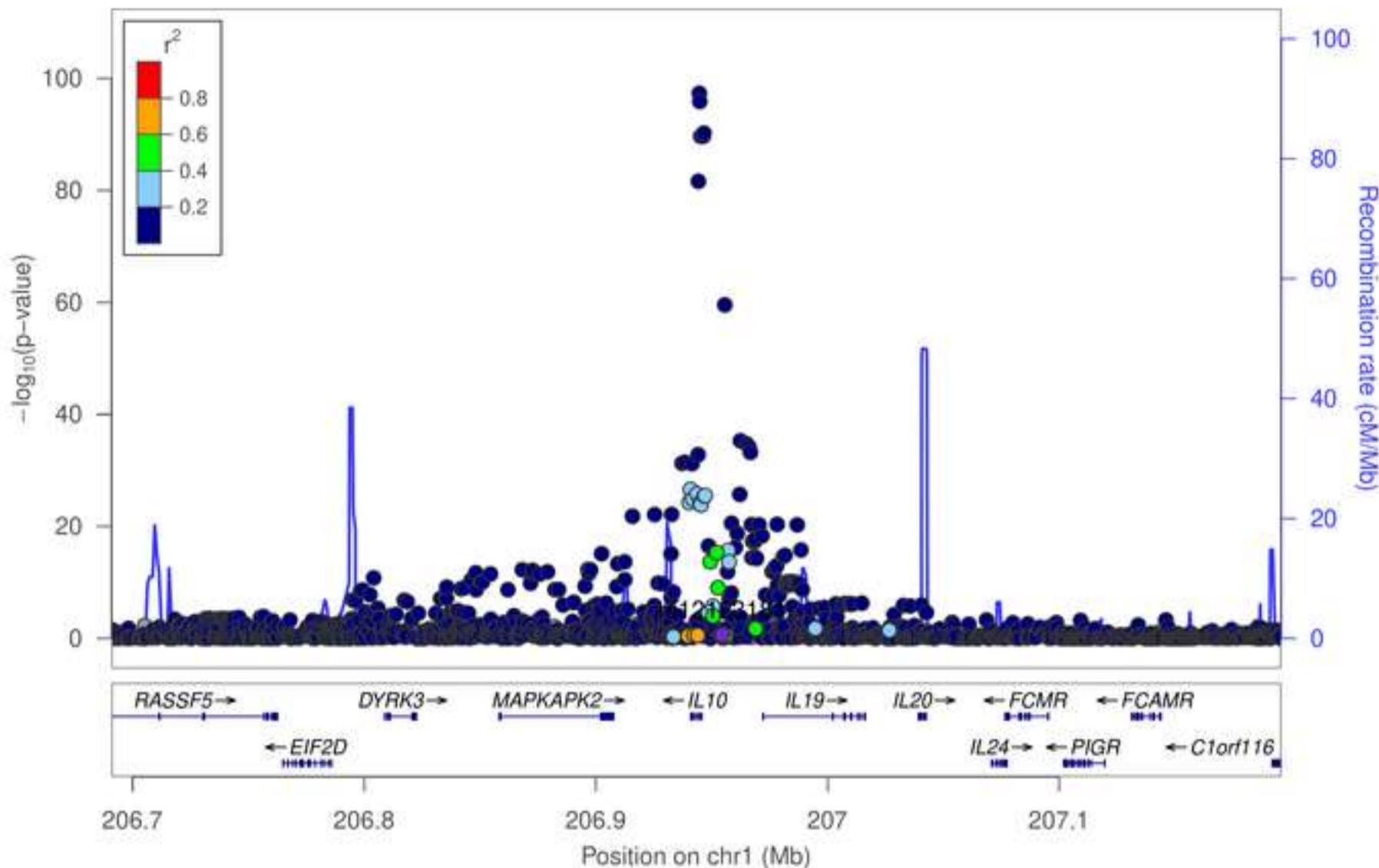
## eQTLGen: HGF (HGF)-rs5745687



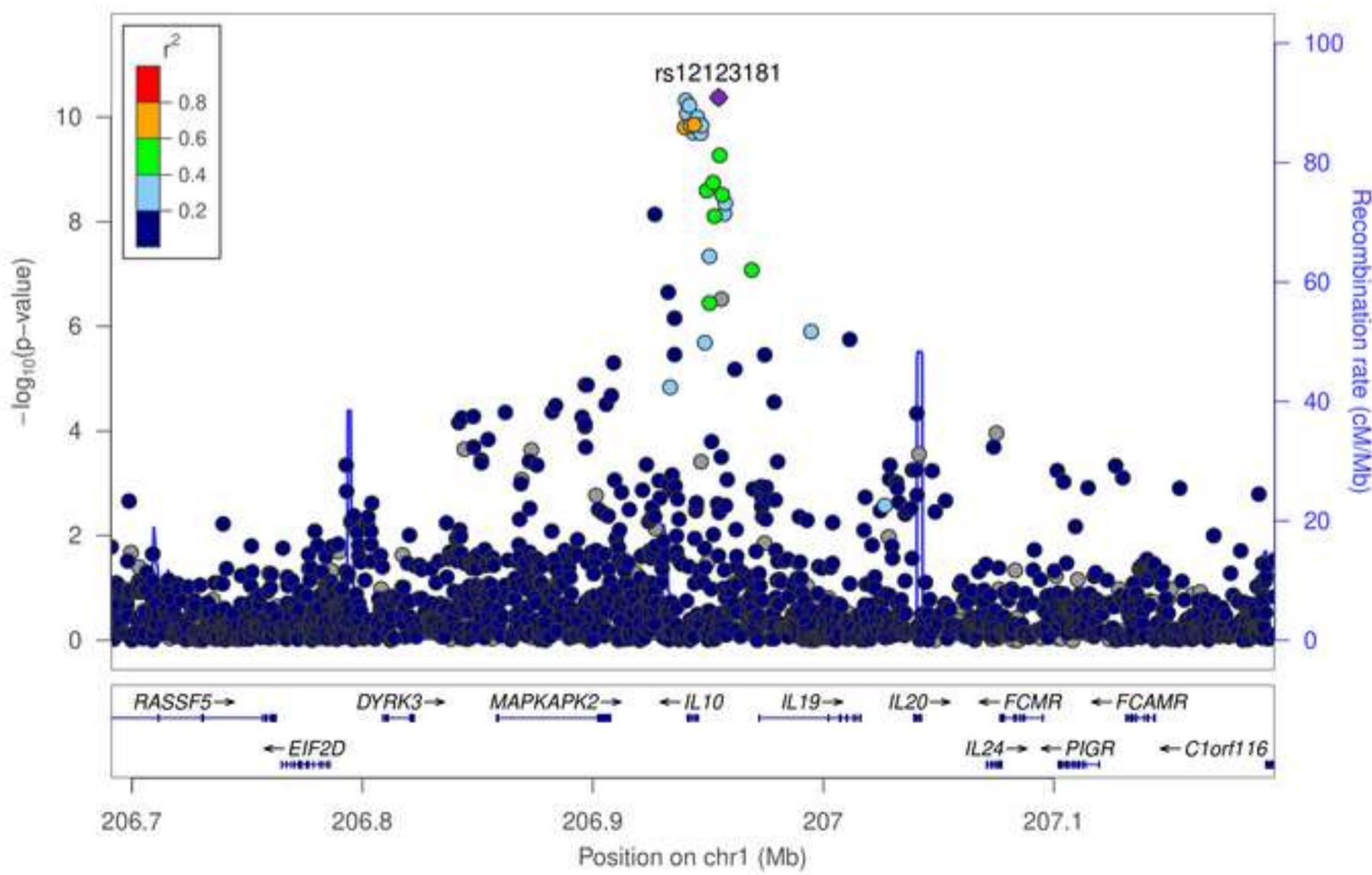
## SCALLOP: HGF (HGF)-rs5745687



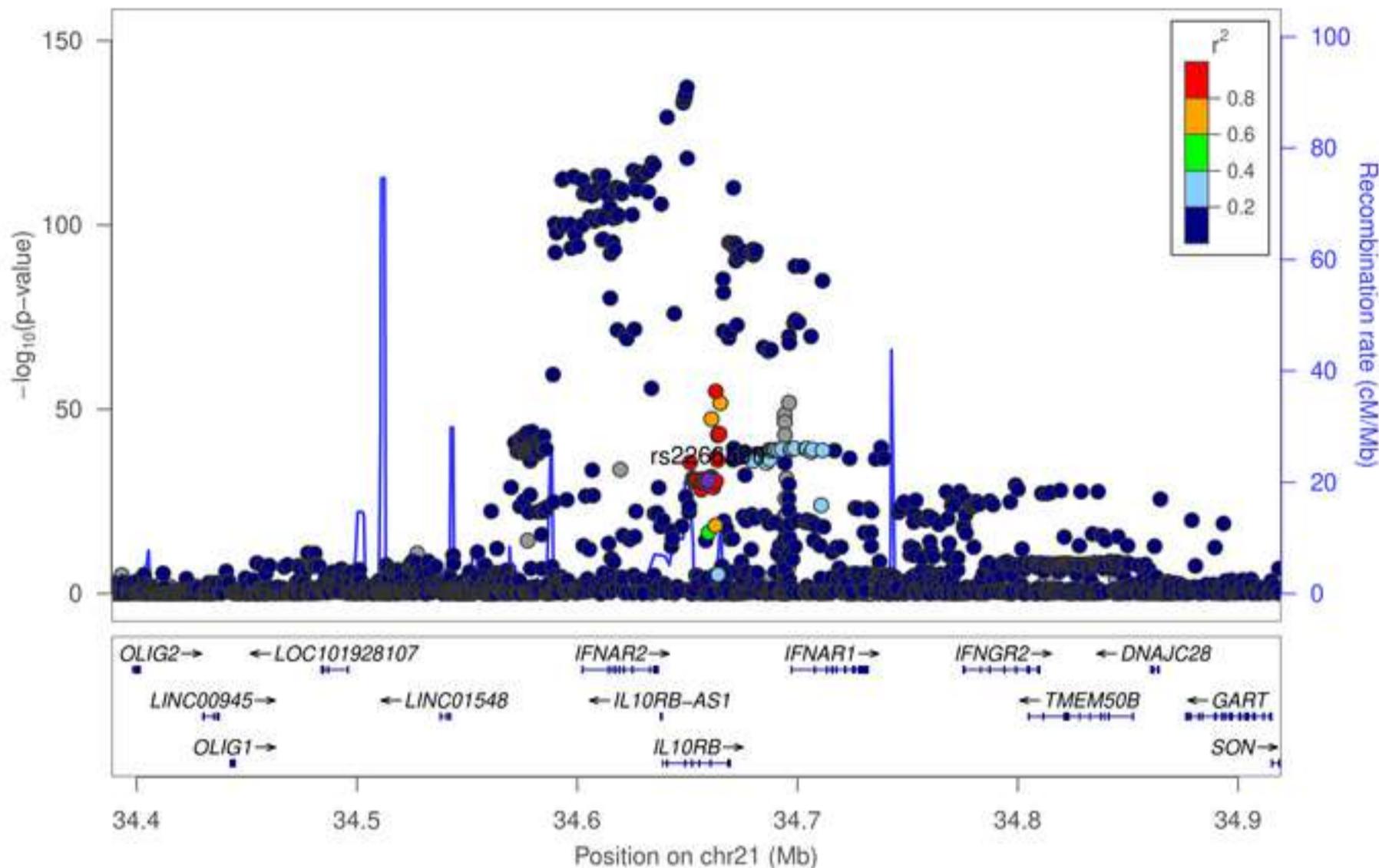
# eQTLGen: IL-10 (IL10)-rs12123181



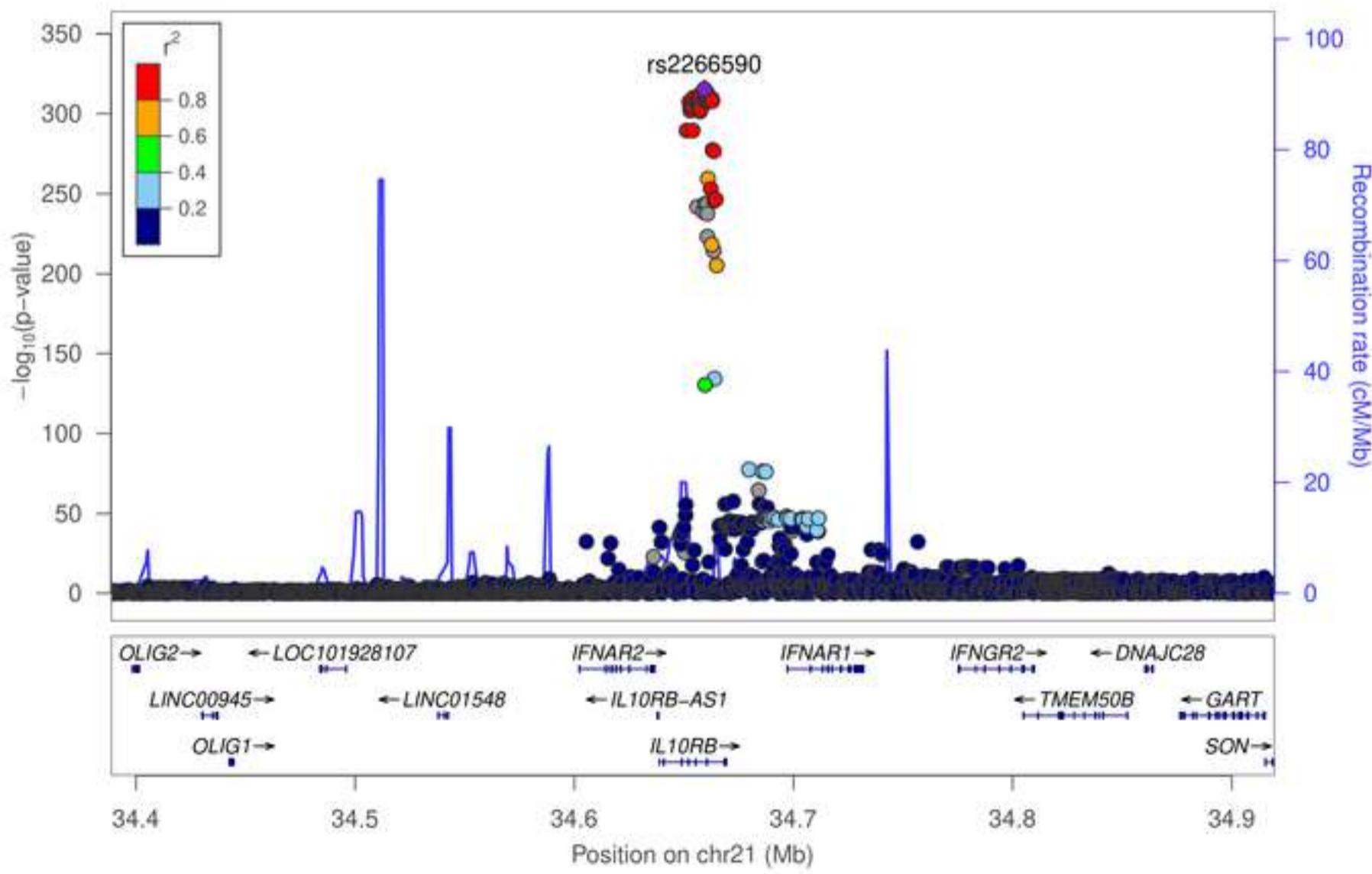
# SCALLOP: IL-10 (IL10)-rs12123181



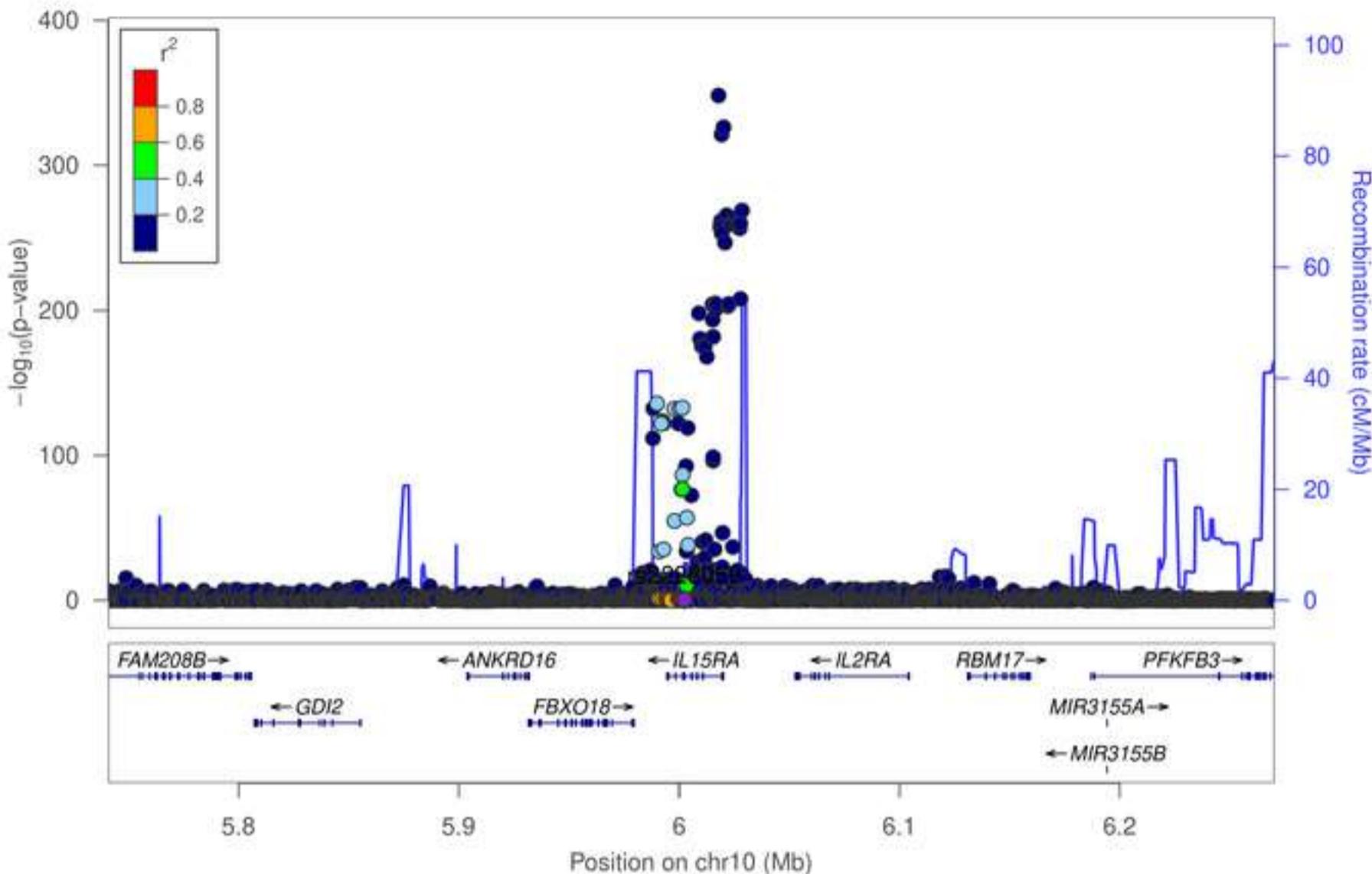
# eQTLGen: IL10RB (IL10RB)-rs2266590



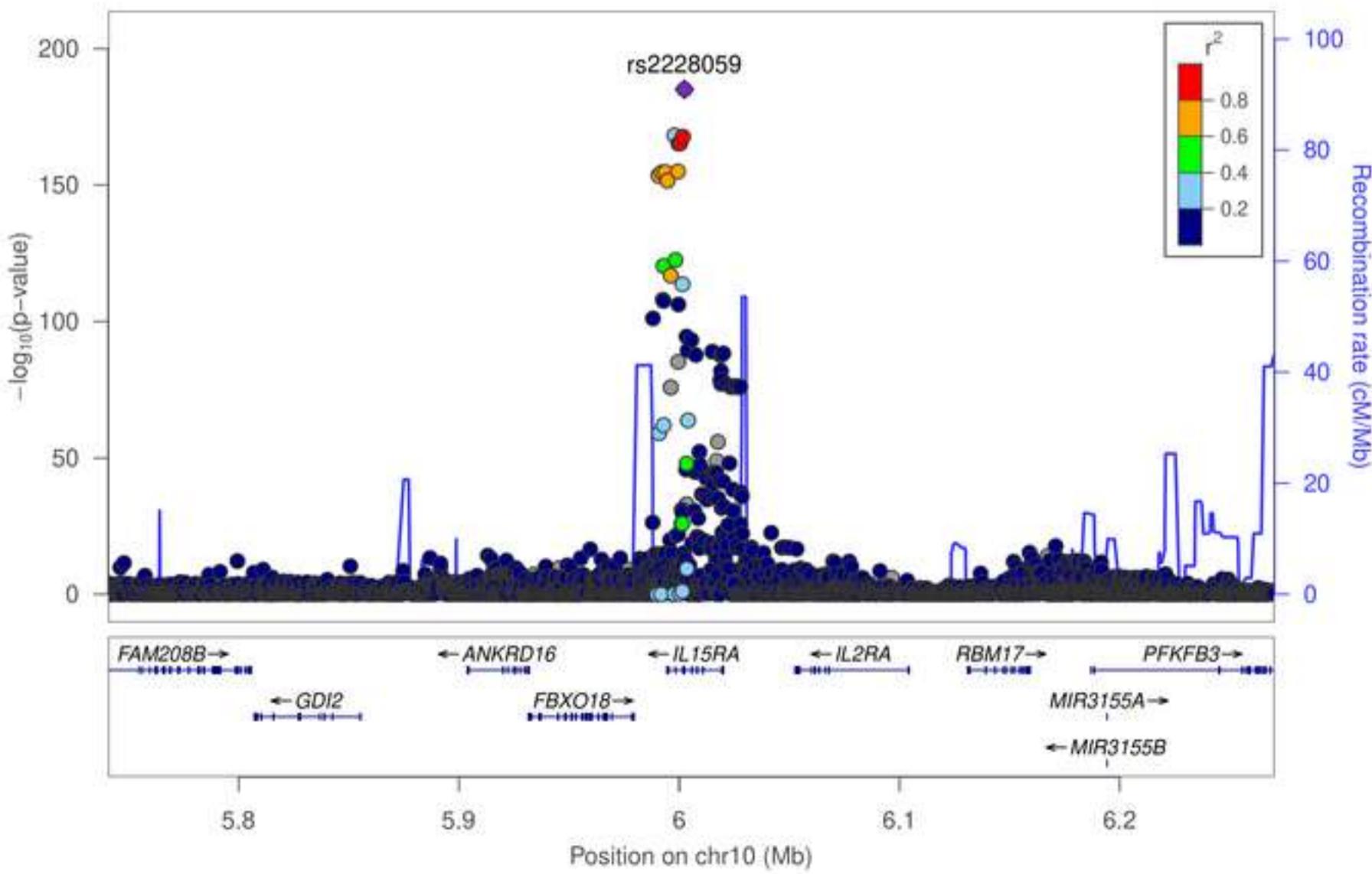
# SCALLOP: IL10RB (IL10RB)-rs2266590



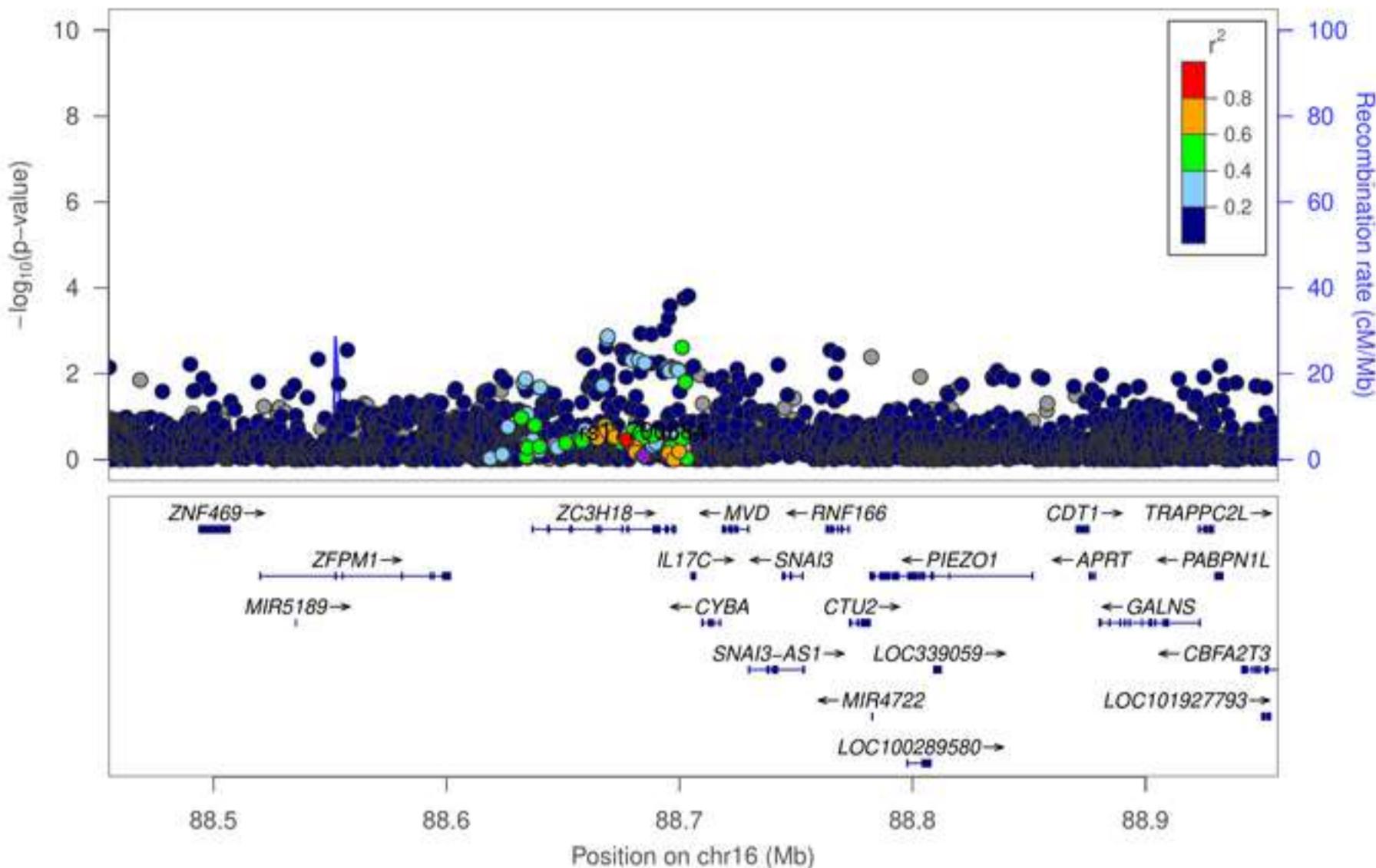
## eQTLGen: IL-15RA (IL15RA)-rs2228059



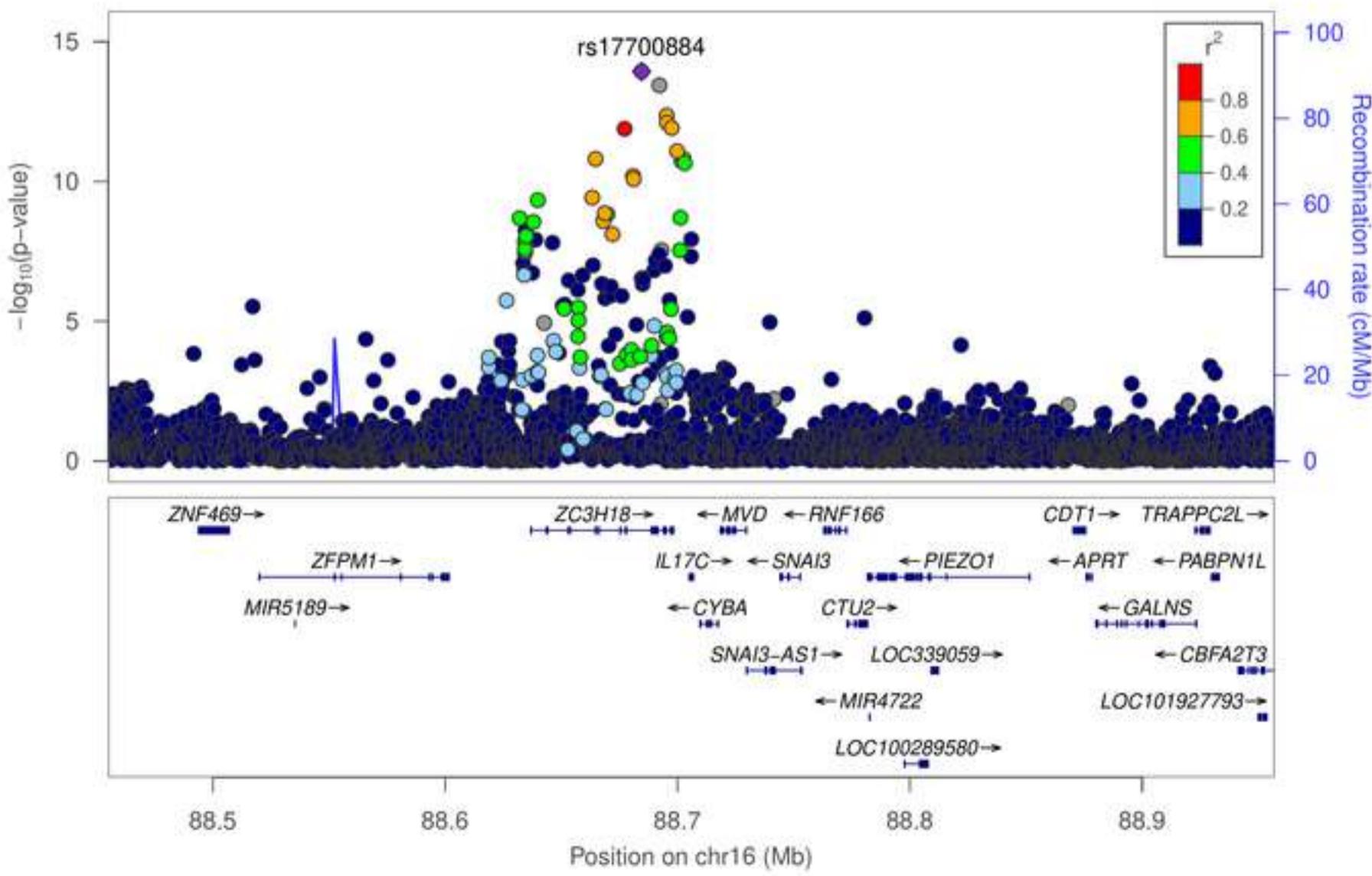
## SCALLOP: IL-15RA (IL15RA)-rs2228059



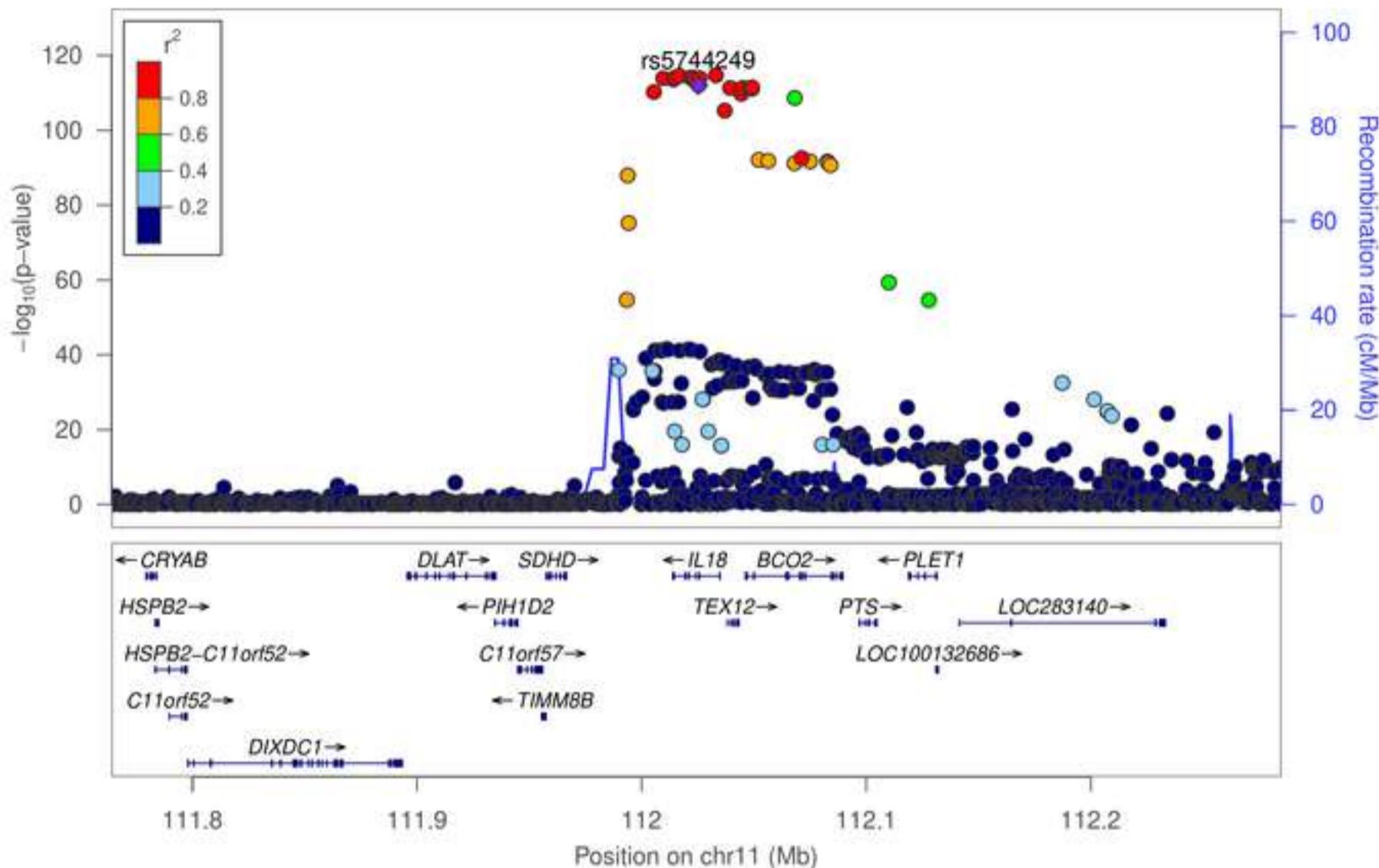
# eQTLGen: IL-17C (IL17C)-rs17700884



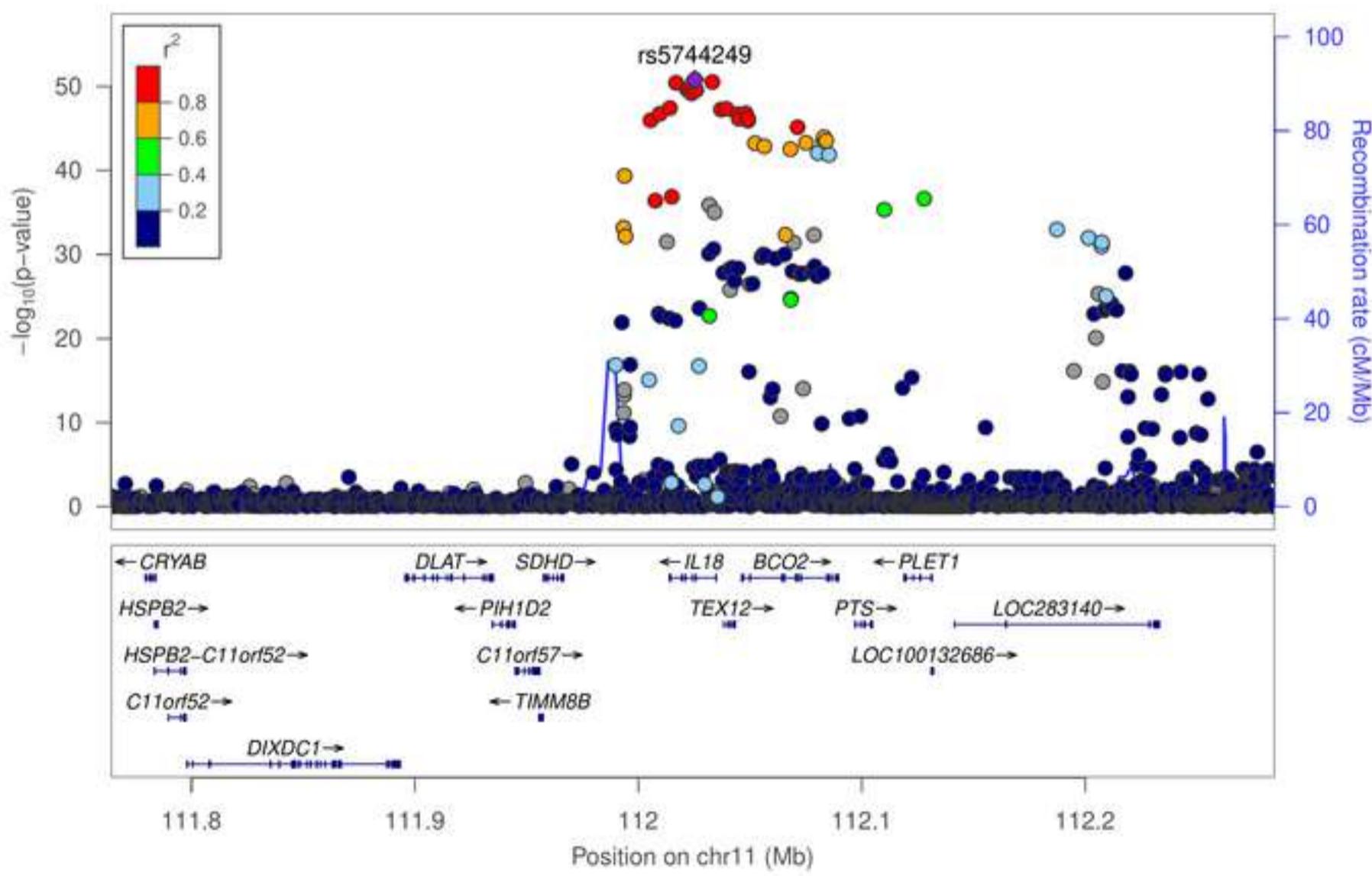
# SCALLOP: IL-17C (IL17C)-rs17700884



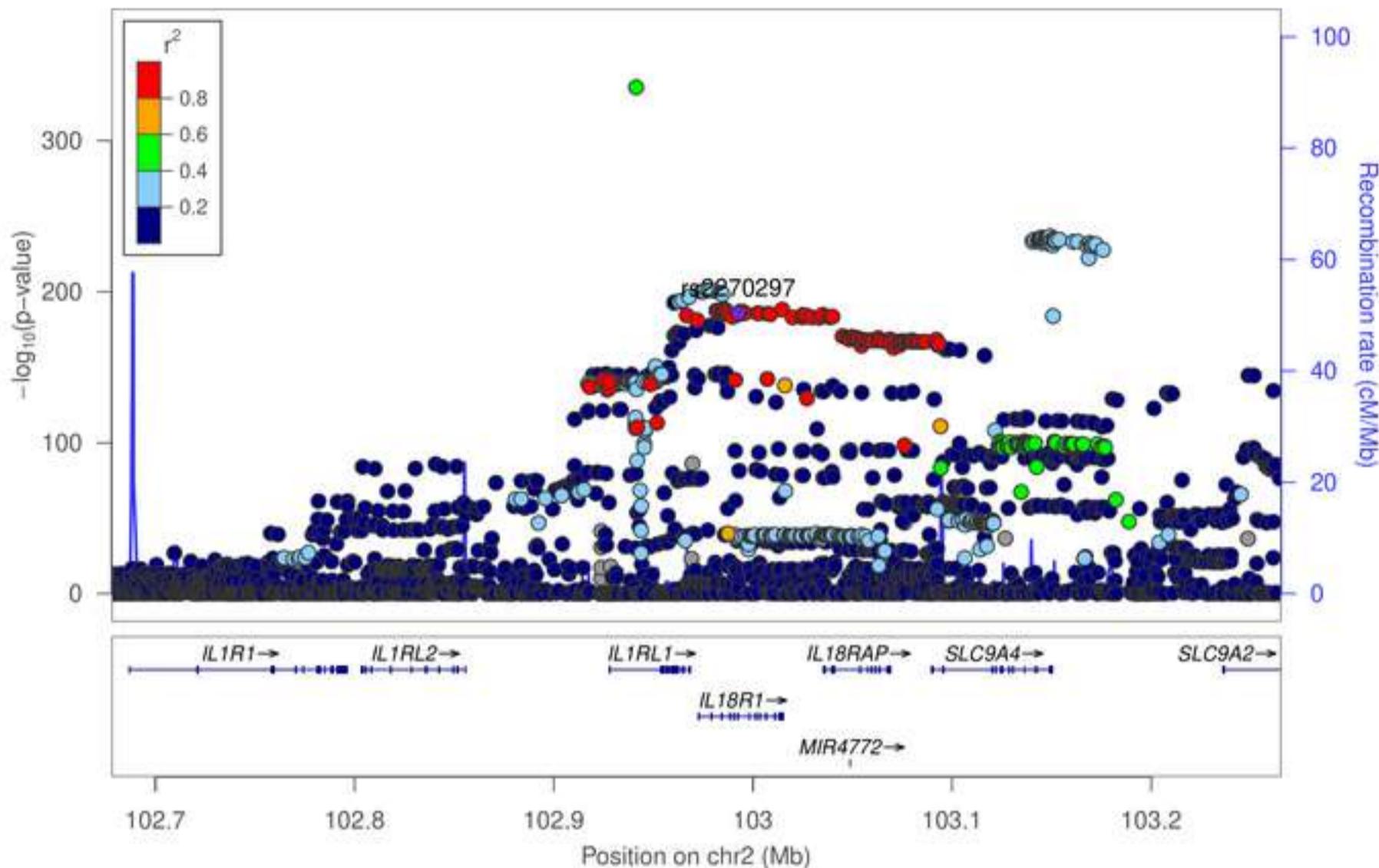
# eQTLGen: IL-18 (IL18)-rs5744249



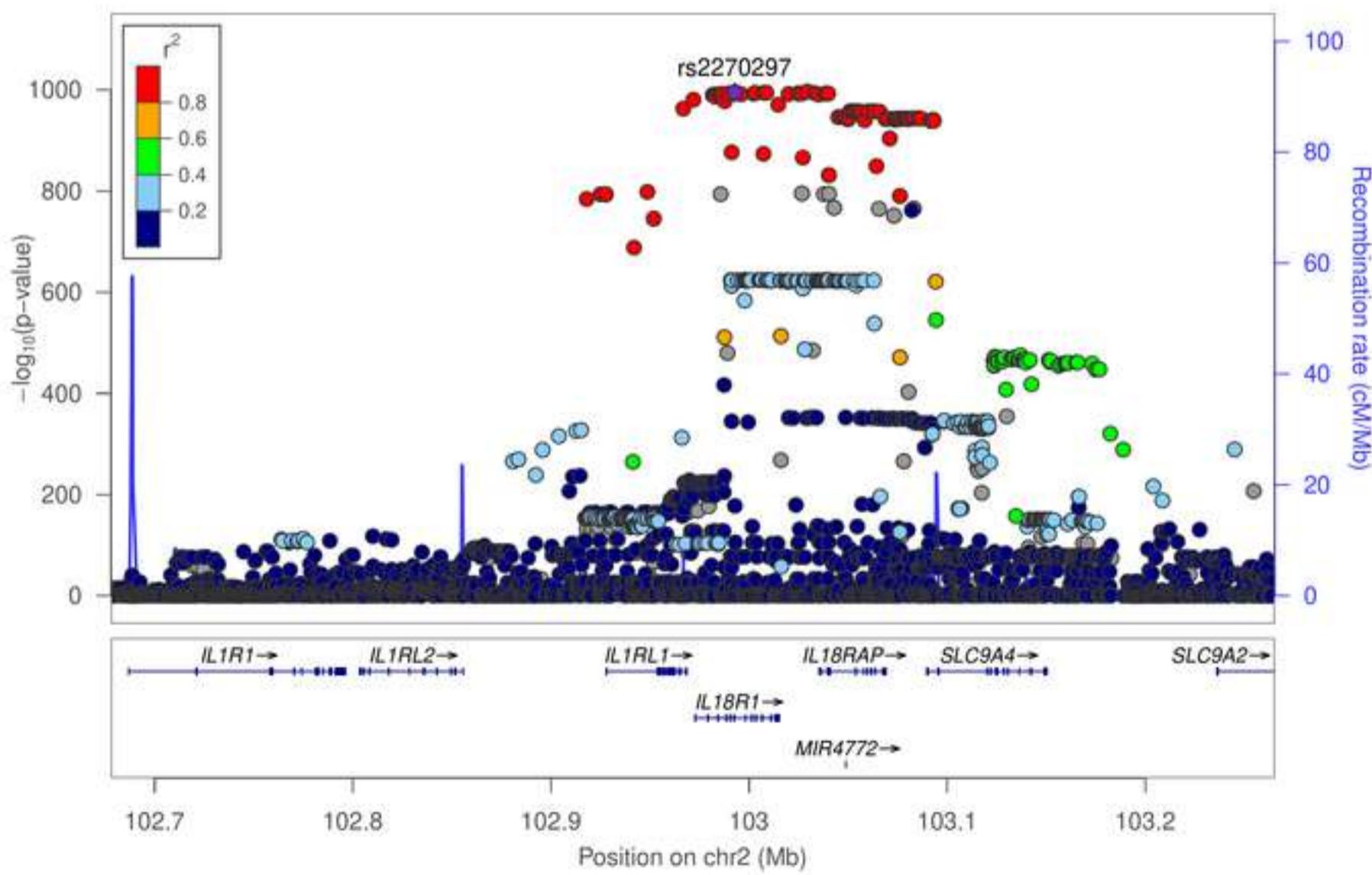
# SCALLOP: IL-18 (IL18)-rs5744249



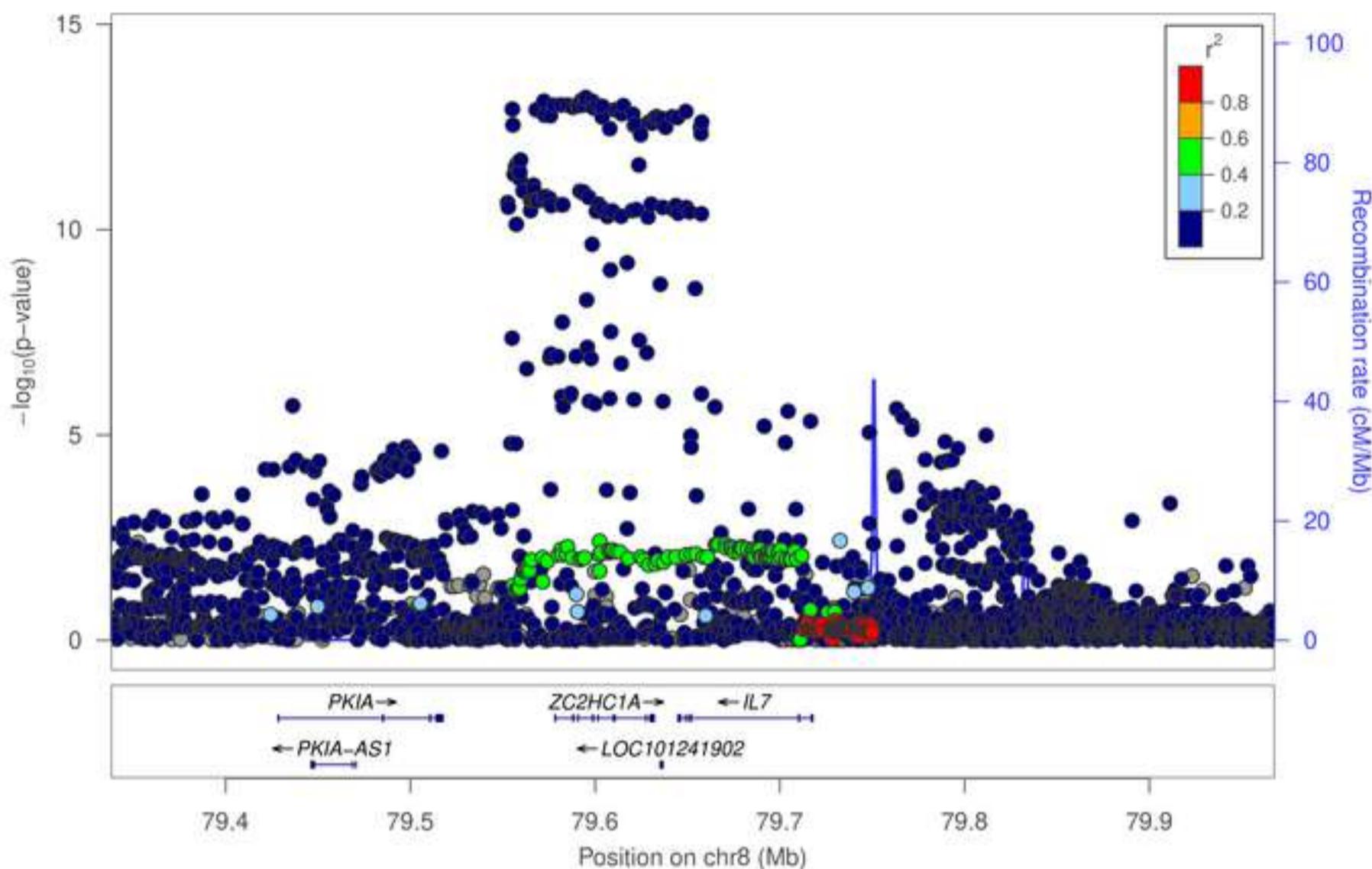
## eQTLGen: IL-18R1 (IL18R1)-rs2270297



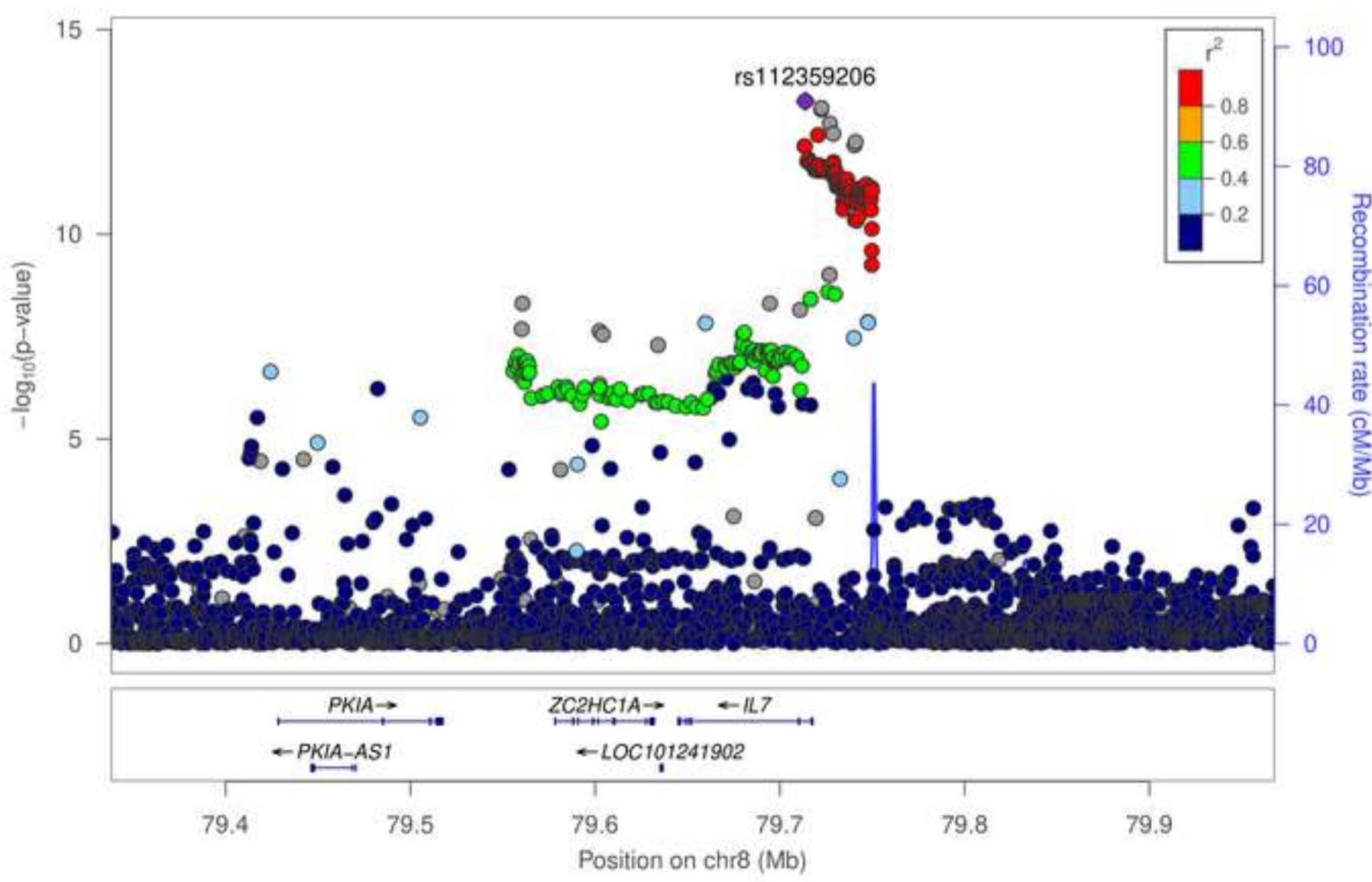
## SCALLOP: IL-18R1 (IL18R1)-rs2270297



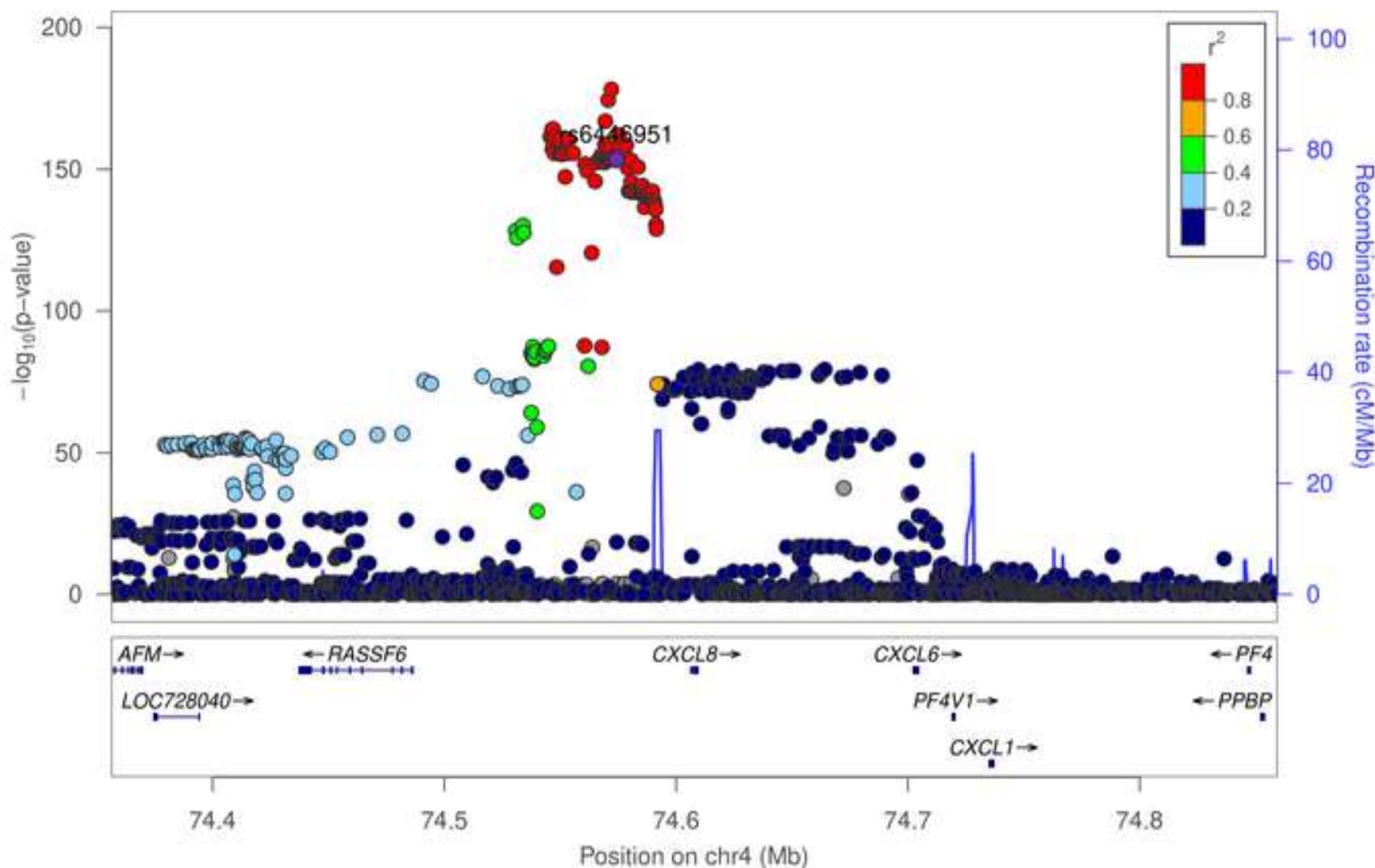
# eQTLGen: IL-7 (IL7)-rs112359206



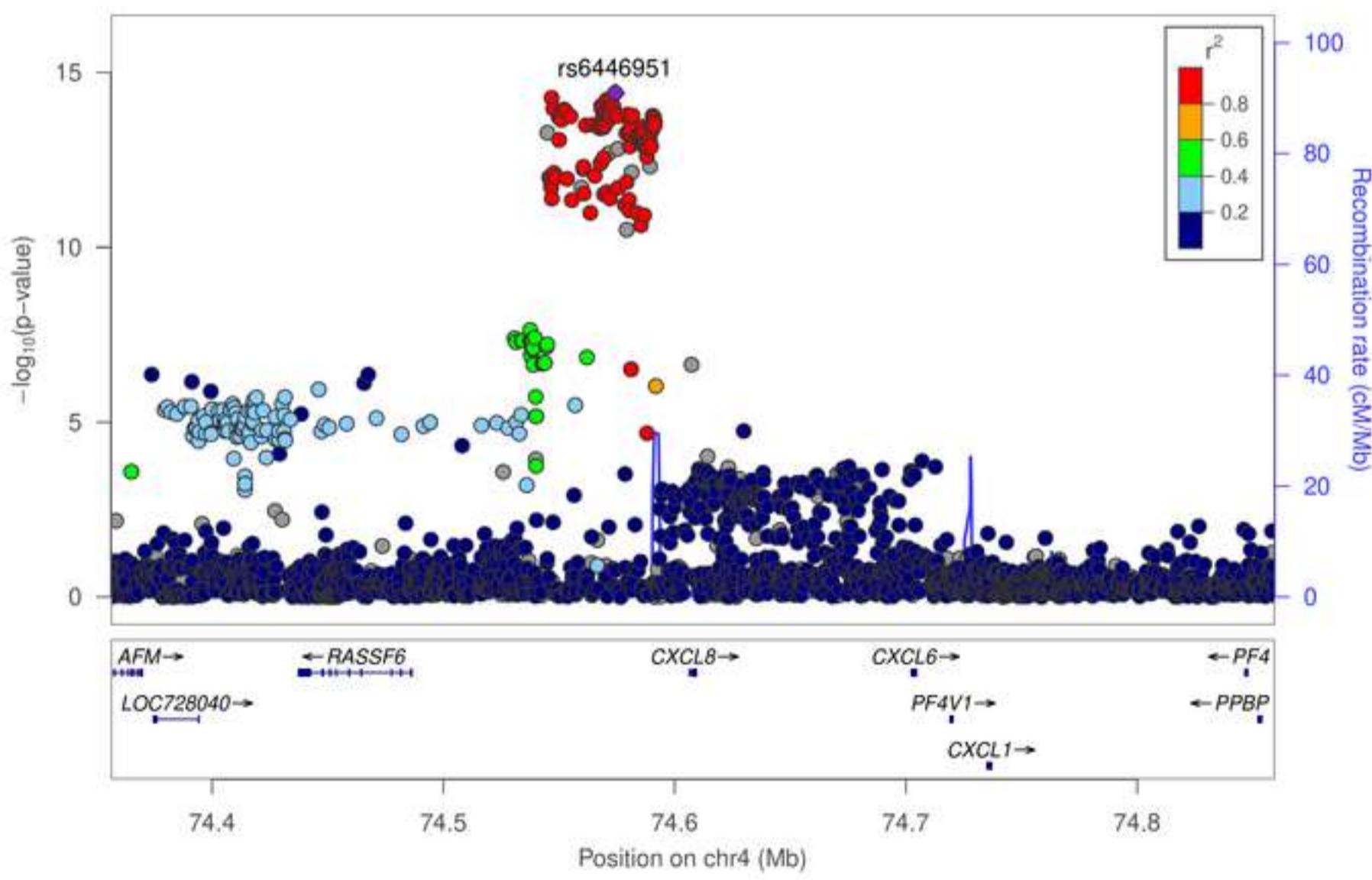
# SCALLOP: IL-7 (IL7)-rs112359206



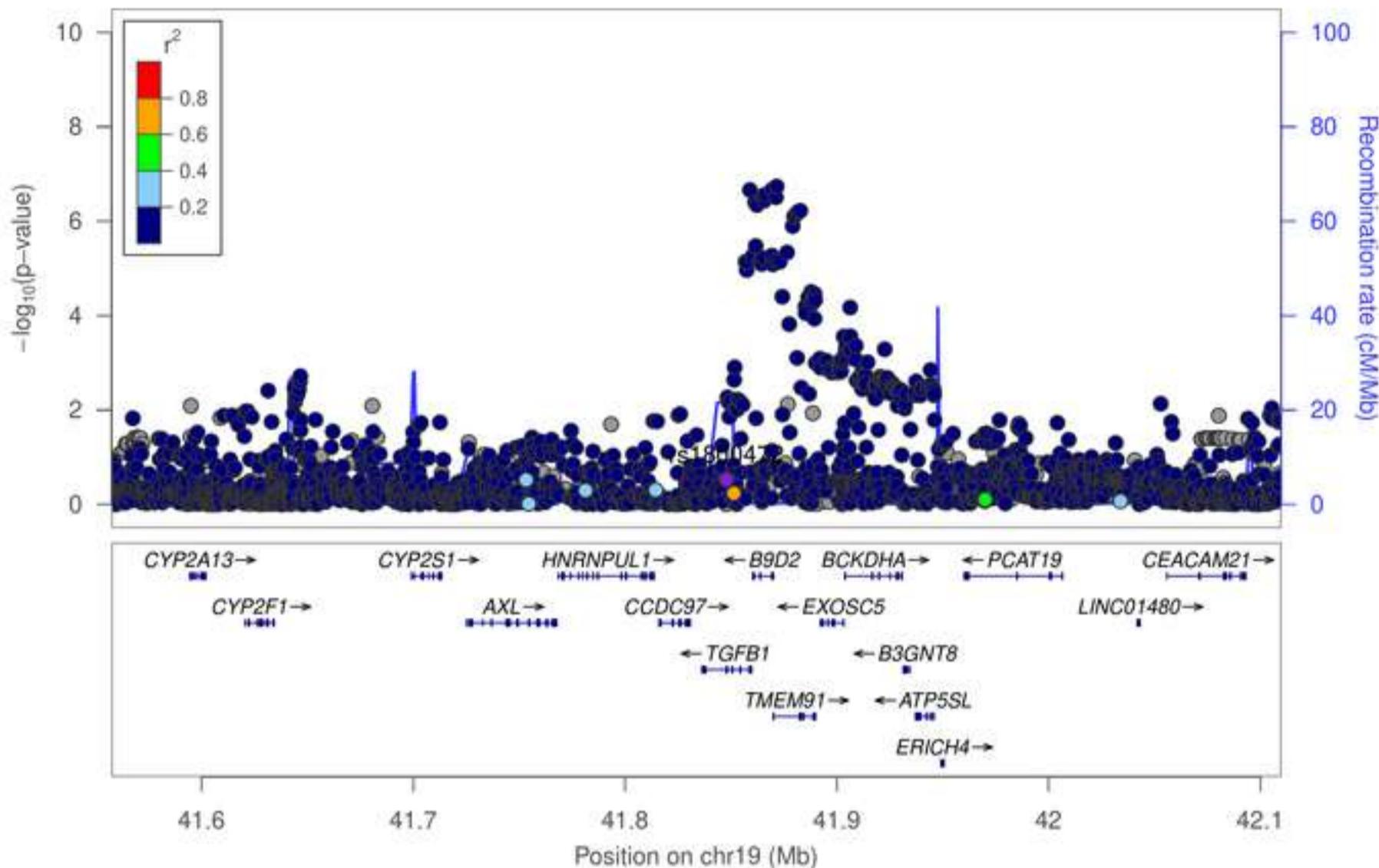
# eQTLGen: IL-8 (IL8)-rs6446951



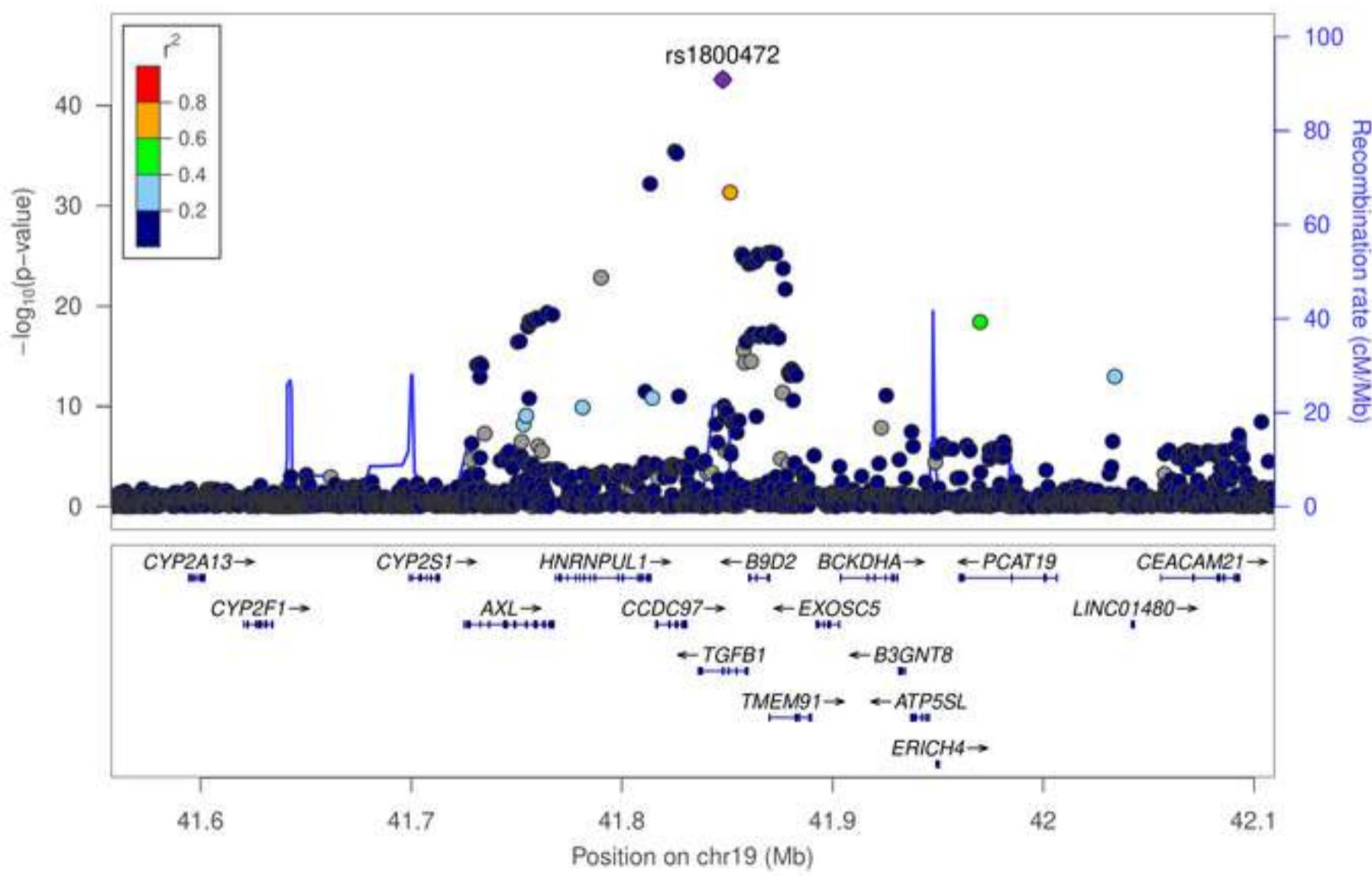
# SCALLOP: IL-8 (IL8)-rs6446951



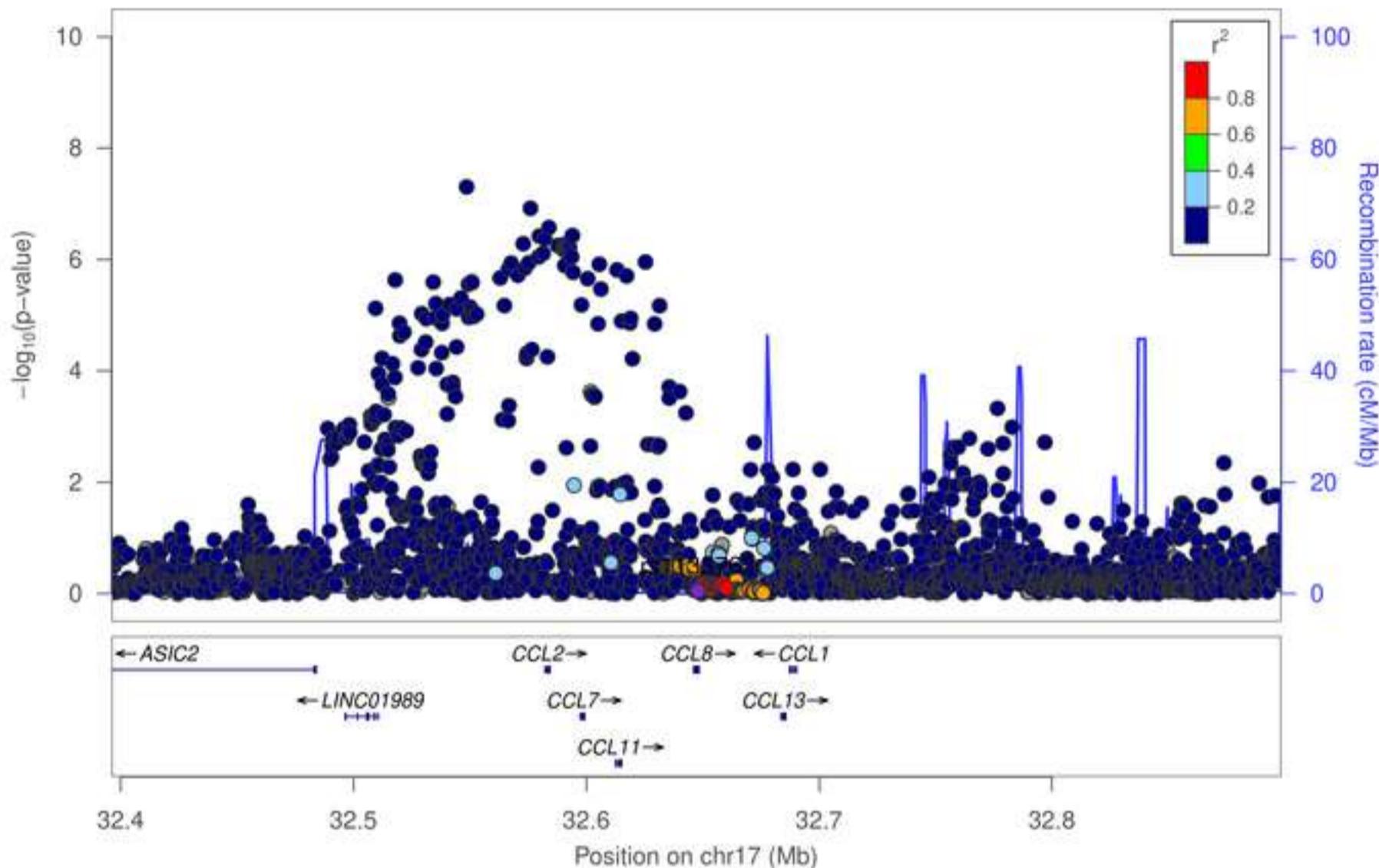
# eQTLGen: LAP (TGFB1)-rs1800472



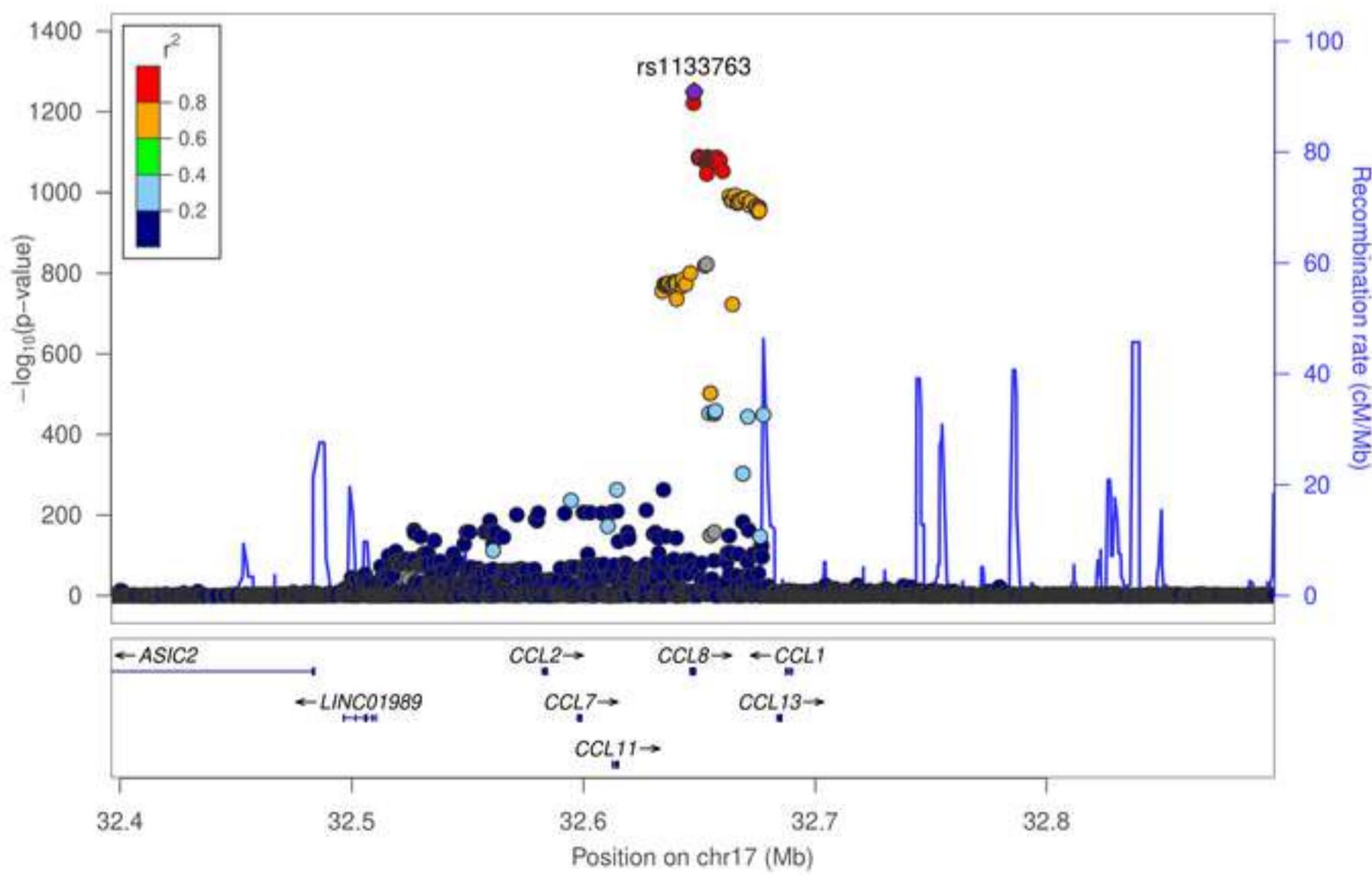
# SCALLOP: LAP (TGFB1)-rs1800472



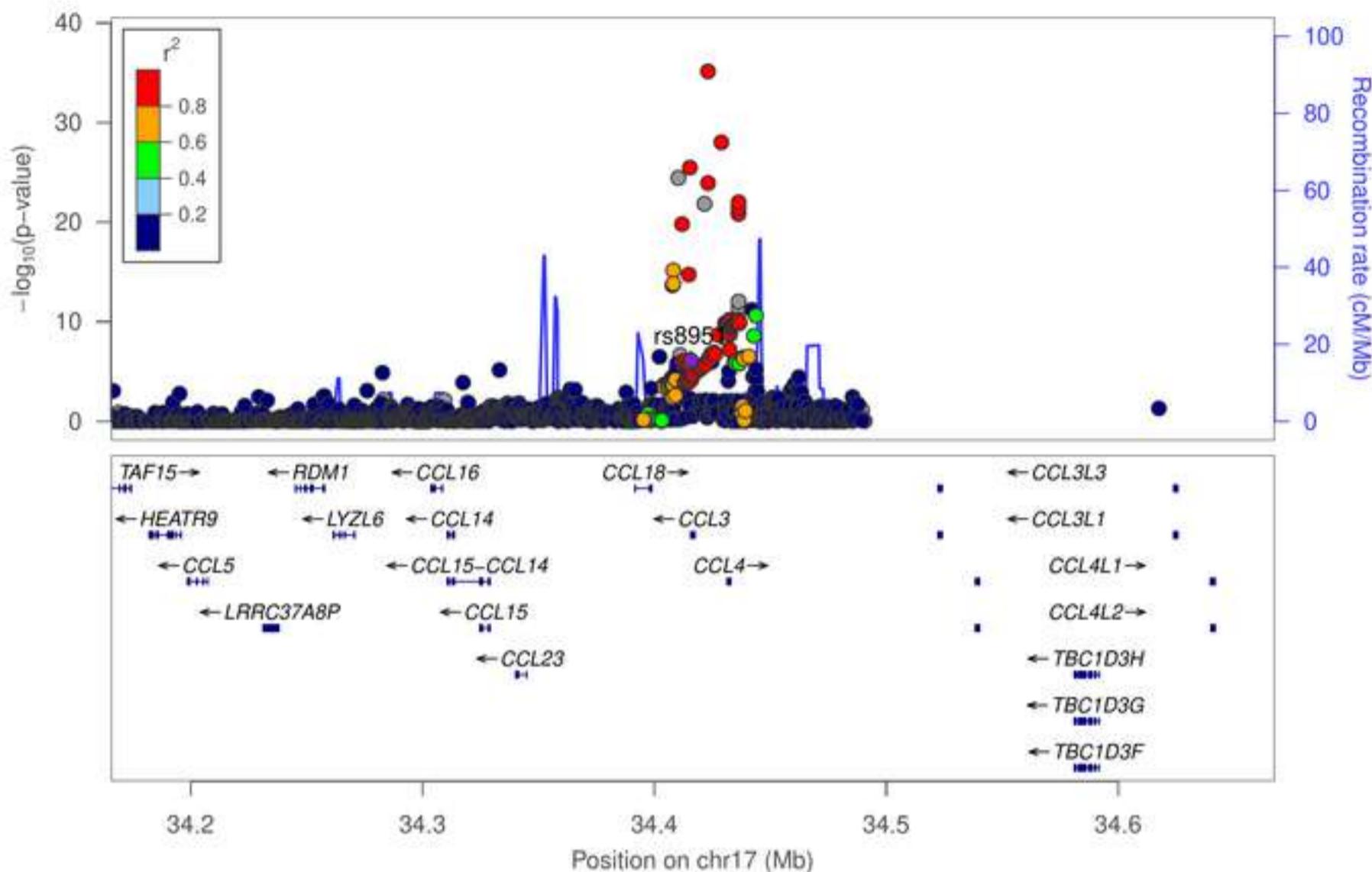
## eQTLGen: MCP–2 (CCL8)–rs1133763



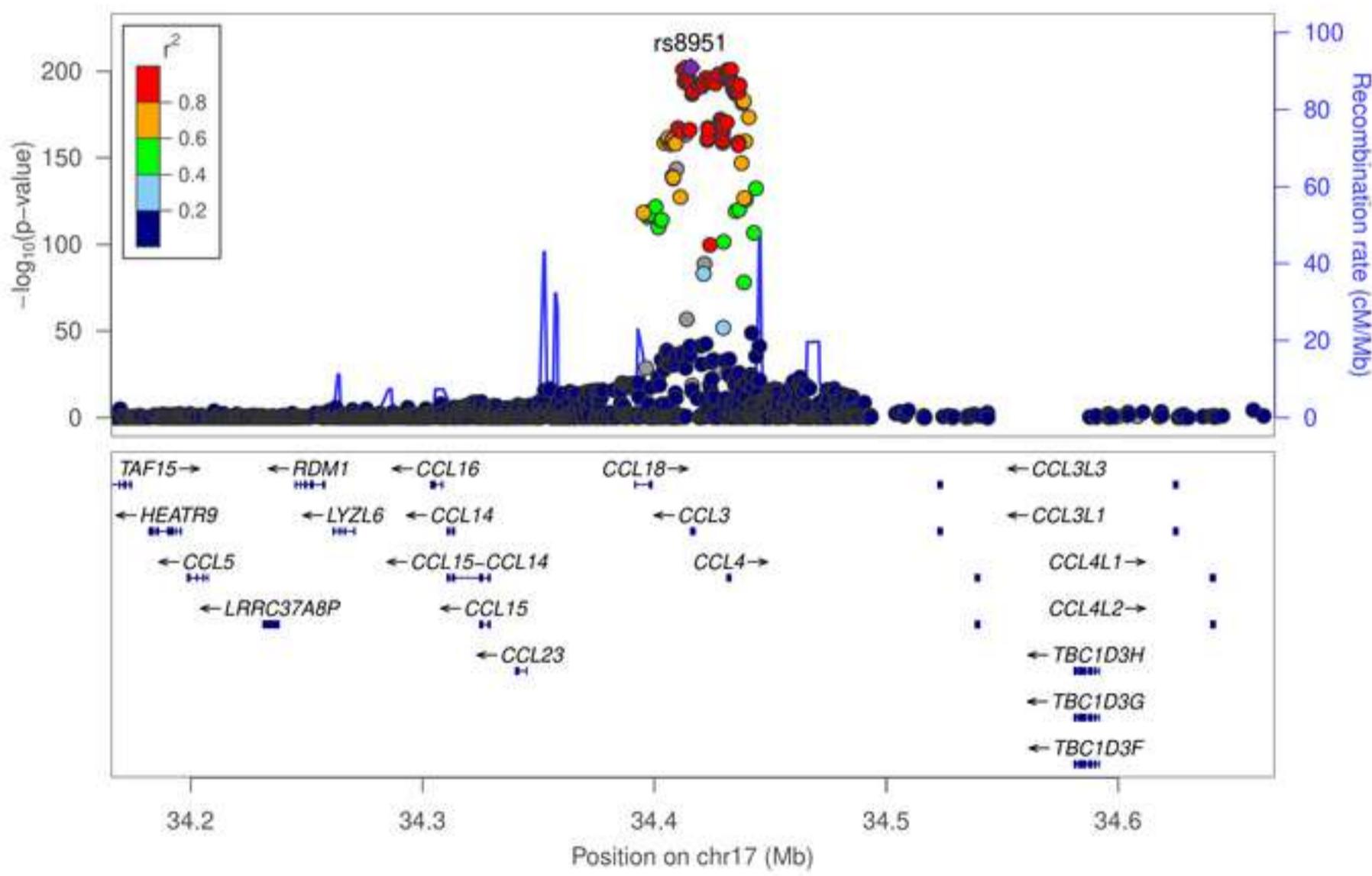
## SCALLOP: MCP–2 (CCL8)–rs1133763



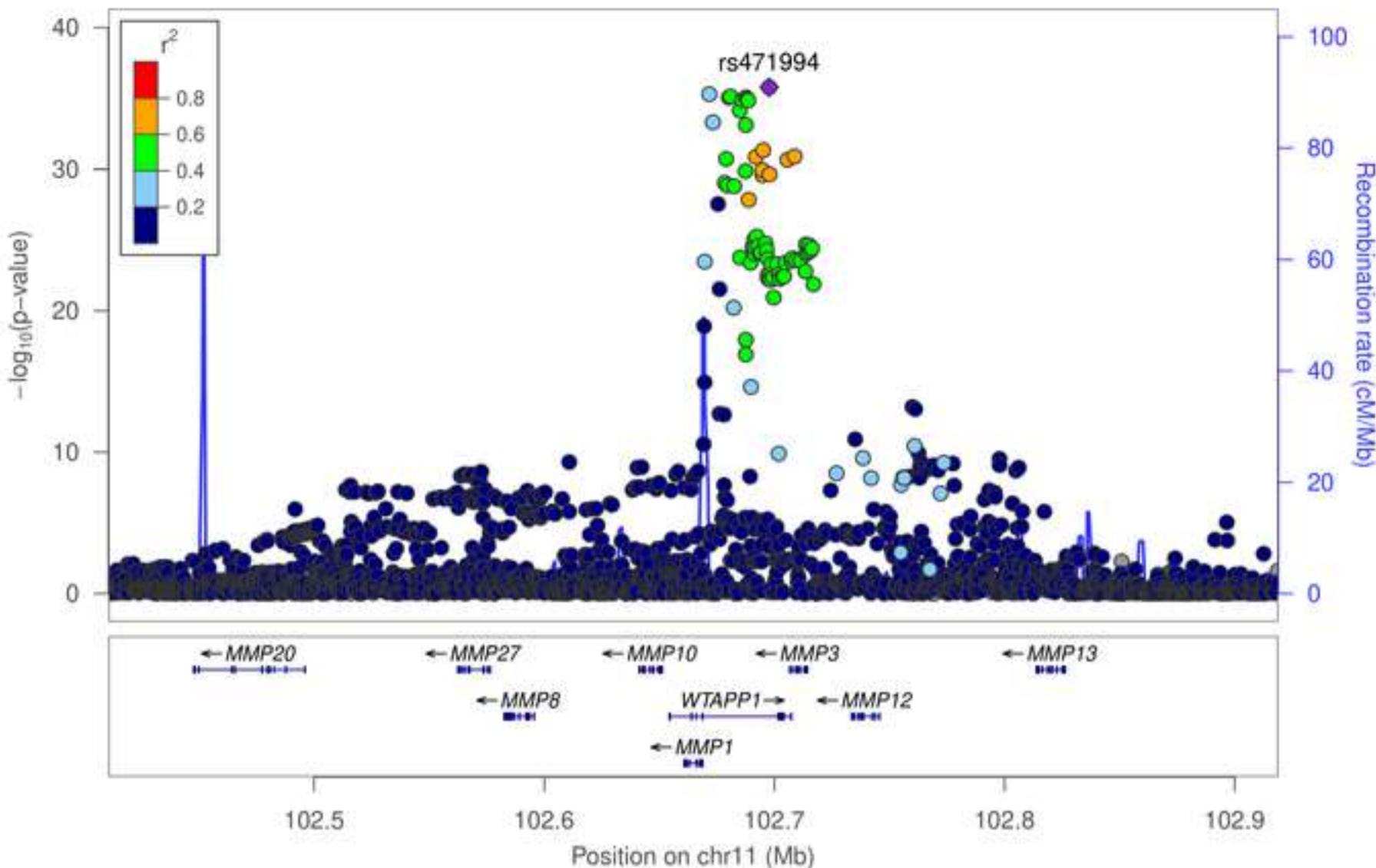
# eQTLGen: MIP-1 (CCL3)-rs8951



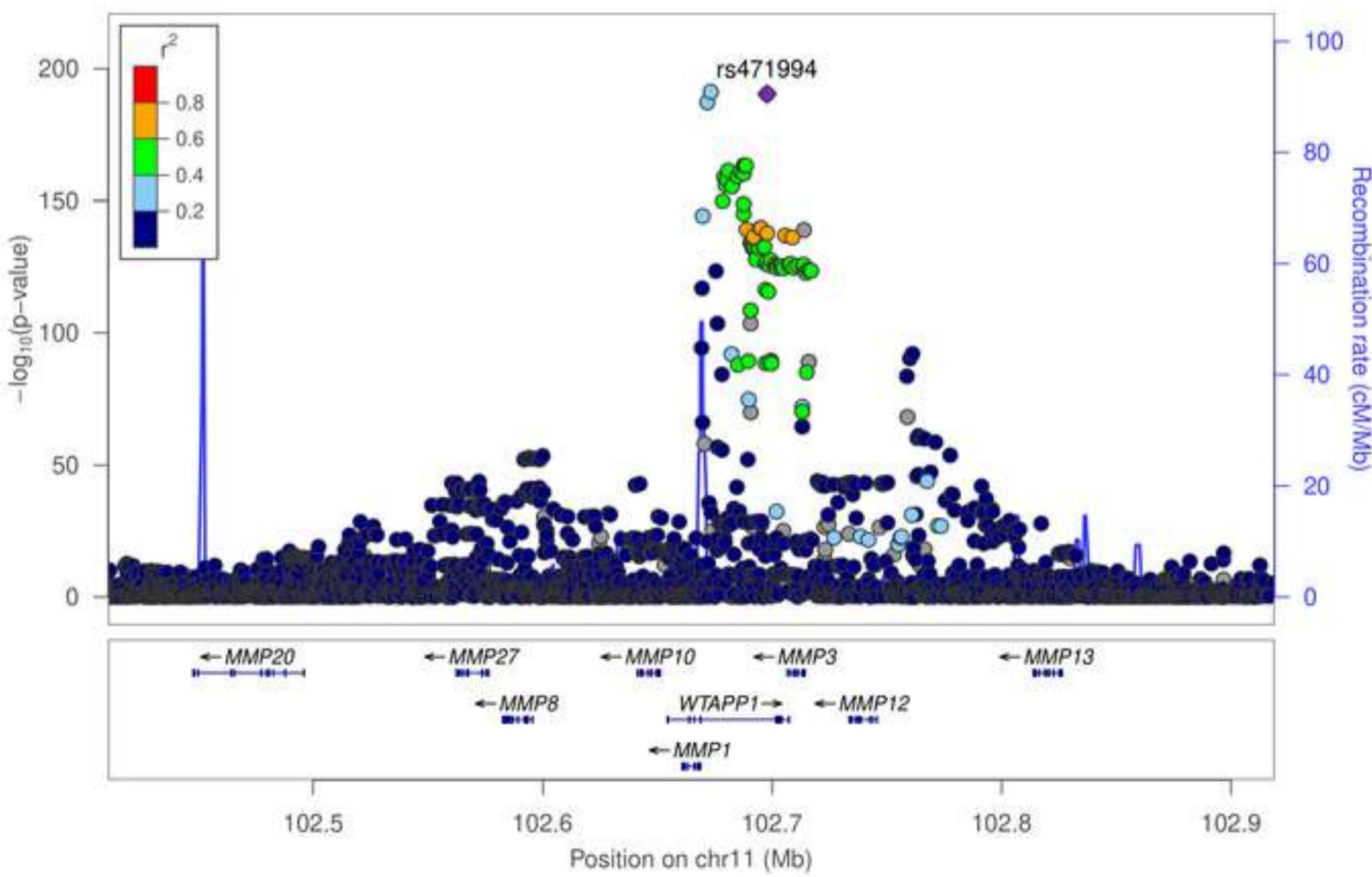
# SCALLOP: MIP-1 (CCL3)-rs8951



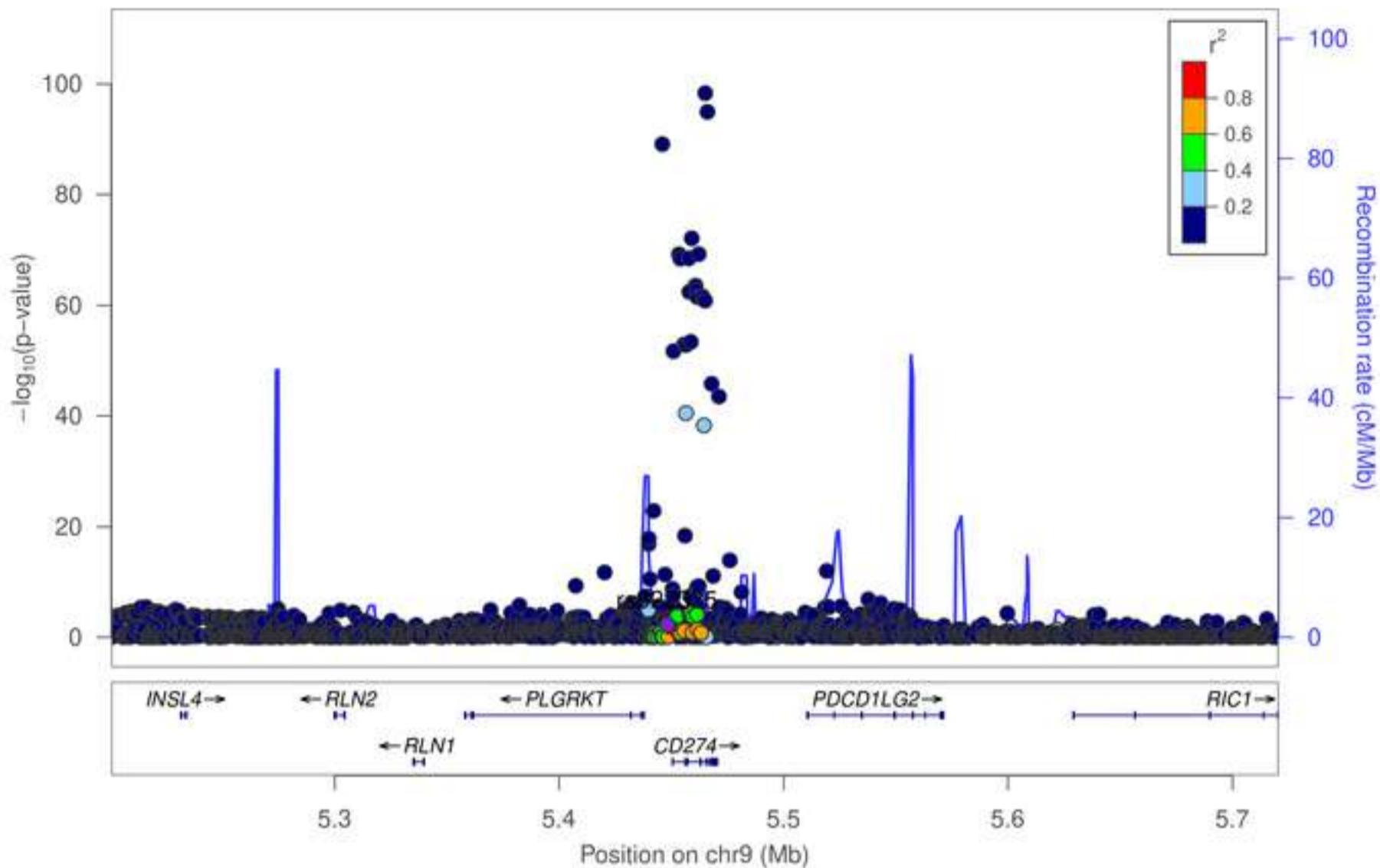
## eQTLGen: MMP-1 (MMP1)-rs471994



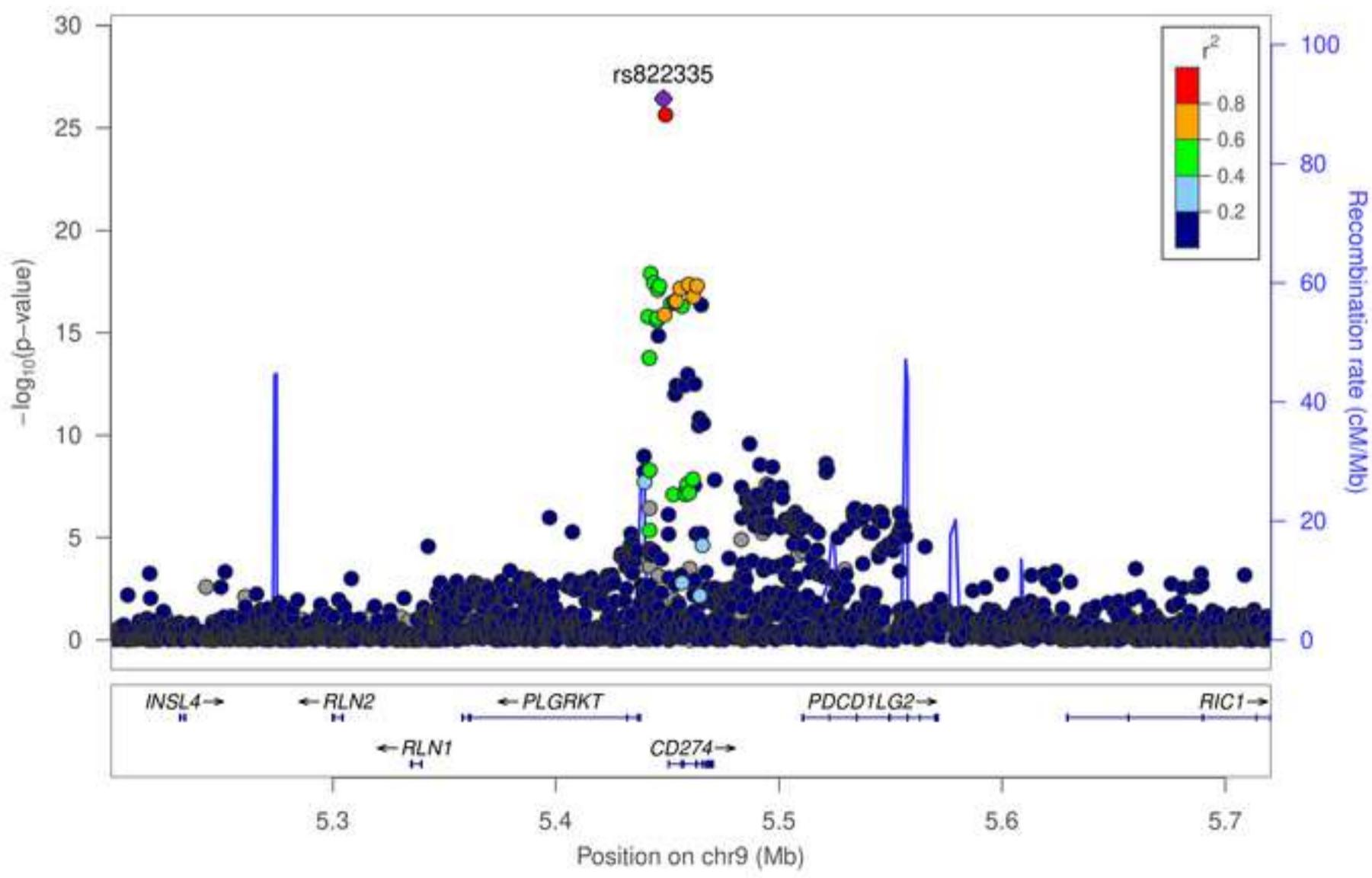
## SCALLOP: MMP-1 (MMP1)-rs471994



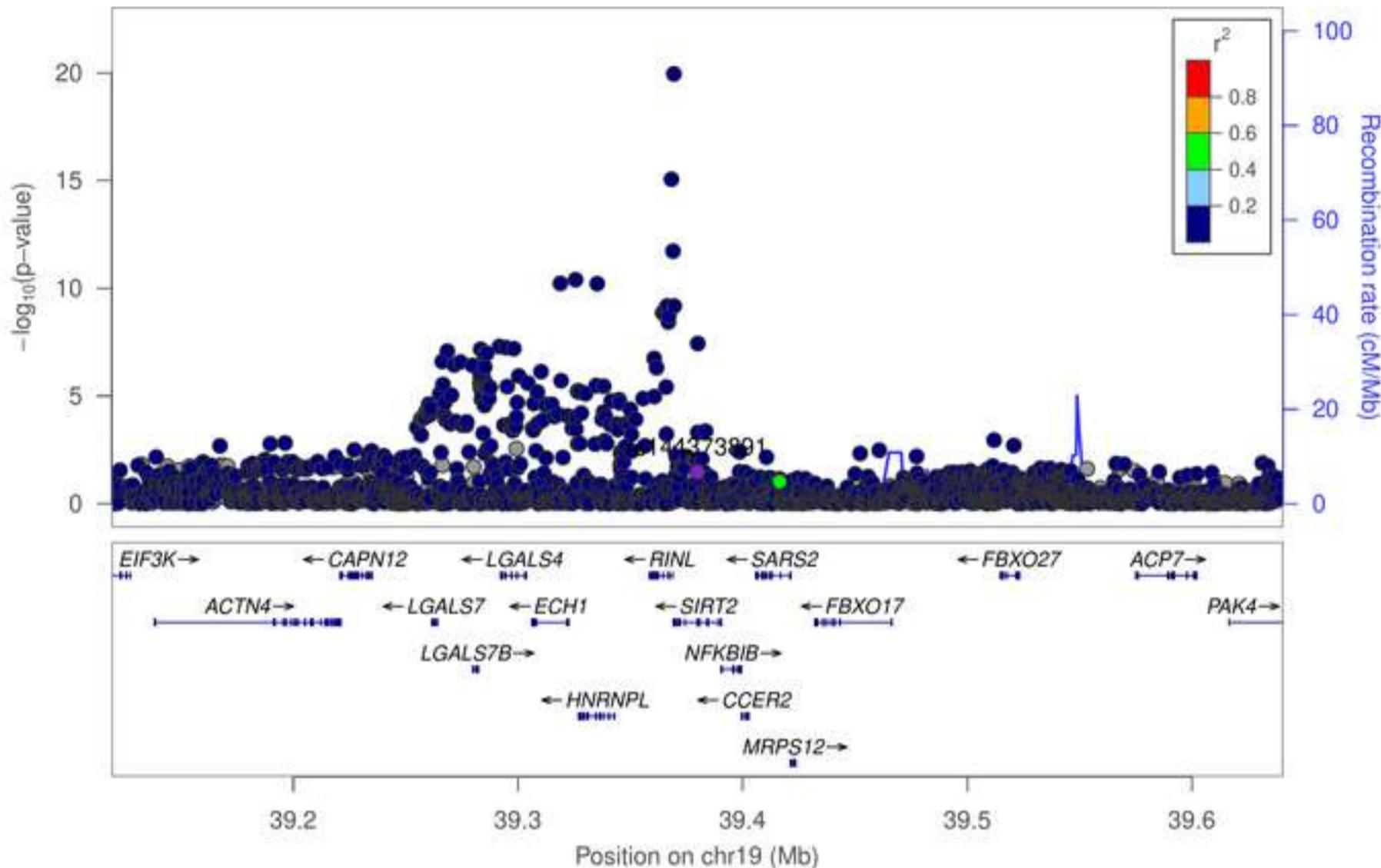
# eQTLGen: PD-L1 (CD274)-rs822335



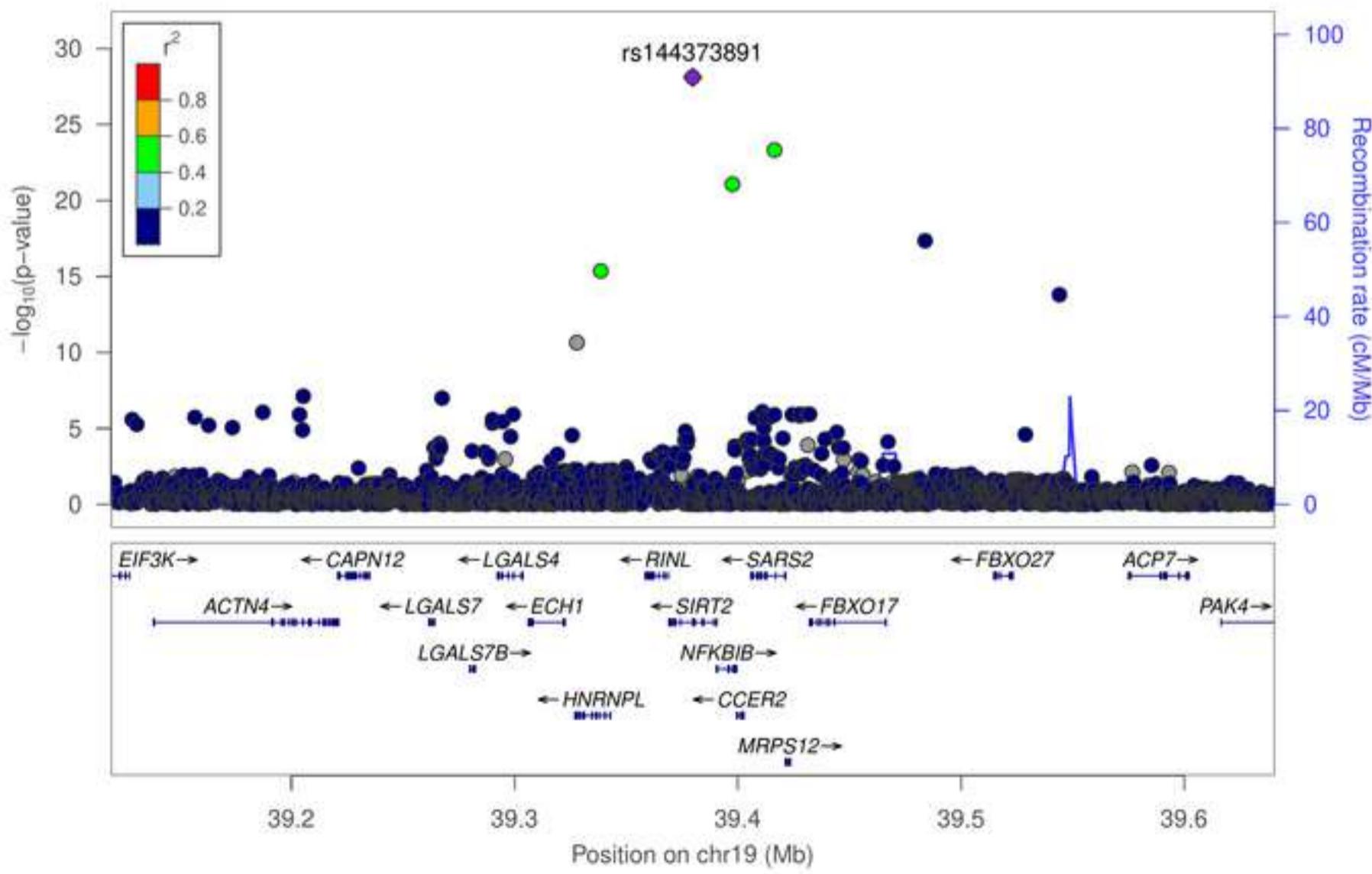
# SCALLOP: PD-L1 (CD274)-rs822335



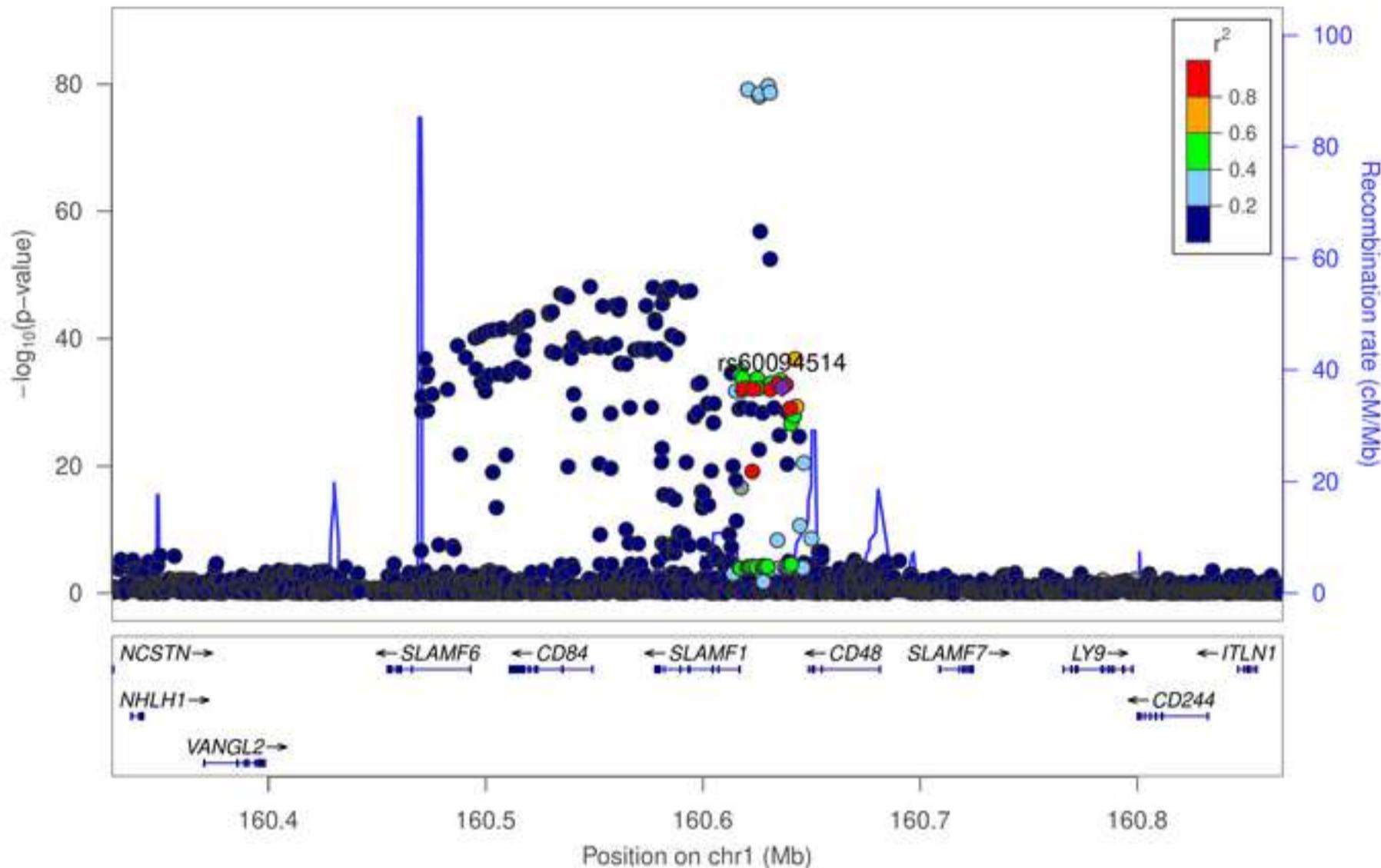
# eQTLGen: SIRT2 (SIRT2)-rs144373891



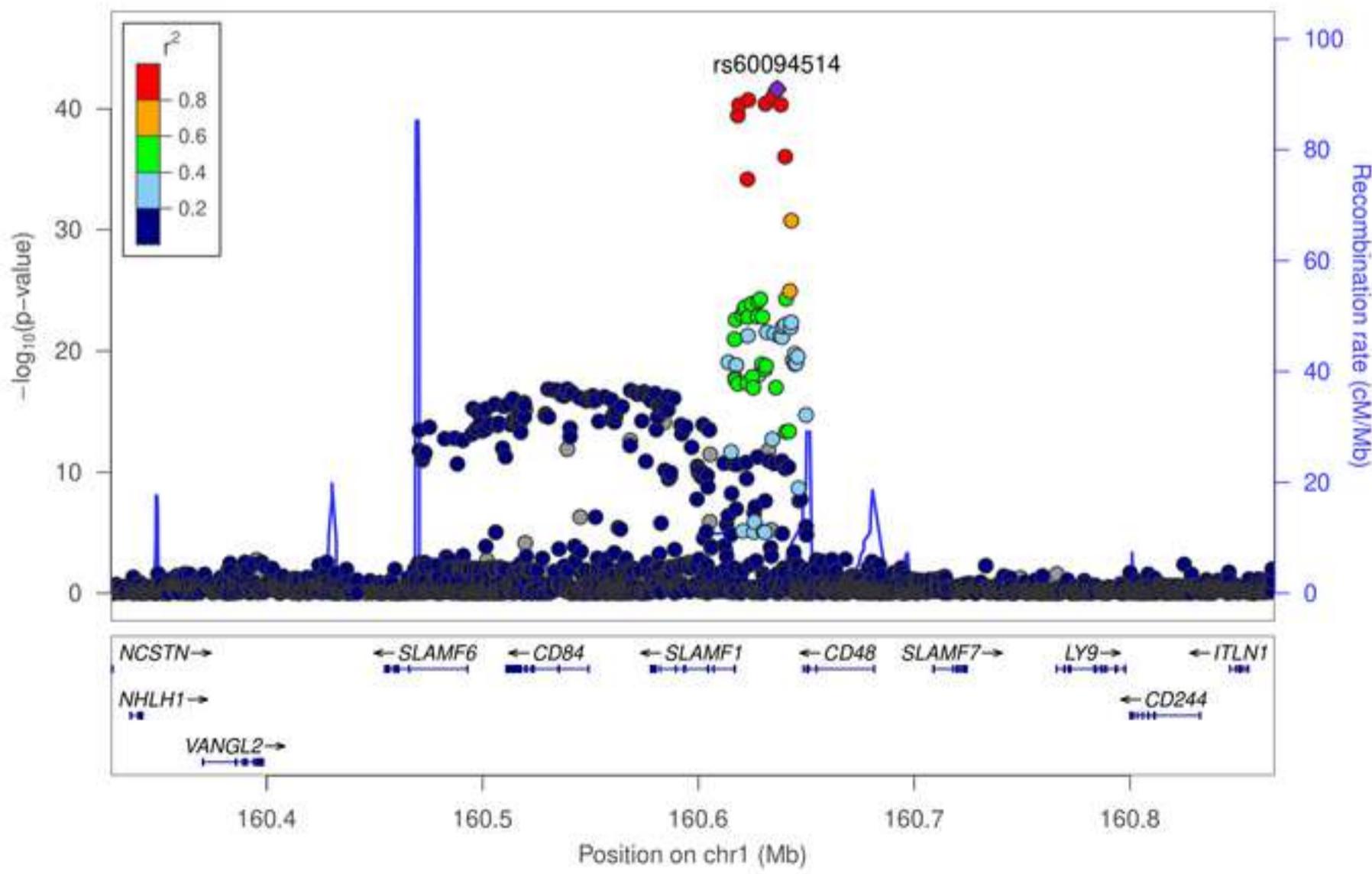
# SCALLOP: SIRT2 (SIRT2)-rs144373891



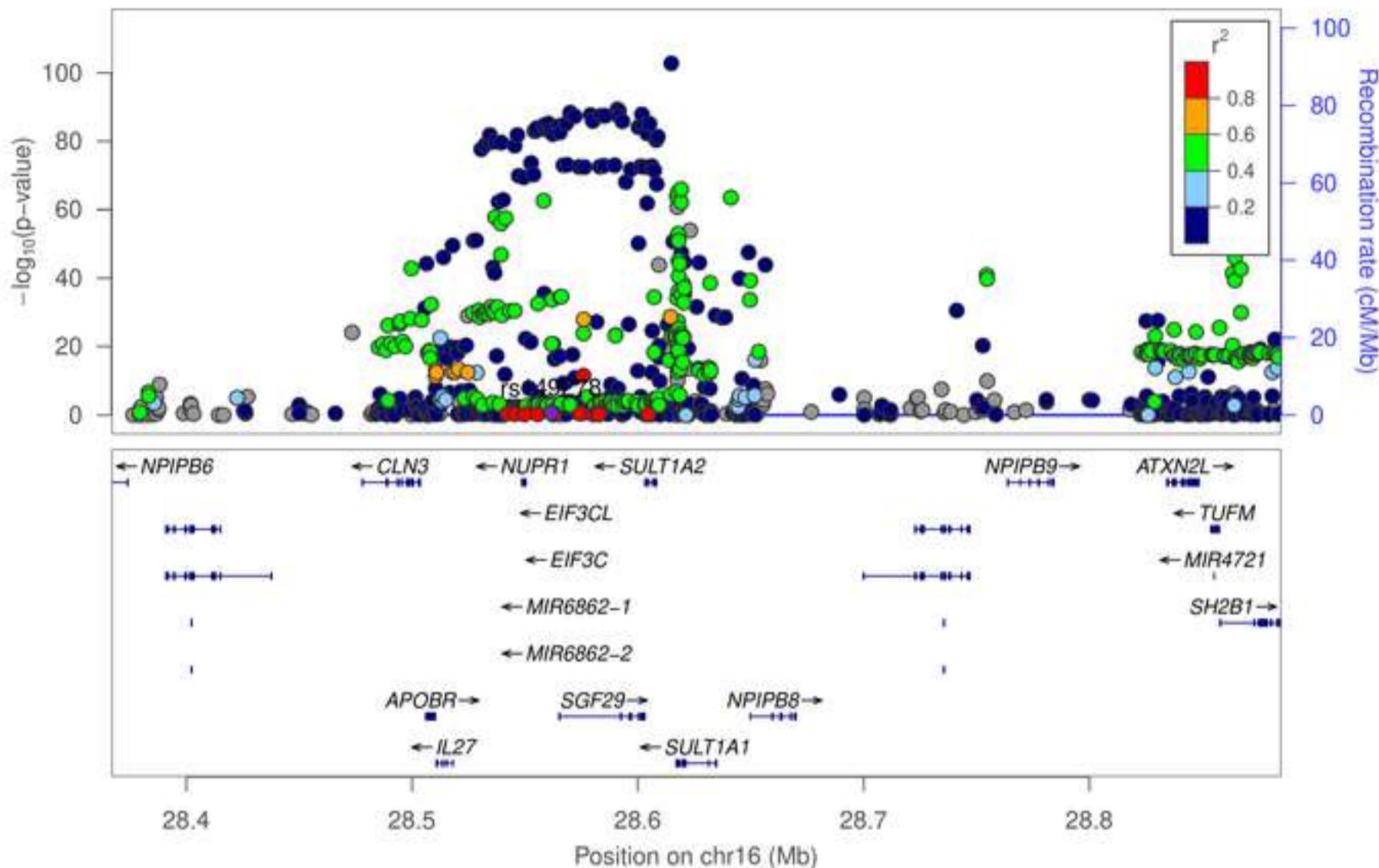
# eQTLGen: SLAMF1 (SLAMF1)-rs60094514



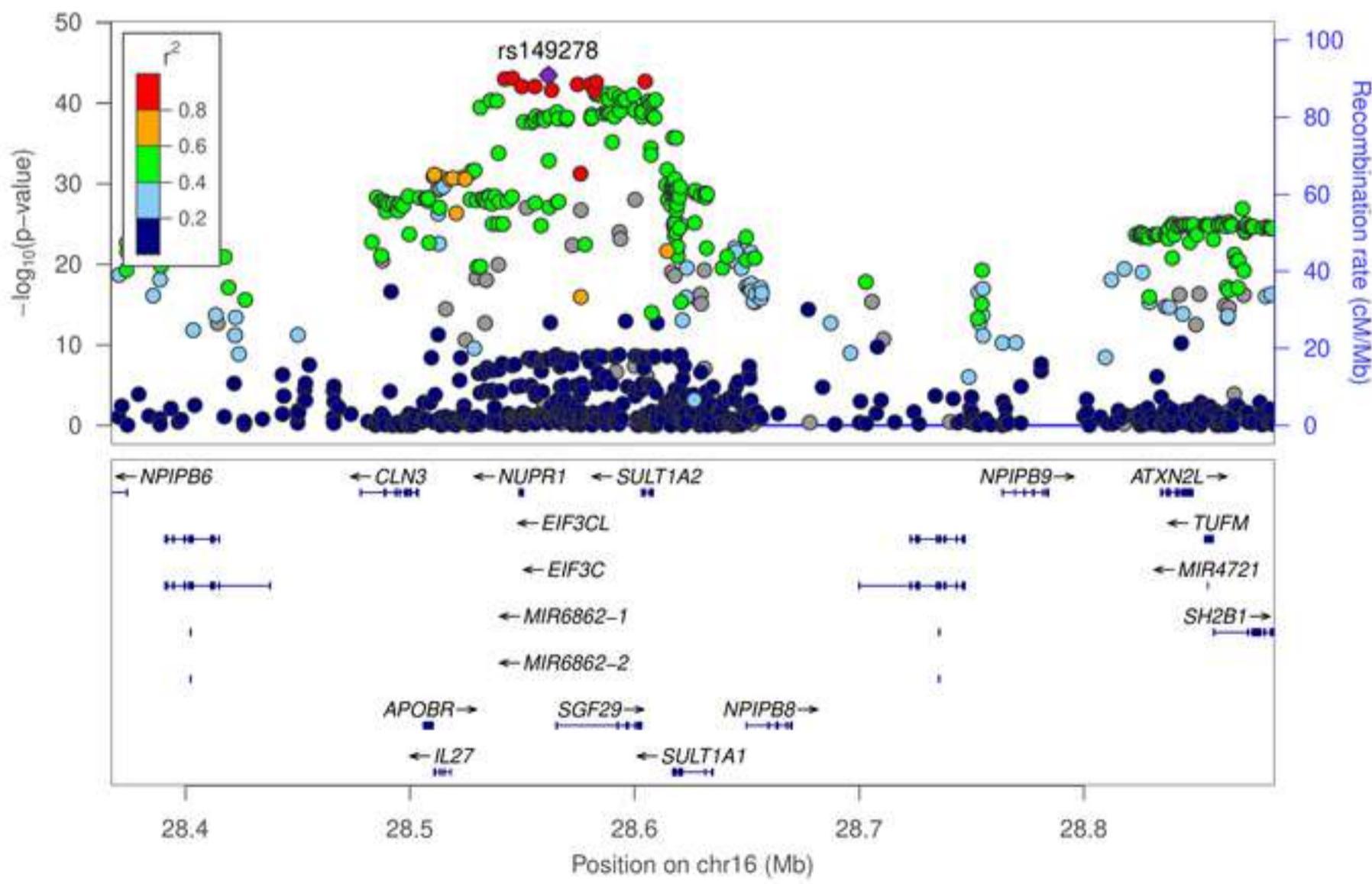
# SCALLOP: SLAMF1 (SLAMF1)-rs60094514



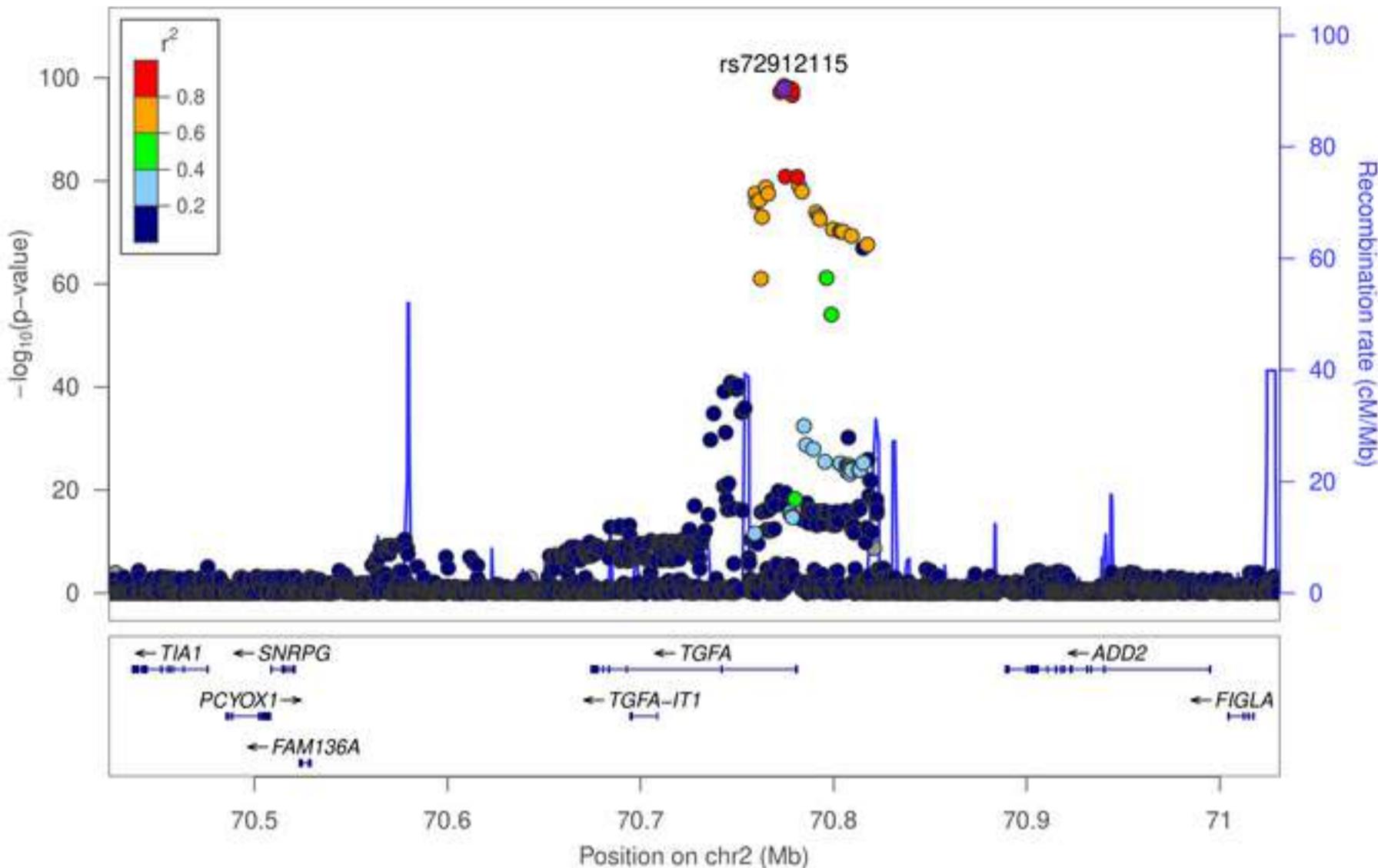
# eQTLGen: ST1A1 (SULT1A1)-rs149278



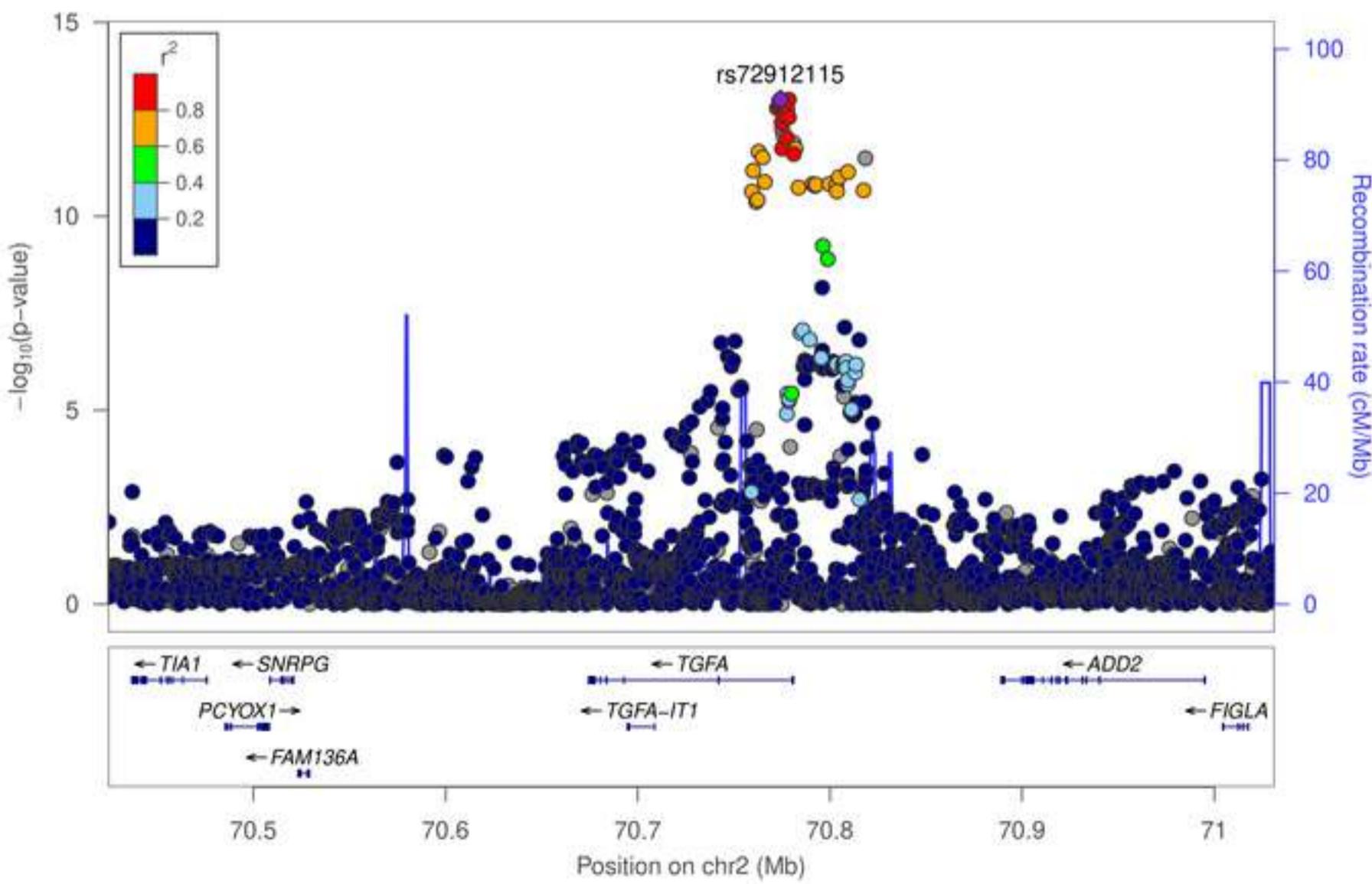
# SCALLOP: ST1A1 (SULT1A1)-rs149278



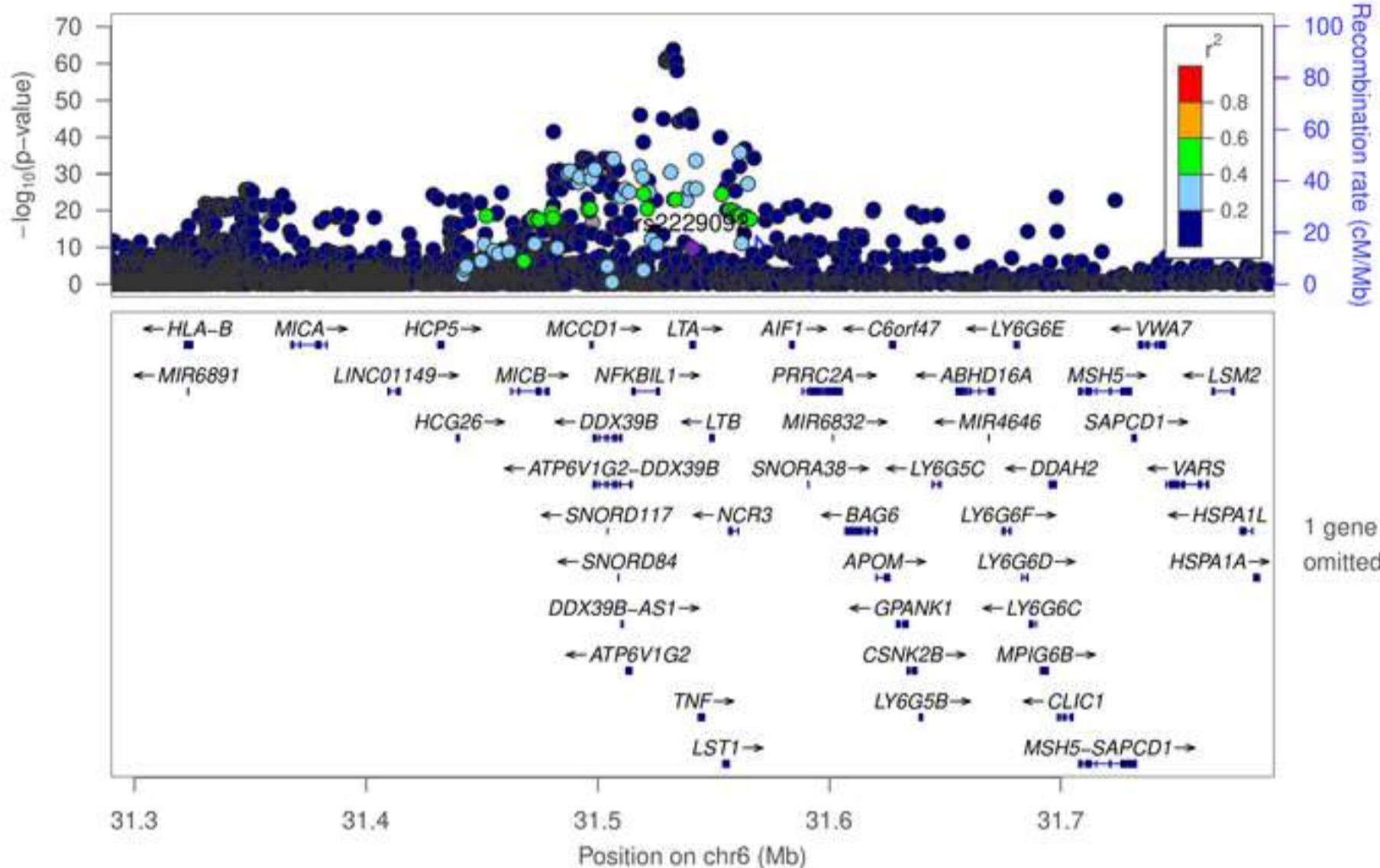
# eQTLGen: TGF-alpha (TGFA)-rs72912115



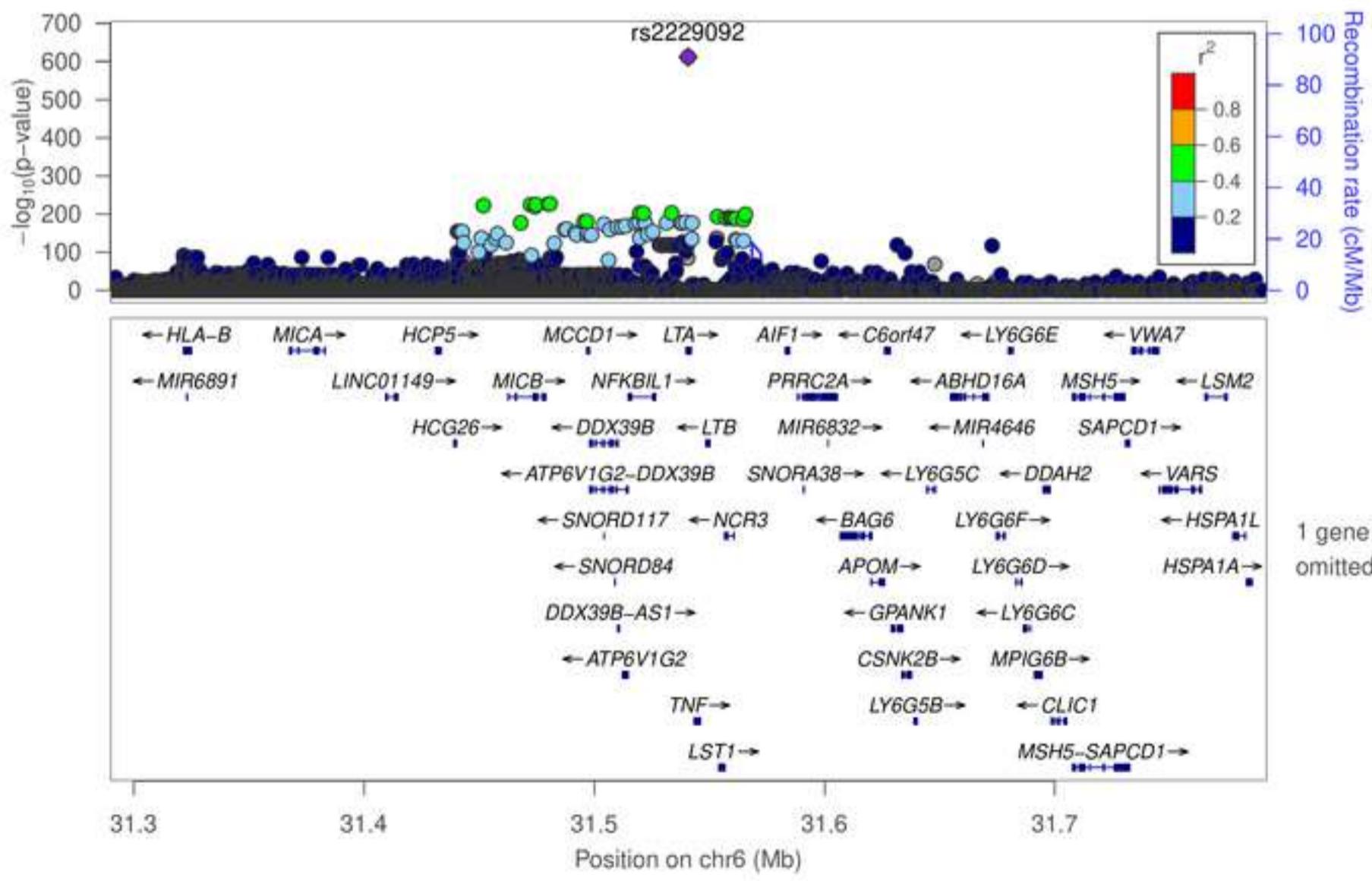
# SCALLOP: TGF-alpha (TGFA)-rs72912115



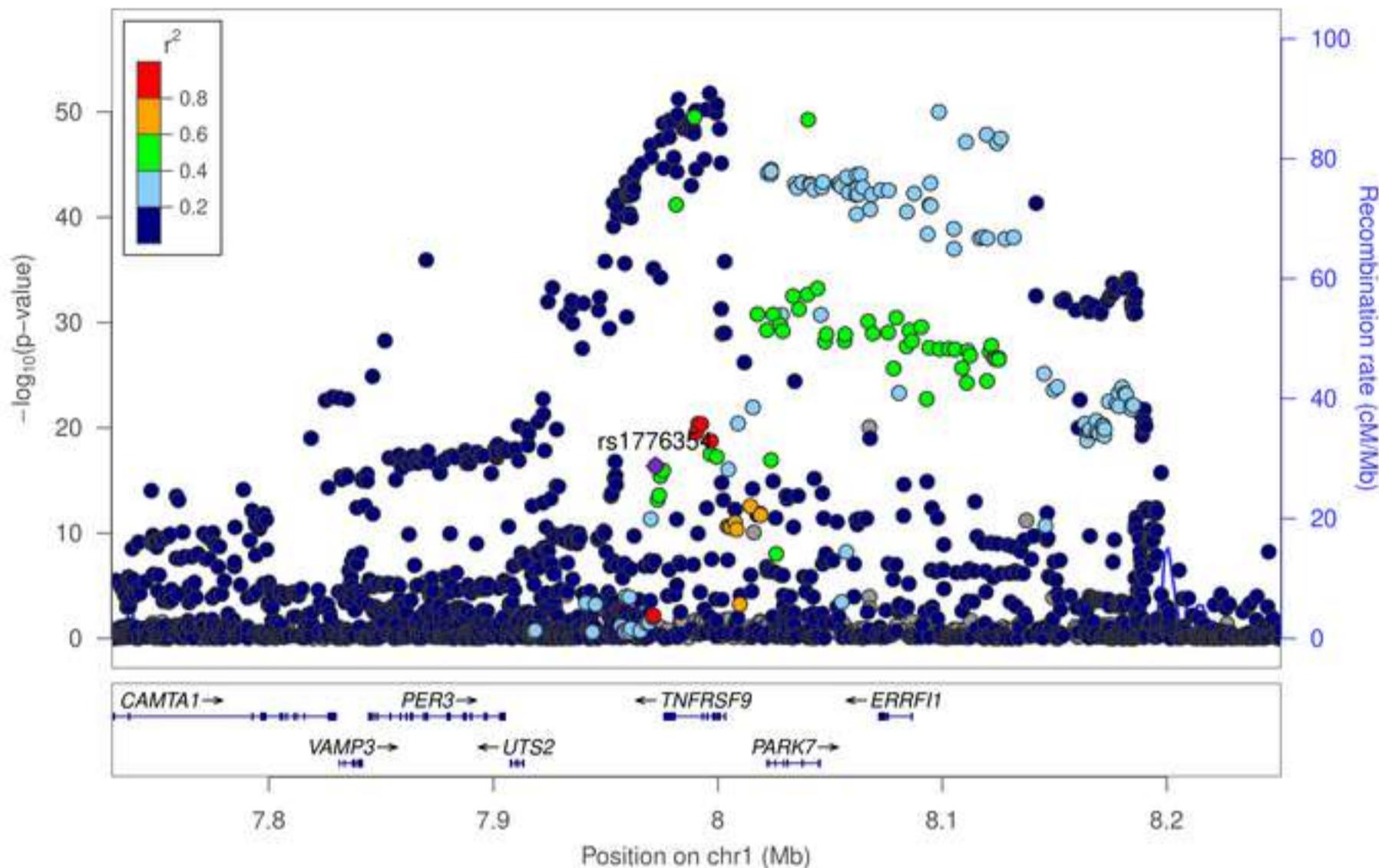
## eQTLGen: TNFB (LTA)-rs2229092



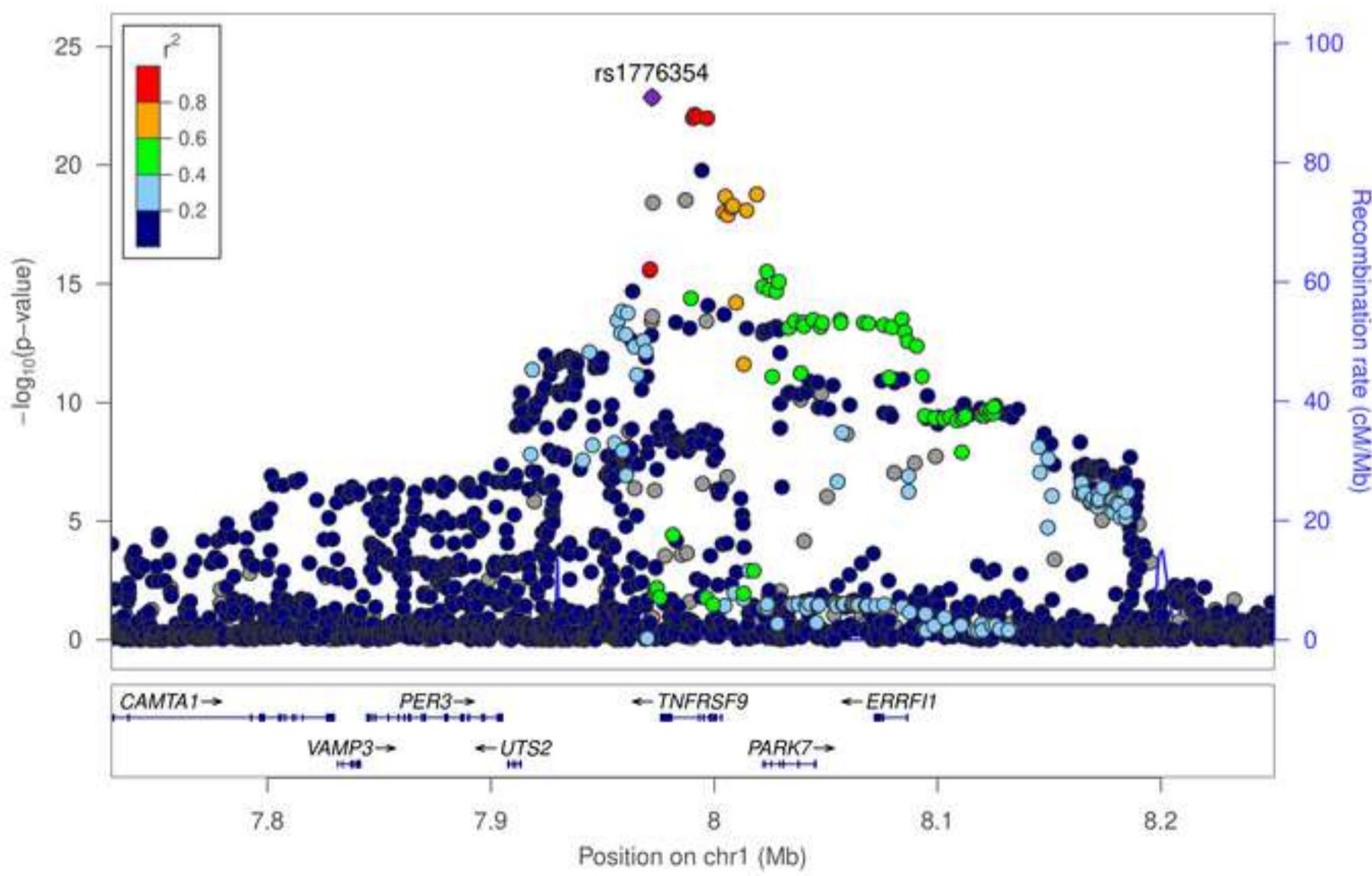
## SCALLOP: TNFB (LTA)-rs2229092



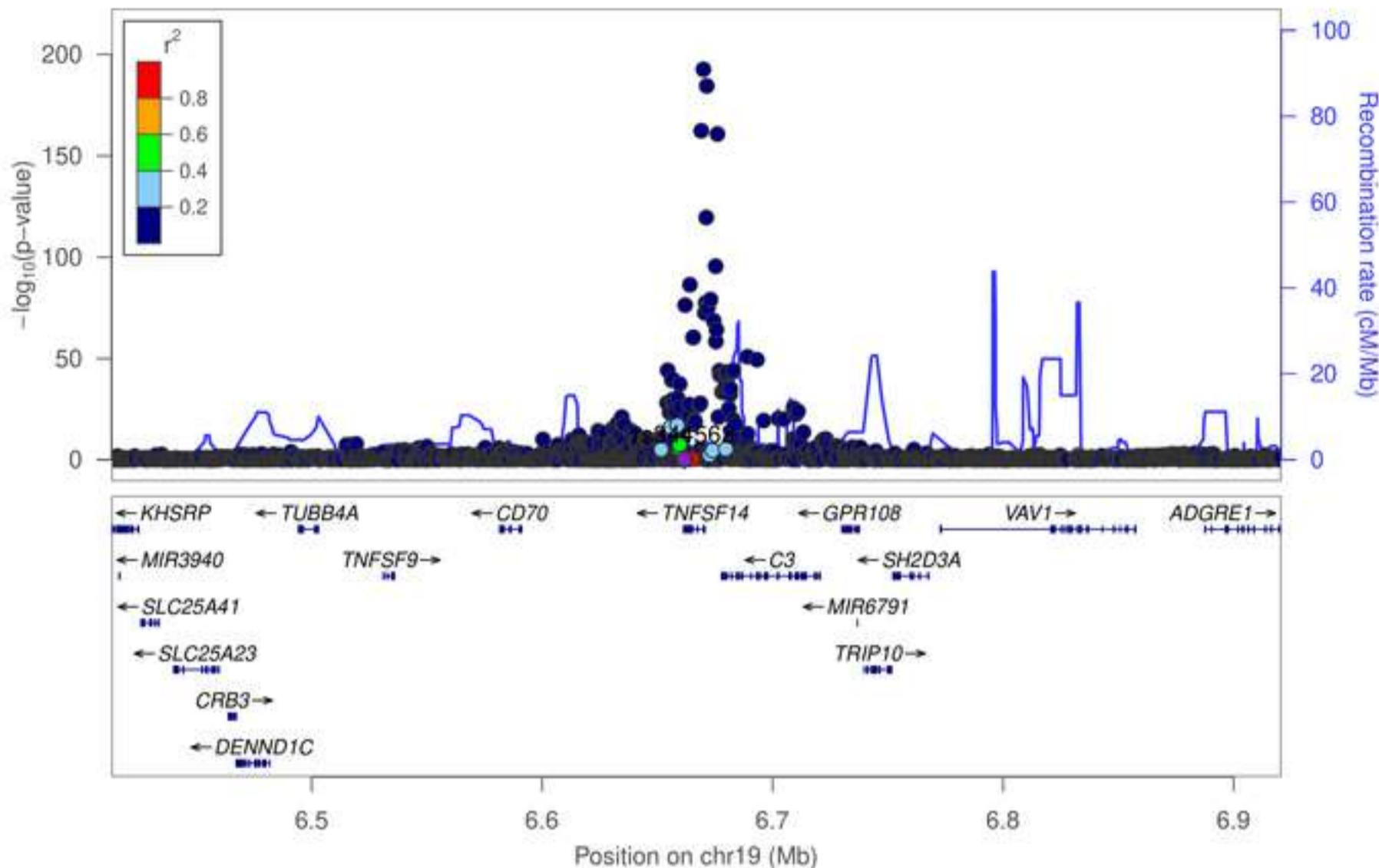
# eQTLGen: TNFRSF9 (TNFRSF9)-rs1776354



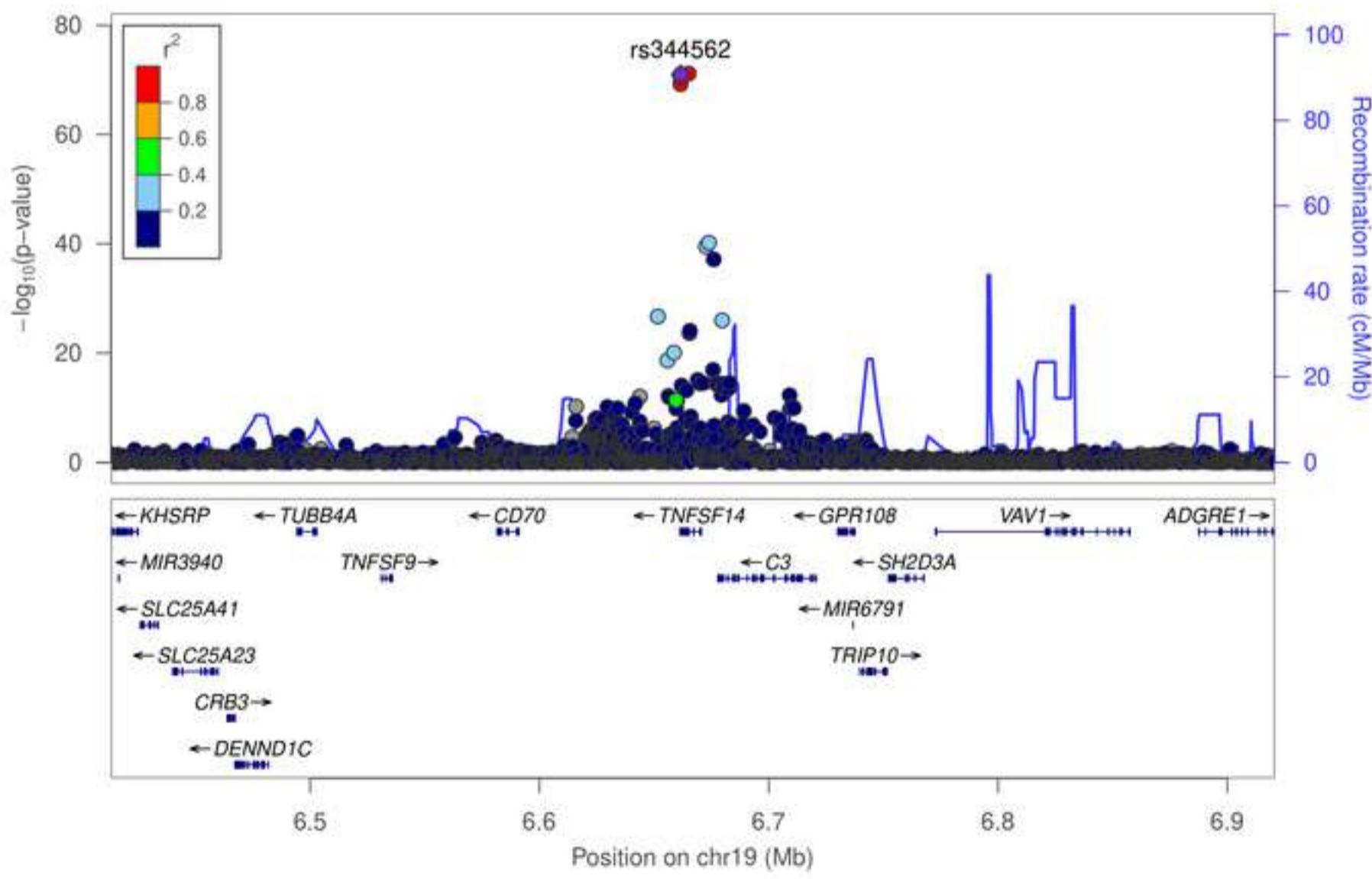
# SCALLOP: TNFRSF9 (TNFRSF9)-rs1776354



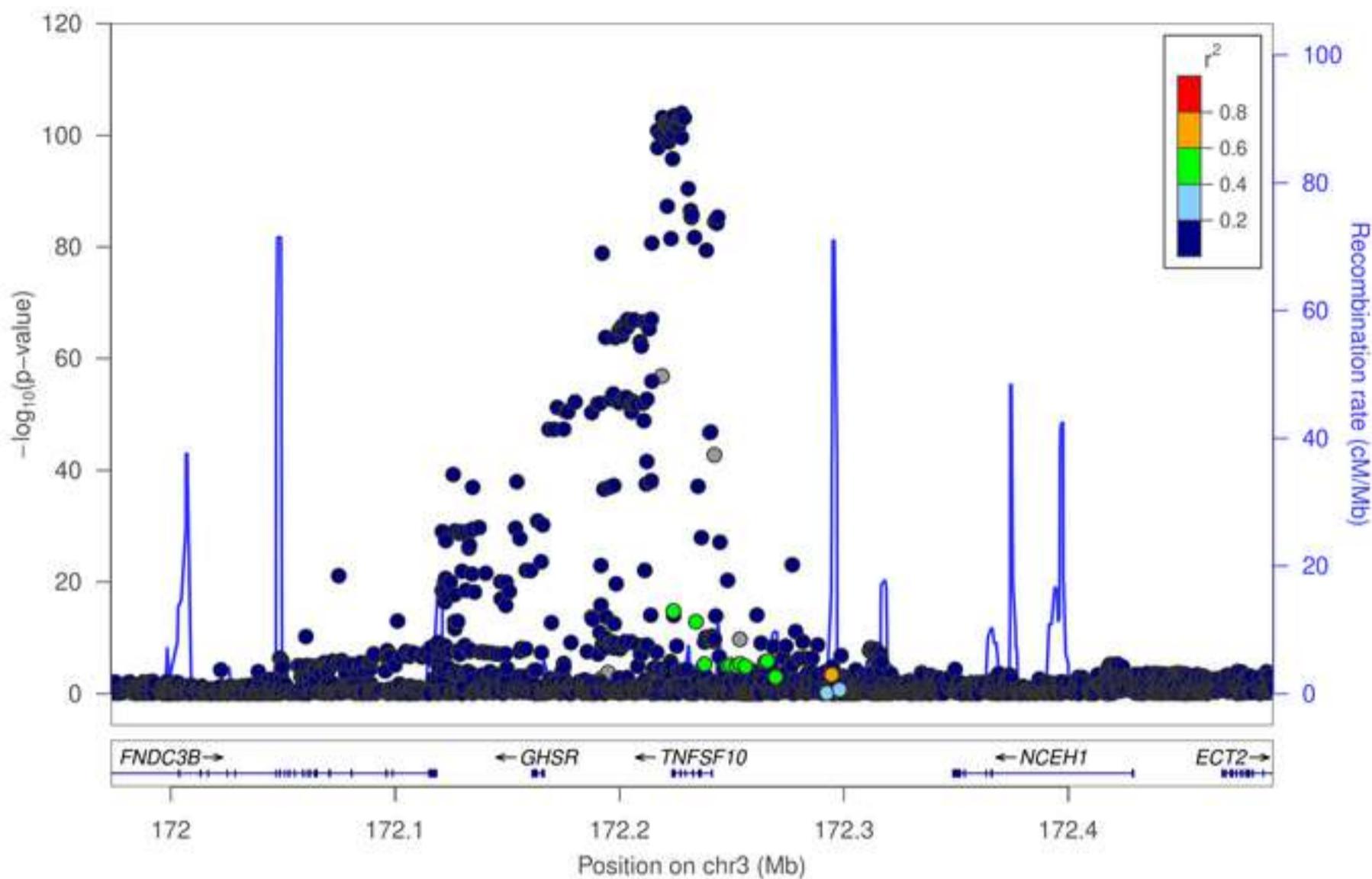
# eQTLGen: TNFSF14 (TNFSF14)-rs344562



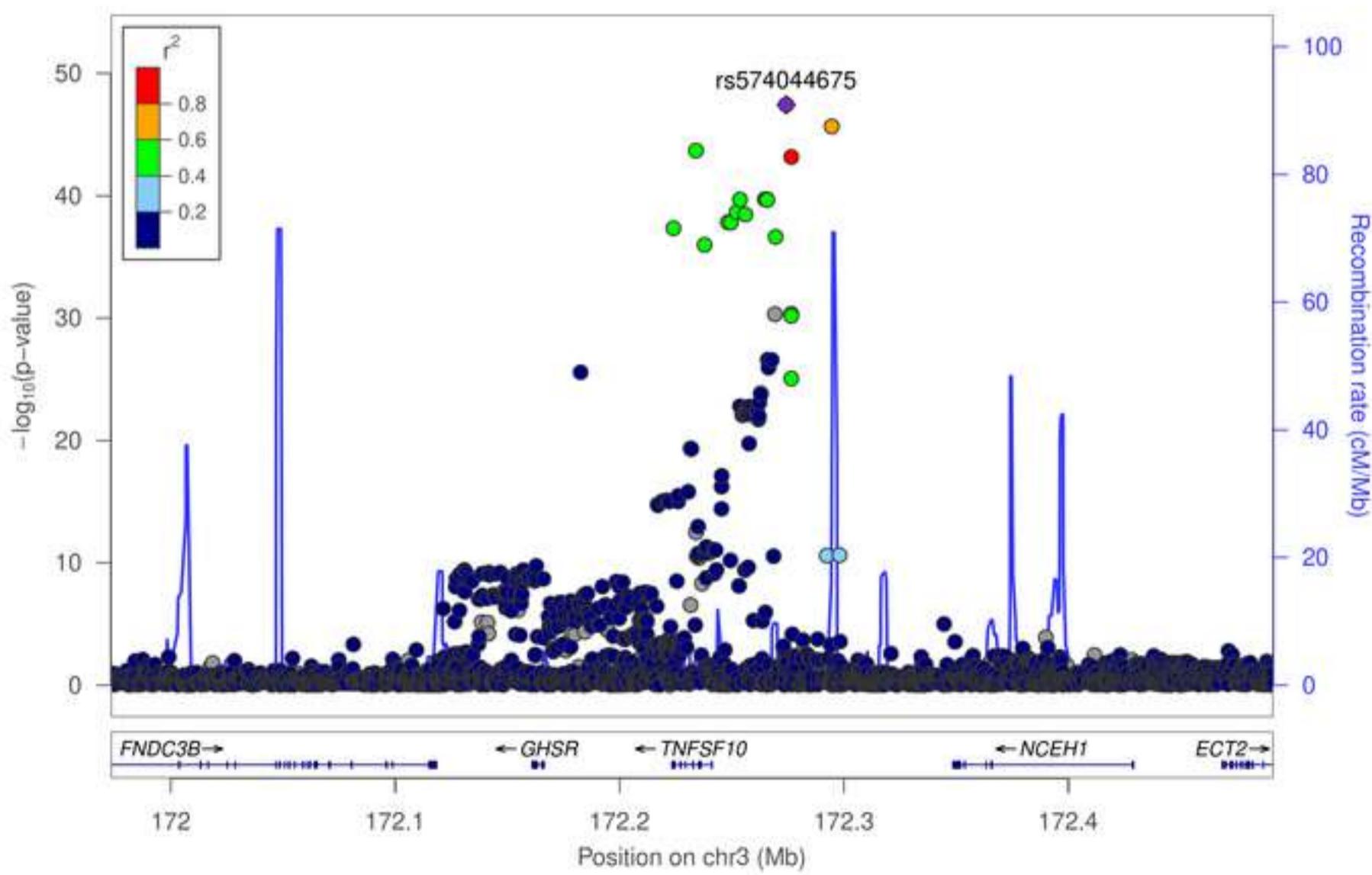
# SCALLOP: TNFSF14 (TNFSF14)-rs344562



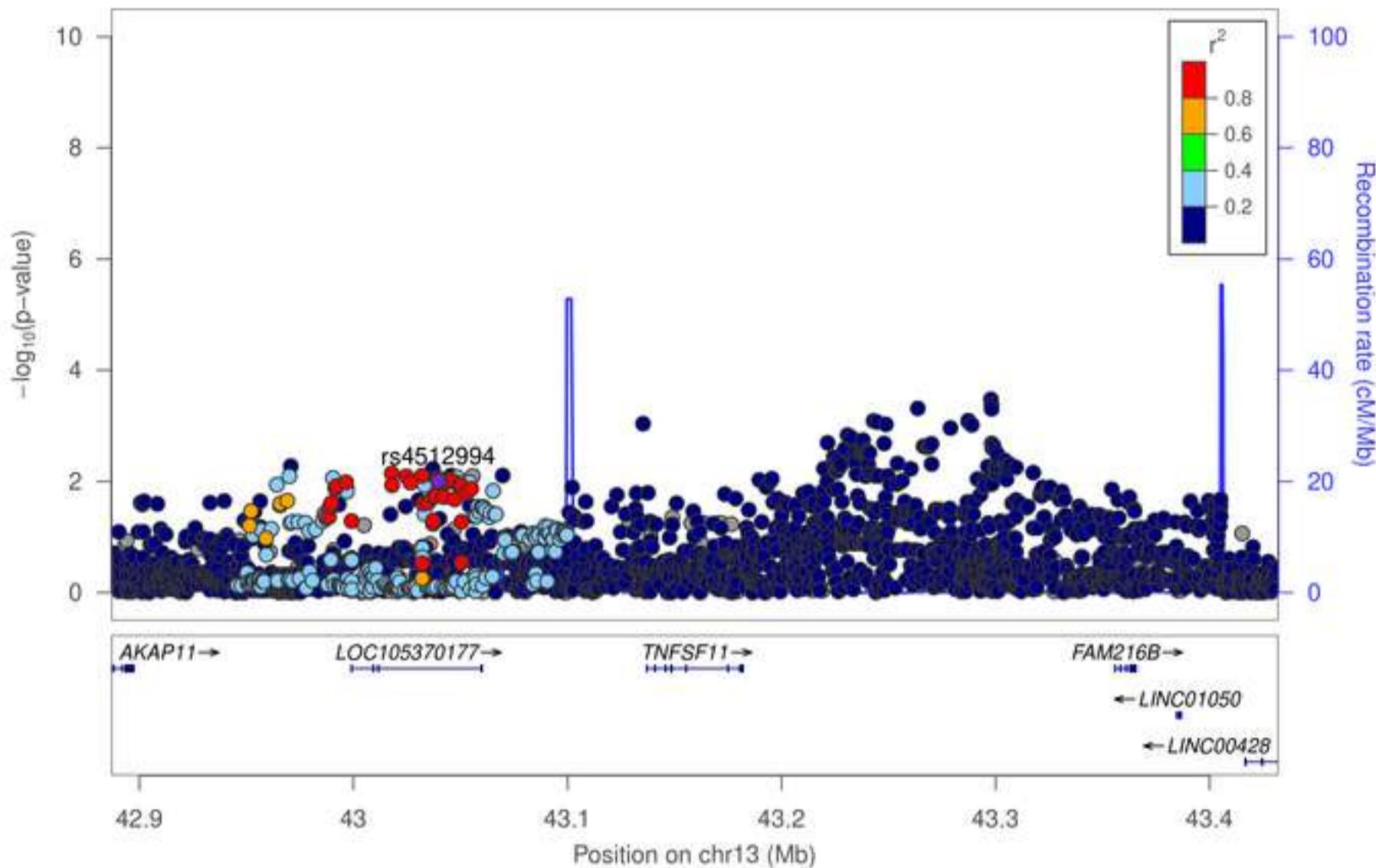
# eQTLGen: TRAIL (TNFSF10)-rs574044675



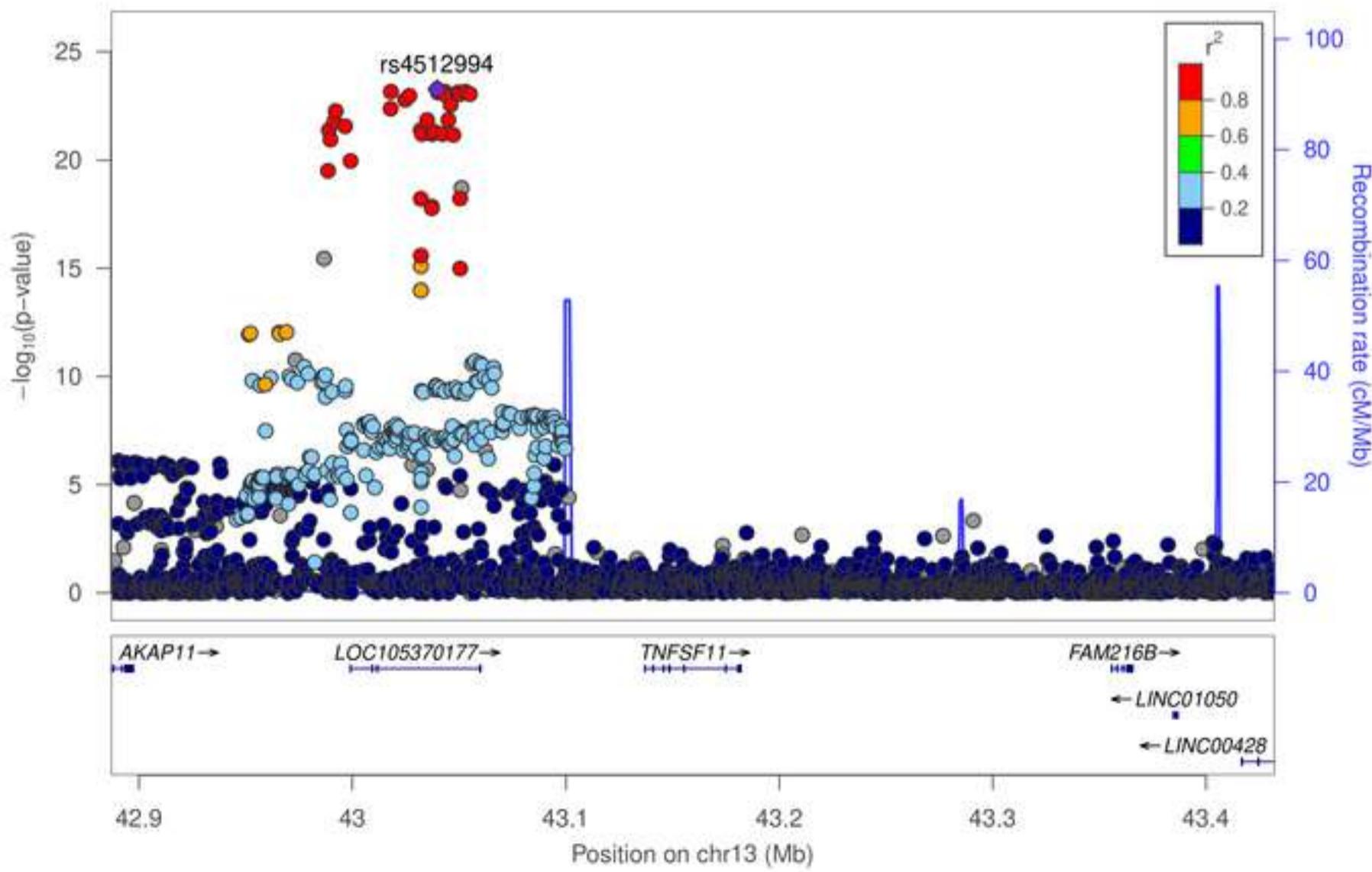
# SCALLOP: TRAIL (TNFSF10)-rs574044675



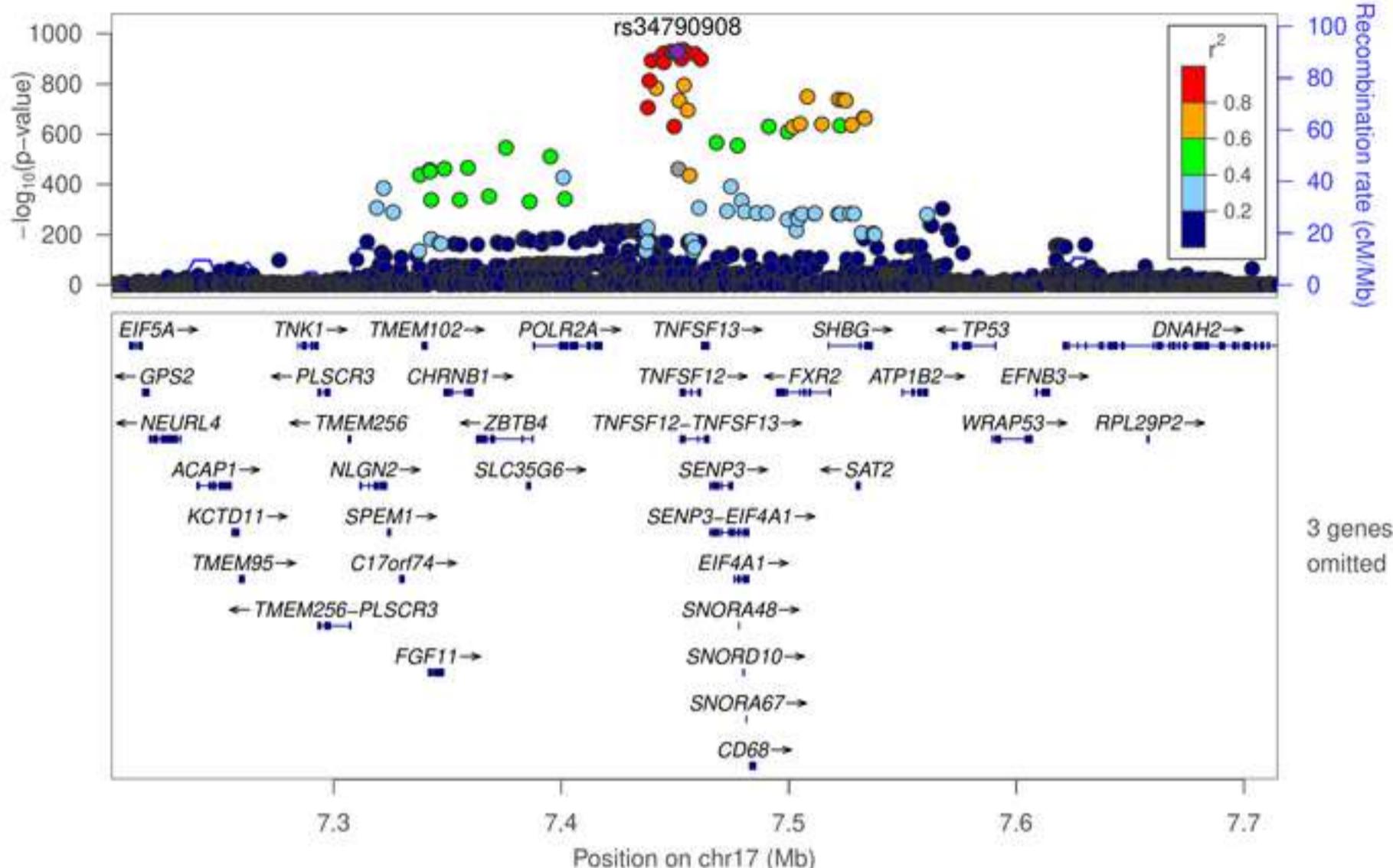
# eQTLGen: TRANCE (TNFSF11)-rs4512994



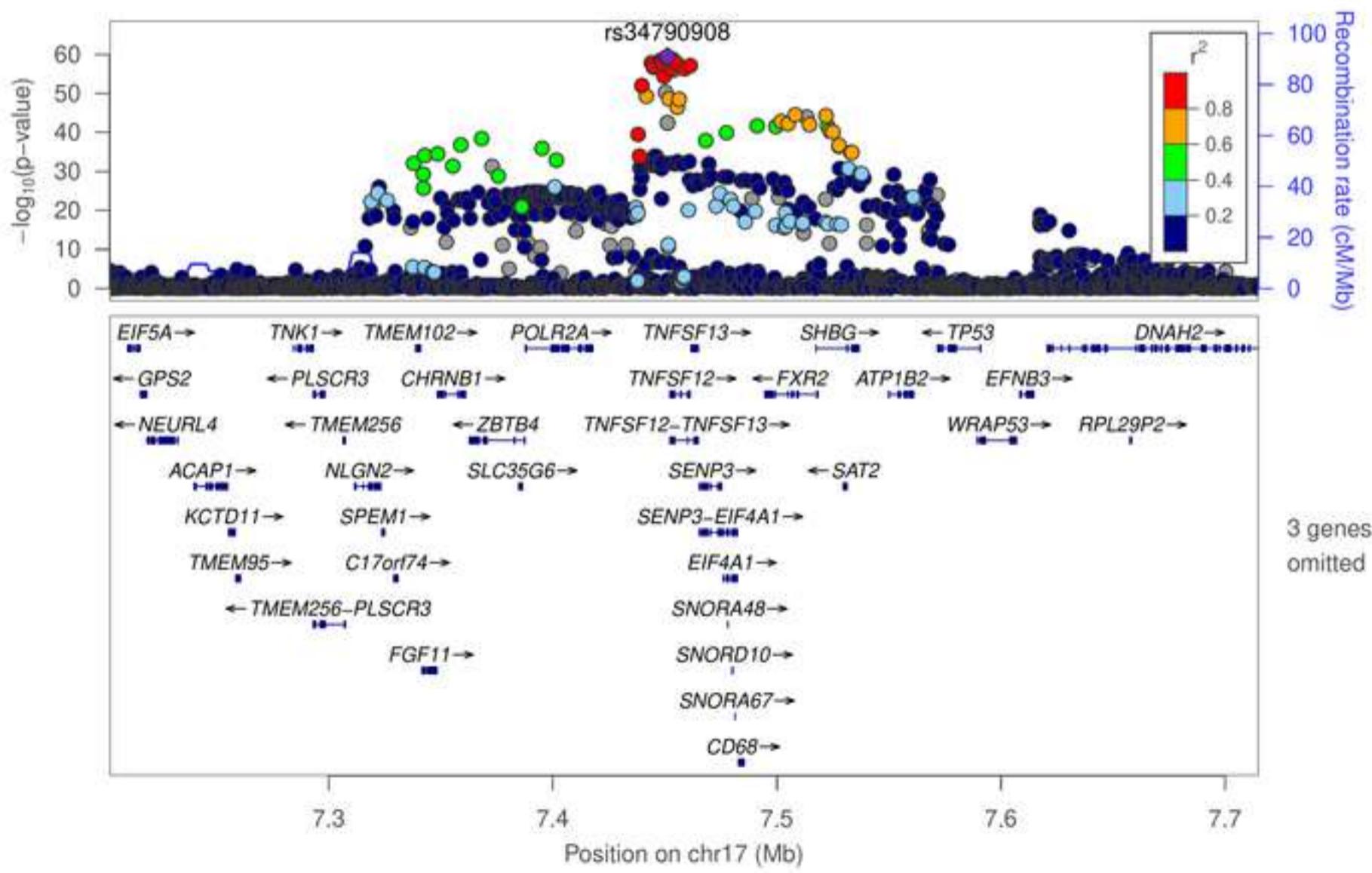
# SCALLOP: TRANCE (TNFSF11)-rs4512994



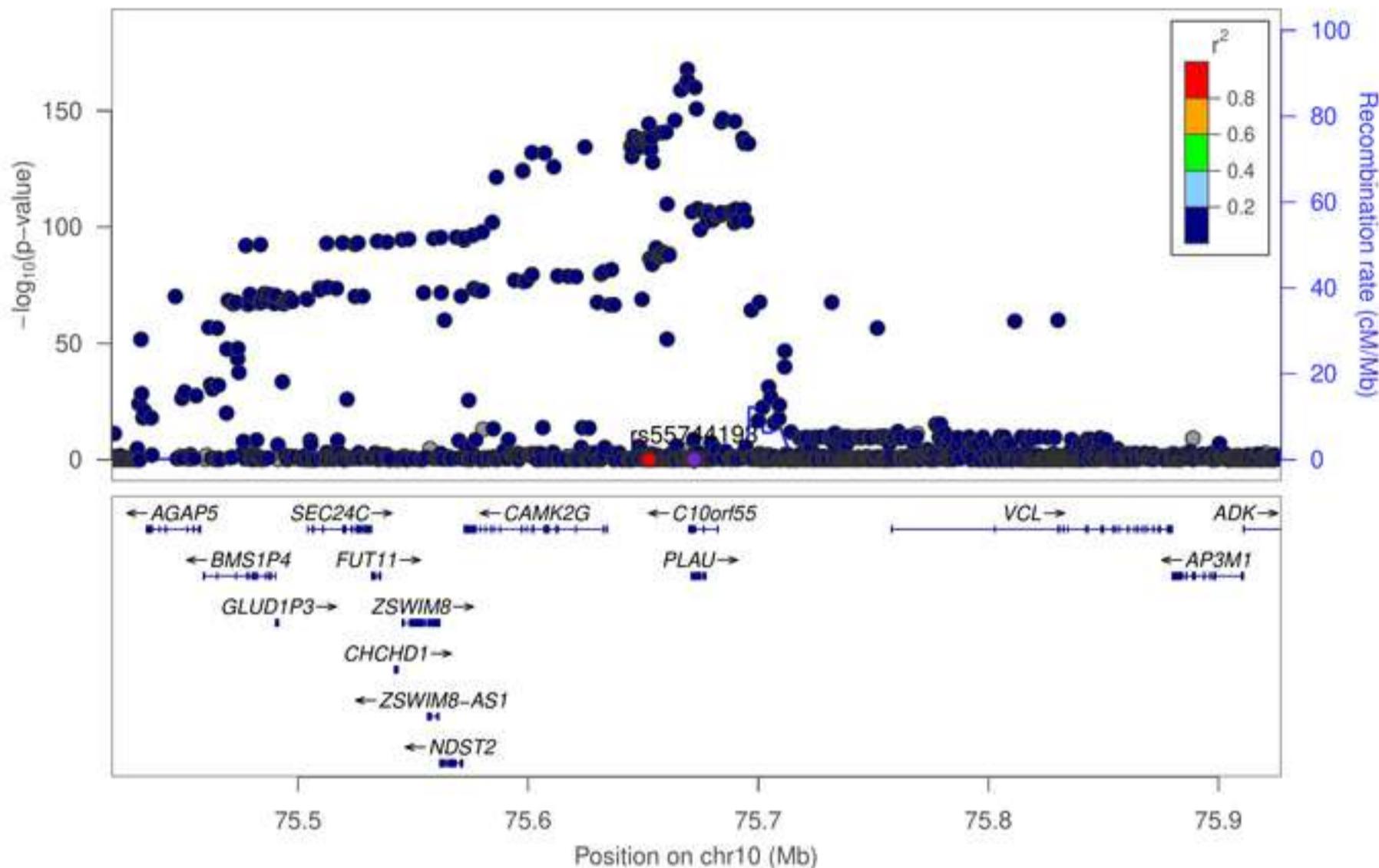
# eQTLGen: TWEAK (TNFSF12)-rs34790908



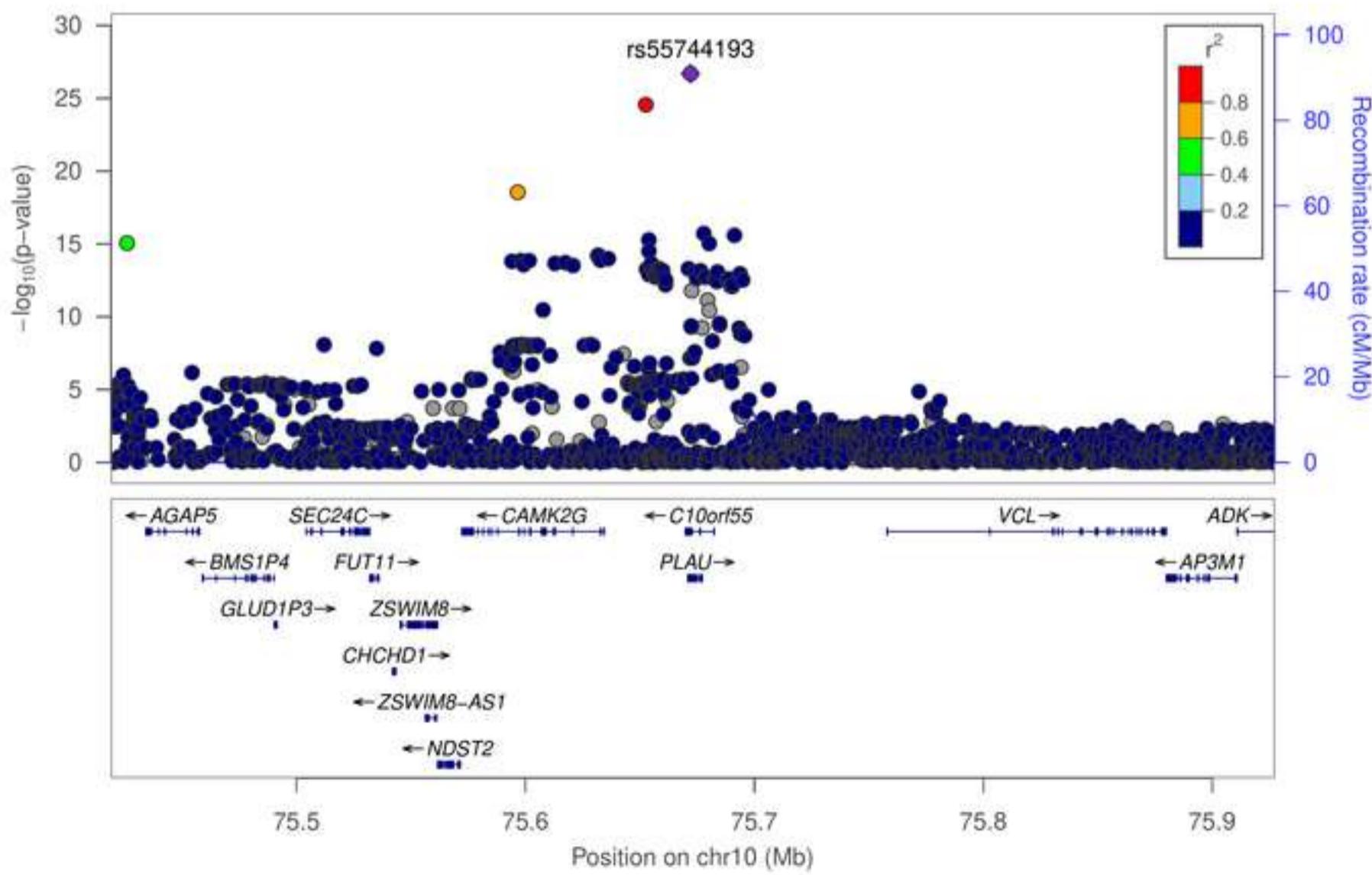
# SCALLOP: TWEAK (TNFSF12)-rs34790908



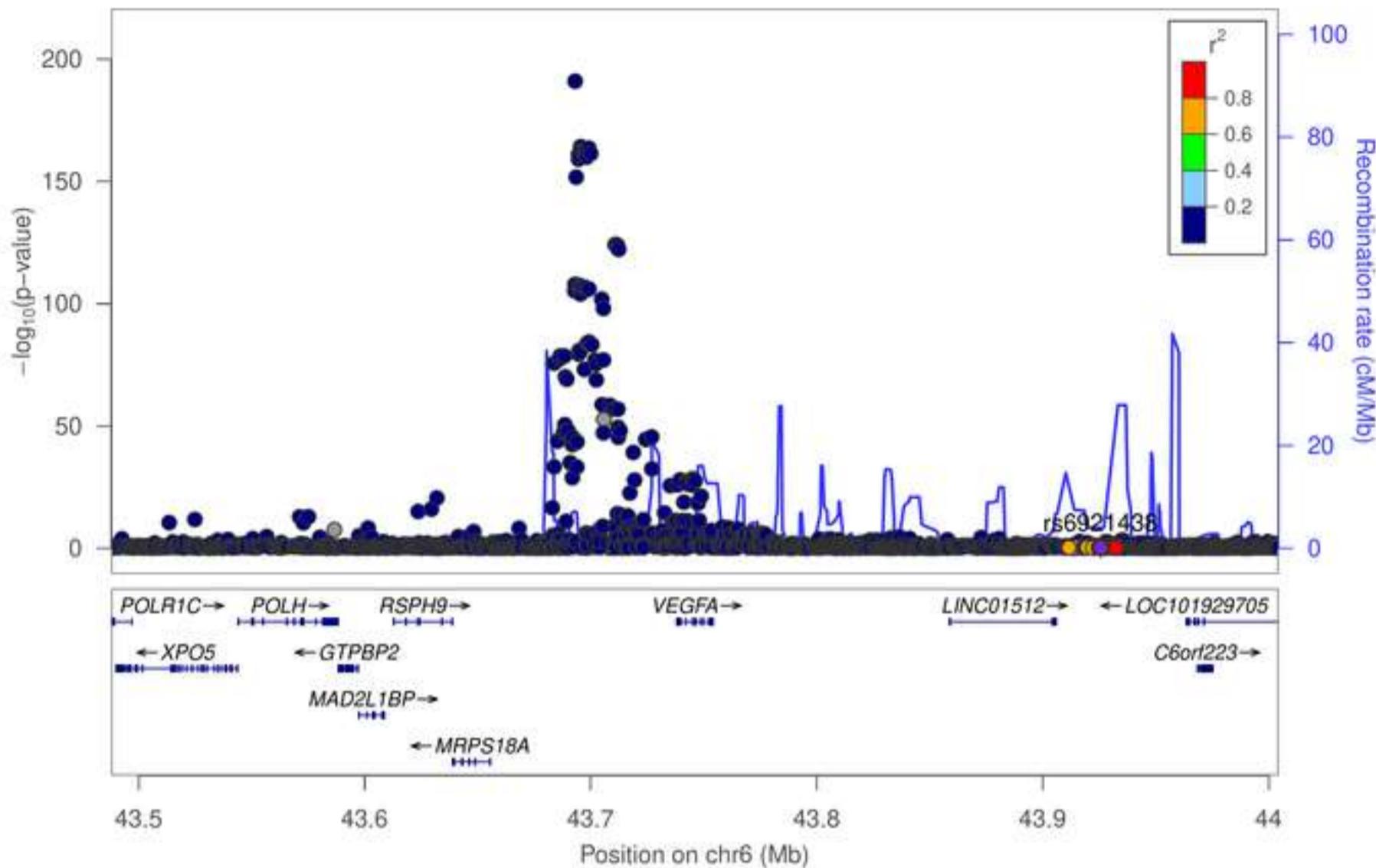
# eQTLGen: uPA (PLAU)-rs55744193



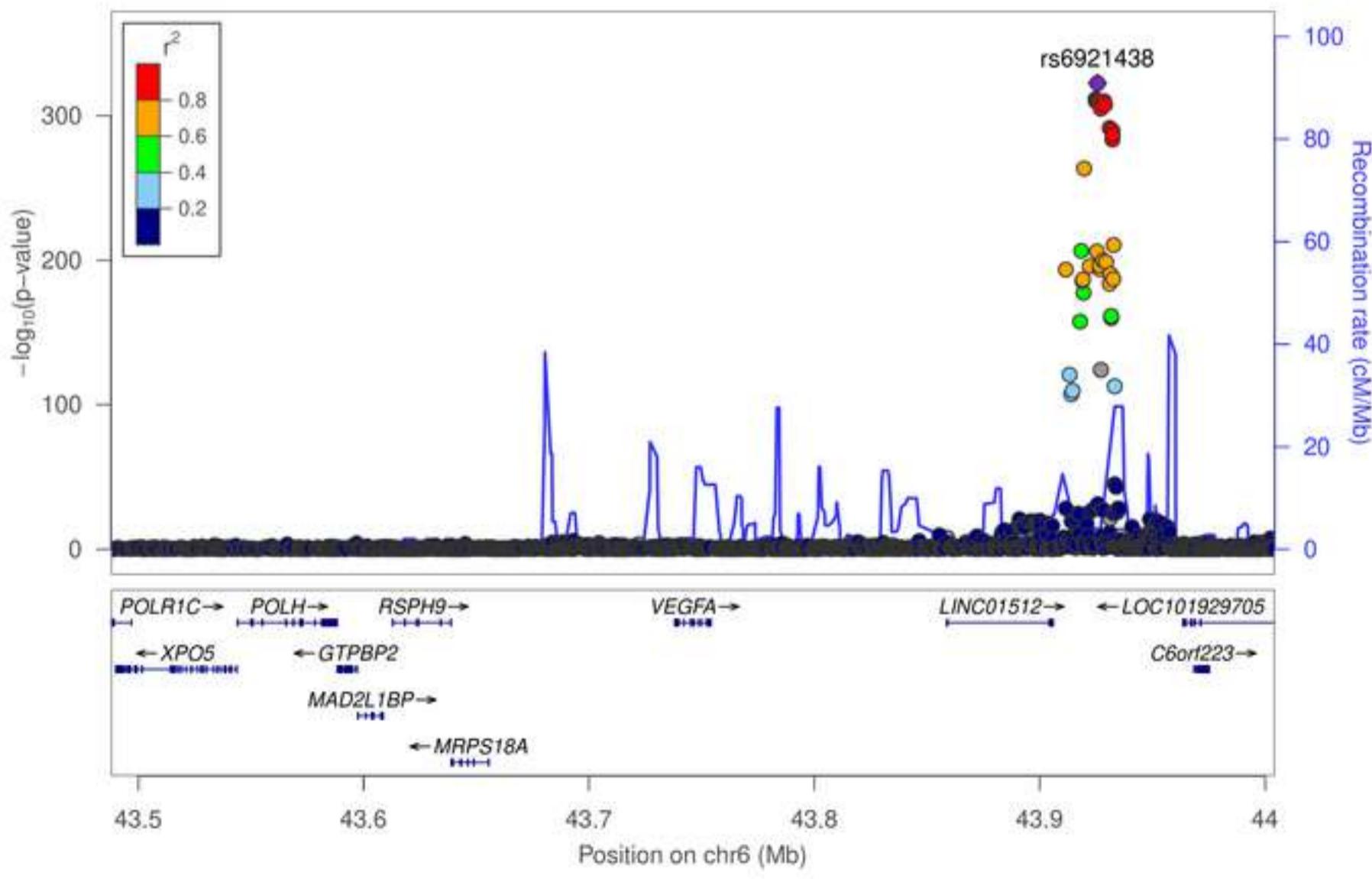
# SCALLOP: uPA (PLAU)-rs55744193



# eQTLGen: VEGF\_A (VEGFA)-rs6921438

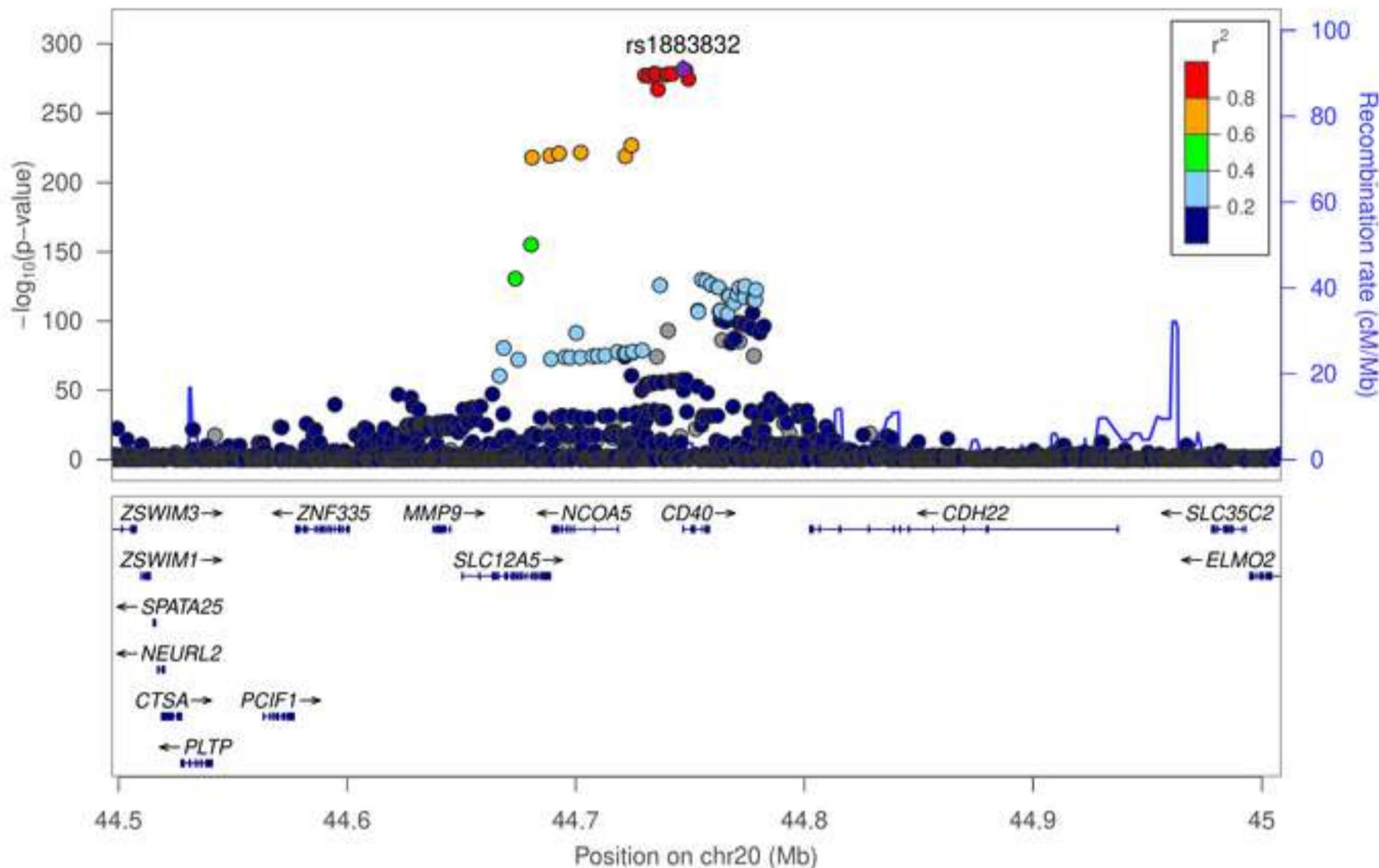


# SCALLOP: VEGF\_A (VEGFA)-rs6921438

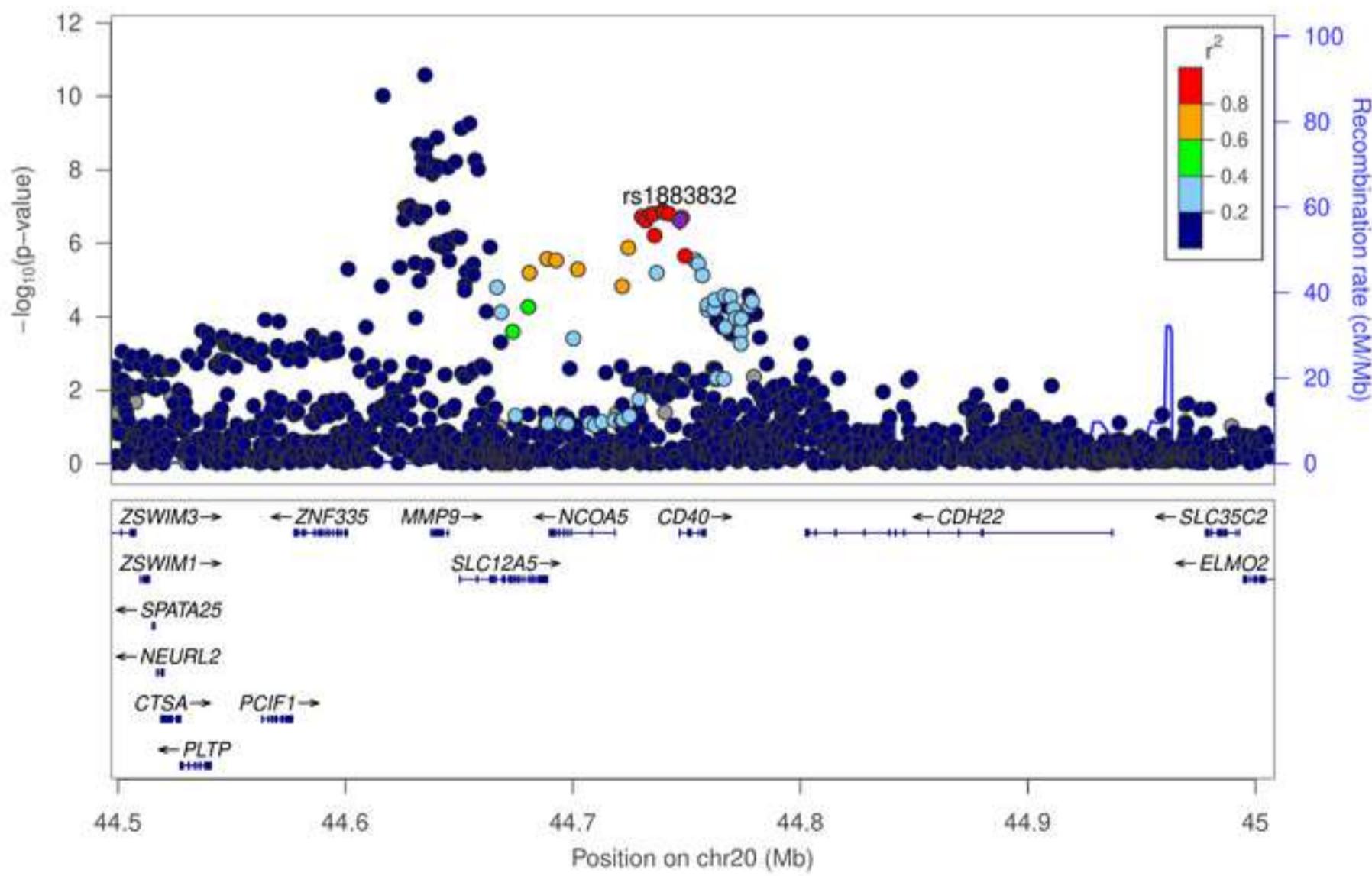


**Supplementary Figure 4.** Regional association plots comparing plasma *cis*-pQTLs and disease associations. ‘LocusZoom’ regional association plots comparing the plasma *cis*-pQTL signals (upper panel) with the relevant disease signals (lower panel) for the 12 protein-disease pairs with significant GSMD results following our initial filters prior to colocalisation testing (see Methods). The sentinel variant for the pQTL is coloured in purple. LD ( $r^2$ ) to the sentinel pQTL is indicated by the colour key. For pQTLs, two-sided  $P$ -values are from meta-analysis of linear regression estimates. For diseases,  $P$ -values are from logistic regression.

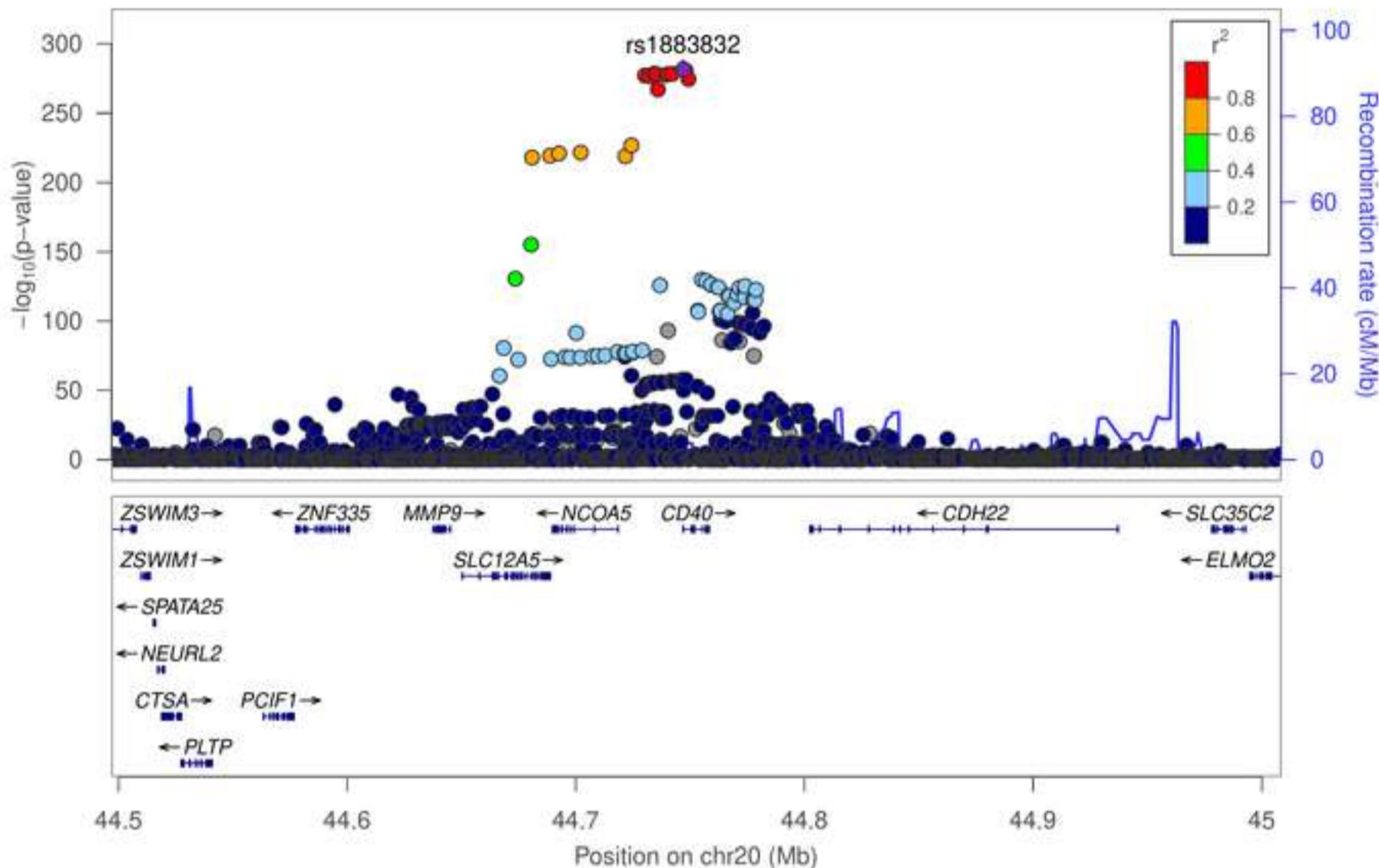
# SCALLOP: CD40–rs1883832



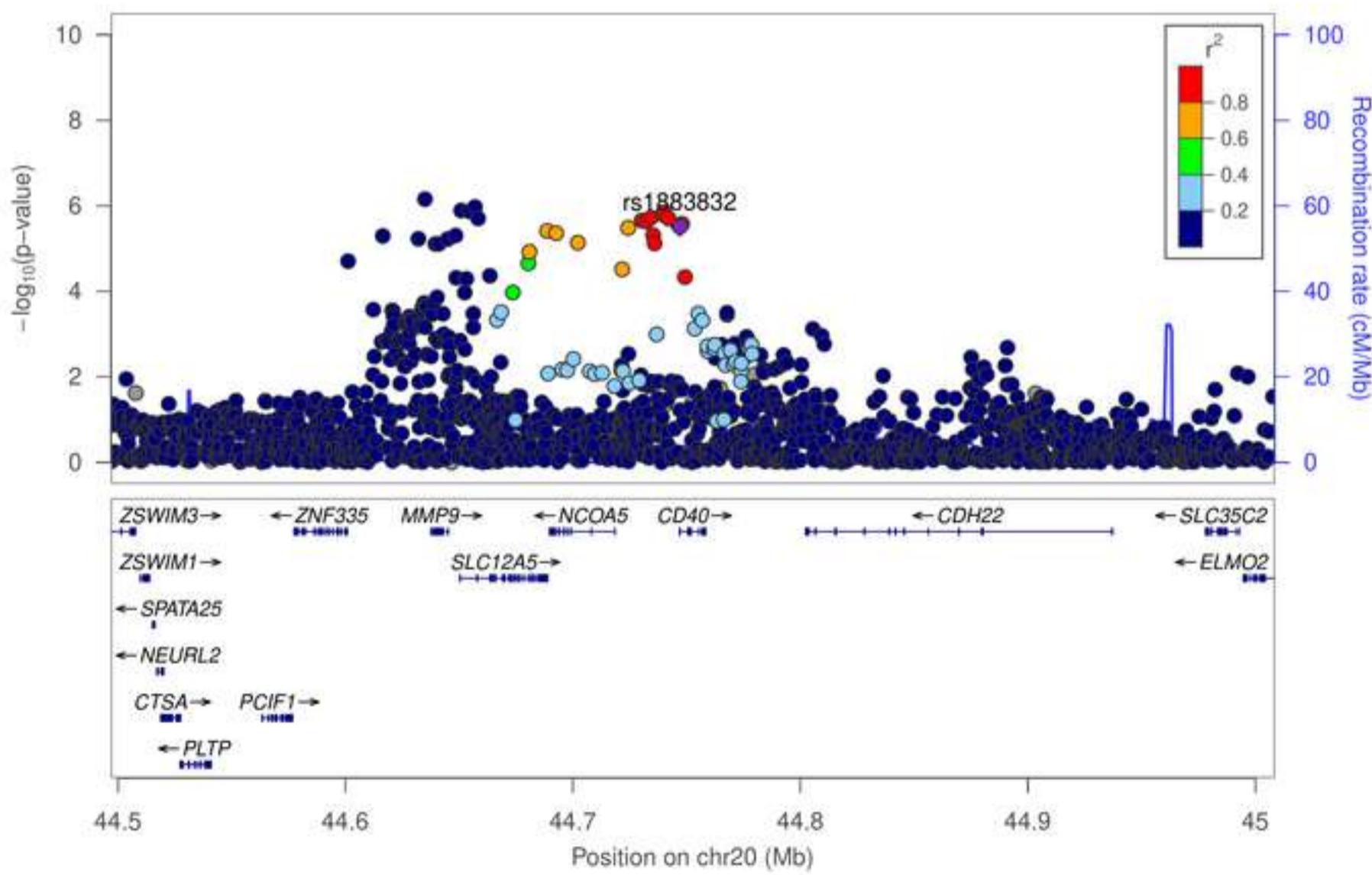
## 'Crohns disease'(ebi-a-GCST004132)–rs1883832



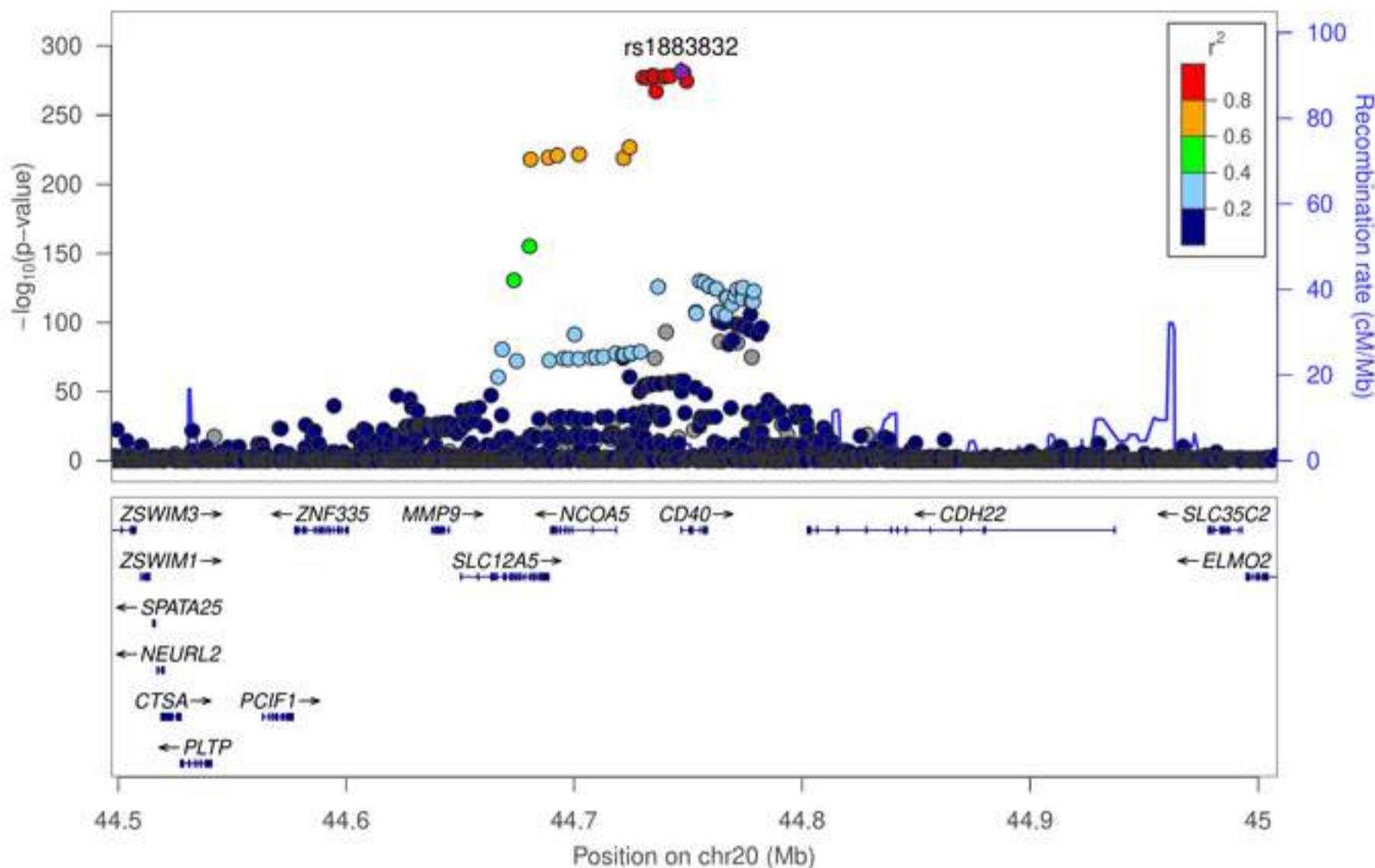
# SCALLOP: CD40–rs1883832



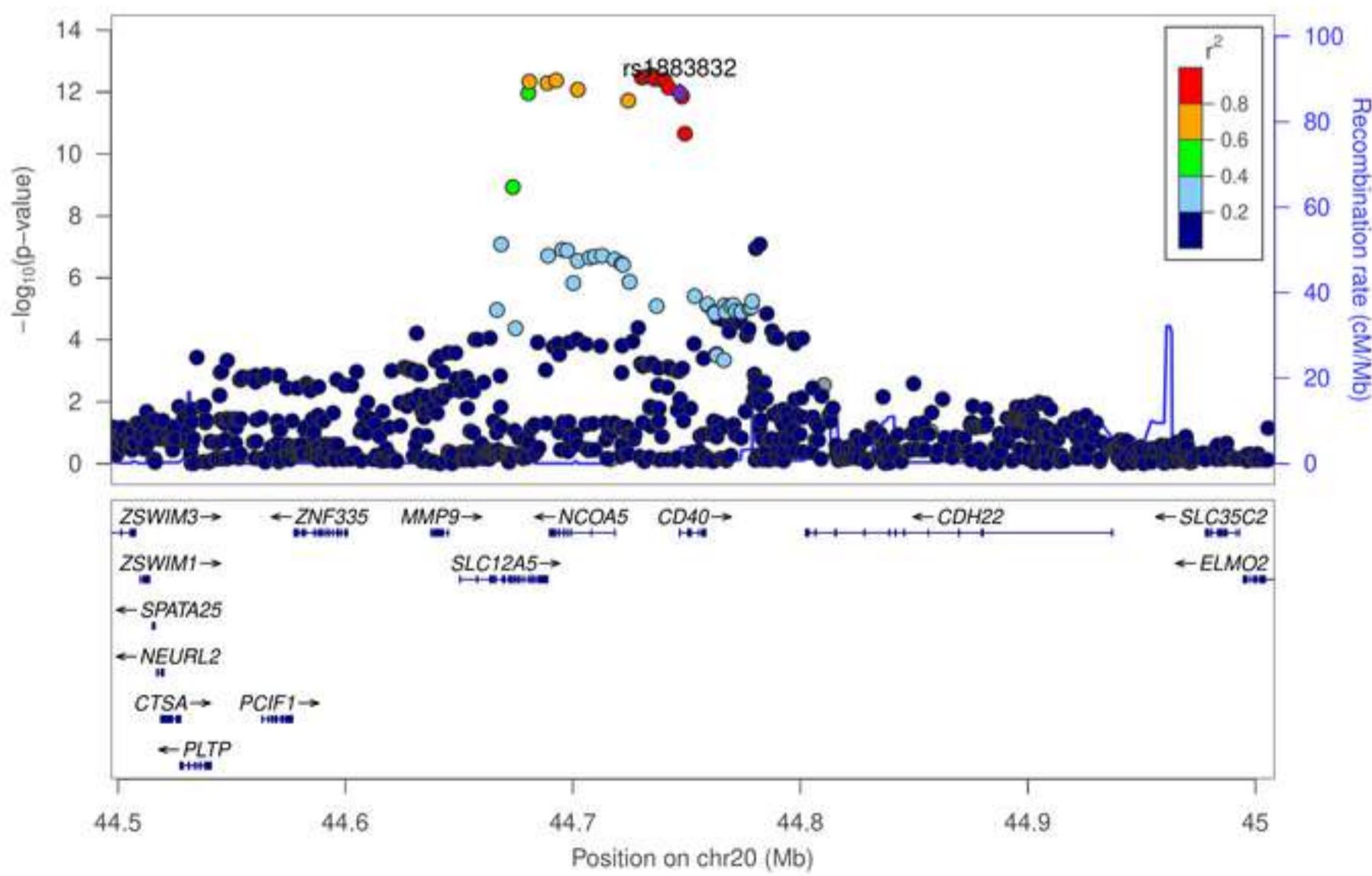
# 'Inflammatory bowel disease'(ebi-a-GCST004131)–rs1883832



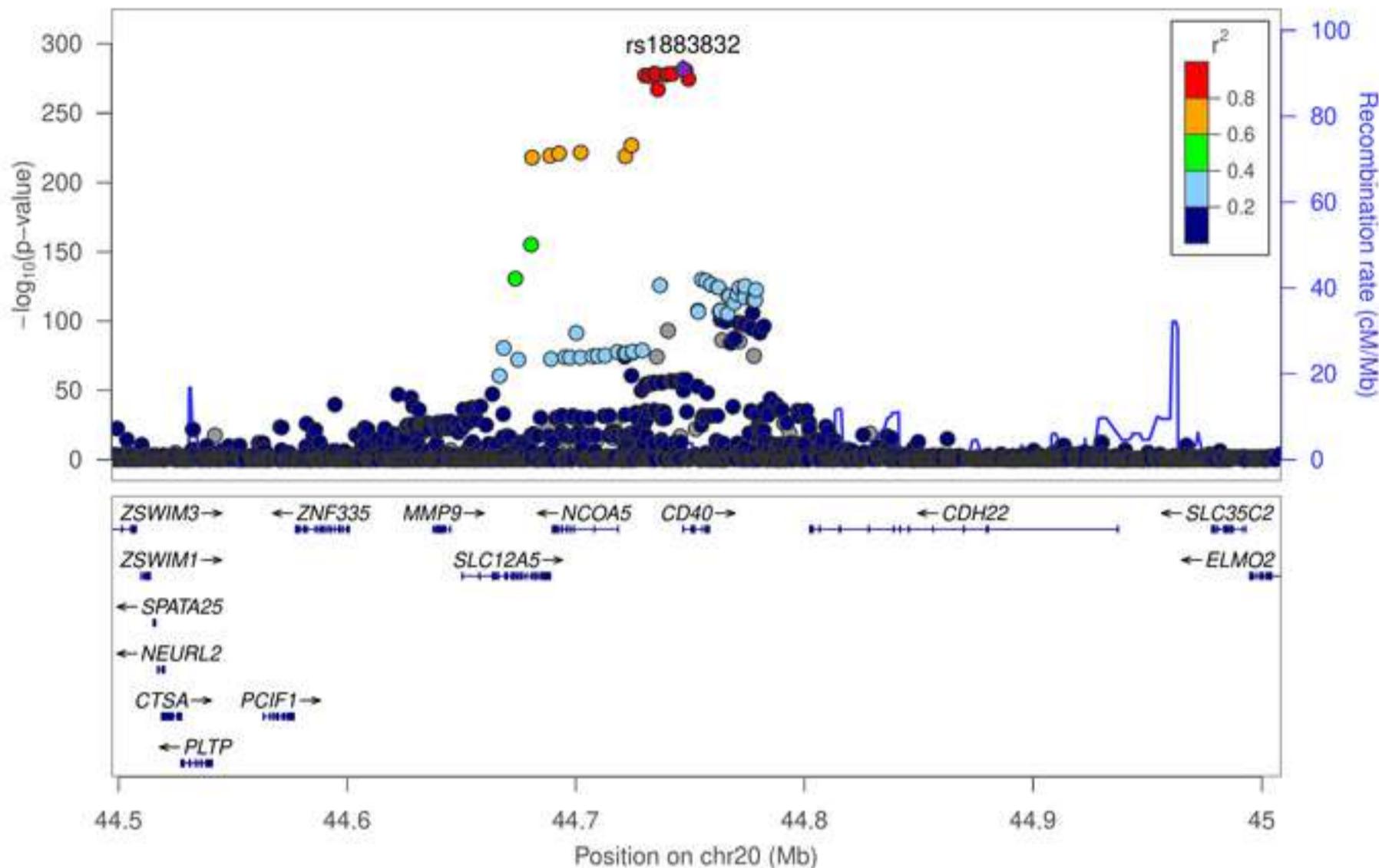
# SCALLOP: CD40–rs1883832



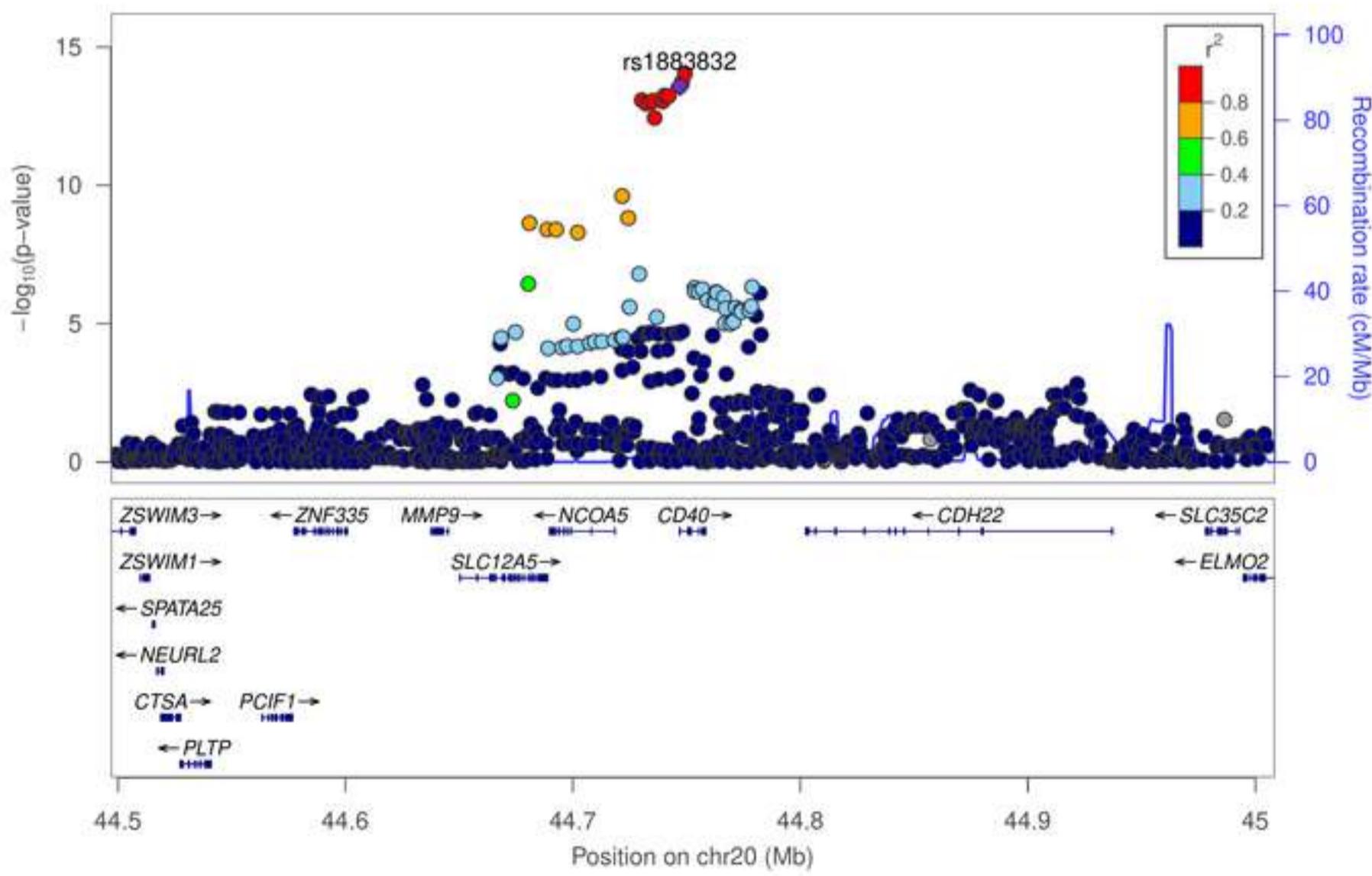
## 'Multiple sclerosis'(ieu–b–18)–rs1883832



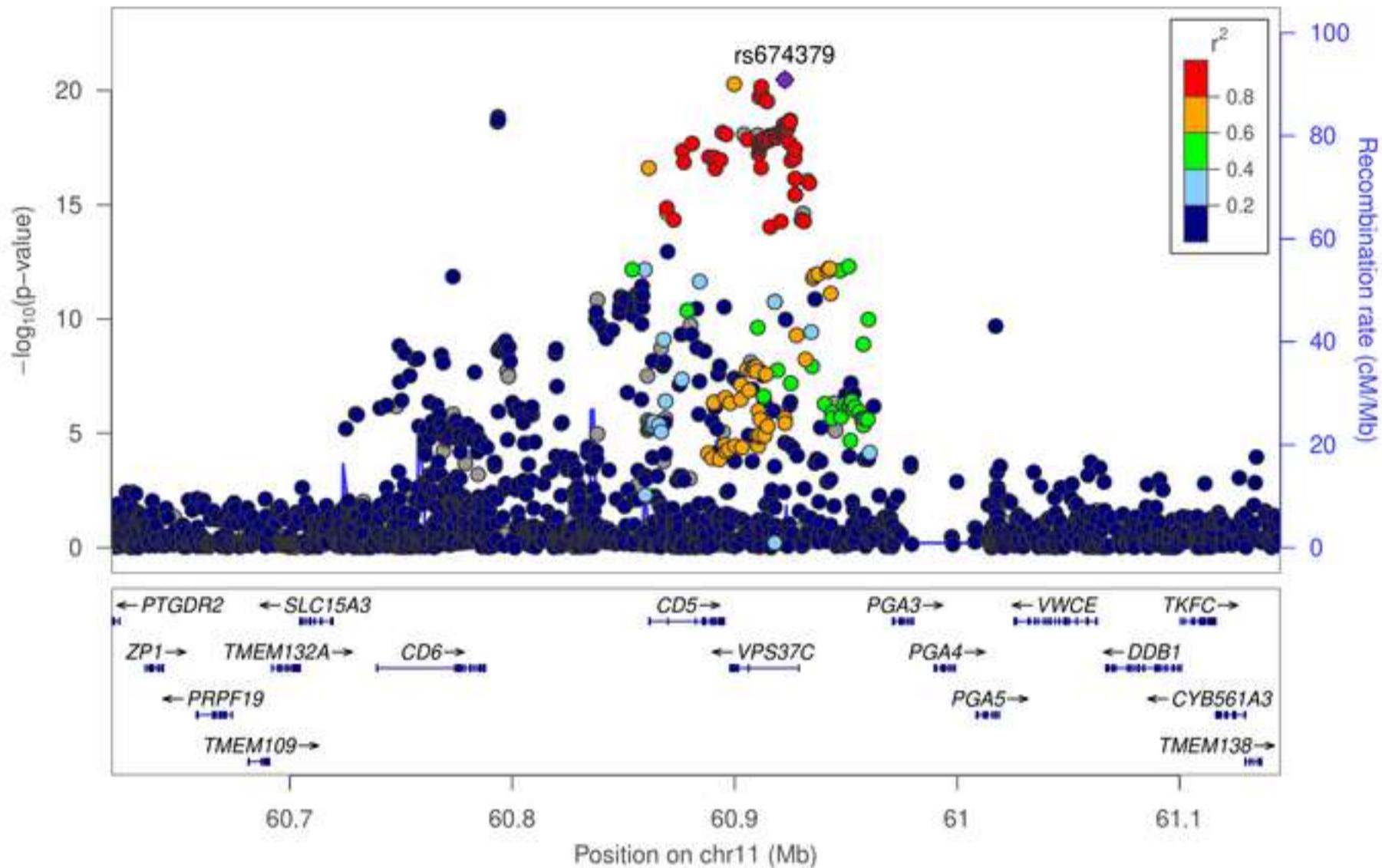
# SCALLOP: CD40–rs1883832



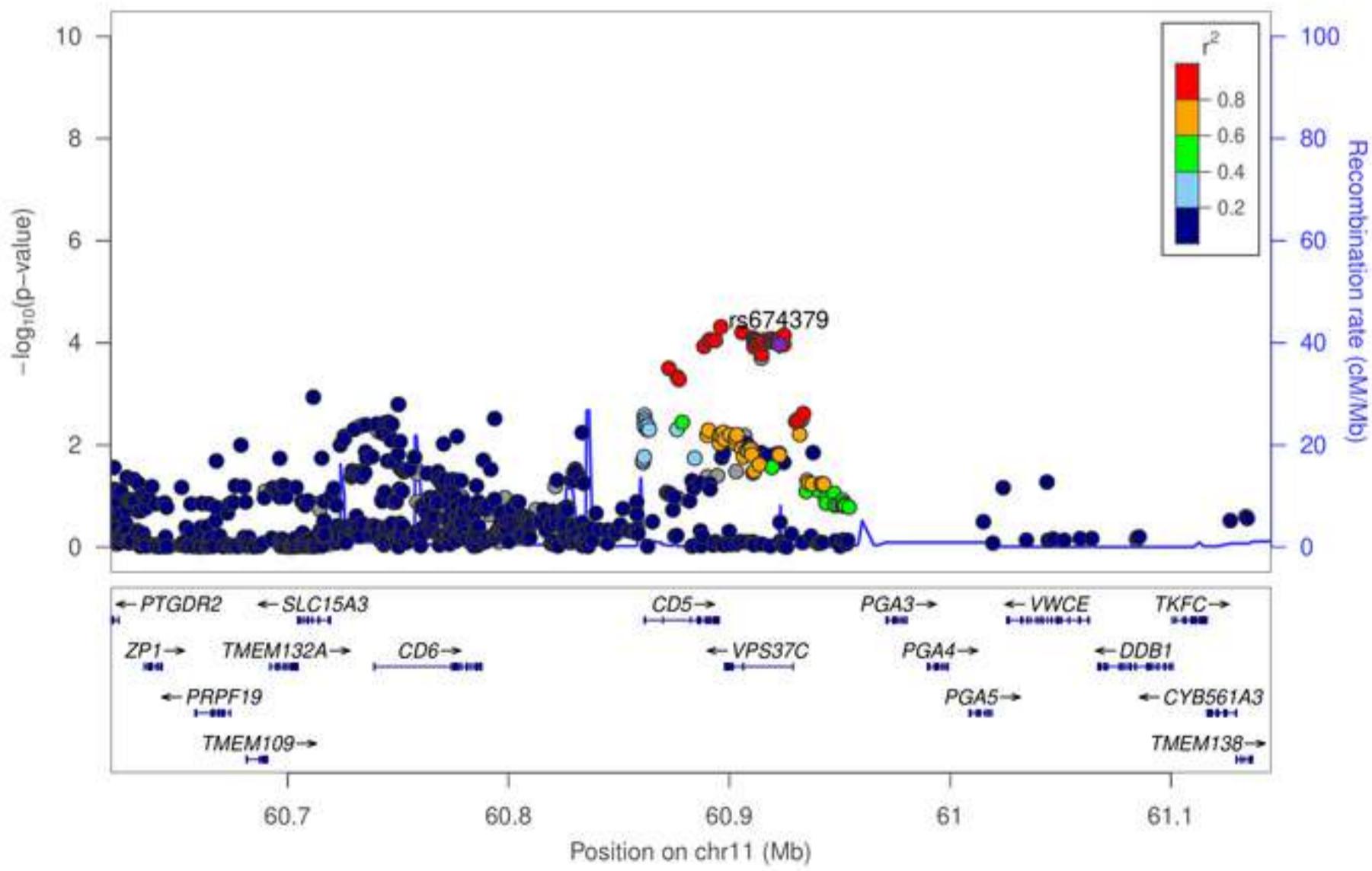
## 'Rheumatoid arthritis'(ieu-a-833)–rs1883832



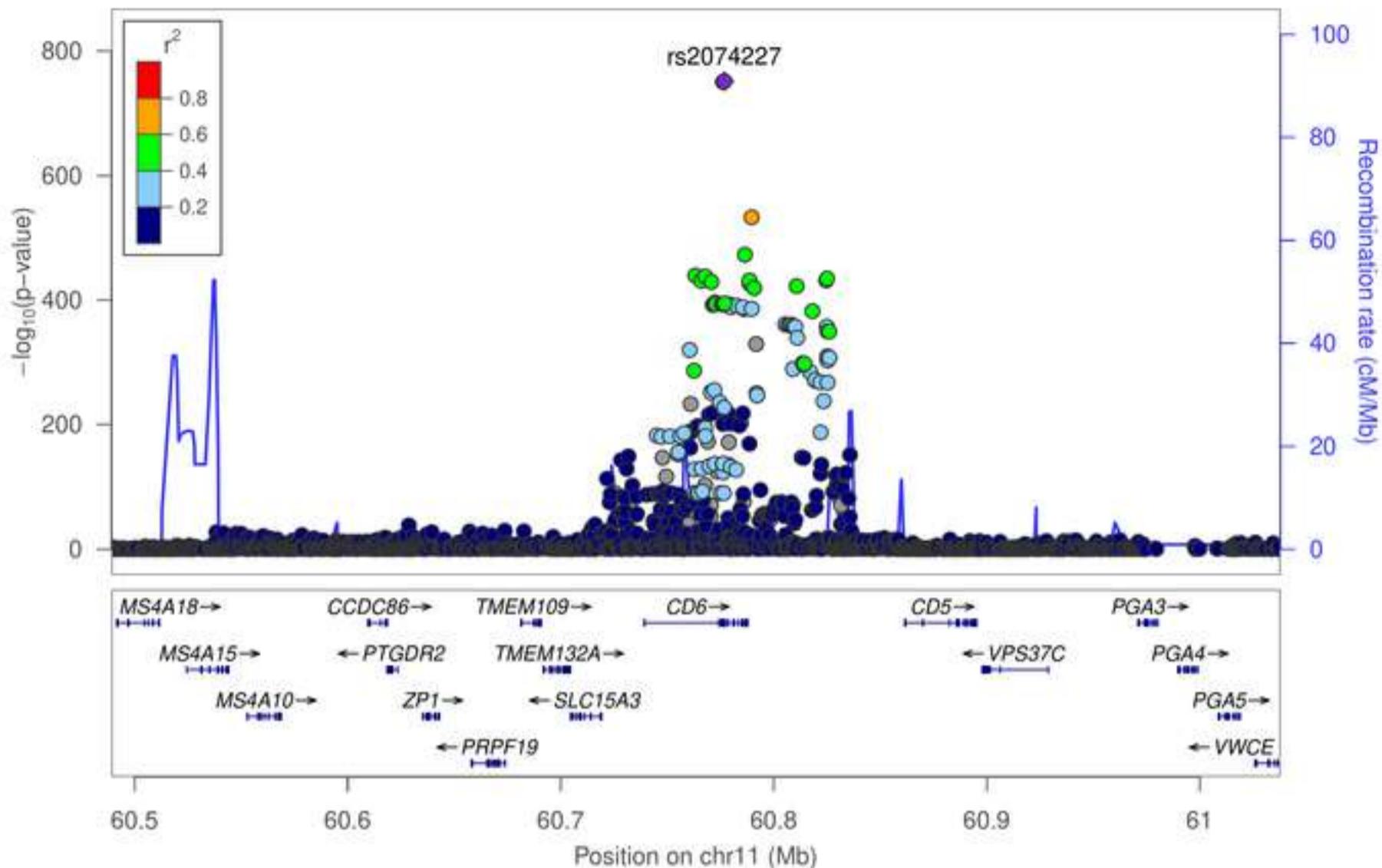
# SCALLOP: CD5–rs674379



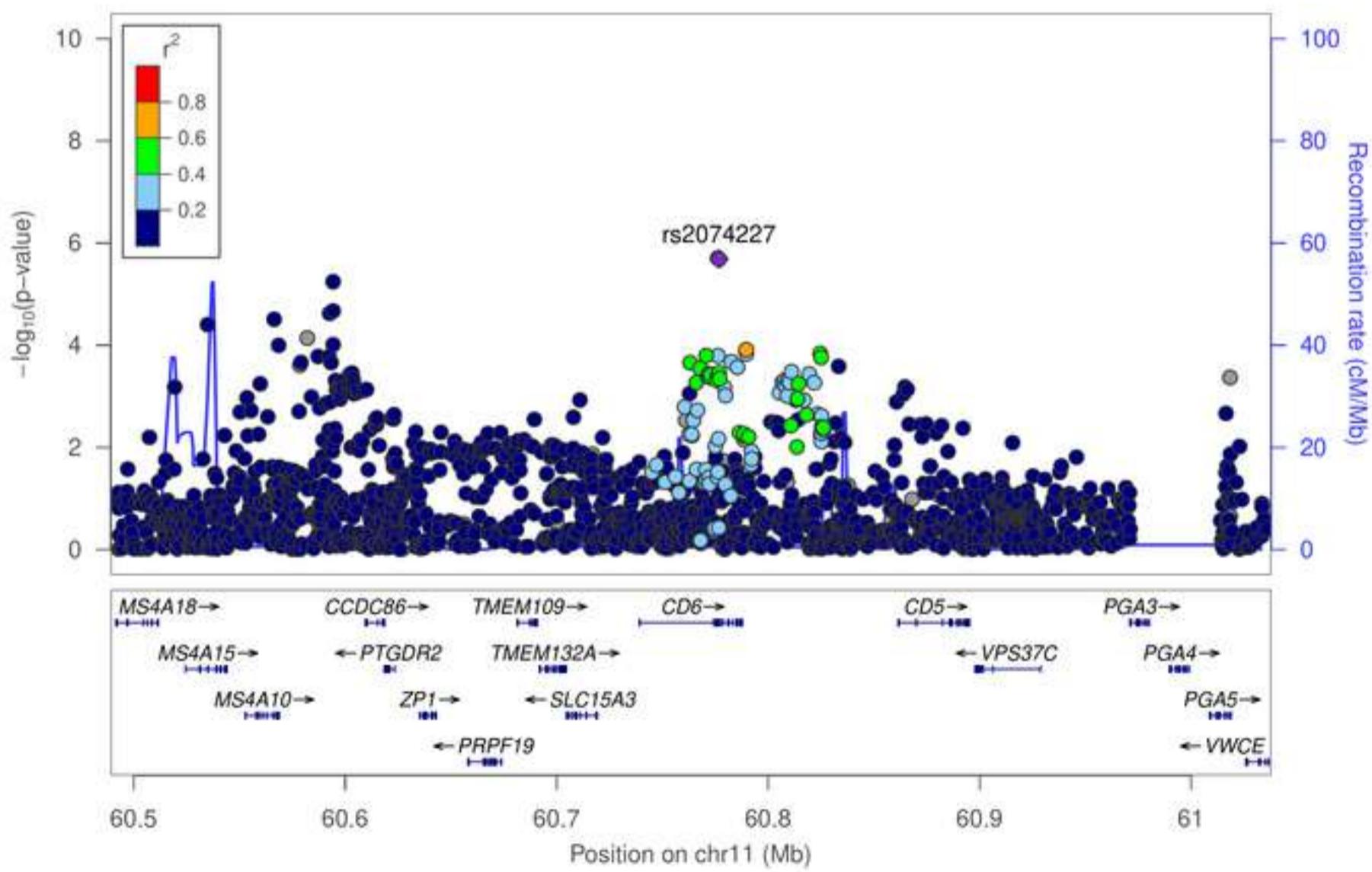
## 'Primary sclerosing cholangitis'(ieu-a-1112)–rs674379



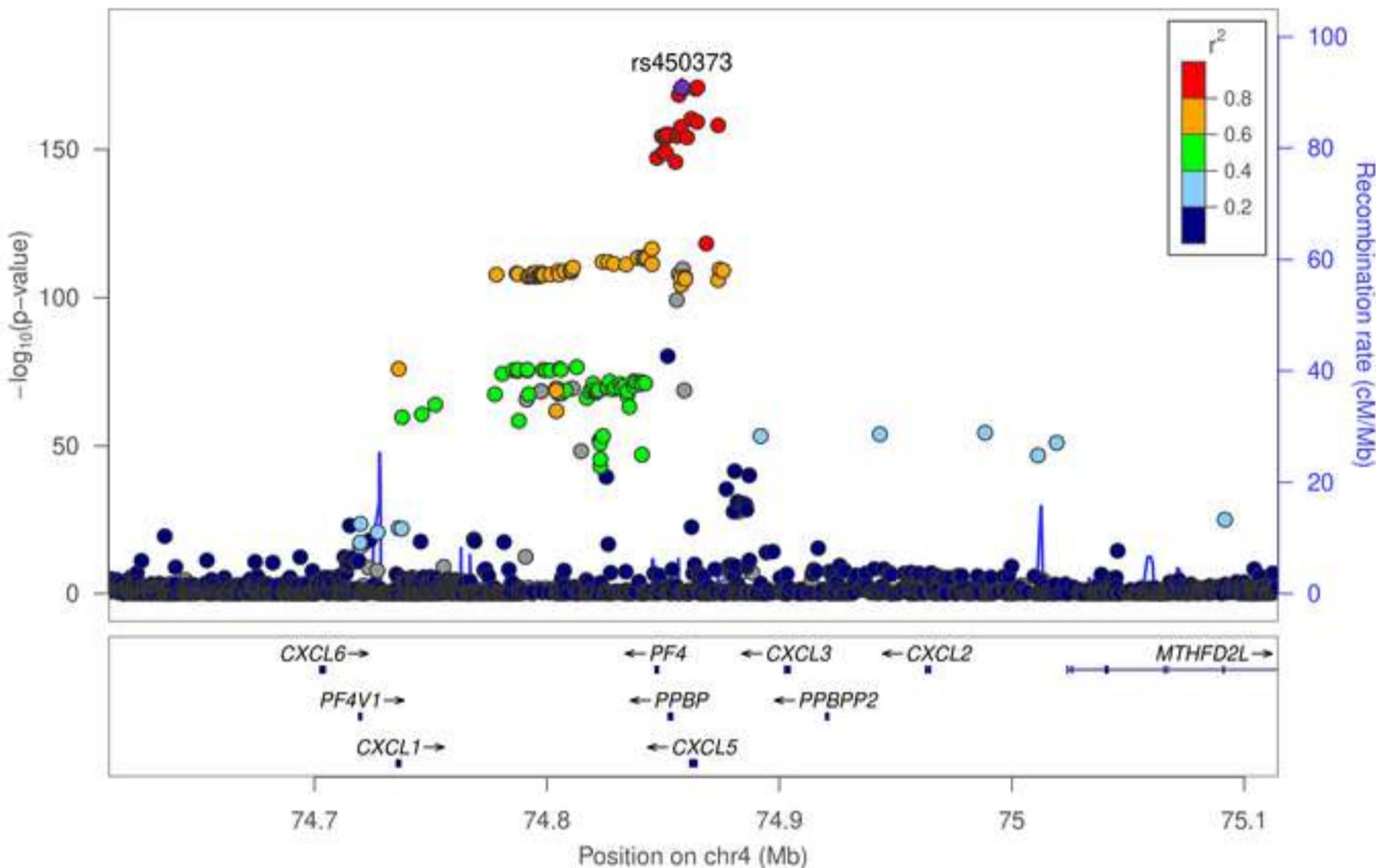
# SCALLOP: CD6–rs2074227



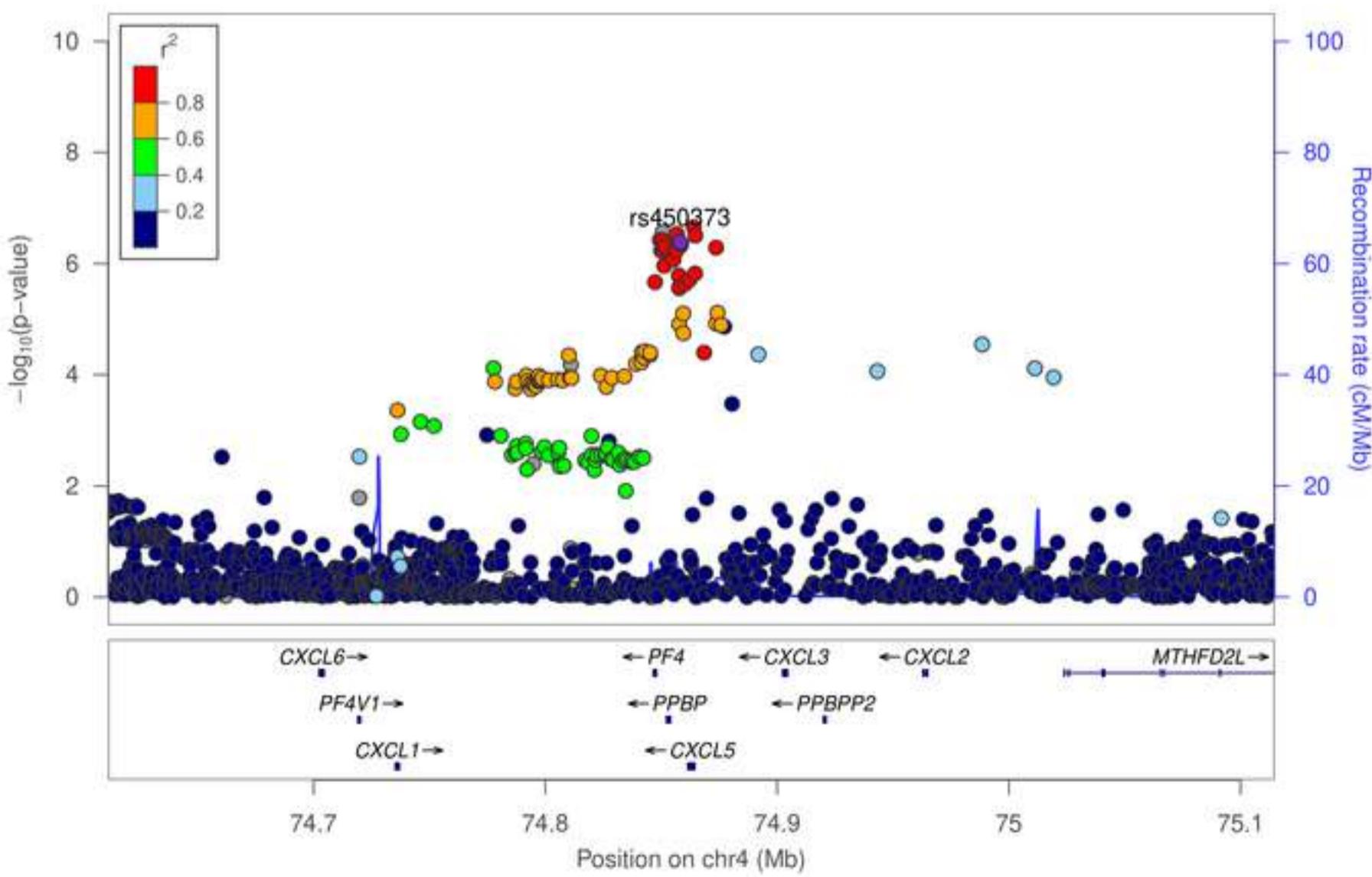
# 'Inflammatory bowel disease'(ebi-a-GCST004131)–rs2074227



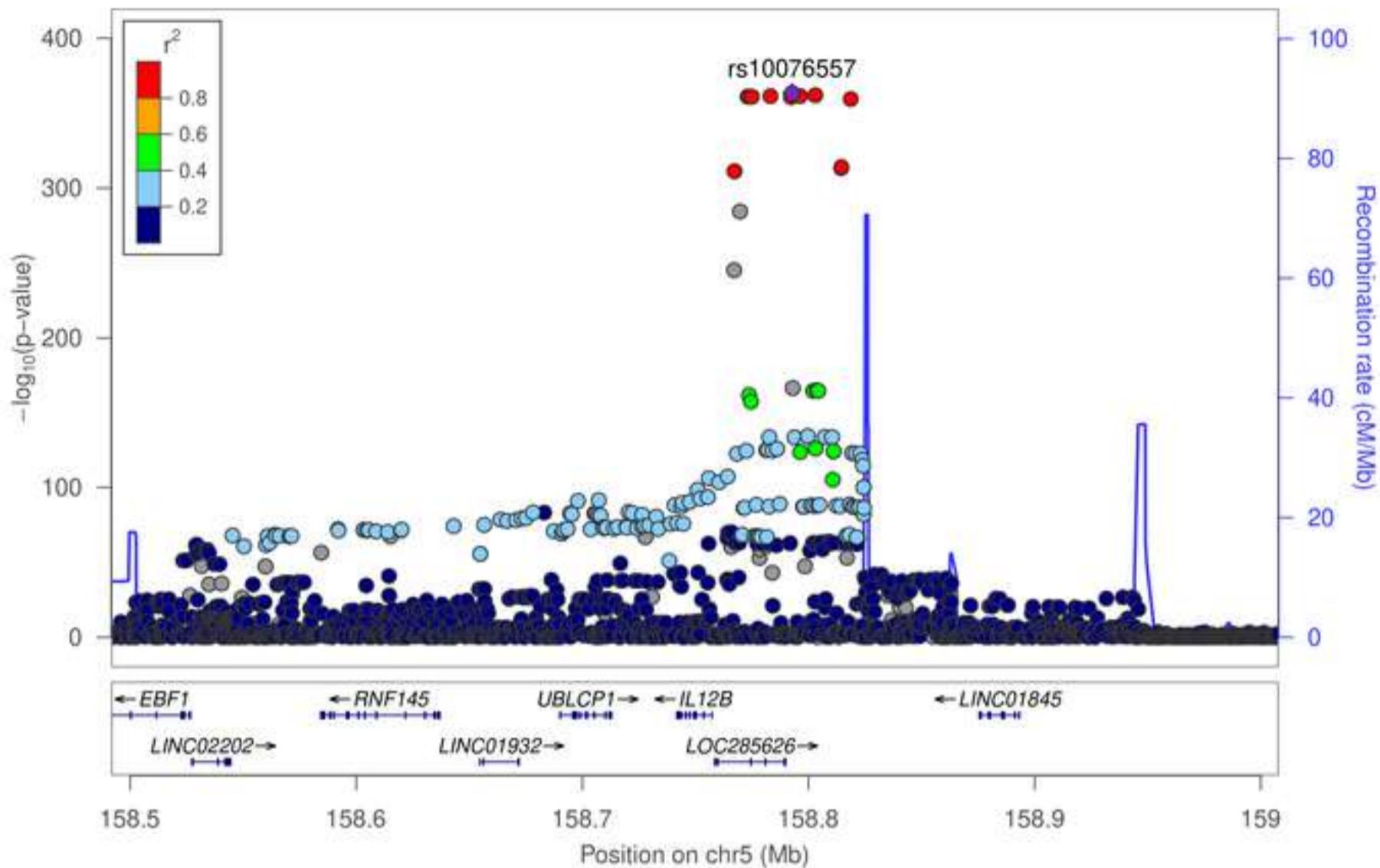
# SCALLOP: CXCL5–rs450373



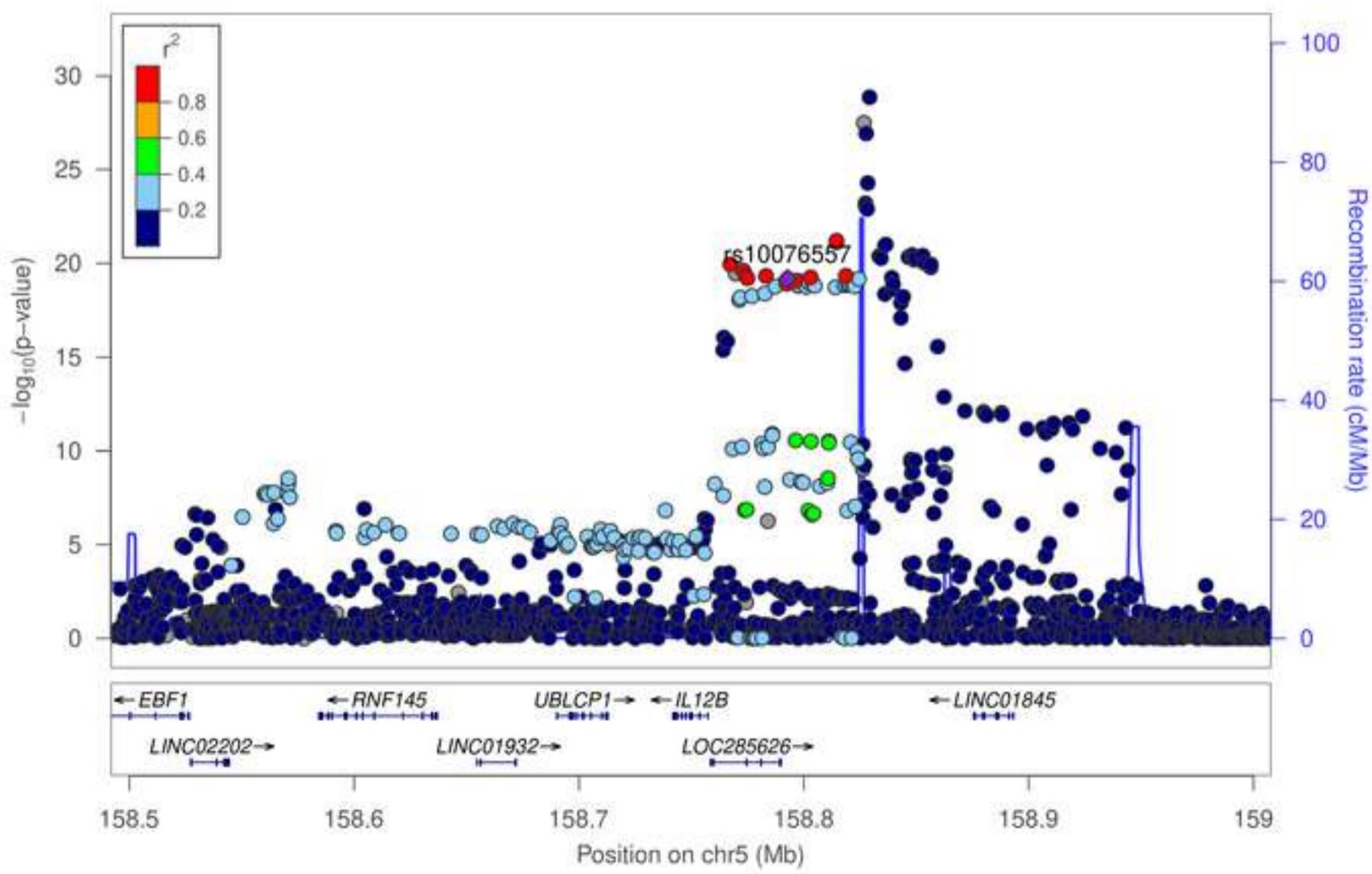
# 'Ulcerative colitis'(ebi-a-GCST004133)–rs450373



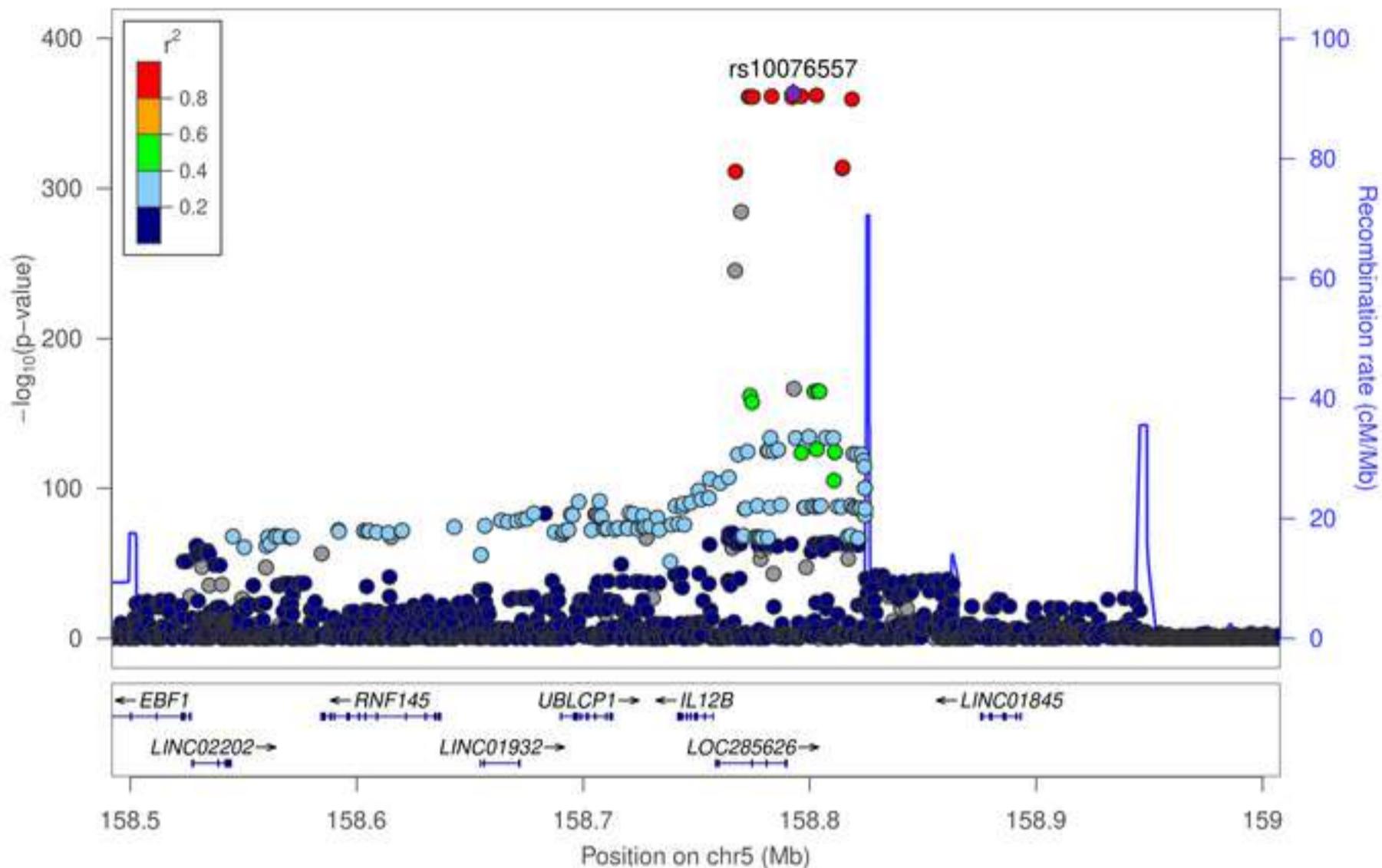
# SCALLOP: IL12B-rs10076557



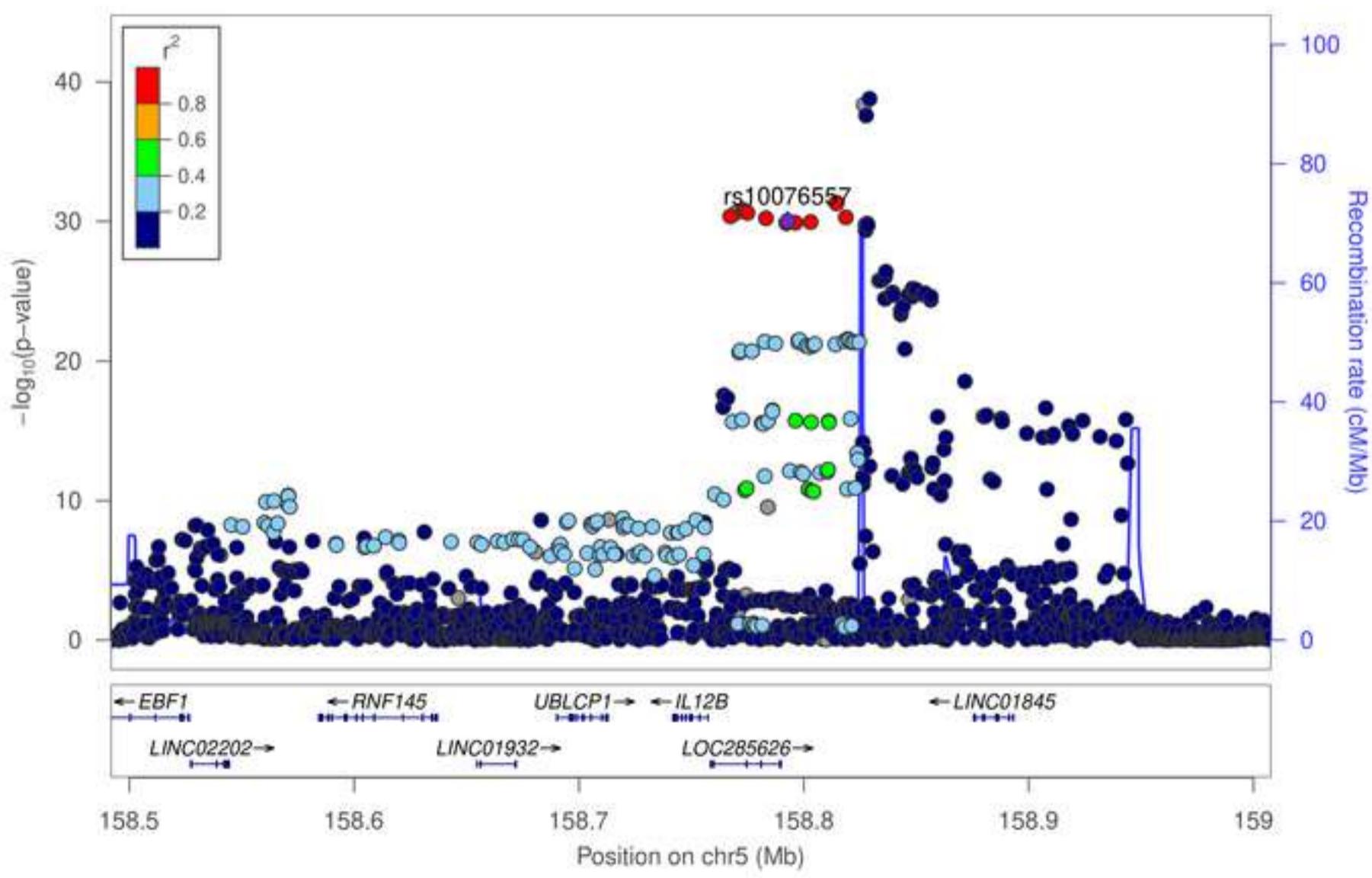
# 'Crohns disease'(ebi-a-GCST004132)-rs10076557



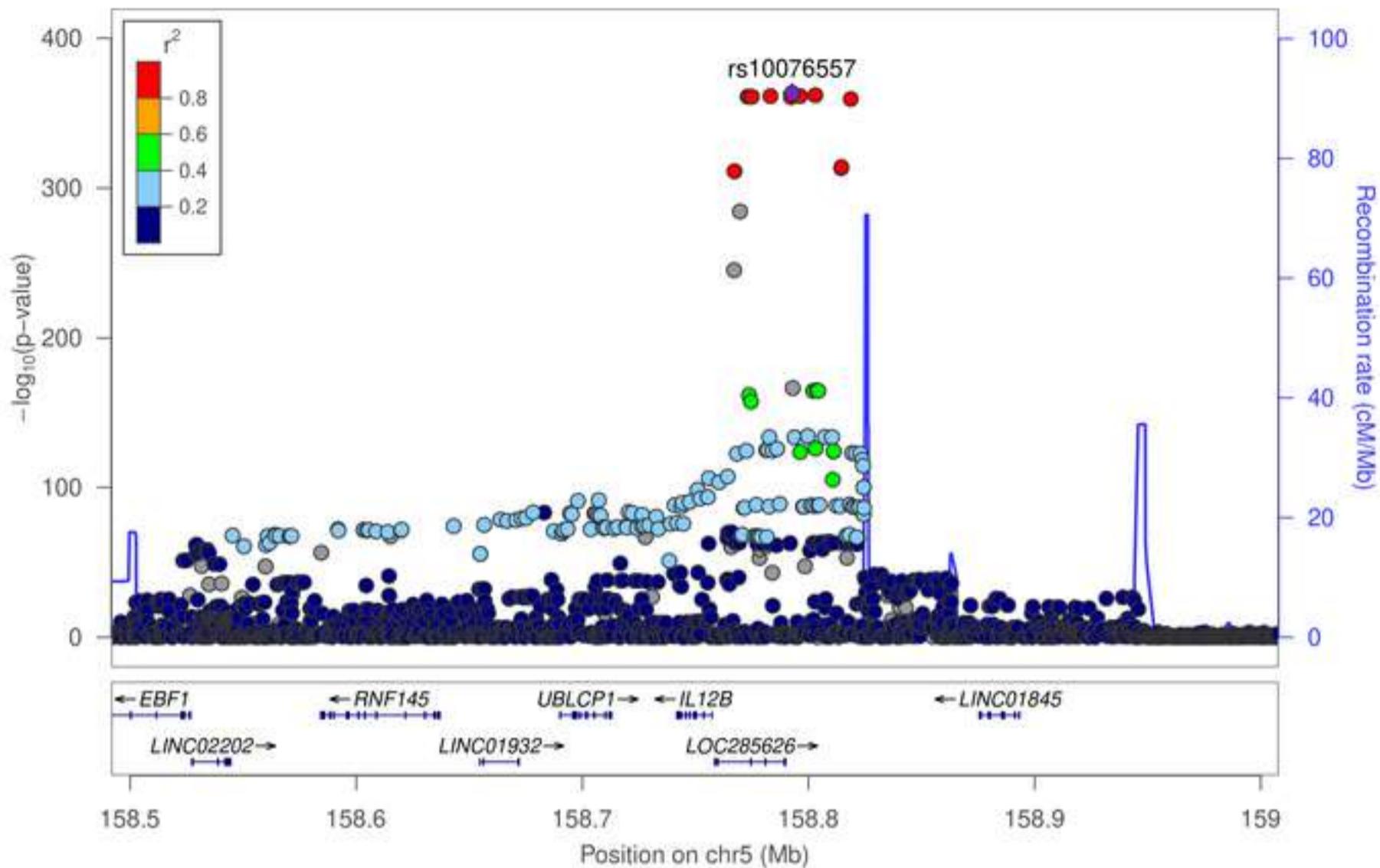
# SCALLOP: IL12B-rs10076557



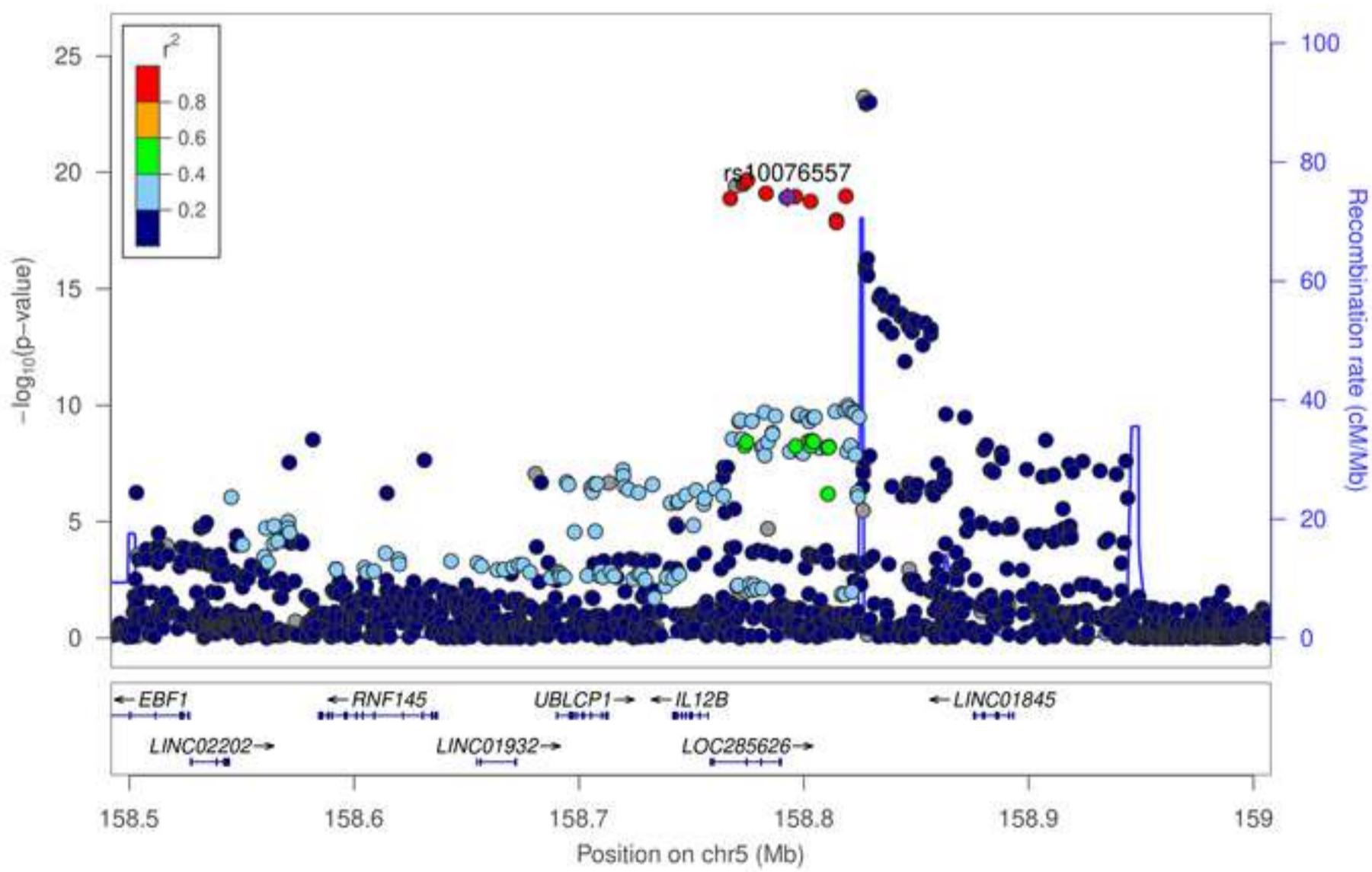
## 'Inflammatory bowel disease'(ebi-a-GCST004131)-rs10076557



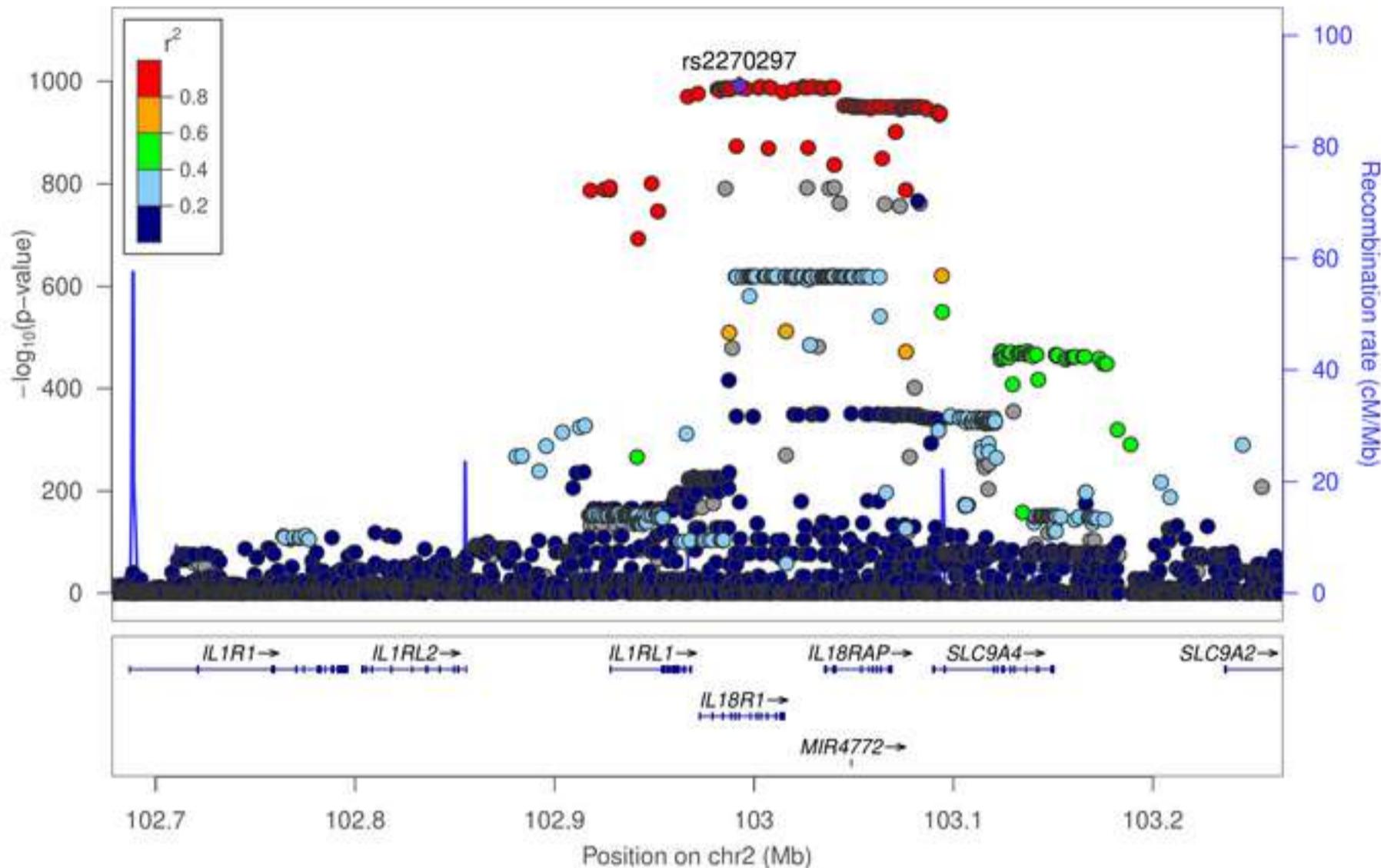
# SCALLOP: IL12B-rs10076557



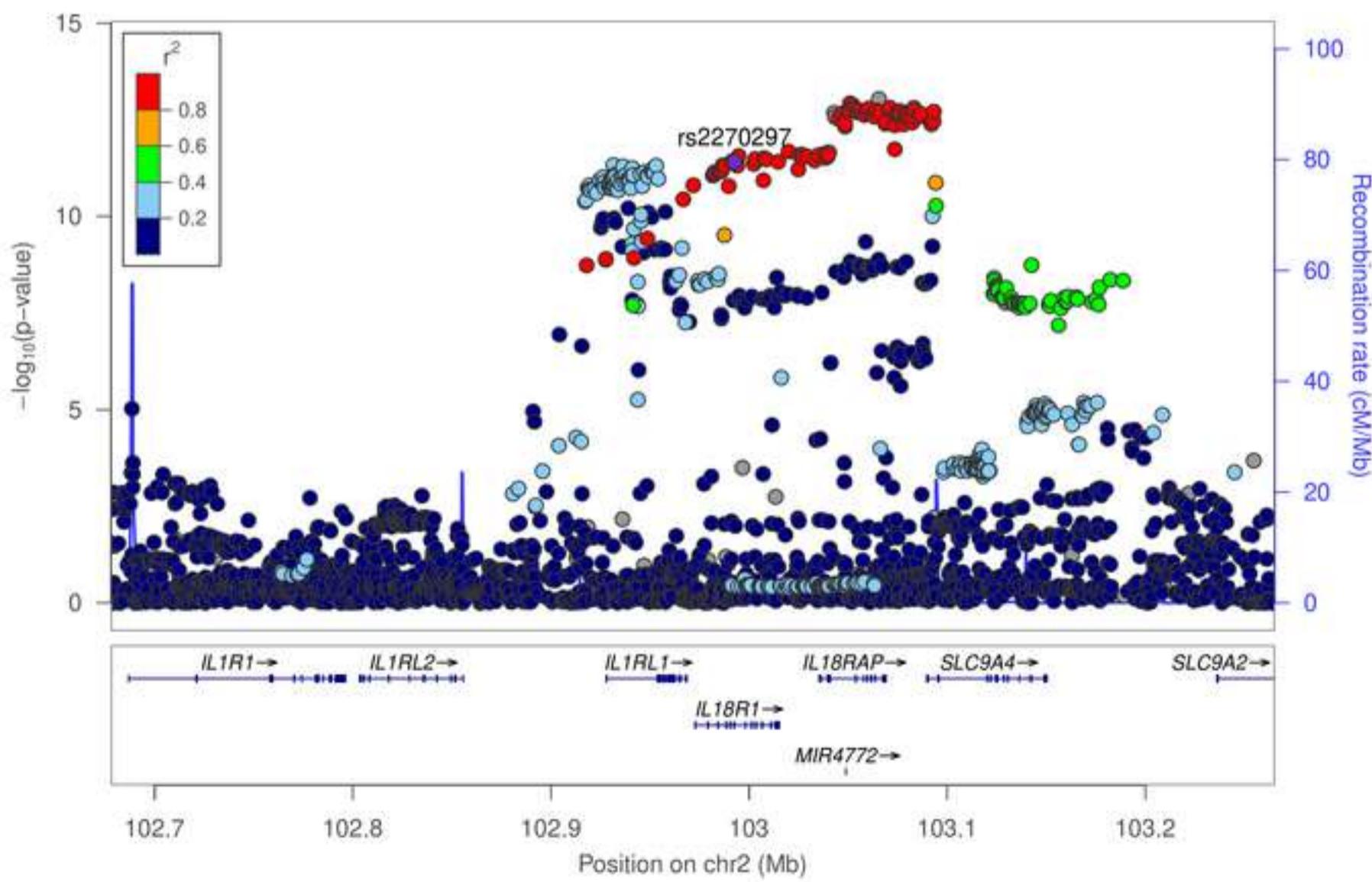
# 'Ulcerative colitis'(ebi-a-GCST004133)-rs10076557



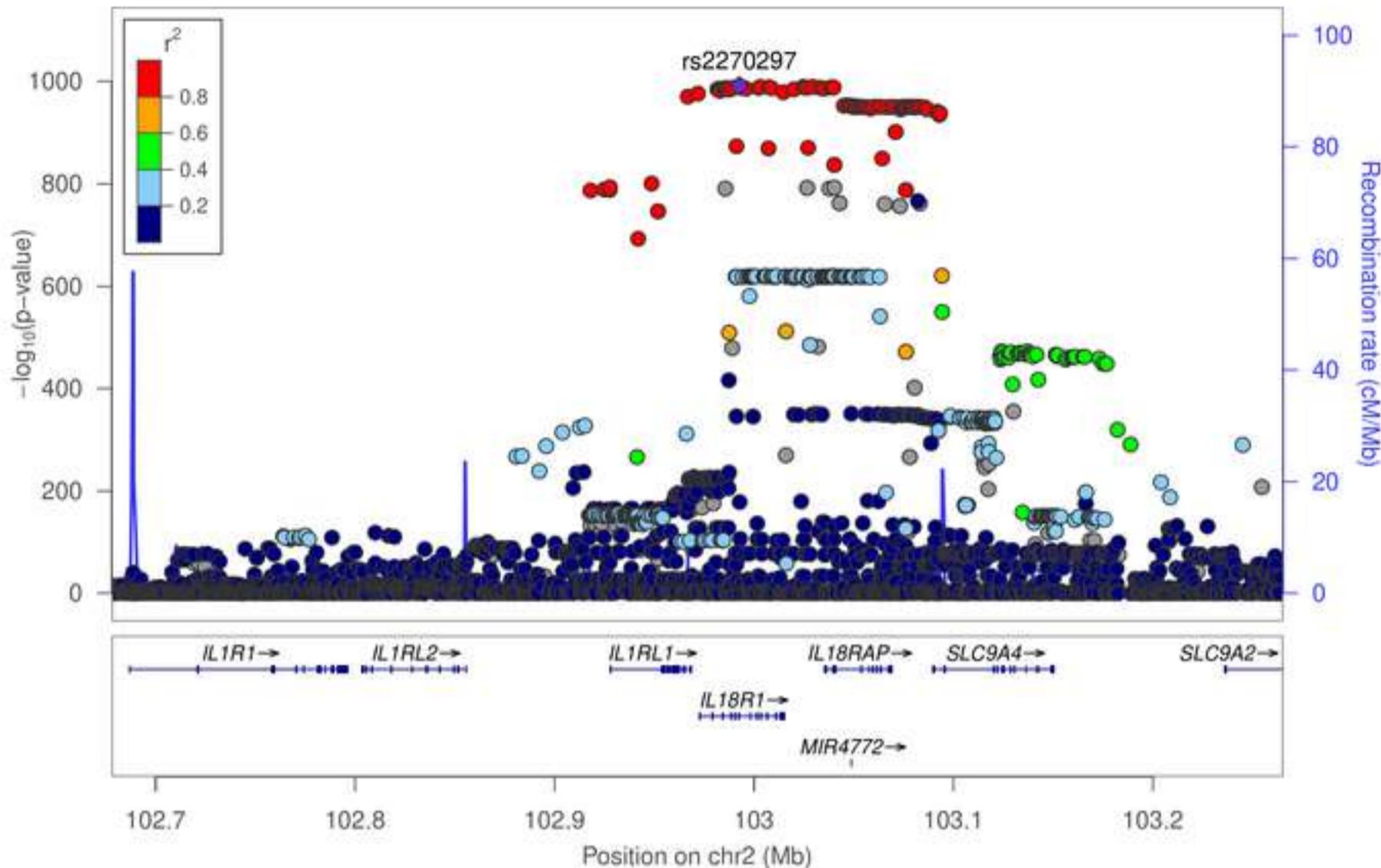
# SCALLOP: IL18R1–rs2270297



# 'Crohns disease'(ebi-a-GCST004132)–rs2270297



# SCALLOP: IL18R1–rs2270297



# Eczema(ieu-a-996)–rs2270297

