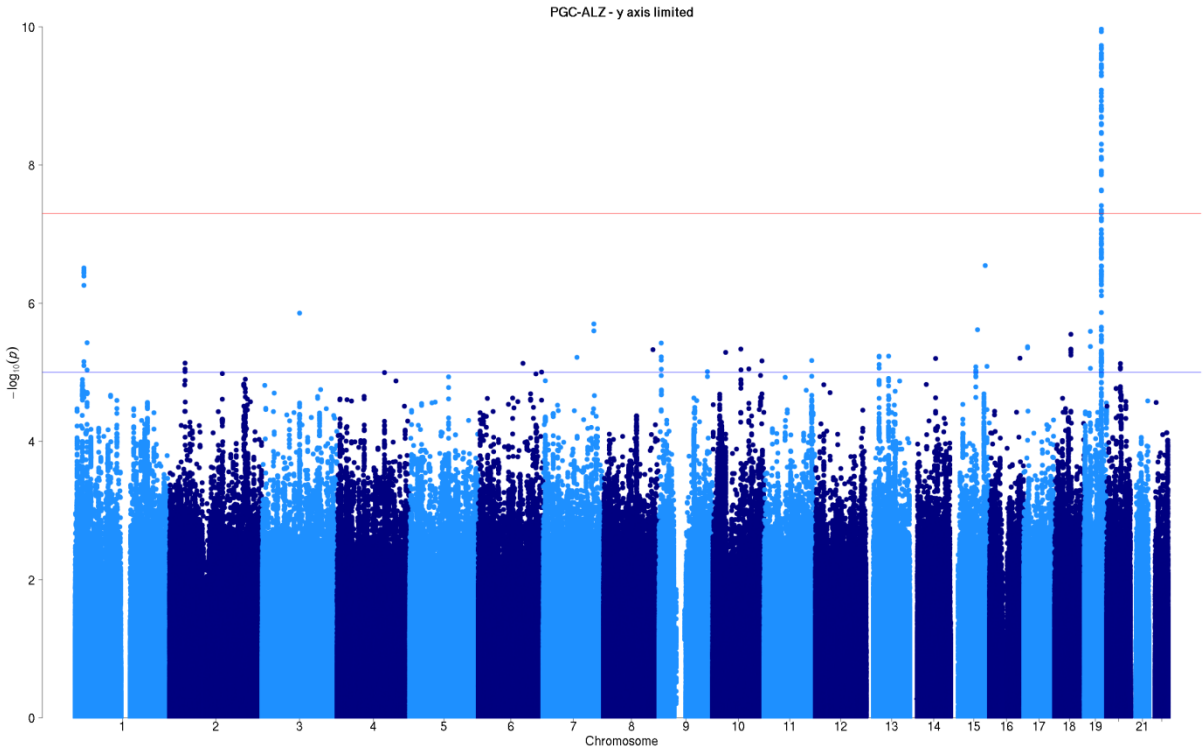
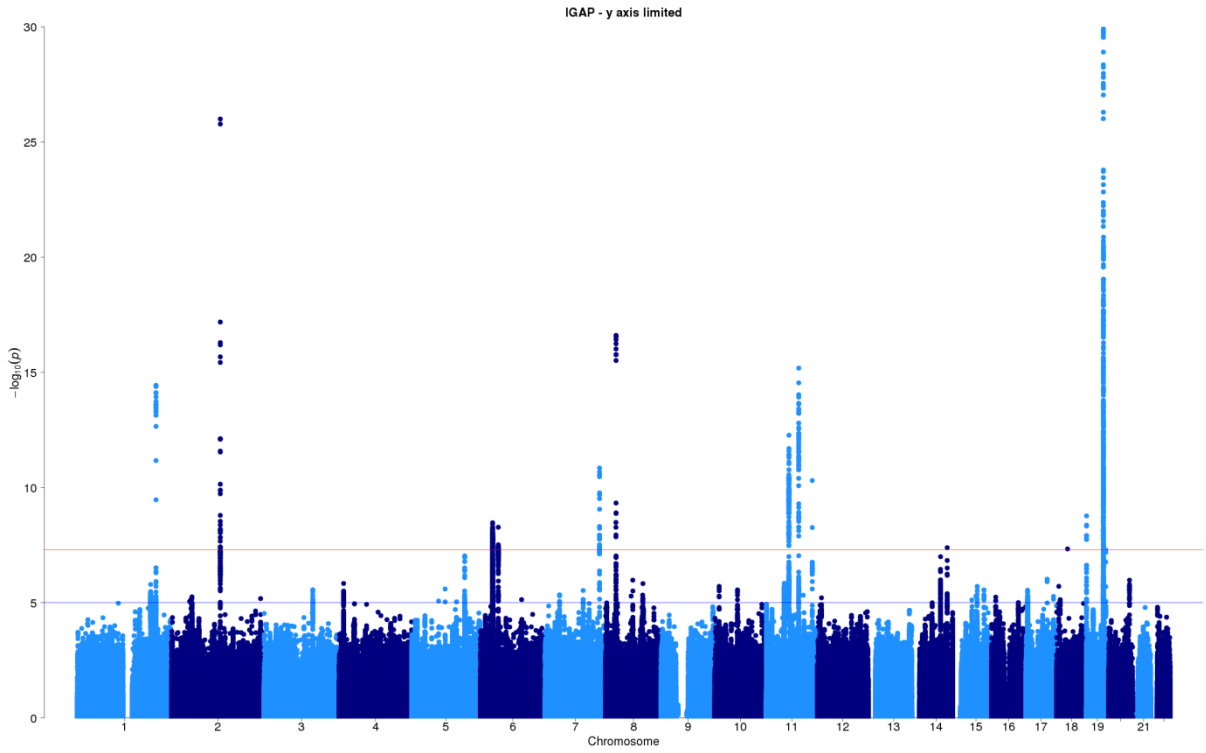
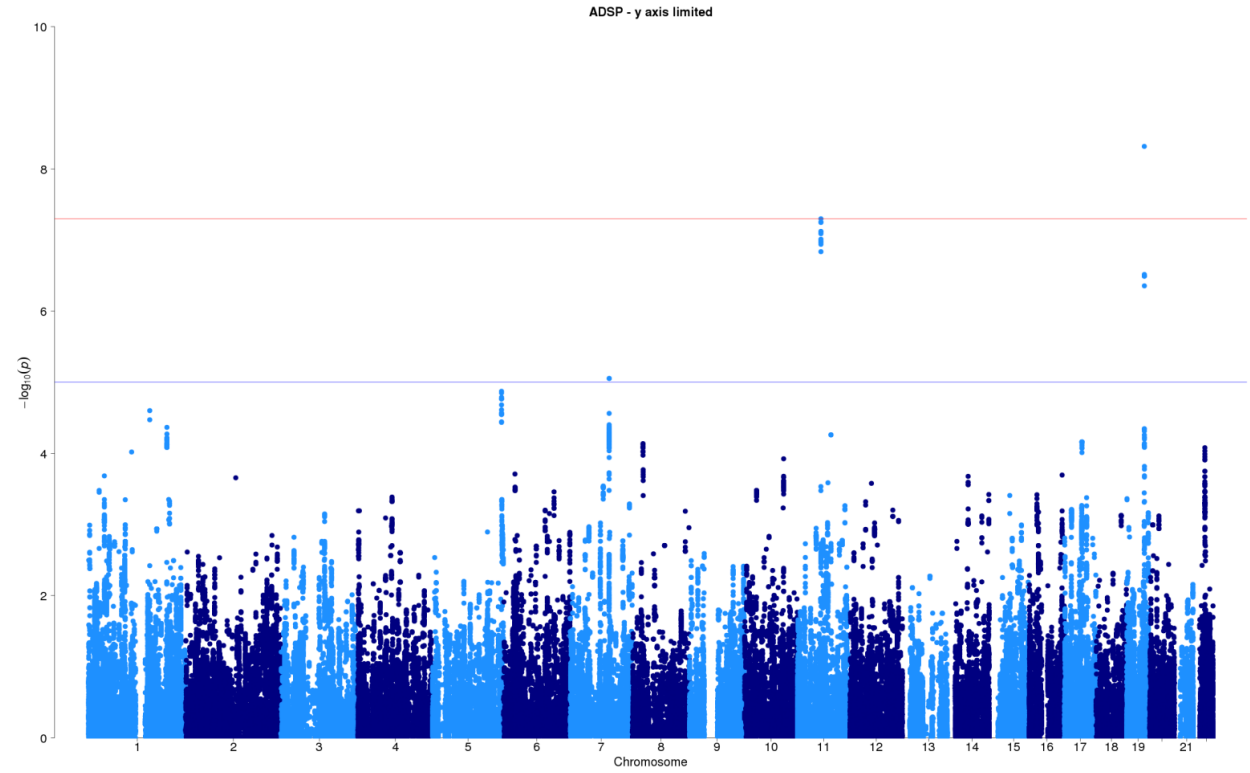
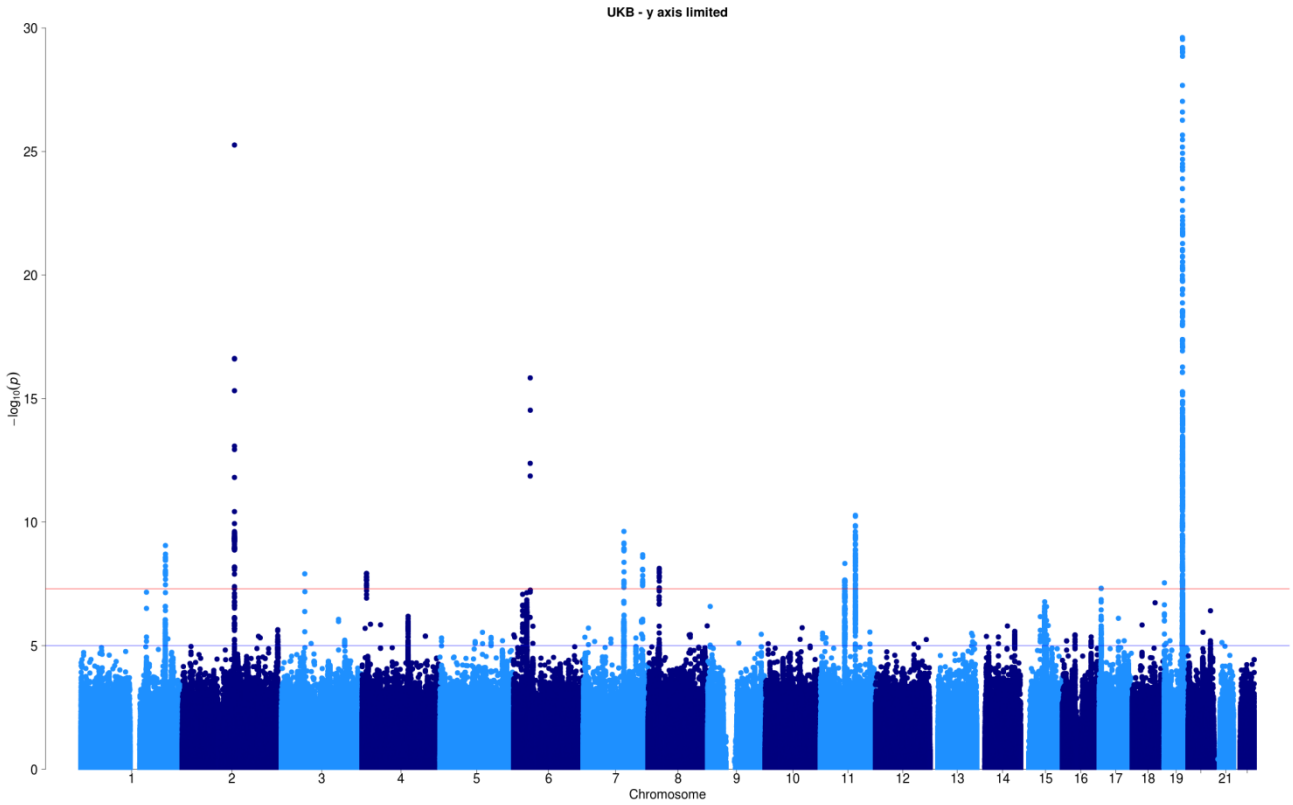
Supplementary Figure 1. Manhattan and QQ plots of single variant association results per main cohort. For each cohort, Manhattan and QQ plots are shown. A) The Manhattan plot displays all associations per variant ordered according to their genomic position on the x-axis and showing the strength of the association with the –log10 transformed *P*-values on the y-axis. The y-axis is limited to enable visualization of non-*APOE* loci. B) The QQ plot displays the expected –log10 transformed *p*-values on the x-axis and the observed –log10 transformed *p*-values on the y-axis.

A

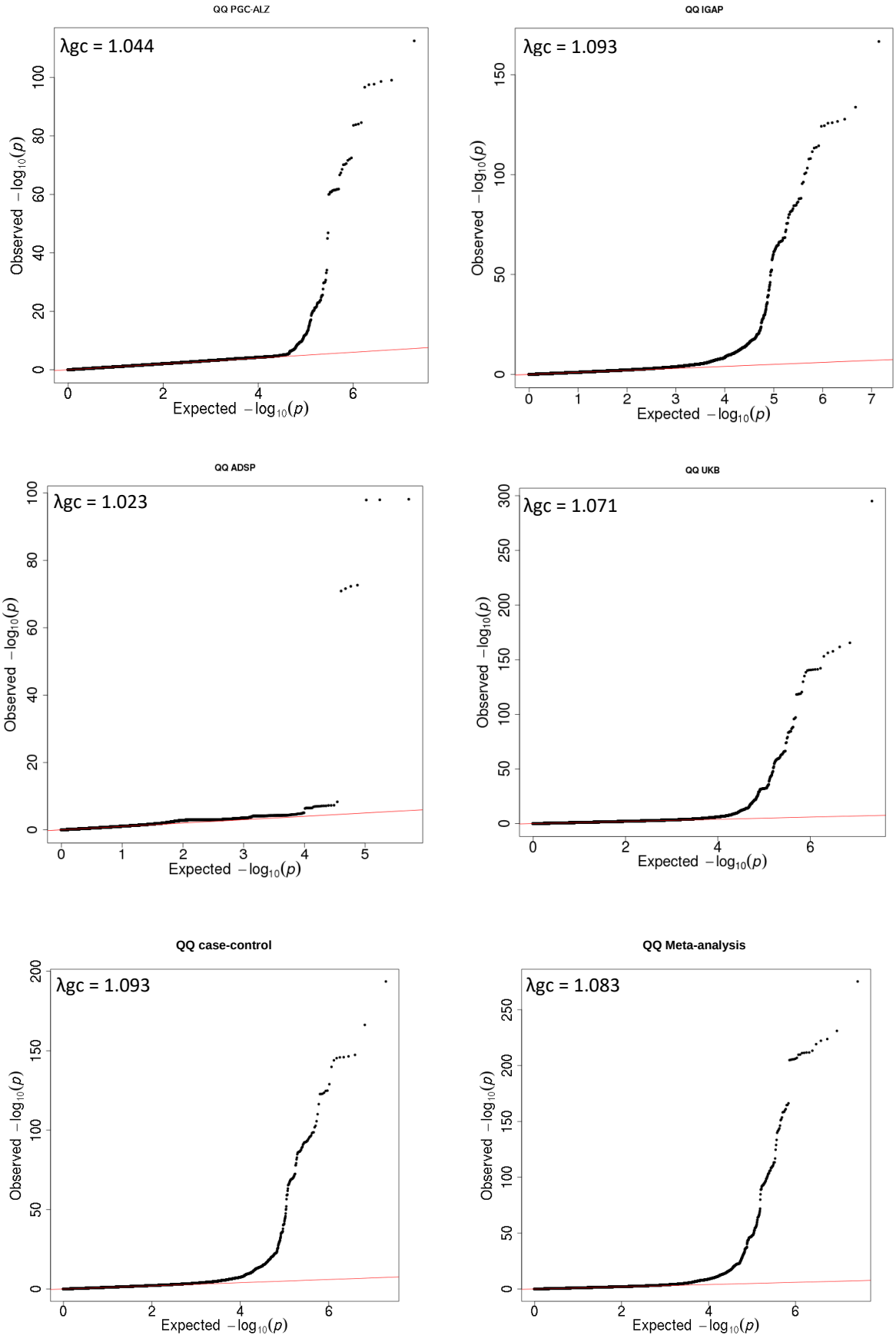




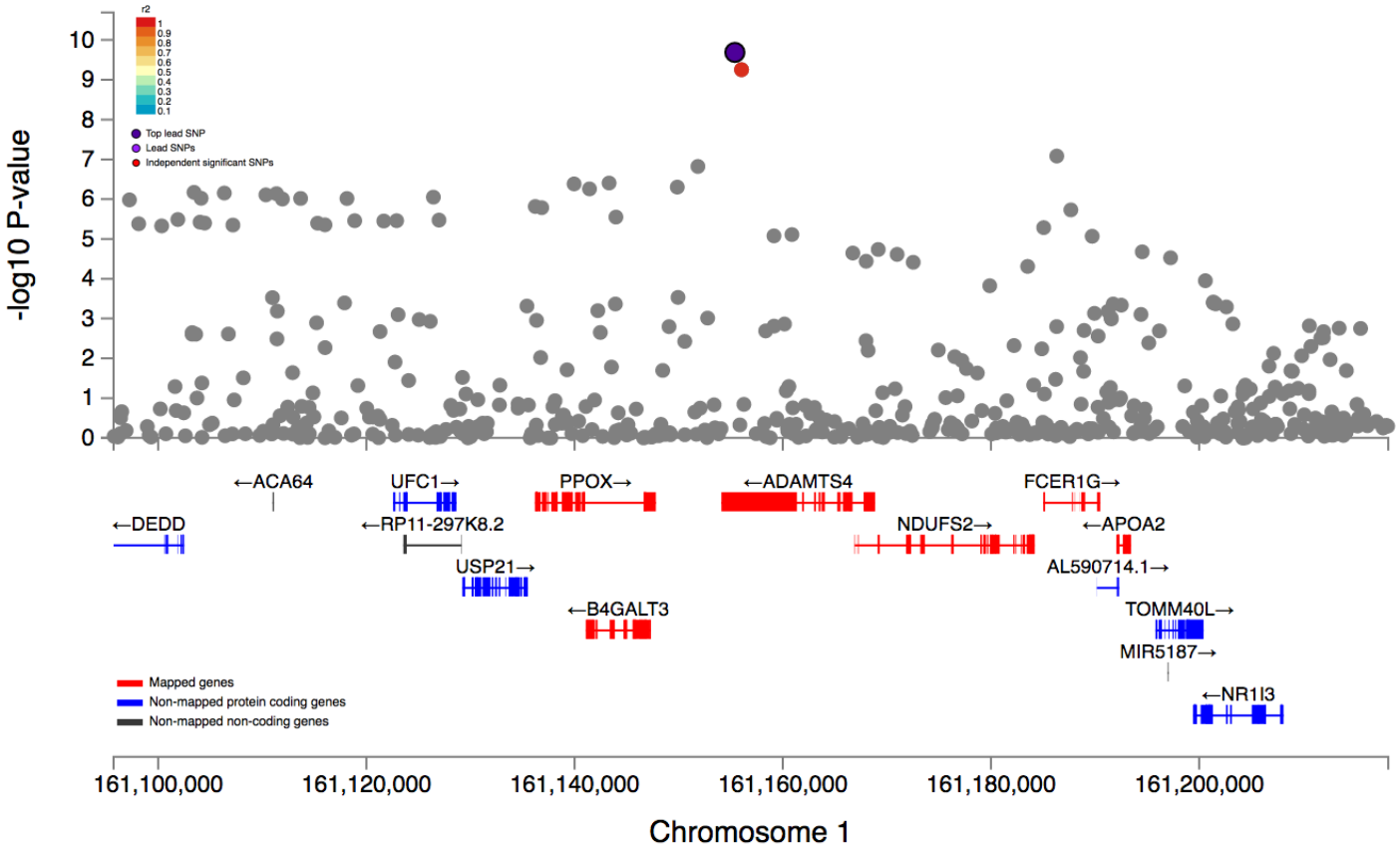

ADSP - y axis limited
10
8
6
4
2
0
$-\log_{10}(p)$
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
21
Chromosome

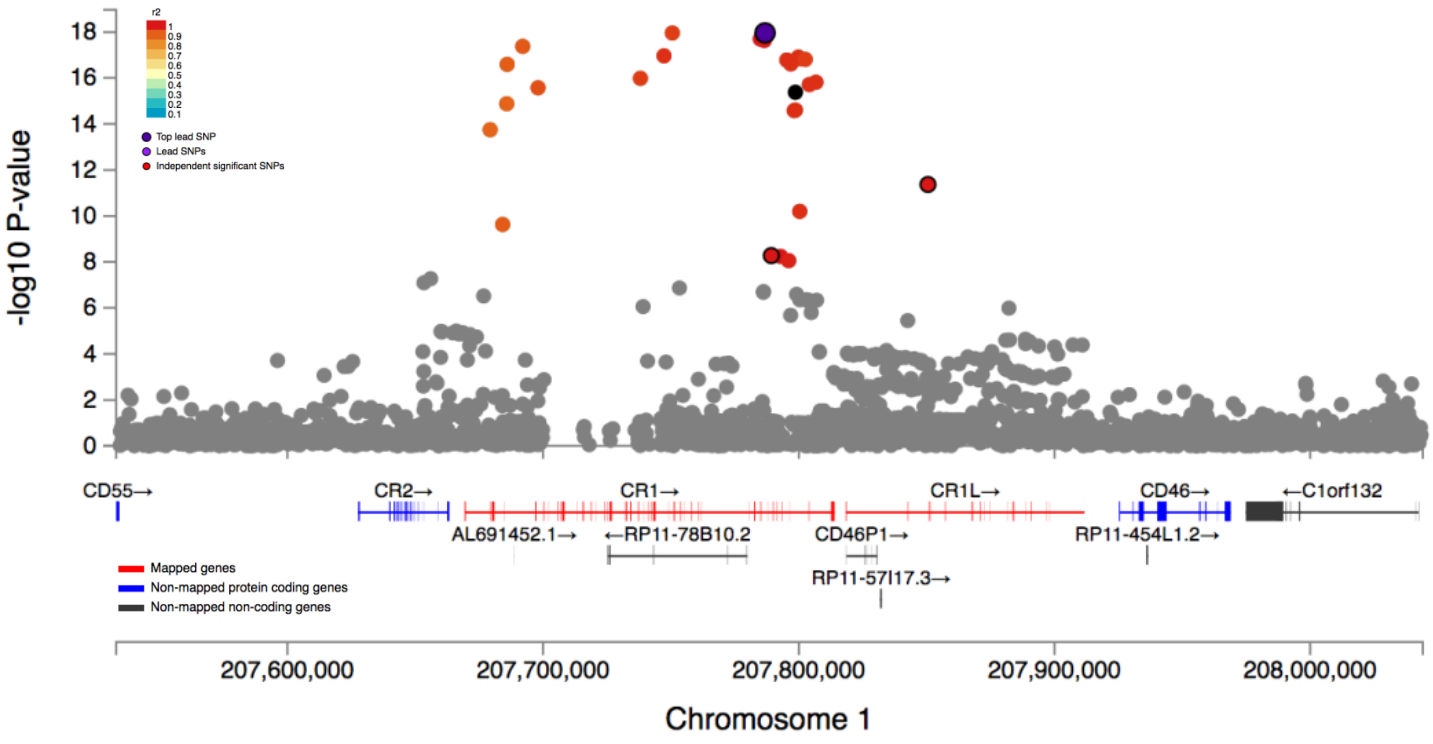

UKB - y axis limited
30
25
20
15
10
5
0
$-\log_{10}(p)$
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
21
Chromosome

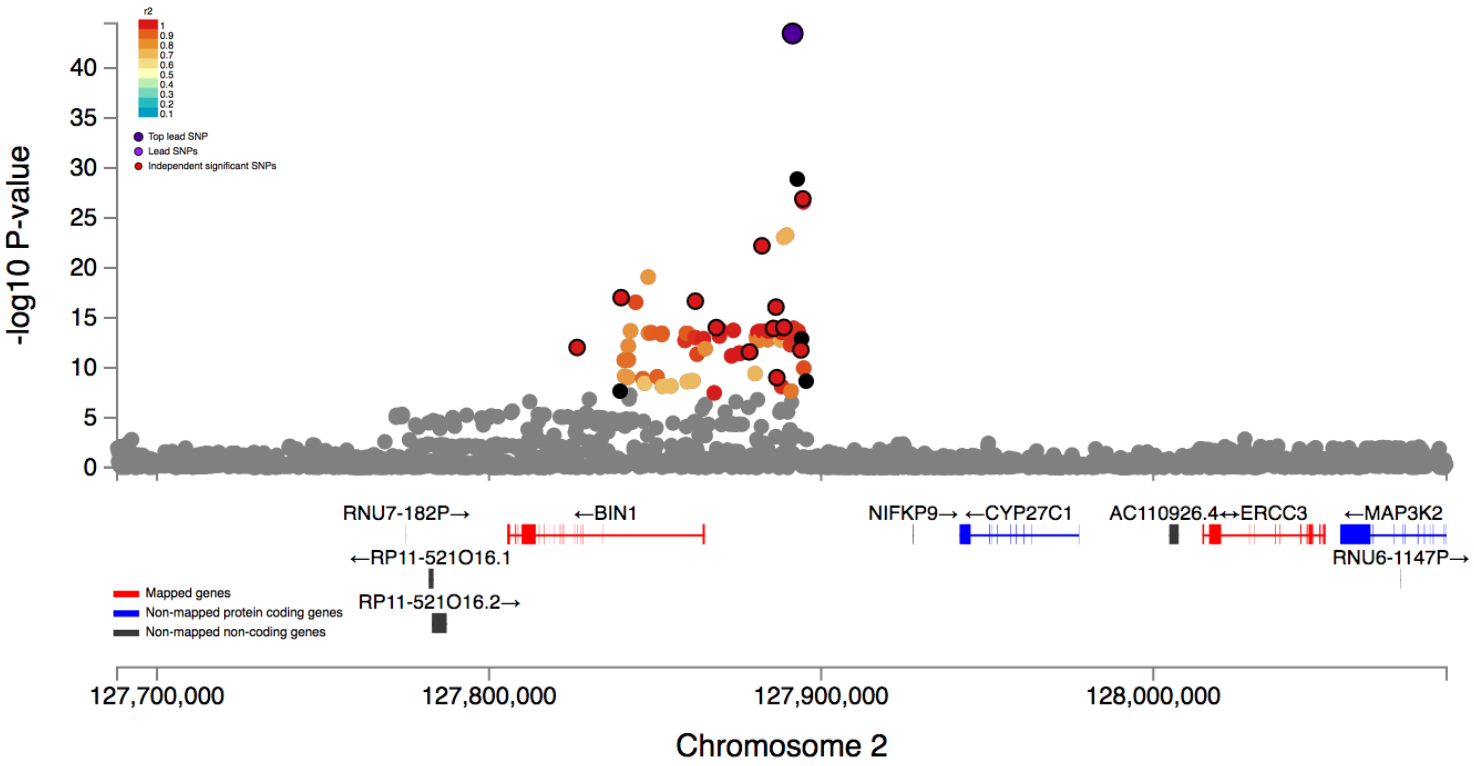
B

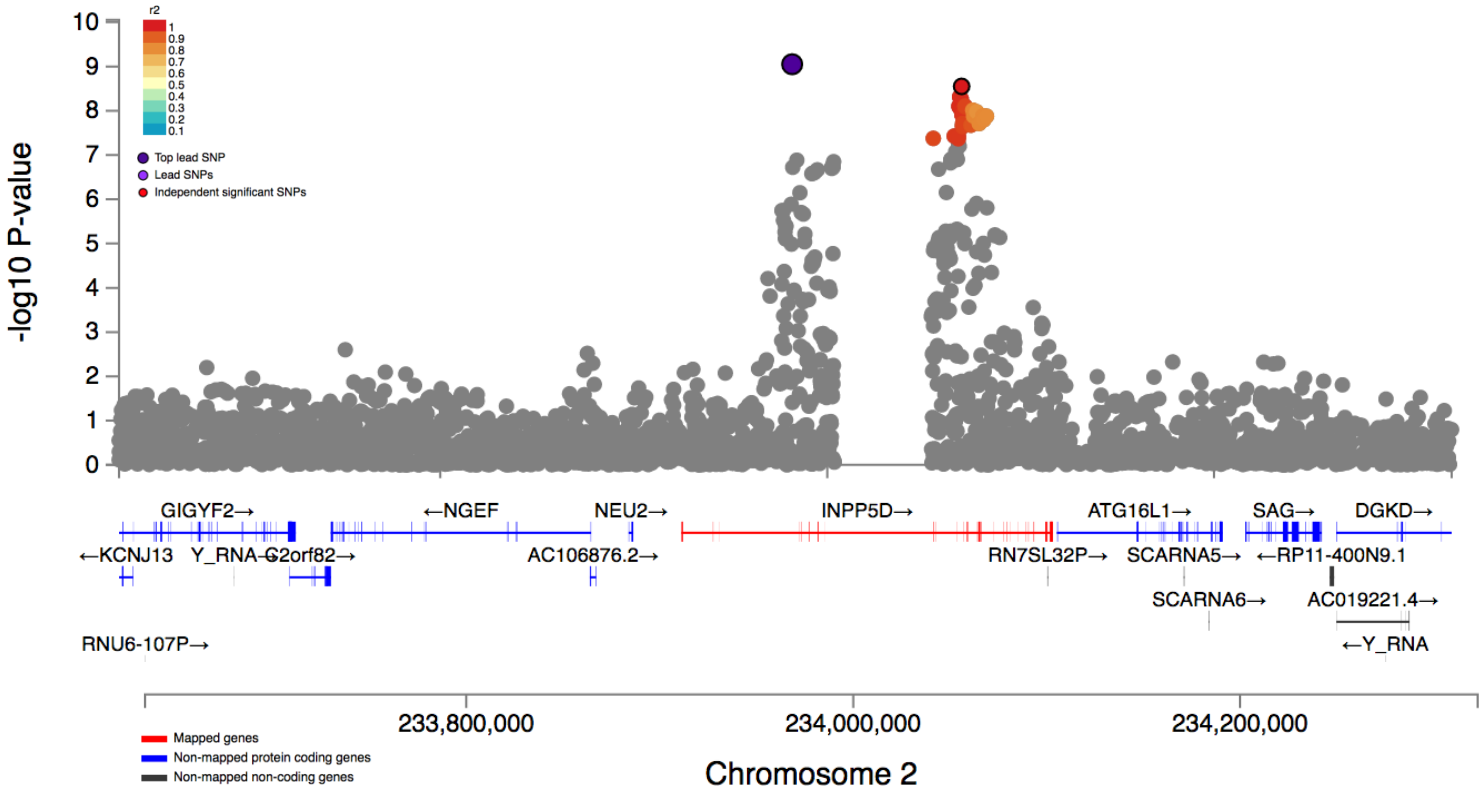

QQ PGC-ALZ
λgc = 1.044
QQ IGAP
λgc = 1.093
QQ ADSP
λgc = 1.023
QQ UKB
λgc = 1.071
QQ case-control
λgc = 1.093
QQ Meta-analysis
λgc = 1.083
Observed $-\log_{10}(p)$
Expected $-\log_{10}(p)$

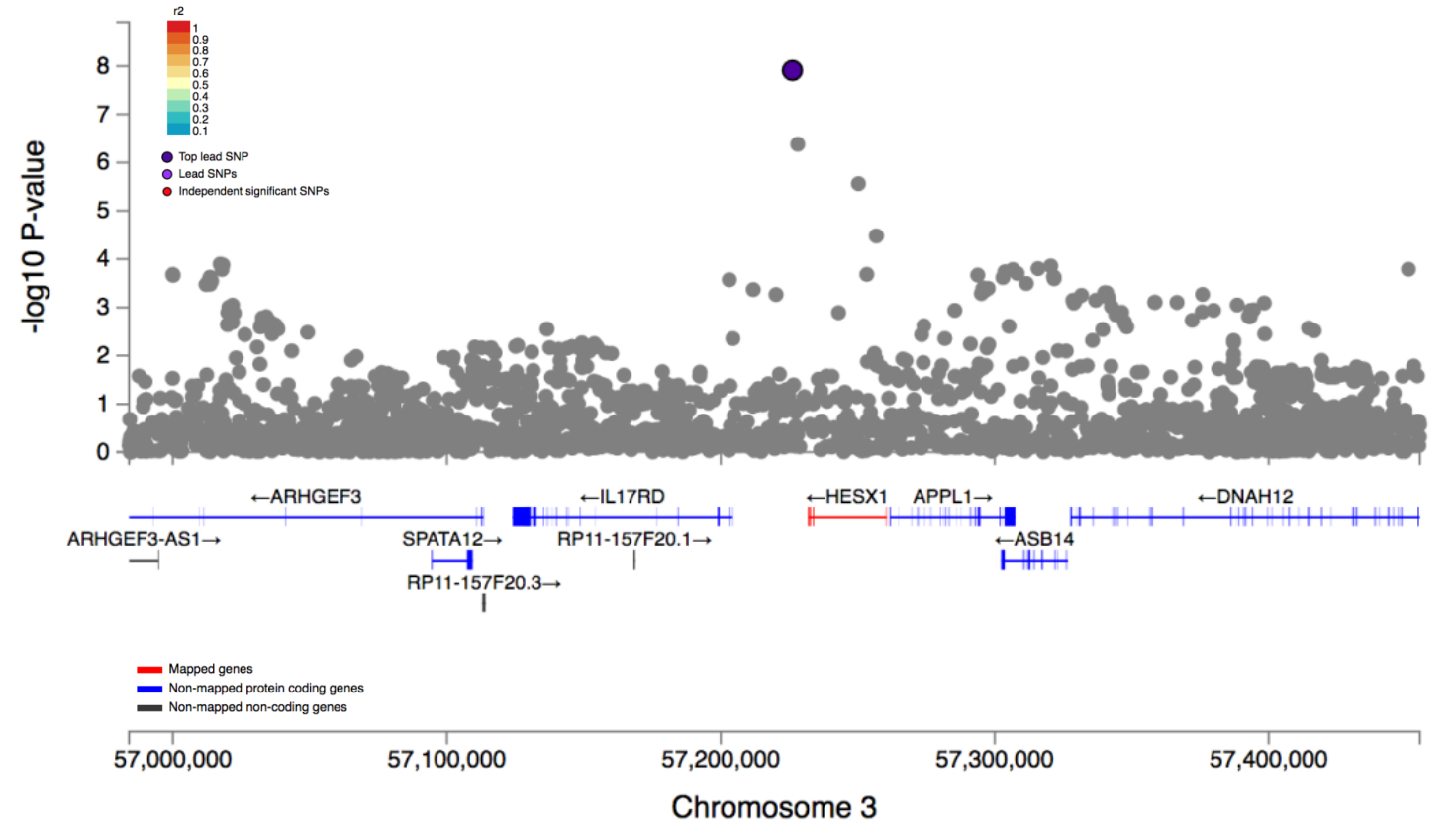
Supplementary Figure 2. Regional plot for the 29 significant loci of the meta-analysis. Every point represents a SNP, which are colour-coded based on the highest r2 to one of the most significant SNPs, if greater or equal to r^2 of 0.6. Other SNPs are coloured in grey. The red colored mapped gene names represent putative causal genes as suggested by FUMA using positional mapping, eQTL data or chromatin interactions.

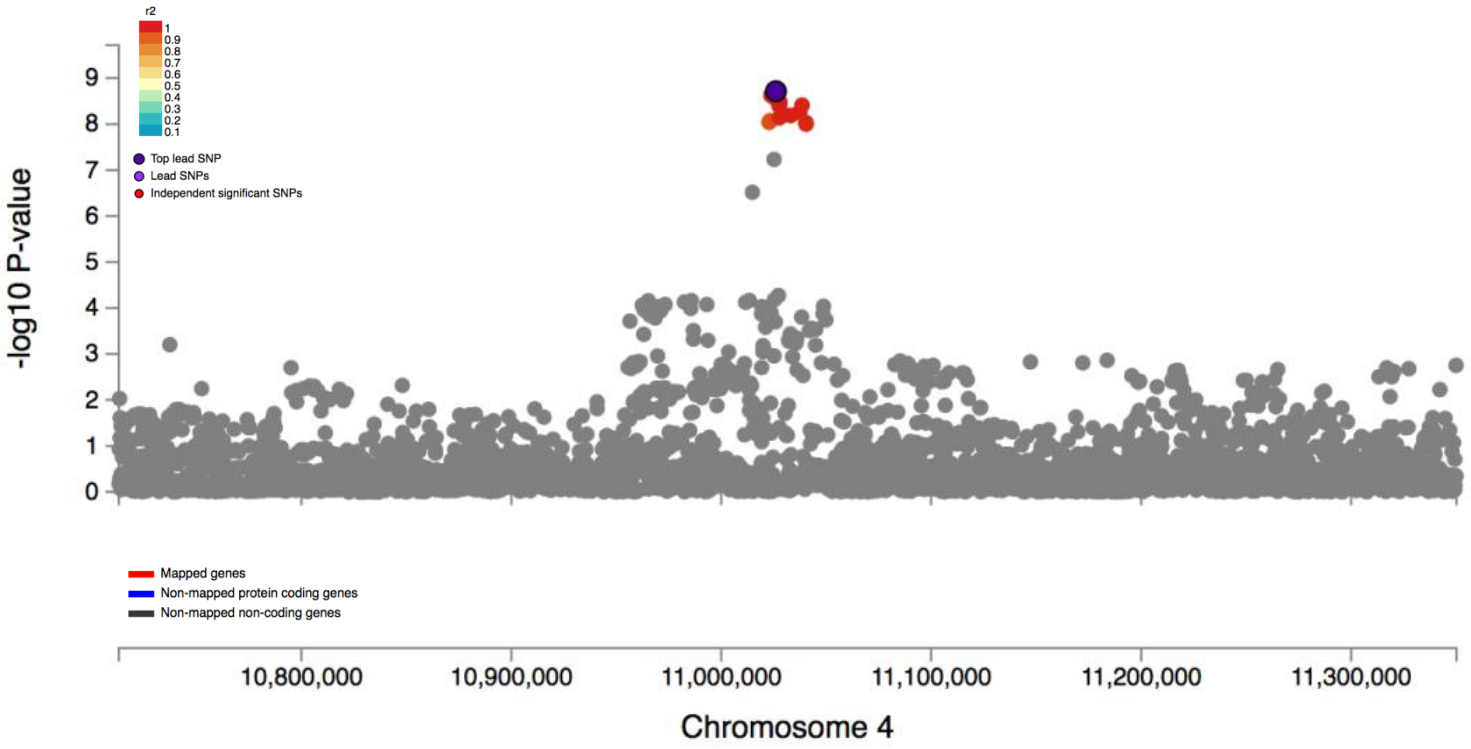


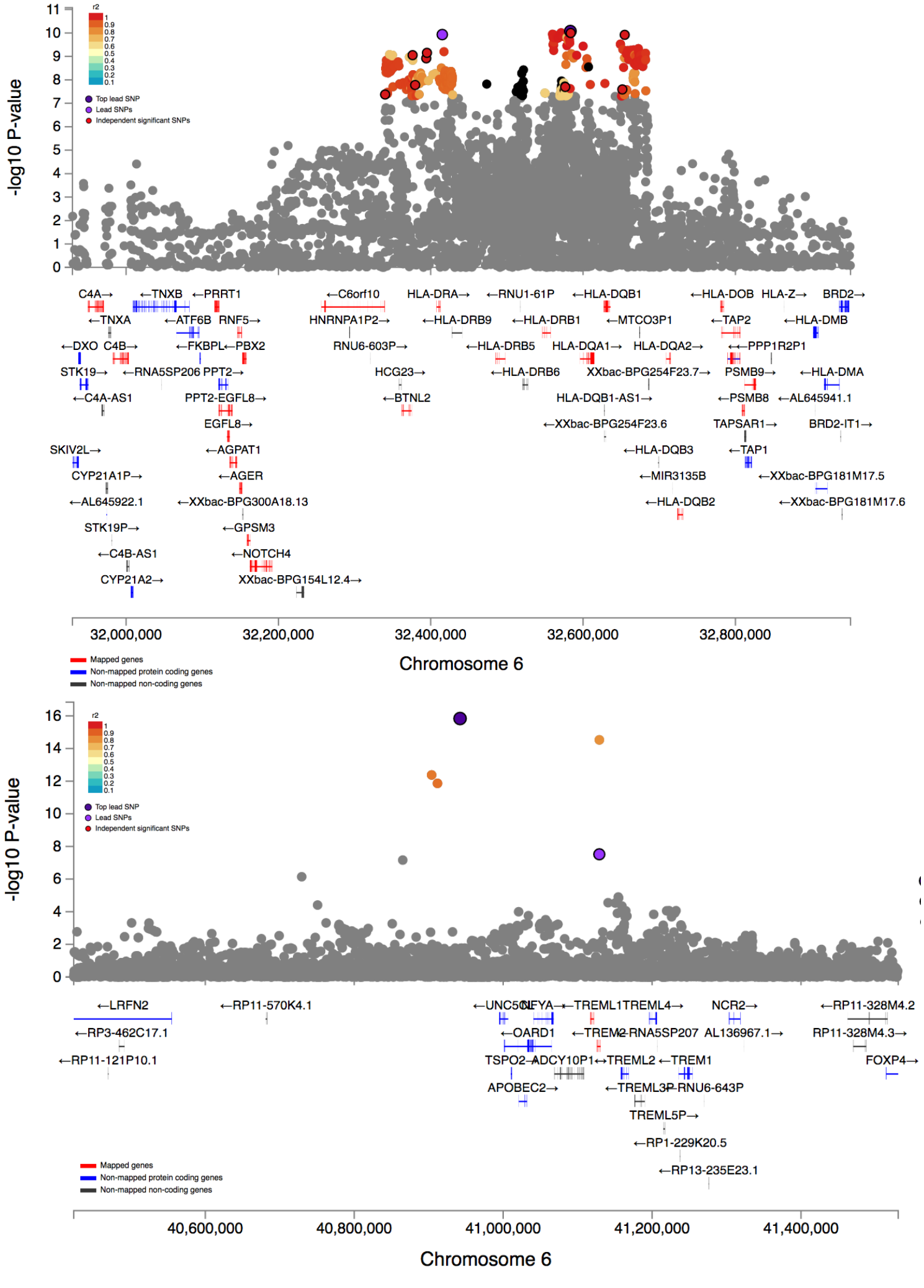


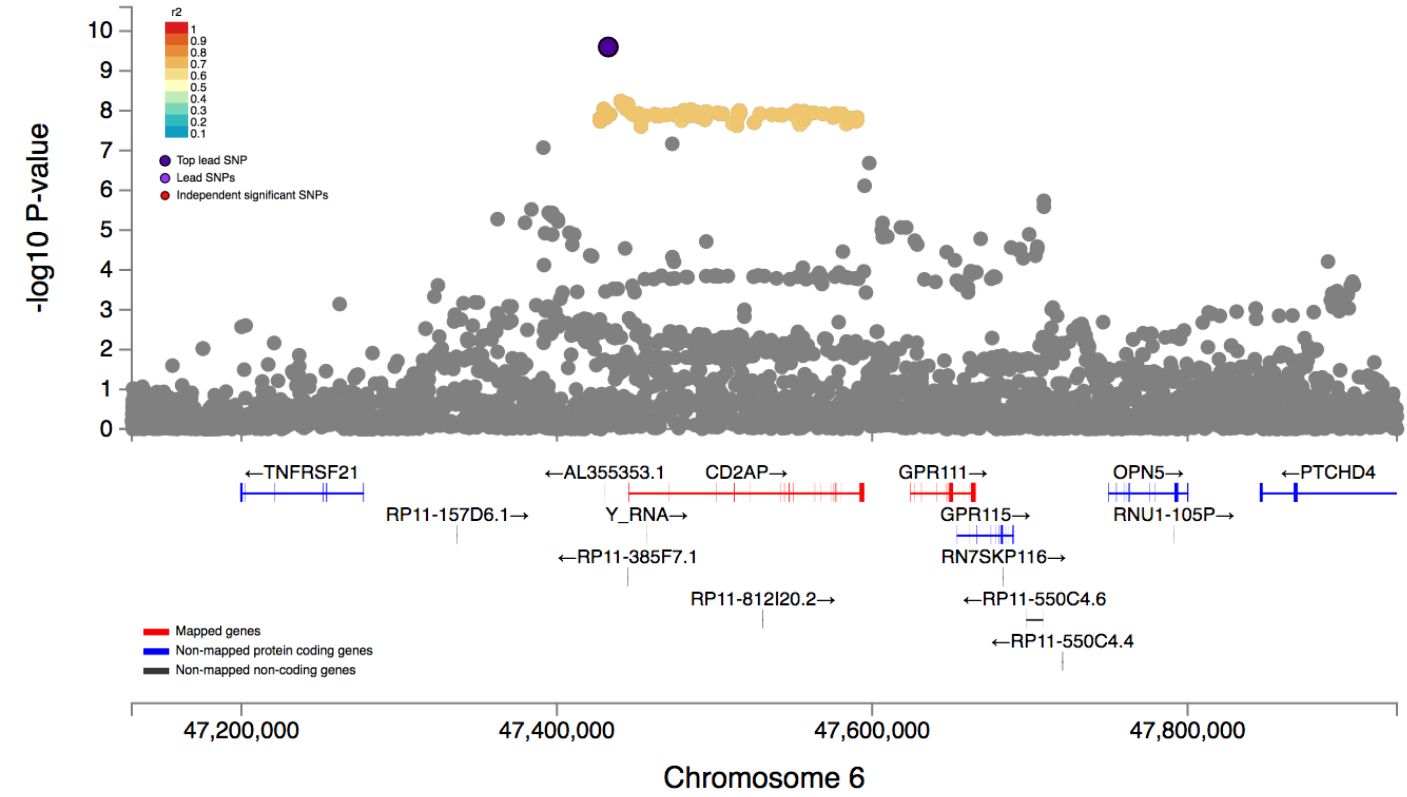

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
40
35
30
25
20
15
10
5
0
RNU7-182P→
←BIN1
NIFKP9→
←CYP27C1
AC110926.4↔ERCC3
←MAP3K2
←RP11-521O16.1
RNU6-1147P→
RP11-521O16.2→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
127,700,000
127,800,000
127,900,000
128,000,000
Chromosome 2

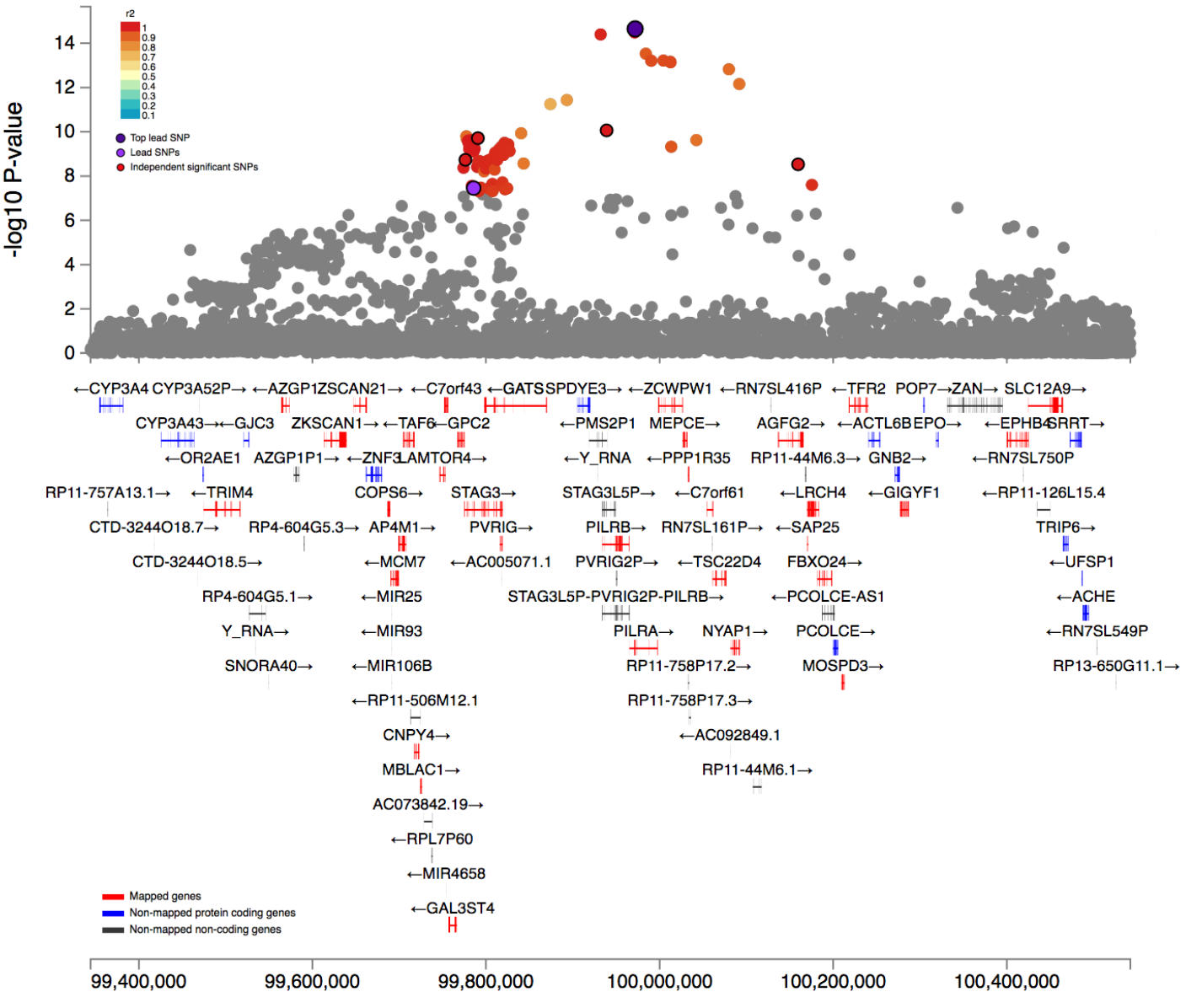

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
10
9
8
7
6
5
4
3
2
1
0
GIGYF2→
←NGEF
NEU2→
INPP5D→
ATG16L1→
SAG→
DGKD→
←KCNJ13
Y_RNA
C2orf82→
AC106876.2→
RN7SL32P→
SCARNA5→
←RP11-400N9.1
SCARNA6→
AC019221.4→
←Y_RNA
RNU6-107P→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
233,800,000
234,000,000
234,200,000
Chromosome 2

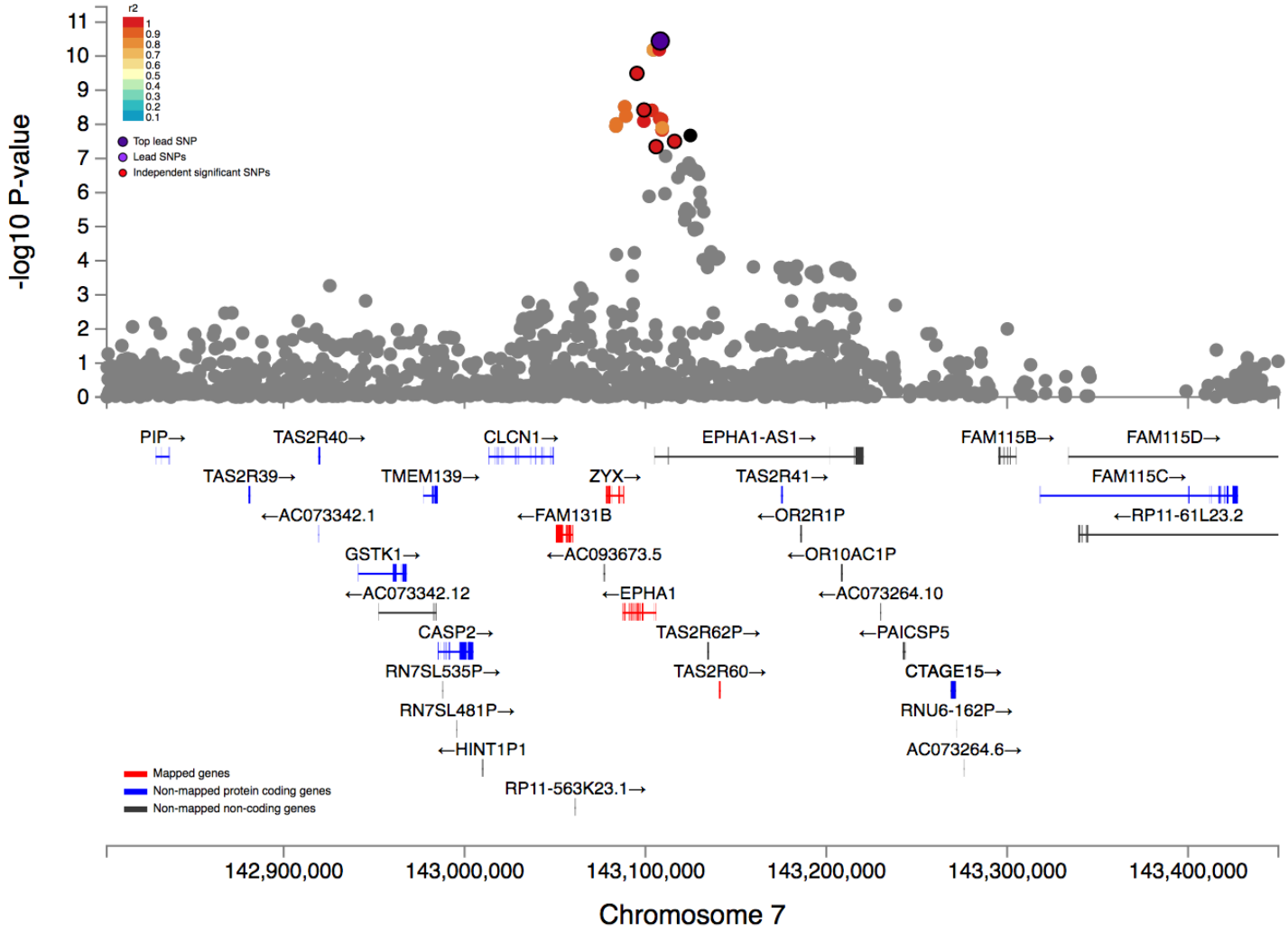

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
←ARHGEF3
←IL17RD
←HESX1
APPL1→
←DNAH12
ARHGEF3-AS1→
SPATA12→
RP11-157F20.1→
←ASB14
RP11-157F20.3→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
57,000,000
57,100,000
57,200,000
57,300,000
57,400,000
Chromosome 3

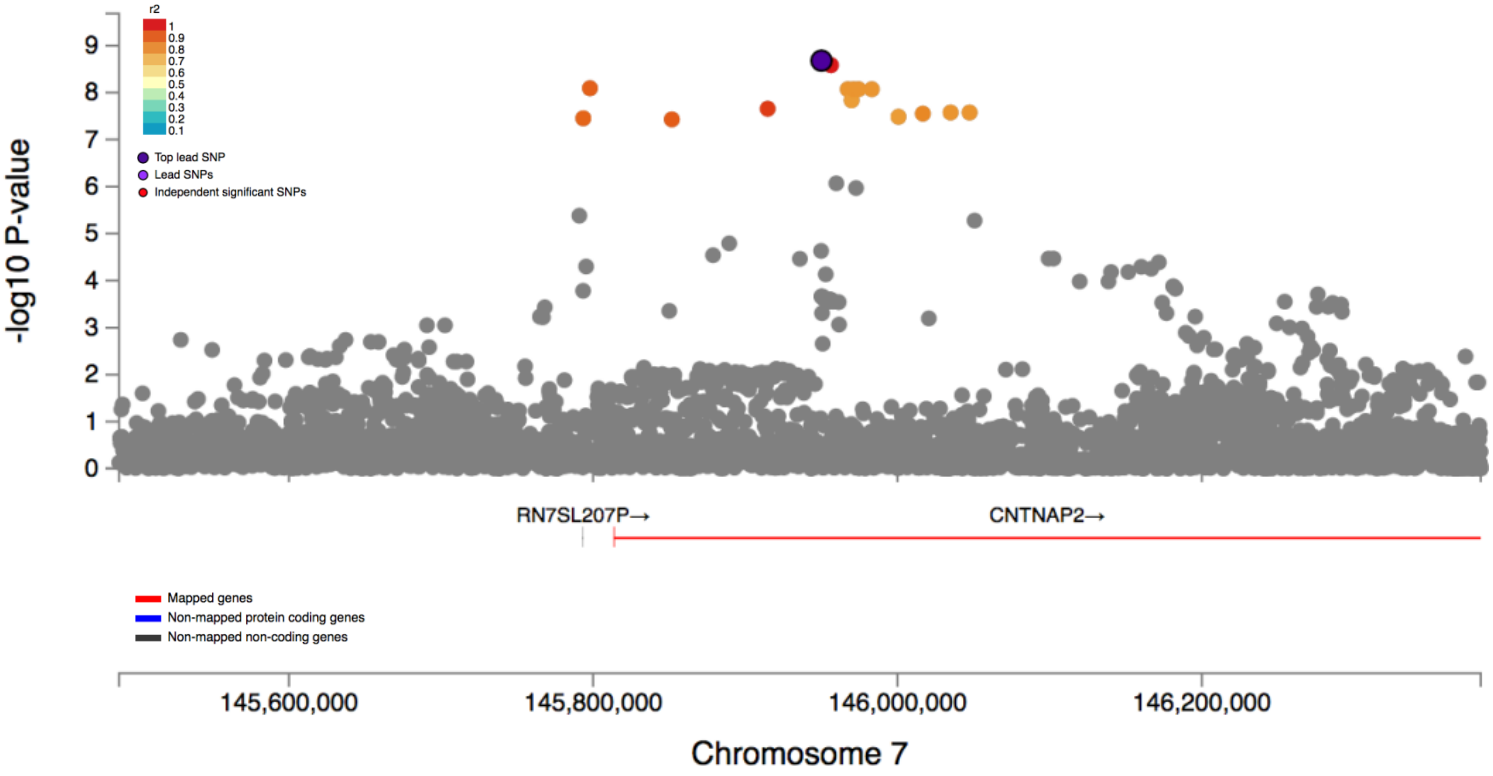

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
9
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
10,800,000
10,900,000
11,000,000
11,100,000
11,200,000
11,300,000
Chromosome 4

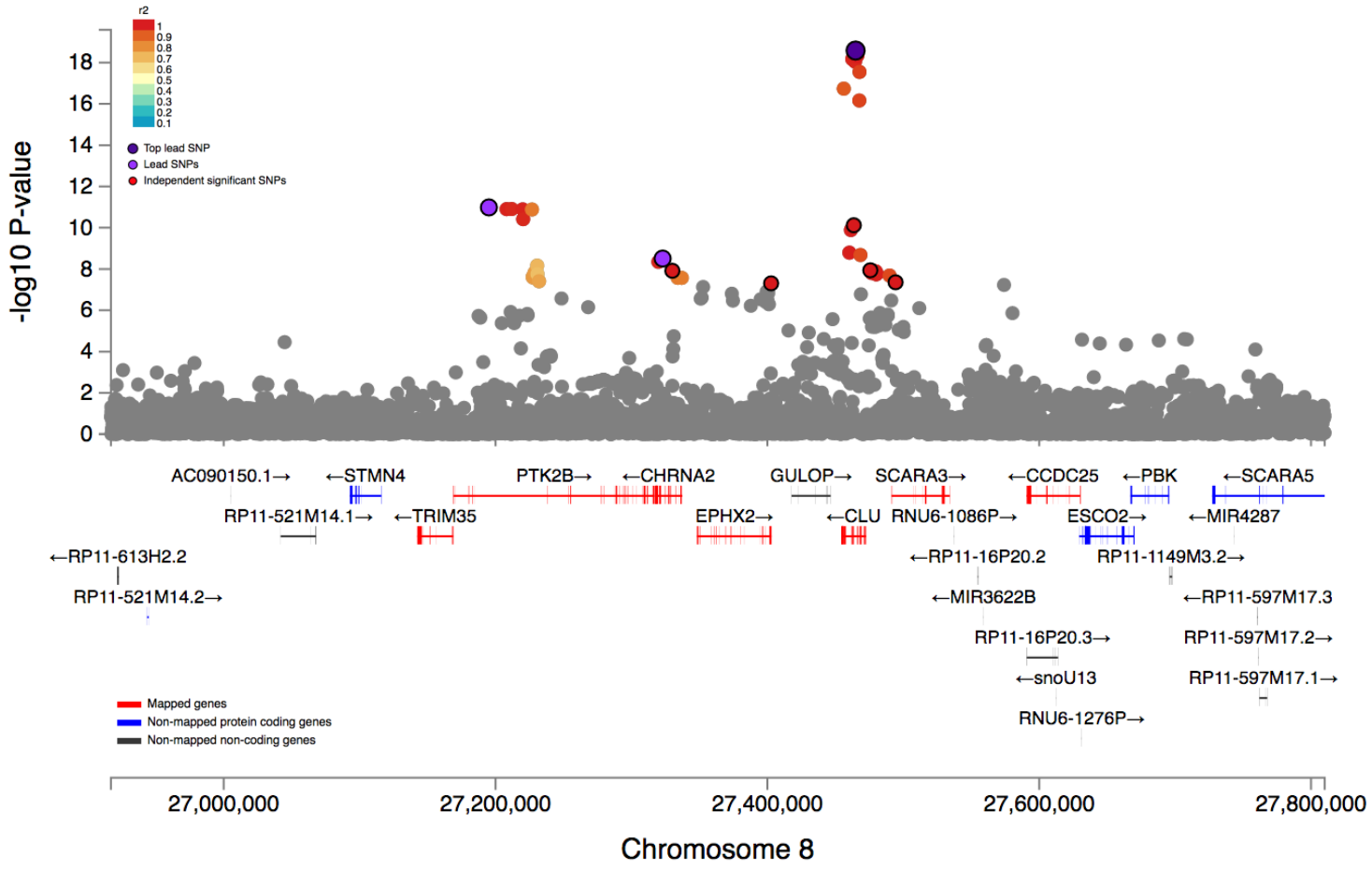

-log10 P-value
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
C4A→ ←TNXB ←PRRT1 ←C6orf10 HLA-DRA→ ←RNU1-61P ←HLA-DQB1 ←HLA-DOB HLA-Z→ BRD2→
←TNXA ←ATF6B RNF5→ HNRNPA1P2→ ←HLA-DRB9 ←HLA-DRB1 ←MTCO3P1 ←TAP2 ←HLA-DMB
←DXO C4B→ ←FKBPL←PBX2 RNU6-603P→ ←HLA-DRB5 HLA-DQA1→ HLA-DQA2→ ←PPP1R2P1
STK19→ ←RNA5SP206 PPT2→ HCG23→ ←HLA-DRB6 XXbac-BPG254F23.7→ PSMB9→ ←HLA-DMA
←C4A-AS1 PPT2-EGFL8→ ←BTNL2 HLA-DQB1-AS1→ ←PSMB8 ←AL645941.1
EGFL8→ ←XXbac-BPG254F23.6 TAPSAR1→ BRD2-IT1→
SKIV2L→ ←AGPAT1 ←HLA-DQB3 ←TAP1
CYP21A1P→ ←AGER ←MIR3135B ←XXbac-BPG181M17.5
←AL645922.1 ←XXbac-BPG300A18.13 ←HLA-DQB2 ←XXbac-BPG181M17.6
STK19P→ ←GPSM3
←C4B-AS1 ←NOTCH4
CYP21A2→ XXbac-BPG154L12.4→
32,000,000
32,200,000
32,400,000
32,600,000
32,800,000
Chromosome 6
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
-log10 P-value
r2
Top lead SNP
Lead SNPs
Independent significant SNPs
←LRFN2 ←RP11-570K4.1 ←UNC5CL NFYA→ ←TREML1 TREML4→ NCR2→ ←RP11-328M4.2
←RP3-462C17.1 ←OARD1 ←TREM2 RNA5SP207 AL136967.1→ RP11-328M4.3→
←RP11-121P10.1 TSPO2 ADCY10P1↔TREML2 ←TREM1 FOXP4→
APOBEC2→ ←TREML3P RNU6-643P
TREML5P→
←RP1-229K20.5
←RP13-235E23.1
40,600,000
40,800,000
41,000,000
41,200,000
41,400,000
Chromosome 6
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes

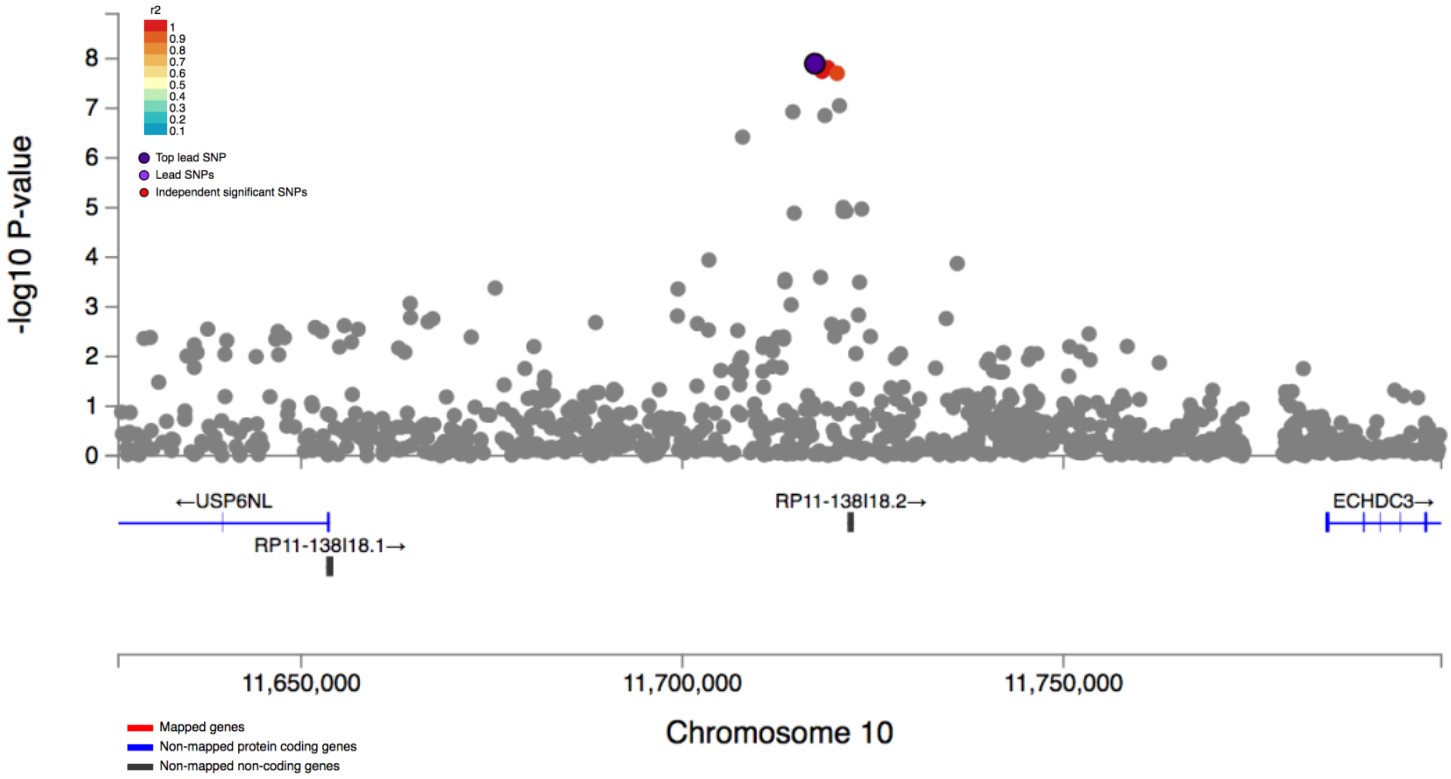

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
10
9
8
7
6
5
4
3
2
1
0
←TNFRSF21
←AL355353.1
CD2AP→
GPR111→
OPN5→
←PTCHD4
RP11-157D6.1→
Y_RNA→
GPR115→
RNU1-105P→
←RP11-385F7.1
RN7SKP116→
RP11-812I20.2→
←RP11-550C4.6
←RP11-550C4.4
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
47,200,000
47,400,000
47,600,000
47,800,000
Chromosome 6

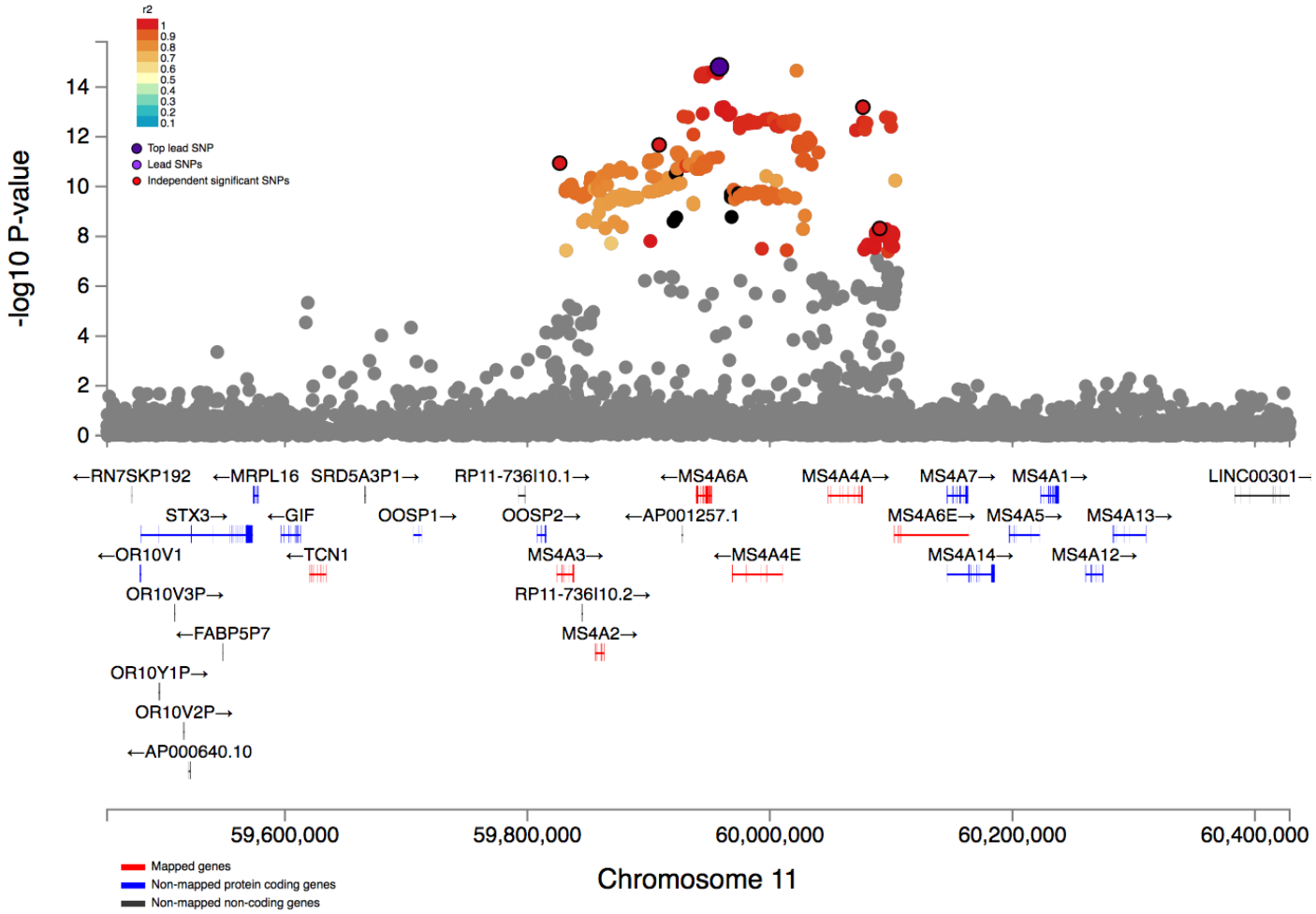

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
14
12
10
8
6
4
2
0
←CYP3A4
CYP3A52P→
←AZGP1
ZSCAN21→
←C7orf43
←GATS
SPDYE3→
←ZCWPW1
←RN7SL416P
←TFR2
POP7→
ZAN→
SLC12A9→
CYP3A43→
←GJC3
ZKSCAN1→
←TAF6
←GPC2
←PMS2P1
MEPCE→
AGFG2→
←ACTL6B
EPO→
←EPHB4
SRRT→
←OR2AE1
AZGP1P1→
←ZNF3
LAMTOR4→
←Y_RNA
←PPP1R35
RP11-44M6.3→
GNB2→
←RN7SL750P
RP11-757A13.1→
←TRIM4
COPS6→
STAG3→
STAG3L5P→
←C7orf61
←LRCH4
←GIGYF1
←RP11-126L15.4
CTD-3244O18.7→
RP4-604G5.3→
AP4M1→
PVRIG→
PILRB→
RN7SL161P→
←SAP25
TRIP6→
CTD-3244O18.5→
←MCM7
←AC005071.1
PVRIG2P→
←TSC22D4
FBXO24→
←UFSP1
RP4-604G5.1→
←MIR25
STAG3L5P-PVRIG2P-PILRB→
←PCOLCE-AS1
←ACHE
Y_RNA→
←MIR93
PILRA→
NYAP1→
PCOLCE→
←RN7SL549P
SNORA40→
←MIR106B
RP11-758P17.2→
MOSPD3→
RP13-650G11.1→
←RP11-506M12.1
RP11-758P17.3→
CNPY4→
←AC092849.1
MBLAC1→
RP11-44M6.1→
AC073842.19→
←RPL7P60
←MIR4658
←GAL3ST4
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
99,400,000
99,600,000
99,800,000
100,000,000
100,200,000
100,400,000
Chromosome 7

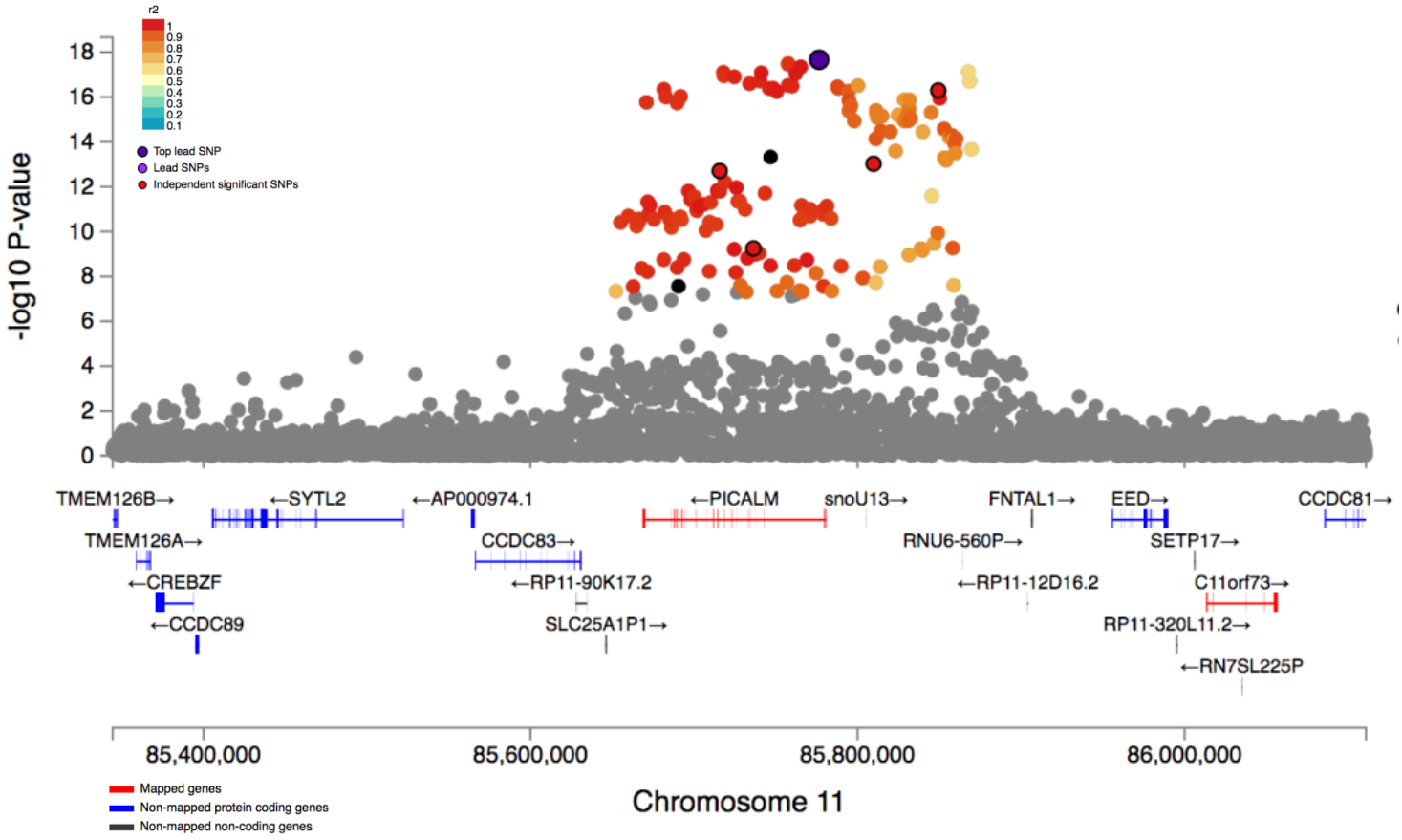

-log10 P-value
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
PIP→
TAS2R40→
CLCN1→
EPHA1-AS1→
FAM115B→
FAM115D→
TAS2R39→
TMEM139→
ZYX→
TAS2R41→
FAM115C→
←AC073342.1
←FAM131B
←OR2R1P
←RP11-61L23.2
GSTK1→
←AC093673.5
←OR10AC1P
←AC073342.12
←EPHA1
←AC073264.10
CASP2→
TAS2R62P→
←PAICSP5
RN7SL535P→
TAS2R60→
CTAGE15→
RN7SL481P→
RNU6-162P→
←HINT1P1
AC073264.6→
RP11-563K23.1→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
142,900,000
143,000,000
143,100,000
143,200,000
143,300,000
143,400,000
Chromosome 7

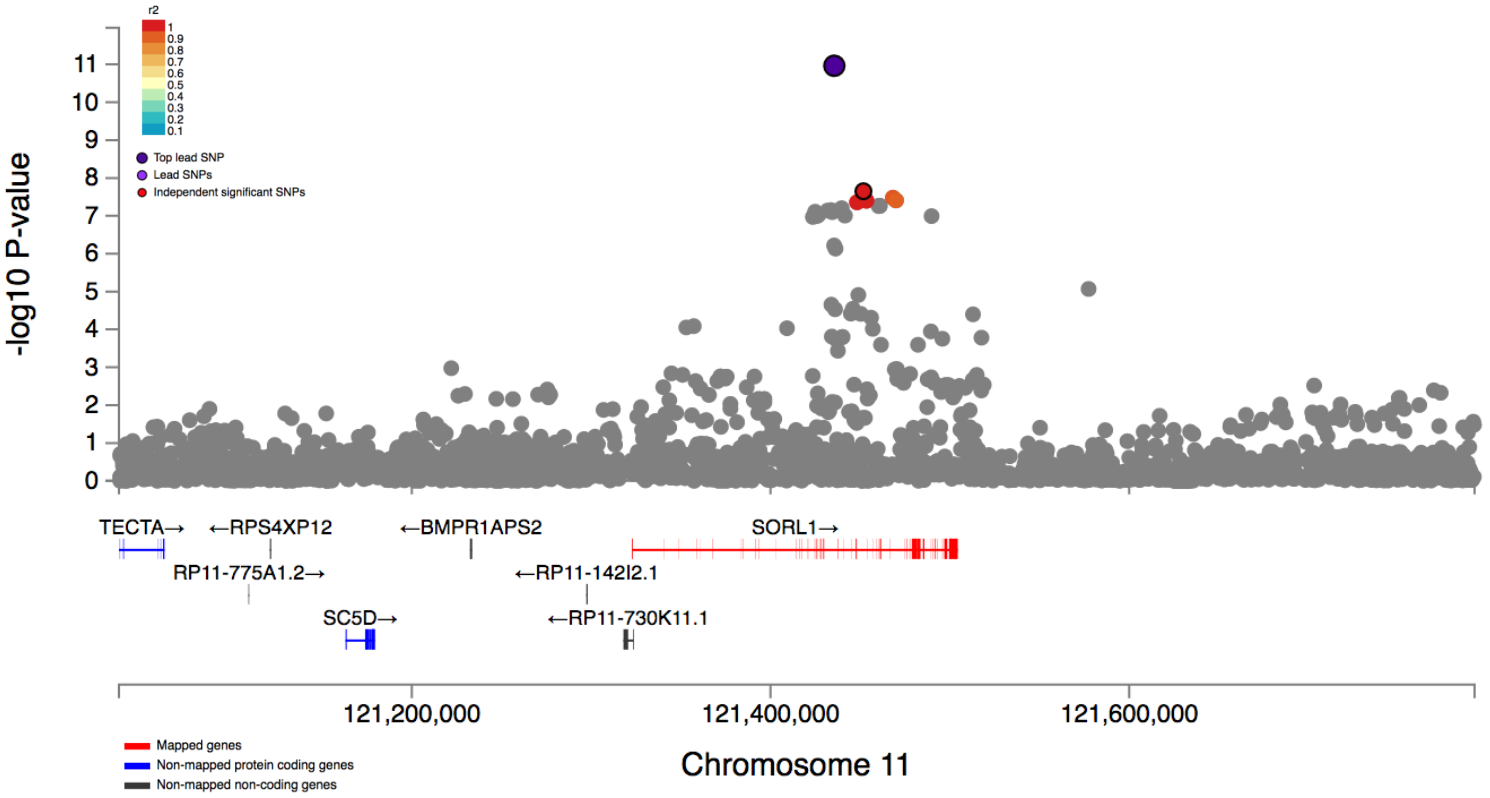

-log10 P-value
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
RN7SL207P→
CNTNAP2→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
145,600,000
145,800,000
146,000,000
146,200,000
Chromosome 7

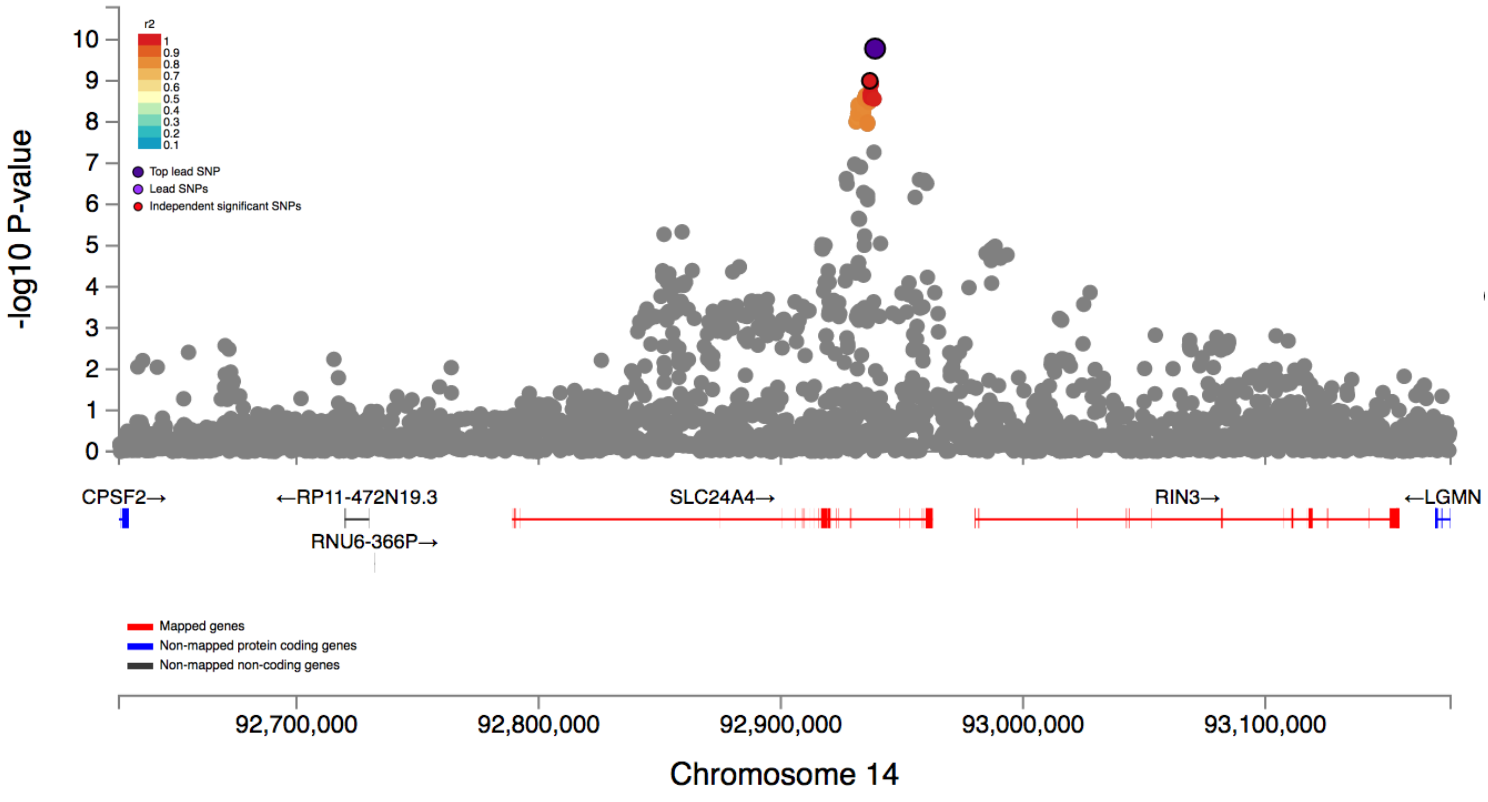

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
2
4
6
8
10
12
14
16
18
AC090150.1→
←STMN4
PTK2B→
←CHRNA2
GULOP→
SCARA3→
←CCDC25
←PBK
←SCARA5
RP11-521M14.1→
←TRIM35
EPHX2→
←CLU
RNU6-1086P→
ESCO2→
←MIR4287
←RP11-613H2.2
←RP11-16P20.2
RP11-1149M3.2→
RP11-521M14.2→
←MIR3622B
←RP11-597M17.3
RP11-16P20.3→
RP11-597M17.2→
←snoU13
RP11-597M17.1→
RNU6-1276P→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
27,000,000
27,200,000
27,400,000
27,600,000
27,800,000
Chromosome 8

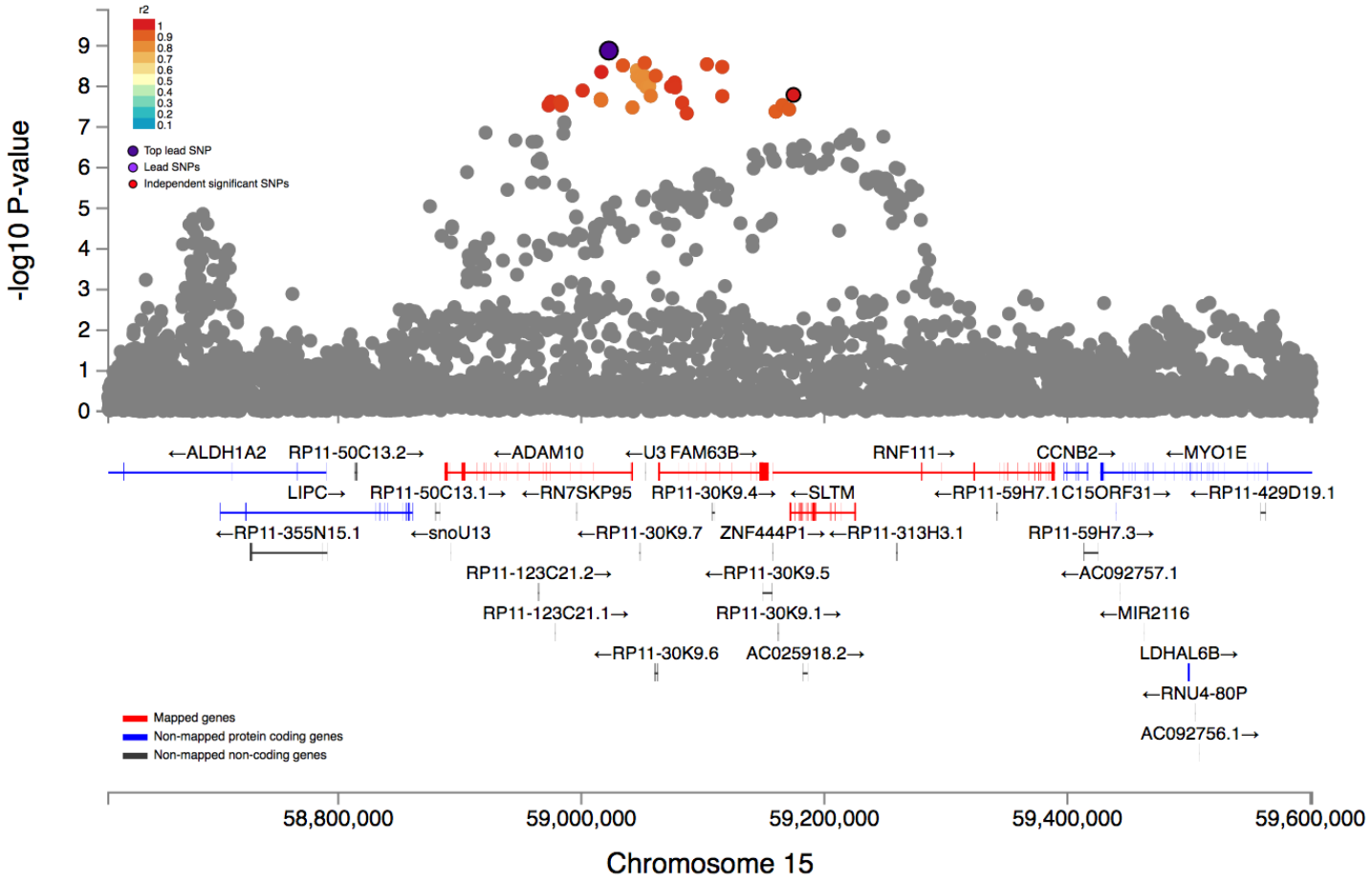

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
←USP6NL
RP11-138I18.1→
RP11-138I18.2→
ECHDC3→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
11,650,000
11,700,000
11,750,000
Chromosome 10

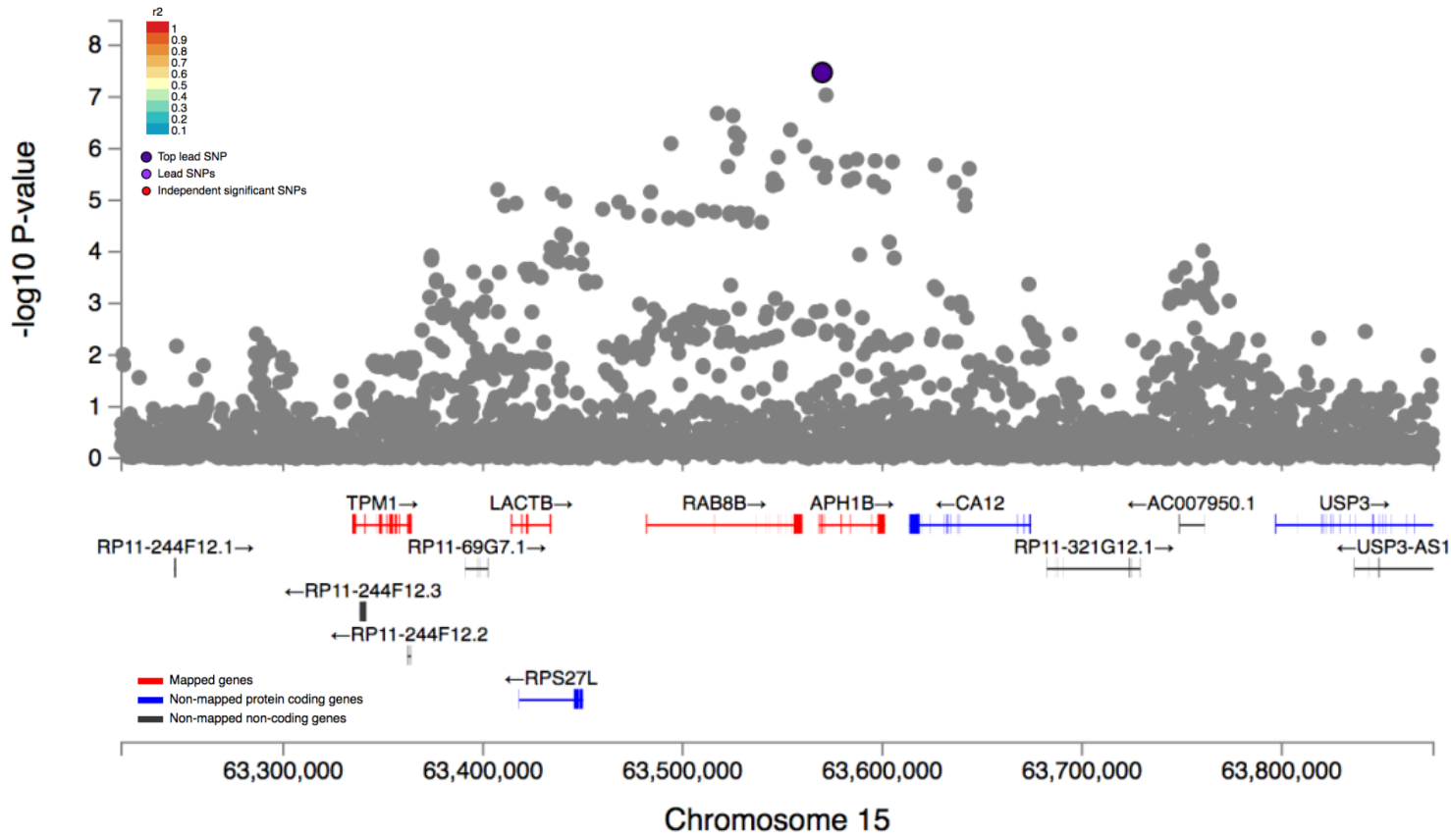

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
2
4
6
8
10
12
14
←RN7SKP192
←MRPL16
SRD5A3P1→
RP11-736I10.1→
←MS4A6A
MS4A4A→
MS4A7→
MS4A1→
LINC00301←
STX3→
←GIF
OOSP1→
OOSP2→
←AP001257.1
MS4A6E→
MS4A5→
MS4A13→
←OR10V1
←TCN1
MS4A3→
←MS4A4E
MS4A14→
MS4A12→
OR10V3P→
RP11-736I10.2→
←FABP5P7
MS4A2→
OR10Y1P→
OR10V2P→
←AP000640.10
59,600,000
59,800,000
60,000,000
60,200,000
60,400,000
Chromosome 11
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes

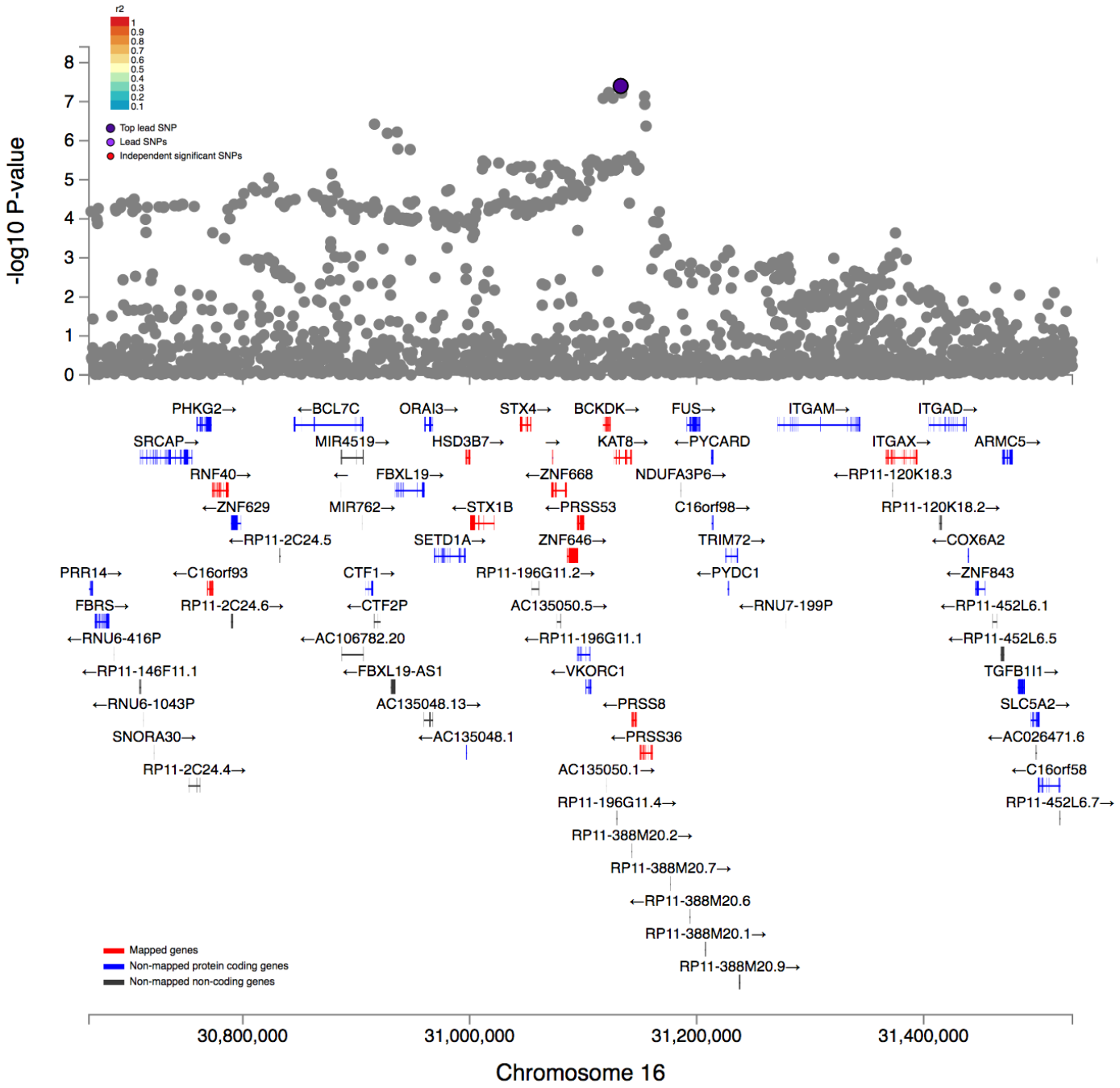

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
2
4
6
8
10
12
14
16
18
TMEM126B→
←SYTL2
←AP000974.1
←PICALM
snoU13→
FNTAL1→
EED→
CCDC81→
TMEM126A→
CCDC83→
RNU6-560P→
SETP17→
←CREBZF
←RP11-90K17.2
←RP11-12D16.2
C11orf73→
←CCDC89
SLC25A1P1→
RP11-320L11.2→
←RN7SL225P
85,400,000
85,600,000
85,800,000
86,000,000
Chromosome 11
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes

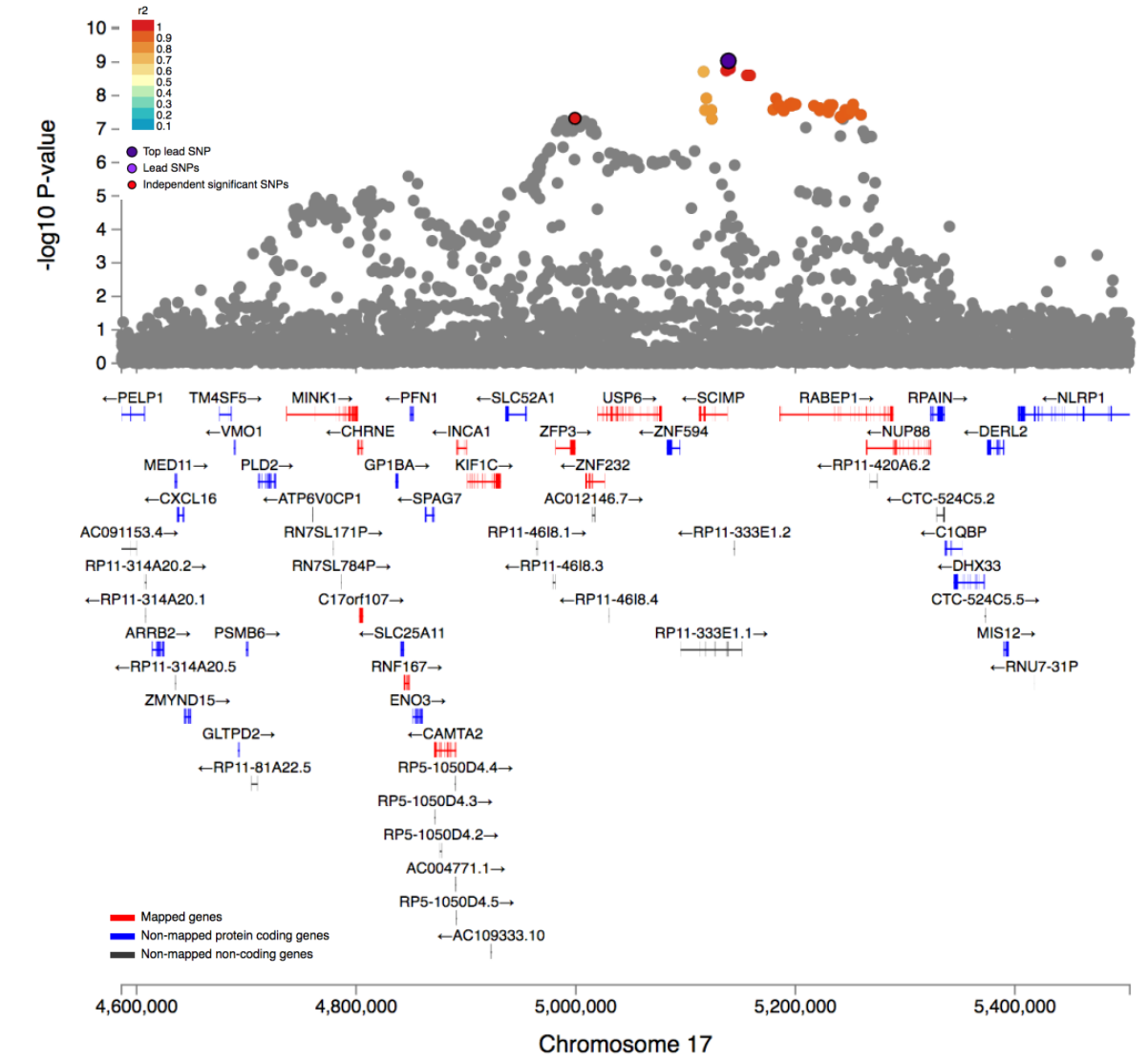

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
11
10
9
8
7
6
5
4
3
2
1
0
TECTA→
←RPS4XP12
←BMPR1APS2
SORL1→
RP11-775A1.2→
←RP11-142I2.1
SC5D→
←RP11-730K11.1
121,200,000
121,400,000
121,600,000
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
Chromosome 11

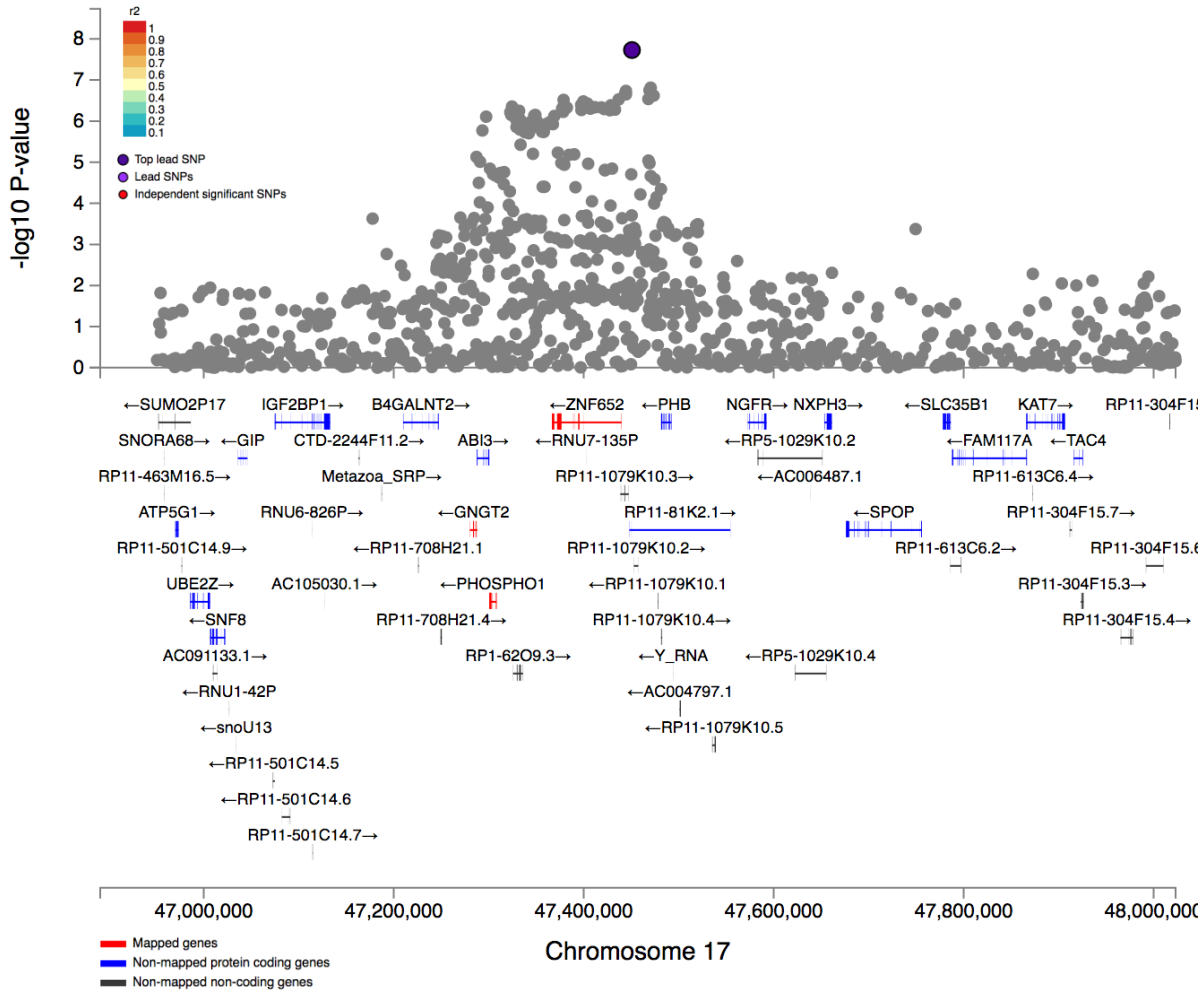

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
10
9
8
7
6
5
4
3
2
1
0
CPSF2→
←RP11-472N19.3
RNU6-366P→
SLC24A4→
RIN3→
←LGMN
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
92,700,000
92,800,000
92,900,000
93,000,000
93,100,000
Chromosome 14

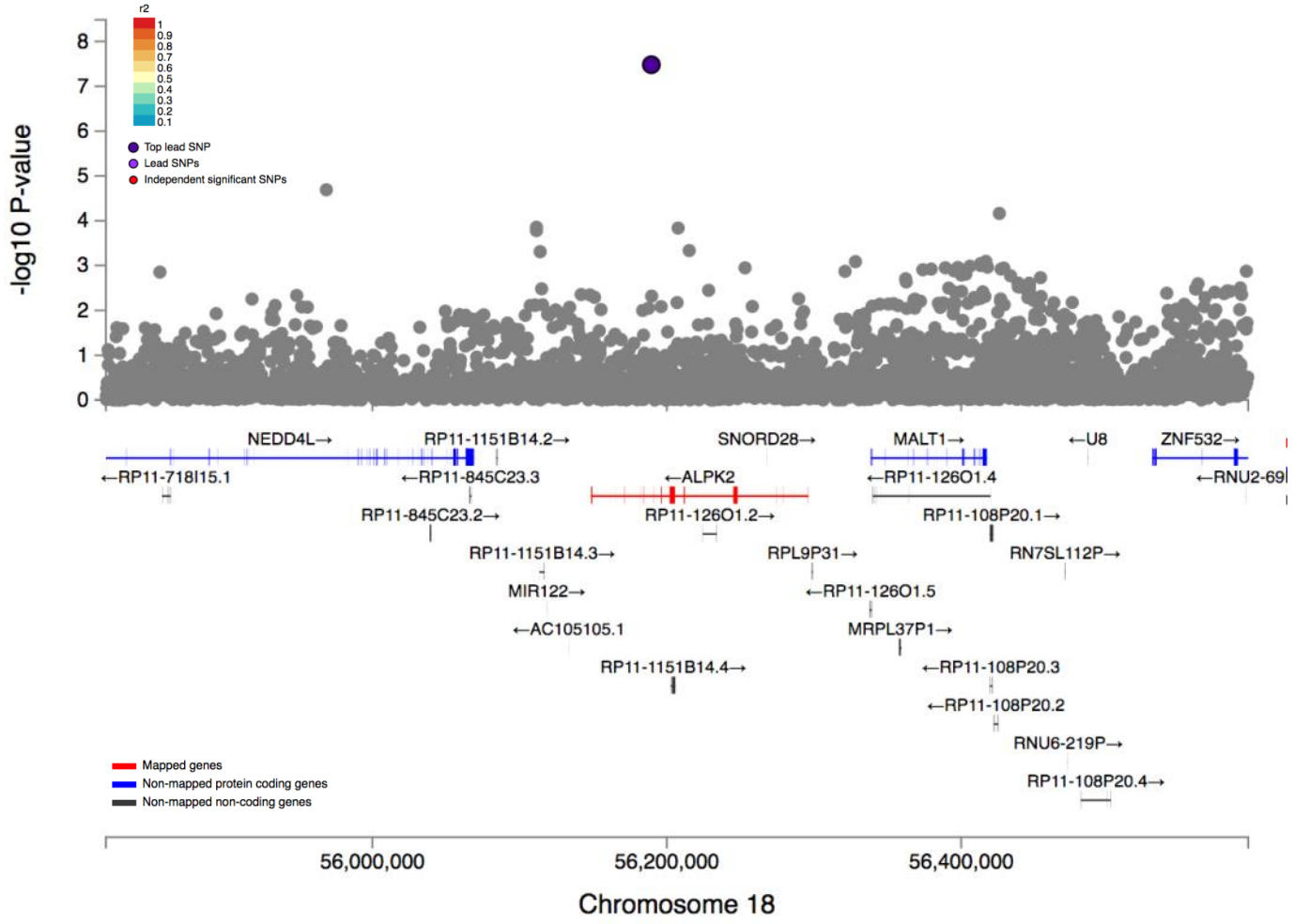

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
9
←ALDH1A2
RP11-50C13.2→
←ADAM10
←U3 FAM63B→
RNF111→
CCNB2→
←MYO1E
LIPC→
RP11-50C13.1→
←RN7SKP95
RP11-30K9.4→
←SLTM
←RP11-59H7.1
C15ORF31→
←RP11-429D19.1
←RP11-355N15.1
←snoU13
←RP11-30K9.7
ZNF444P1→
←RP11-313H3.1
RP11-59H7.3→
RP11-123C21.2→
←RP11-30K9.5
←AC092757.1
RP11-123C21.1→
RP11-30K9.1→
←MIR2116
←RP11-30K9.6
AC025918.2→
LDHAL6B→
←RNU4-80P
AC092756.1→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
58,800,000
59,000,000
59,200,000
59,400,000
59,600,000
Chromosome 15

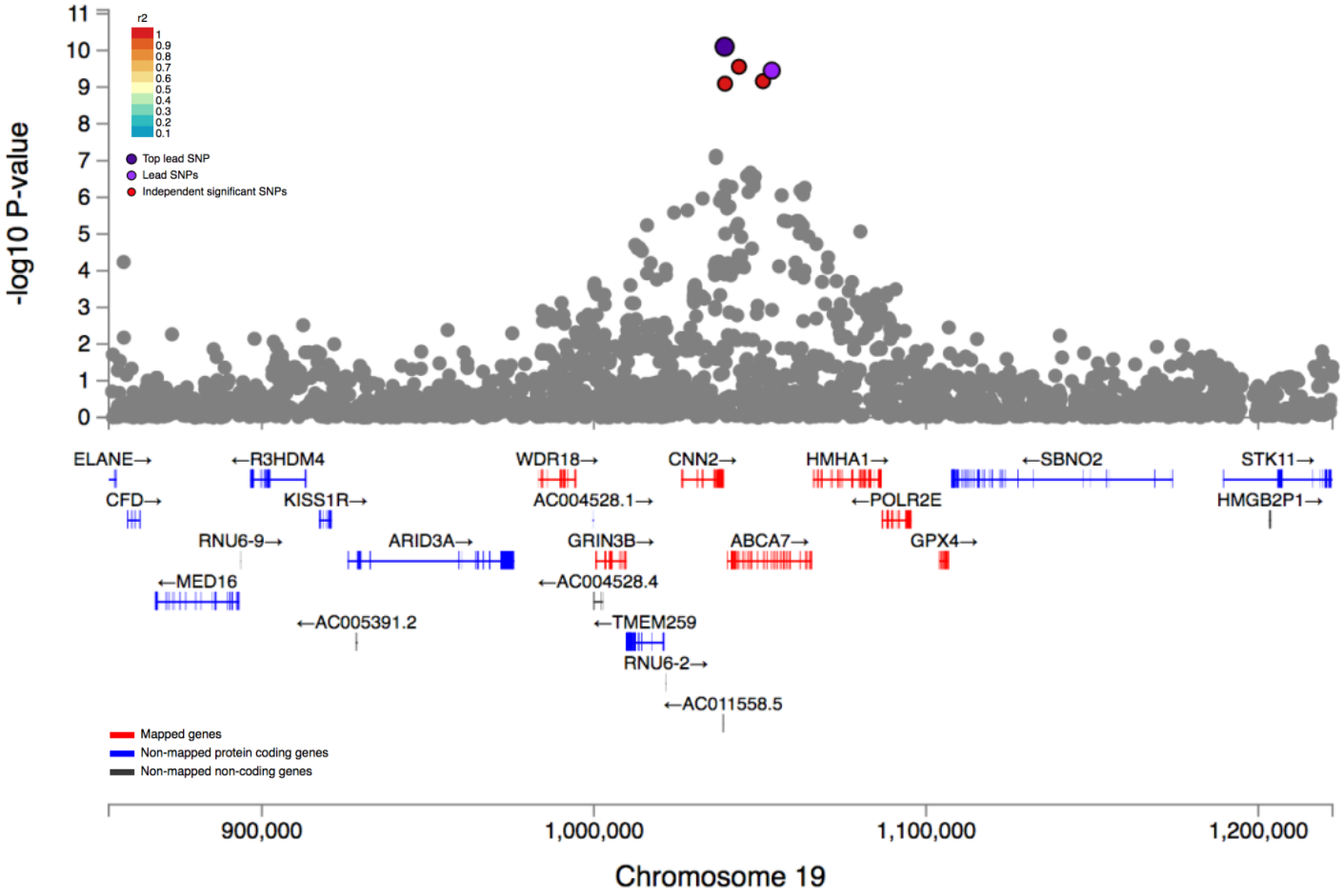

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
TPM1→
LACTB→
RAB8B→
APH1B→
←CA12
←AC007950.1
USP3→
RP11-244F12.1→
RP11-69G7.1→
RP11-321G12.1→
←USP3-AS1
←RP11-244F12.3
←RP11-244F12.2
←RPS27L
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
63,300,000
63,400,000
63,500,000
63,600,000
63,700,000
63,800,000
Chromosome 15

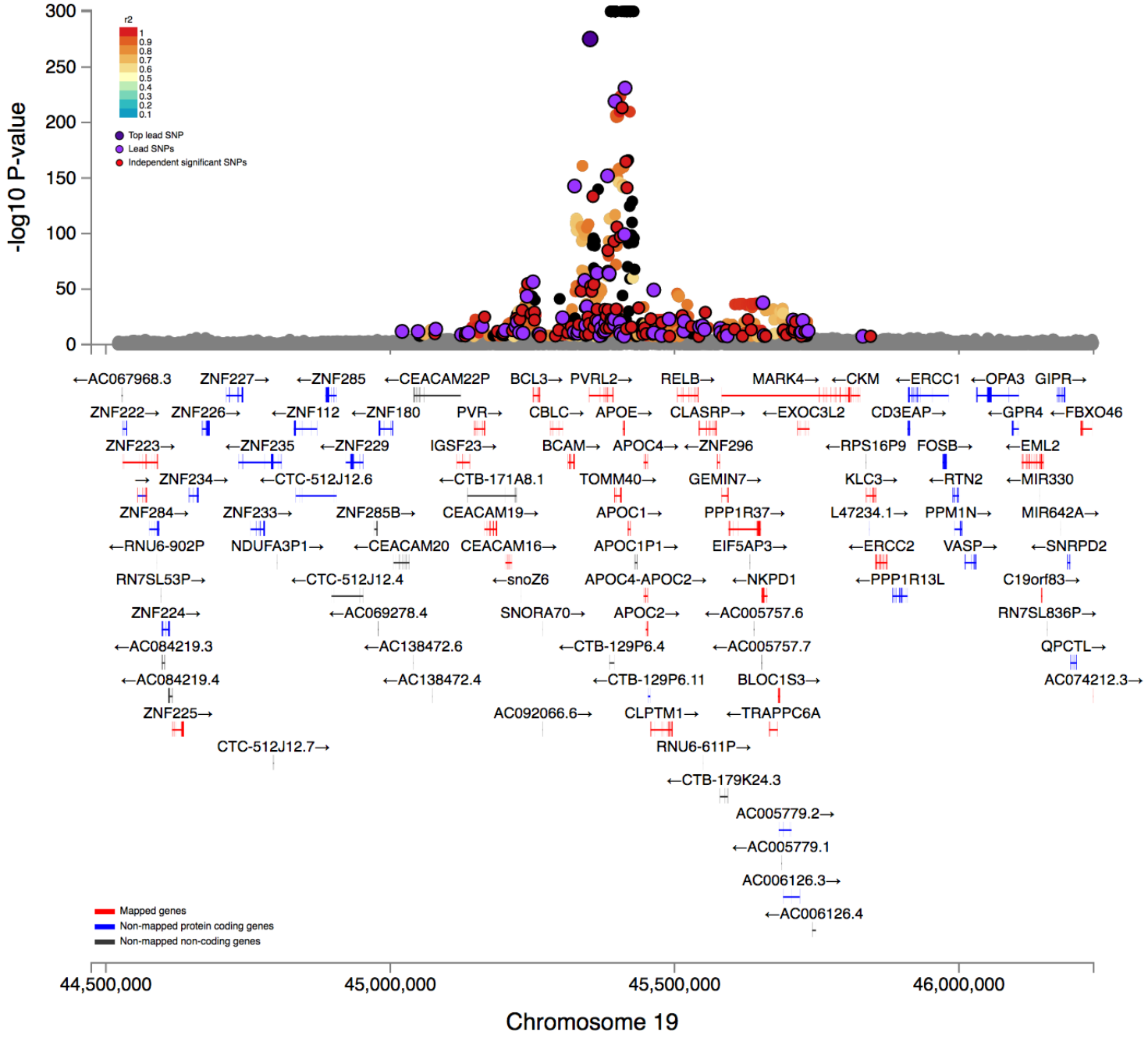

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
0
1
2
3
4
5
6
7
8
PHKG2→
←BCL7C
ORAI3→
STX4→
BCKDK→
FUS→
ITGAM→
ITGAD→
SRCAP→
MIR4519→
HSD3B7→
→
KAT8→
←PYCARD
ITGAX→
ARMC5→
RNF40→
←
FBXL19→
←ZNF668
NDUFA3P6→
←RP11-120K18.3
←ZNF629
MIR762→
←STX1B
←PRSS53
C16orf98→
RP11-120K18.2→
←RP11-2C24.5
SETD1A→
ZNF646→
TRIM72→
←COX6A2
PRR14→
←C16orf93
CTF1→
RP11-196G11.2→
←PYDC1
←ZNF843
FBRS→
RP11-2C24.6→
←CTF2P
AC135050.5→
←RNU7-199P
←RP11-452L6.1
←RNU6-416P
←AC106782.20
←RP11-196G11.1
←RP11-452L6.5
←RP11-146F11.1
←FBXL19-AS1
←VKORC1
TGFB1I1→
←RNU6-1043P
AC135048.13→
←PRSS8
SLC5A2→
SNORA30→
←AC135048.1
←PRSS36
←AC026471.6
RP11-2C24.4→
AC135050.1→
←C16orf58
RP11-196G11.4→
RP11-452L6.7→
RP11-388M20.2→
RP11-388M20.7→
←RP11-388M20.6
RP11-388M20.1→
RP11-388M20.9→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
30,800,000
31,000,000
31,200,000
31,400,000
Chromosome 16

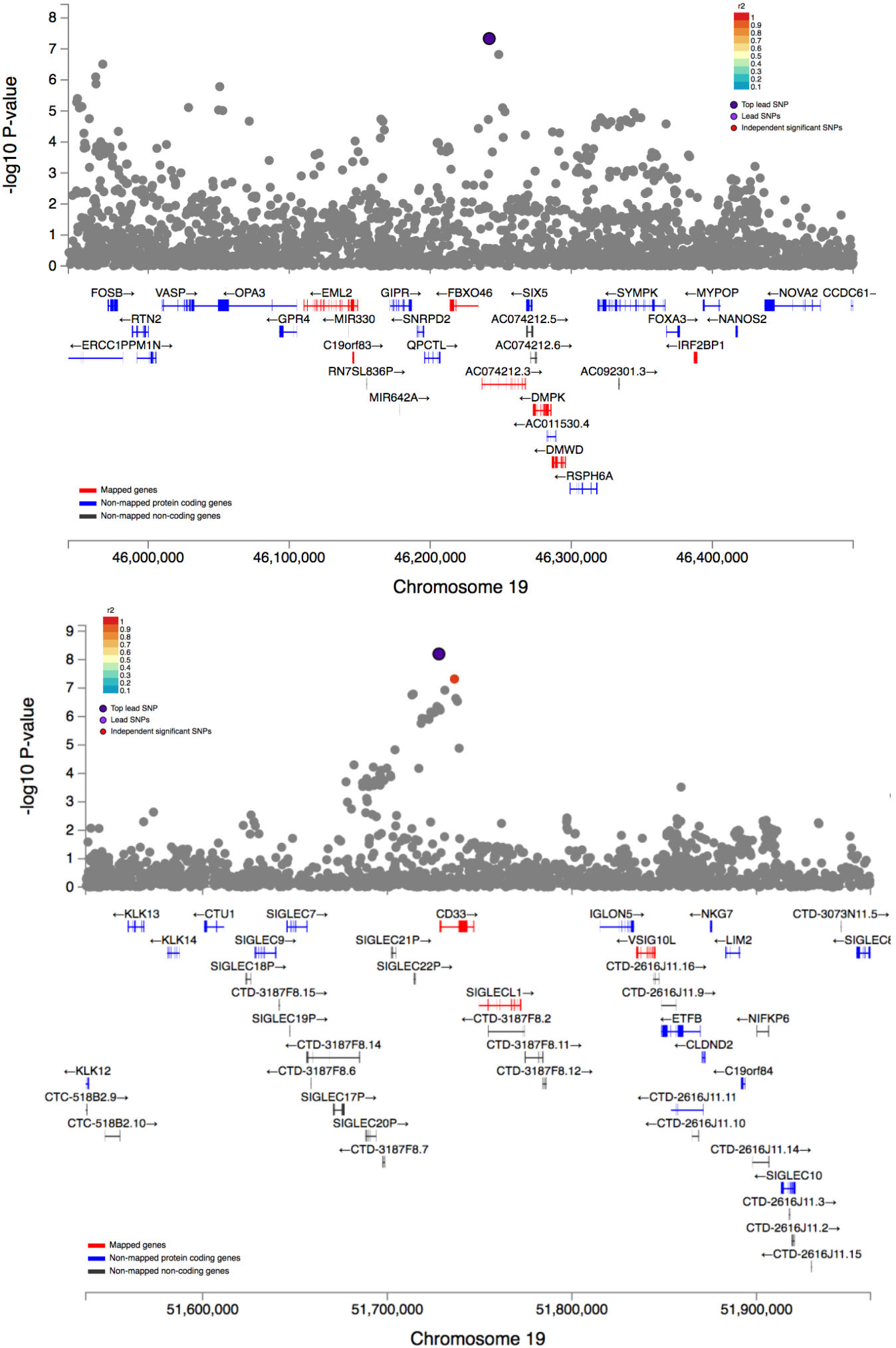

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
10
9
8
7
6
5
4
3
2
1
0
←PELP1
TM4SF5→
MINK1→
←PFN1
←SLC52A1
USP6→
←SCIMP
RABEP1→
RPAIN→
←NLRP1
←VMO1
←CHRNE
←INCA1
ZFP3→
←ZNF594
←NUP88
←DERL2
MED11→
PLD2→
GP1BA→
KIF1C→
←ZNF232
←RP11-420A6.2
←CXCL16
←ATP6V0CP1
←SPAG7
AC012146.7→
←CTC-524C5.2
AC091153.4→
RN7SL171P→
RP11-46I8.1→
←RP11-333E1.2
←C1QBP
RP11-314A20.2→
RN7SL784P→
←RP11-46I8.3
←DHX33
←RP11-314A20.1
C17orf107→
←RP11-46I8.4
CTC-524C5.5→
ARRB2→
PSMB6→
←SLC25A11
RP11-333E1.1→
MIS12→
←RP11-314A20.5
RNF167→
←RNU7-31P
ZMYND15→
ENO3→
GLTPD2→
←CAMTA2
←RP11-81A22.5
RP5-1050D4.4→
RP5-1050D4.3→
RP5-1050D4.2→
AC004771.1→
RP5-1050D4.5→
←AC109333.10
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
4,600,000
4,800,000
5,000,000
5,200,000
5,400,000
Chromosome 17

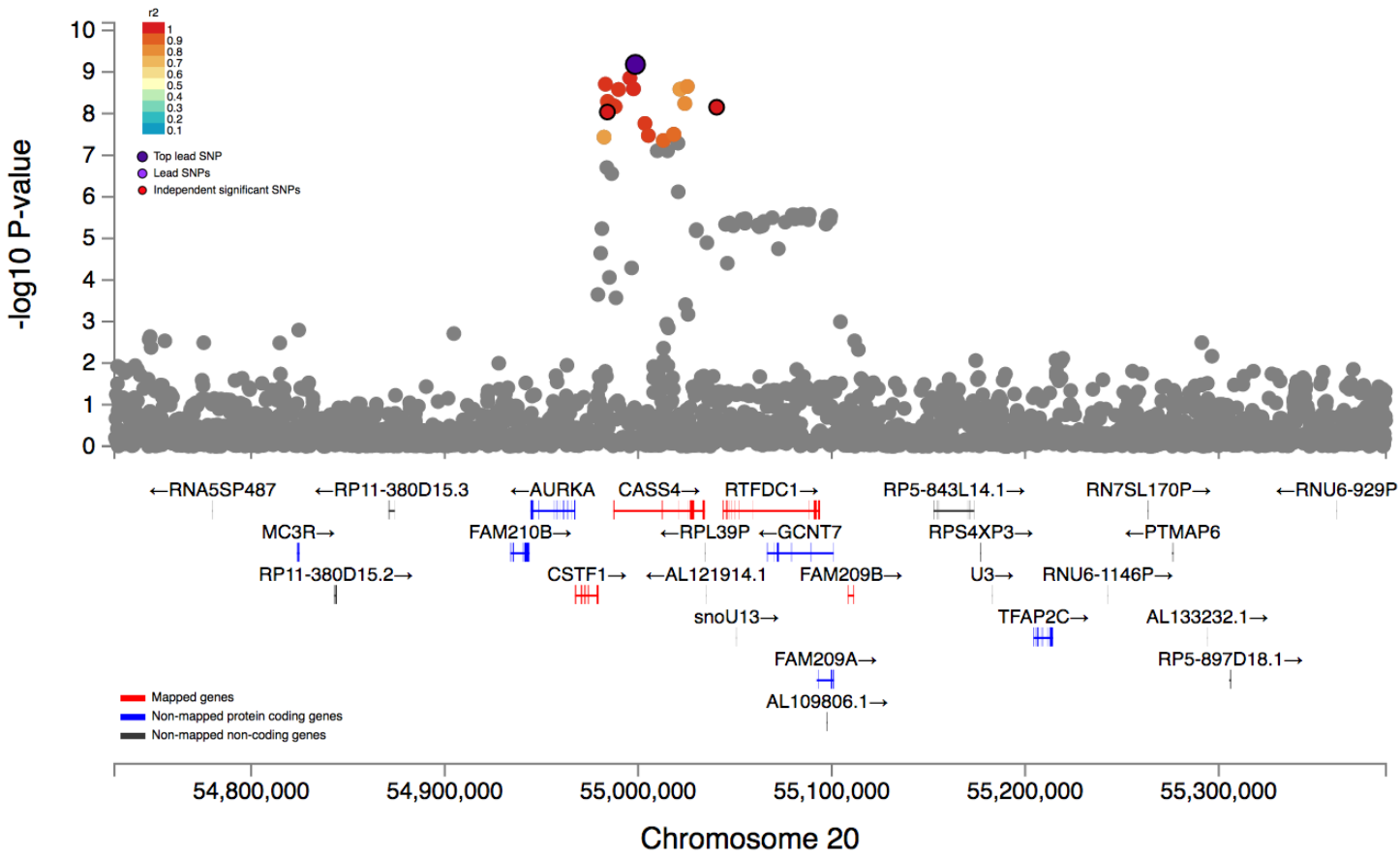

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
8
7
6
5
4
3
2
1
0
←SUMO2P17
IGF2BP1→
B4GALNT2→
←ZNF652
←PHB
NGFR→
NXPH3→
←SLC35B1
KAT7→
SNORA68→
←GIP
CTD-2244F11.2→
ABI3→
←RNU7-135P
←RP5-1029K10.2
←FAM117A
←TAC4
RP11-463M16.5→
Metazoa_SRP→
RP11-1079K10.3→
←AC006487.1
RP11-613C6.4→
ATP5G1→
RNU6-826P→
←GNGT2
RP11-81K2.1→
←SPOP
RP11-304F15.7→
RP11-501C14.9→
←RP11-708H21.1
RP11-1079K10.2→
RP11-613C6.2→
UBE2Z→
AC105030.1→
←PHOSPHO1
←RP11-1079K10.1
RP11-304F15.3→
←SNF8
RP11-708H21.4→
RP11-1079K10.4→
RP11-304F15.4→
AC091133.1→
RP1-62O9.3→
←Y_RNA
←RP5-1029K10.4
←RNU1-42P
←AC004797.1
←snoU13
←RP11-1079K10.5
←RP11-501C14.5
←RP11-501C14.6
RP11-501C14.7→
47,000,000
47,200,000
47,400,000
47,600,000
47,800,000
48,000,000
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
Chromosome 17


r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
NEDD4L→
RP11-1151B14.2→
SNORD28→
MALT1→
←U8
ZNF532→
←RP11-718I15.1
←RP11-845C23.3
←ALPK2
←RP11-126O1.4
←RNU2-69
RP11-845C23.2→
RP11-126O1.2→
RP11-108P20.1→
RP11-1151B14.3→
RPL9P31→
RN7SL112P→
MIR122→
←RP11-126O1.5
←AC105105.1
MRPL37P1→
RP11-1151B14.4→
←RP11-108P20.3
←RP11-108P20.2
RNU6-219P→
RP11-108P20.4→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
56,000,000
56,200,000
56,400,000
Chromosome 18


r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
ELANE→
←R3HDM4
WDR18→
CNN2→
HMHA1→
←SBNO2
STK11→
CFD→
KISS1R→
AC004528.1→
←POLR2E
HMGB2P1→
RNU6-9→
ARID3A→
GRIN3B→
ABCA7→
GPX4→
←MED16
←AC004528.4
←AC005391.2
←TMEM259
RNU6-2→
←AC011558.5
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
900,000
1,000,000
1,100,000
1,200,000
Chromosome 19

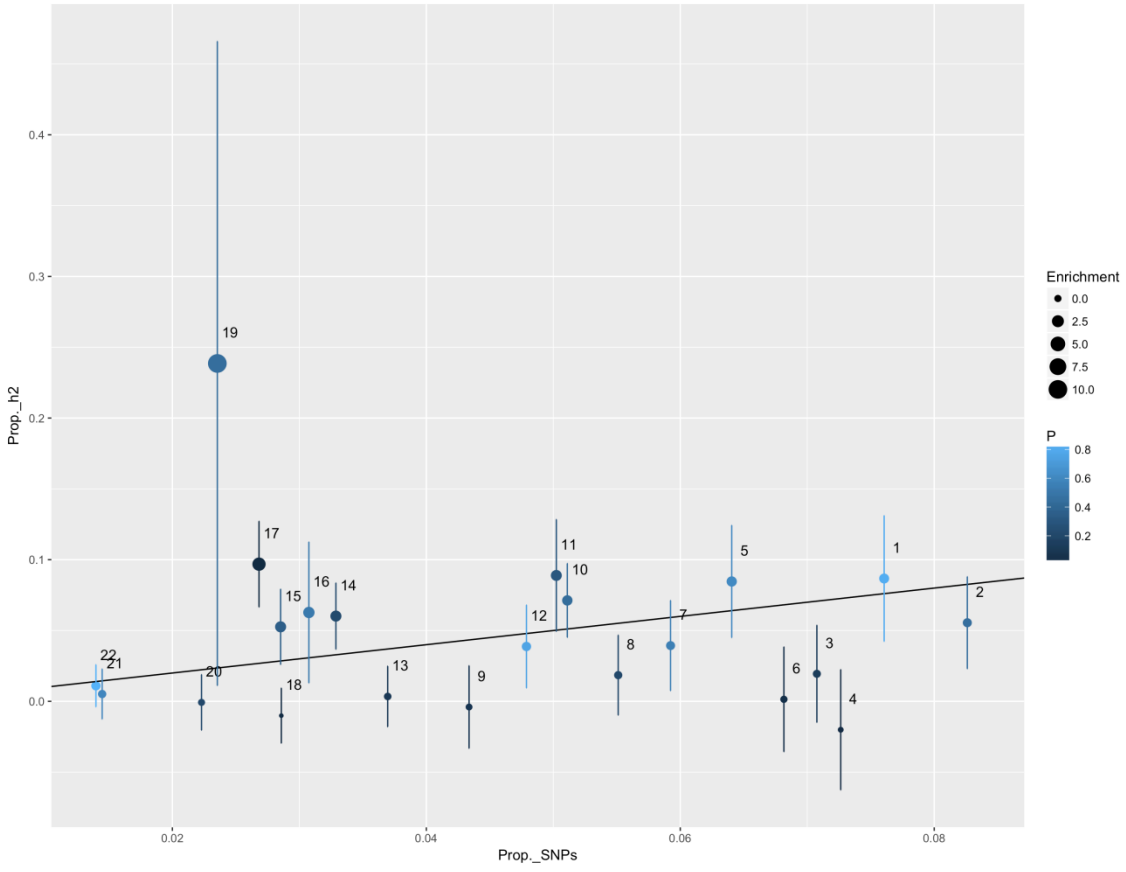

-log10 P-value
300
250
200
150
100
50
0
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
←AC067968.3
ZNF227→
←ZNF285
←CEACAM22P
BCL3→
PVRL2→
RELB→
MARK4→
←CKM
←ERCC1
←OPA3
GIPR→
ZNF222→
ZNF226→
←ZNF112
←ZNF180
PVR→
CBLC→
APOE→
CLASRP→
←EXOC3L2
CD3EAP→
←GPR4
←FBXO46
ZNF223→
←ZNF235
←ZNF229
IGSF23→
BCAM→
APOC4→
←ZNF296
←RPS16P9
FOSB→
←EML2
→ ZNF234→
←CTC-512J12.6
←CTB-171A8.1
TOMM40→
GEMIN7→
KLC3→
←RTN2
←MIR330
ZNF284→
ZNF233→
ZNF285B→
CEACAM19→
APOC1→
PPP1R37→
L47234.1→
PPM1N→
MIR642A→
←RNU6-902P
NDUFA3P1→
←CEACAM20
CEACAM16→
APOC1P1→
EIF5AP3→
←ERCC2
VASP→
←SNRPD2
RN7SL53P→
←CTC-512J12.4
←snoZ6
APOC4-APOC2→
←NKPD1
←PPP1R13L
C19orf83→
ZNF224→
←AC069278.4
SNORA70→
APOC2→
←AC005757.6
RN7SL836P→
←AC084219.3
←AC138472.6
←CTB-129P6.4
←AC005757.7
QPCTL→
←AC084219.4
←AC138472.4
←CTB-129P6.11
BLOC1S3→
AC074212.3→
ZNF225→
AC092066.6→
CLPTM1→
←TRAPPC6A
CTC-512J12.7→
RNU6-611P→
←CTB-179K24.3
AC005779.2→
←AC005779.1
AC006126.3→
←AC006126.4
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
44,500,000
45,000,000
45,500,000
46,000,000
Chromosome 19


-log10 P-value
r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
FOSB→
VASP→
←OPA3
←EML2
GIPR→
←FBXO46
←SIX5
←SYMPK
←MYPOP
←NOVA2
CCDC61–
←RTN2
←GPR4
←MIR330
←SNRPD2
AC074212.5→
FOXA3→
←NANOS2
←ERCC1PPM1N→
C19orf83→
QPCTL→
AC074212.6→
←IRF2BP1
RN7SL836P→
AC074212.3→
AC092301.3→
MIR642A→
←DMPK
←AC011530.4
←DMWD
←RSPH6A
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
46,000,000
46,100,000
46,200,000
46,300,000
46,400,000
Chromosome 19
-log10 P-value
r2
Top lead SNP
Lead SNPs
Independent significant SNPs
←KLK13
←CTU1
SIGLEC7→
CD33→
IGLON5→
←NKG7
CTD-3073N11.5→
←KLK14
SIGLEC9→
SIGLEC21P→
←VSIG10L
←LIM2
←SIGLEC6
SIGLEC18P→
SIGLEC22P→
CTD-2616J11.16→
CTD-3187F8.15→
CTD-2616J11.9→
SIGLECL1→
SIGLEC19P→
←CTD-3187F8.2
←ETFB
←NIFKP6
←CTD-3187F8.14
CTD-3187F8.11→
←CLDND2
←KLK12
←CTD-3187F8.6
CTD-3187F8.12→
←C19orf84
CTC-518B2.9→
SIGLEC17P→
←CTD-2616J11.11
CTC-518B2.10→
SIGLEC20P→
←CTD-2616J11.10
←CTD-3187F8.7
CTD-2616J11.14→
←SIGLEC10
CTD-2616J11.3→
CTD-2616J11.2→
←CTD-2616J11.15
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
51,600,000
51,700,000
51,800,000
51,900,000
Chromosome 19

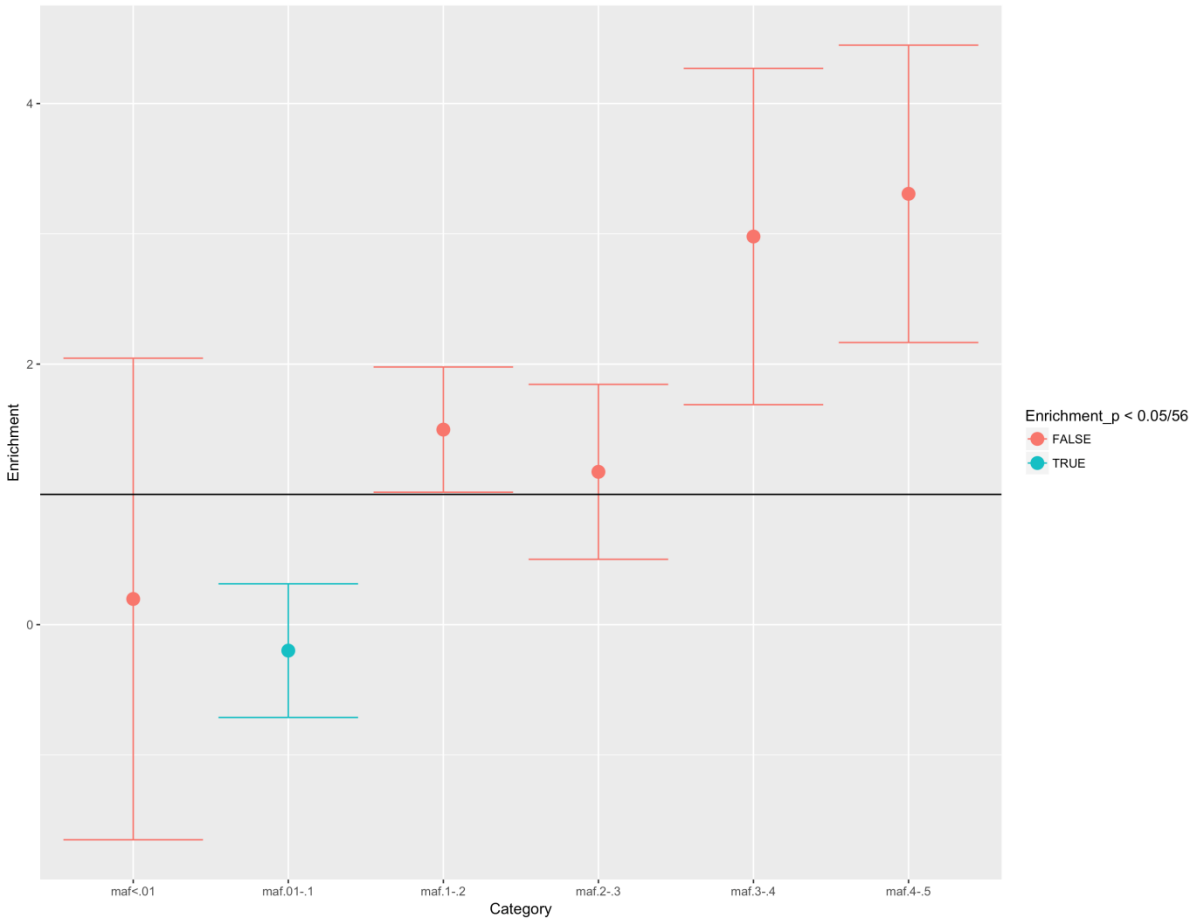

r2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Top lead SNP
Lead SNPs
Independent significant SNPs
-log10 P-value
10
9
8
7
6
5
4
3
2
1
0
←RNA5SP487
←RP11-380D15.3
←AURKA
CASS4→
RTFDC1→
RP5-843L14.1→
RN7SL170P→
←RNU6-929P
MC3R→
FAM210B→
←RPL39P
←GCNT7
RPS4XP3→
←PTMAP6
RP11-380D15.2→
CSTF1→
←AL121914.1
FAM209B→
U3→
RNU6-1146P→
snoU13→
TFAP2C→
AL133232.1→
FAM209A→
RP5-897D18.1→
AL109806.1→
Mapped genes
Non-mapped protein coding genes
Non-mapped non-coding genes
54,800,000
54,900,000
55,000,000
55,100,000
55,200,000
55,300,000
Chromosome 20

Supplementary Figure 3. Partitioned heritability results for the meta-analysis. Variants were binned by chromosome or minor allele frequency and tested for a significant over- or underrepresentation as to what is expected by chance. A) Enrichment results for heritability calculations where variants have been partitioned per chromosome. B) Enrichment results for heritability calculations where variants have been partitioned into multiple categories based on minor allele frequency.

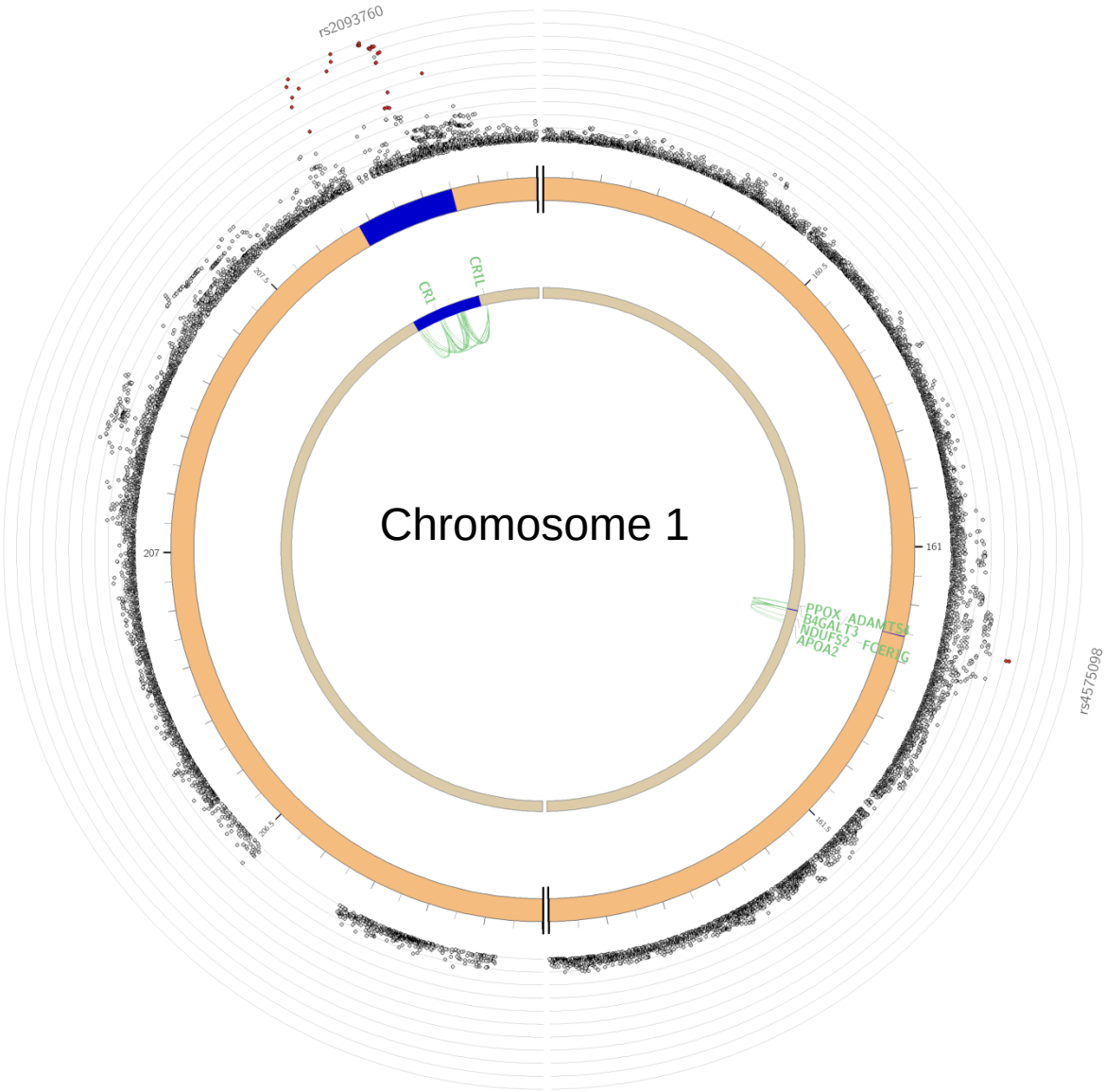
A

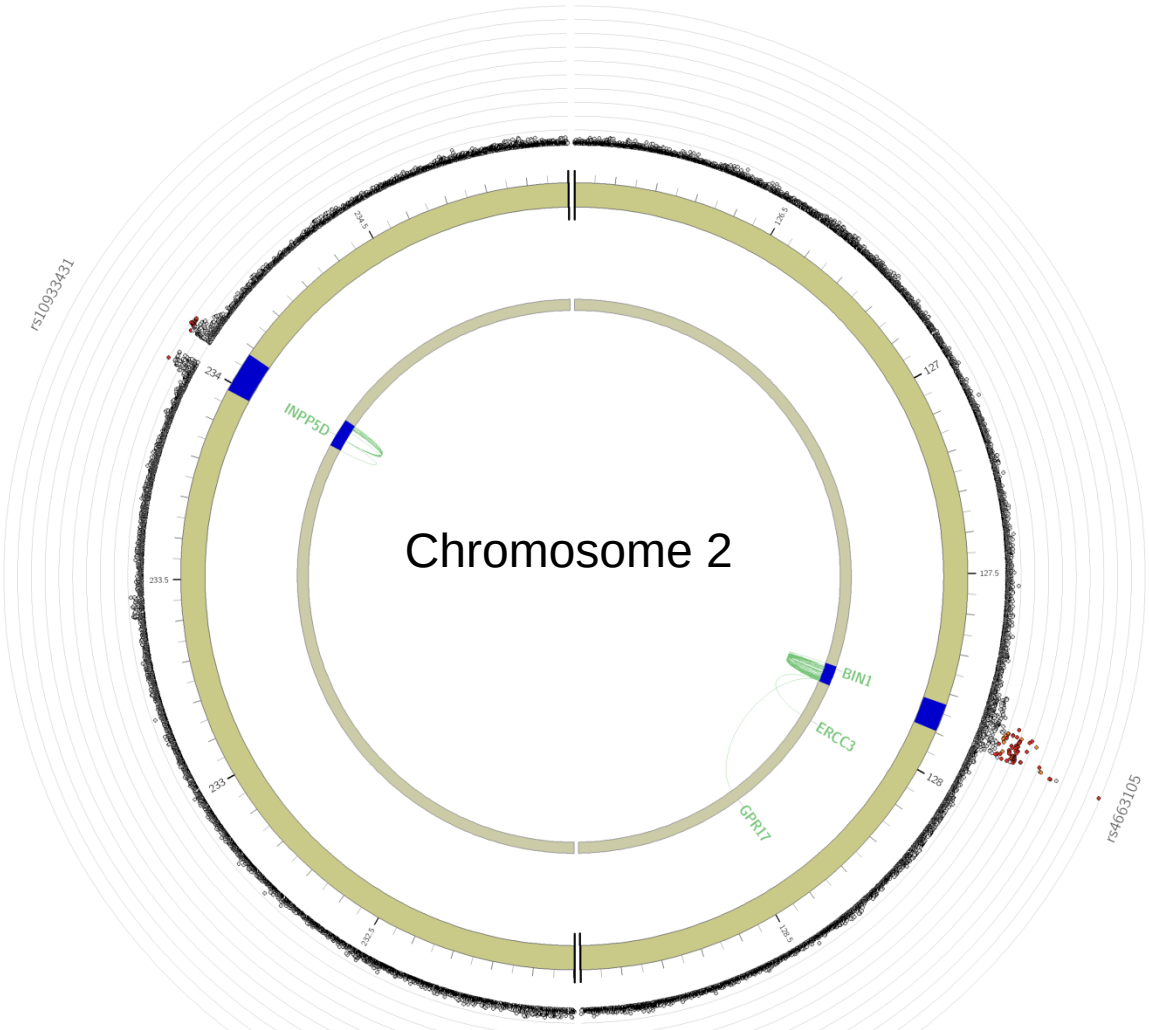


B

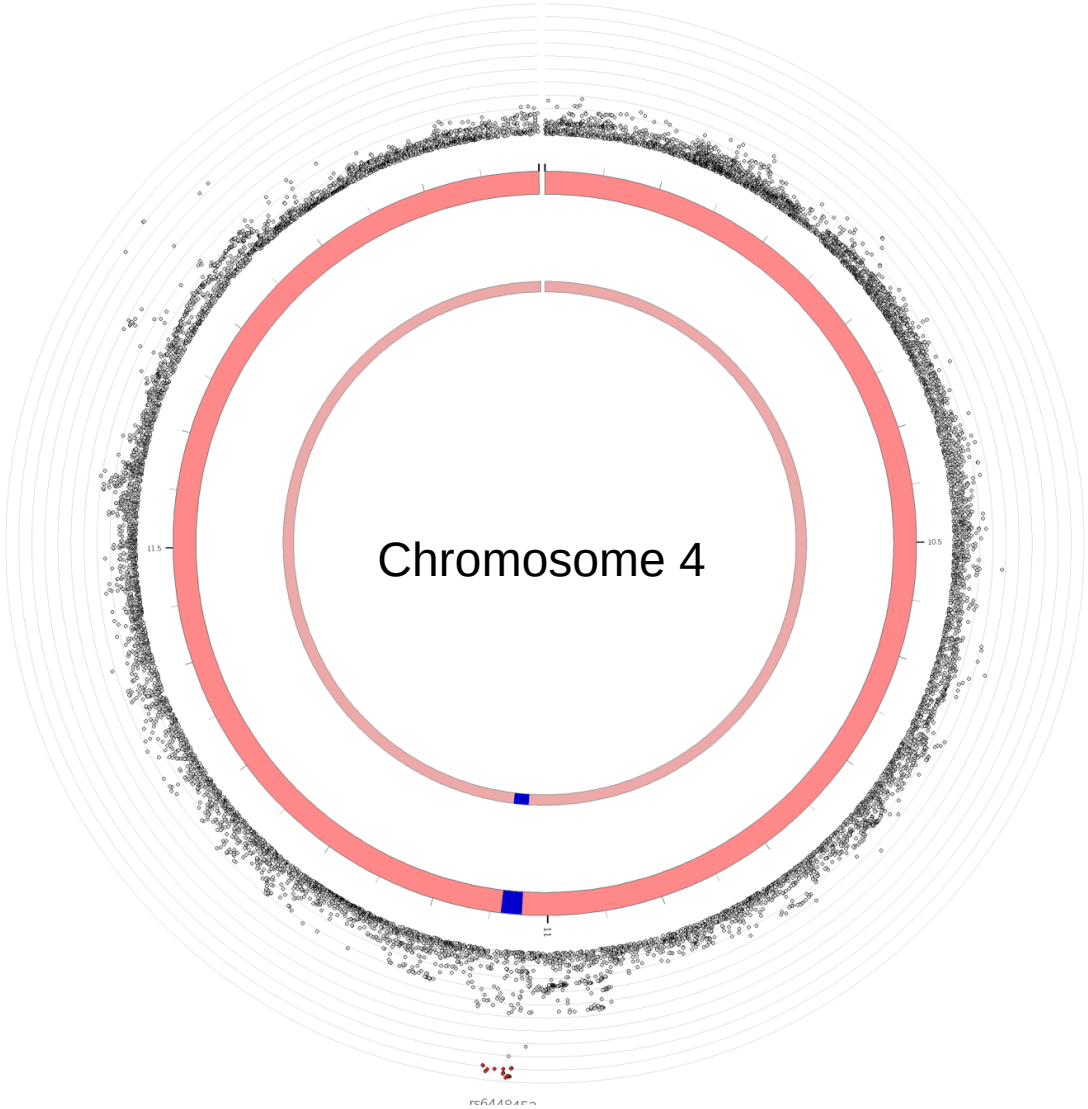


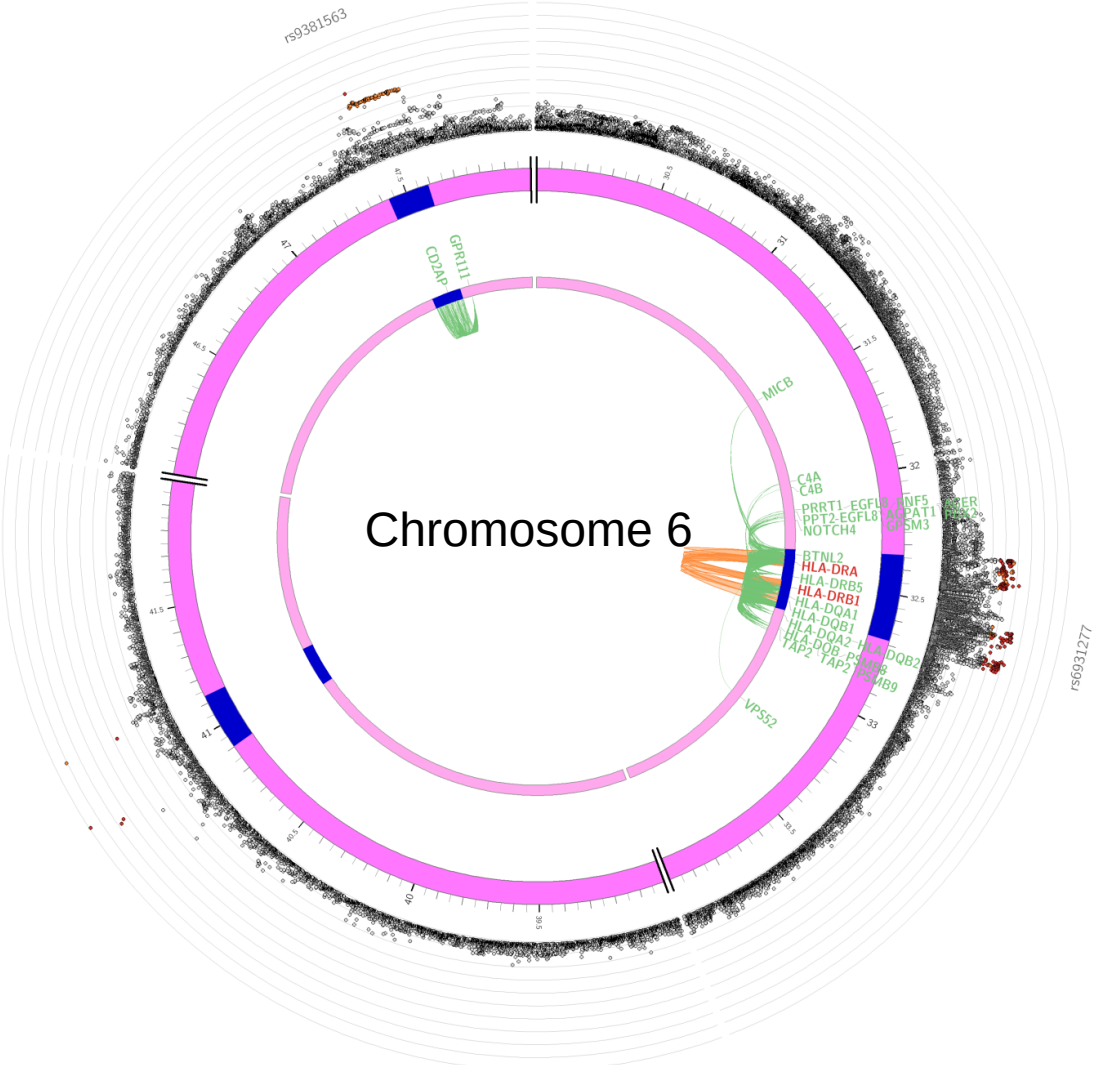
Supplementary Figure 4. Full circos plots of chromatin interactions and eQTLs for all chromosomes with significantly associated loci. The distinct layers and colors correspond to various features. The outer layer contains zoomed in Manhattan plots containing only SNPs with P < 0.05. SNPs in genomic risk loci are color-coded as a function of their maximum r2 to the one of the independent significant SNPs in the locus, as follows: red (r2 > 0.8), orange (r2 > 0.6), green (r2 > 0.4) and blue (r2 > 0.2). SNPs that are not in LD with any of the independent significant SNPs (with r2 ≤ 0.2) are grey. The second layer displays the position of the genomic risk loci in blue. The third layer contains the mapped genes that are implicated by chromatin interactions and/or eQTL analysis (orange = chromatin interaction; green = eQTL; red = chromatin interaction and eQTL).

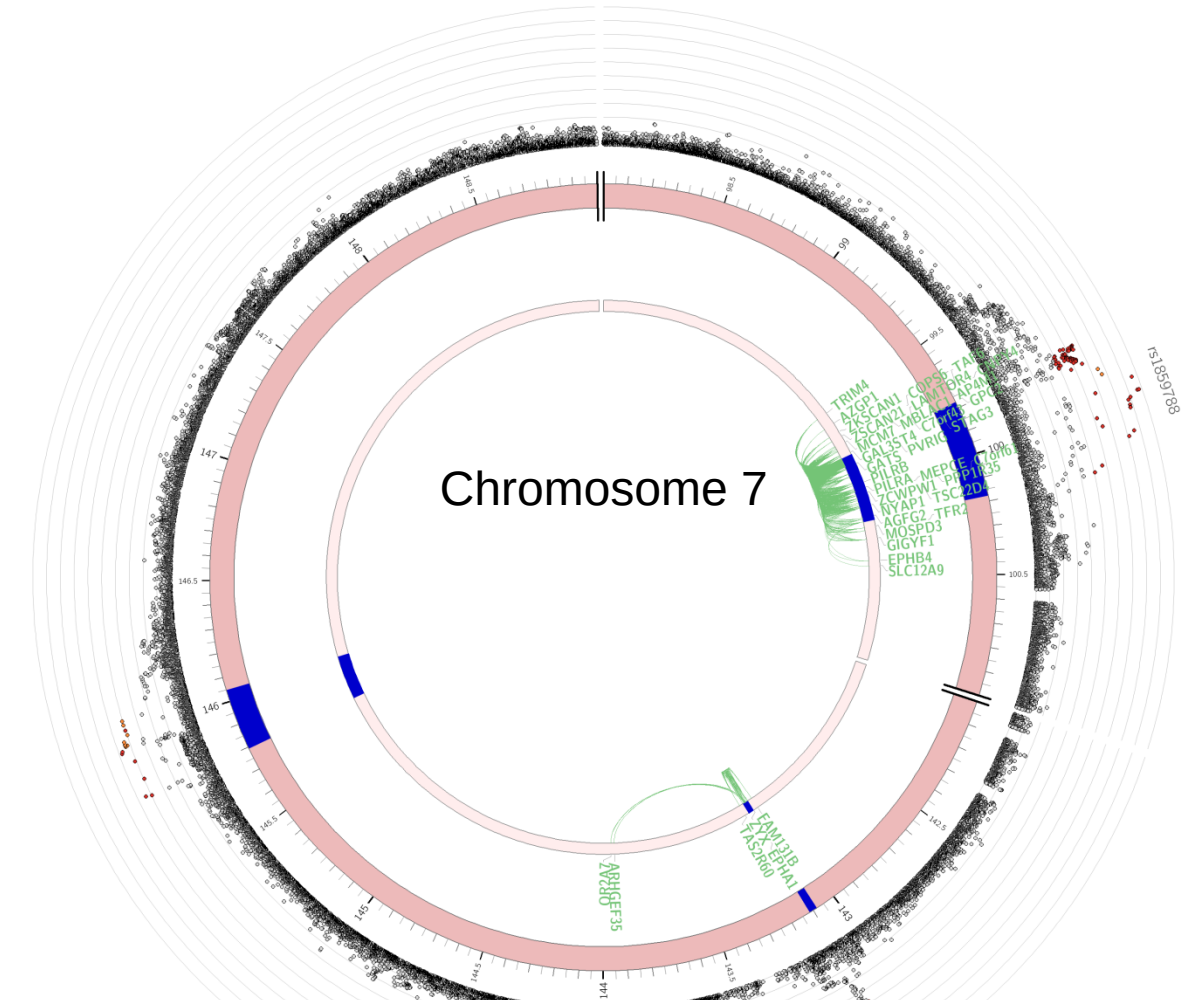


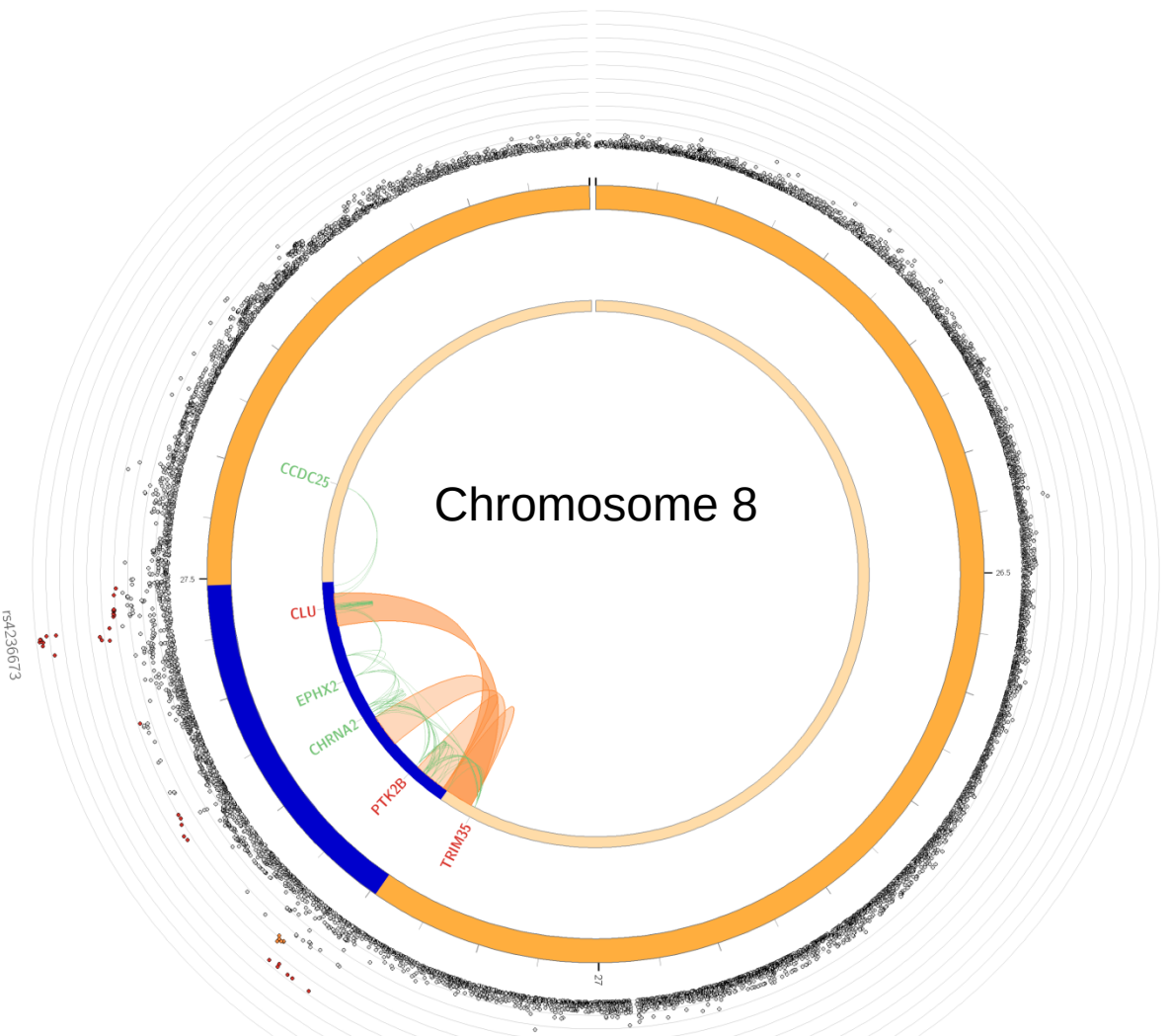

Chromosome 2
rs10933431
rs4663105
INPP5D
BIN1
ERCC3
GPR17
234
233.5
233
232.5
234.5
126.5
127
127.5
128
128.5

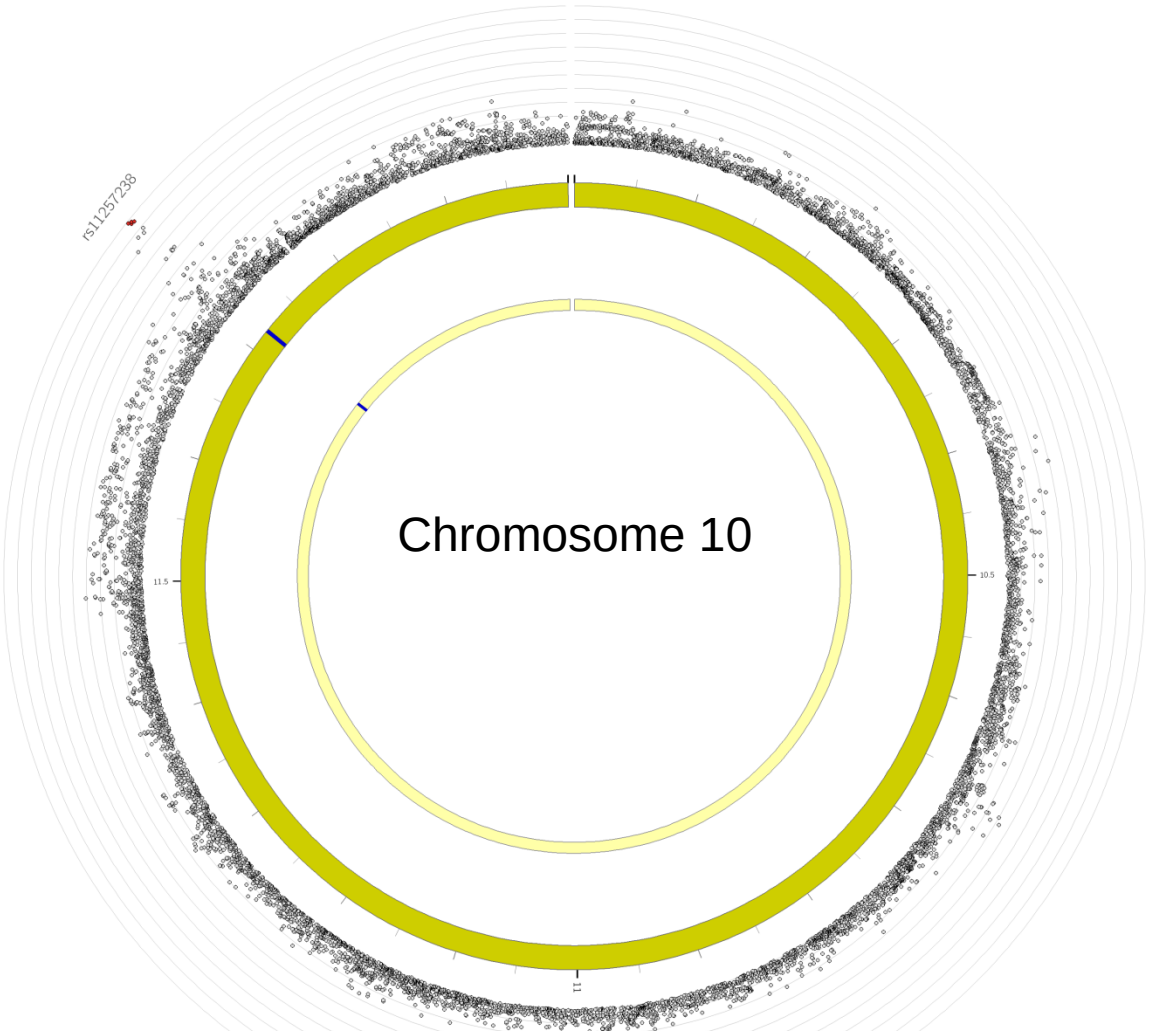

Chromosome 3
57.5
57
56.5

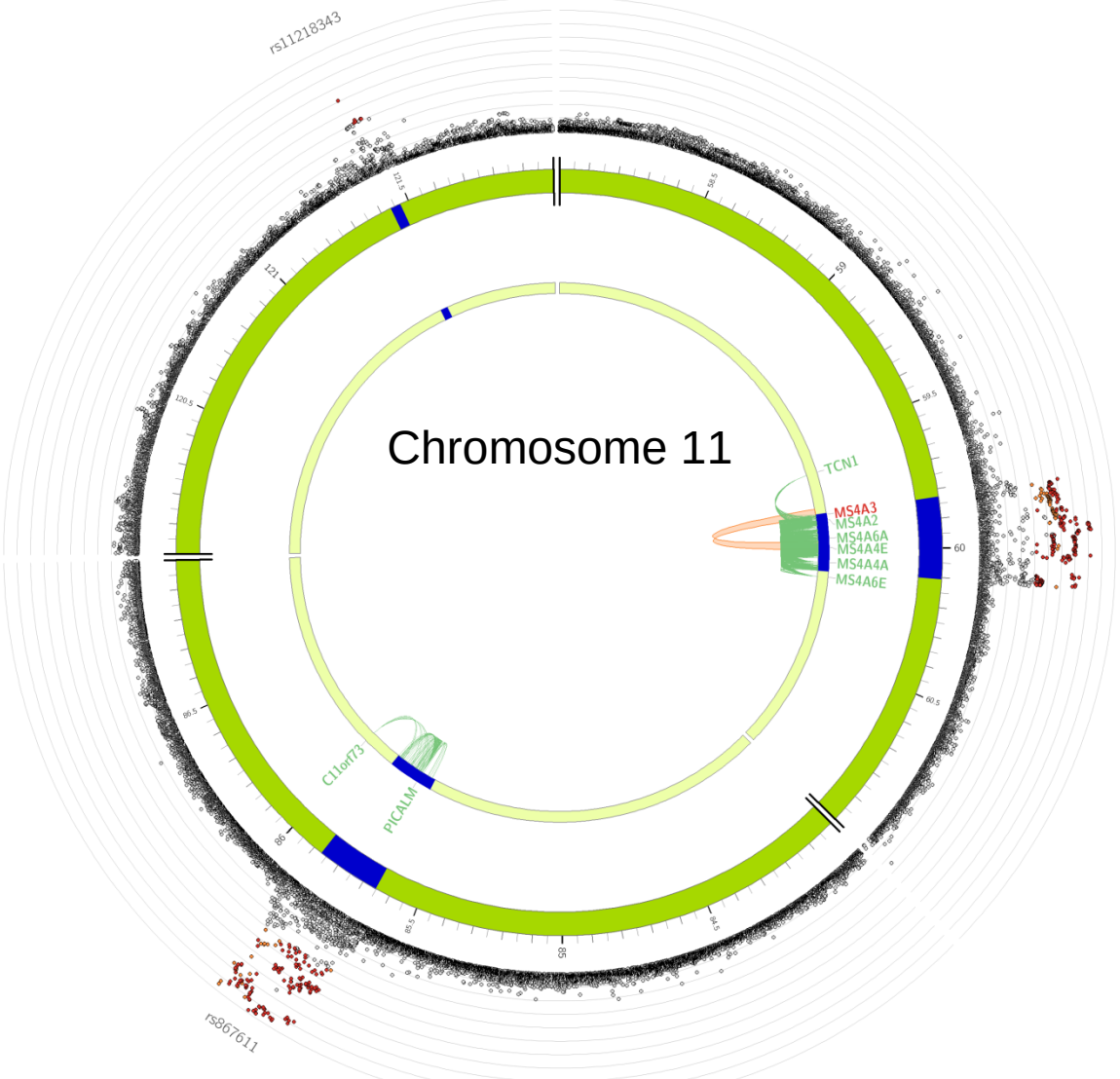

Chromosome 4

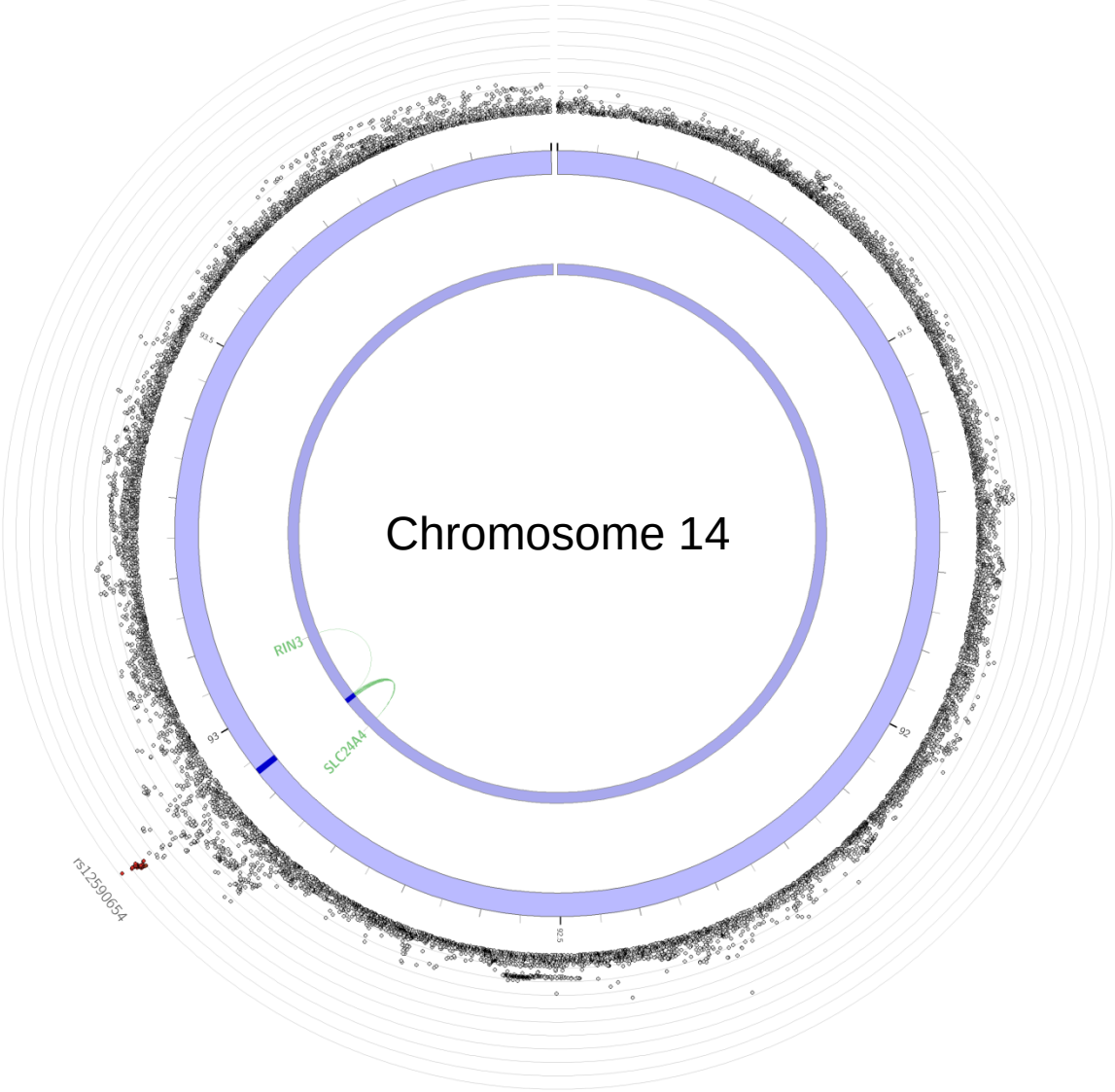

rs9381563
Chromosome 6
CD2AP
GPR111
MICB
C4A
C4B
PRRT1-EGFL8
PPT2-EGFL8
NOTCH4
BTNL2
HLA-DRA
HLA-DRB5
HLA-DRB1
HLA-DQA1
HLA-DQB1
HLA-DQA2
HLA-DQB2
TAP2
PSMB8
PSMB9
VPS52
rs6931277

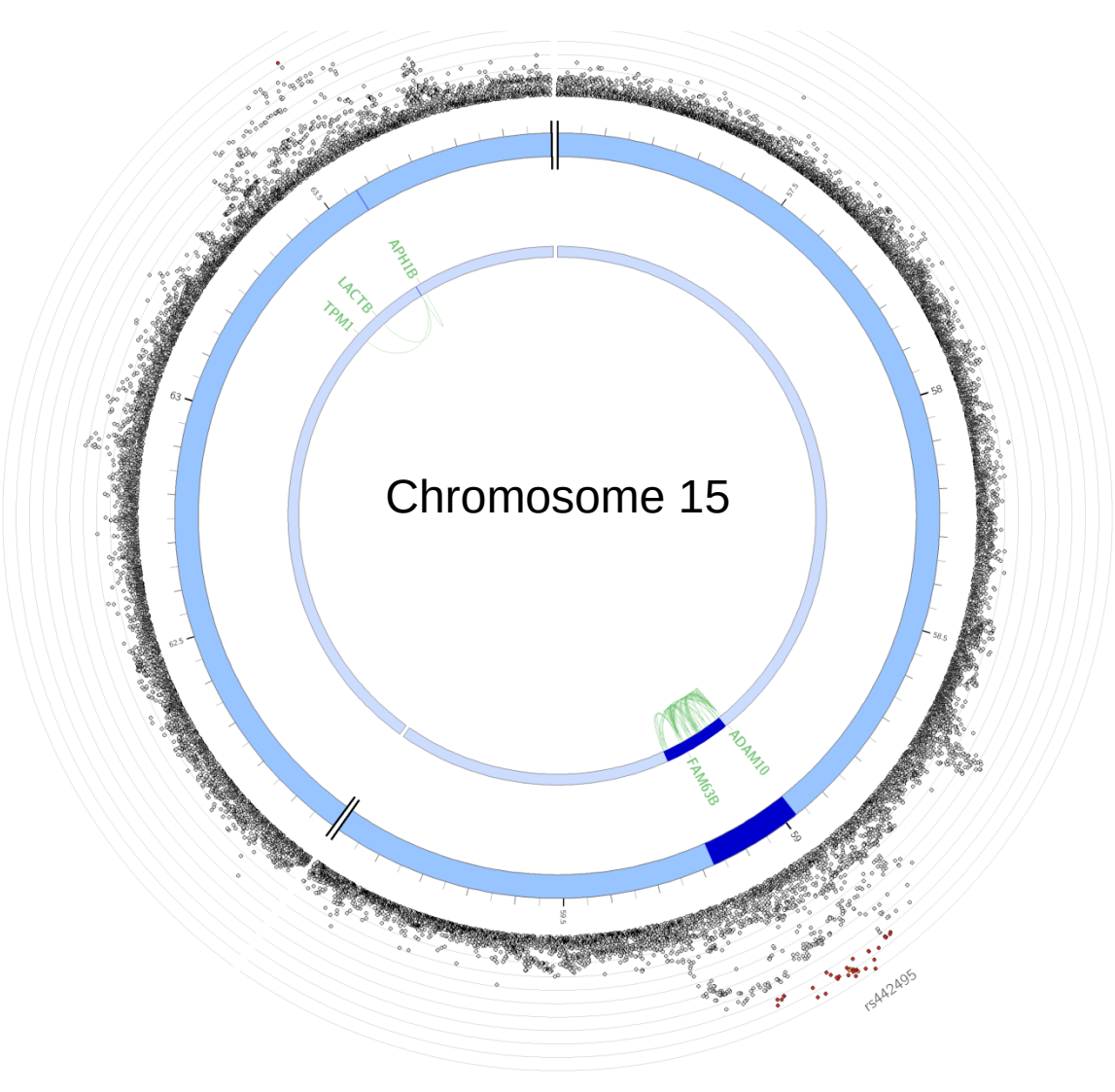

Chromosome 7
rs1859788
TRIM4
AZGP1
ZKSCAN1
ZKSCAN21
MCM7
GAL3ST4
GALE
PILRB
PILRA
AGFG2
TFR2
MOSPD3
GIGYF1
EPHB4
SLC12A9
STAG3
ARHGEF35
FAM131B
EPHA1
TAS2R60

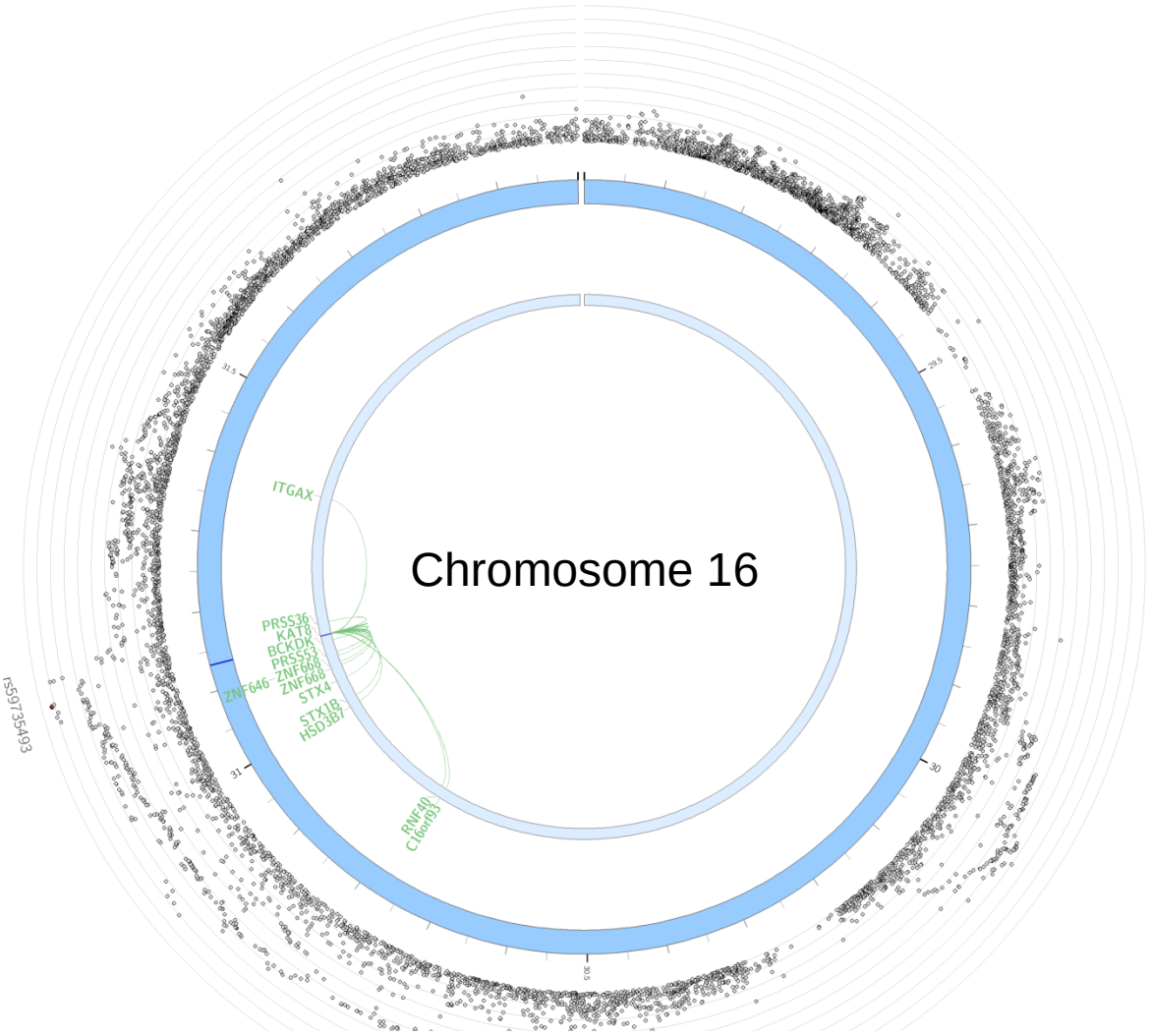

Chromosome 8
rs4236673
CCDC25
CLU
EPHX2
CHRNA2
PTK2B
TRIM35

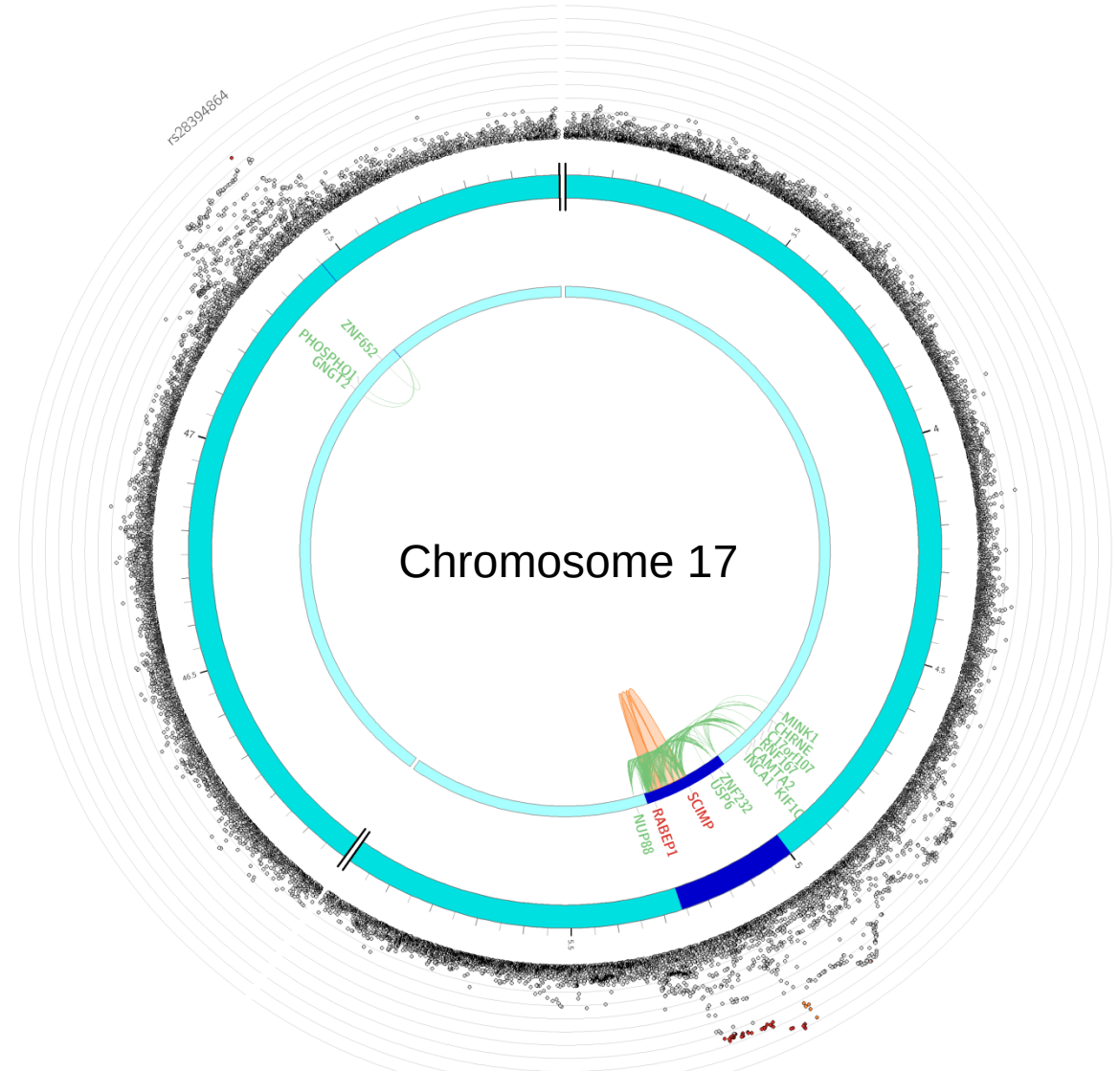

rs11257238
Chromosome 10
11.5
10.5
11

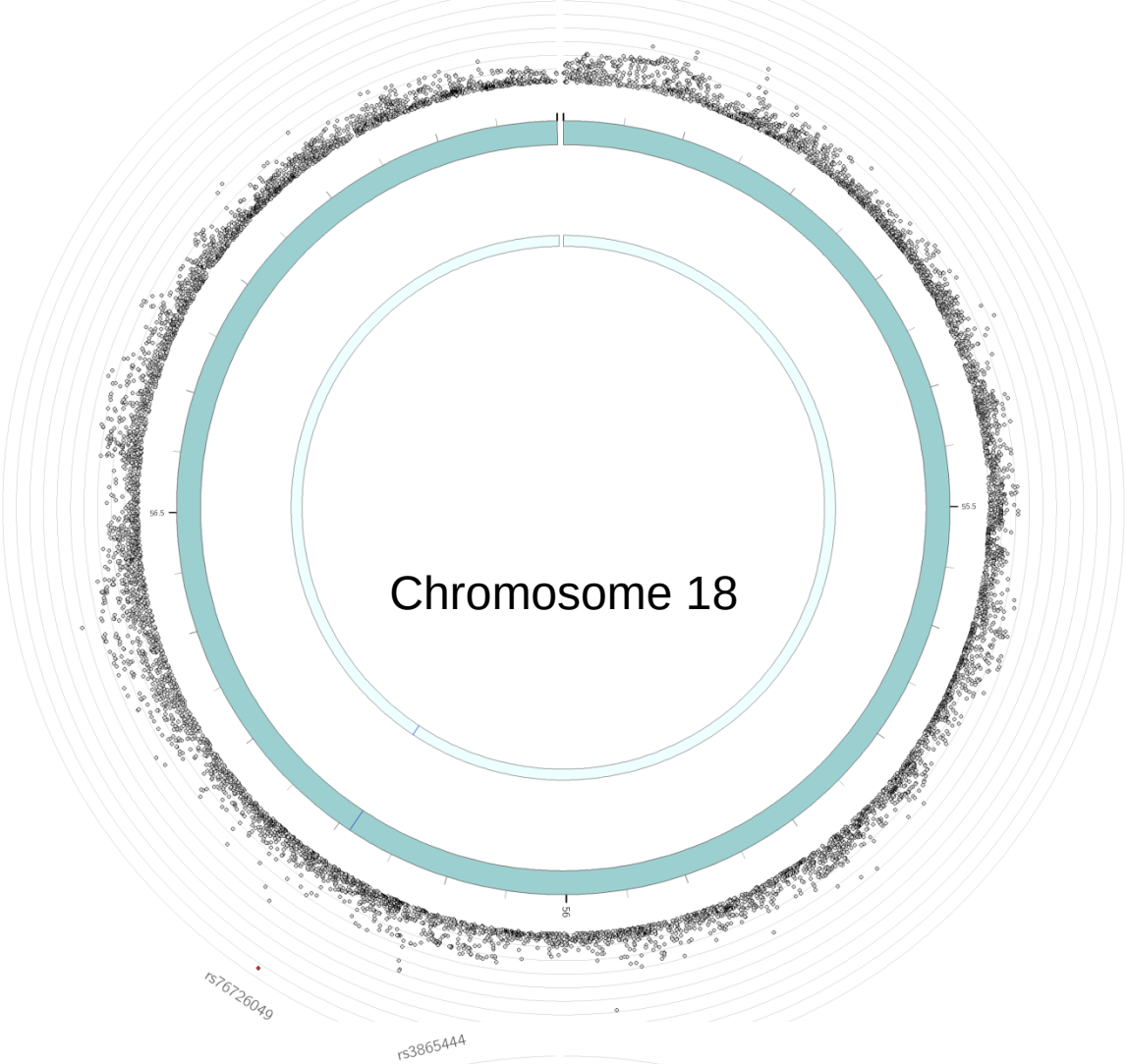

rs11218343
Chromosome 11
TCN1
MS4A3
MS4A2
MS4A6A
MS4A4E
MS4A4A
MS4A6E
C11orf73
PICALM
rs2081545
rs867611

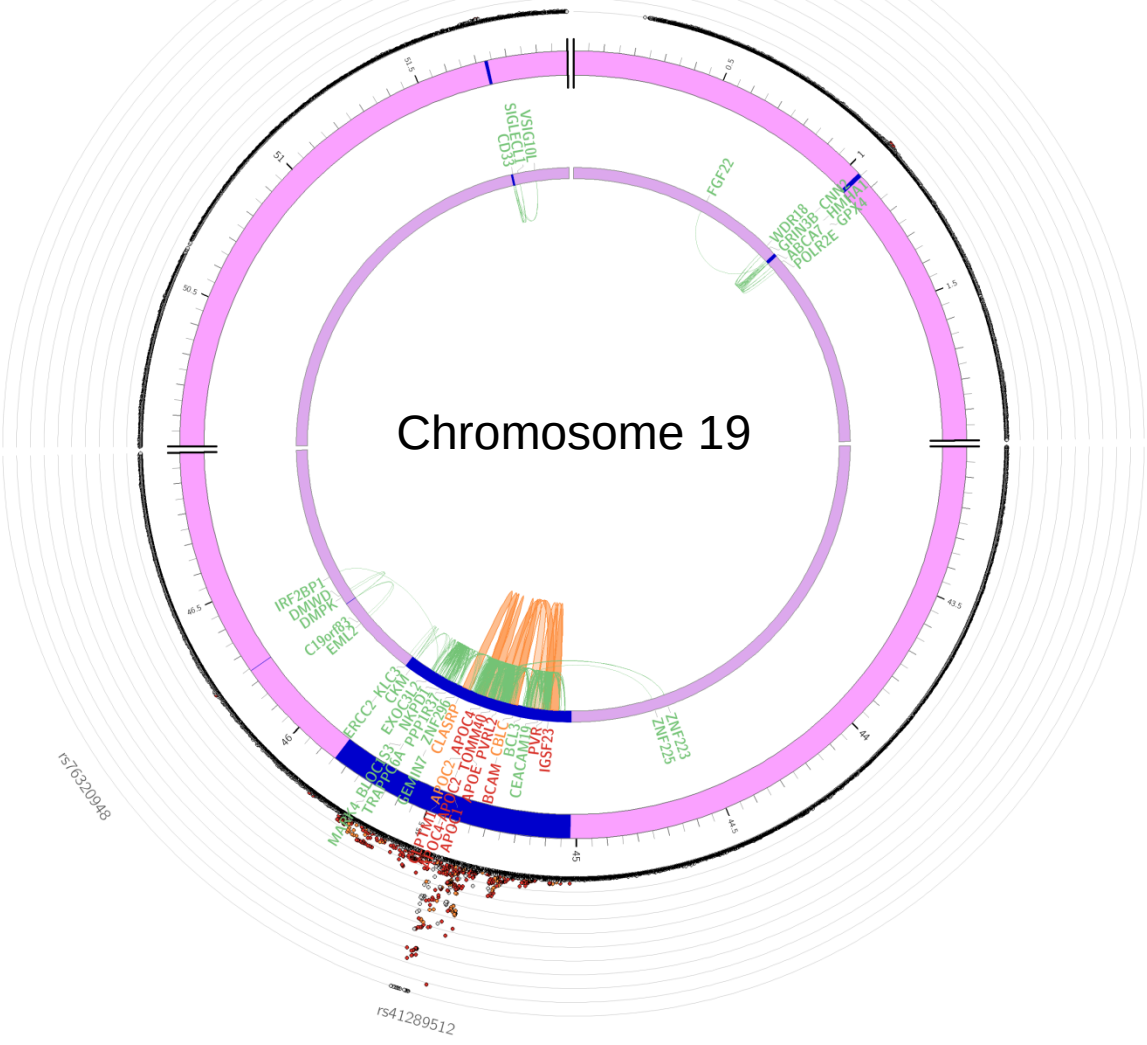

Chromosome 14
RIN3
SLC24A4
rs12590654
93.5
93
92.5
91.5
92

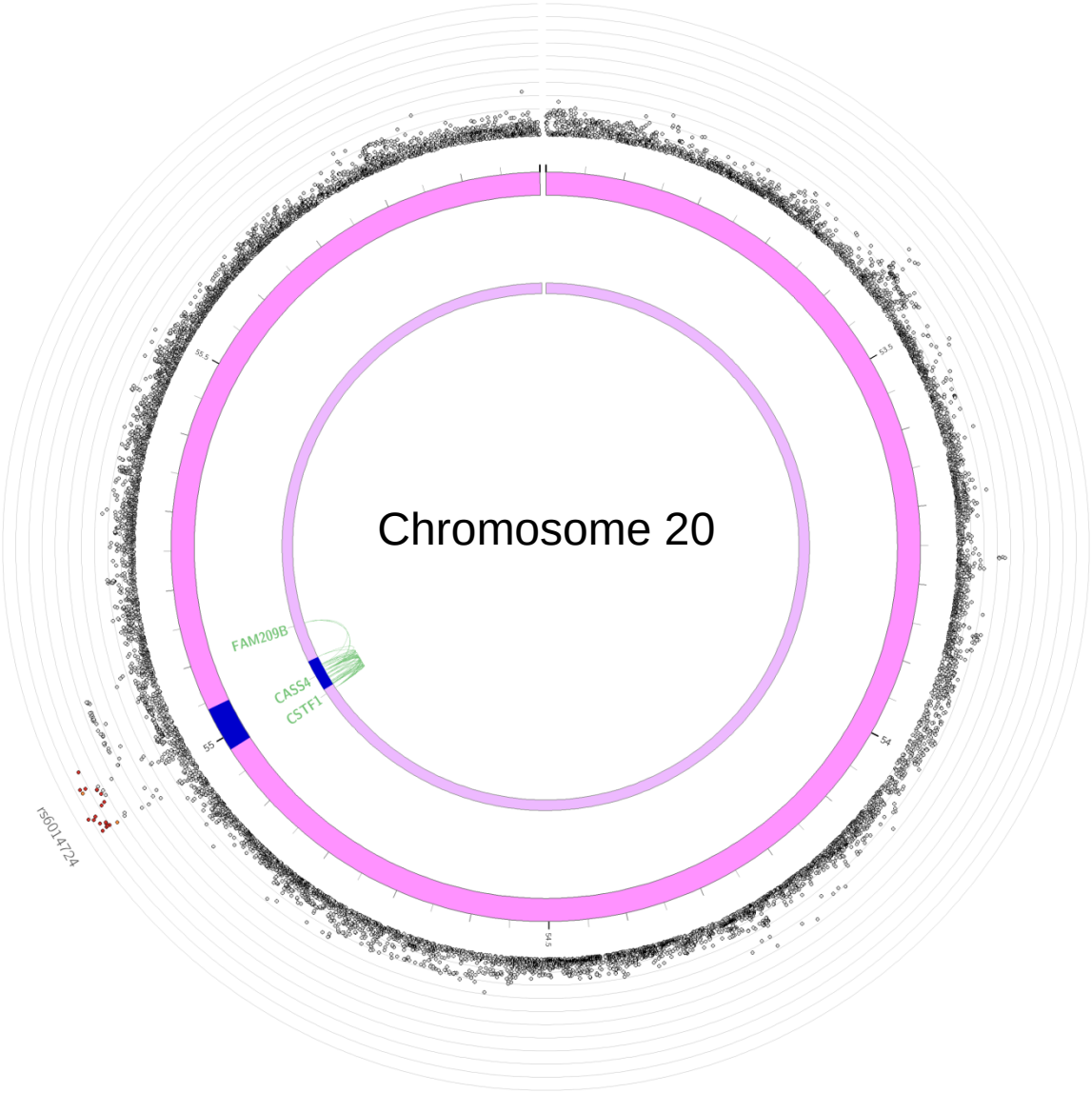

Chromosome 15
APH1B
LACTB
TPM1
ADAM10
FAM63B
rs442495
63.5
63
62.5
59.5
59
58.5
58
57.5


Chromosome 16
rs59735493
ITGAX
PRSS36
KAT8
BCKDK
PRSS53
ZNF668
ZNF668
STX4
STX1B
H5D3B7
ZNF646
RNF40
C16orf93


Chromosome 17
rs28394864
ZNF652
PHOSPHO1
GNGT2
MINK1
CHRNE
SCIMP
RABEPT
NUP88
ZNF232
USP6

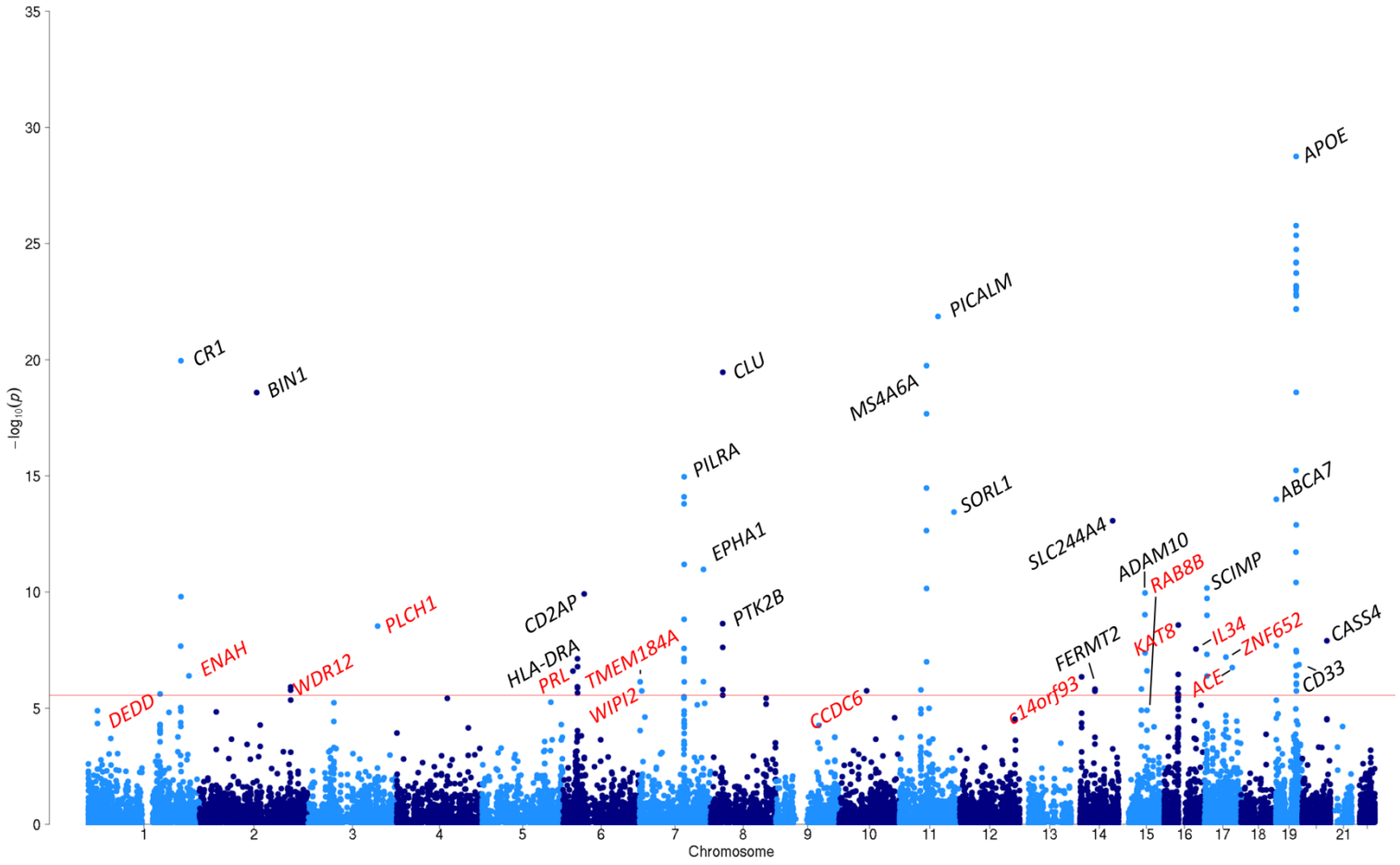

Chromosome 18
56.5
55.5
56
rs76726049
rs3865444


Chromosome 19
51
50.5
46.5
46
45
44.5
44
43.5
1.5
1
0.5
51.5
SIGLEC11
CD33
FGF22
WDR18
GRIN3B
ABCA7
IPOLR2E
CNN2
TIMM17A
GPX4
IRF2BP1
DMWD
DMPK
C19orf83
EML2
ERCC2
KLC3
CEACAM19
BCL3
PVR
IGSF23
ZNF223
ZNF225
rs76320948
rs41289512

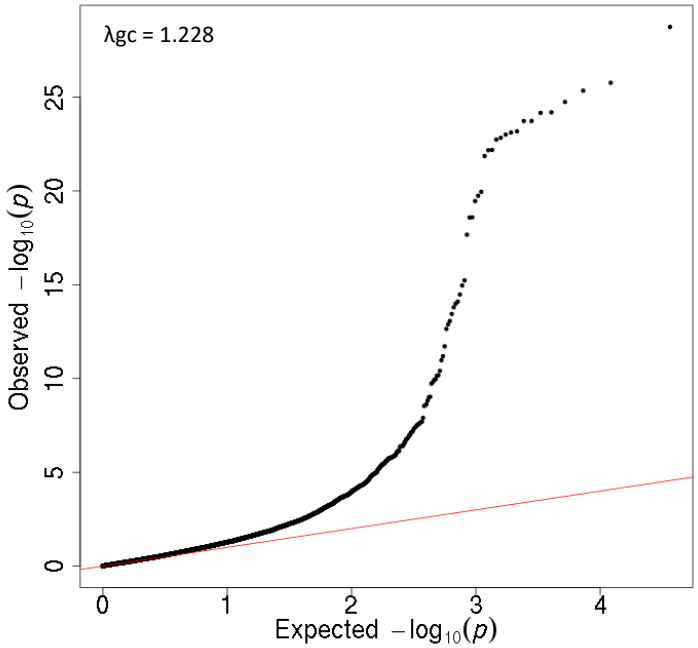

Chromosome 20
FAM209B
CASS4
CSTF1
rs6014724

Supplementary Figure 5. Gene-based association results with MAGMA. A) The Manhattan plot displays all associations per gene ordered according to their genomic position (start of gene) on the x-axis and showing the strength of the association with the –log10 transformed *P*-values on the y-axis. Every locus with at least one significant gene-based association is labelled with the most significant gene name (black = known AD loci/genes, red = novel AD genes). B) The QQ plot displays the expected –log10 transformed *p*-values on the x-axis and the observed –log10 transformed *p*-values on the y-axis.

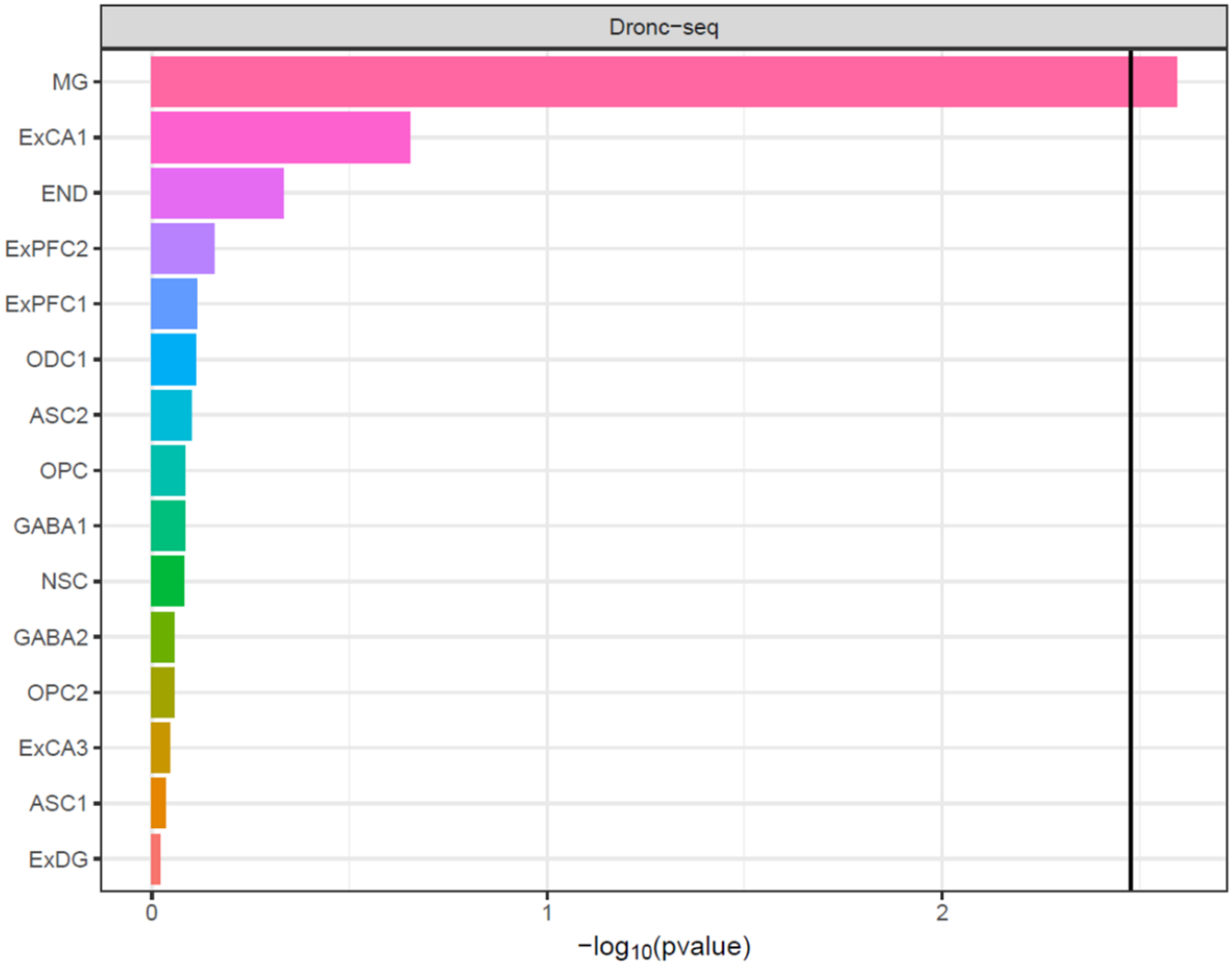
A



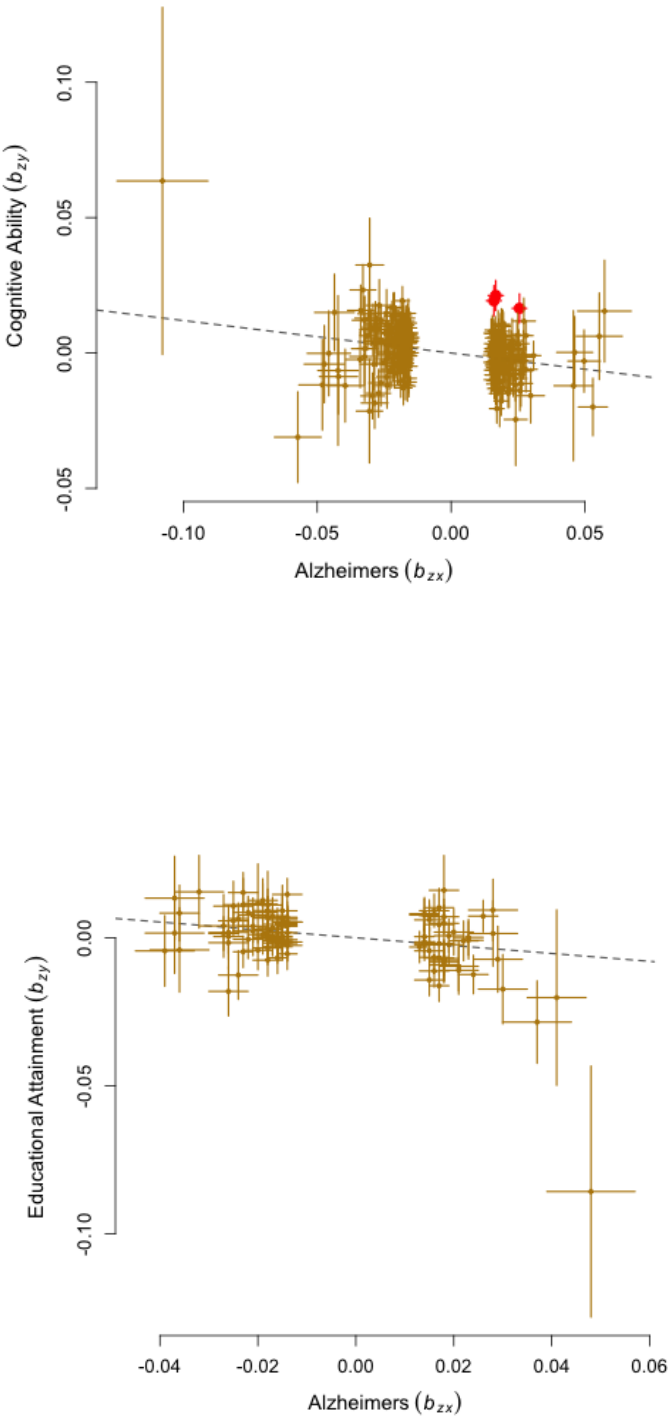
B

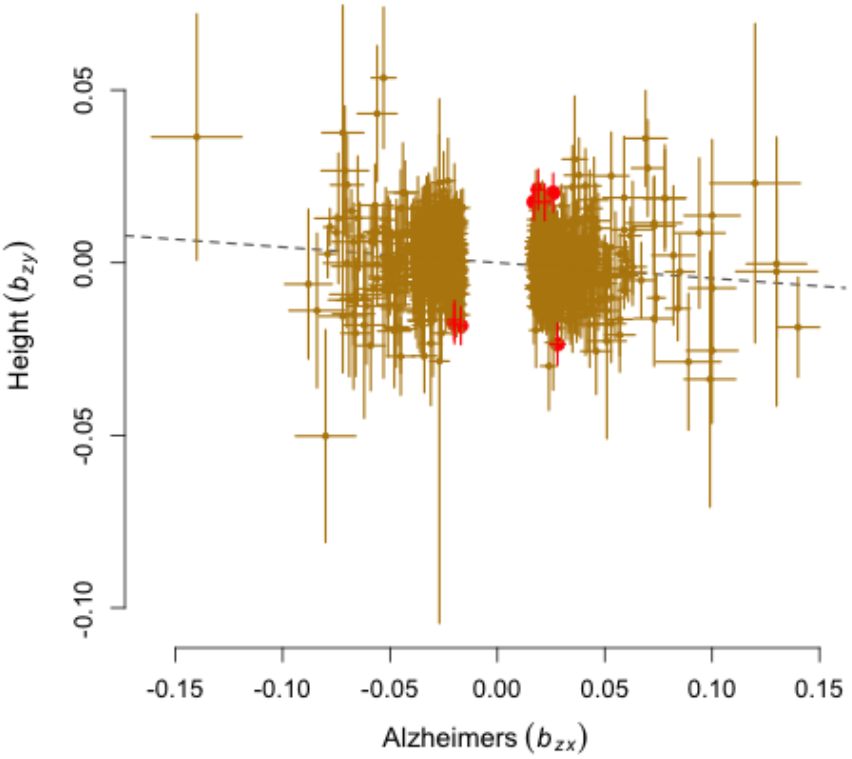


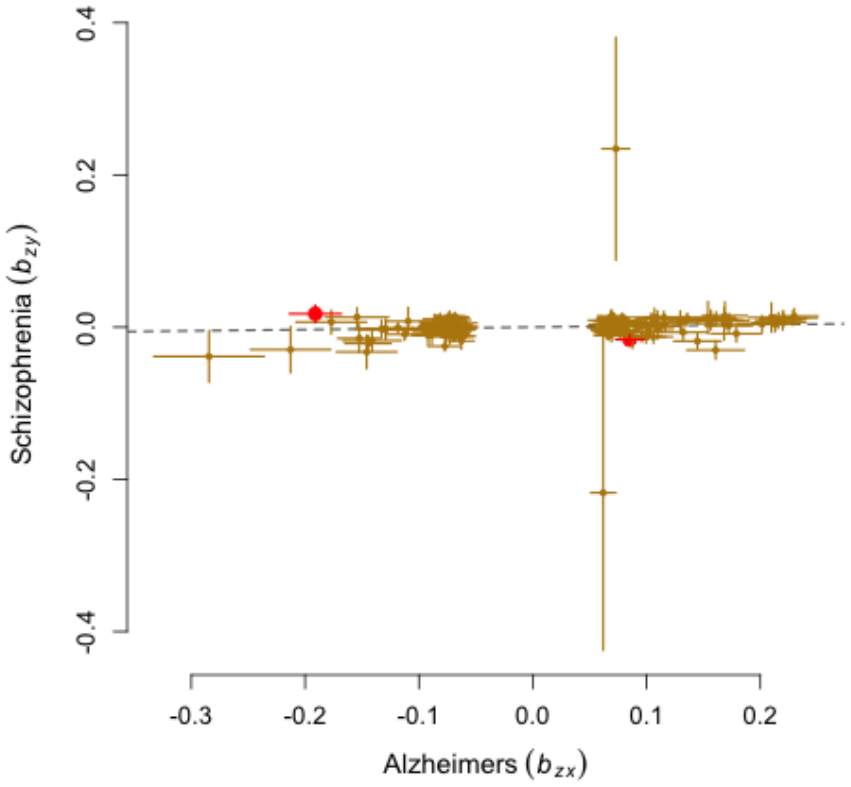
Supplementary Figure 6. Single-cell expression gene-set results of human brain tissue. The black vertical line indicates the significance threshold correcting for number of tests within category. MG = microglia; ExCA1 = Hippocampal CA 1 pyramidal neurons; END = Endothelial cells; ExPFC2 = Prefrontal glutamergic neurons 2; ExPFC1 = Prefrontal glutamergic neurons 1; ODC1 = Oligodendrocytes; ASC2 = Astrocytes 2; OPC = Oligodendrocyte precursor cells 1; GABA1 = GABAergic interneurons 1; NSC = Neuronal stem cells; GABA2 = GABAergic interneurons 2; OPC2 = Oligodendrocyte precursor cells 2; ExCA3 = Hippocampal CA 3 pyramidal neurons; ASC1 = Astrocytes 1; ExDG = Dentate gyrus granule neurons.

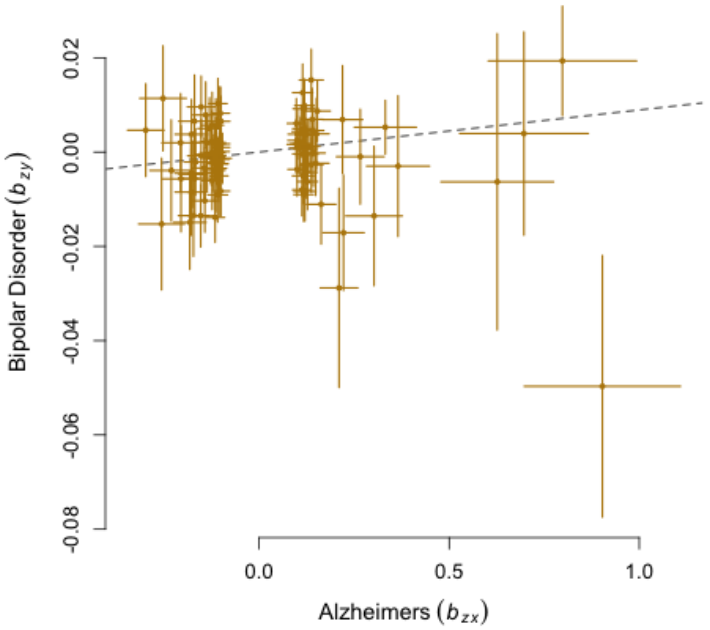


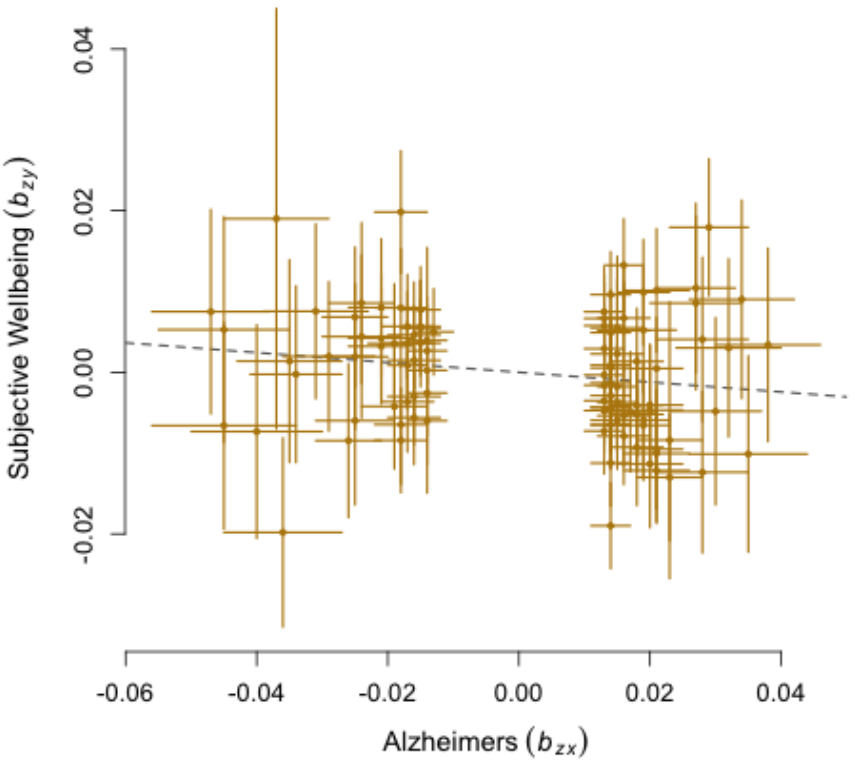
Supplementary Figure 7. Mendelian Randomization tests for the effect of correlated phenotypes on risk for Alzheimer's disease. For independent significant SNPs from each correlated phenotype, effect sizes of the SNPs for Alzheimer's disease (b_{zy}) are shown on the x-axis and effect sizes for correlated phenotypes are on the y-axis (b_{zx}). The dotted line represents a line with slope of (b_{xy}) and an intercept of 0.Red dots represent outliers that were excluded for the Mendelian Randomization analysis.

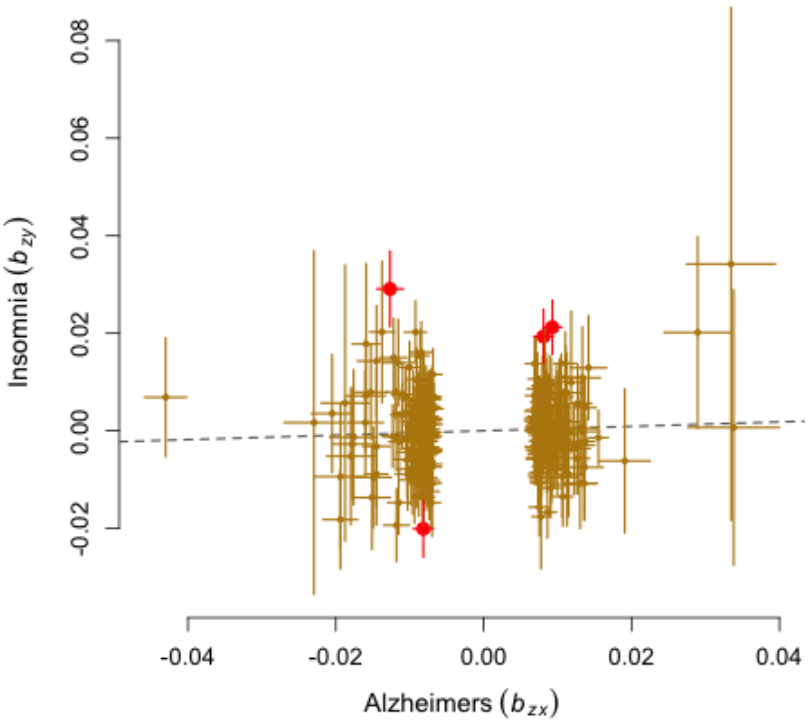


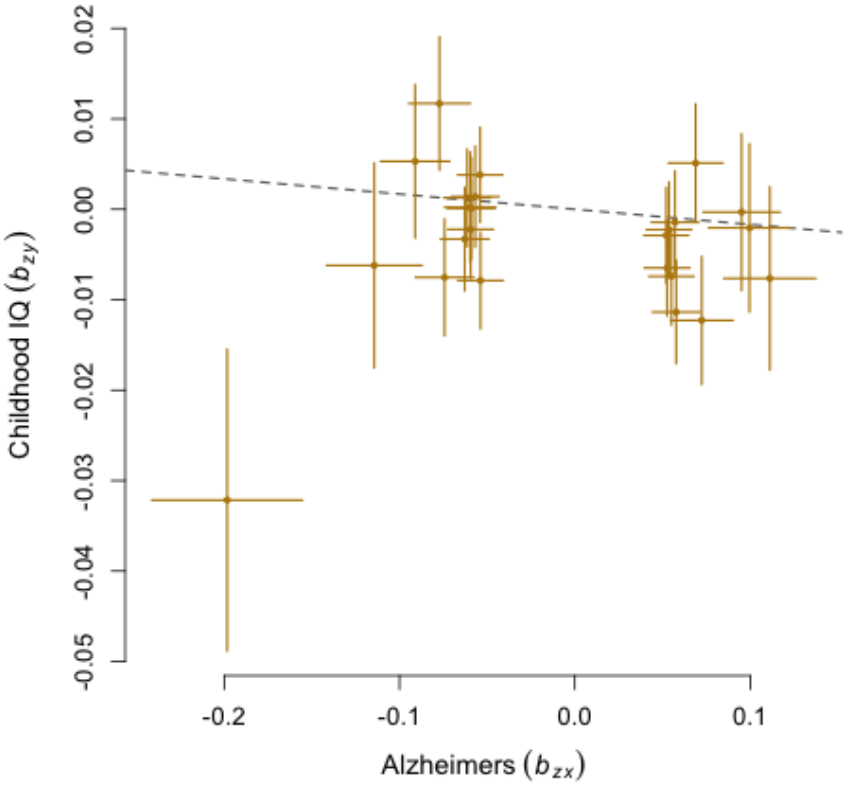

Height (b_{zy})
0.05
0.00
-0.05
-0.10
-0.15
-0.10
-0.05
0.00
0.05
0.10
0.15
Alzheimers (b_{zx})

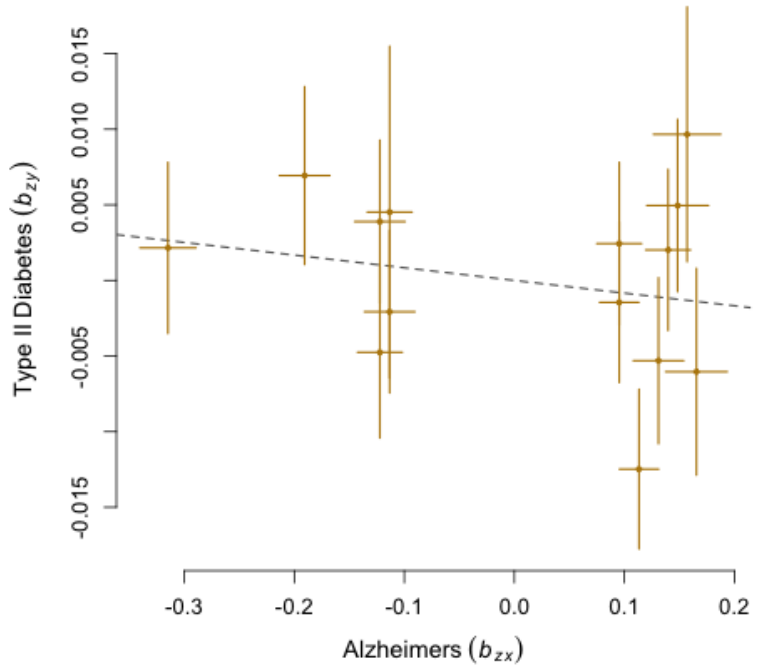

Schizophrenia (b_{zy})
0.4
0.2
0.0
-0.2
-0.4
-0.3
-0.2
-0.1
0.0
0.1
0.2
Alzheimers (b_{zx})

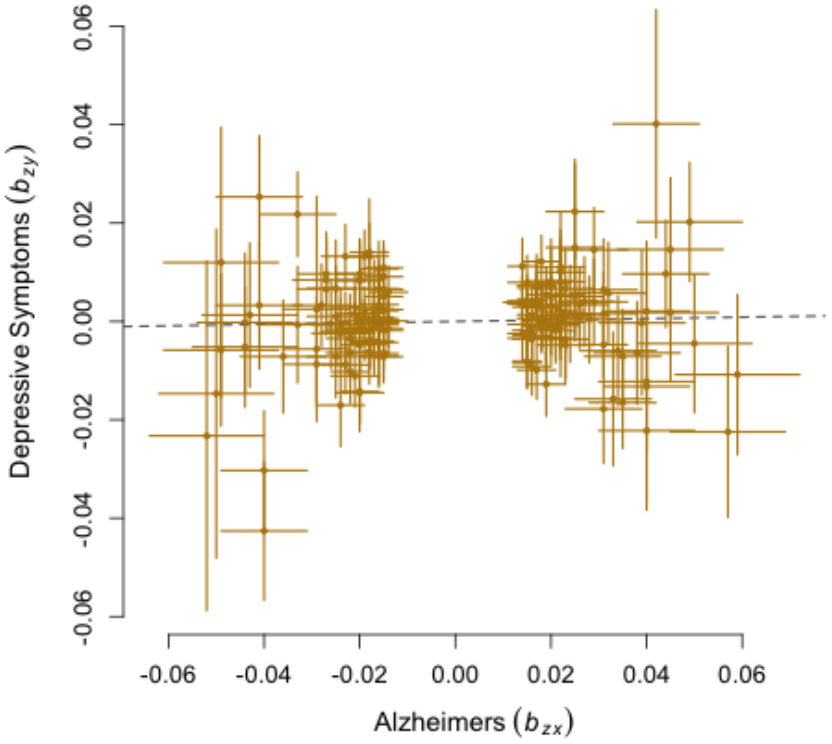

Bipolar Disorder (b_{zy})
0.02
0.00
-0.02
-0.04
-0.06
-0.08
0.0
0.5
1.0
Alzheimers (b_{zx})

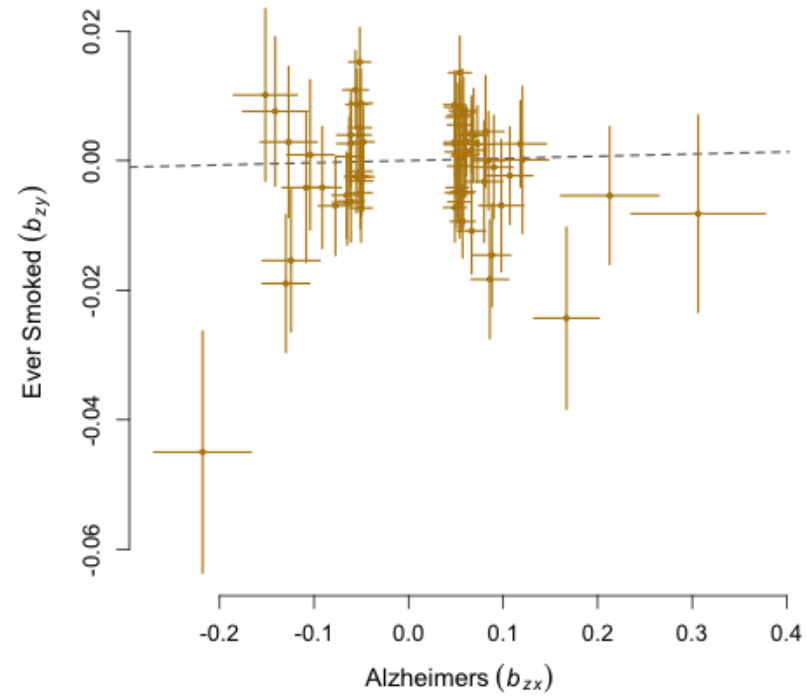

Subjective Wellbeing (b_{zy})
0.04
0.02
0.00
-0.02
-0.06
-0.04
-0.02
0.00
0.02
0.04
Alzheimers (b_{zx})

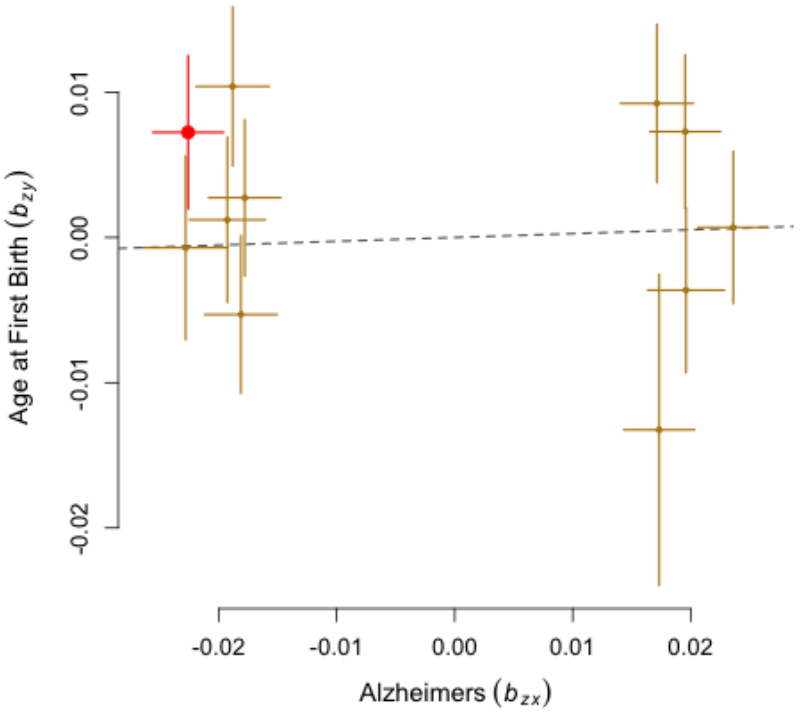

Insomnia (b_{zy})
0.08
0.06
0.04
0.02
0.00
-0.02
-0.04
-0.02
0.00
0.02
0.04
Alzheimers (b_{zx})

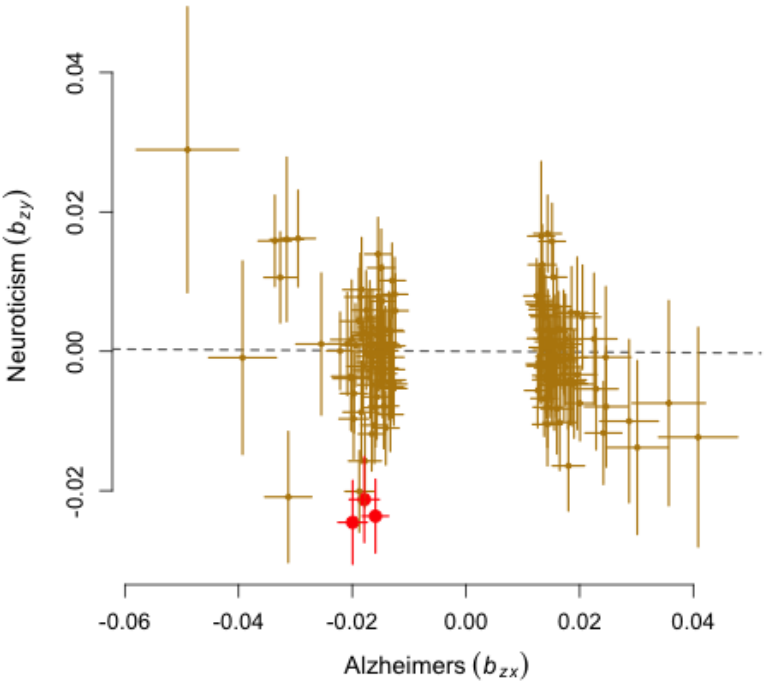

Childhood IQ (b_{zy})
0.02
0.01
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.2
-0.1
0.0
0.1
Alzheimers (b_{zx})


Type II Diabetes (b_{zy})
0.015
0.010
0.005
-0.005
-0.015
-0.3
-0.2
-0.1
0.0
0.1
0.2
Alzheimers (b_{zx})


Depressive Symptoms (b_{zy})
0.06
0.04
0.02
0.00
-0.02
-0.04
-0.06
-0.06
-0.04
-0.02
0.00
0.02
0.04
0.06
Alzheimers (b_{zx})


Ever Smoked (b_{zy})
0.02
0.00
-0.02
-0.04
-0.06
-0.2
-0.1
0.0
0.1
0.2
0.3
0.4
Alzheimers (b_{zx})


Age at First Birth (b_{zy})
0.01
0.00
-0.01
-0.02
-0.02
-0.01
0.00
0.01
0.02
Alzheimers (b_{zx})


Neuroticism (b_{zy})
0.04
0.02
0.00
-0.02
-0.06
-0.04
-0.02
0.00
0.02
0.04
Alzheimers (b_{zx})