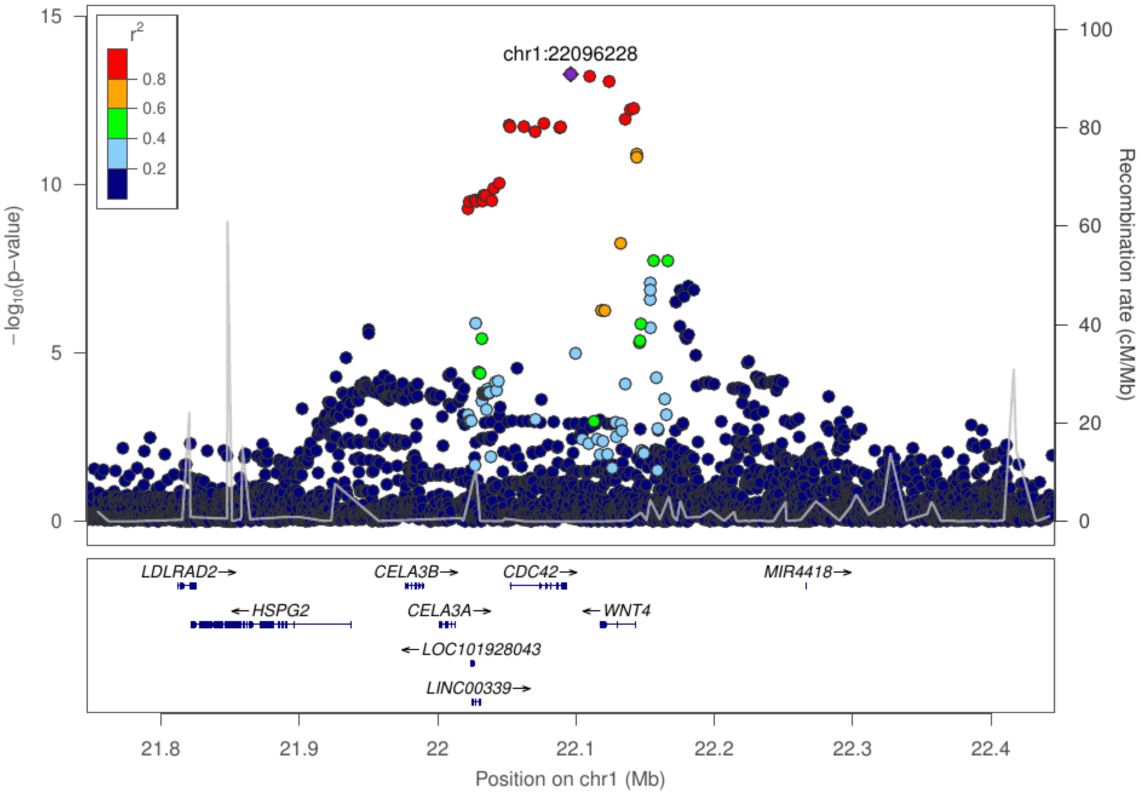
Supplementary Information

Variants associating with uterine leiomyoma highlight genetic background shared by various cancers and hormone-related traits

Rafnar **et al.**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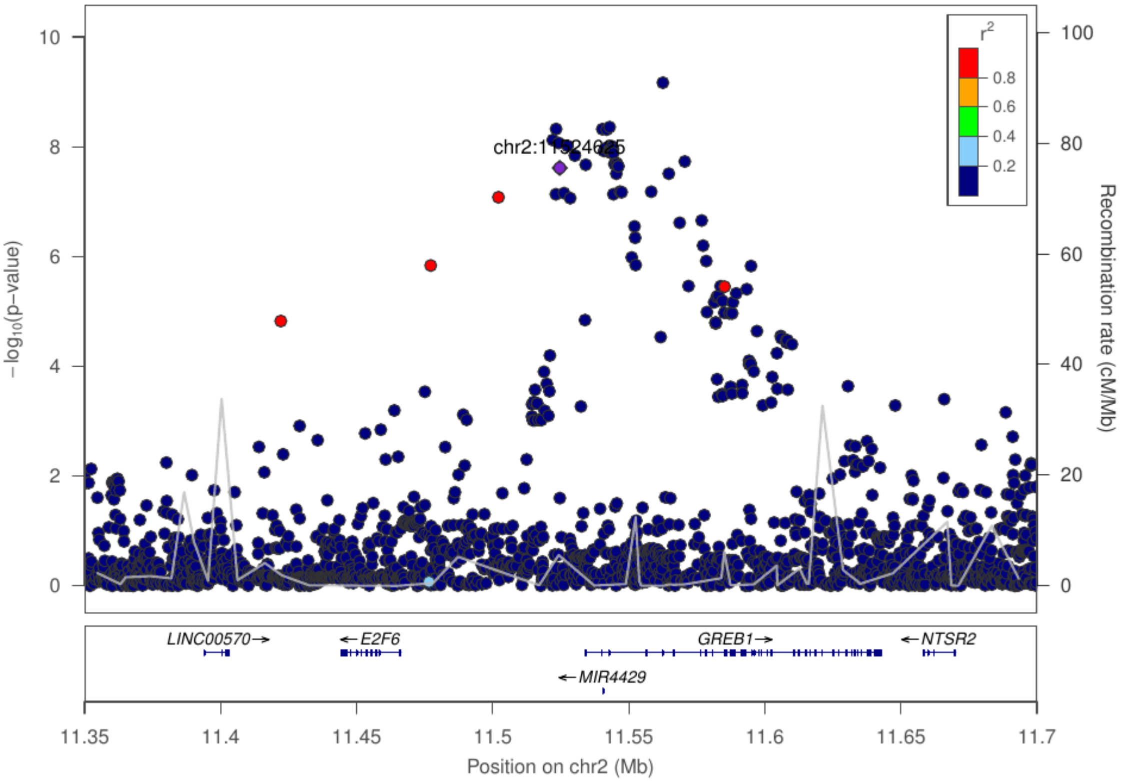
0.8
0.6
0.4
0.2
chr1:22096228
15
10
5
0
−log₁₀(p−value)
100
80
60
40
20
0
Recombination rate (cM/Mb)
LDLRAD2→
←HSPG2
CELA3B→
CELA3A→
←LOC101928043
LINC00339→
CDC42→
←WNT4
MIR4418→
21.8
21.9
22
22.1
22.2
22.3
22.4
Position on chr1 (Mb)


r^2
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0.6
0.4
0.2
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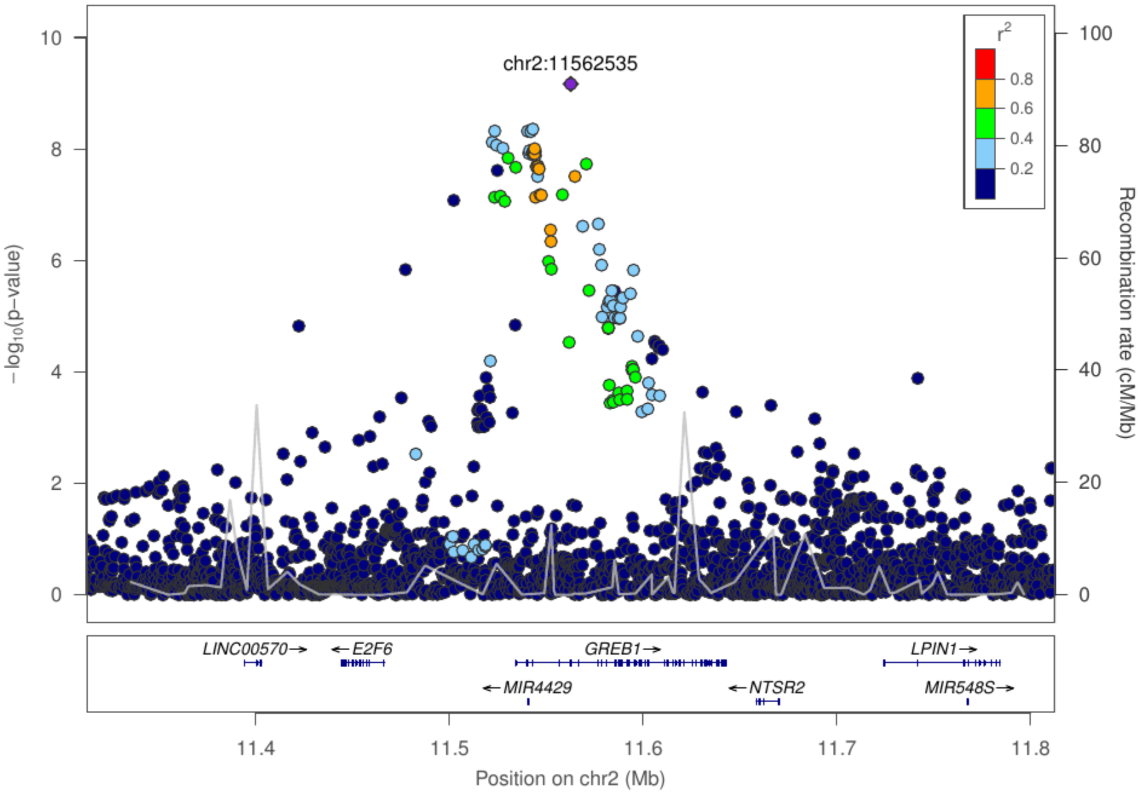
8
6
4
2
0
−log₁₀(p−value)
100
80
60
40
20
0
Recombination rate (cM/Mb)
LINC00570→
←E2F6
GREB1→
←MIR4429
←NTSR2
11.35
11.4
11.45
11.5
11.55
11.6
11.65
11.7
Position on chr2 (Mb)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r2
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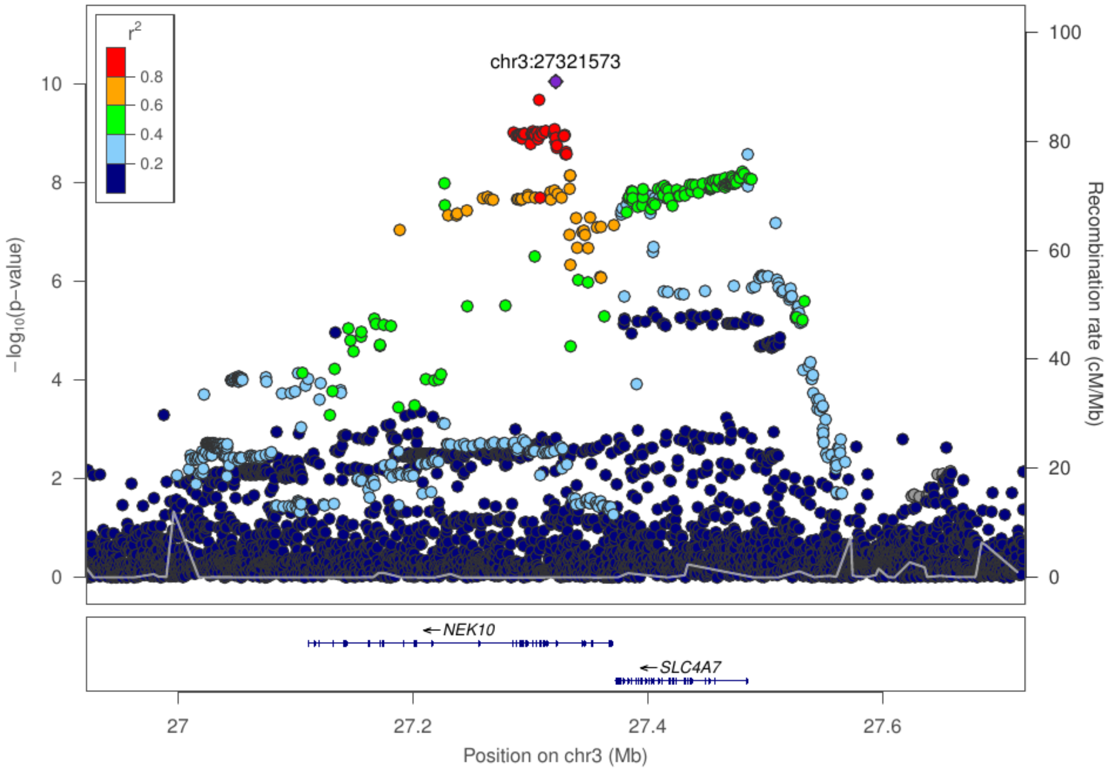
0.6
0.4
0.2
−log10(p−value)
10
8
6
4
2
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
LINC00570→
←E2F6
GREB1→
LPIN1→
←MIR4429
←NTSR2
MIR548S→
11.4
11.5
11.6
11.7
11.8
Position on chr2 (Mb)


chr3:27321573
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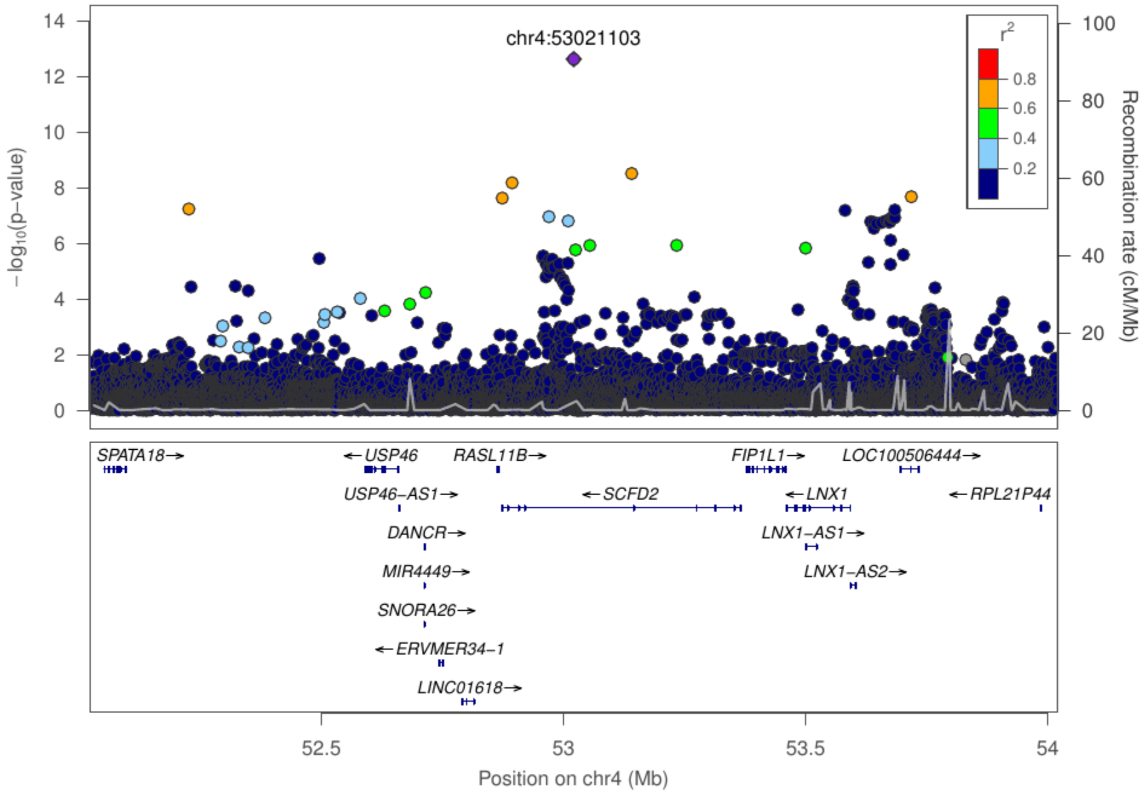
0.6
0.4
0.2
−log10(p−value)
10
8
6
4
2
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
←NEK10
←SLC4A7
27
27.2
27.4
27.6
Position on chr3 (Mb)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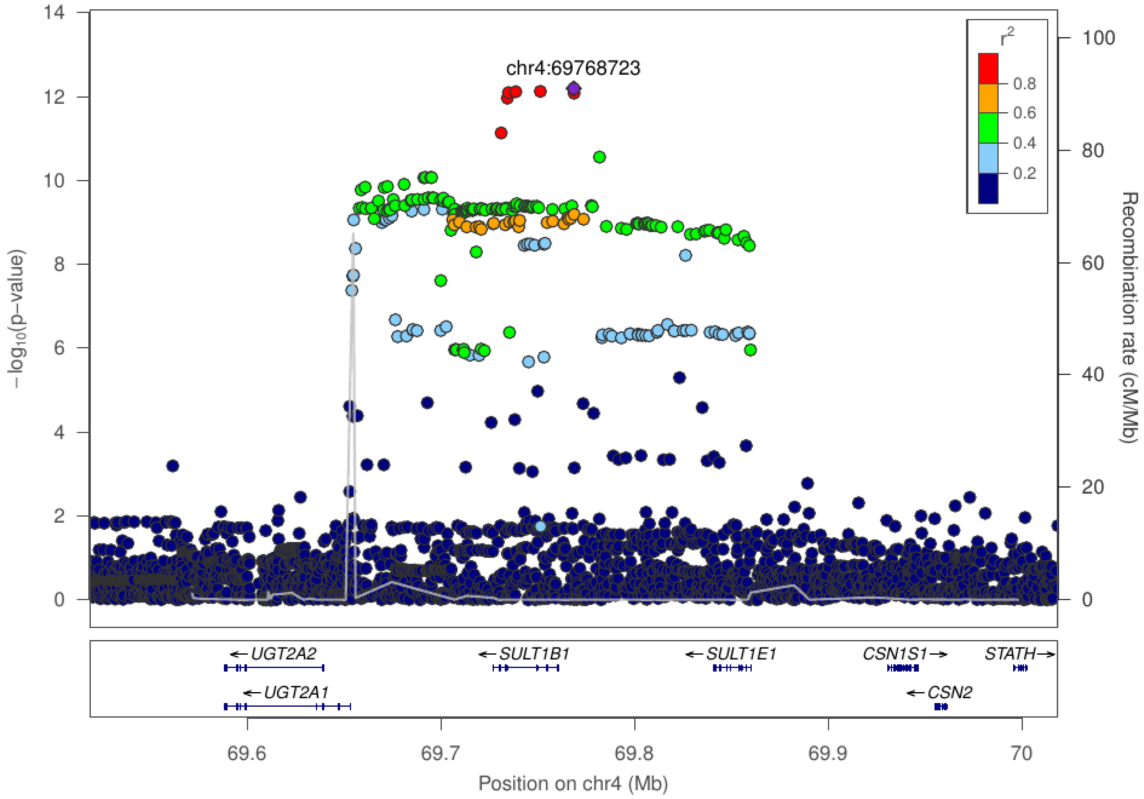
0.8
0.6
0.4
0.2
− log10(p−value)
Recombination rate (cM/Mb)
14
12
10
8
6
4
2
0
100
80
60
40
20
0
SPATA18
USP46
RASL11B
FIP1L1
LOC100506444
USP46−AS1
SCFD2
LNX1
RPL21P44
DANCR
LNX1−AS1
MIR4449
LNX1−AS2
SNORA26
ERVMER34−1
LINC01618
52.5
53
53.5
54
Position on chr4 (Mb)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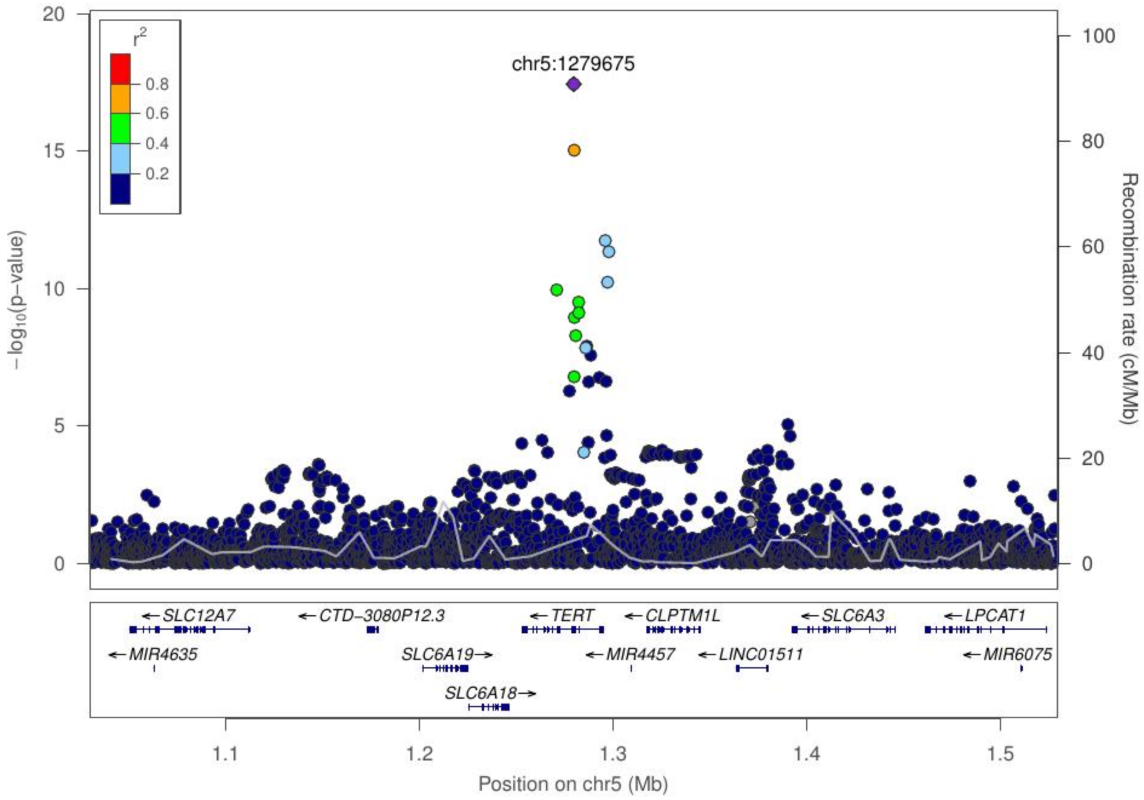
r2
0.8
0.6
0.4
0.2
− log10(p−value)
Recombination rate (cM/Mb)
14
12
10
8
6
4
2
0
100
80
60
40
20
0
UGT2A2
SULT1B1
SULT1E1
CSN1S1
STATH
UGT2A1
CSN2
69.6
69.7
69.8
69.9
70
Position on chr4 (Mb)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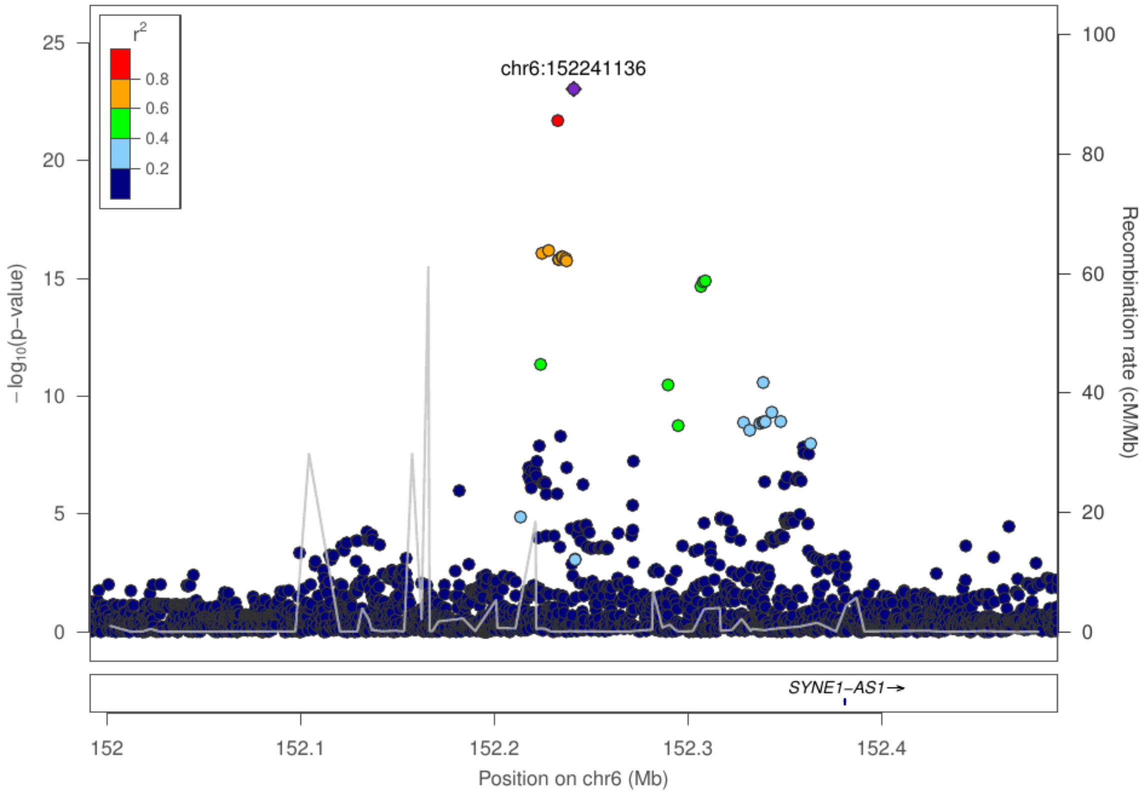
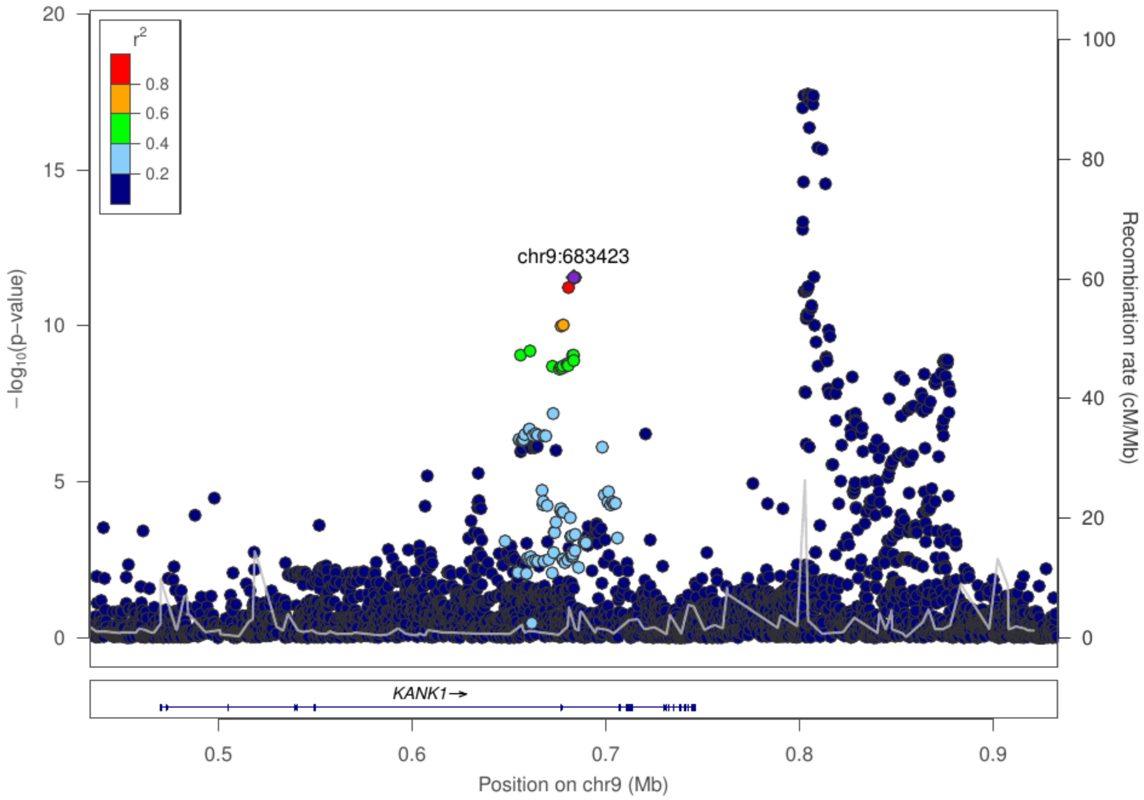
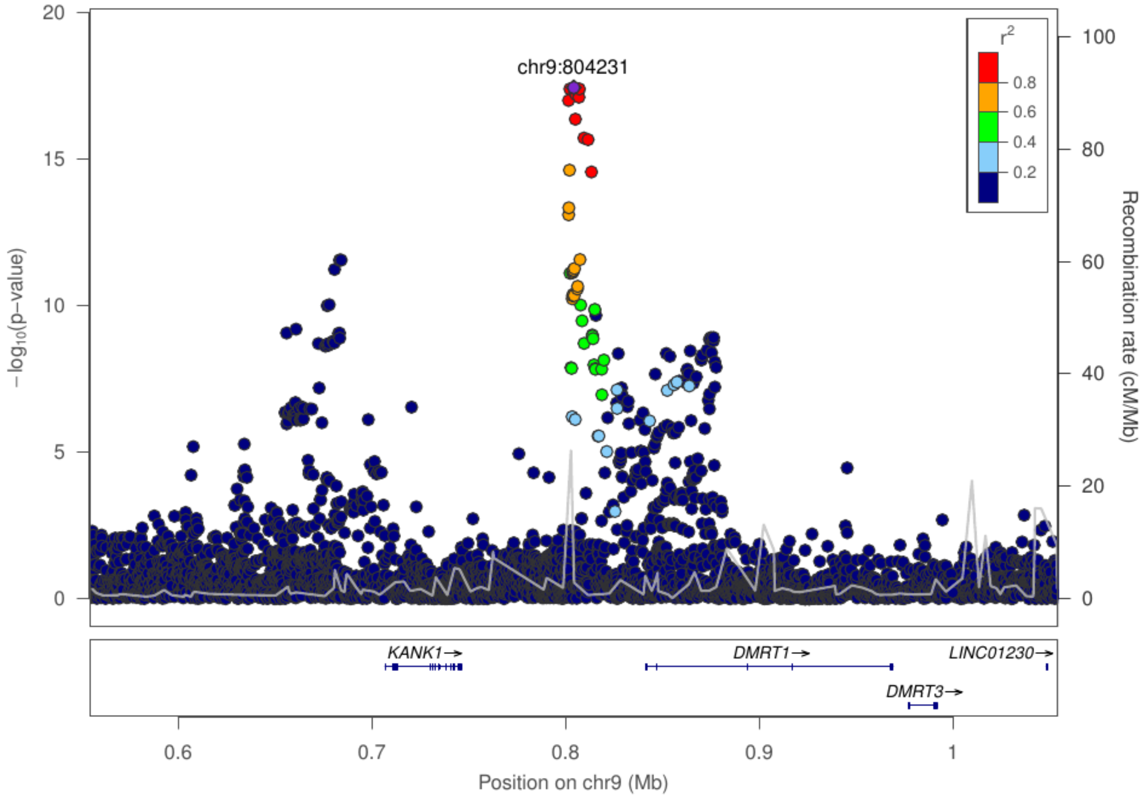
0.6
0.4
0.2
chr5:1279675
− log$_{10}$(p−value)
20
15
10
5
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
SLC12A7
CTD−3080P12.3
TERT
CLPTM1L
SLC6A3
LPCAT1
MIR4635
SLC6A19
MIR4457
LINC01511
MIR6075
SLC6A18
1.1
1.2
1.3
1.4
1.5
Position on chr5 (Mb)


r^2
0.8
0.6
0.4
0.2
chr6:152241136
− log$_{10}$(p−value)
25
20
15
10
5
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
SYNE1−AS1
152
152.1
152.2
152.3
152.4
Position on chr6 (Mb)


chr9:683423
r2
0.8
0.6
0.4
0.2
−log10(p−value)
0
5
10
15
20
Recombination rate (cM/Mb)
0
20
40
60
80
100
KANK1→
0.5
0.6
0.7
0.8
0.9
Position on chr9 (Mb)


chr9:804231
r2
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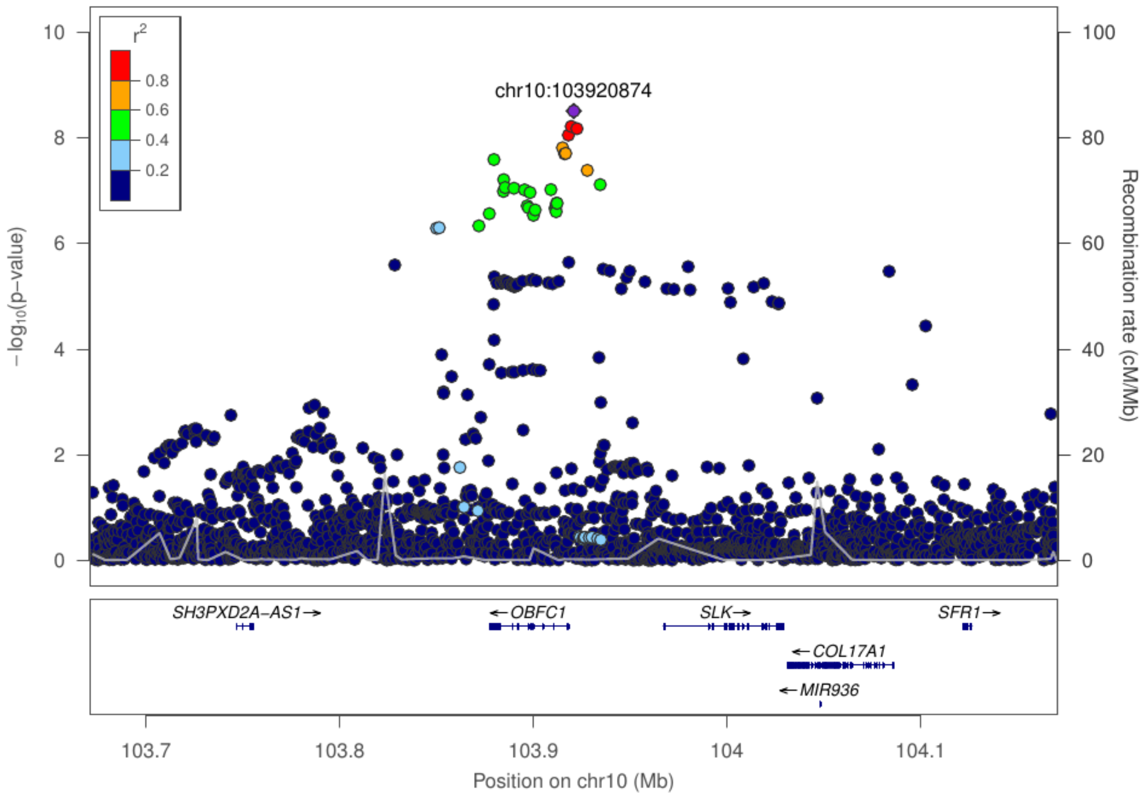
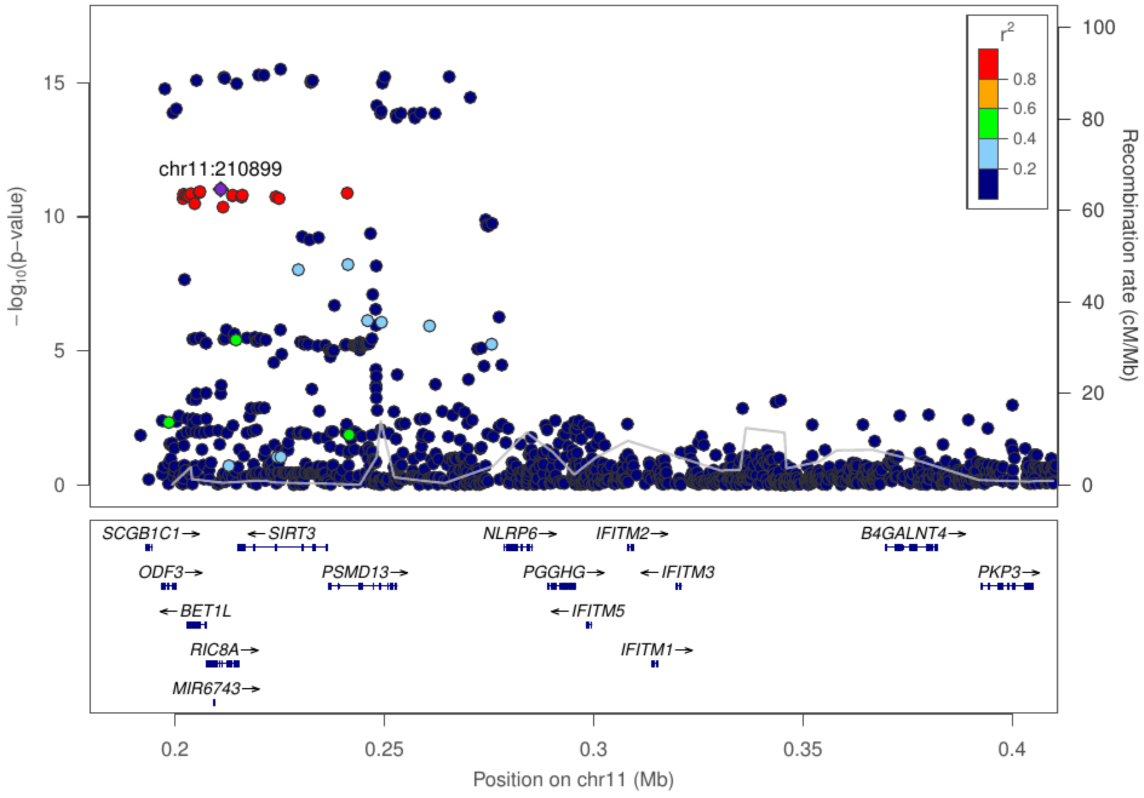
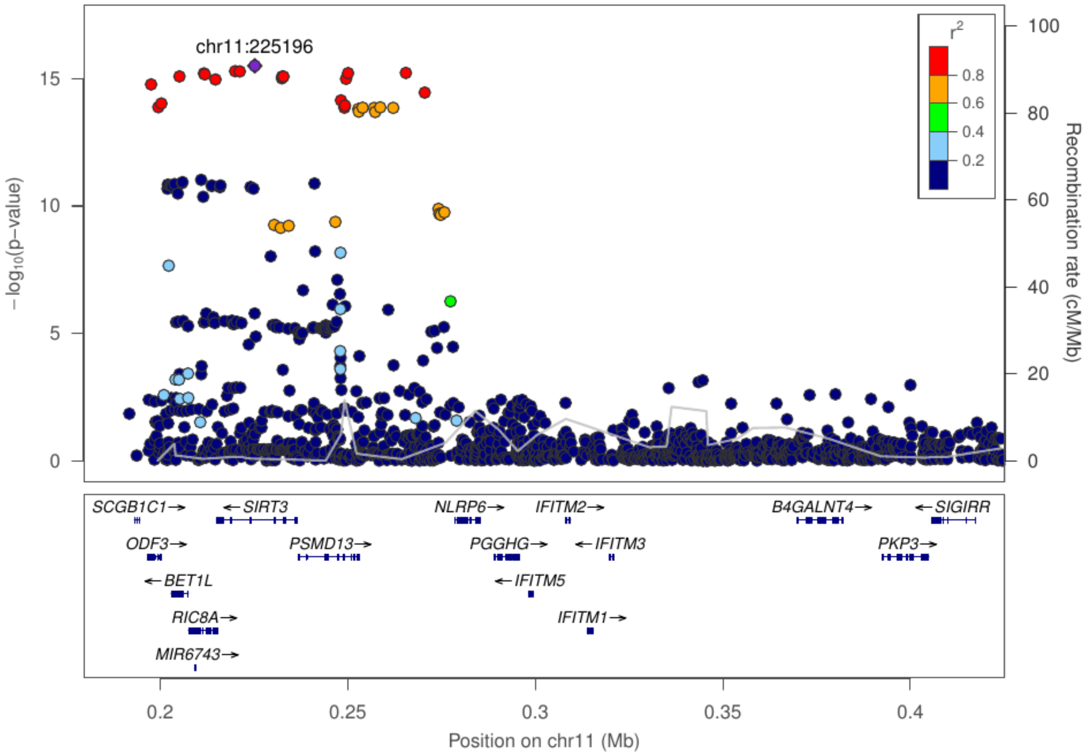
0.6
0.4
0.2
−log10(p−value)
0
5
10
15
20
Recombination rate (cM/Mb)
0
20
40
60
80
100
KANK1→
DMRT1→
LINC01230→
DMRT3→
0.6
0.7
0.8
0.9
1
Position on chr9 (Mb)


r²
0.8
0.6
0.4
0.2
chr10:103920874
−log₁₀(p−value)
Recombination rate (cM/Mb)
SH3PXD2A−AS1→
←OBFC1
SLK→
SFR1→
←COL17A1
←MIR936
103.7
103.8
103.9
104
104.1
Position on chr10 (Mb)


r²
0.8
0.6
0.4
0.2
chr11:210899
−log₁₀(p−value)
Recombination rate (cM/Mb)
SCGB1C1→
←SIRT3
NLRP6→
IFITM2→
B4GALNT4→
ODF3→
PSMD13→
PGGHG→
←IFITM3
PKP3→
←BET1L
←IFITM5
RIC8A→
IFITM1→
MIR6743→
0.2
0.25
0.3
0.35
0.4
Position on chr11 (Mb)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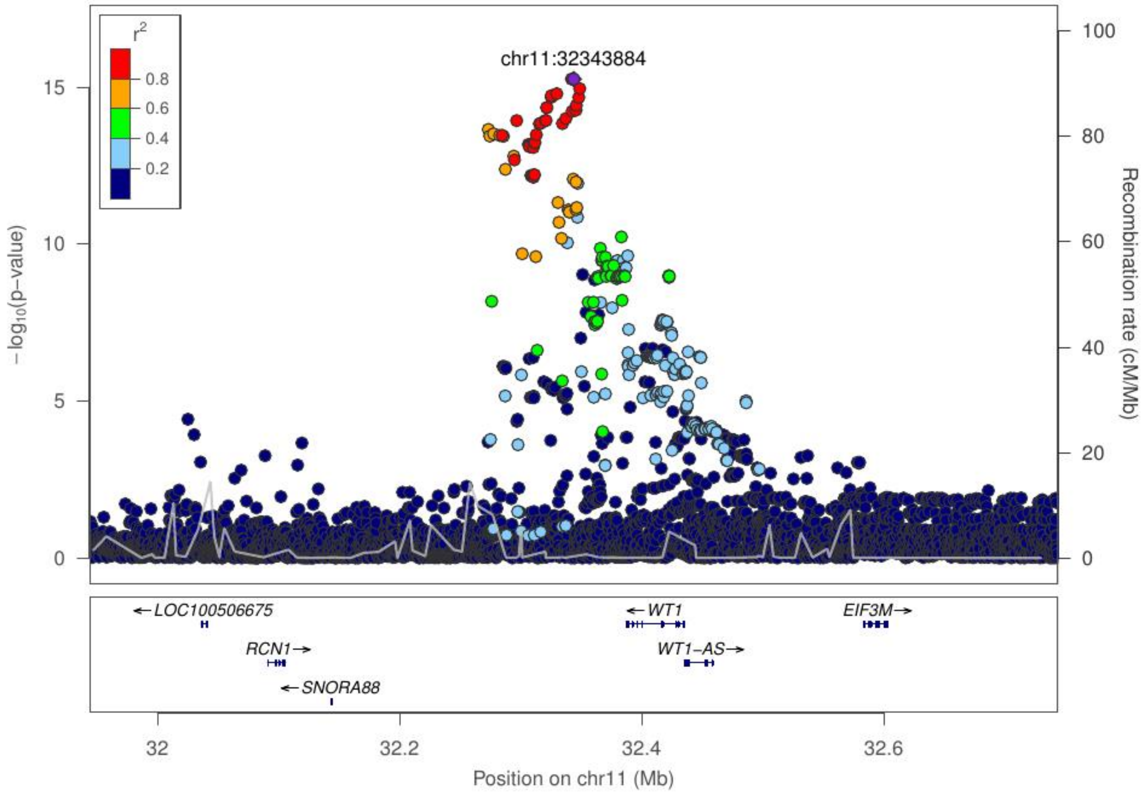
r²
0.8
0.6
0.4
0.2
− log₁₀(p−value)
0
5
10
15
Recombination rate (cM/Mb)
0
20
40
60
80
100
SCGB1C1→
←SIRT3
NLRP6→
IFITM2→
B4GALNT4→
←SIGIRR
ODF3→
PSMD13→
PGGHG→
←IFITM3
PKP3→
←BET1L
←IFITM5
RIC8A→
IFITM1→
MIR6743→
0.2
0.25
0.3
0.35
0.4
Position on chr11 (Mb)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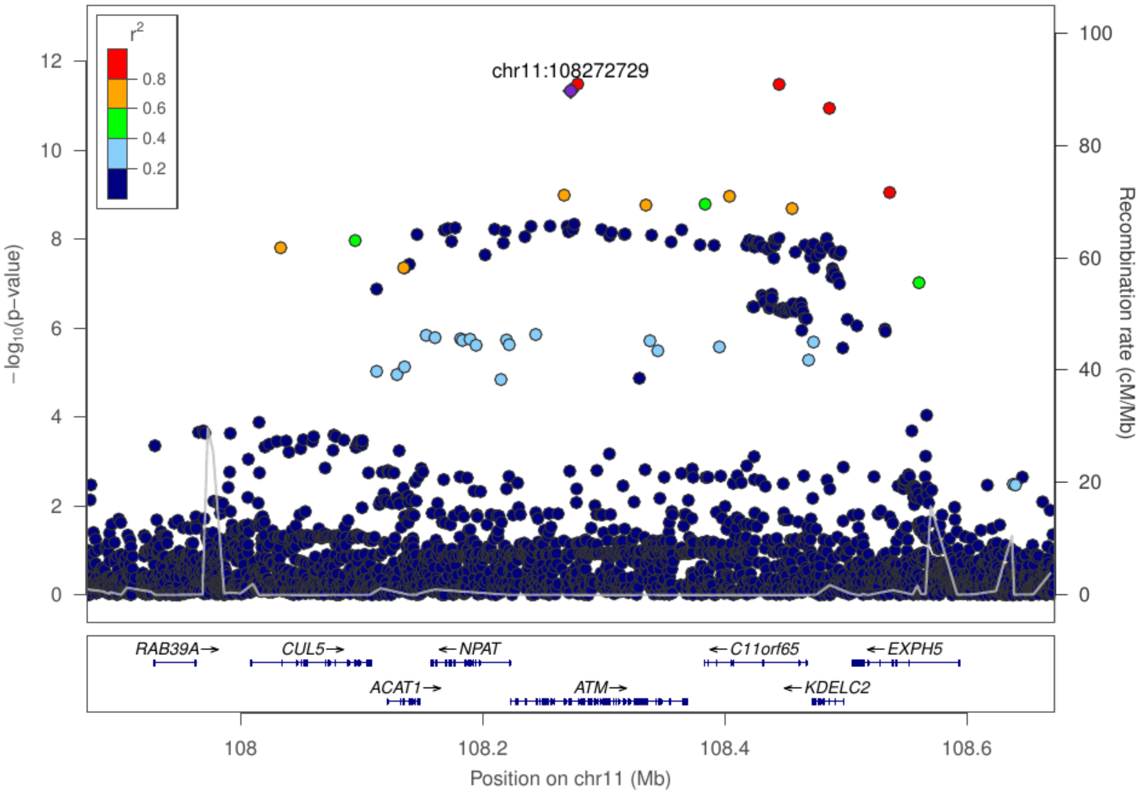
r²
0.8
0.6
0.4
0.2
− log₁₀(p−value)
0
5
10
15
Recombination rate (cM/Mb)
0
20
40
60
80
100
←LOC100506675
←WT1
EIF3M→
RCN1→
WT1−AS→
←SNORA88
32
32.2
32.4
32.6
Position on chr11 (Mb)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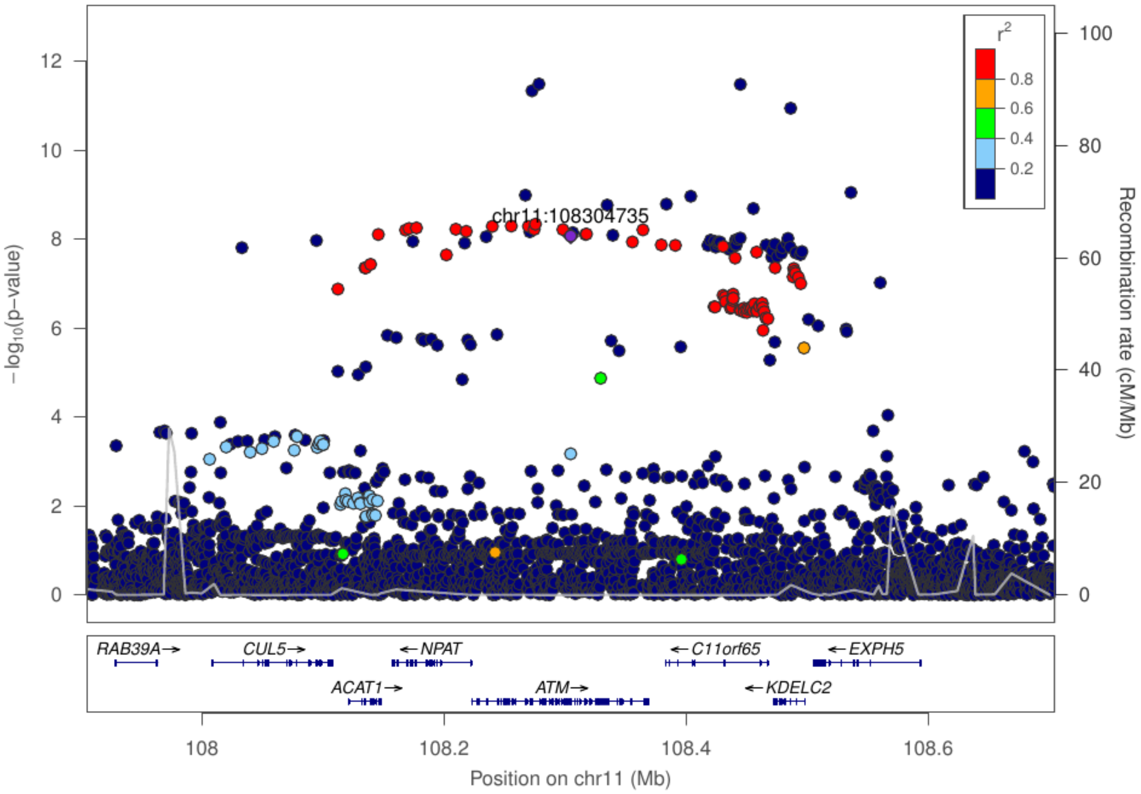
0.6
0.4
0.2
chr11:108272729
12
10
8
6
4
2
0
−log₁₀(p−value)
100
80
60
40
20
0
Recombination rate (cM/Mb)
RAB39A→
CUL5→
←NPAT
←C11orf65
←EXPH5
ACAT1→
ATM→
←KDELC2
108
108.2
108.4
108.6
Position on chr11 (Mb)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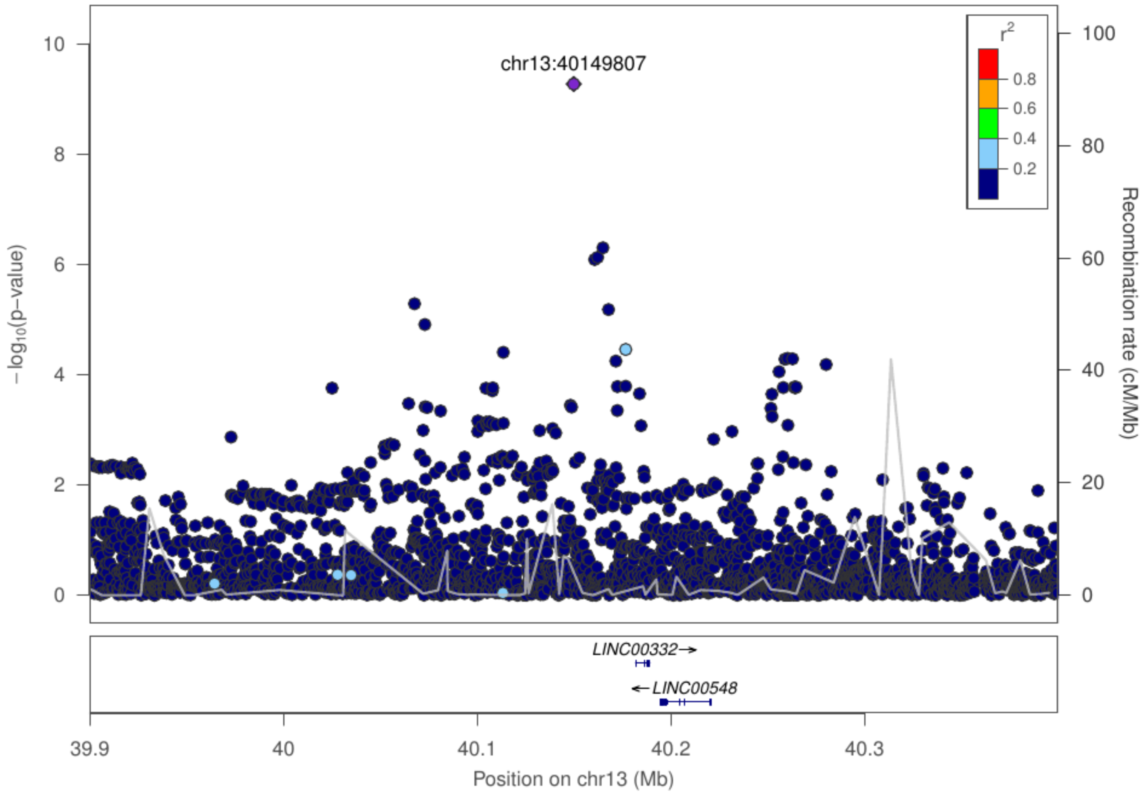
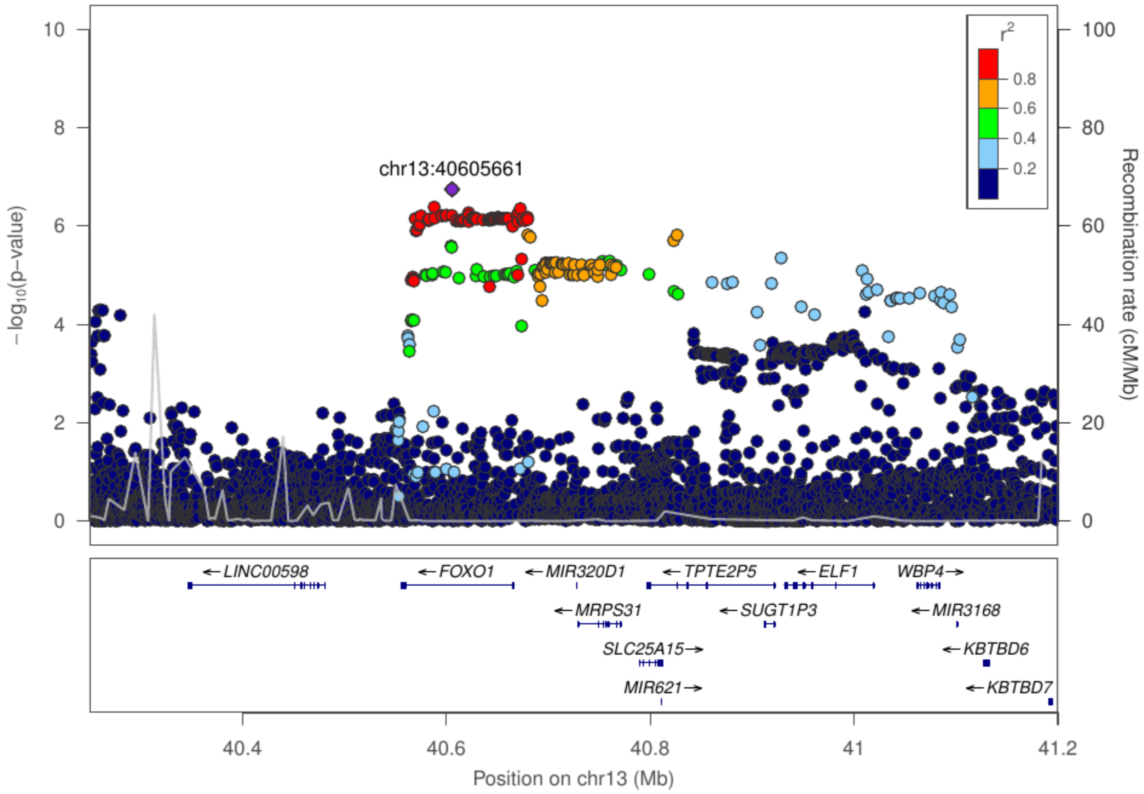
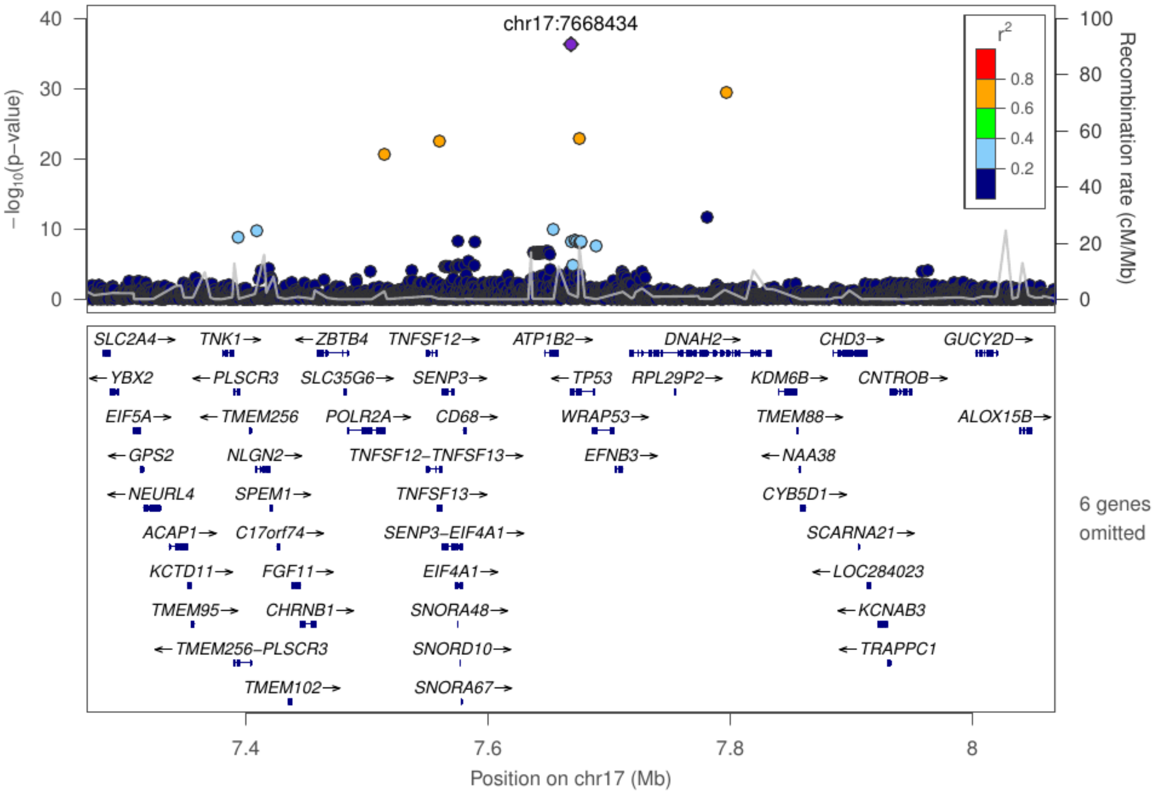
0.6
0.4
0.2
chr11:108304735
12
10
8
6
4
2
0
−log₁₀(p−value)
100
80
60
40
20
0
Recombination rate (cM/Mb)
RAB39A→
CUL5→
←NPAT
←C11orf65
←EXPH5
ACAT1→
ATM→
←KDELC2
108
108.2
108.4
108.6
Position on chr11 (Mb)


chr13:40149807
r2
0.8
0.6
0.4
0.2
−log10(p−value)
0
2
4
6
8
10
Recombination rate (cM/Mb)
0
20
40
60
80
100
LINC00332→
←LINC00548
39.9
40
40.1
40.2
40.3
Position on chr13 (Mb)


chr13:40605661
r2
0.8
0.6
0.4
0.2
−log10(p−value)
0
2
4
6
8
10
Recombination rate (cM/Mb)
0
20
40
60
80
100
←LINC00598
←FOXO1
←MIR320D1
←TPTE2P5
←ELF1
WBP4→
←MRPS31
←SUGT1P3
←MIR3168
SLC25A15→
←KBTBD6
MIR621→
←KBTBD7
40.4
40.6
40.8
41
41.2
Position on chr13 (Mb)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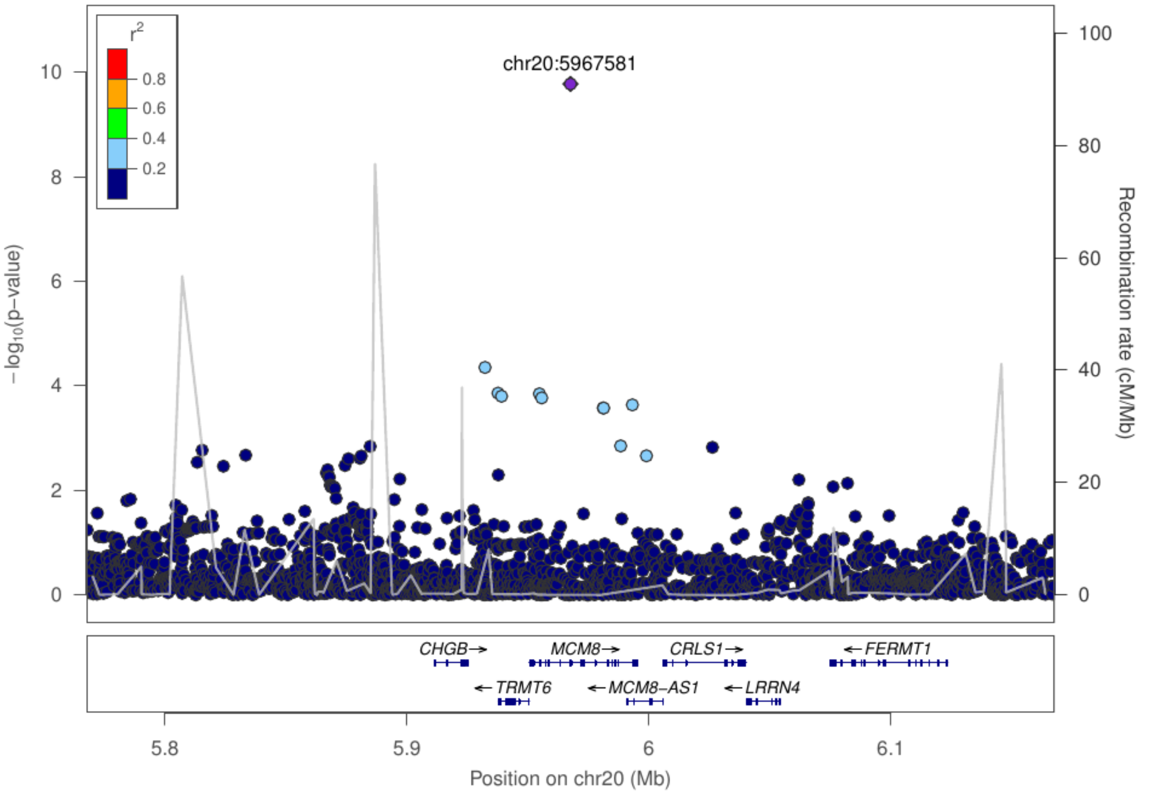
r²
0.8
0.6
0.4
0.2
− log₁₀(p−value)
40
30
20
10
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
SLC2A4→
TNK1→
←ZBTB4
TNFSF12→
ATP1B2→
DNAH2→
CHD3→
GUCY2D→
←YBX2
←PLSCR3
SLC35G6→
SENP3→
←TP53
RPL29P2→
KDM6B→
CNTROB→
EIF5A→
←TMEM256
POLR2A→
CD68→
WRAP53→
TMEM88→
ALOX15B→
←GPS2
NLGN2→
TNFSF12−TNFSF13→
EFNB3→
←NAA38
←NEURL4
SPEM1→
TNFSF13→
CYB5D1→
ACAP1→
C17orf74→
SENP3−EIF4A1→
SCARNA21→
KCTD11→
FGF11→
EIF4A1→
←LOC284023
TMEM95→
CHRNB1→
SNORA48→
←KCNAB3
←TMEM256−PLSCR3
SNORD10→
←TRAPPC1
TMEM102→
SNORA67→
6 genes
omitted
7.4
7.6
7.8
8
Position on chr17 (Mb)


chr20:5967581
r²
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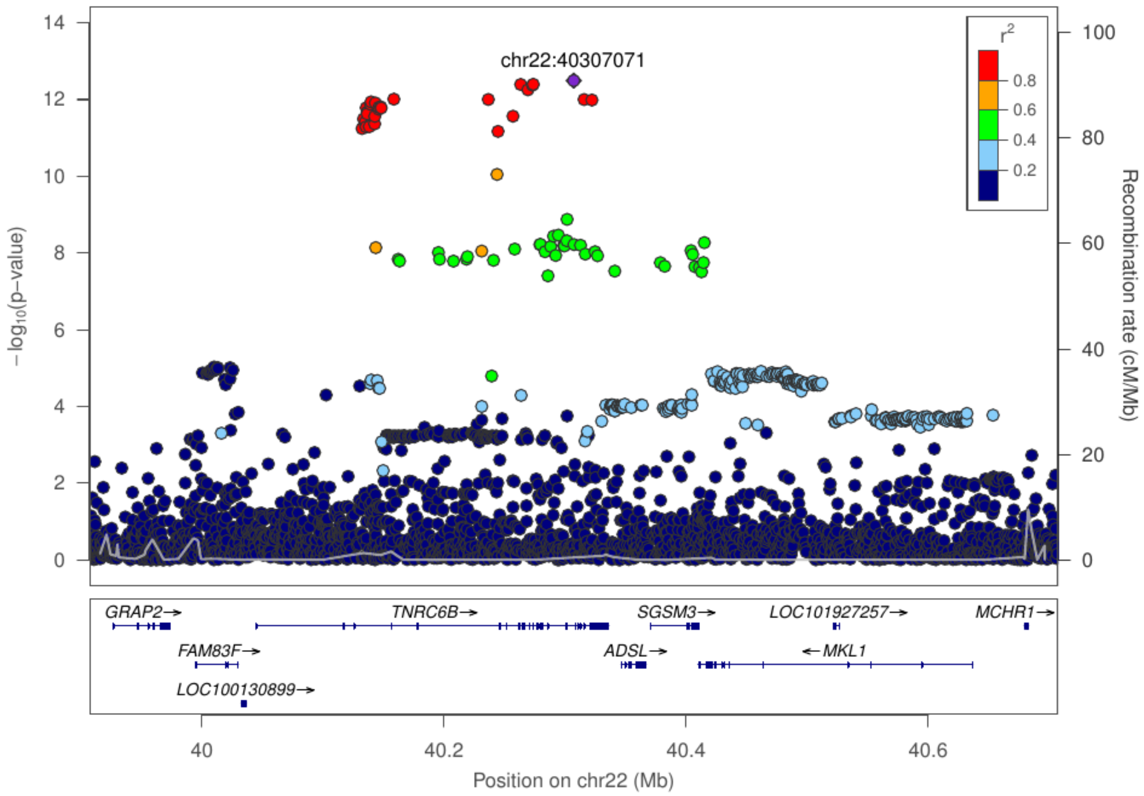
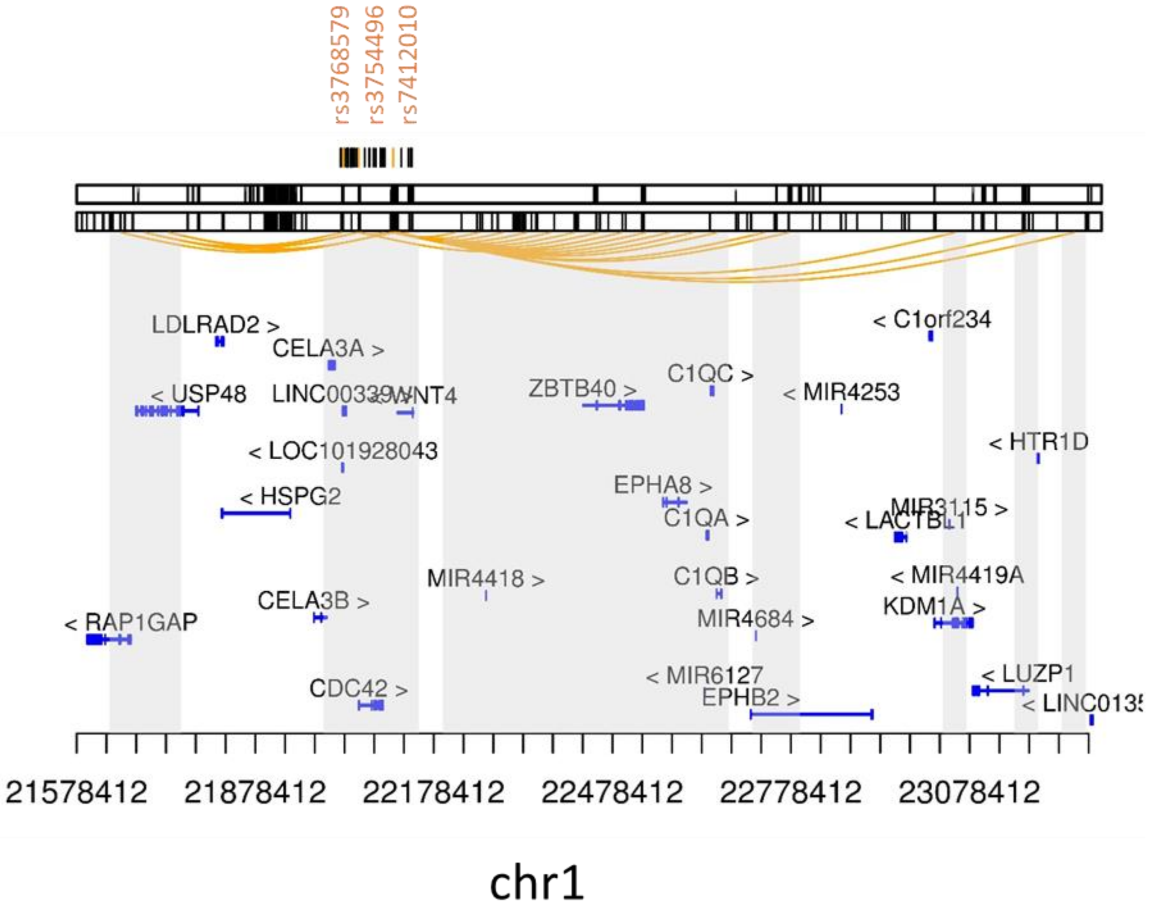
0.6
0.4
0.2
− log₁₀(p−value)
10
8
6
4
2
0
100
80
60
40
20
0
Recombination rate (cM/Mb)
CHGB→
MCM8→
CRLS1→
←FERMT1
←TRMT6
←MCM8−AS1
←LRRN4
5.8
5.9
6
6.1
Position on chr20 (Mb)



Supplementary figure 1. Locus plots for variants associating with leiomyoma from meta-analysis of Icelandic and UK Biobank GWAS datasets. P values (−log10) of variant associations with leiomyoma in the meta-analysis are plotted against their NCBI Build 38 positions. Known genes in the regions are shown underneath each plot, taken from the UCSC Genes track in the UCSC Genome Browser. Only high-quality markers are displayed with a 400kb window around the lead variant.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CELA3B >
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CDC42 >
MIR4418 >
ZBTB40 >
C1QC >
EPHA8 >
C1QA >
C1QB >
MIR4684 >
< MIR6127
EPHB2 >
< MIR4253
< C1orf234
< HTR1D
MIR3115 >
< LACTBL1
< MIR4419A
KDM1A >
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< LINC0135
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22178412
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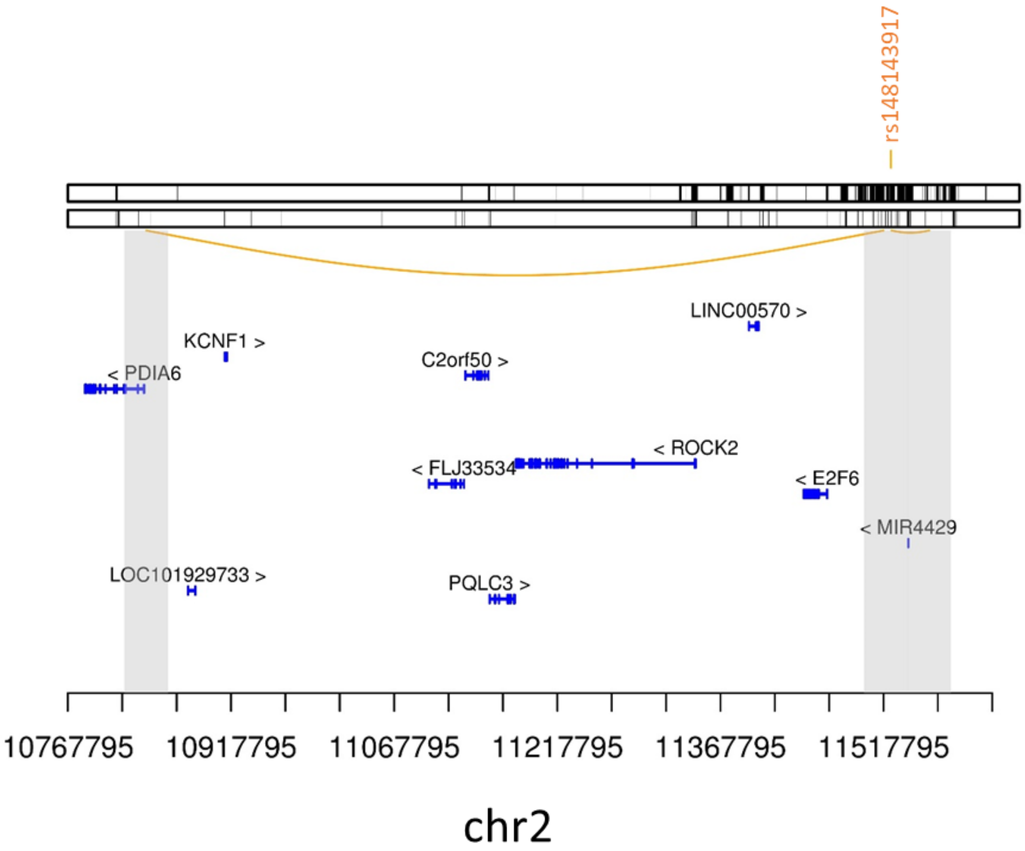
22778412
23078412
chr1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LINC00570 >
KCNF1 >
C2orf50 >
< PDIA6
< ROCK2
< FLJ33534
< E2F6
< MIR4429
LOC101929733 >
PQLC3 >
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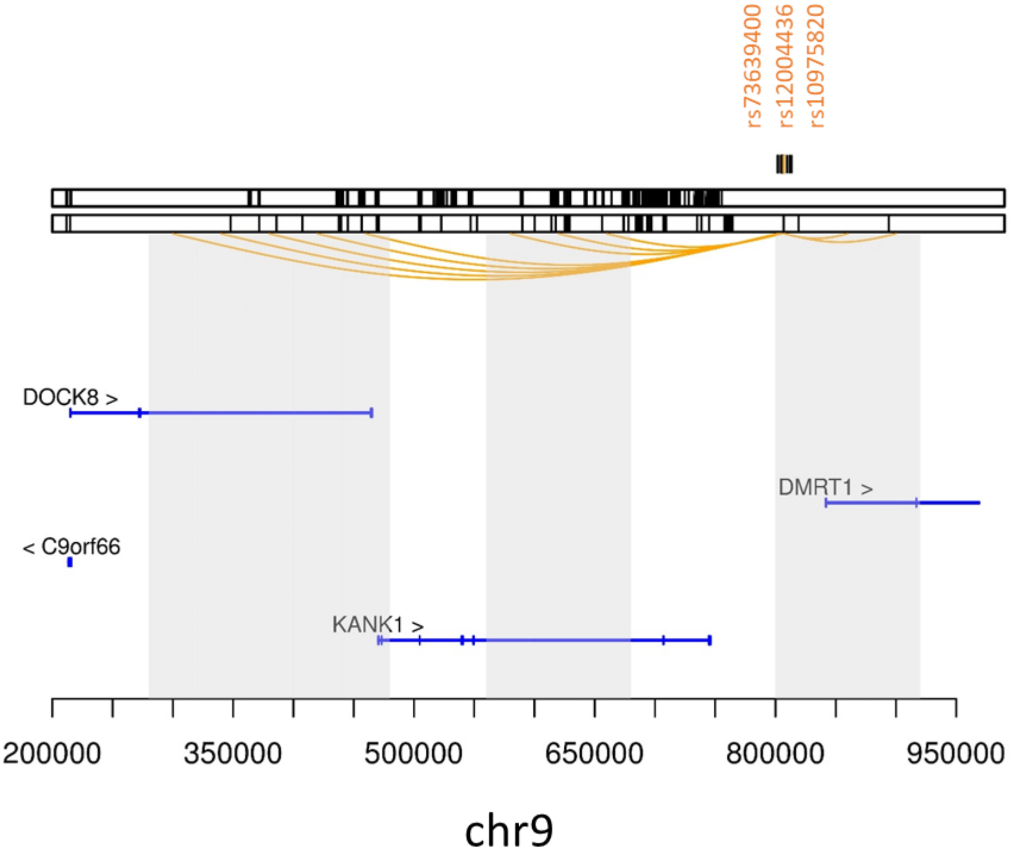
10917795
11067795
11217795
11367795
11517795
chr2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rs10975820
DOCK8 >
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KANK1 >
DMRT1 >
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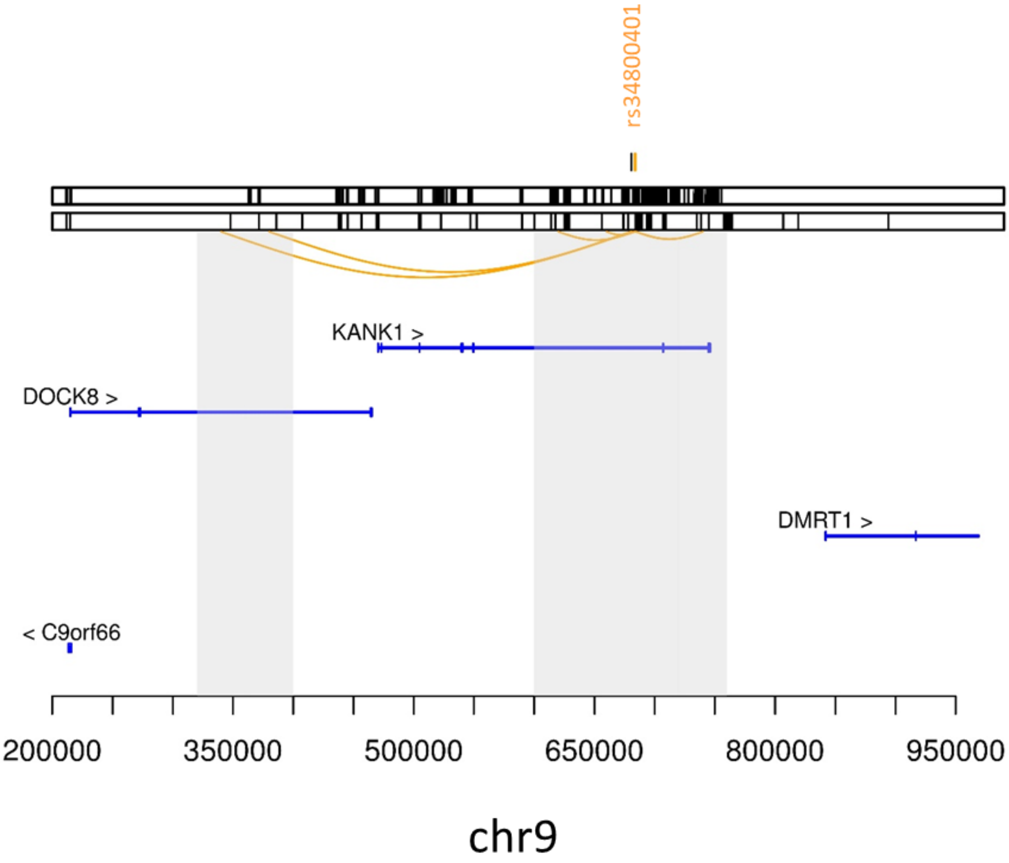
350000
500000
650000
800000
950000
chr9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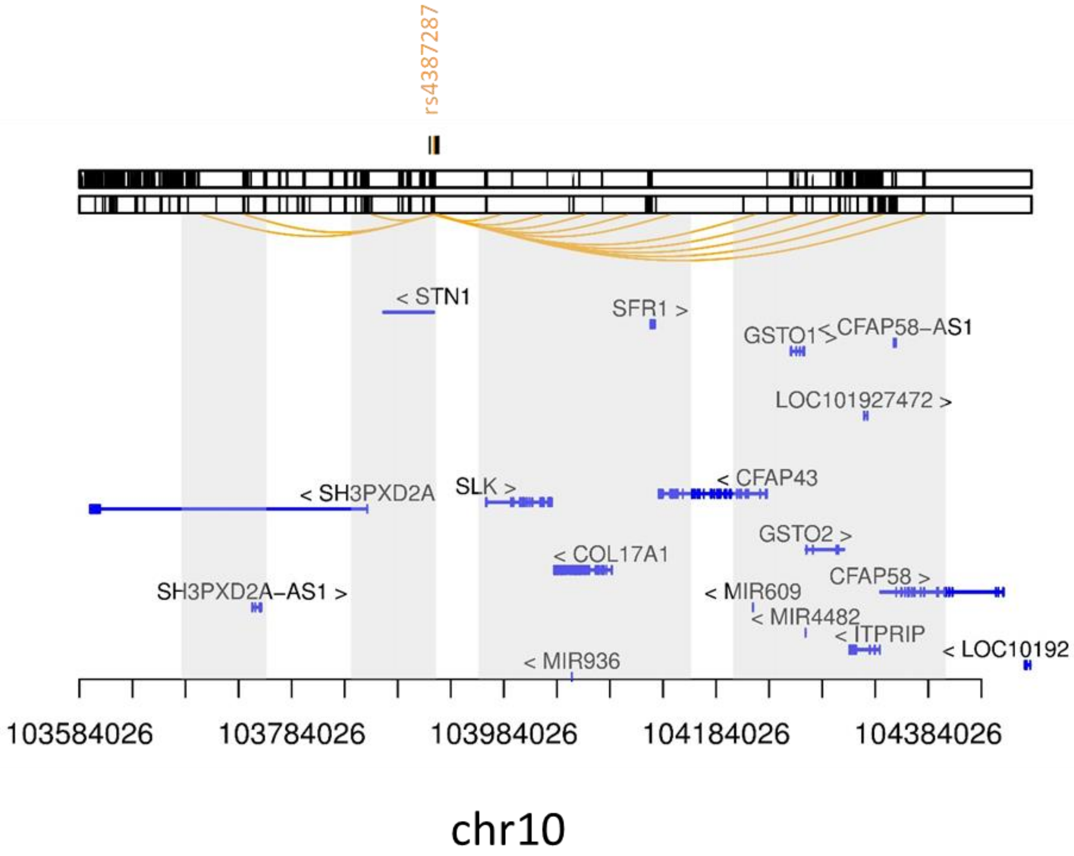
KANK1 >
DOCK8 >
DMRT1 >
< C9orf66
200000
350000
500000
650000
800000
950000
chr9


rs4387287
< STN1
SFR1 >
GSTO1 >
< CFAP58-AS1
LOC101927472 >
< SH3PXD2A
SLK >
< CFAP43
GSTO2 >
< COL17A1
SH3PXD2A-AS1 >
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CFAP58 >
< MIR4482
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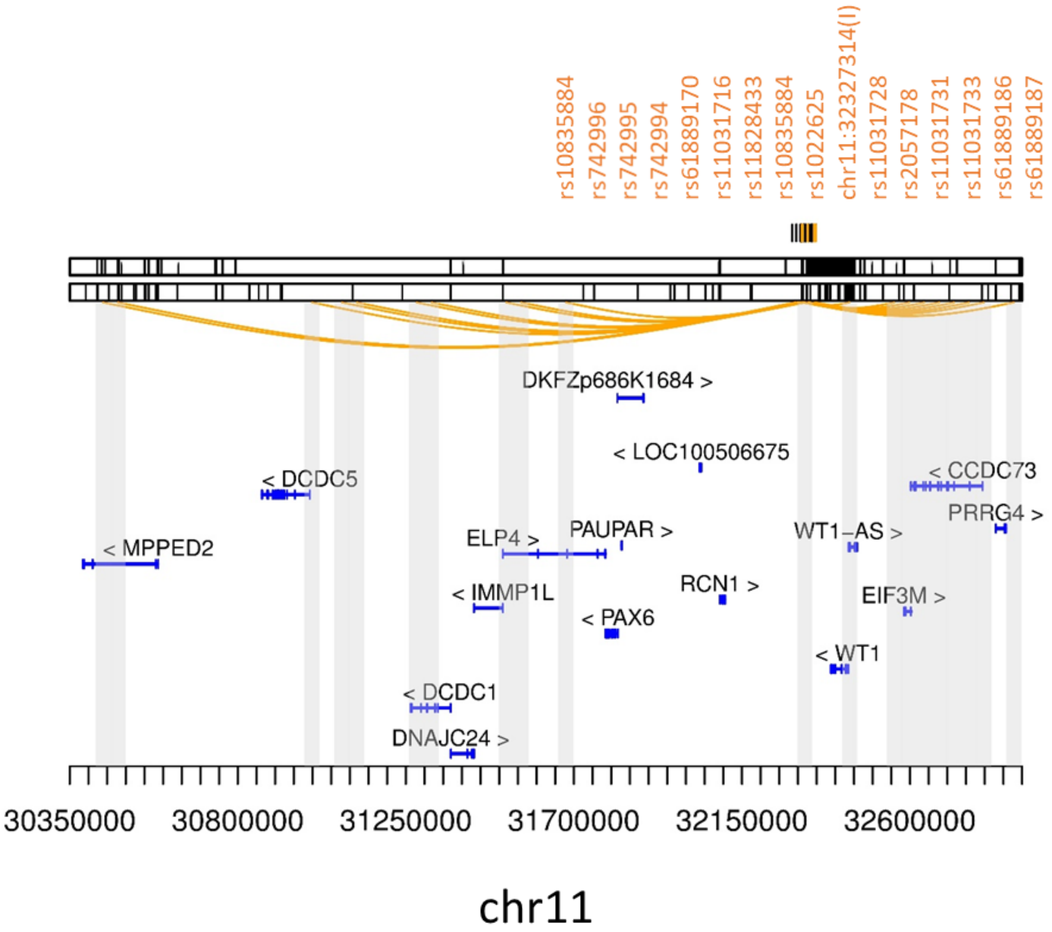
< MIR936
103584026
103784026
103984026
104184026
104384026
chr10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rs742995
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rs61889170
rs11031716
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rs1022625
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rs11031728
rs2057178
rs11031731
rs11031733
rs61889186
rs61889187
DKFZp686K1684 >
< LOC100506675
< DCDC5
< CCDC73
PRRG4 >
ELP4 >
PAUPAR >
WT1−AS >
< MPPED2
RCN1 >
EIF3M >
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< WT1
< DCDC1
DNAJC24 >
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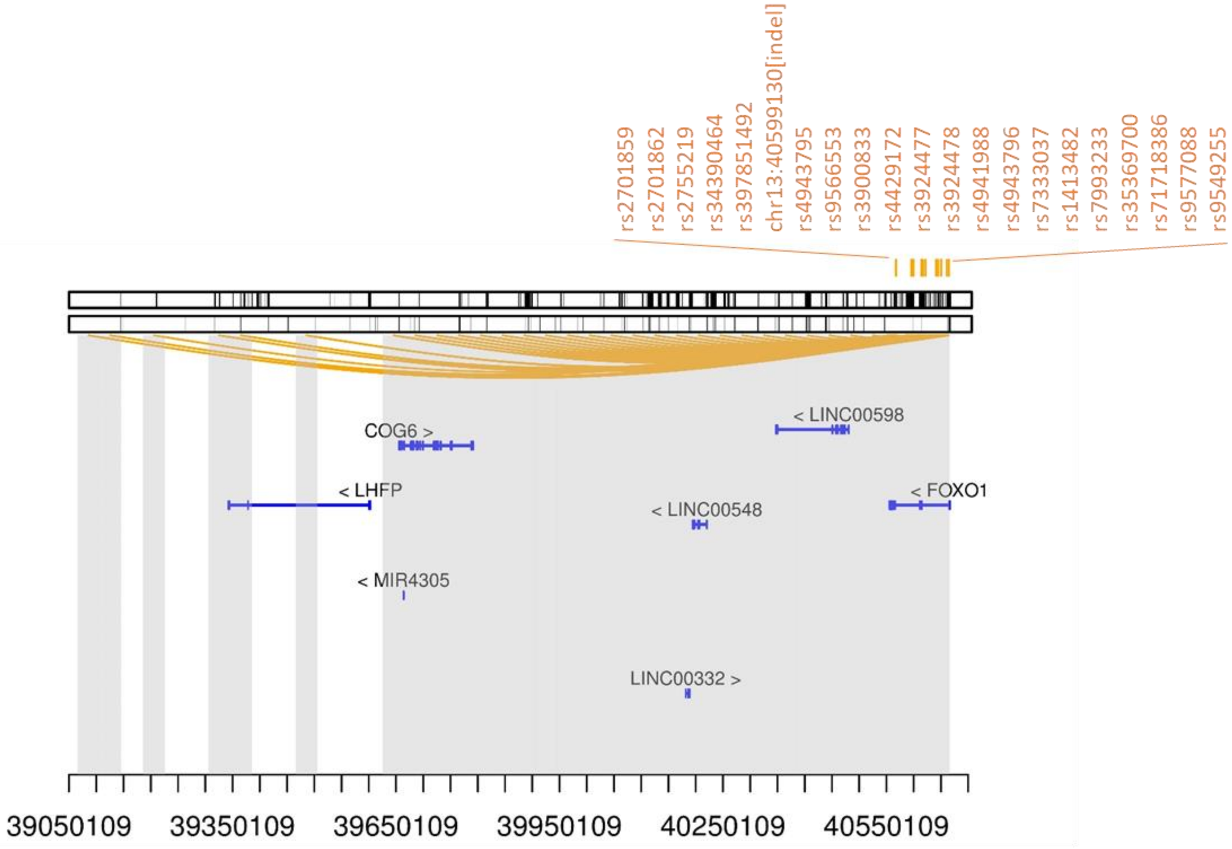
31700000
32150000
32600000
chr11


rs2701859
rs2701862
rs2755219
rs34390464
rs397851492
chr13:40599130[indel]
rs4943795
rs9566553
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rs3924477
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rs7333037
rs1413482
rs7993233
rs35369700
rs71718386
rs9577088
rs9549255
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COG6 >
< LHFP
< FOXO1
< LINC00548
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LINC00332 >
39050109
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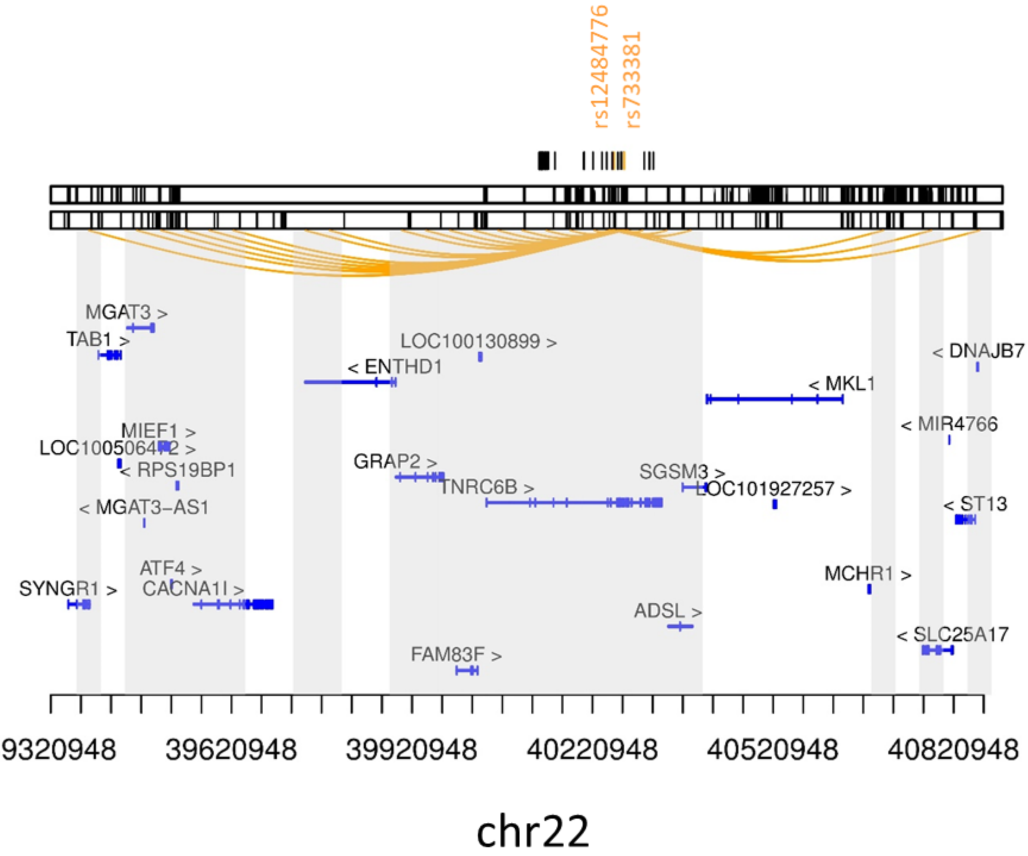
39650109
39950109
40250109
40550109

chr13



Supplementary figure 2. Leiomyoma risk variants intersecting with regulatory regions and their candidate target genes.