SI GUIDE

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Description: Supplementary Figures.

Supplementary Data

Title of file for HTML: Supplementary Data 1
Description: Sample counts by SLE status

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Description: Complete list of associations by ancestry and tier (nonHLA).

Title of file for HTML: Supplementary Data 3
Description: Posterior probabilities for HLA imputation

Title of file for HTML: Supplementary Data 4
Description: Classical HLA associations.

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Description: HLA stepwise model results

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Description: SNP associations, post-adjustment for HLA alleles.

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Description: SLE risk for DRB1 homozygotes and heterozygotes

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Description: Secondary top meta-analysis and transancestral-mapping Regions.

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Title of file for HTML: Supplementary Data 10
Description: Deviations in average risk-allele admixture.

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Description: Binomial test of CEU vs YRI admixture deviations.

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Description: cisEQTLs for regions in Tier 1 and Tier 2

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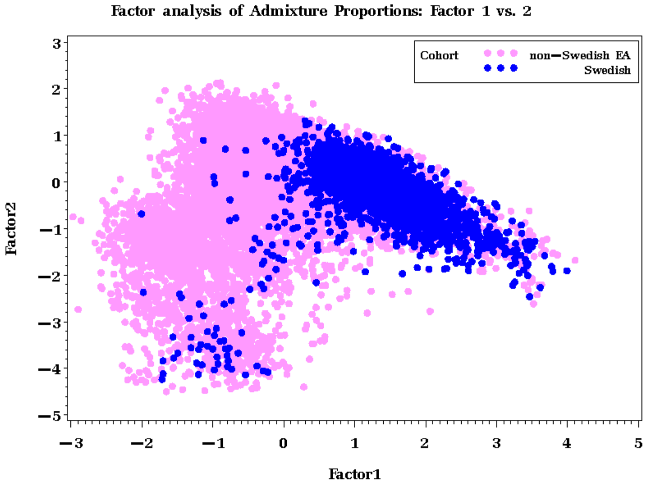
Title of file for HTML: Supplementary Data 14
Description: Prioritized SLE risk genes.

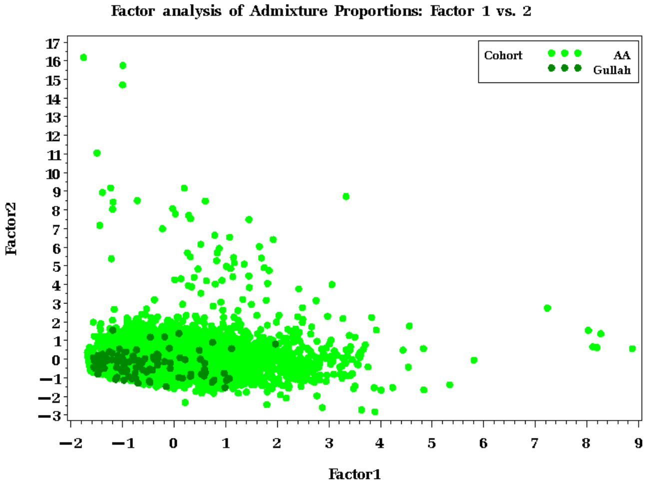
Title of file for HTML: Peer Review File
Description:

Supplementary Figure 1. Admixture by ancestry.

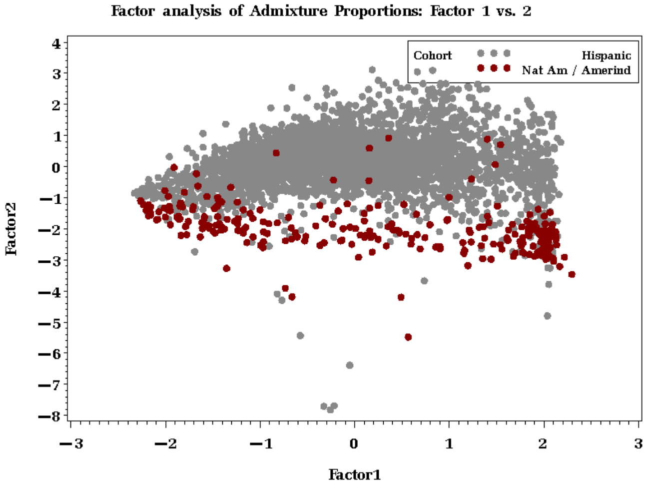
a. European Ancestry



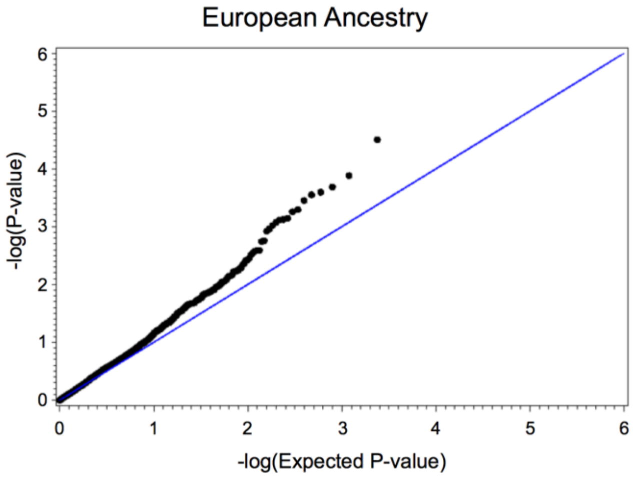
b. African American

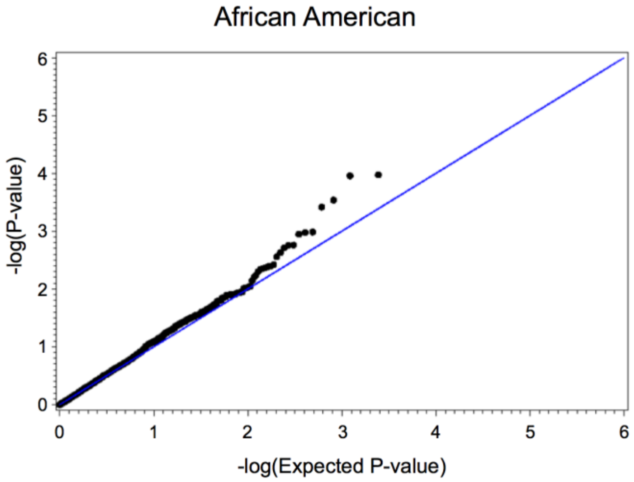


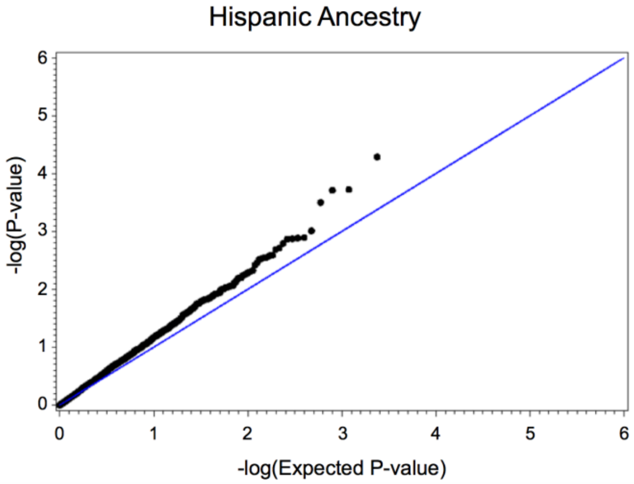
c. Hispanic Ancestry



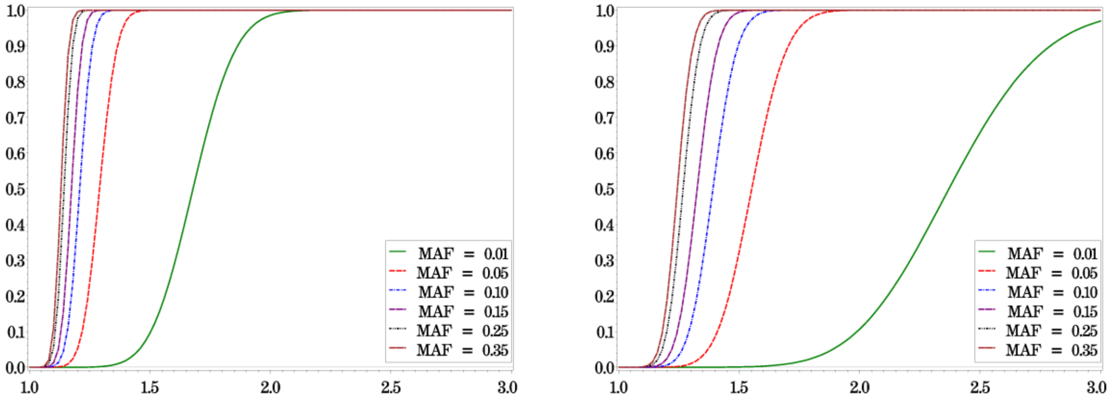
Supplementary Figure 2. PP-plot by ancestry.


European Ancestry

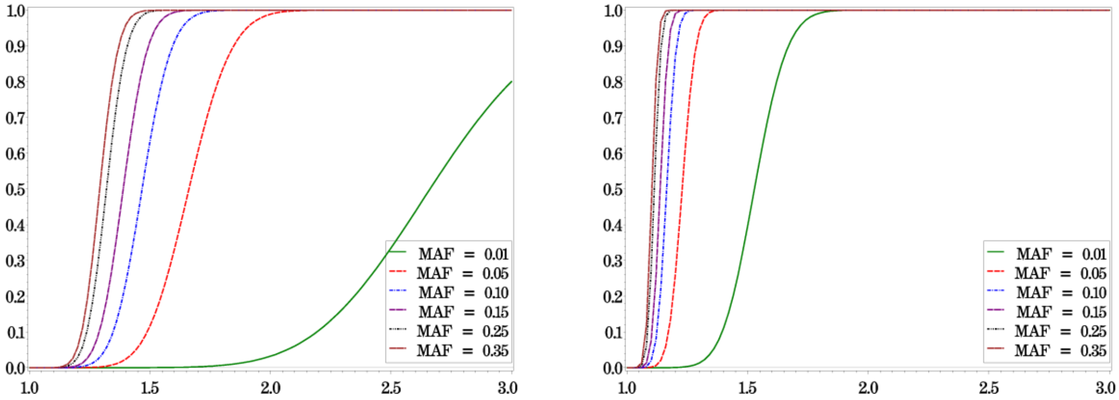

African American


Hispanic Ancestry

Supplementary Figure 3. Power by ancestry (α=5x10^{-8}).

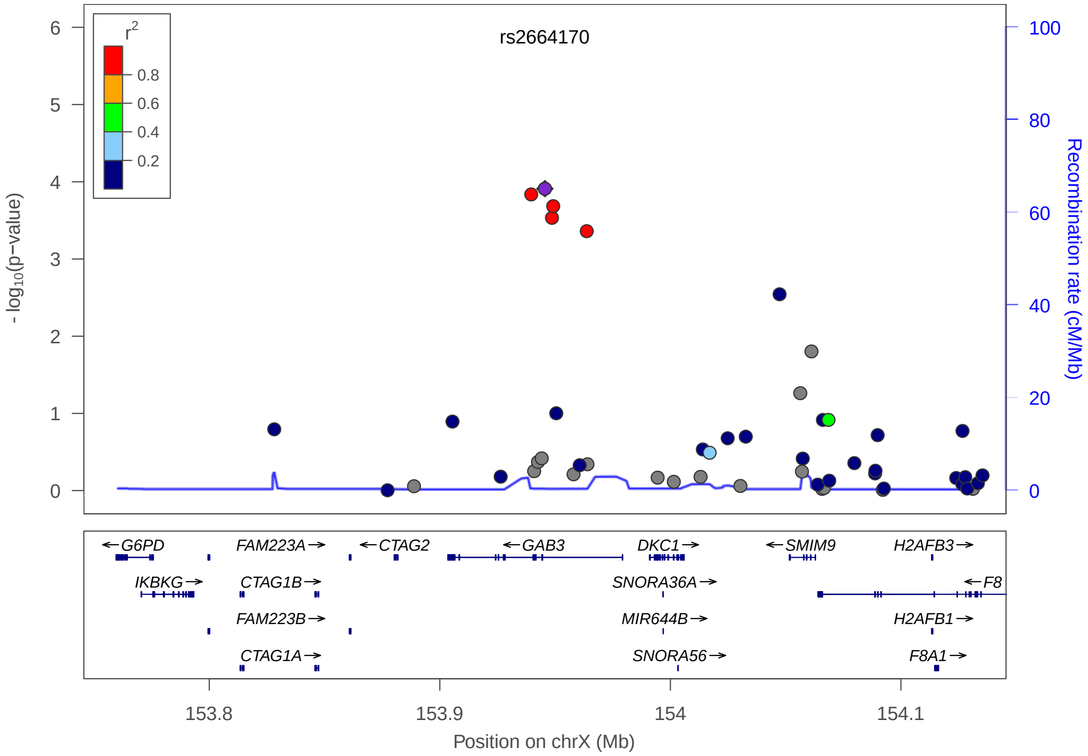

a. European Ancestry

b. African American


c. Hispanic Ancestry

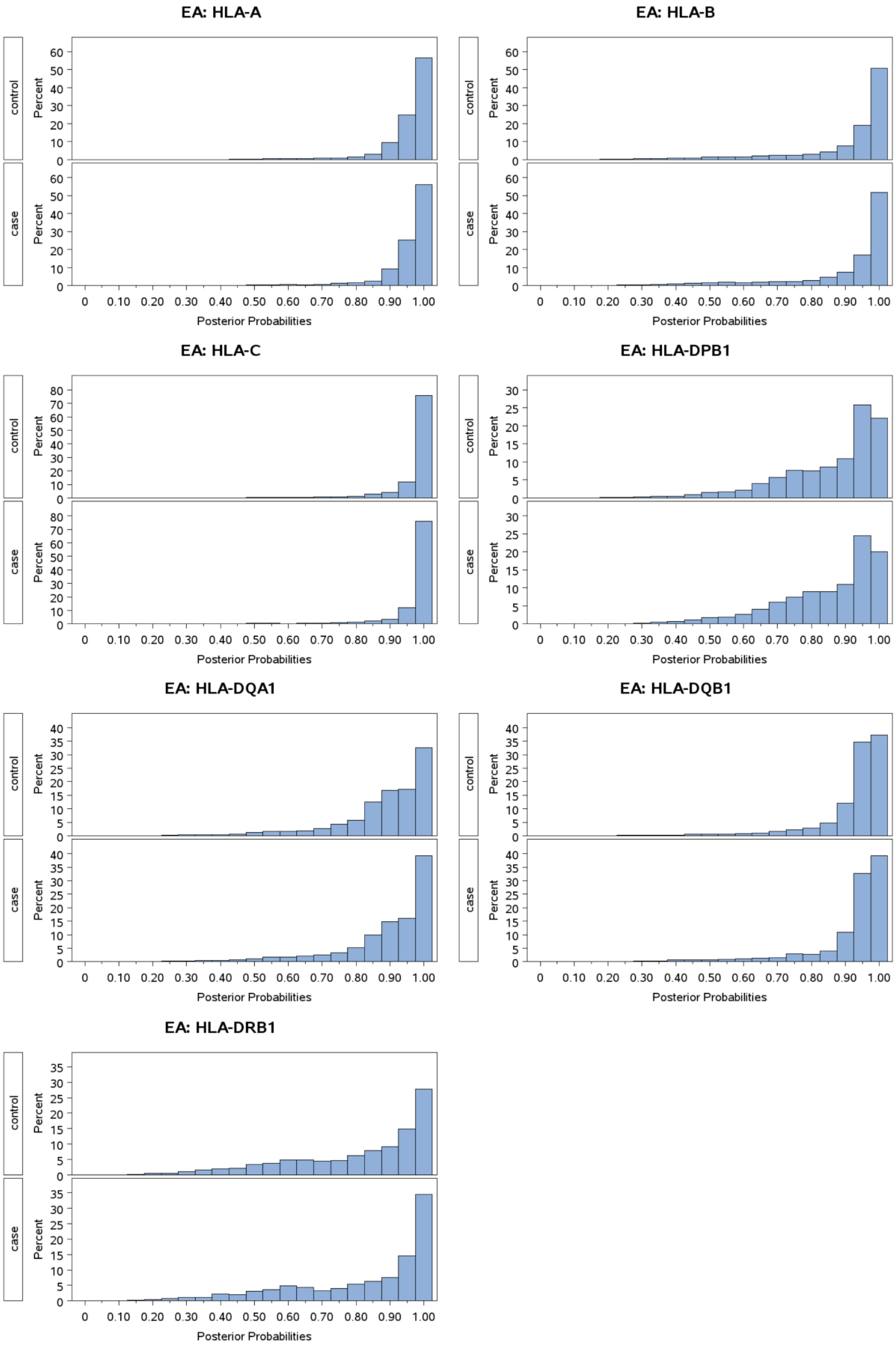
d. Meta-analysis

Supplementary Figure 4. Meta-analysis of chromosome X region of association (female only).

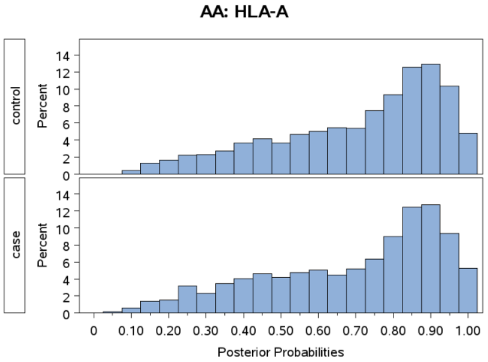


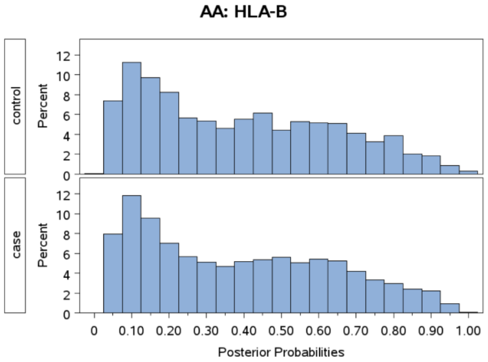
Supplementary Figure 5. Posterior probability distributions for best guess HLA imputed alleles.

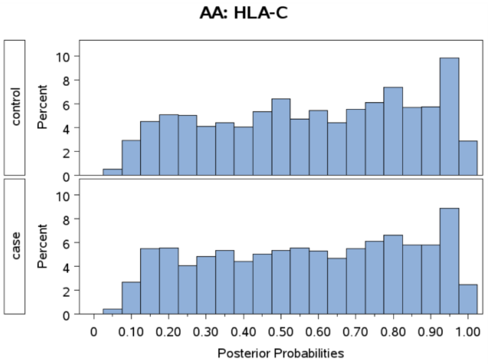
a. European Ancestry

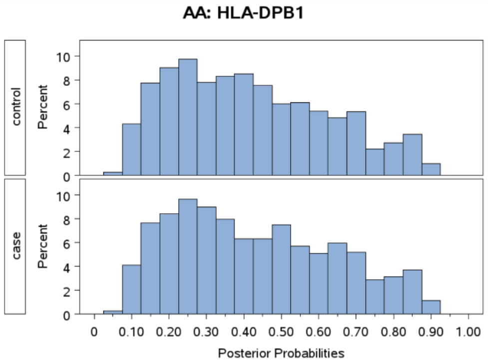


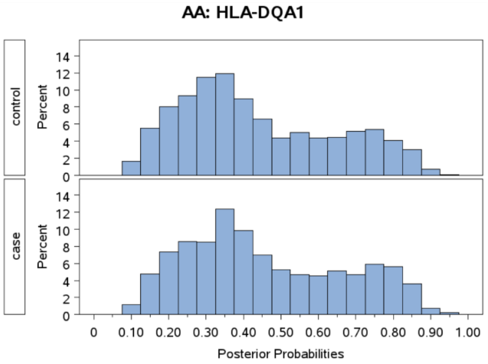
b. African American

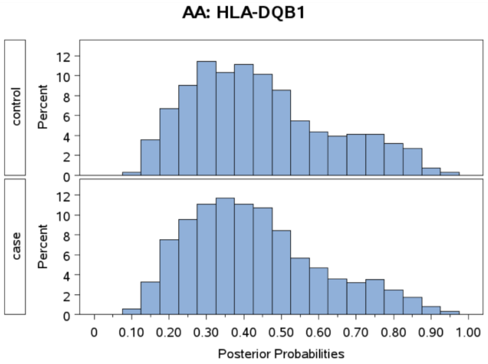

AA: HLA-A

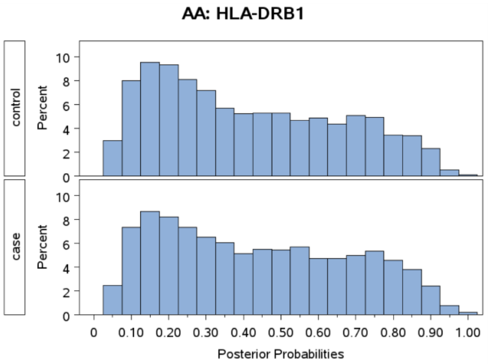

AA: HLA-B


AA: HLA-C

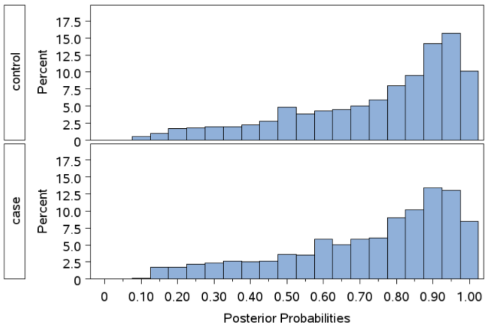

AA: HLA-DPB1

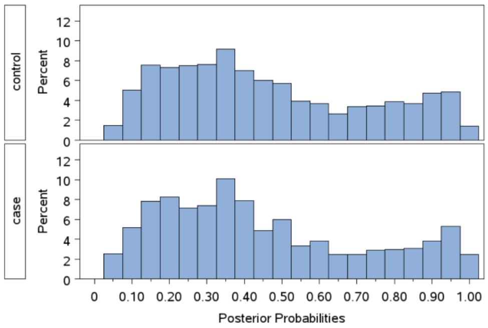

AA: HLA-DQA1

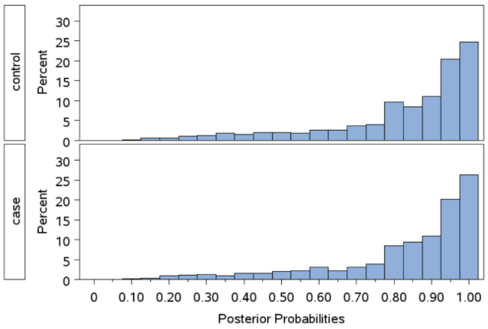

AA: HLA-DQB1

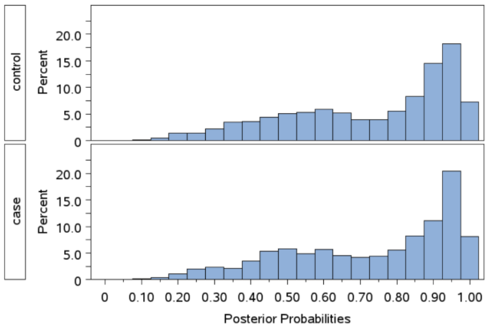

AA: HLA-DRB1

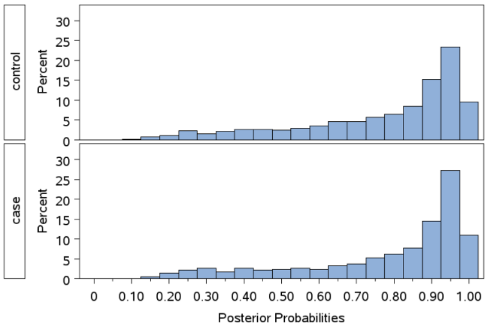
c. Hispanic Ancestry

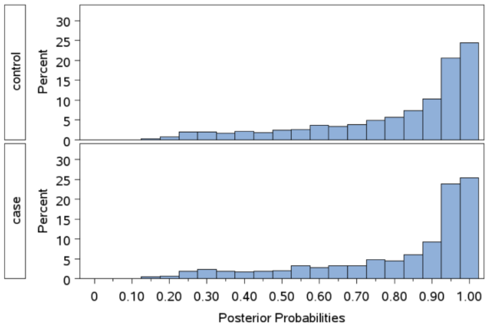

HA: HLA-A

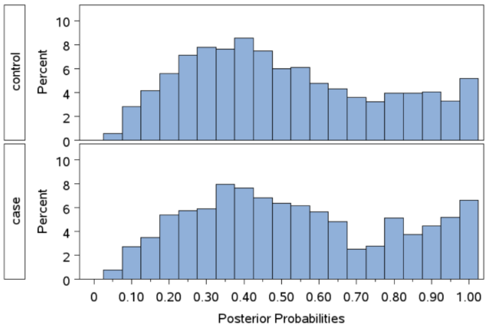

HA: HLA-B


HA: HLA-C


HA: HLA-DPB1

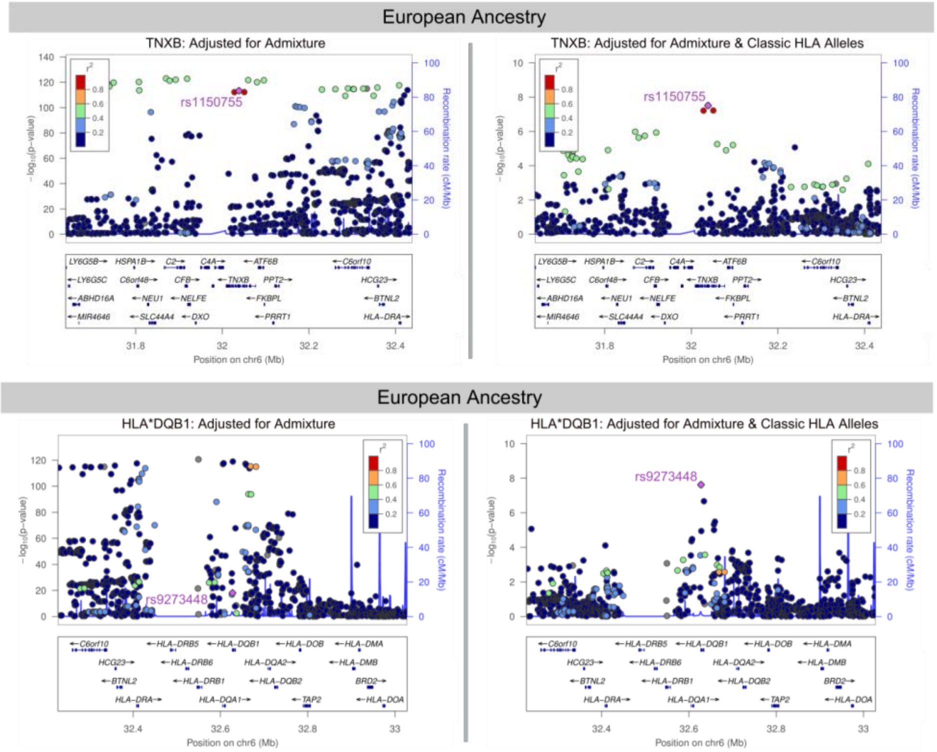

HA: HLA-DQA1


HA: HLA-DQB1

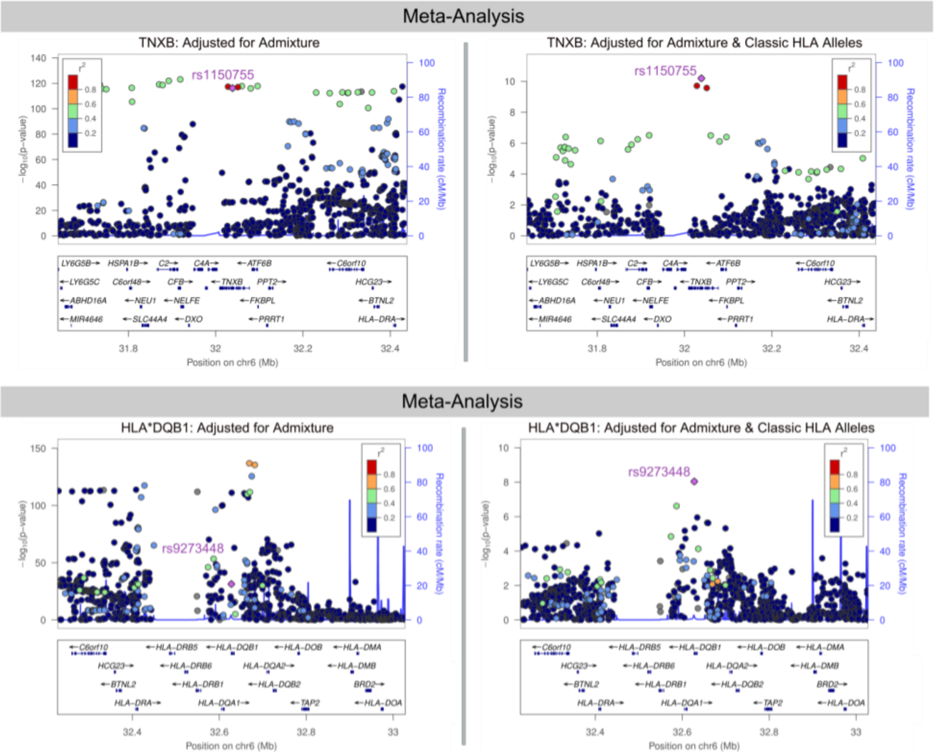

HA: HLA-DRB1

Supplementary Figure 6. Plots of SNP associations meeting genome-wide significance, post-adjustment for Classical HLA alleles.

a. European Ancestry

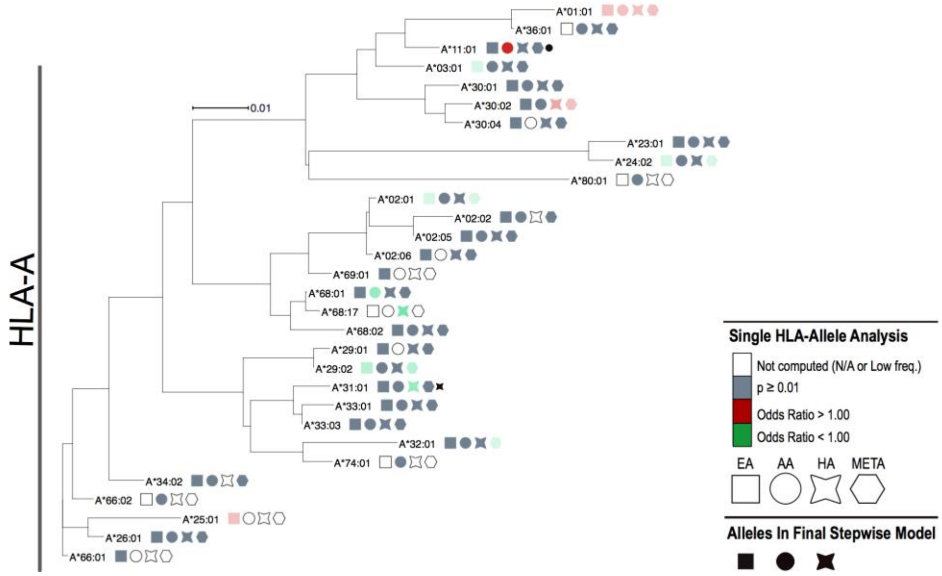


b. Meta Analysis

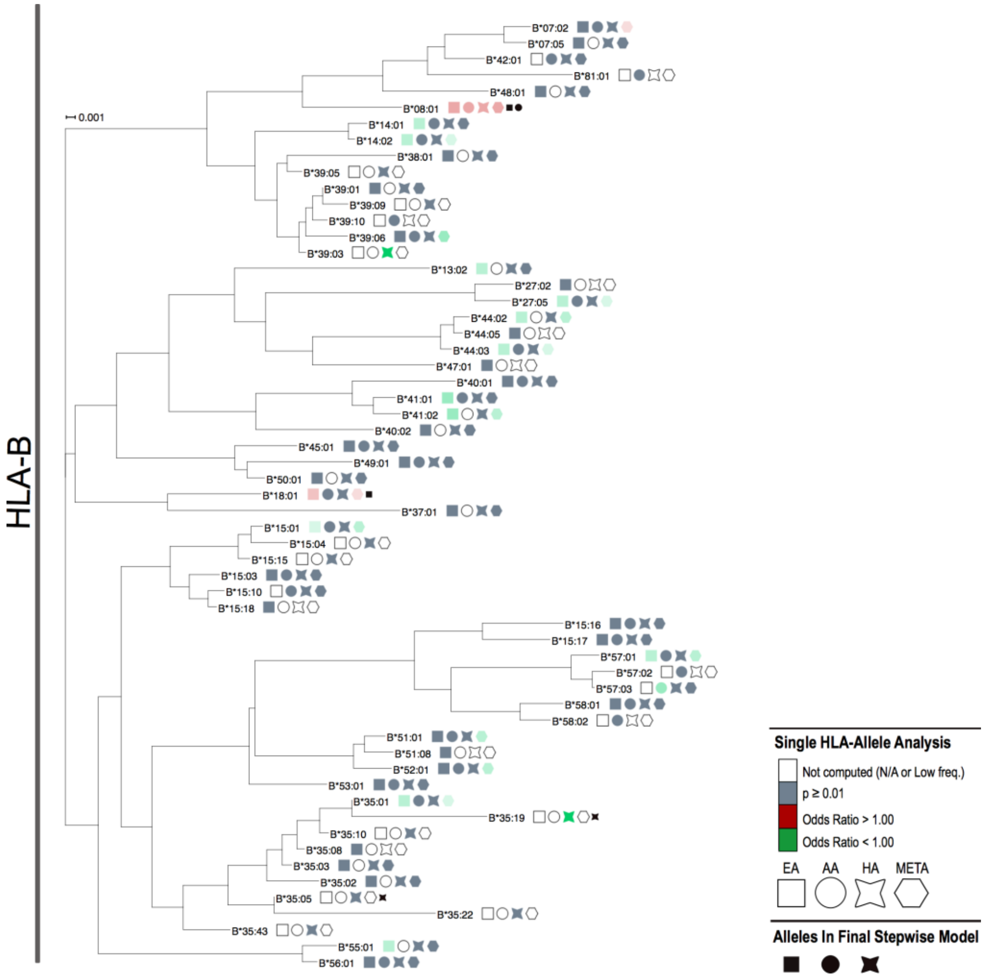


Supplementary Figure 7. Clustering of HLA alleles by amino acid sequence similarity. For each HLA gene, the odds ratios for each cohort are overlain if the SLE association p-value was less than 0.01. Alleles that were present in the multi-locus model from the stepwise procedure are also denoted. This process aims to identify clusters with shared SLE risk or not-risk odds ratios across the three cohorts. Such clusters help identify potential amino acid sequences contributing to SLE risk.

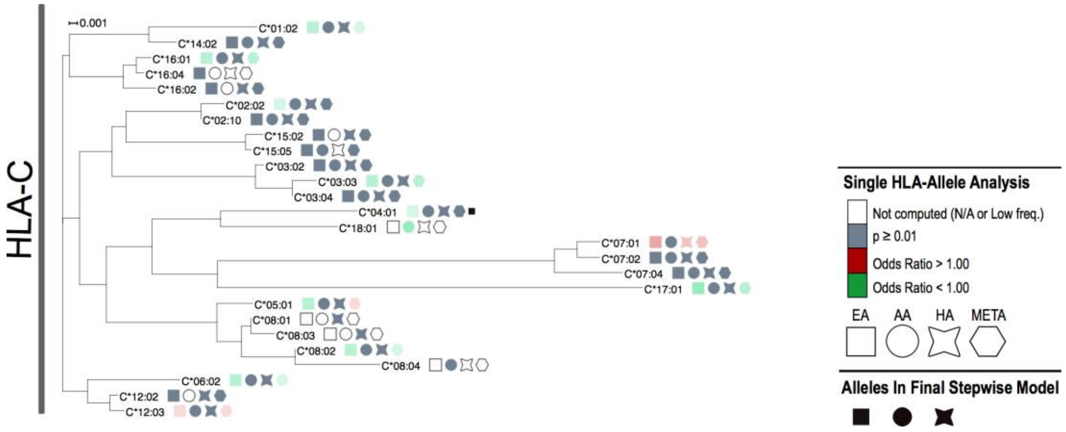
a. HLA-A



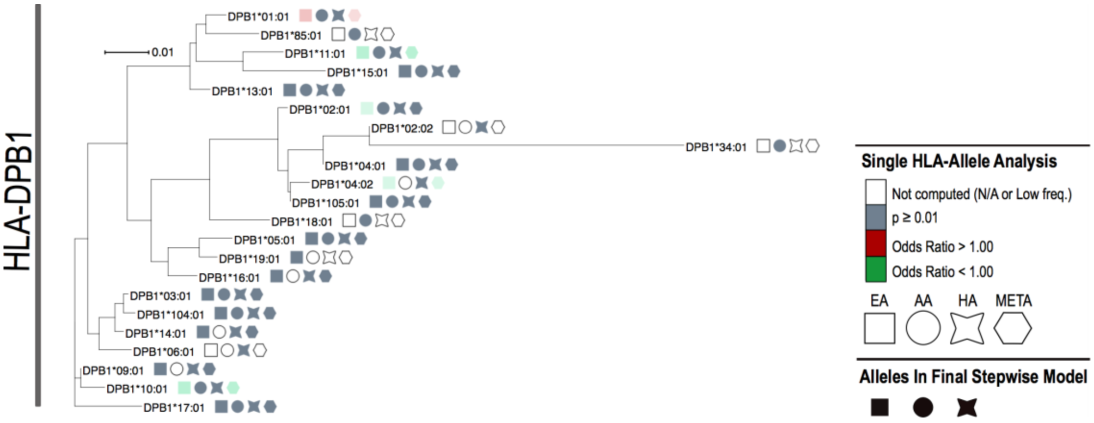
b. HLA-B



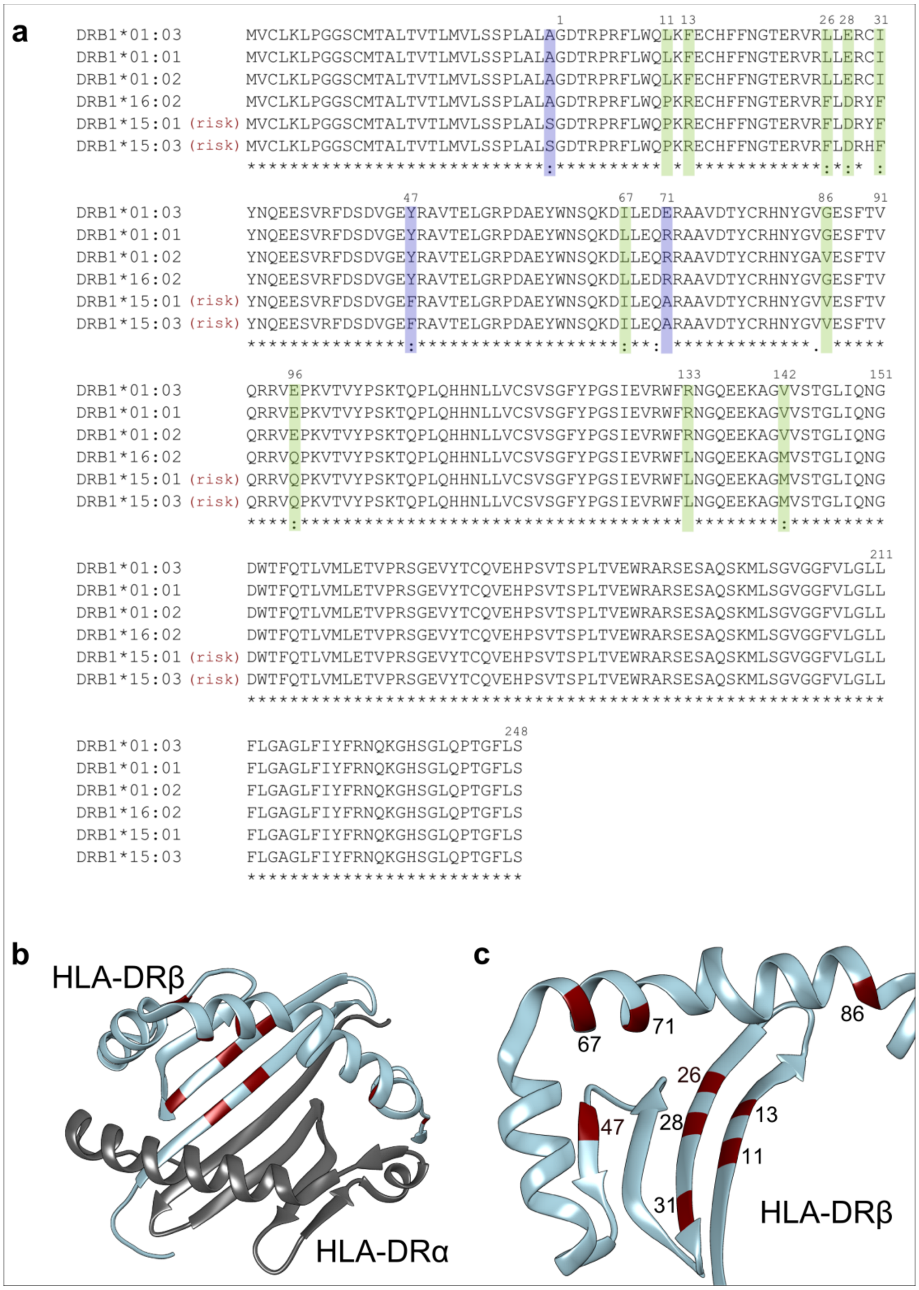
c. HLA-C



d. HLA-DPB1



Supplementary Figure 8. Amino acids within DRB1*15 SLE risk cluster. (a) Multiple sequence alignment performed by CLUSTAL-omega of HLA-DRB1 alleles with a Percent Identity score of at least 95 with HLA-DRB1*15:01 or 15:03, two alleles associated with SLE risk in at least three populations (Figure 3). Numbering begins after signal peptide. Amino acids unique to the two risk alleles (positions -1, 47, and 71) are highlighted in purple. Positions in which the two risk alleles share an amino acid with less than half of the non-risk peptides in this cluster are highlighted in green. (b) Three dimensional ribbon model of HLA-DR protein. This structure is based on Protein Data Bank entry 3pdo. Amino acid positions noted in (a) are highlighted in red. (c) An enlarged view of the HLA-DRβ subunit, rotated for another view of noted amino acids in binding pocket.



```
                                              1        11 13          26 28 31
DRB1*01:03        MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQLKFECHFFNGTERVRLLERCI
DRB1*01:01        MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQLKFECHFFNGTERVRLLERCI
DRB1*01:02        MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQLKFECHFFNGTERVRLLERCI
DRB1*16:02        MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQPKRECHFFNGTERVRFLDRYF
DRB1*15:01 (risk) MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF
DRB1*15:03 (risk) MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRHF
                  ****************************:********** * ************:*:* :

                                47                  67  71             86   91
DRB1*01:03        YNQEESVRFDSDVGEYRAVTELGRPDAEYWNSQKDILEDERAAVDTYCRHNYGVGESFTV
DRB1*01:01        YNQEESVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQRRAAVDTYCRHNYGVGESFTV
DRB1*01:02        YNQEESVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQRRAAVDTYCRHNYGAVESFTV
DRB1*16:02        YNQEESVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEDRRAAVDTYCRHNYGVGESFTV
DRB1*15:01 (risk) YNQEESVRFDSDVGEFRAVTELGRPDAEYWNSQKDILEQARAAVDTYCRHNYGVVESFTV
DRB1*15:03 (risk) YNQEESVRFDSDVGEFRAVTELGRPDAEYWNSQKDILEQARAAVDTYCRHNYGVVESFTV
                  ***************:*******************:**: *************. *****

                      96                              133      142         151
DRB1*01:03        QRRVEPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG
DRB1*01:01        QRRVEPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG
DRB1*01:02        QRRVEPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG
DRB1*16:02        QRRVQPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG
DRB1*15:01 (risk) QRRVQPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG
DRB1*15:03 (risk) QRRVQPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG
                  ****:************************************ ********:*********

                                                                           211
DRB1*01:03        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*01:01        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*01:02        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*16:02        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*15:01 (risk) DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*15:03 (risk) DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
                  ************************************************************

                                         248
DRB1*01:03        FLGAGLFIYFRNQKGHSGLQPTGFLS
DRB1*01:01        FLGAGLFIYFRNQKGHSGLQPTGFLS
DRB1*01:02        FLGAGLFIYFRNQKGHSGLQPTGFLS
DRB1*16:02        FLGAGLFIYFRNQKGHSGLQPTGFLS
DRB1*15:01        FLGAGLFIYFRNQKGHSGLQPTGFLS
DRB1*15:03        FLGAGLFIYFRNQKGHSGLQPTGFLS
                  **************************
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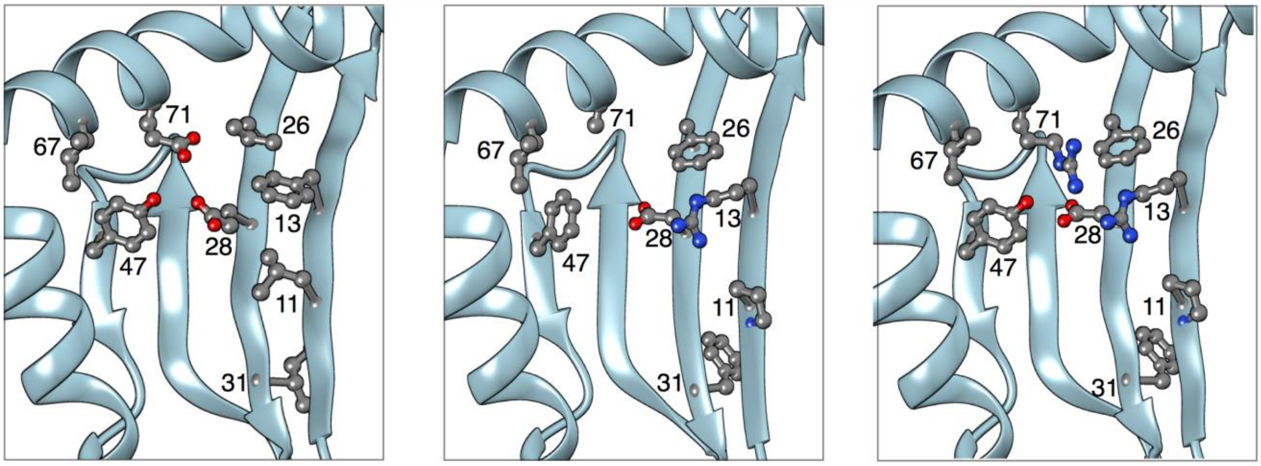
Supplementary Figure 9. Three dimensional ribbon model of classical HLA alleles. Three dimensional ribbon model of classical HLA alleles representative of binding-pocket amino acids that distinguish among risk and non-risk alleles in the DRB1*01; 16; 15 cluster (Figure 3a, Supplementary figure 10.) Non-polar, hydrophobic Phe47 Ala71 (Pocket 7) residues are unique to the two risk alleles (DRB1*15:01 and 15:03) within this cluster. Contrastingly, the non-risk alleles (DRB1*01:03, 01:01, 01:02, 16:02) exhibit a polar Tyr47 and either a polar Arg71 or polar Glu71. Focusing on amino acids sequences with at least 95% identity, allows for the ability to isolate potential regions of biochemical influence on SLE risk. In this case, SLE risk alleles DRB1*15:01 and 15:03 are unique from non-risk alleles via a hydrophobic space in DRB1 pocket 7. Proteins were modeled with SWISS-MODEL using Protein Data Bank Entry 3pdo.1.B as the template. 3-D visualizations were created via Chimera.

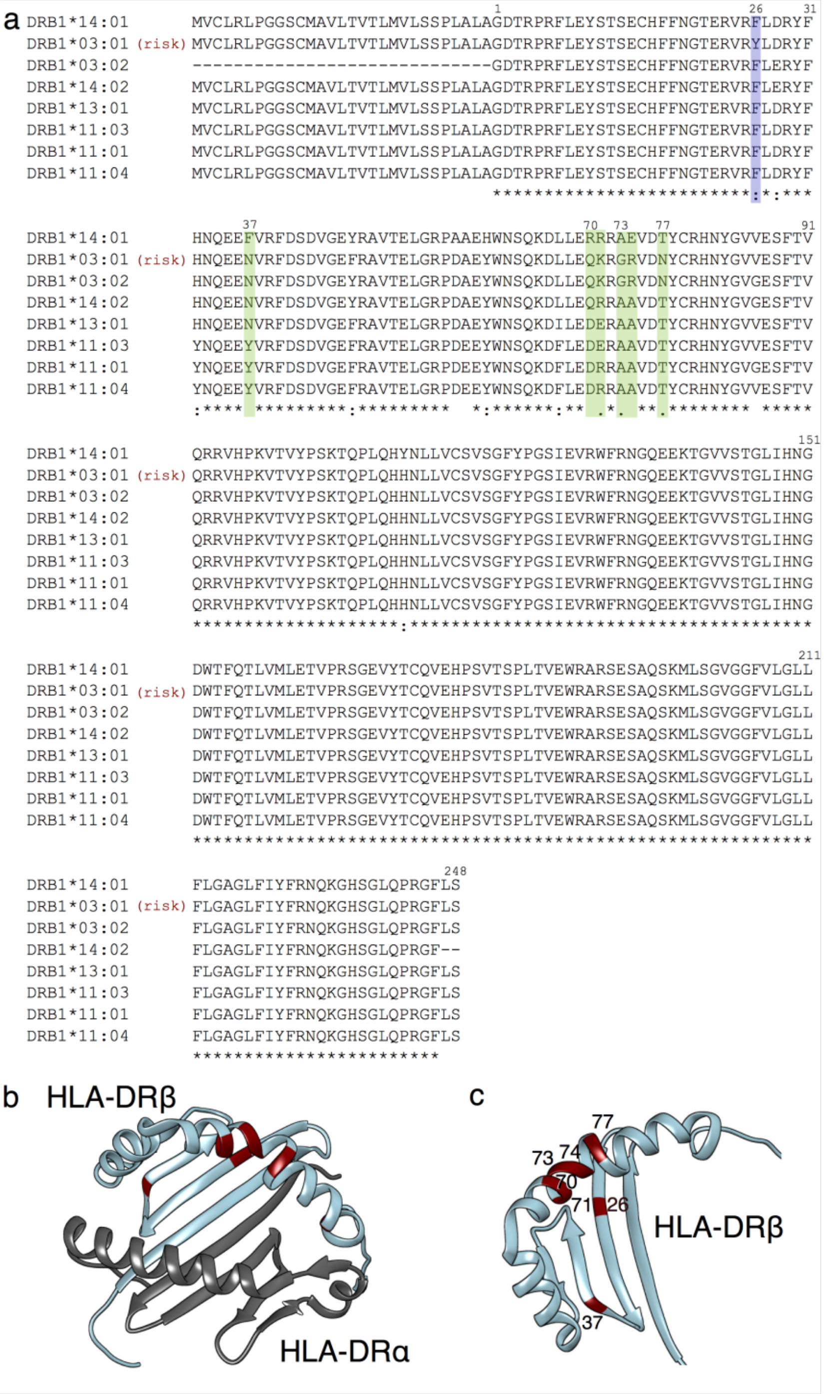


DRB1*01:03

DRB1*15:01
DRB1*15:03

DRB1*16:02

Supplementary Figure 10. DRB1*03 cluster sequence alignment. (a) Multiple sequence alignment performed by CLUSTAL-omega of HLA-DRB1 alleles with a Percent Identity score of at least 95 with SLE risk allele, HLA-DRB1*03:01. Numbering begins after signal peptide. DRB1*03:01 uniquely holds a polar Tyr26, compared to the non-polar Phe26 of the non-risk alleles within this cluster. Positions in which the risk allele shared an amino acid with 50% or less of the non-risk peptides in this cluster are highlighted in green. Most of these amino acids spanned the designated ‘Shared Epitope Region’. (b) Three-dimensional representation of the DR and DRB1 protein. Amino acids of interest from the sequence alignment are highlighted in the models which were created using Chimera.



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                                               1                       26   31
DRB1*14:01        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF
DRB1*03:01 (risk) MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRYLDRYF
DRB1*03:02        -----------------------------GDTRPRFLEYSTSECHFFNGTERVRFLERYF
DRB1*14:02        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLERYF
DRB1*13:01        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF
DRB1*11:03        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF
DRB1*11:01        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF
DRB1*11:04        MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF
                                               *************************:*:***

                      37                               70 73  77            91
DRB1*14:01        HNQEEFVRFDSDVGEYRAVTELGRPAAEHWNSQKDLLERRRAEVDTYCRHNYGVVESFTV
DRB1*03:01 (risk) HNQEENVRFDSDVGEFRAVTELGRPDAEYWNSQKDLLEQKRGRVDNYCRHNYGVVESFTV
DRB1*03:02        HNQEENVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRGRVDNYCRHNYGVGESFTV
DRB1*14:02        HNQEENVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQRRAAVDTYCRHNYGVGESFTV
DRB1*13:01        HNQEENVRFDSDVGEFRAVTELGRPDAEYWNSQKDILEDERAAVDTYCRHNYGVVESFTV
DRB1*11:03        YNQEEYVRFDSDVGEFRAVTELGRPDEEYWNSQKDFLEDERAAVDTYCRHNYGVVESFTV
DRB1*11:01        YNQEEYVRFDSDVGEFRAVTELGRPDEEYWNSQKDFLEDRRAAVDTYCRHNYGVGESFTV
DRB1*11:04        YNQEEYVRFDSDVGEFRAVTELGRPDEEYWNSQKDFLEDRRAAVDTYCRHNYGVVESFTV
                  :**** *********:*********  *:******:** .*. **.******** *****

                                                                           151
DRB1*14:01        QRRVHPKVTVYPSKTQPLQHYNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*03:01 (risk) QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*03:02        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*14:02        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*13:01        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*11:03        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*11:01        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
DRB1*11:04        QRRVHPKVTVYPSKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG
                  ********************:***************************************

                                                                           211
DRB1*14:01        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*03:01 (risk) DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*03:02        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*14:02        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*13:01        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*11:03        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*11:01        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
DRB1*11:04        DWTFQTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL
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                                         248
DRB1*14:01        FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*03:01 (risk) FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*03:02        FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*14:02        FLGAGLFIYFRNQKGHSGLQPRGF--
DRB1*13:01        FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*11:03        FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*11:01        FLGAGLFIYFRNQKGHSGLQPRGFLS
DRB1*11:04        FLGAGLFIYFRNQKGHSGLQPRGFLS
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Supplementary Figure 11. Sequence Alignment of DQA1*01 cluster. Sequence alignment comparing SLE risk allele DQA1*01:02 to non-risk alleles with 95% sequence identity (DQA1*01:03, *01:01, *01:04, and *01:05). Met207 is the only amino acid unique to risk allele DQA1*01:02 from it's non-risk neighbors. Positions in which the risk allele shared an amino acid with 50% or less of the non-risk peptides in this cluster are highlighted in green (Gln34).

```
                                        1                                34 37
DQA1*01:03       MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQFTHEFDGDEQFYV
DQA1*01:02(risk) MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEQFYV
DQA1*01:01       MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEEFYV
DQA1*01:04       MILNKALLLGALALTTMMSPCGGEGIVADHVASCGVNLYQFYGPSGQYTHEFDGDEEFYV
DQA1*01:05       MILNKALLLGALALTTMMSPCGGEGIVADHVASCGVNLYQFYGPSGQYTHEFDGDEEFYV
                 ****************:******* **********************:********:***

                                                                            97
DQA1*01:03       DLEKKETAWRWPEFSKFGGFDPQGALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK
DQA1*01:02(risk) DLERKETAWRWPEFSKFGGFDPQGALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK
DQA1*01:01       DLERKETAWRWPEFSKFGGFDPQGALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK
DQA1*01:04       DLERKETAWRWPEFSKFGGFDPQGALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK
DQA1*01:05       DLERKETAWRWPEFSKFGGFDPQGALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK
                 ***:********************************************************

                                                                           157
DQA1*01:03       SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHAVTEGVSETSFLSKSDHSFFKISYLTFL
DQA1*01:02(risk) SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL
DQA1*01:01       SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL
DQA1*01:04       SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL
DQA1*01:05       SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL
                 *******************************::***************************

                                                                207        217
DQA1*01:03       PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII
DQA1*01:02(risk) PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLMGIVVGTVFII
DQA1*01:01       PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII
DQA1*01:04       PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCTLGLSVGLVGIVVGTVFII
DQA1*01:05       PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII
                 *****************************************:*******:**********

                              217
DQA1*01:03       QGLRSVGASRHQGPL
DQA1*01:02(risk) QGLRSVGASRHQGPL
DQA1*01:01       QGLRSVGASRHQGPL
DQA1*01:04       QGLRSVGASRHQGPL
DQA1*01:05       QGLRSVGASRHQGPL
                 ***************
```

Supplementary Figure 12. Sequence alignment of DQA1*05 cluster. Sequence alignment comparing SLE risk allele DQA1*05:01 to non-risk alleles with 95% sequence identity (DQA1*05:05 and *05:03). Thr-13 and Ala159 are the only differences among these three alleles are highlighted below.

```
                           -13          1                                    37
DQA1*05:05        MILNKALMLGTLALTTVMSPCGGEDIVADHVASYGVNLYQSYGPSGQYTHEFDGDEQFYV
DQA1*05:03        MILNKALMLGALALTTVMSPCGGEDIVADHVASYGVNLYQSYGPSGQYTHEFDGDEQFYV
DQA1*05:01 (risk) MILNKALMLGALALTTVMSPCGGEDIVADHVASYGVNLYQSYGPSGQYTHEFDGDEQFYV
                  **********:*************************************************

                                                                             97
DQA1*05:05        DLGRKETVWCLPVLRQFRFDPQFALTNIAVLKHNLNSLIKRSNSTAATNEVPEVTVFSKS
DQA1*05:03        DLGRKETVWCLPVLRQFRFDPQFALTNIAVLKHNLNSLIKRSNSTAATNEVPEVTVFSKS
DQA1*05:01 (risk) DLGRKETVWCLPVLRQFRFDPQFALTNIAVLKHNLNSLIKRSNSTAATNEVPEVTVFSKS
                  ************************************************************

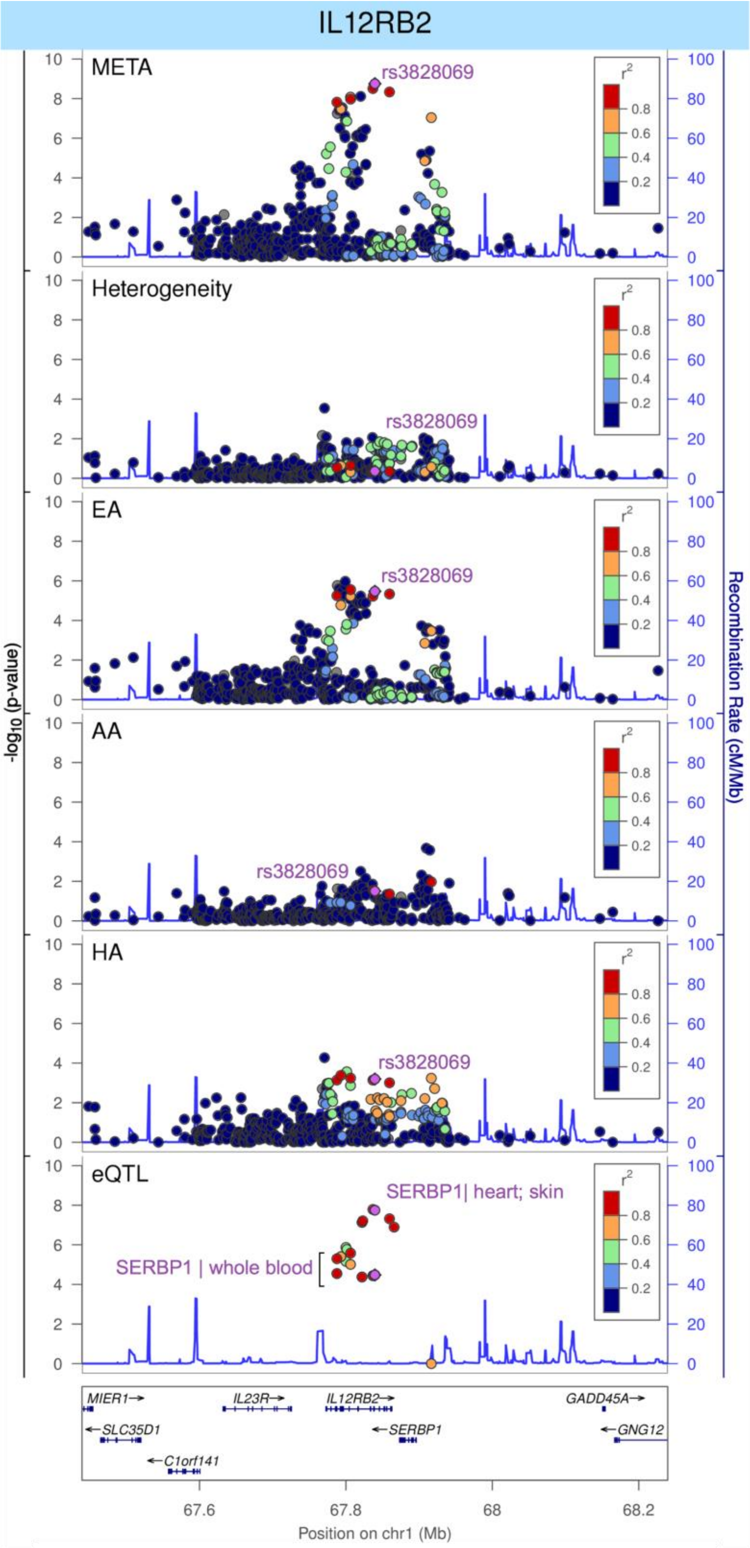
                                                                            157
DQA1*05:05        PVTLGQPNILICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTLLP
DQA1*05:03        PVTLGQPNILICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTLLP
DQA1*05:01 (risk) PVTLGQPNILICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTLLP
                  ************************************************************

                                                                            217
DQA1*05:05        SAEESYDCKVEHWGLDKPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFIIR
DQA1*05:03        SSEESYDCKVEHWGLDKPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFIIR
DQA1*05:01 (risk) SAEESYDCKVEHWGLDKPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFIIR
                  *:**********************************************************

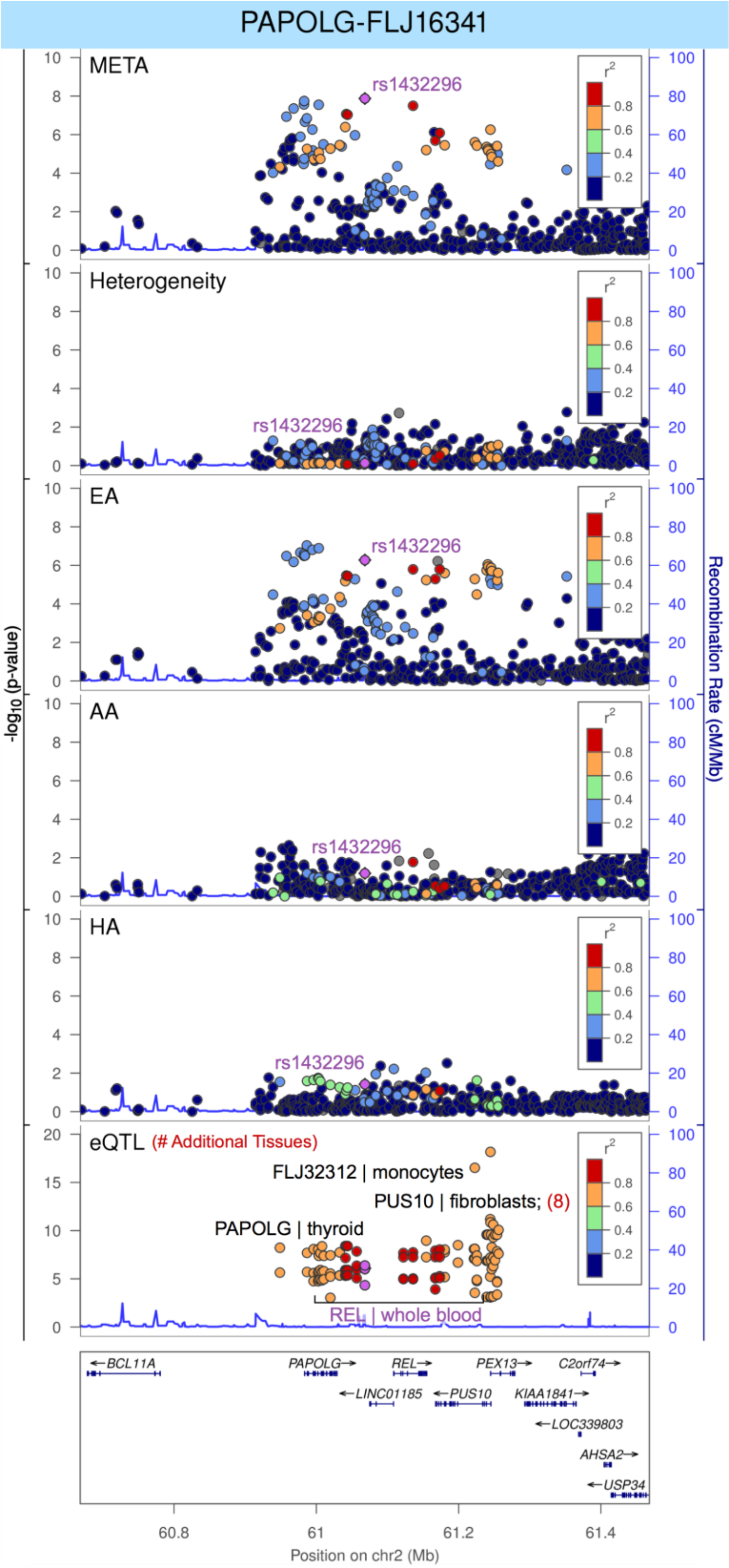
DQA1*05:05        GLRSVGASRHQGPL
DQA1*05:03        GLRSVGASRHQGPL
DQA1*05:01 (risk) GLRSVGASRHQGPL
                  **************
```

Supplementary Figure 13. Plots of novel Tier 1 meta-analysis and transancestral-mapping regions. Plots appear in the order found in Table 3a. Individual plots were created using LocusZoom standalone software (http://locuszoom.sph.umich.edu/)

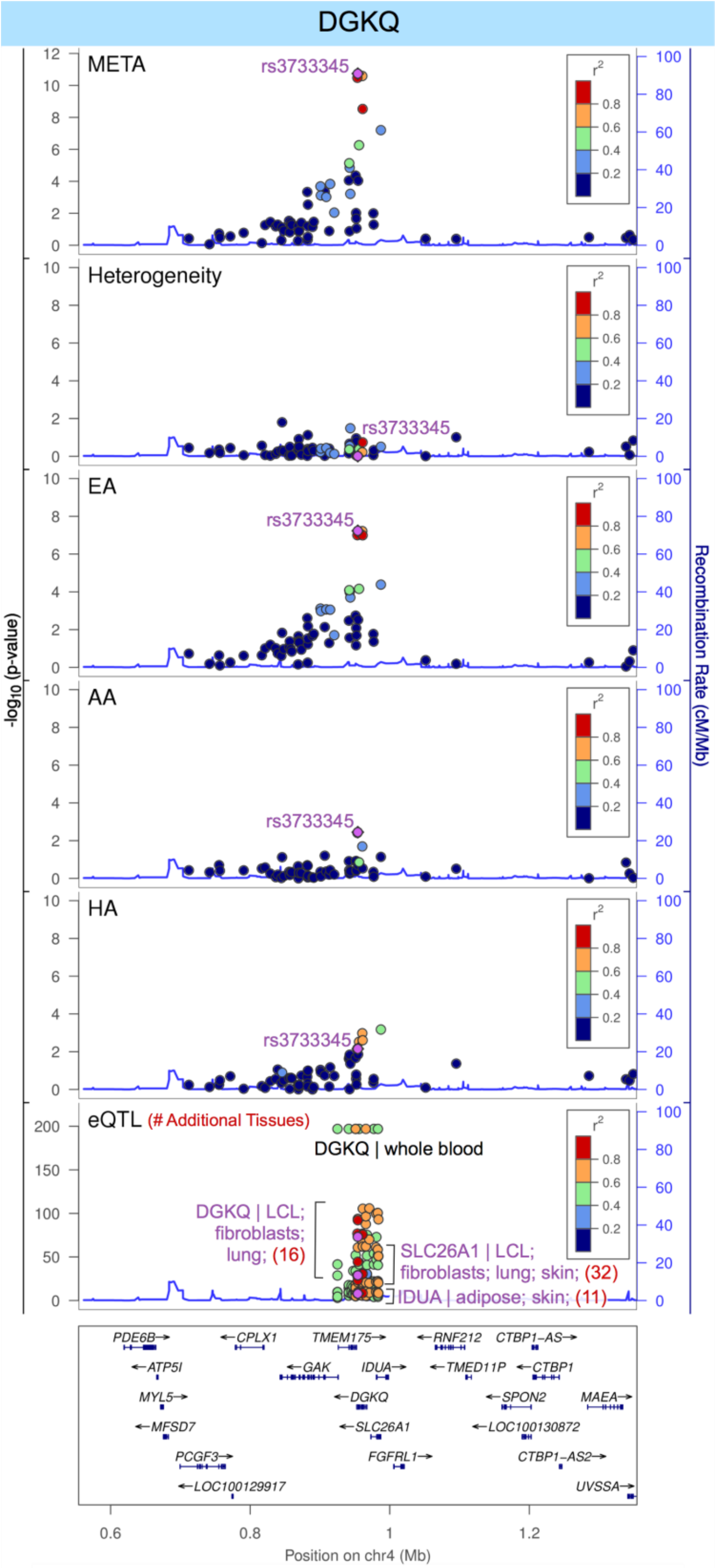
a. IL12RB2



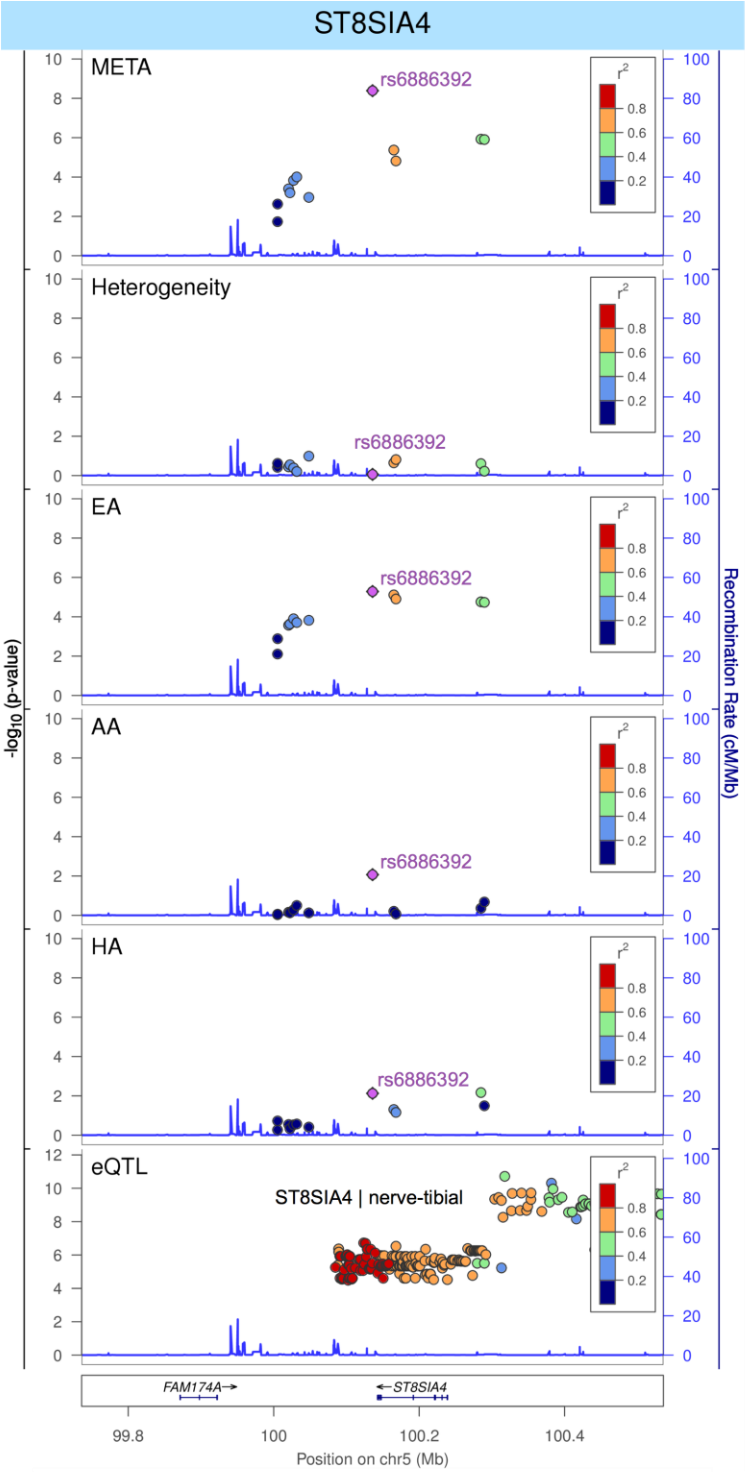
b. PAPOLG-FLJ16341



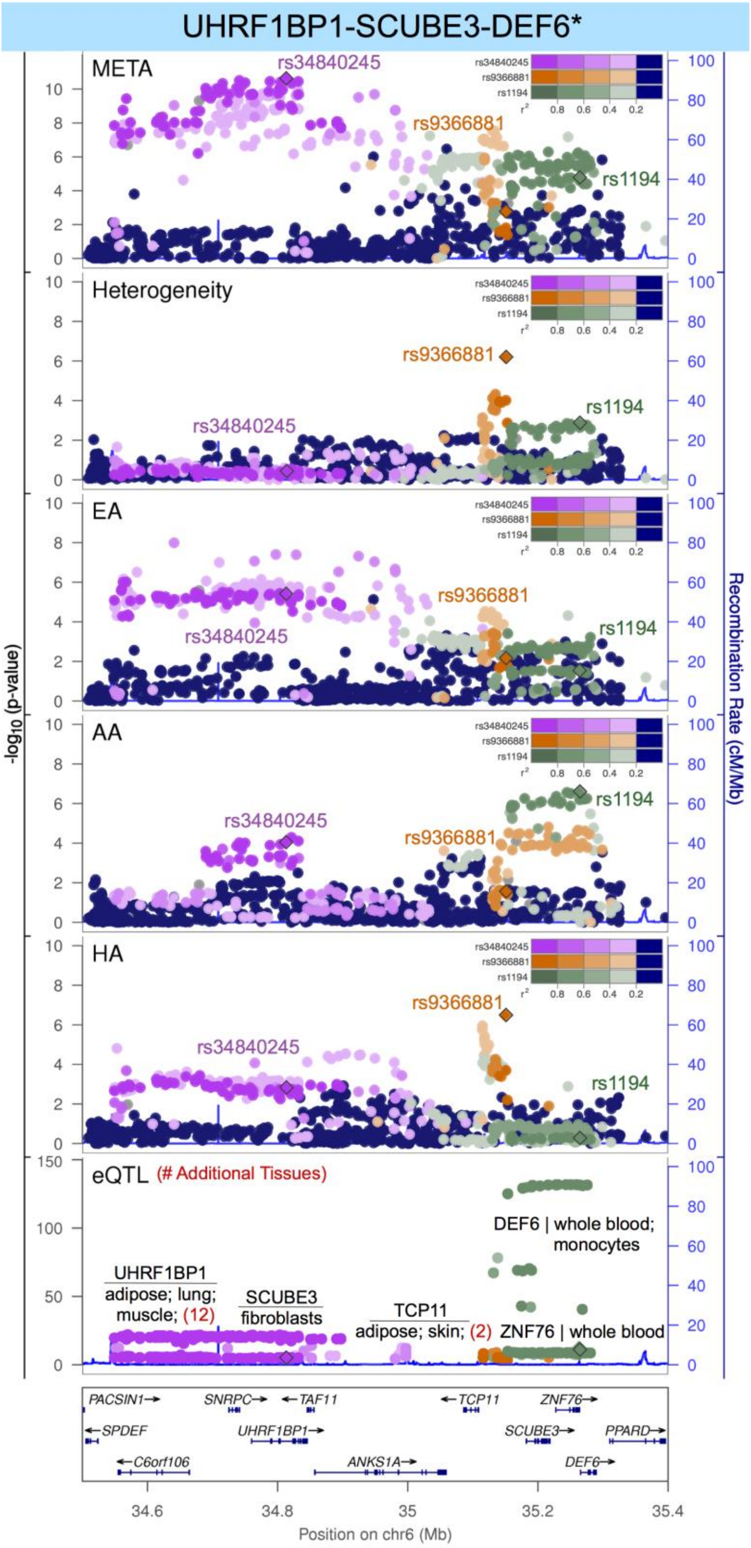
c. DGKQ


DGKQ
META
rs3733345
Heterogeneity
rs3733345
EA
rs3733345
AA
rs3733345
HA
rs3733345
eQTL (# Additional Tissues)
DGKQ | whole blood
DGKQ | LCL; fibroblasts; lung; (16)
SLC26A1 | LCL; fibroblasts; lung; skin; (32)
IDUA | adipose; skin; (11)
r^2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
0
2
4
6
8
10
12
50
100
150
200
20
40
60
80
100
PDE6B→
←CPLX1
TMEM175→
←RNF212
CTBP1−AS→
←ATP5I
←GAK
IDUA→
←TMED11P
←CTBP1
MYL5→
←DGKQ
←SPON2
MAEA→
←MFSD7
←SLC26A1
←LOC100130872
PCGF3→
FGFRL1→
CTBP1−AS2→
←LOC100129917
UVSSA→
0.6
0.8
1
1.2
Position on chr4 (Mb)

d. ST8SIA4

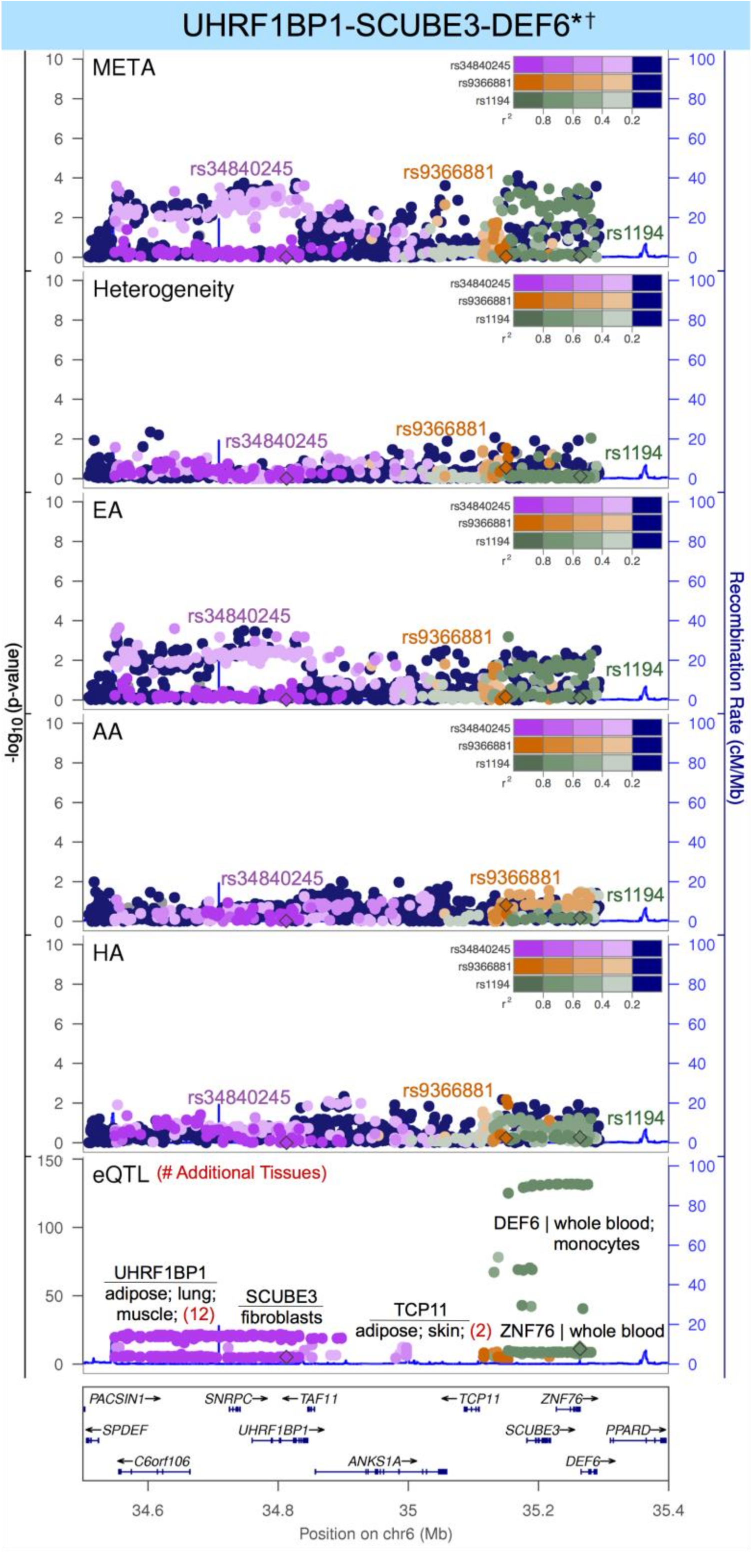

ST8SIA4
META
Heterogeneity
EA
AA
HA
eQTL
rs6886392
ST8SIA4 | nerve-tibial
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
FAM174A
ST8SIA4
99.8
100
100.2
100.4
Position on chr5 (Mb)

e. UHRF1BP1-SCUBE3-DEF6 (SLE SNP associations adjusted for Classical HLA alleles)



*SLE SNP associations adjusted for Classic HLA alleles

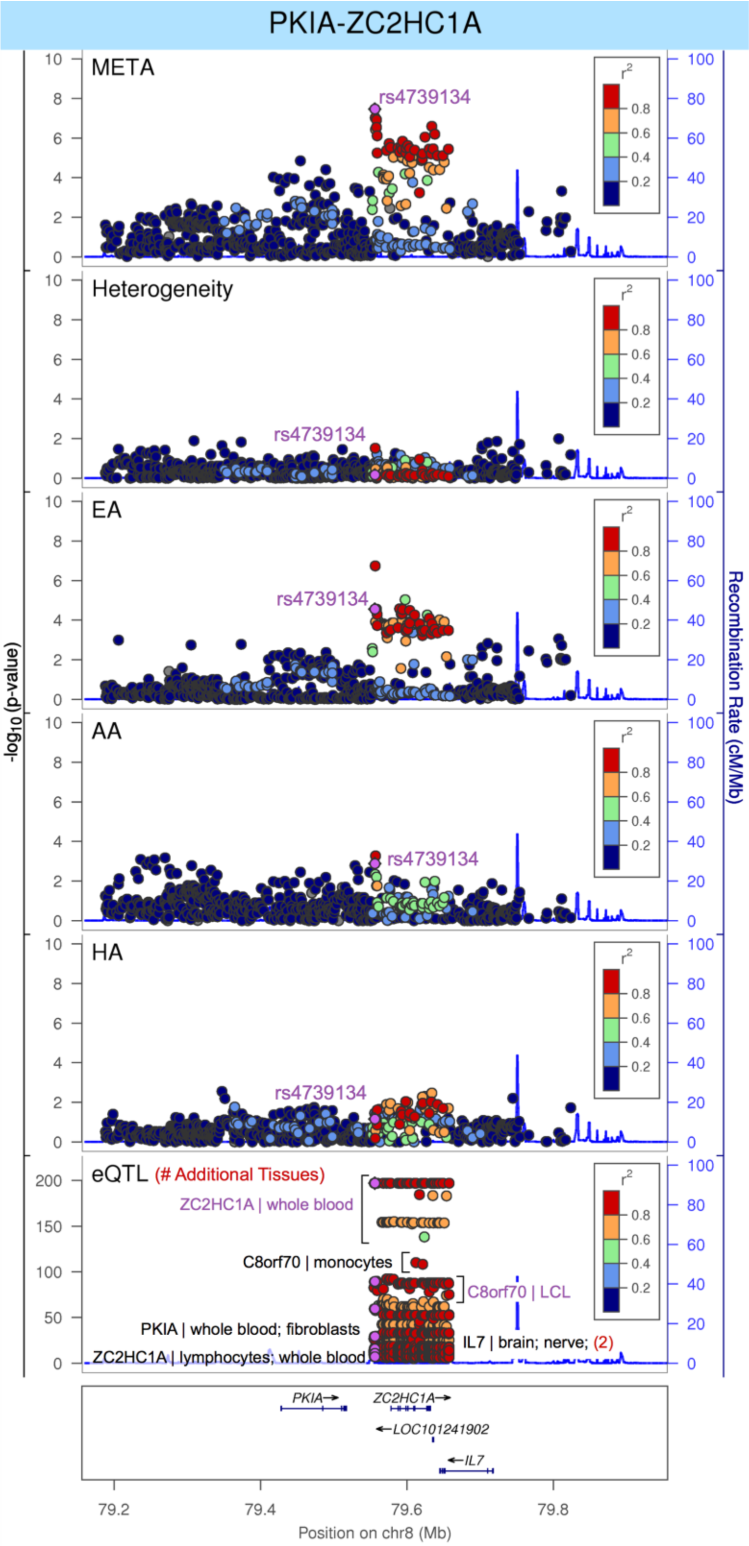
f. UHRF1BP1-SCUBE3-DEF6 (SLE SNP associations adjusted for Classical HLA alleles, and top 3 ancestry-specific SNPs: *rs34840245, rs9366881, rs1194*)



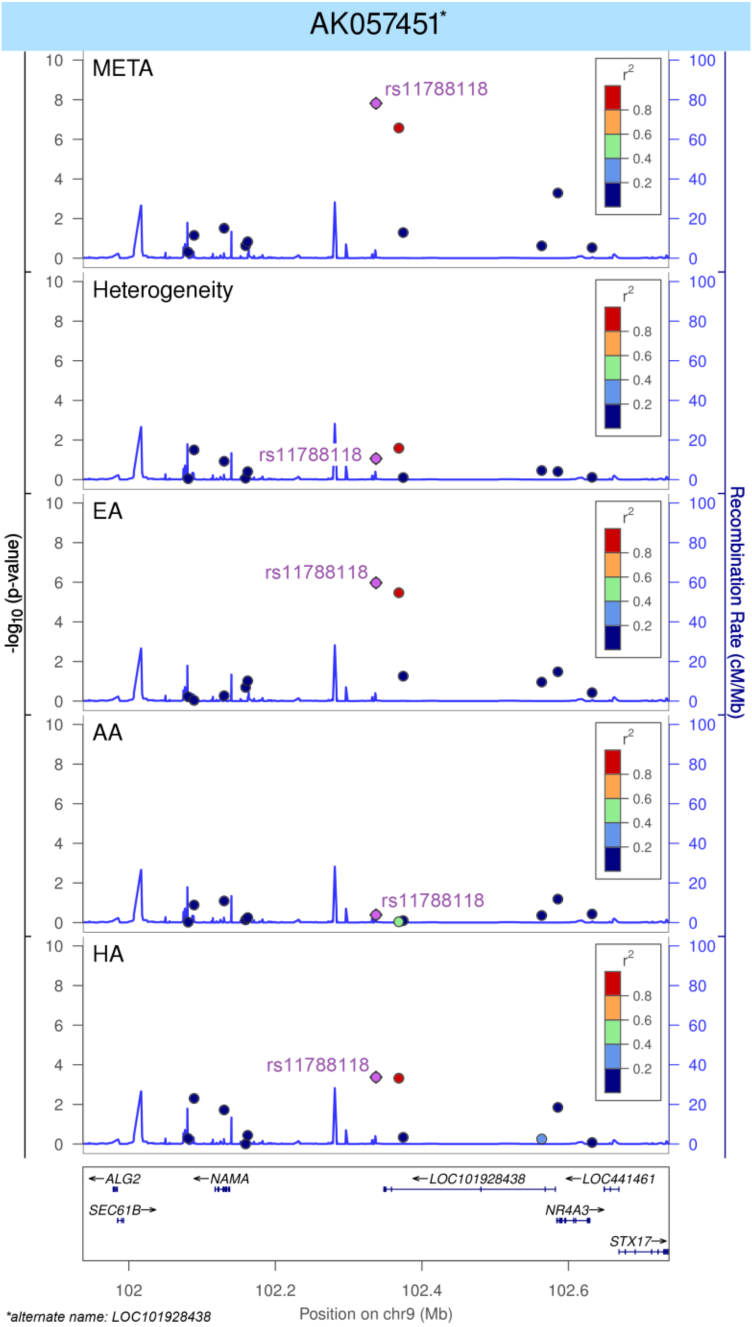
** SLE SNP associations adjusted for Classic HLA alleles*

†Post-adjustment for top 3 SNPs in region: rs34840245; rs9366881; rs1194

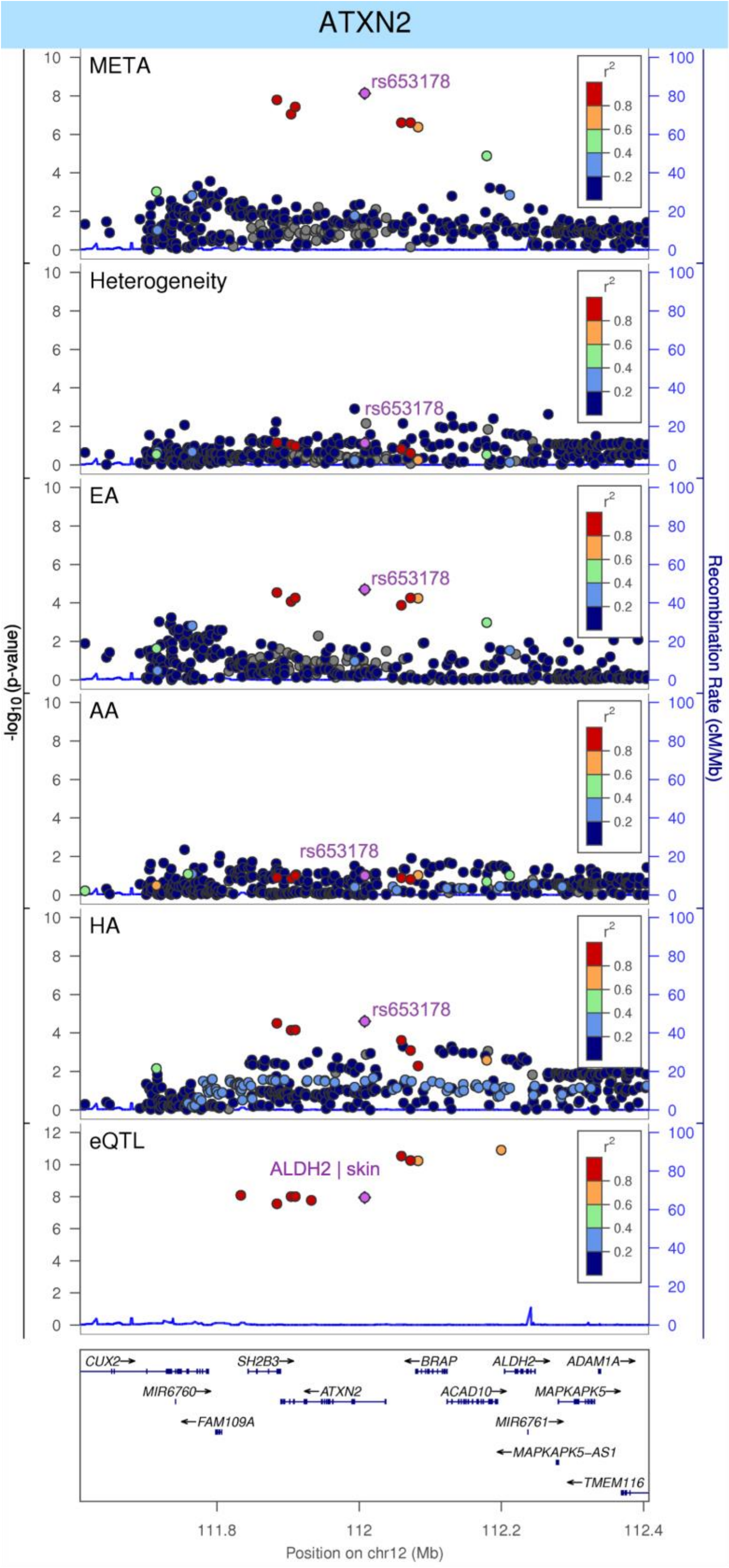
g. PKIA-ZC2HC1A



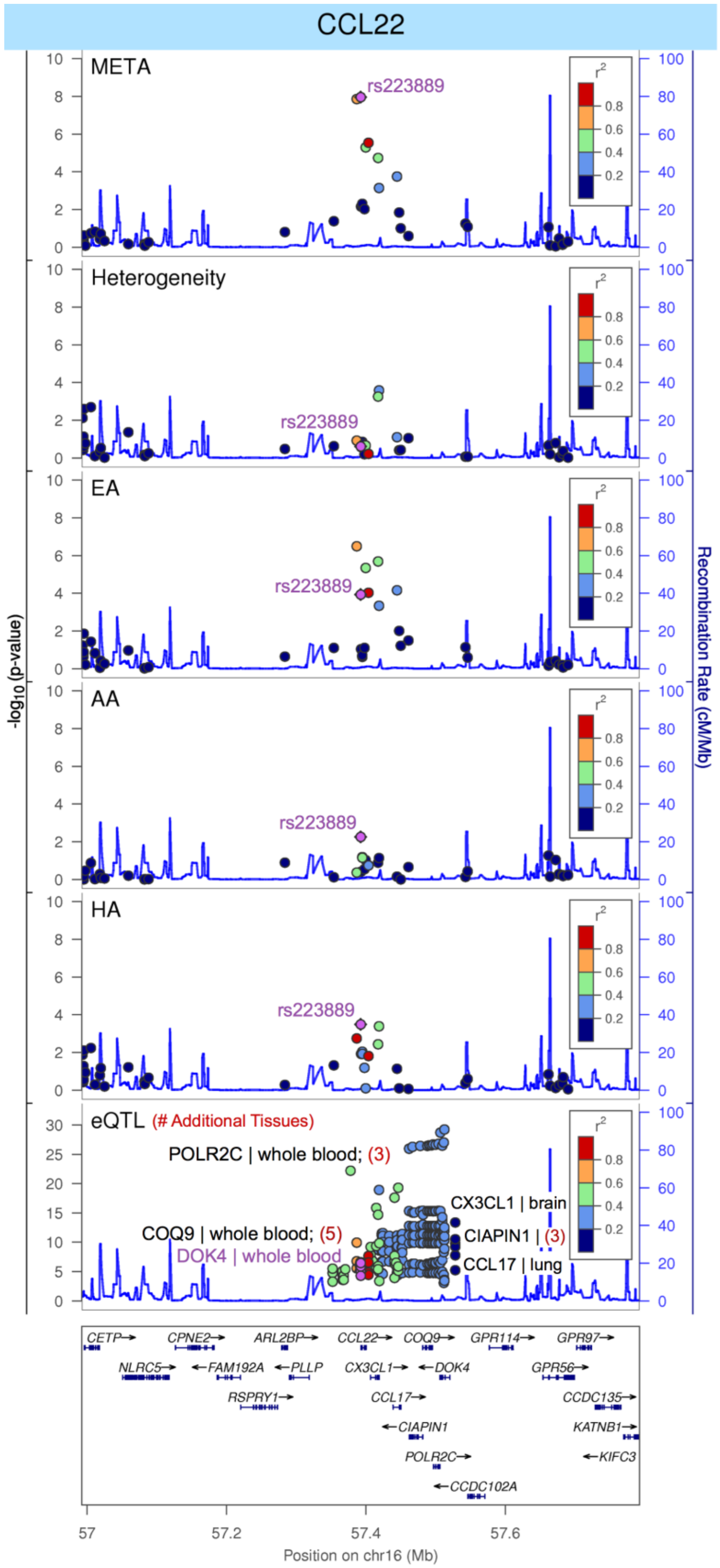
h. AK057451


AK057451*
META
Heterogeneity
EA
AA
HA
rs11788118
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
0
2
4
6
8
10
20
40
60
80
100
ALG2
NAMA
LOC101928438
LOC441461
SEC61B
NR4A3
STX17
102
102.2
102.4
102.6
Position on chr9 (Mb)
*alternate name: LOC101928438

i. ATXN2

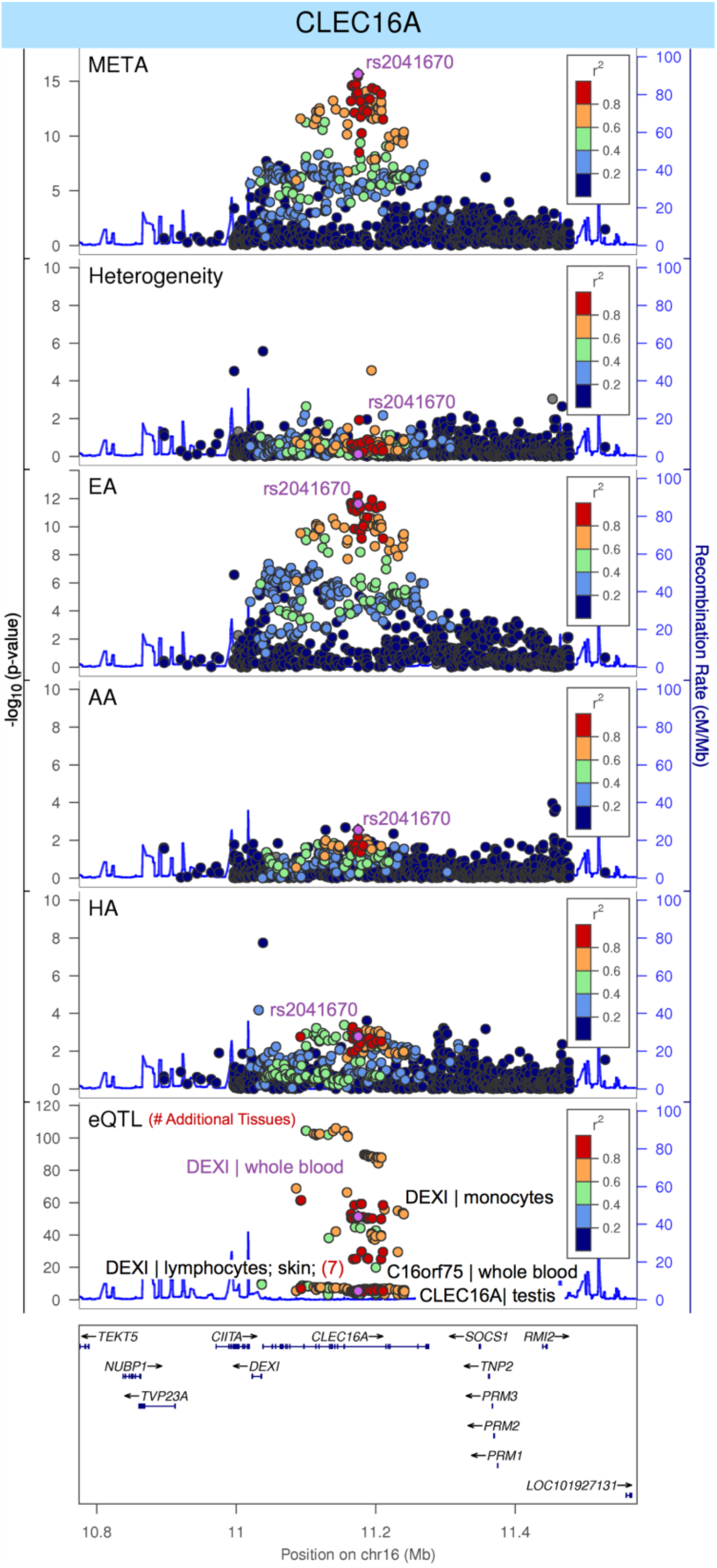

ATXN2
META
rs653178
Heterogeneity
rs653178
EA
rs653178
AA
rs653178
HA
rs653178
eQTL
ALDH2 | skin
r^2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
CUX2
SH2B3
BRAP
ALDH2
ADAM1A
MIR6760
ATXN2
ACAD10
MAPKAPK5
FAM109A
MIR6761
MAPKAPK5-AS1
TMEM116
111.8
112
112.2
112.4
Position on chr12 (Mb)

j. CCL22



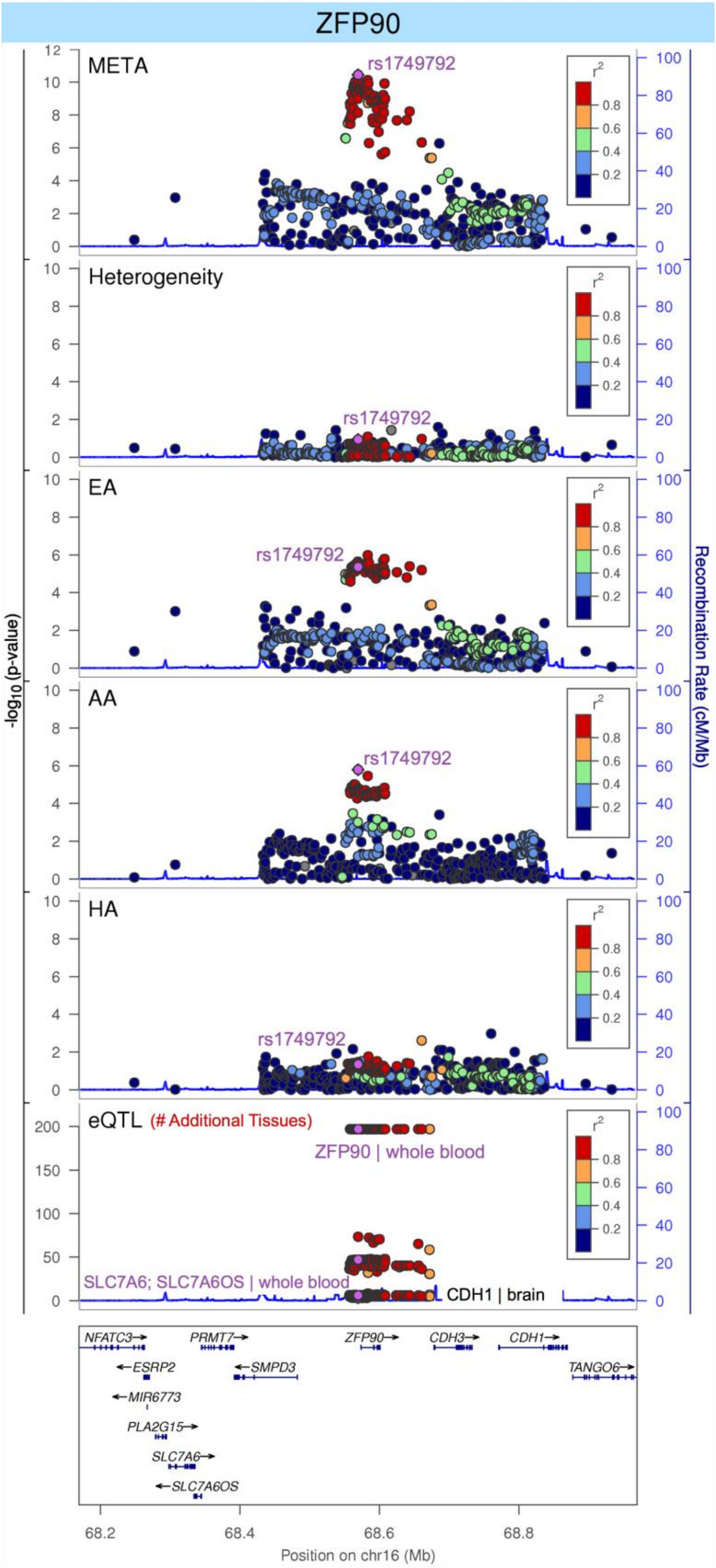
CCL22
META
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
rs223889
r^2
0.8
0.6
0.4
0.2
0
2
4
6
8
10
5
15
20
25
30
100
80
60
40
20
$-\log_{10}$(p-value)
Recombination Rate (cM/Mb)
POLR2C | whole blood; (3)
CX3CL1 | brain
CIAPIN1 | (3)
COQ9 | whole blood; (5)
DOK4 | whole blood
CCL17 | lung
CETP→
CPNE2→
ARL2BP→
CCL22→
COQ9→
GPR114→
GPR97→
NLRC5→
←FAM192A
←PLLP
CX3CL1→
←DOK4
GPR56→
RSPRY1→
CCL17→
CCDC135→
←CIAPIN1
KATNB1→
POLR2C→
←KIFC3
←CCDC102A
57
57.2
57.4
57.6
Position on chr16 (Mb)

k. CLEC16A



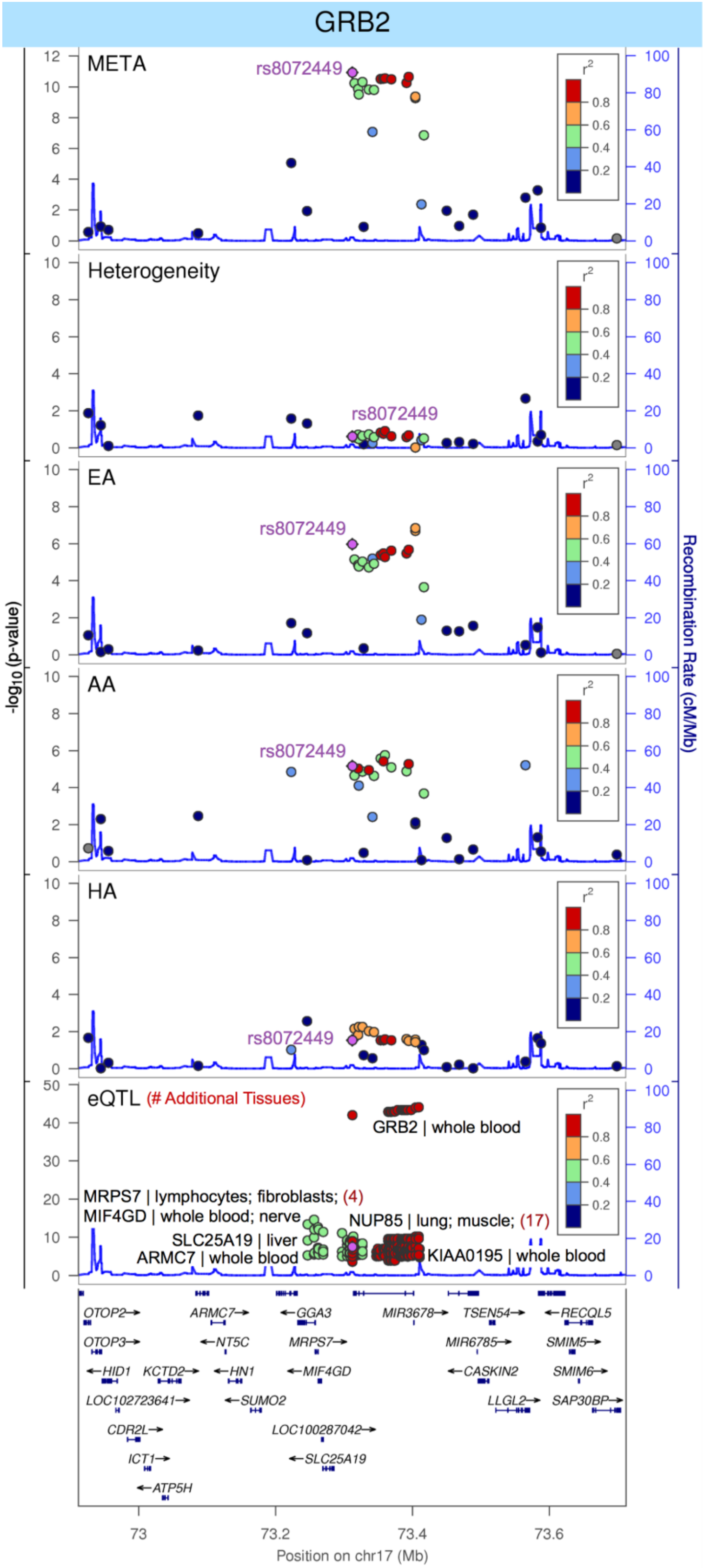
CLEC16A
META
rs2041670
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
DEXI | whole blood
DEXI | monocytes
DEXI | lymphocytes; skin; (7)
C16orf75 | whole blood
CLEC16A| testis
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
TEKT5
NUBP1
TVP23A
CIITA
DEXI
CLEC16A
SOCS1
TNP2
PRM3
PRM2
PRM1
RMI2
LOC101927131
10.8
11
11.2
11.4
Position on chr16 (Mb)

I. ZFP90

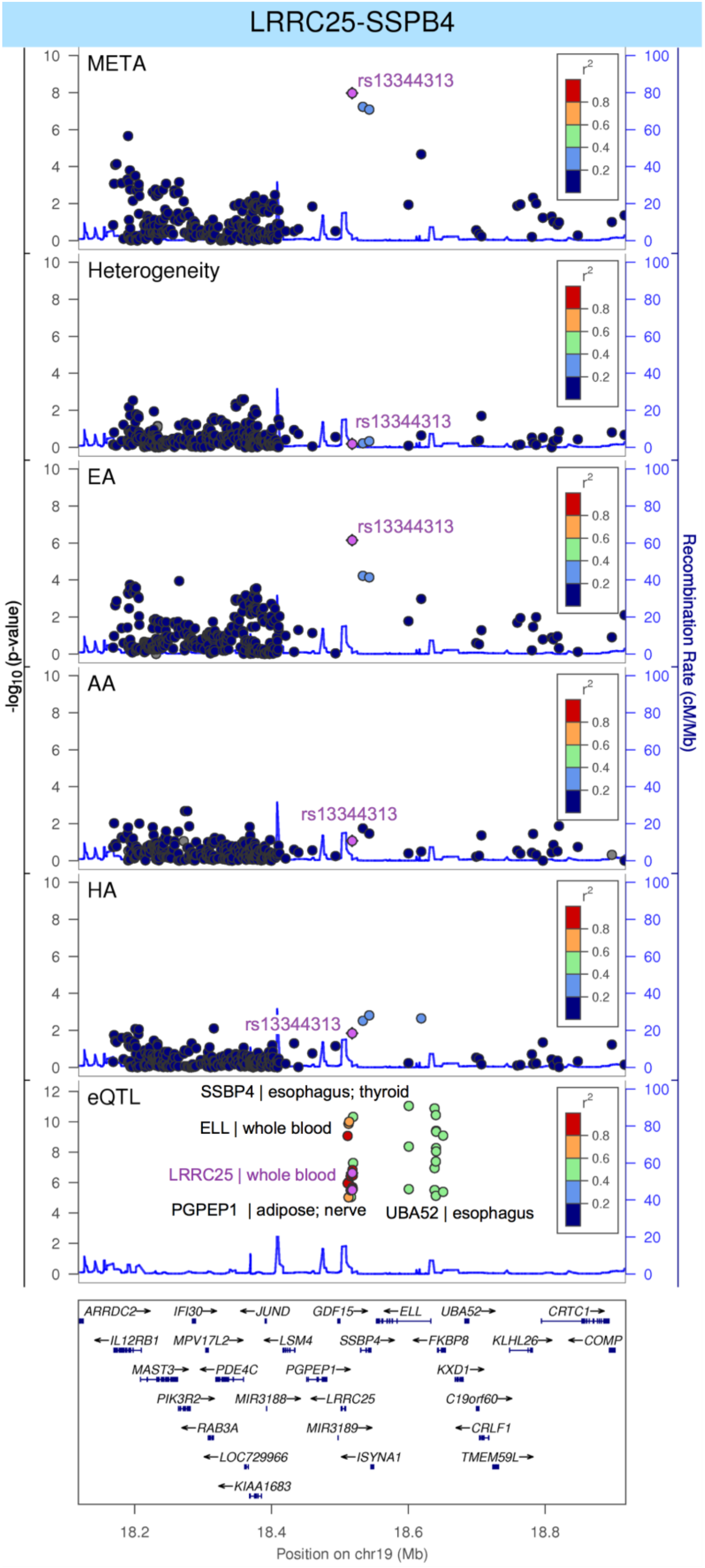


ZFP90
META
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
rs1749792
ZFP90 | whole blood
SLC7A6; SLC7A6OS | whole blood
CDH1 | brain
-log10 (p-value)
Recombination Rate (cM/Mb)
r²
0.8
0.6
0.4
0.2
NFATC3
PRMT7
ZFP90
CDH3
CDH1
ESRP2
SMPD3
TANGO6
MIR6773
PLA2G15
SLC7A6
SLC7A6OS
68.2
68.4
68.6
68.8
Position on chr16 (Mb)

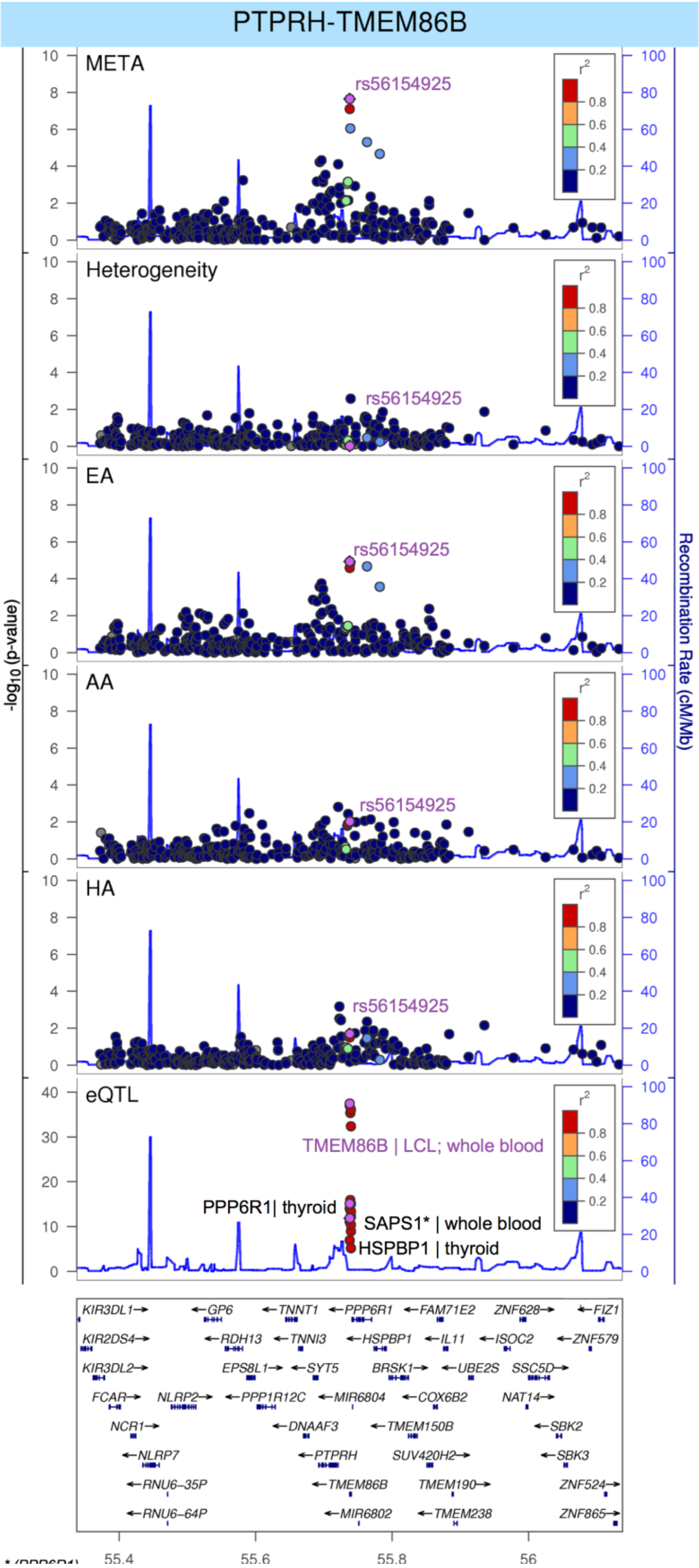
m. GRB2


GRB2
META
Heterogeneity
EA
AA
HA
rs8072449
eQTL (# Additional Tissues)
GRB2 | whole blood
MRPS7 | lymphocytes; fibroblasts; (4)
MIF4GD | whole blood; nerve
NUP85 | lung; muscle; (17)
SLC25A19 | liver
ARMC7 | whole blood
KIAA0195 | whole blood
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
OTOP2→
OTOP3→
←HID1
KCTD2→
LOC102723641→
CDR2L→
ICT1→
←ATP5H
ARMC7→
←NT5C
←HN1
←SUMO2
←GGA3
MRPS7→
←MIF4GD
LOC100287042→
←SLC25A19
MIR3678→
TSEN54→
MIR6785→
←CASKIN2
LLGL2→
←RECQL5
SMIM5→
SMIM6→
SAP30BP→
73
73.2
73.4
73.6
Position on chr17 (Mb)

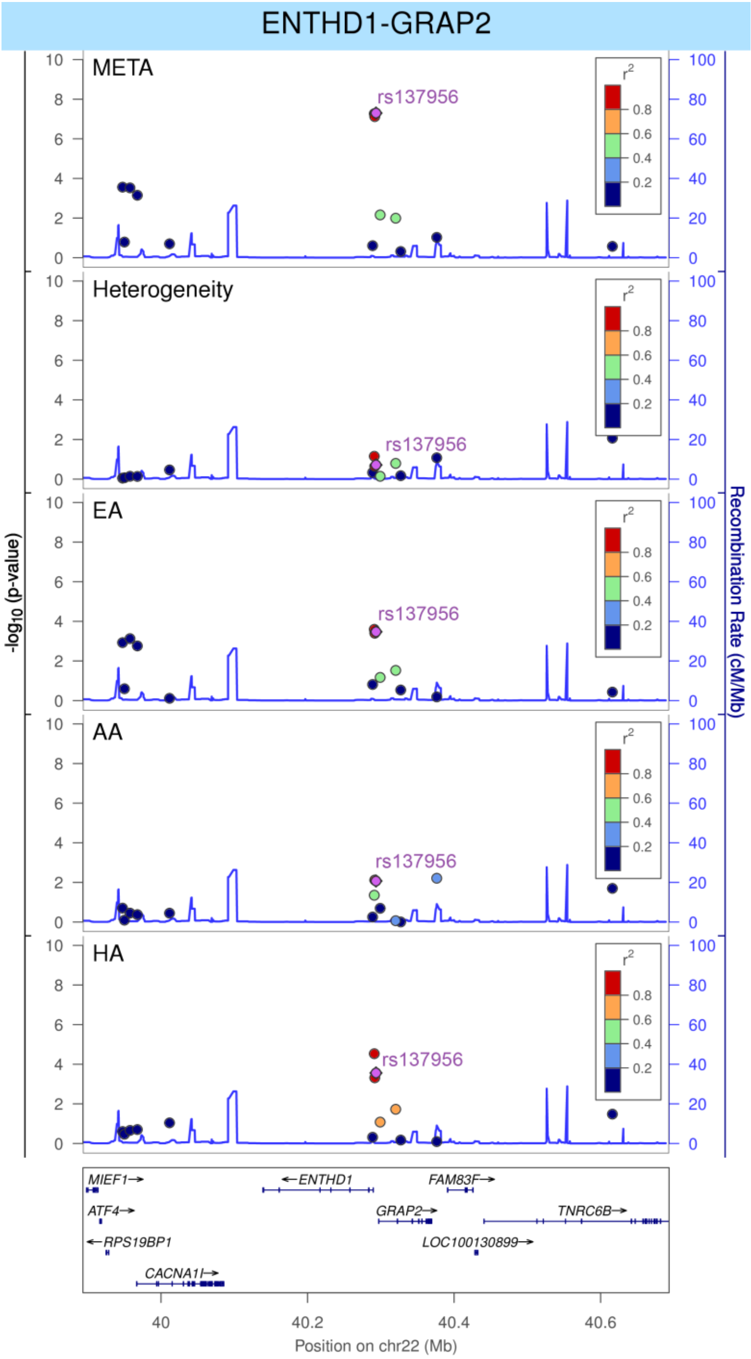
n. LRRC25-SSPB4



o. PTPRH-TMEM86B

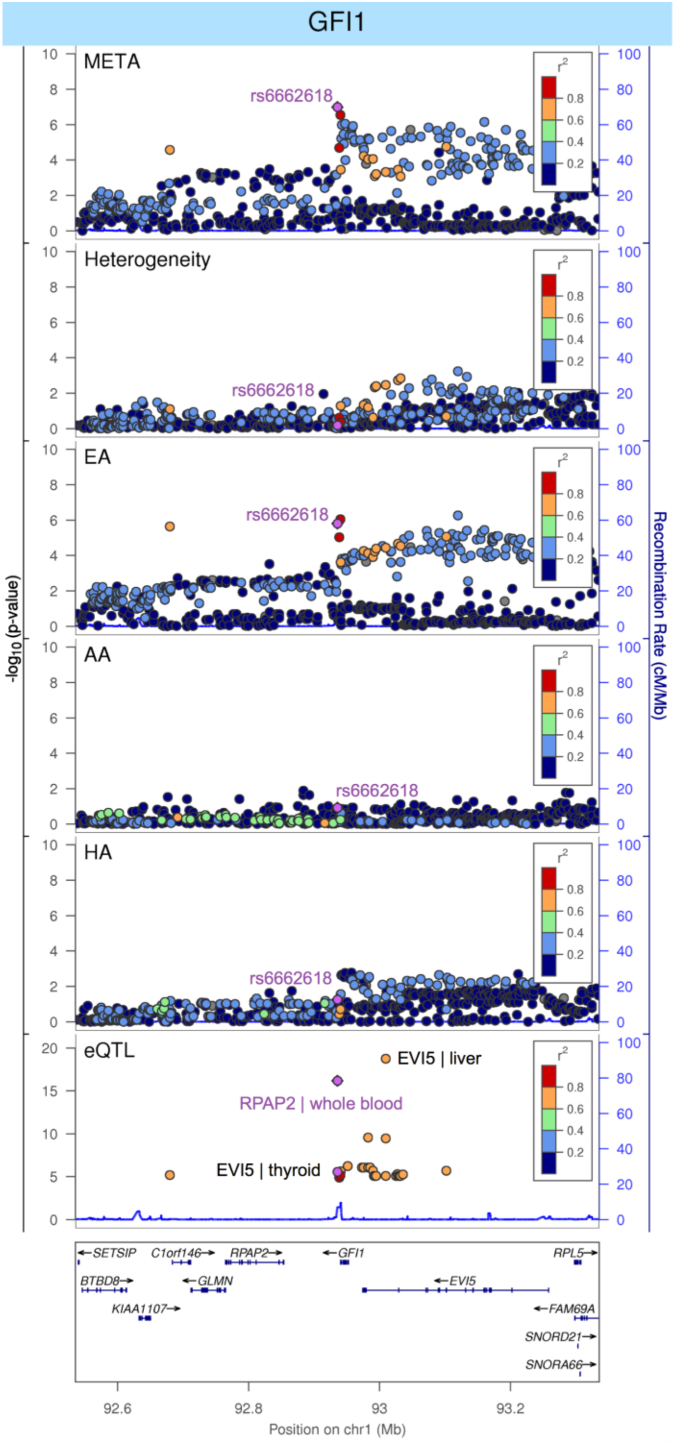


p. ENTHD1-GRAP2

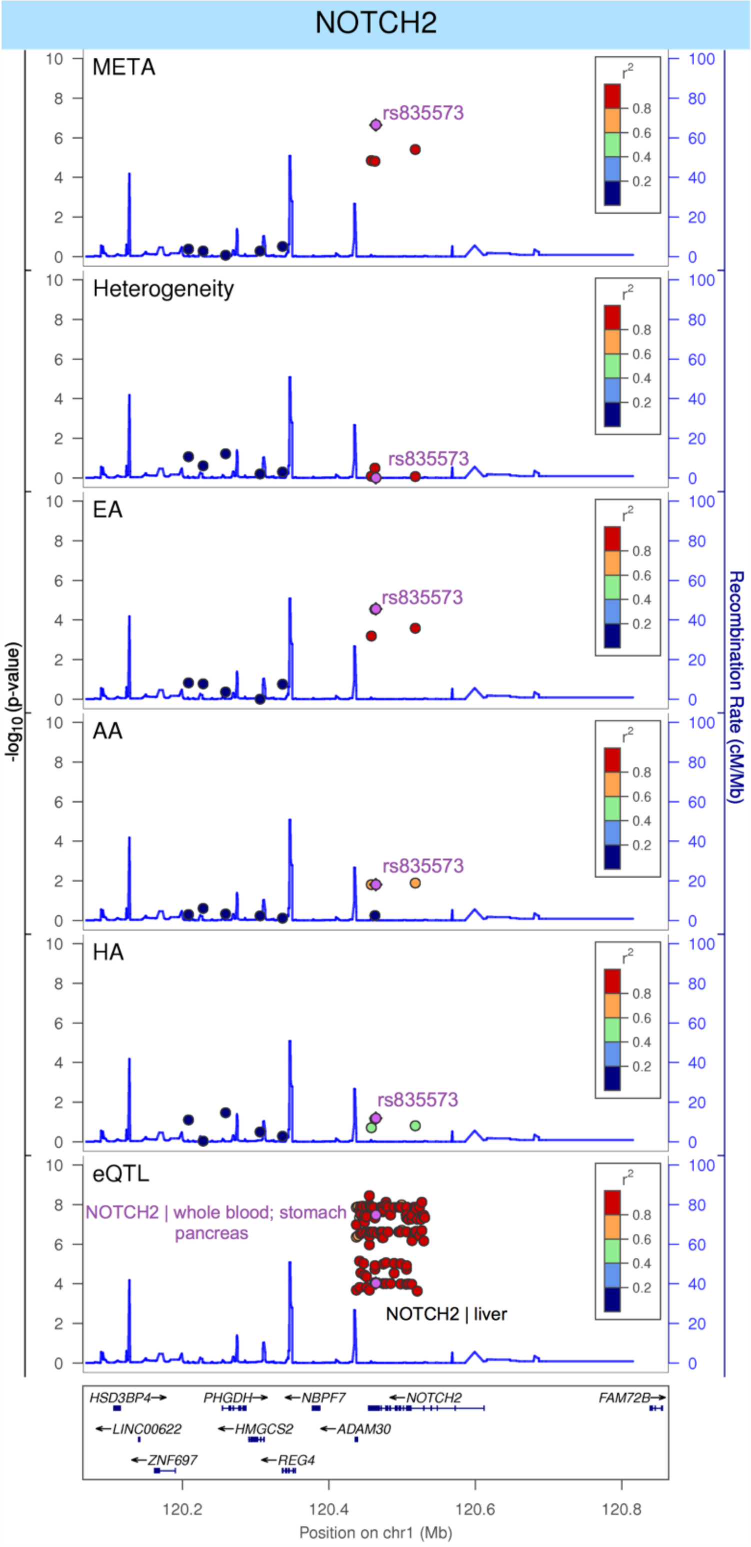


Supplementary Figure 14. Plots of novel Tier 2 meta-analysis and transancestral-mapping regions. Plots appear in the order found in Table 3b. Individual plots were created using LocusZoom standalone software (*http://locuszoom.sph.umich.edu/*).

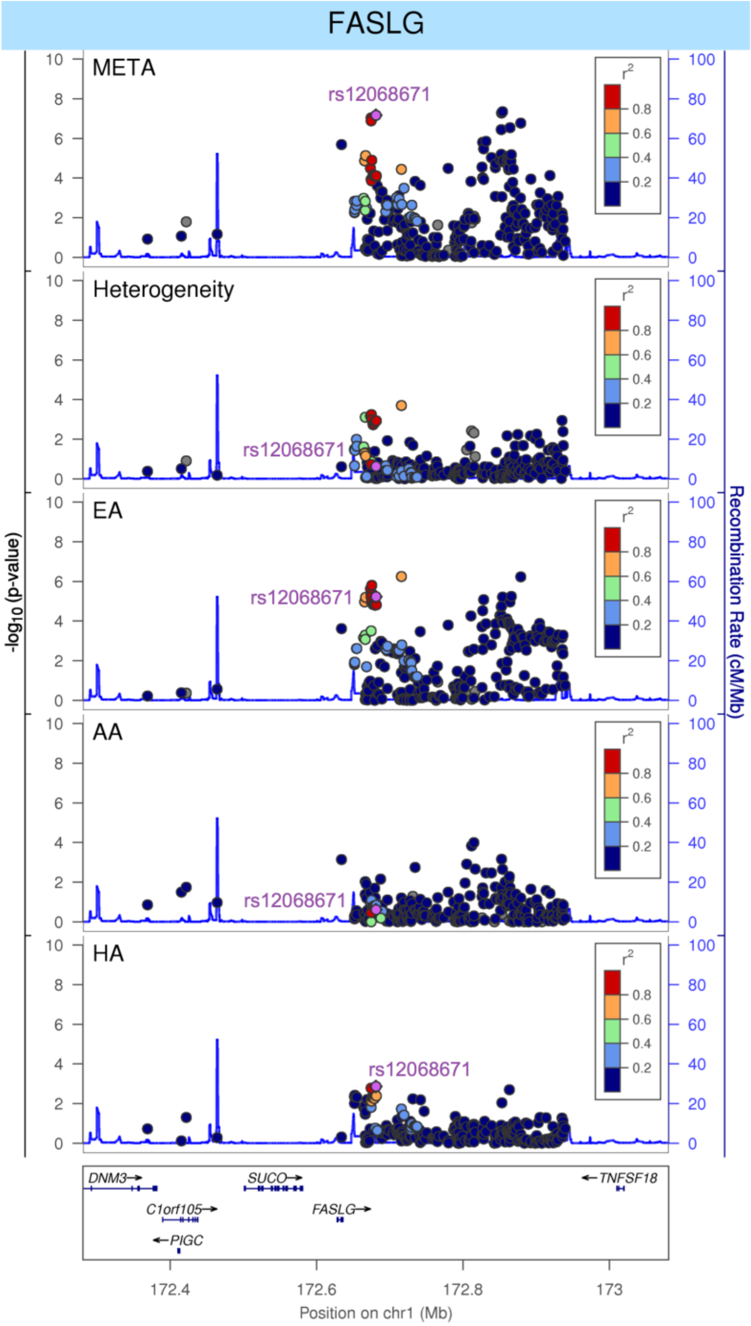
a. GFI1



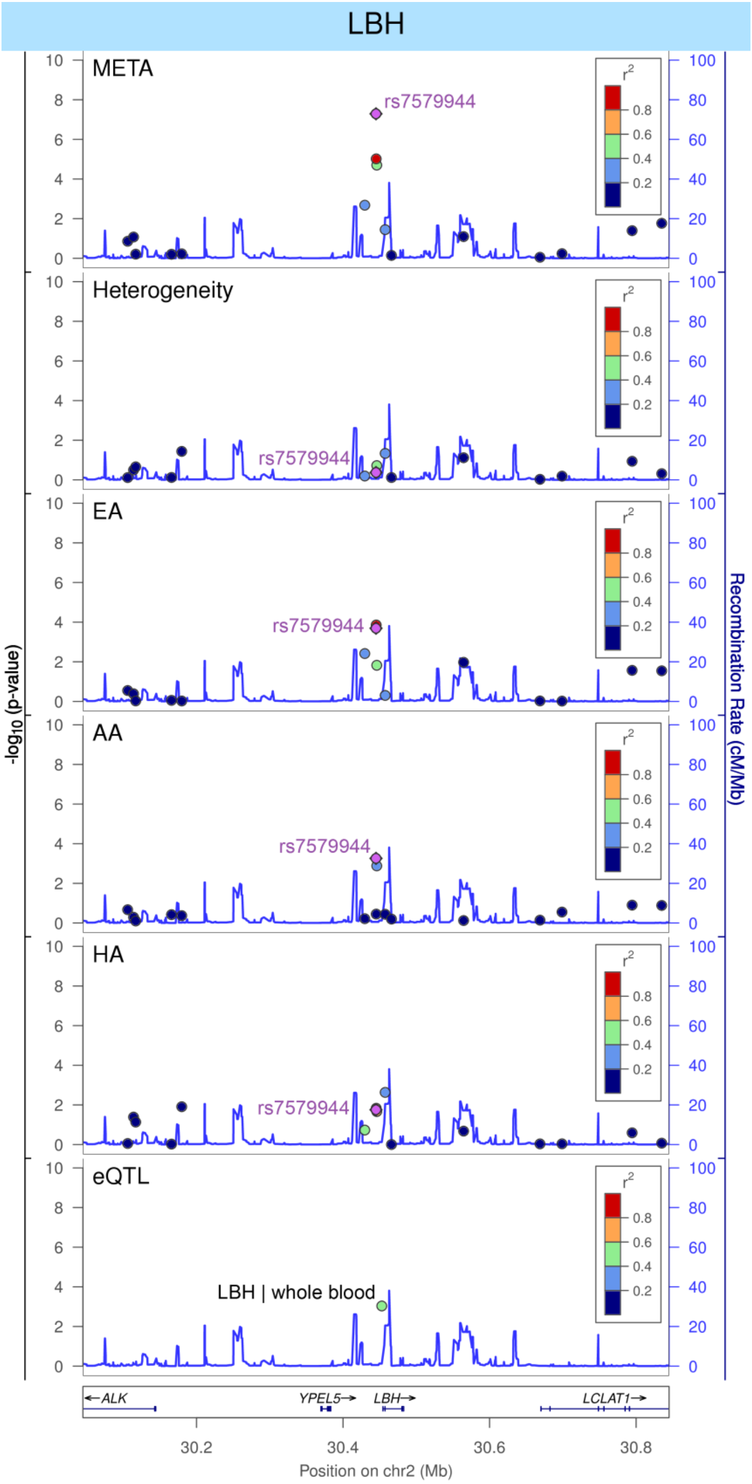
b. NOTCH2


NOTCH2
META
Heterogeneity
EA
AA
HA
eQTL
rs835573
r^2
0.8
0.6
0.4
0.2
0
2
4
6
8
10
20
40
60
80
100
-log$_{10}$(p-value)
Recombination Rate (cM/Mb)
NOTCH2 | whole blood; stomach
pancreas
NOTCH2 | liver
HSD3BP4
PHGDH
NBPF7
NOTCH2
FAM72B
LINC00622
HMGCS2
ADAM30
ZNF697
REG4
120.2
120.4
120.6
120.8
Position on chr1 (Mb)

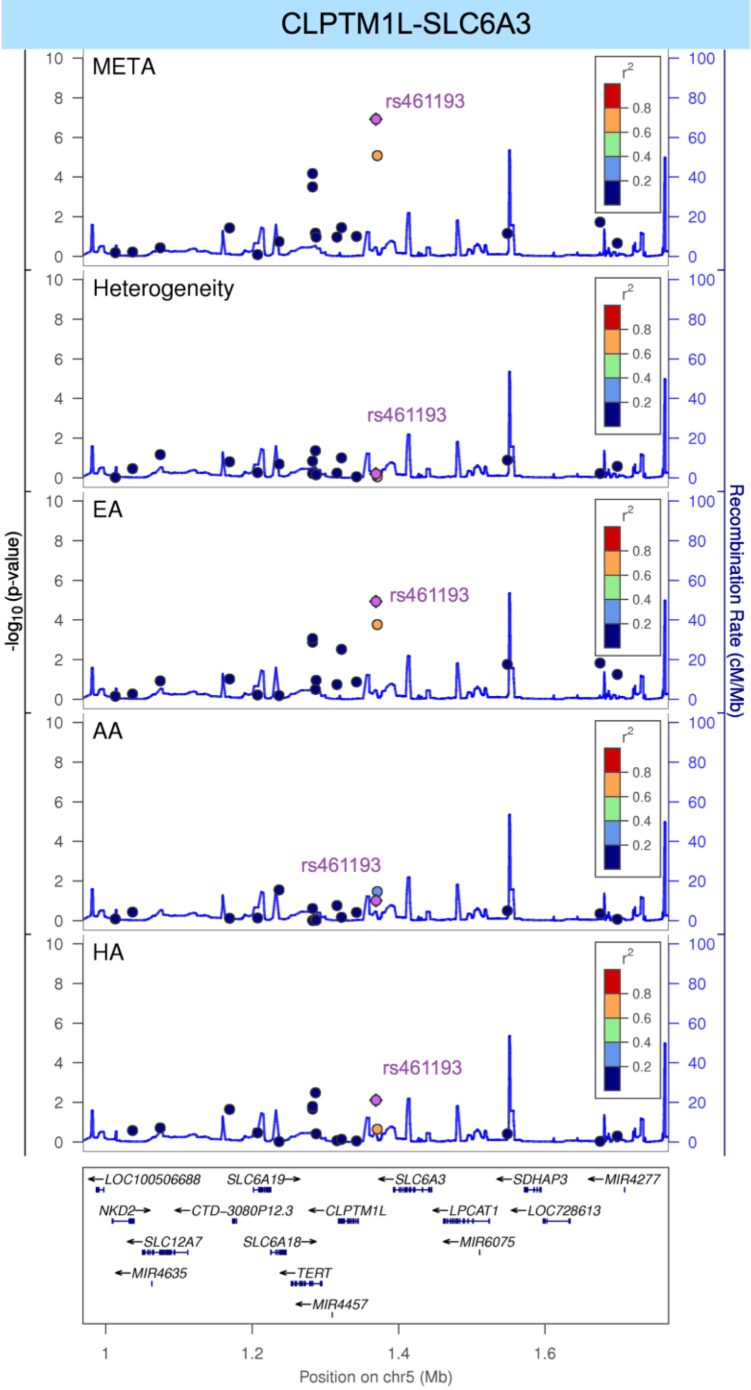
c. FASLG


FASLG
META
Heterogeneity
EA
AA
HA
rs12068671
-log10 (p-value)
Recombination Rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
0
2
4
6
8
10
20
40
60
80
100
DNM3
C1orf105
PIGC
SUCO
FASLG
TNFSF18
172.4
172.6
172.8
173
Position on chr1 (Mb)

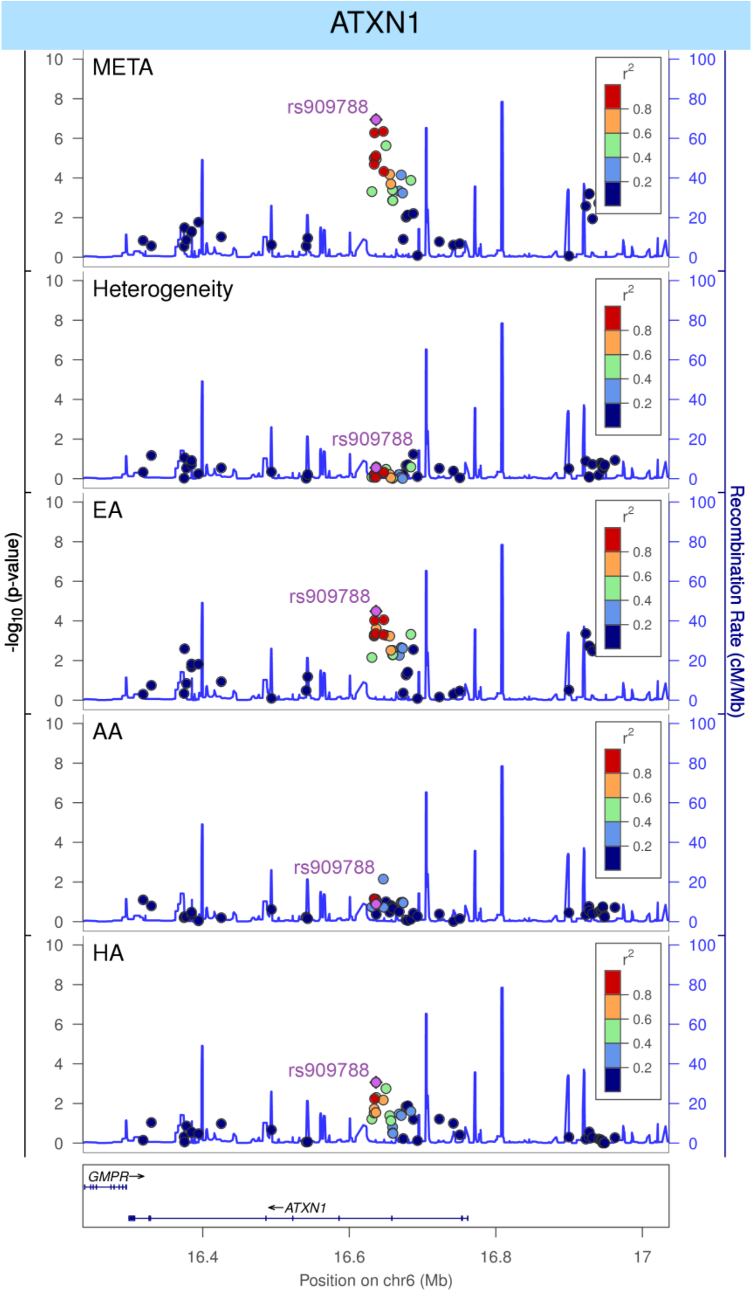
d. LBH


LBH
META
rs7579944
Heterogeneity
rs7579944
EA
rs7579944
AA
rs7579944
HA
rs7579944
eQTL
LBH | whole blood
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
0
2
4
6
8
10
0
20
40
60
80
100
ALK
YPEL5
LBH
LCLAT1
30.2
30.4
30.6
30.8
Position on chr2 (Mb)

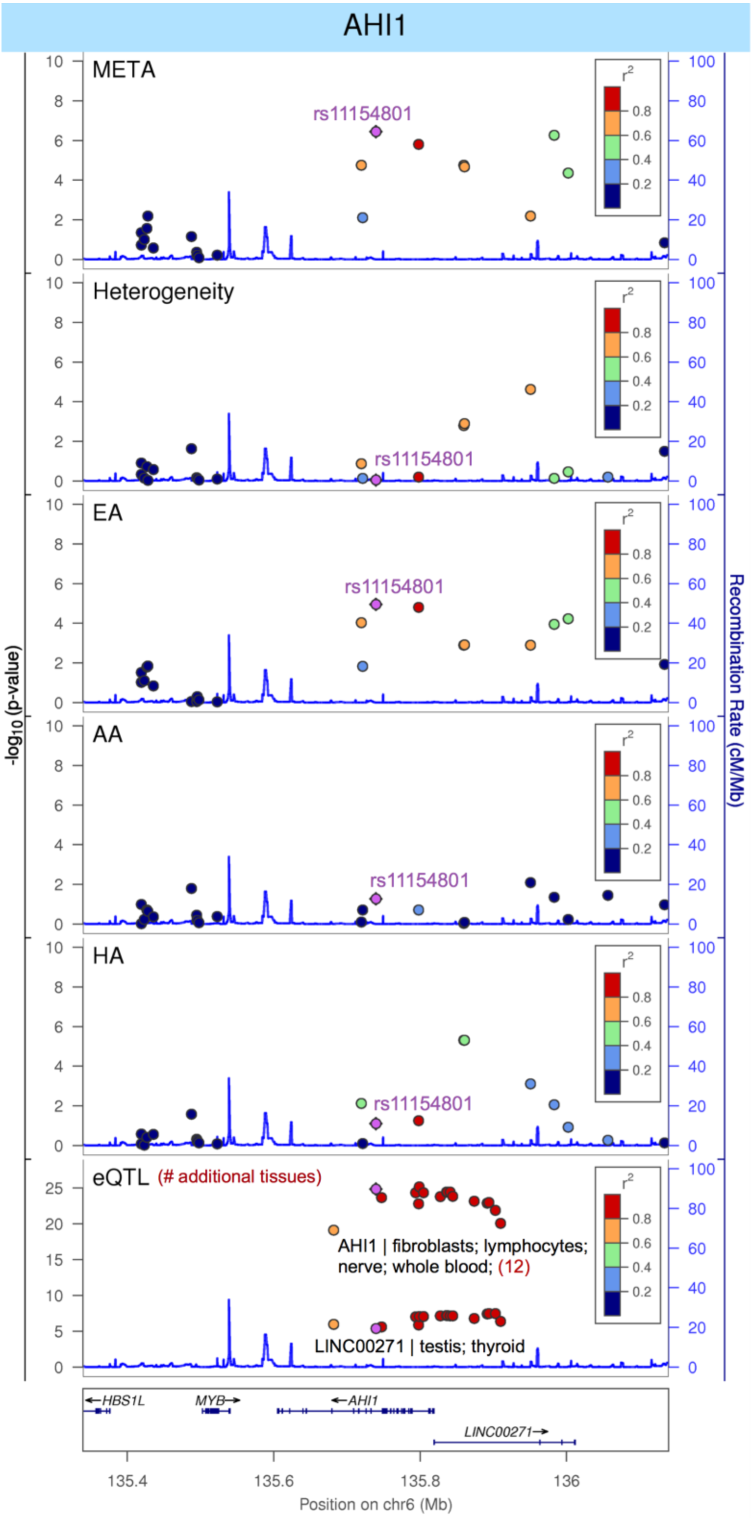
e. CLPTM1L-SLC6A3



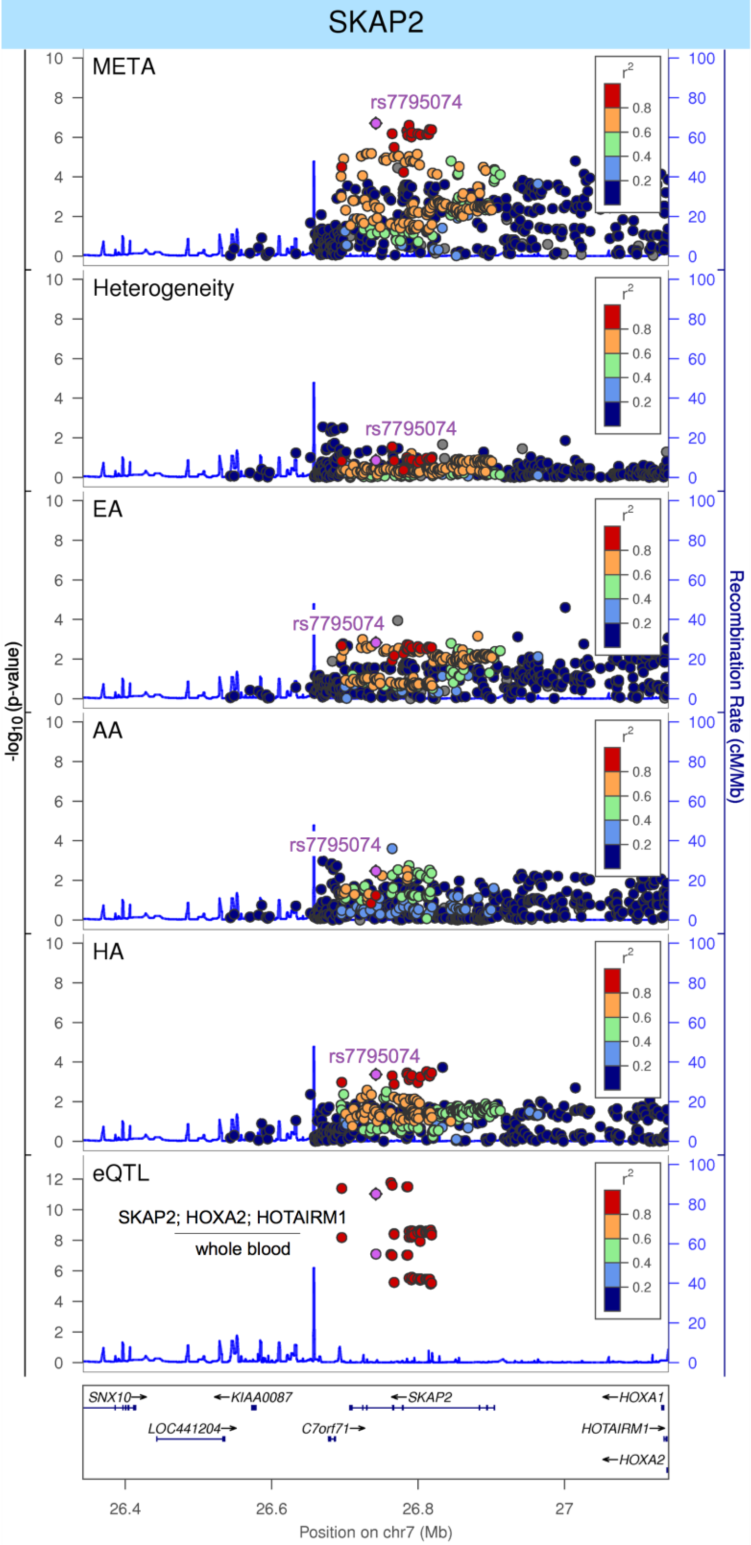
f. ATXN1


ATXN1
META
Heterogeneity
EA
AA
HA
rs909788
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
GMPR
ATXN1
16.4
16.6
16.8
17
Position on chr6 (Mb)

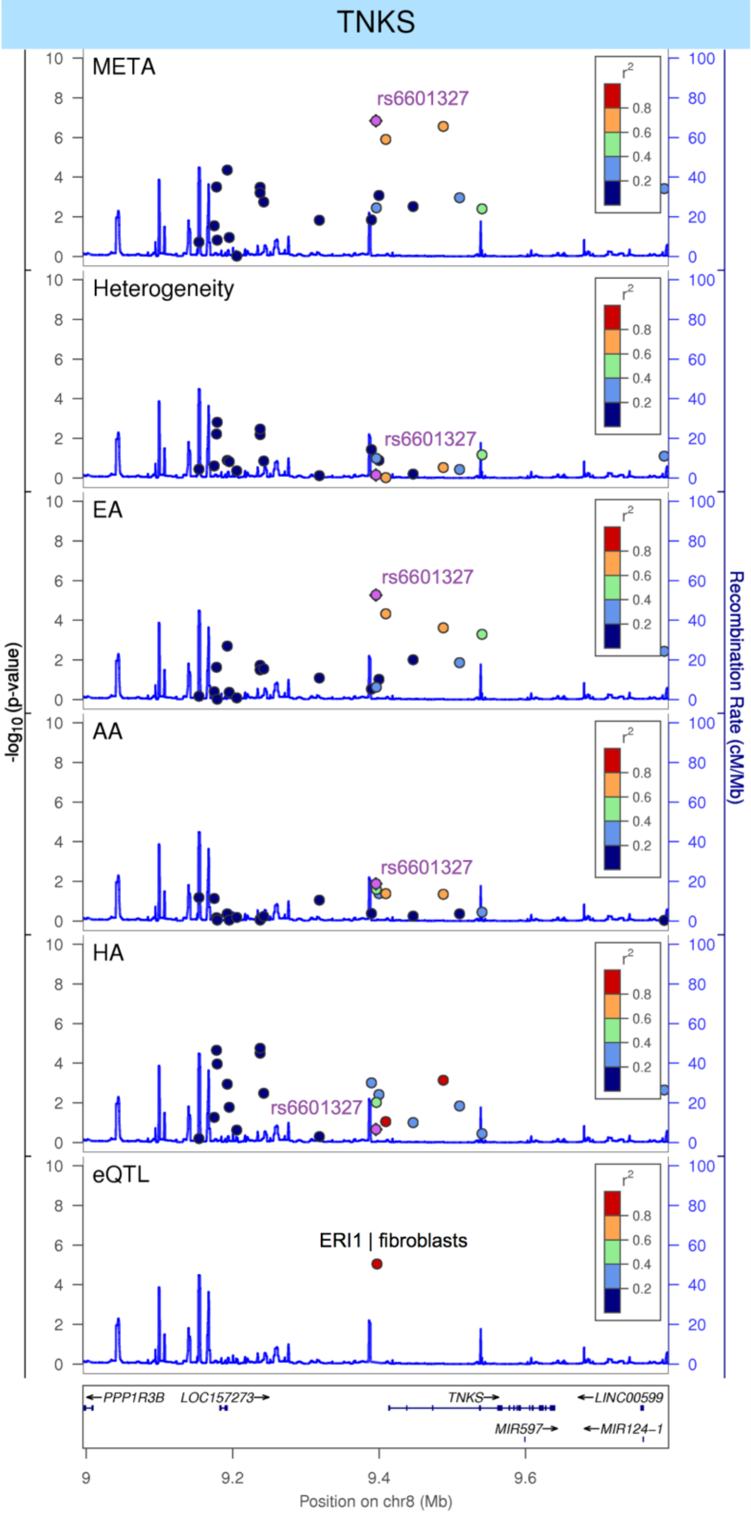
g. AHI1


AHI1
META
Heterogeneity
EA
AA
HA
eQTL (# additional tissues)
rs11154801
r2
0.8
0.6
0.4
0.2
AHI1 | fibroblasts; lymphocytes; nerve; whole blood; (12)
LINC00271 | testis; thyroid
-log10 (p-value)
Recombination Rate (cM/Mb)
HBS1L
MYB
AHI1
LINC00271
135.4
135.6
135.8
136
Position on chr6 (Mb)

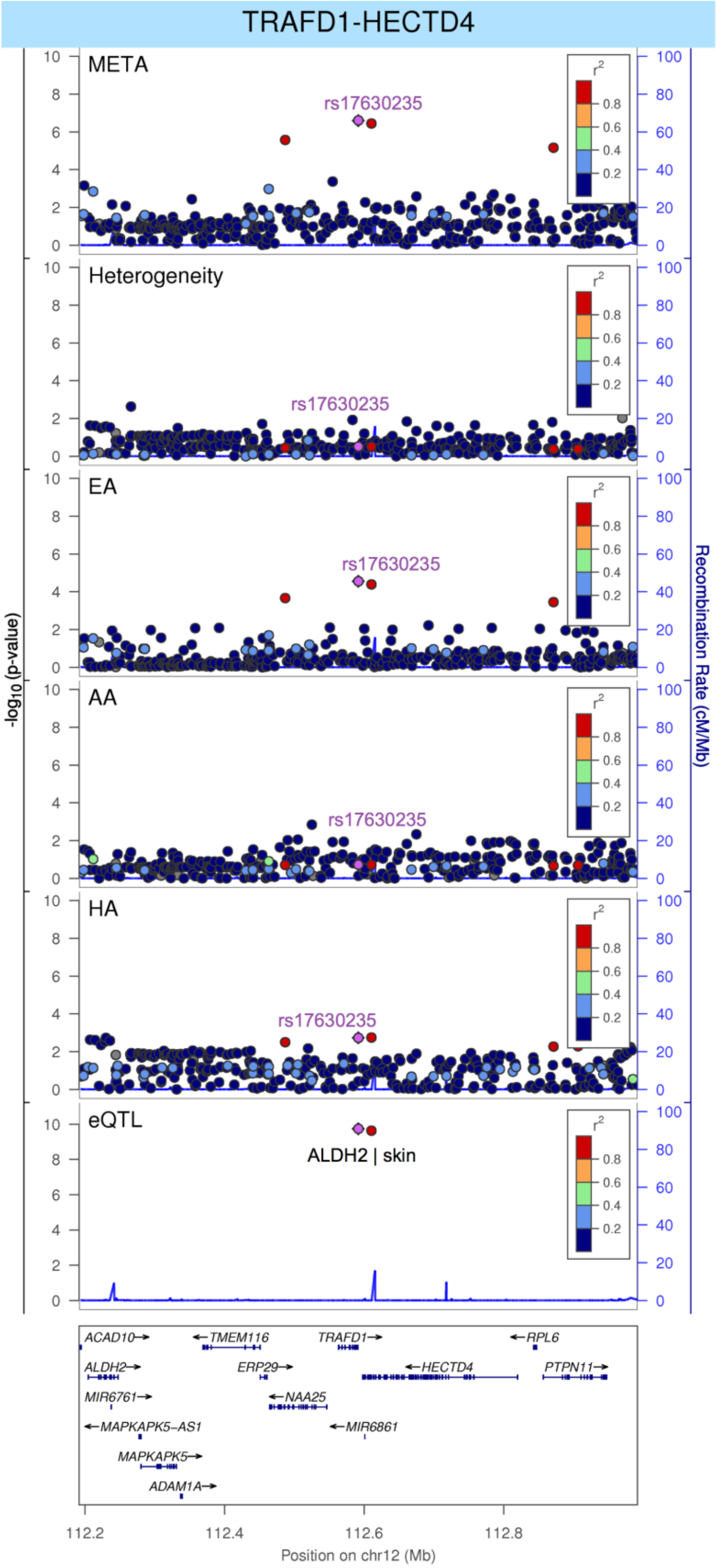
h. SKAP2


SKAP2
META
Heterogeneity
EA
AA
HA
eQTL
rs7795074
SKAP2; HOXA2; HOTAIRM1
whole blood
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
SNX10→
←KIAA0087
←SKAP2
←HOXA1
LOC441204→
C7orf71→
HOTAIRM1→
←HOXA2
26.4
26.6
26.8
27
Position on chr7 (Mb)

i. TNKS

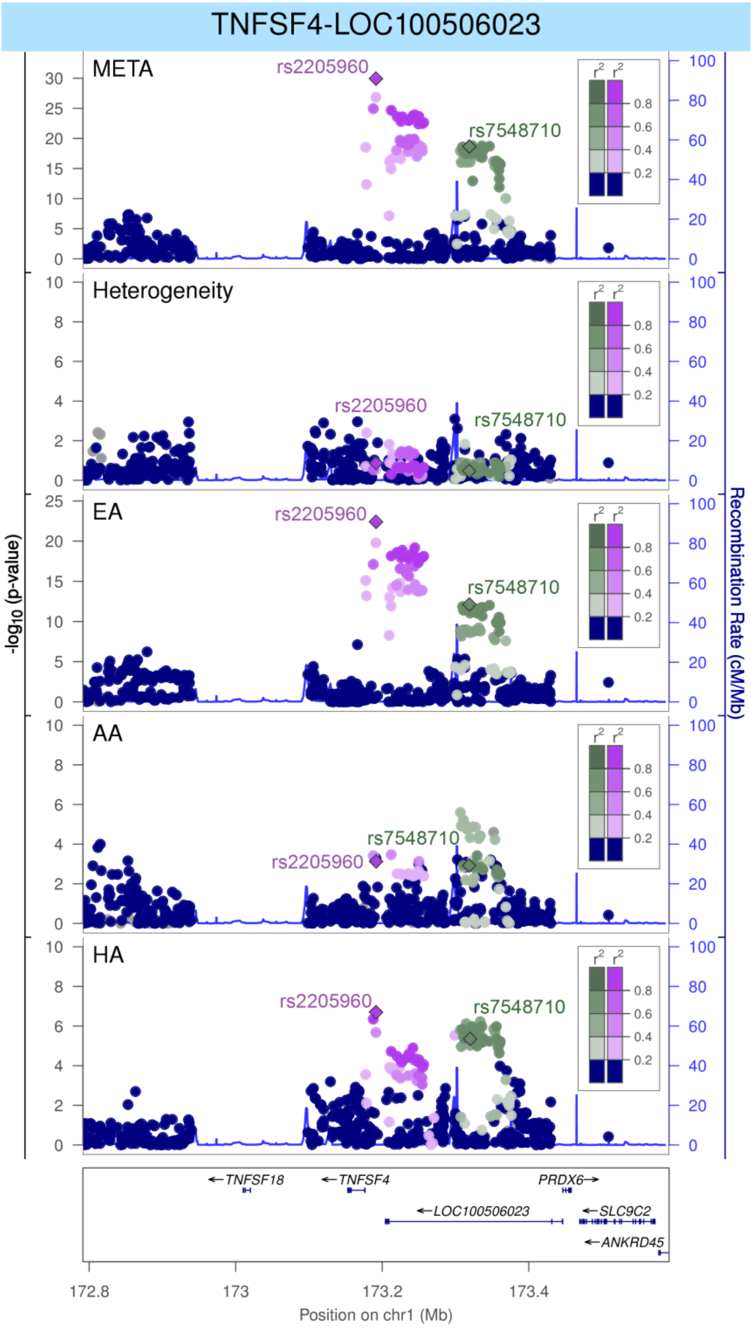

TNKS
META
Heterogeneity
EA
AA
HA
eQTL
rs6601327
ERI1 | fibroblasts
r^2
0.8
0.6
0.4
0.2
0
2
4
6
8
10
20
40
60
80
100
$-\log_{10}$(p-value)
Recombination Rate (cM/Mb)
←PPP1R3B
LOC157273→
TNKS→
←LINC00599
MIR597→
←MIR124–1
9
9.2
9.4
9.6
Position on chr8 (Mb)

j. TRAFD1-HECTD4

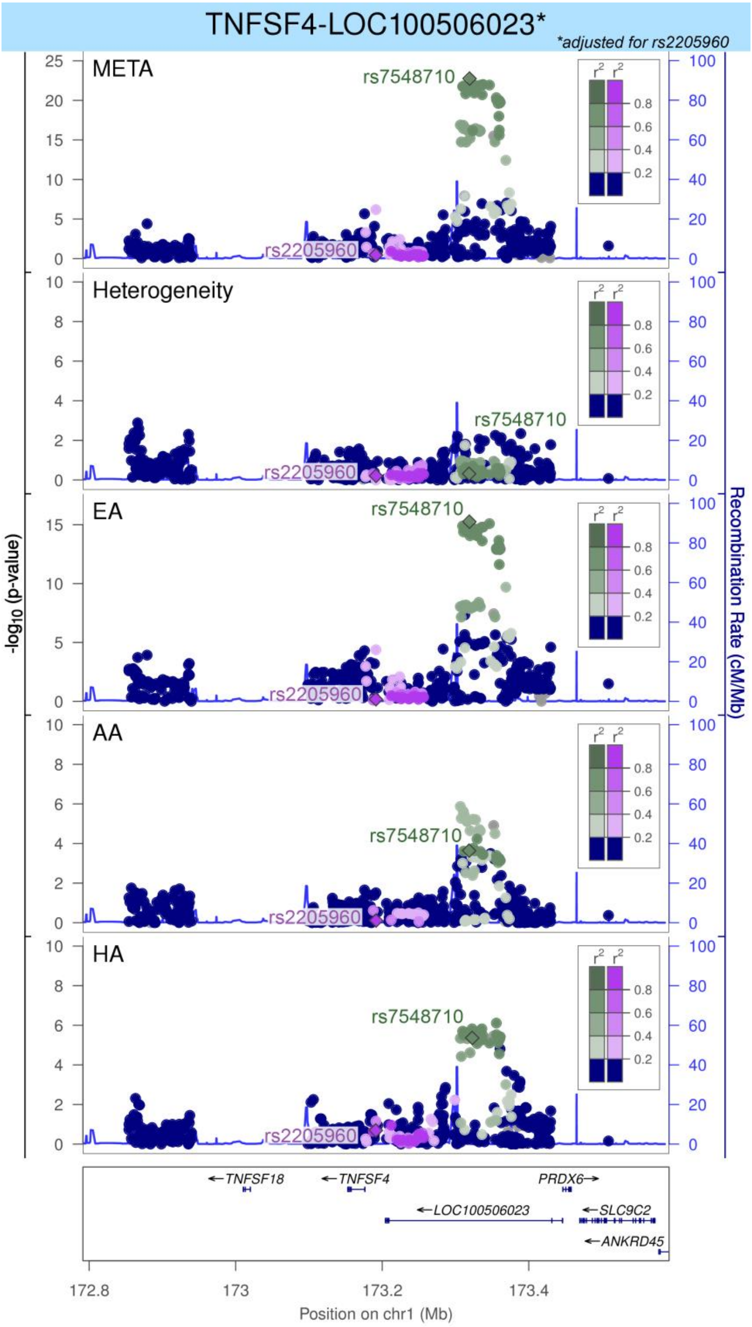


Supplementary Figure 15. Plots of Tier 1 meta-analysis regions noted for transancestral-mapping. Plots appear in the order found in Table 4. Individual plots were created using LocusZoom standalone software (*http://locuszoom.sph.umich.edu/*).

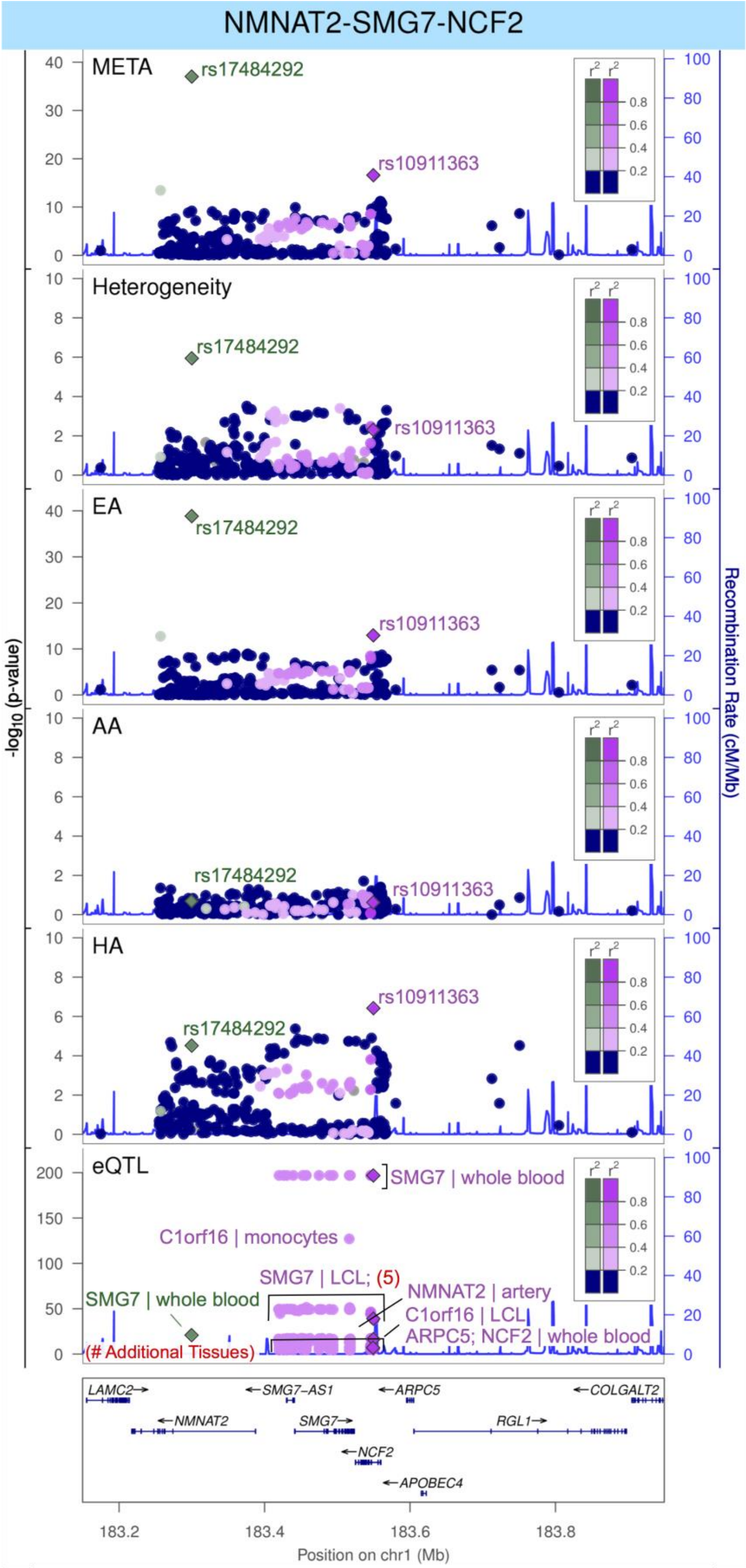
a. TNFSF4-LOC100506023



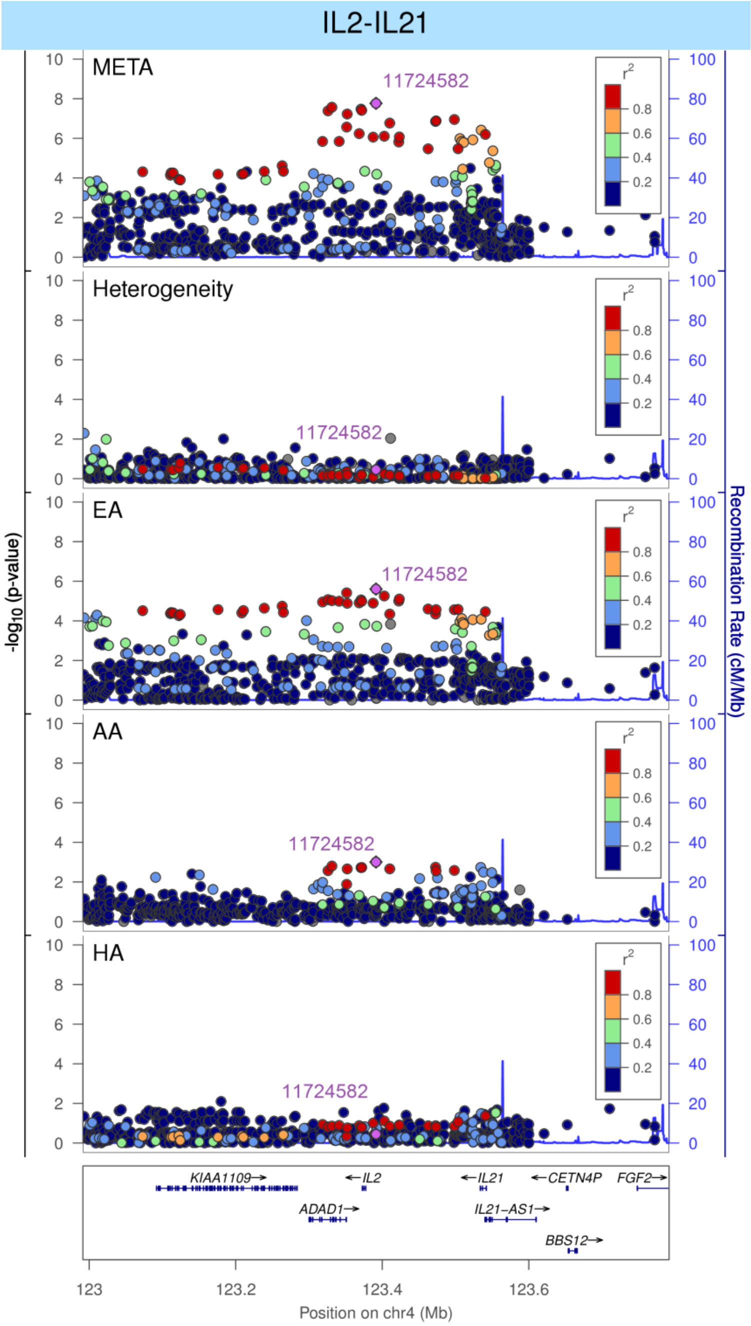
b. TNFSF4-LOC100506023



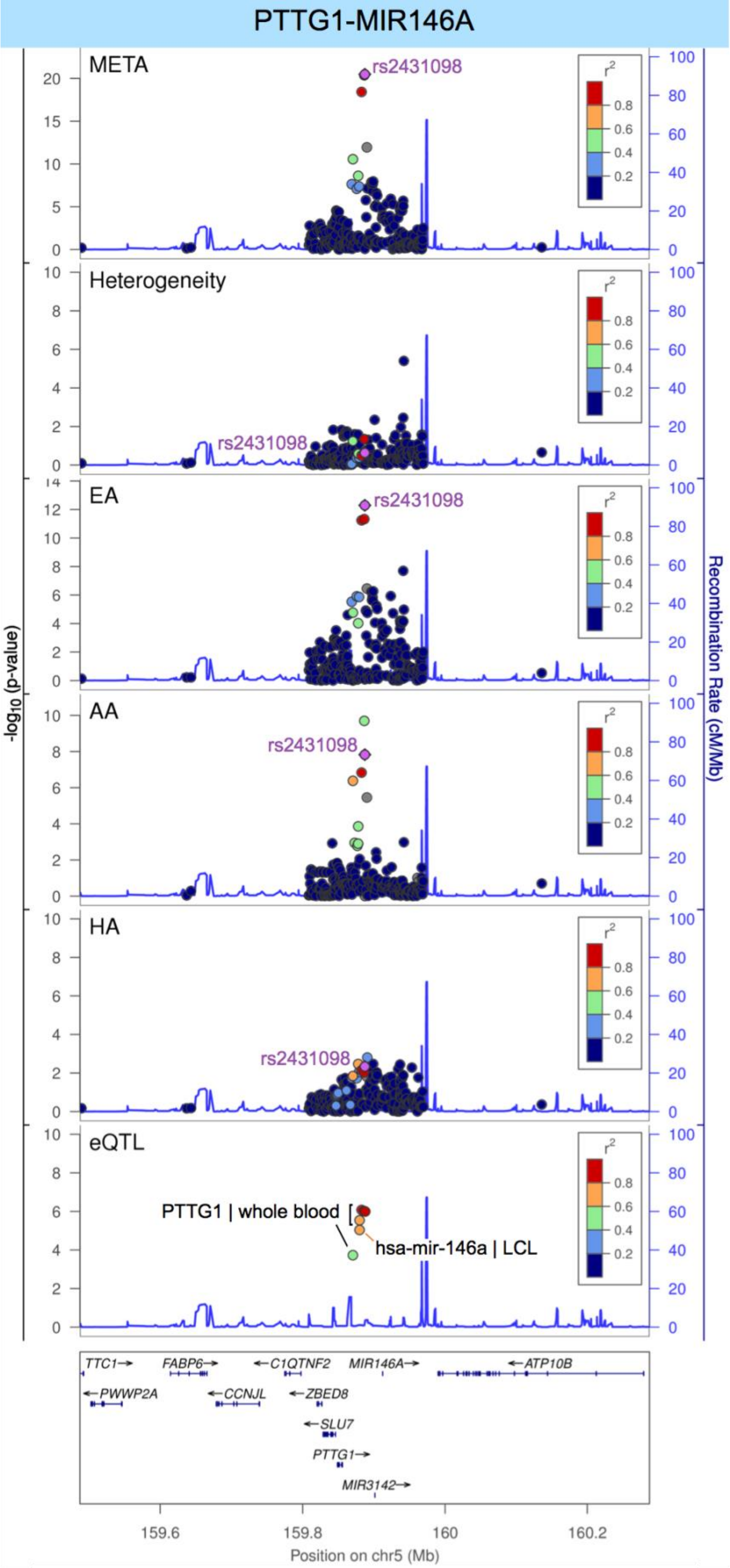
c. NMNAT2-SMG7-NCF2



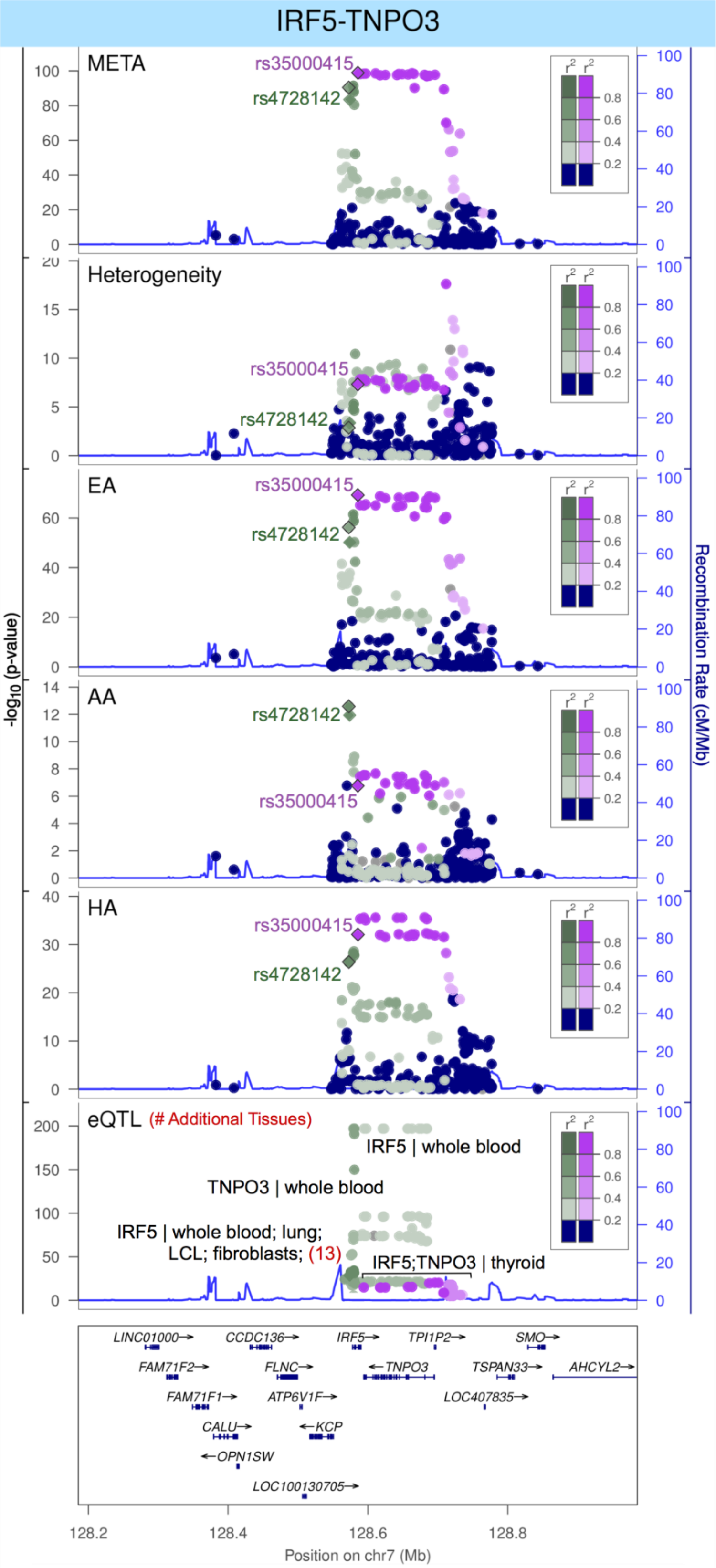
d. IL2-IL21


IL2-IL21
META
Heterogeneity
EA
AA
HA
11724582
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
KIAA1109
IL2
IL21
CETN4P
FGF2
ADAD1
IL21-AS1
BBS12
123
123.2
123.4
123.6
Position on chr4 (Mb)

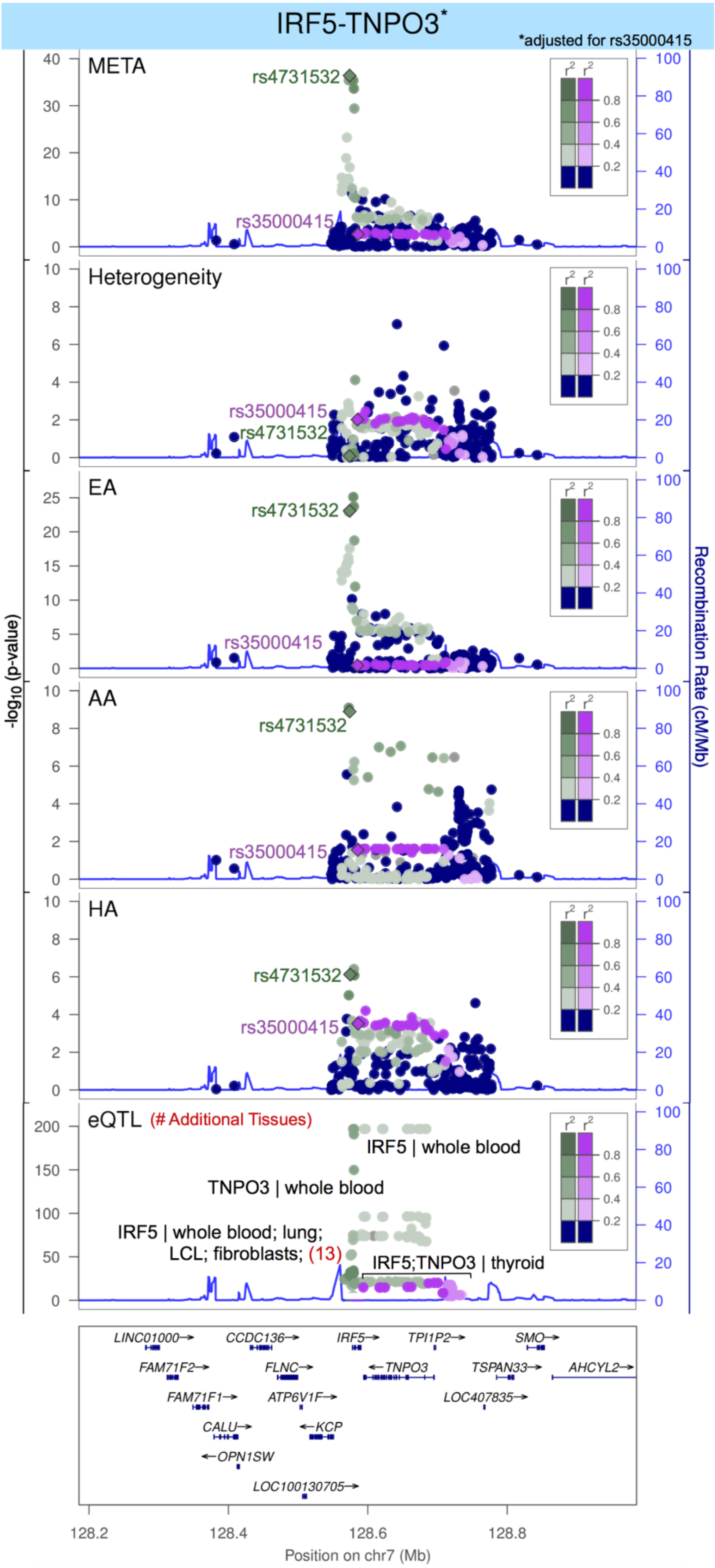
e. PTTG1-MIR146A



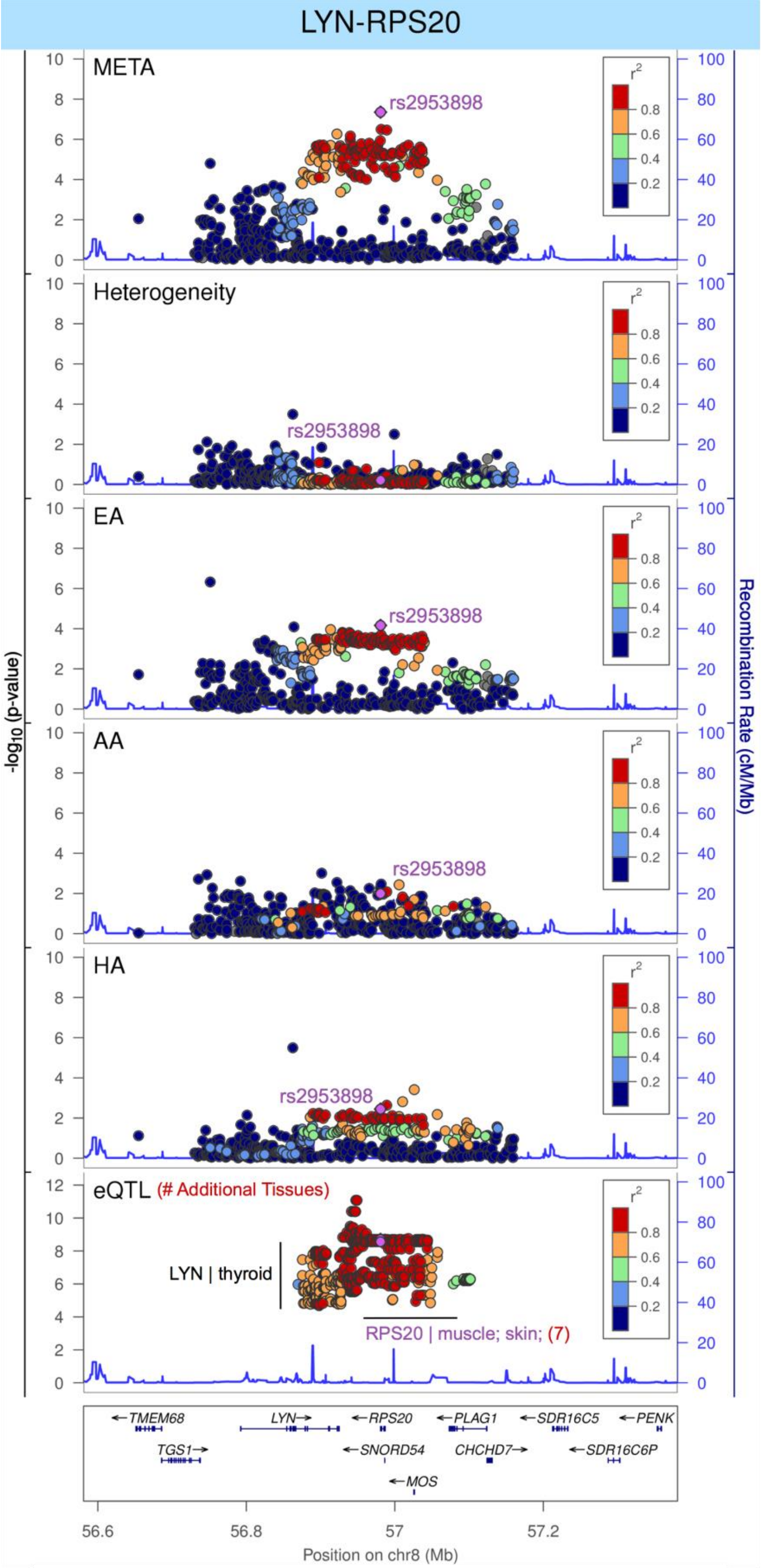
f. IRF5-TNPO3


IRF5-TNPO3
META
rs35000415
rs4728142
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
IRF5 | whole blood
TNPO3 | whole blood
IRF5 | whole blood; lung; LCL; fibroblasts; (13)
IRF5;TNPO3 | thyroid
-log10 (p-value)
Recombination Rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
LINC01000
CCDC136
IRF5
TPI1P2
SMO
FAM71F2
FLNC
TNPO3
TSPAN33
AHCYL2
FAM71F1
ATP6V1F
LOC407835
CALU
KCP
OPN1SW
LOC100130705
128.2
128.4
128.6
128.8
Position on chr7 (Mb)

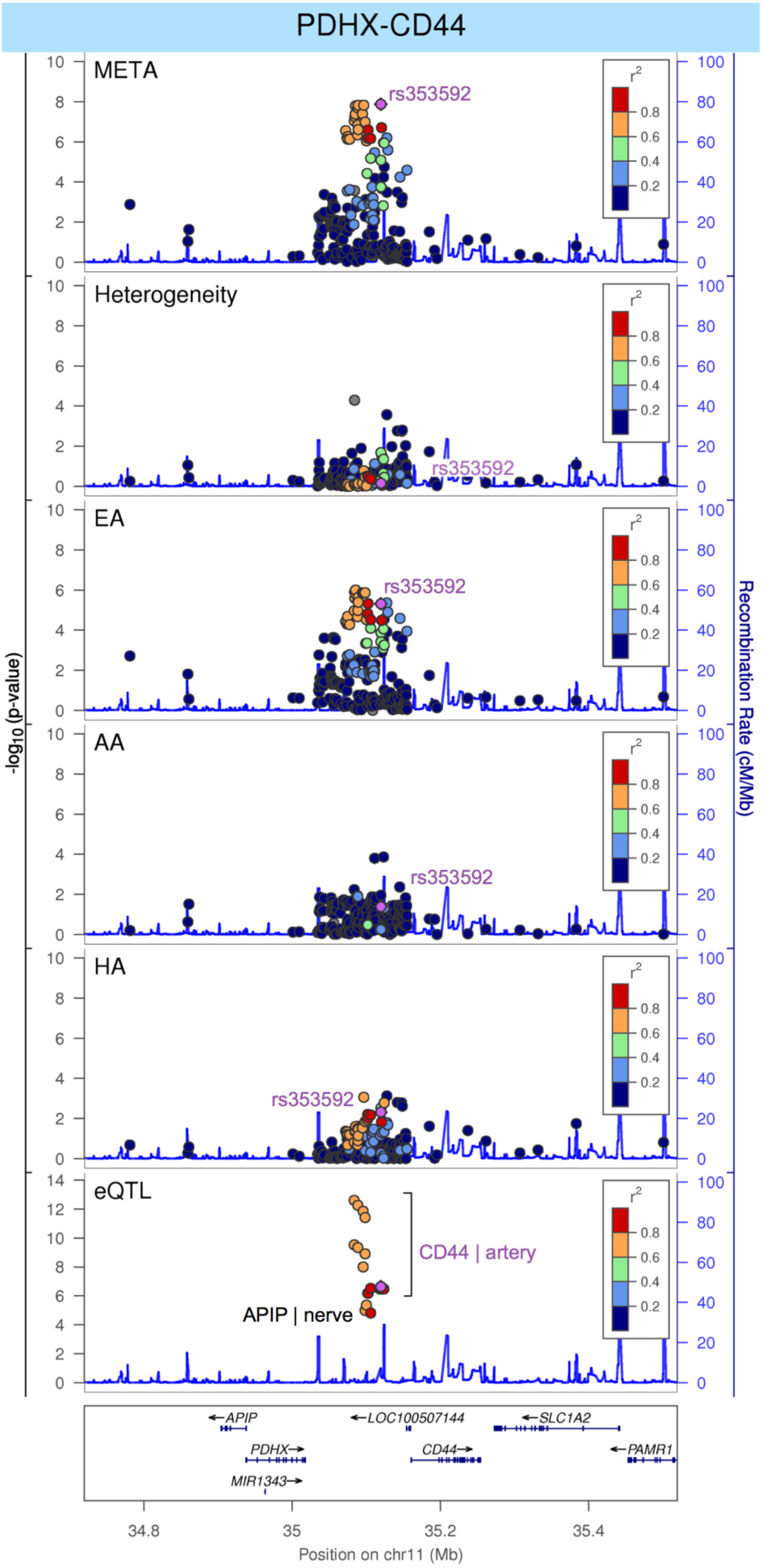
g. IRF5-TNPO3 (adjusted for rs350004115)



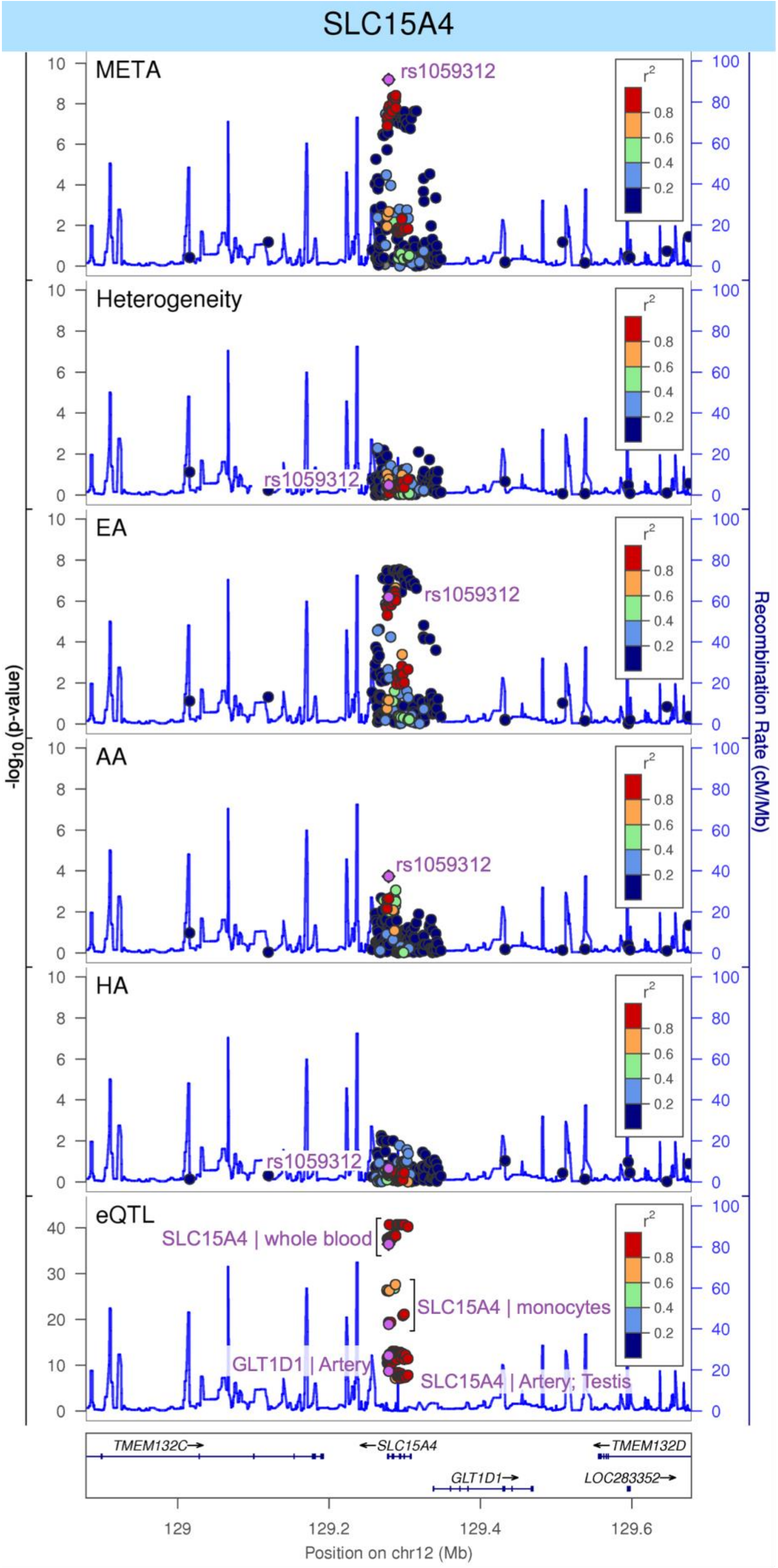
h. LYN-RPS20


LYN-RPS20
META
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
rs2953898
LYN | thyroid
RPS20 | muscle; skin; (7)
r²
0.8
0.6
0.4
0.2
-log₁₀ (p-value)
Recombination Rate (cM/Mb)
TMEM68
LYN
RPS20
PLAG1
SDR16C5
PENK
TGS1
SNORD54
CHCHD7
SDR16C6P
MOS
56.6
56.8
57
57.2
Position on chr8 (Mb)

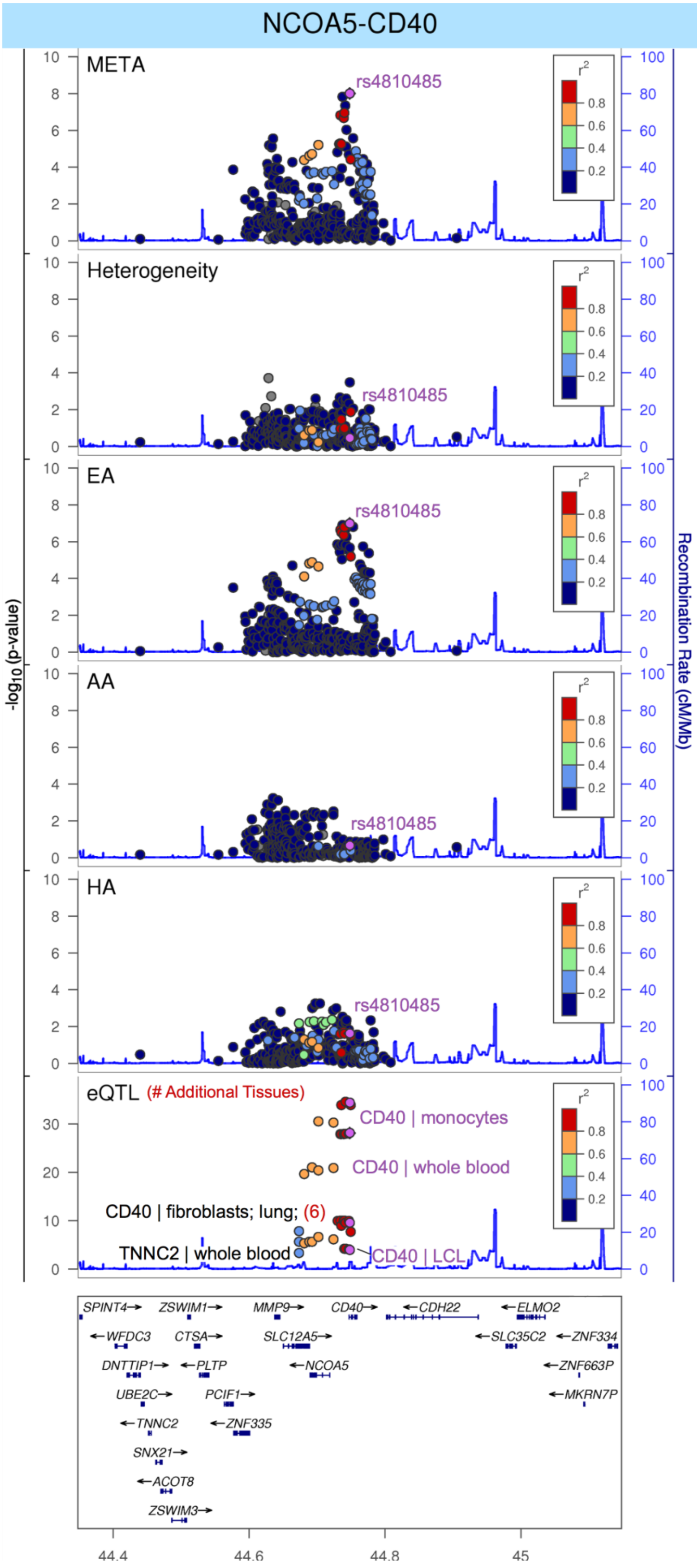
i. PDHX-CD44


PDHX-CD44
META
Heterogeneity
EA
AA
HA
eQTL
rs353592
CD44 | artery
APIP | nerve
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
APIP
LOC100507144
SLC1A2
PDHX
CD44
PAMR1
MIR1343
34.8
35
35.2
35.4
Position on chr11 (Mb)

j. SLC15A4

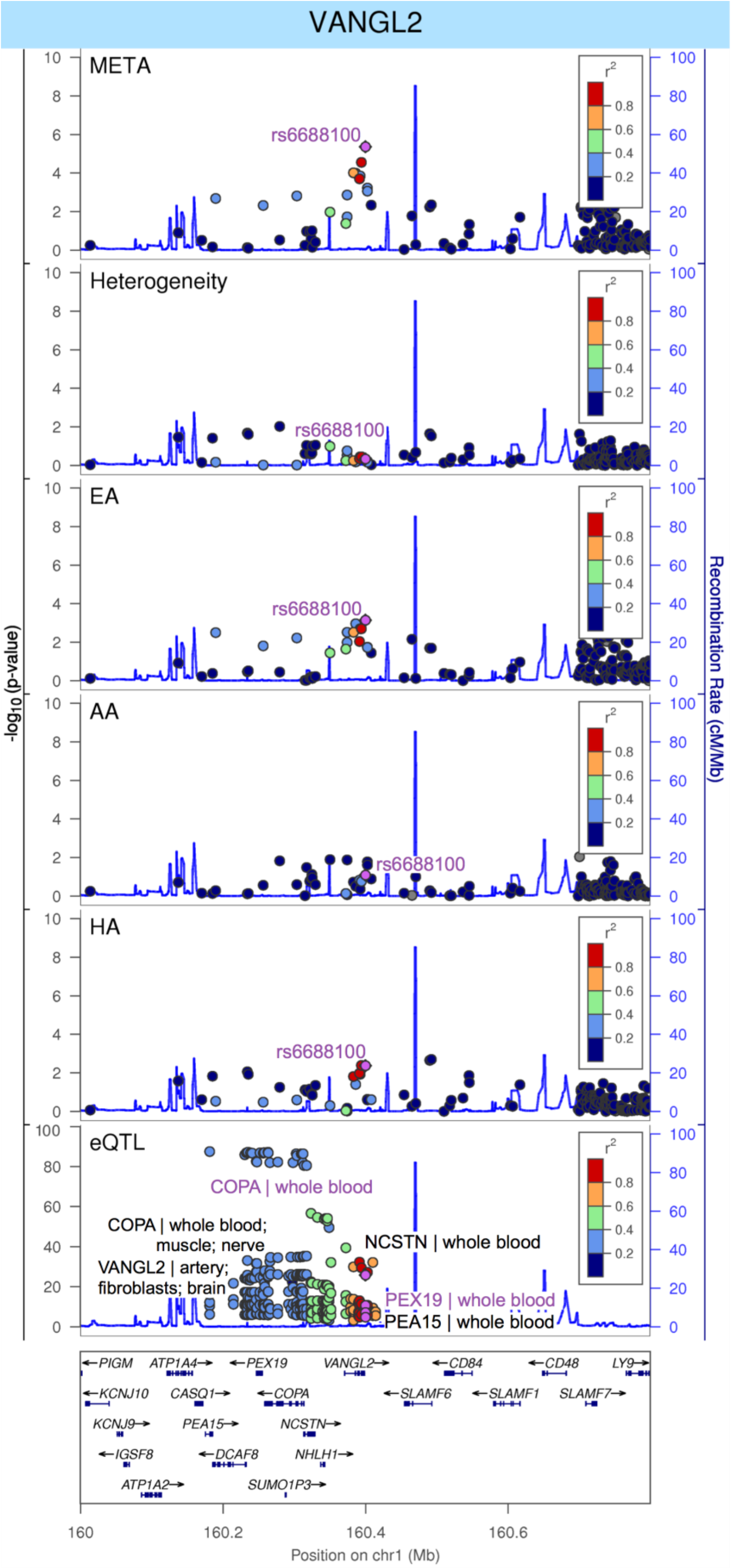

SLC15A4
META
Heterogeneity
EA
AA
HA
eQTL
rs1059312
SLC15A4 | whole blood
SLC15A4 | monocytes
GLT1D1 | Artery
SLC15A4 | Artery; Testis
r^2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
TMEM132C→
←SLC15A4
←TMEM132D
GLT1D1→
LOC283352→
129
129.2
129.4
129.6
Position on chr12 (Mb)

k. NCOA5-CD40

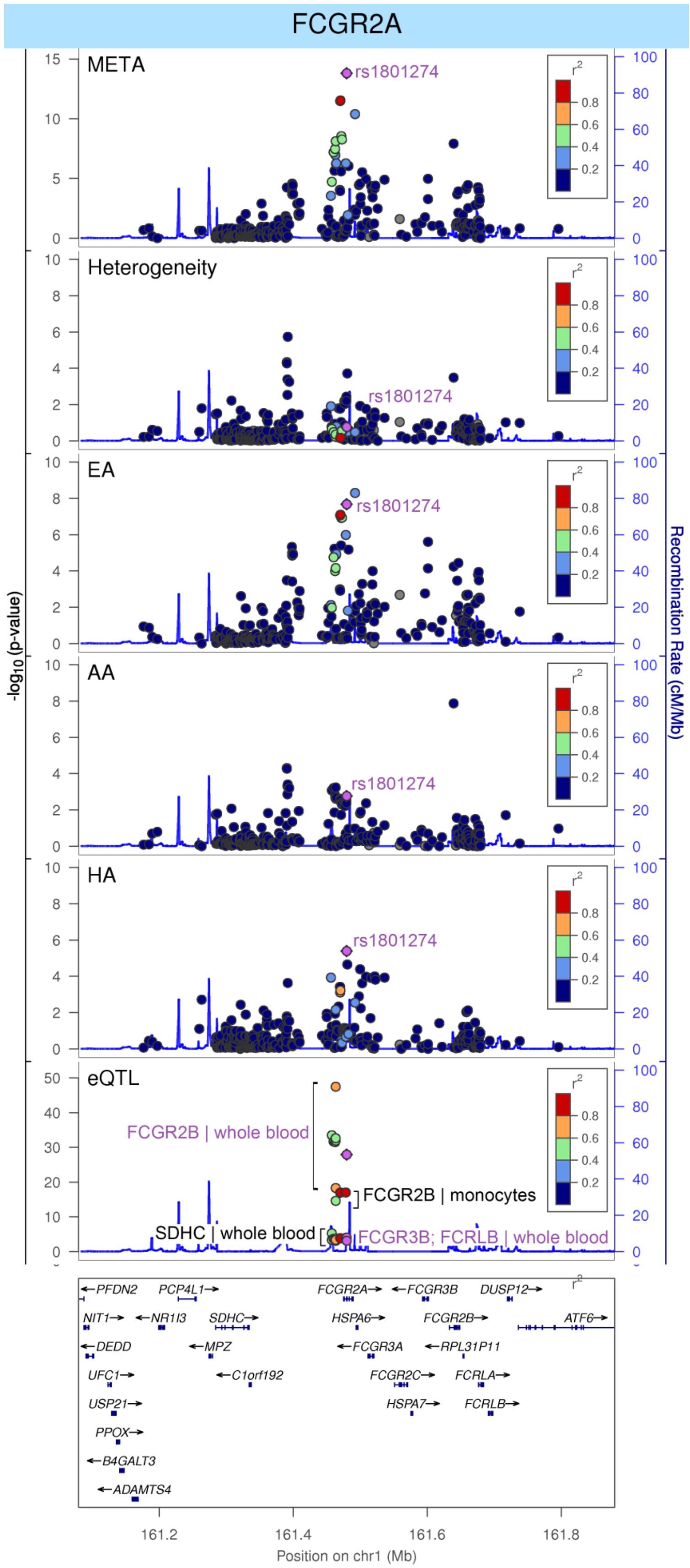

NCOA5-CD40
META
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
rs4810485
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
0
2
4
6
8
10
20
30
40
60
80
100
CD40 | monocytes
CD40 | whole blood
CD40 | fibroblasts; lung; (6)
TNNC2 | whole blood
CD40 | LCL
SPINT4→
ZSWIM1→
MMP9→
CD40→
←CDH22
←ELMO2
←WFDC3
CTSA→
SLC12A5→
←SLC35C2
←ZNF334
DNTTIP1→
←PLTP
←NCOA5
←ZNF663P
UBE2C→
PCIF1→
←MKRN7P
←TNNC2
←ZNF335
SNX21→
←ACOT8
ZSWIM3→
44.4
44.6
44.8
45

Supplementary Figure 16. Plots of additional meta-analysis regions noted for transancestral-mapping (p-value$_{\text{fdr}}$ <0.001). Plots appear in the order found in Supplementary Data 8. Individual plots were created using LocusZoom standalone software (*http://locuszoom.sph.umich.edu/*).

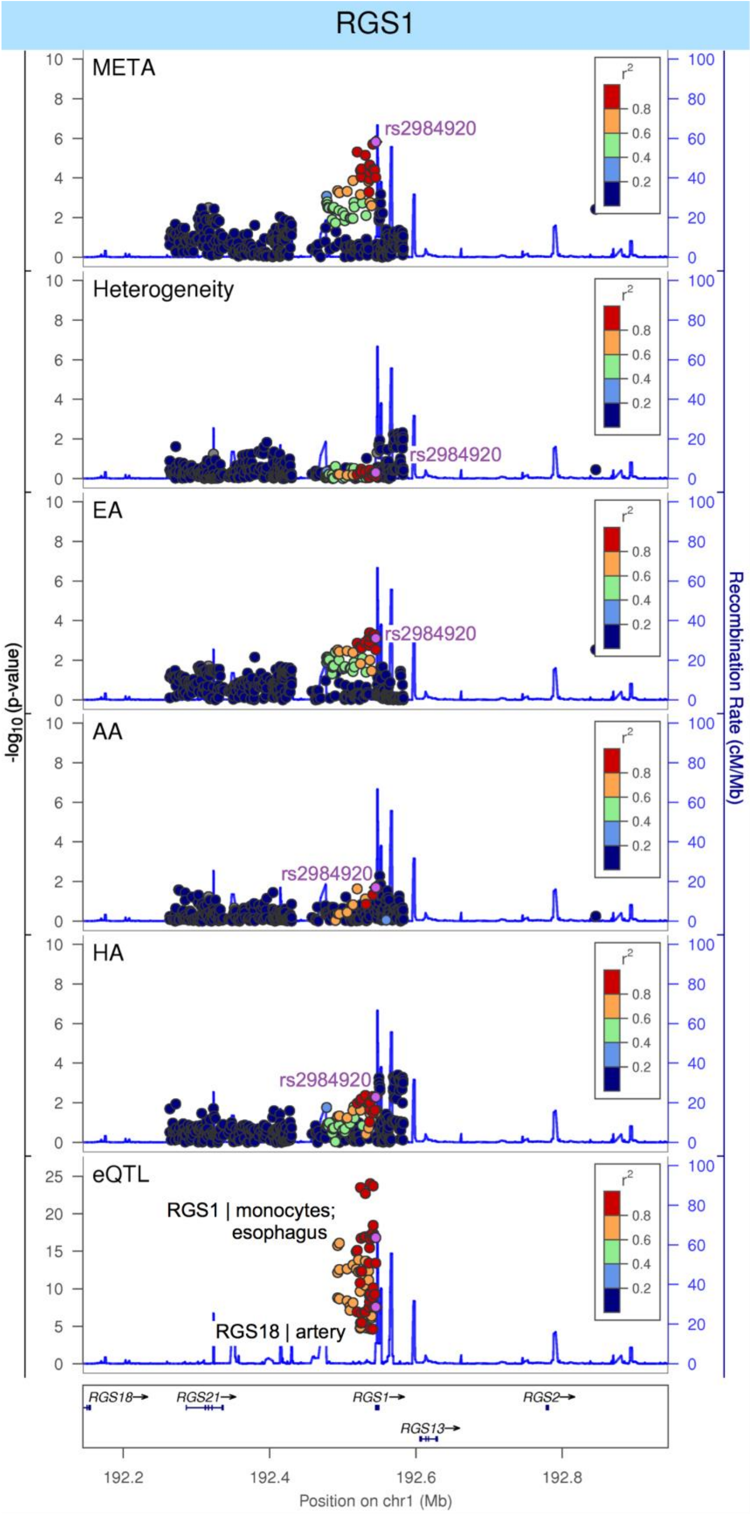
a. VANGL2



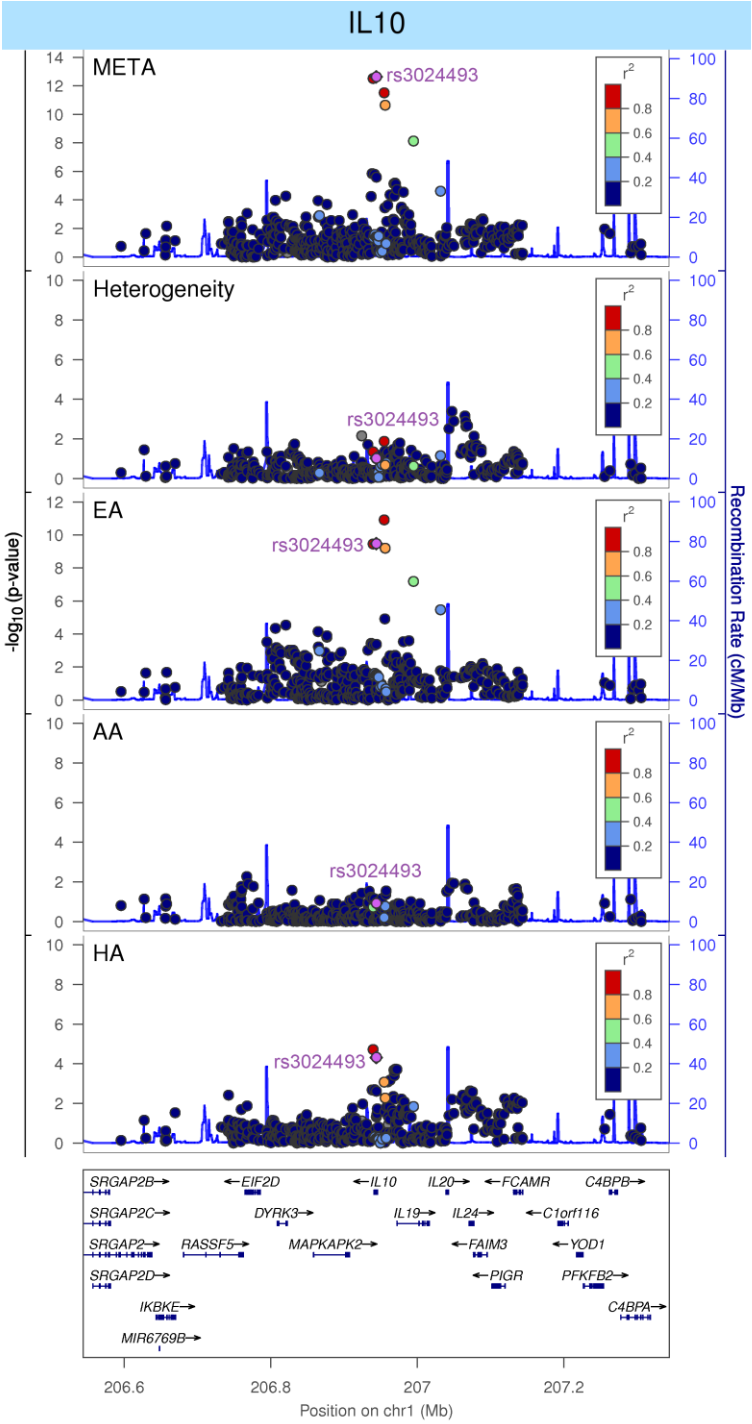
b. FCGR2A


FCGR2A
META
Heterogeneity
EA
AA
HA
eQTL
rs1801274
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
FCGR2B | whole blood
FCGR2B | monocytes
SDHC | whole blood
FCGR3B; FCRLB | whole blood
←PFDN2
PCP4L1→
FCGR2A→
←FCGR3B
DUSP12→
NIT1→
←NR1I3
SDHC→
HSPA6→
FCGR2B→
ATF6→
←DEDD
←MPZ
←FCGR3A
←RPL31P11
UFC1→
←C1orf192
FCGR2C→
FCRLA→
USP21→
HSPA7→
FCRLB→
PPOX→
←B4GALT3
←ADAMTS4
161.2
161.4
161.6
161.8
Position on chr1 (Mb)

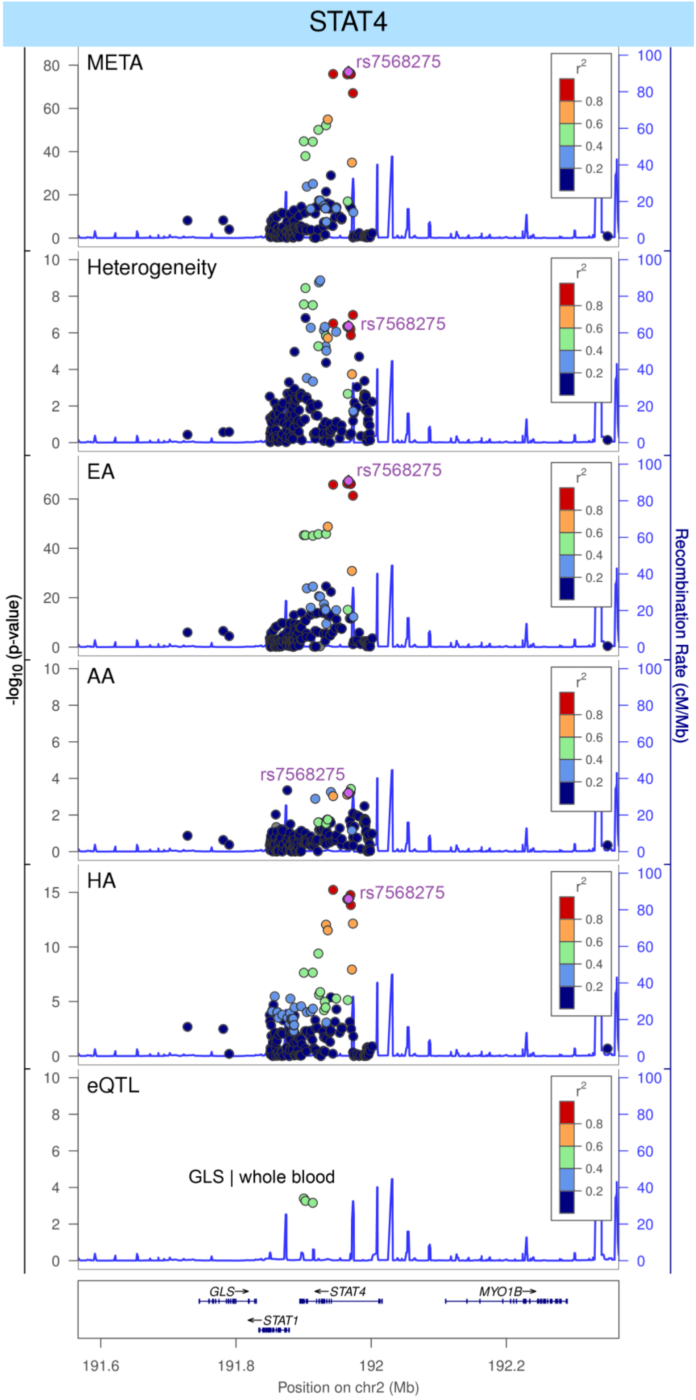
c. RGS1


RGS1
META
Heterogeneity
EA
AA
HA
eQTL
rs2984920
RGS1 | monocytes; esophagus
RGS18 | artery
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
RGS18→
RGS21→
RGS1→
RGS13→
RGS2→
192.2
192.4
192.6
192.8
Position on chr1 (Mb)

d. IL10

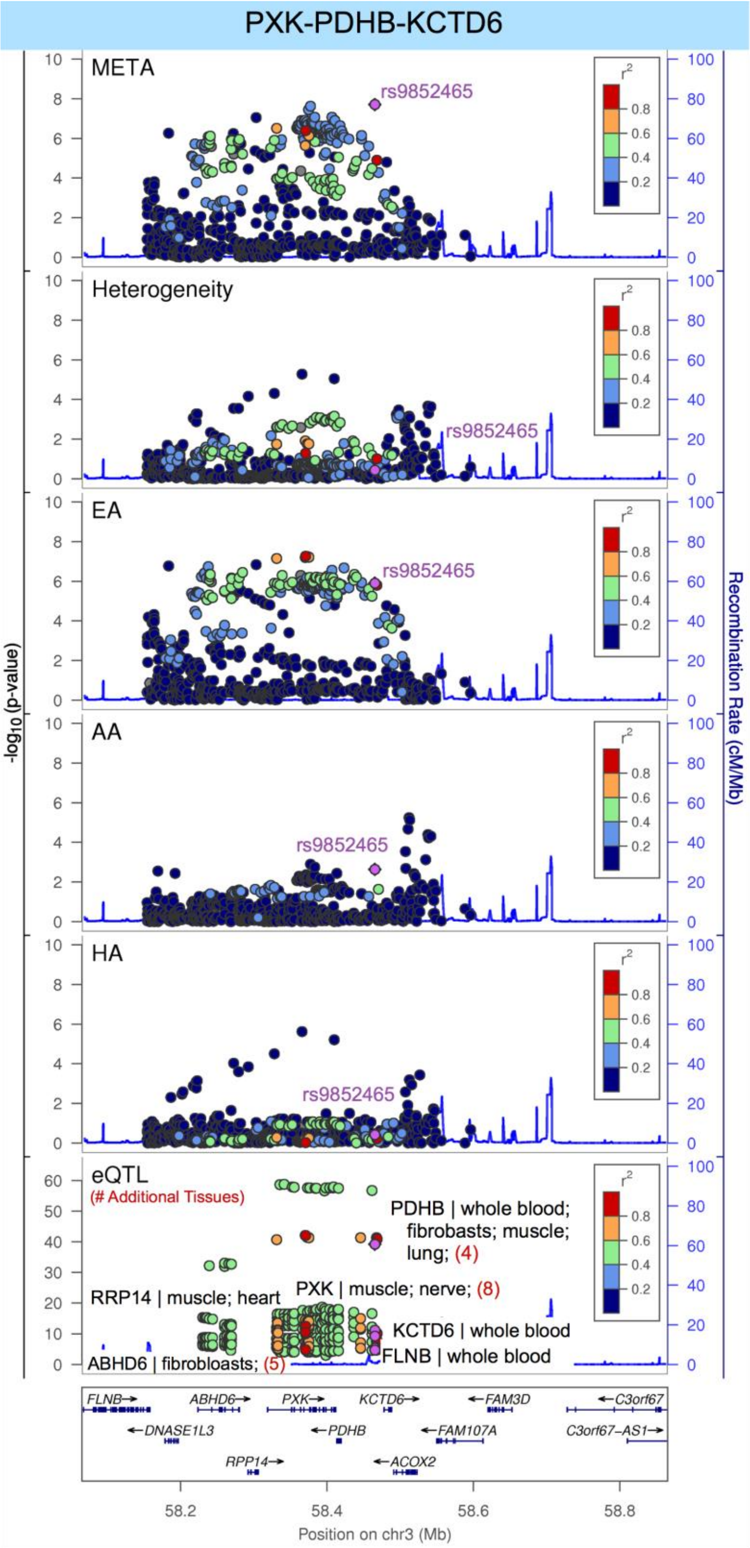

IL10
META
rs3024493
Heterogeneity
rs3024493
EA
rs3024493
AA
rs3024493
HA
rs3024493
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
0
2
4
6
8
10
12
14
0
20
40
60
80
100
SRGAP2B→
←EIF2D
←IL10
IL20→
←FCAMR
C4BPB→
SRGAP2C→
DYRK3→
IL19→
IL24→
←C1orf116
SRGAP2→
RASSF5→
MAPKAPK2→
←FAIM3
←YOD1
SRGAP2D→
←PIGR
PFKFB2→
IKBKE→
C4BPA→
MIR6769B→
206.6
206.8
207
207.2
Position on chr1 (Mb)

e. STAT4

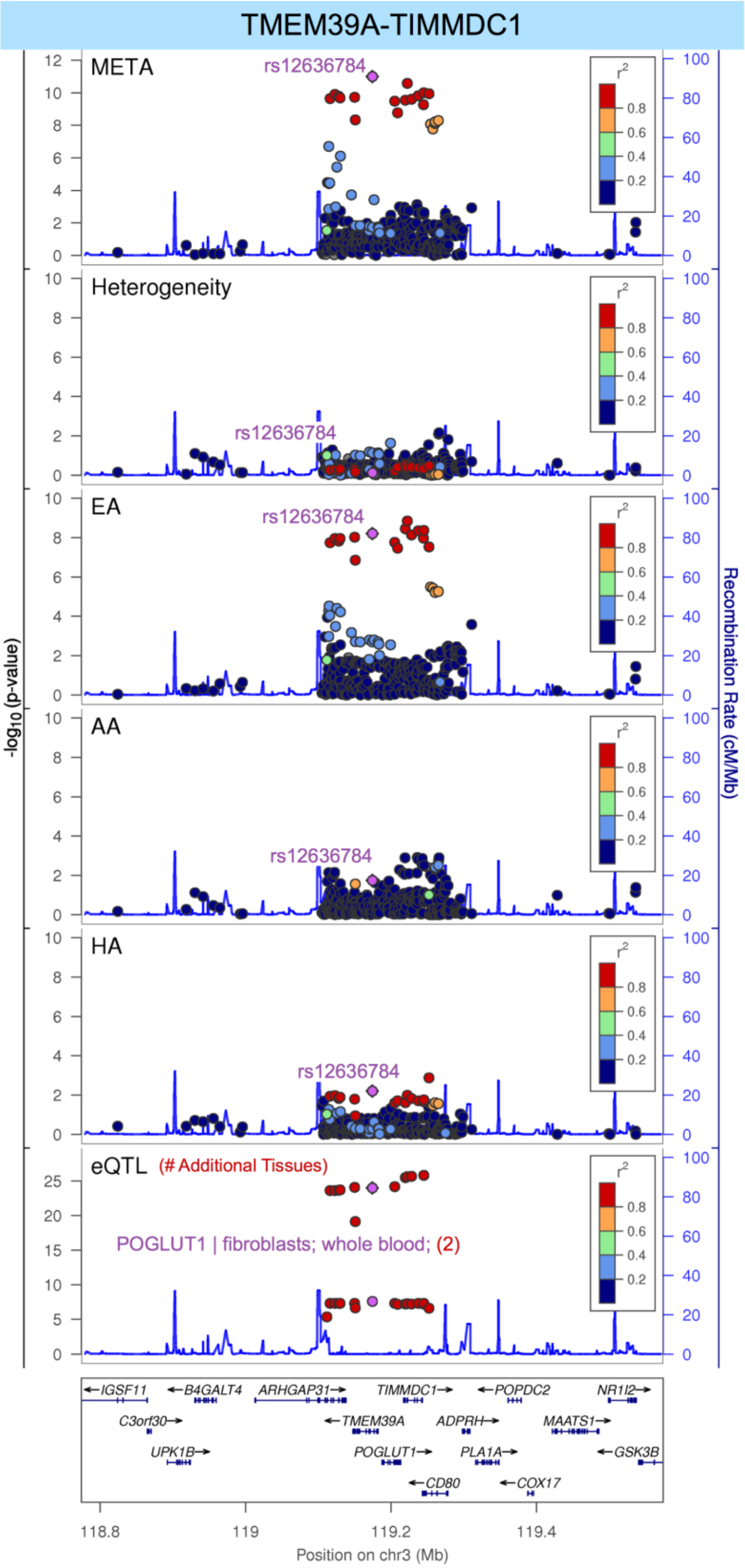


STAT4
META
Heterogeneity
EA
AA
HA
eQTL
rs7568275
GLS | whole blood
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
GLS
STAT4
STAT1
MYO1B
191.6
191.8
192
192.2
Position on chr2 (Mb)

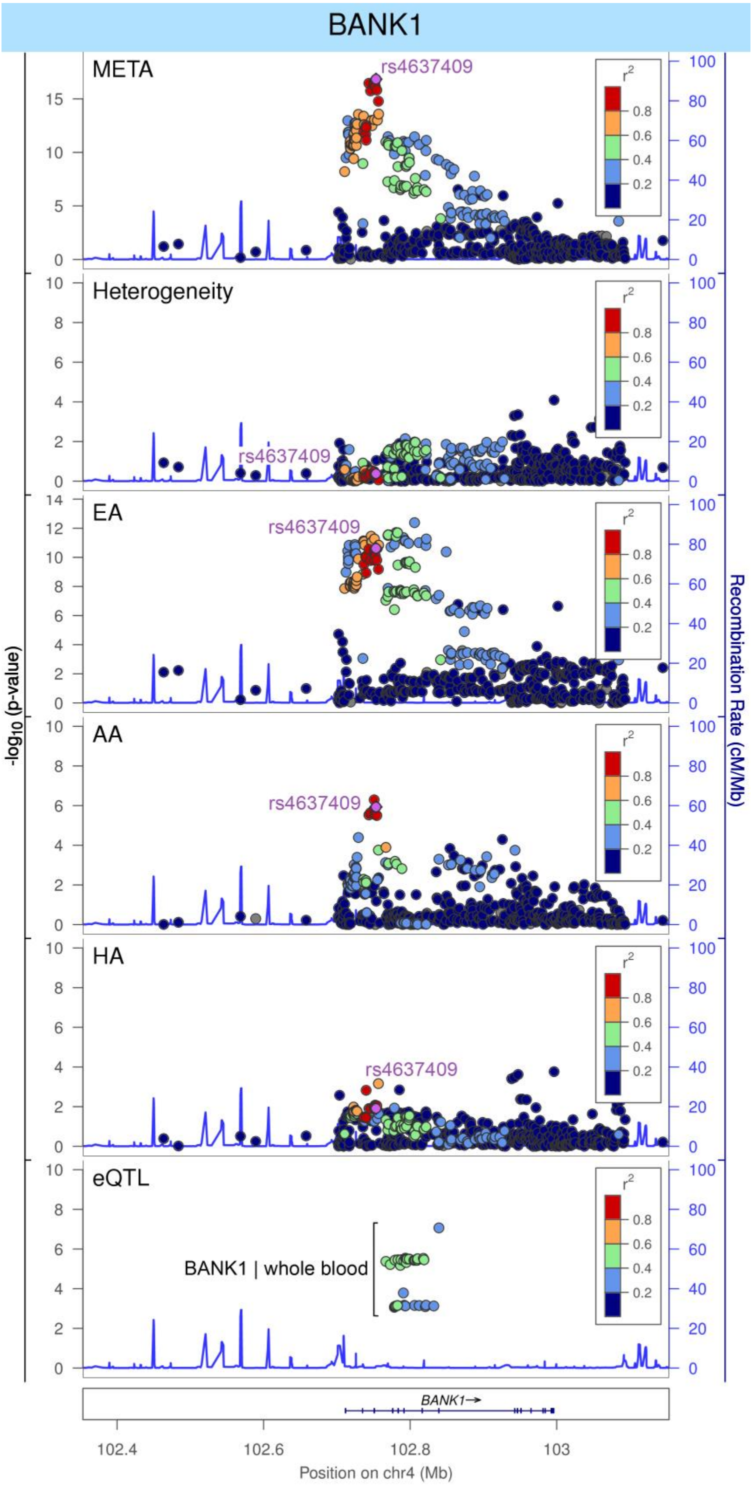
f. PXK-PDHB-KCTD6



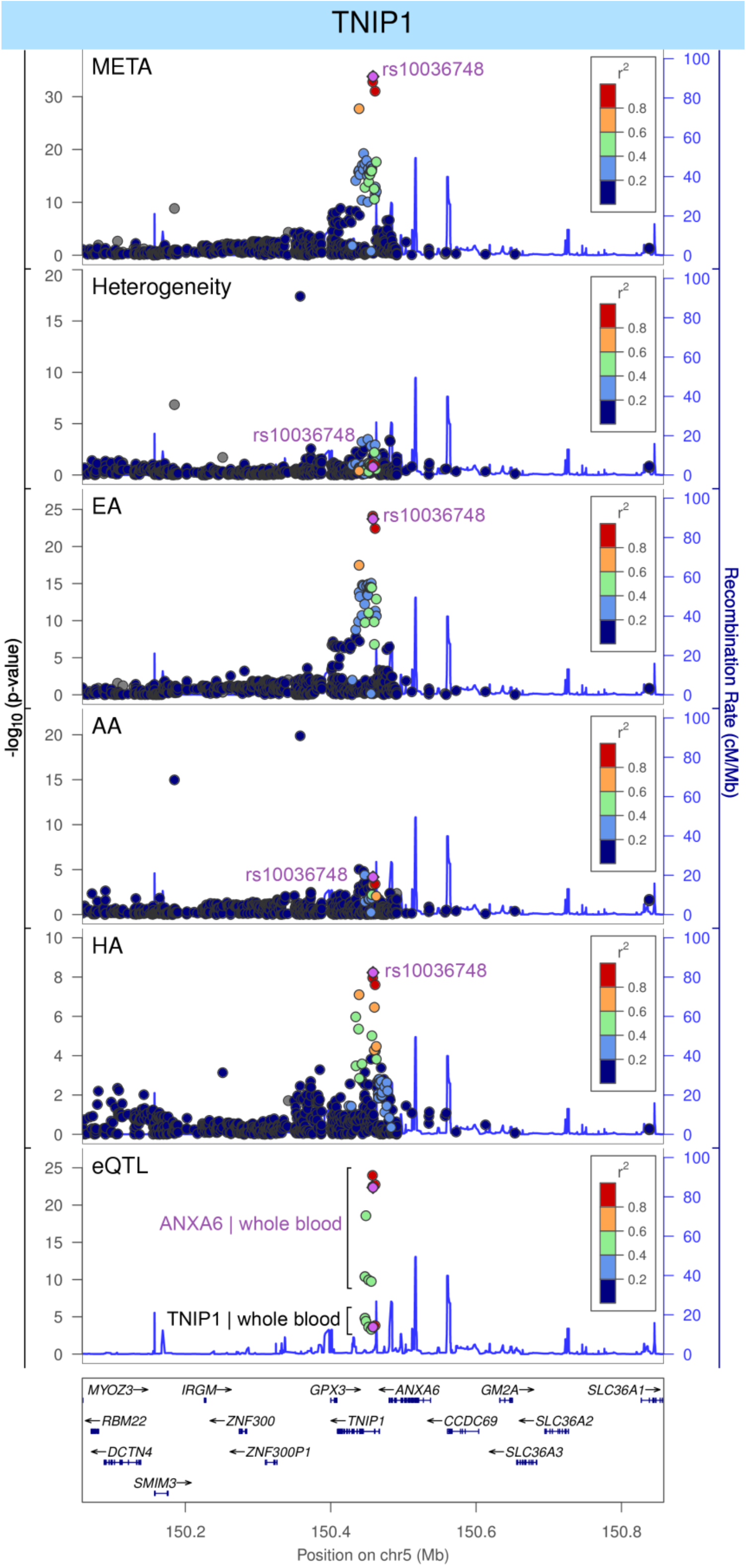
g. TMEM39A-TIMMDC1



h. BANK1

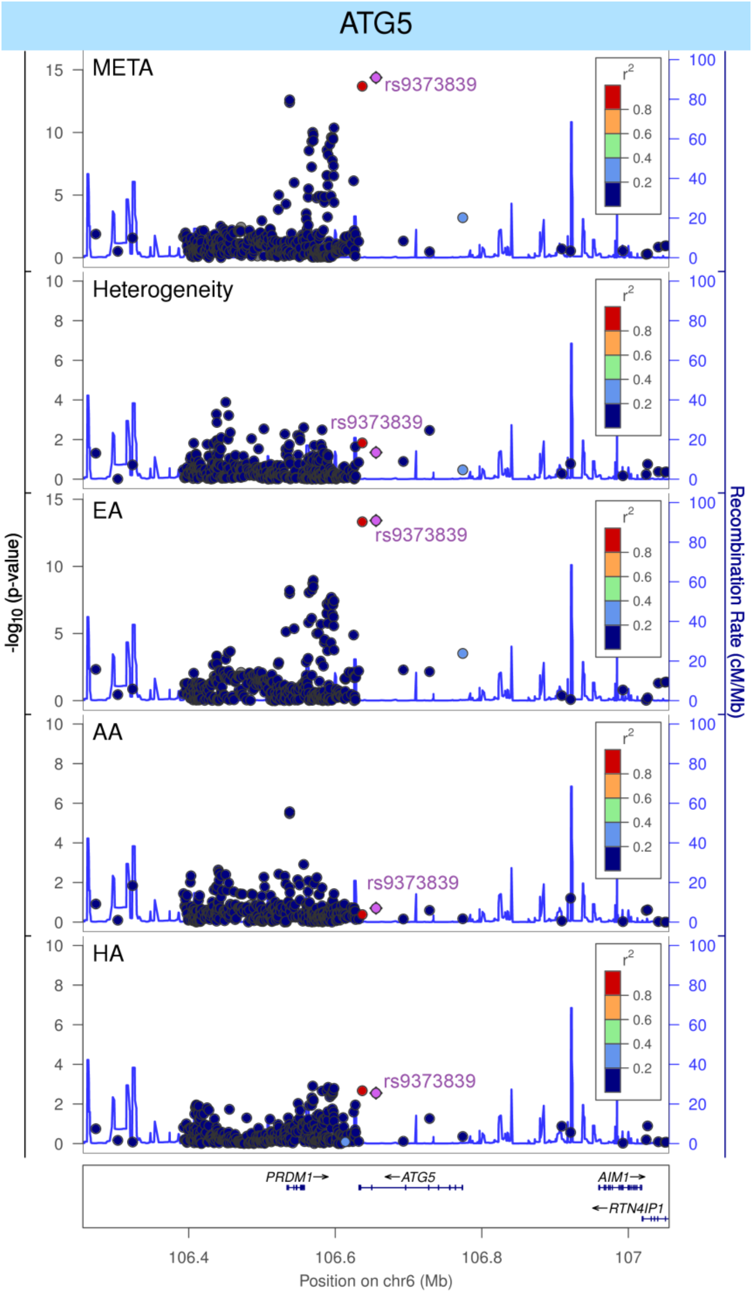

BANK1
META
Heterogeneity
EA
AA
HA
eQTL
rs4637409
BANK1 | whole blood
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
BANK1→
102.4
102.6
102.8
103
Position on chr4 (Mb)

i. TNIP1

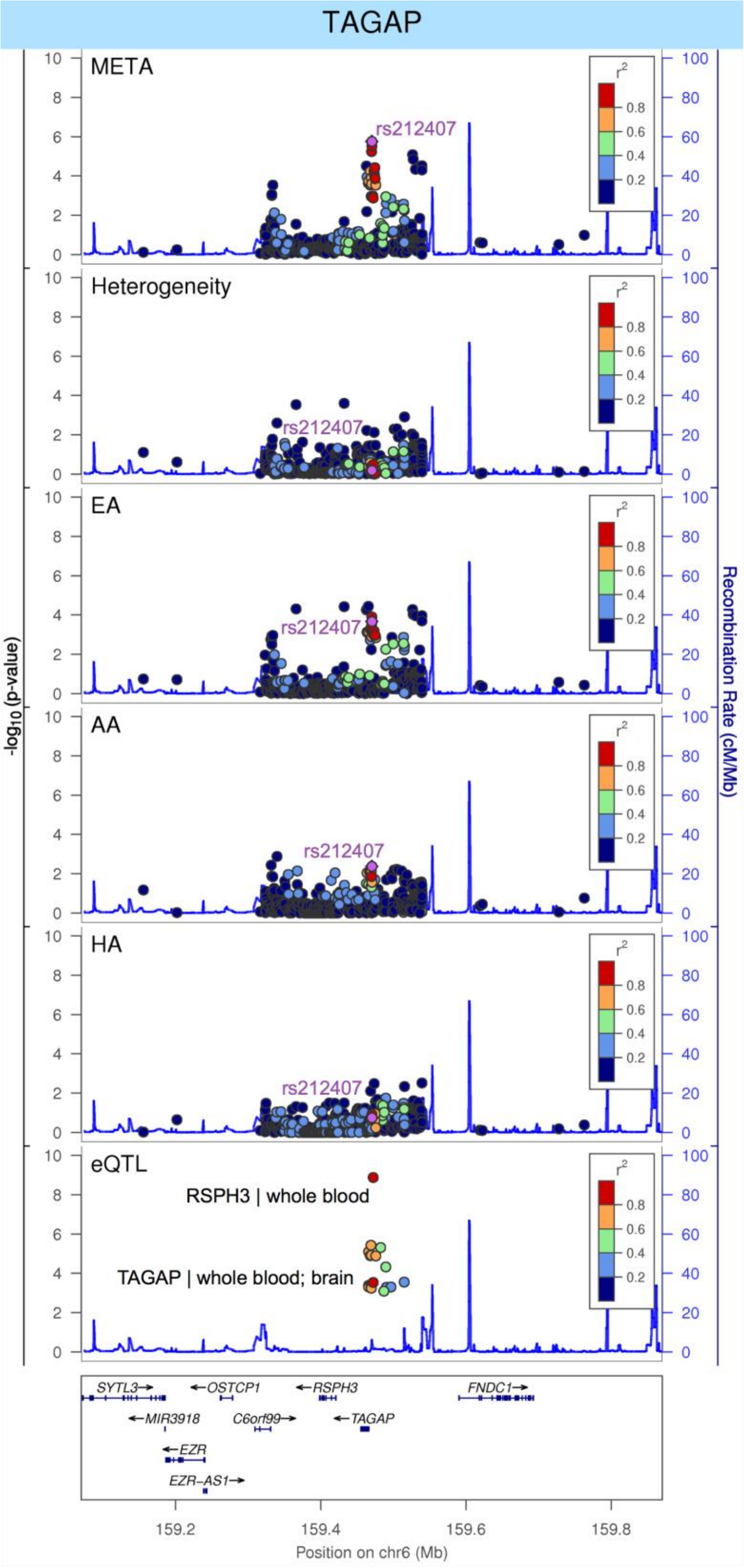


TNIP1
META
rs10036748
Heterogeneity
rs10036748
EA
rs10036748
AA
rs10036748
HA
rs10036748
eQTL
ANXA6 | whole blood
TNIP1 | whole blood
r^2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
MYOZ3→
IRGM→
GPX3→
←ANXA6
GM2A→
SLC36A1→
←RBM22
←ZNF300
←TNIP1
←CCDC69
←SLC36A2
←DCTN4
←ZNF300P1
←SLC36A3
SMIM3→
150.2
150.4
150.6
150.8
Position on chr5 (Mb)

j. ATG5

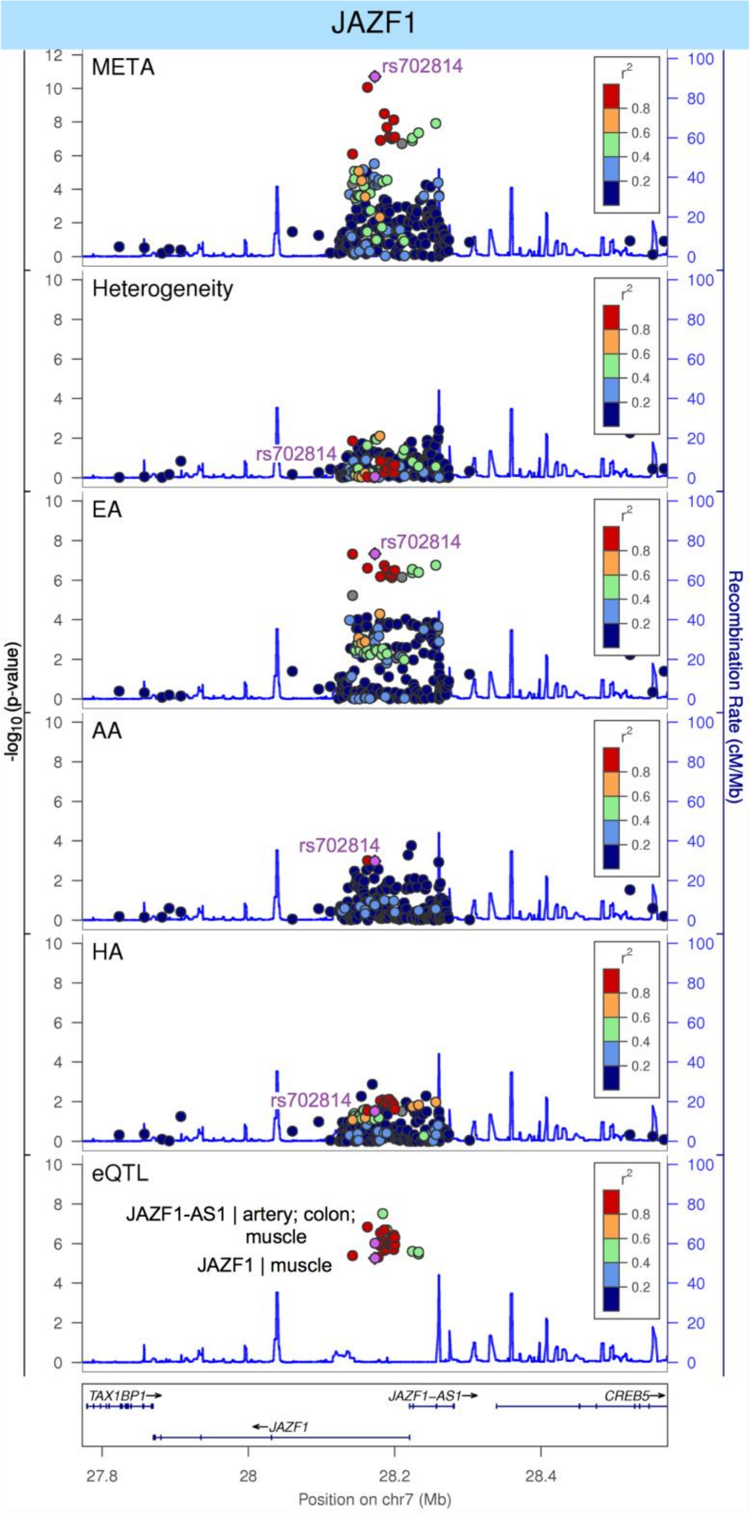

ATG5
META
Heterogeneity
EA
AA
HA
rs9373839
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
PRDM1→
←ATG5
AIM1→
←RTN4IP1
106.4
106.6
106.8
107
Position on chr6 (Mb)

k. TAGAP

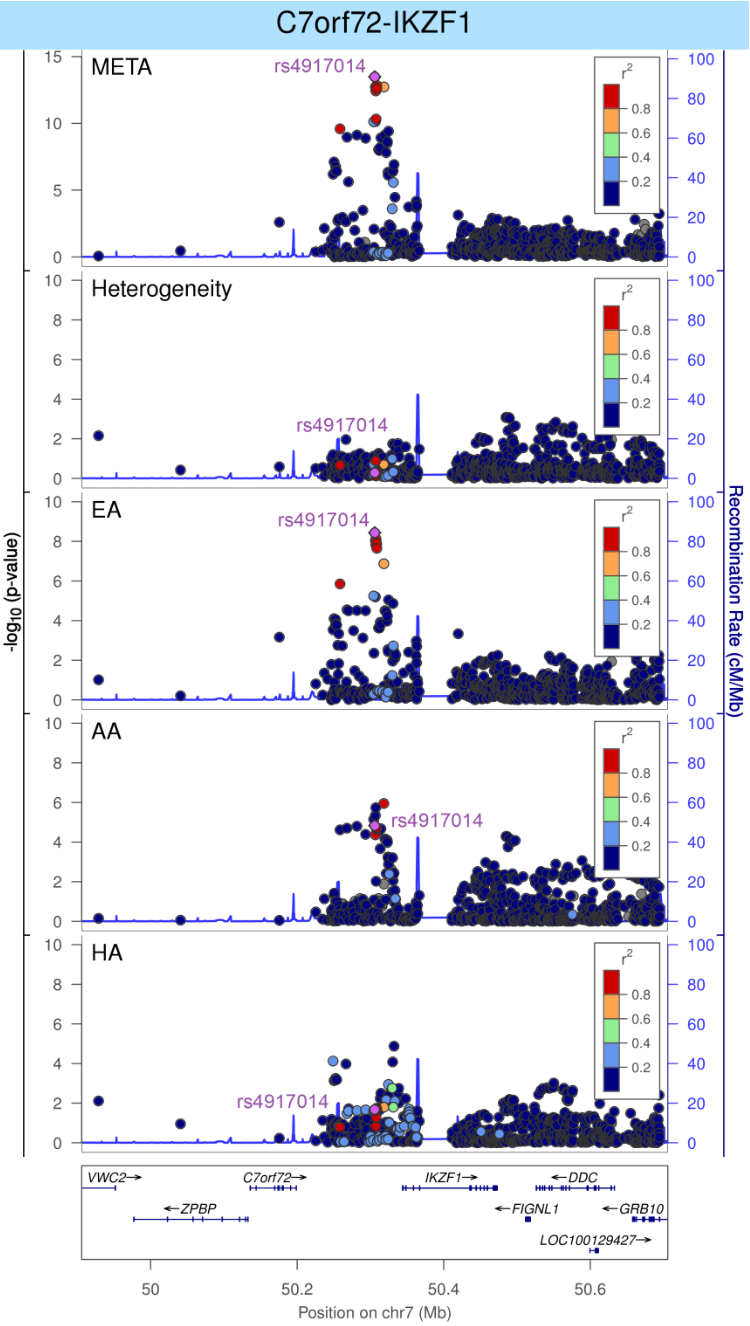


TAGAP
META
Heterogeneity
EA
AA
HA
eQTL
rs212407
RSPH3 | whole blood
TAGAP | whole blood; brain
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
SYTL3
OSTCP1
RSPH3
FNDC1
MIR3918
C6orf99
TAGAP
EZR
EZR-AS1
159.2
159.4
159.6
159.8
Position on chr6 (Mb)

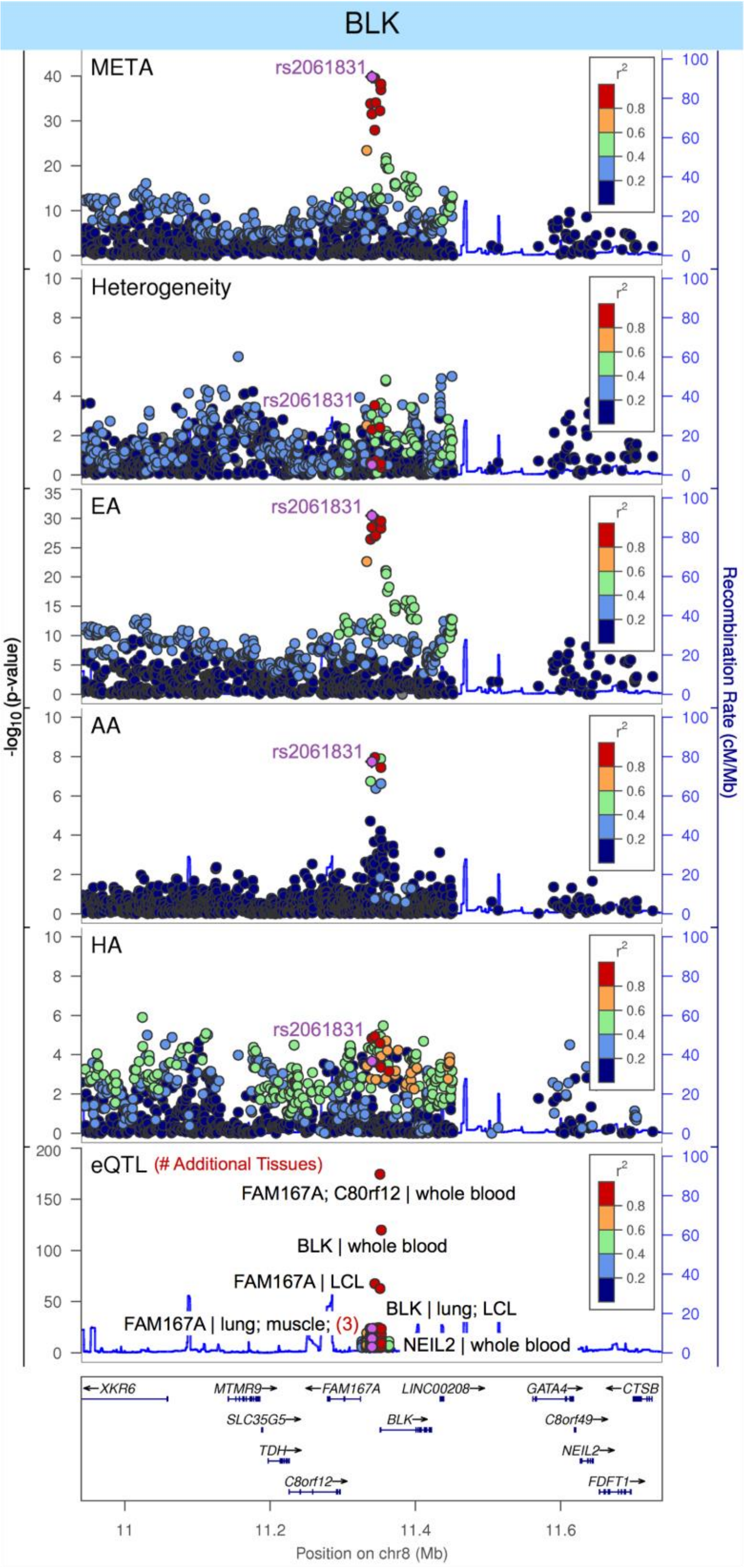
I. JAZF1


JAZF1
META
Heterogeneity
EA
AA
HA
eQTL
rs702814
JAZF1-AS1 | artery; colon; muscle
JAZF1 | muscle
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
TAX1BP1→
JAZF1-AS1→
CREB5→
←JAZF1
27.8
28
28.2
28.4
Position on chr7 (Mb)

m. C7orf72-IKZF1

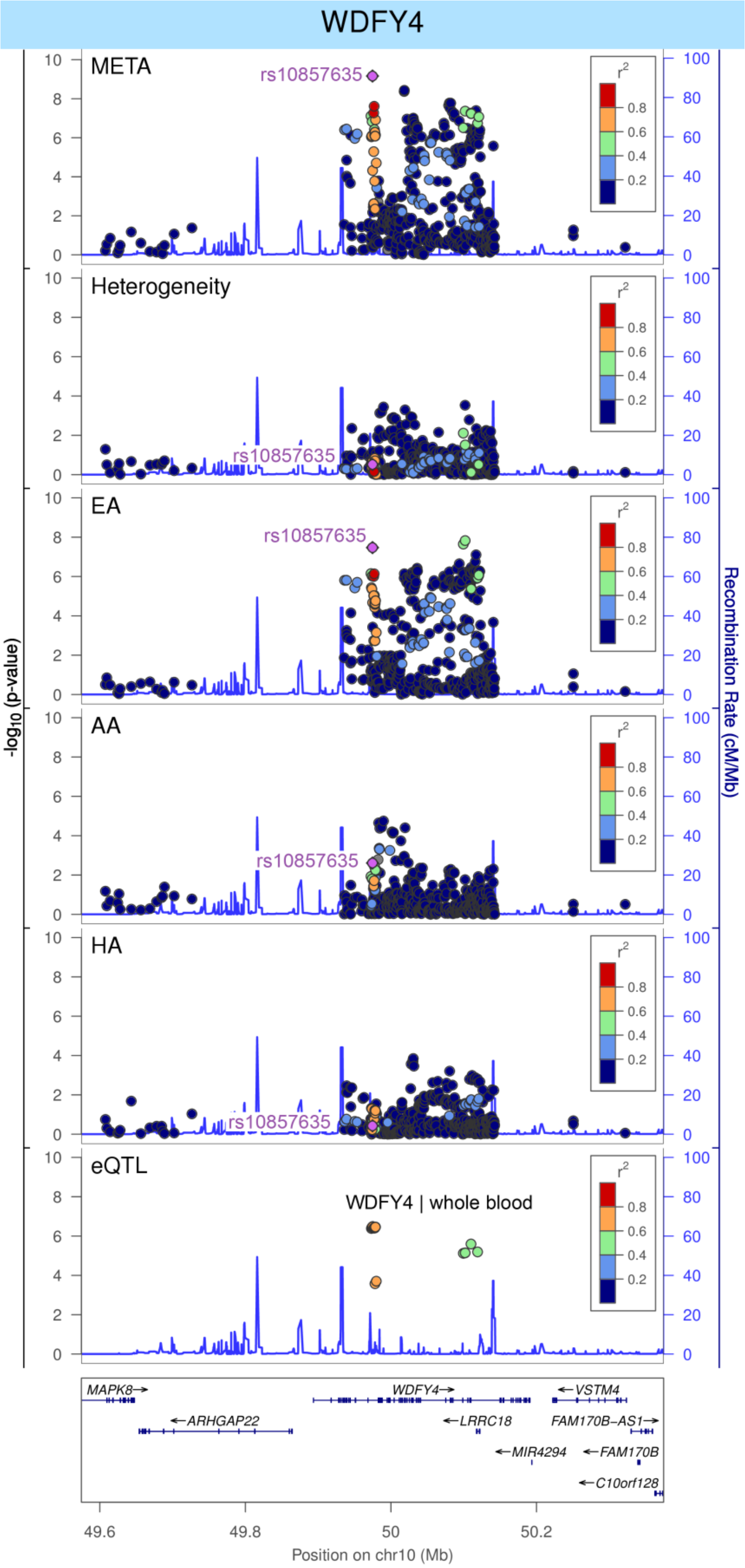


n. BLK

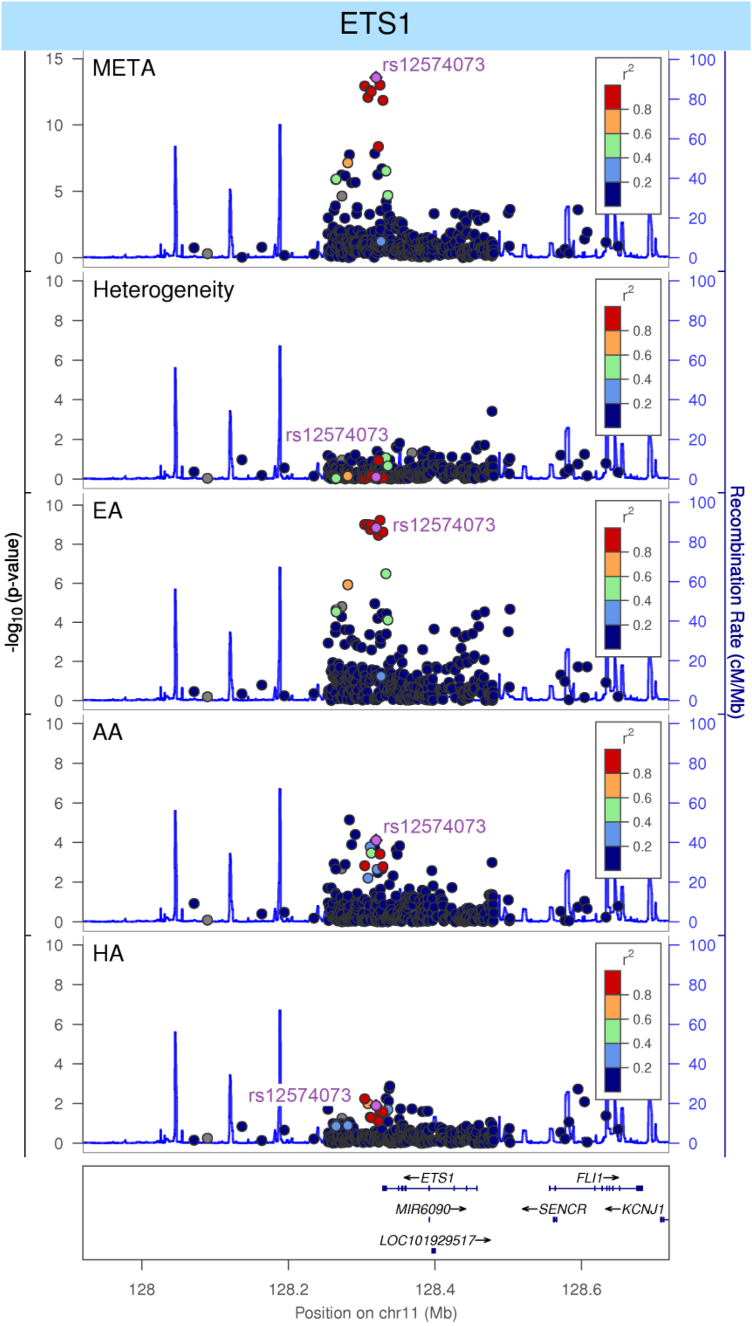


BLK
META
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
rs2061831
r²
0.8
0.6
0.4
0.2
-log$_{10}$ (p-value)
Recombination Rate (cM/Mb)
FAM167A; C80rf12 | whole blood
BLK | whole blood
FAM167A | LCL
BLK | lung; LCL
FAM167A | lung; muscle; (3)
NEIL2 | whole blood
←XKR6
MTMR9→
←FAM167A
LINC00208→
GATA4→
←CTSB
SLC35G5→
BLK→
C8orf49→
TDH→
NEIL2→
C8orf12→
FDFT1→
11
11.2
11.4
11.6
Position on chr8 (Mb)

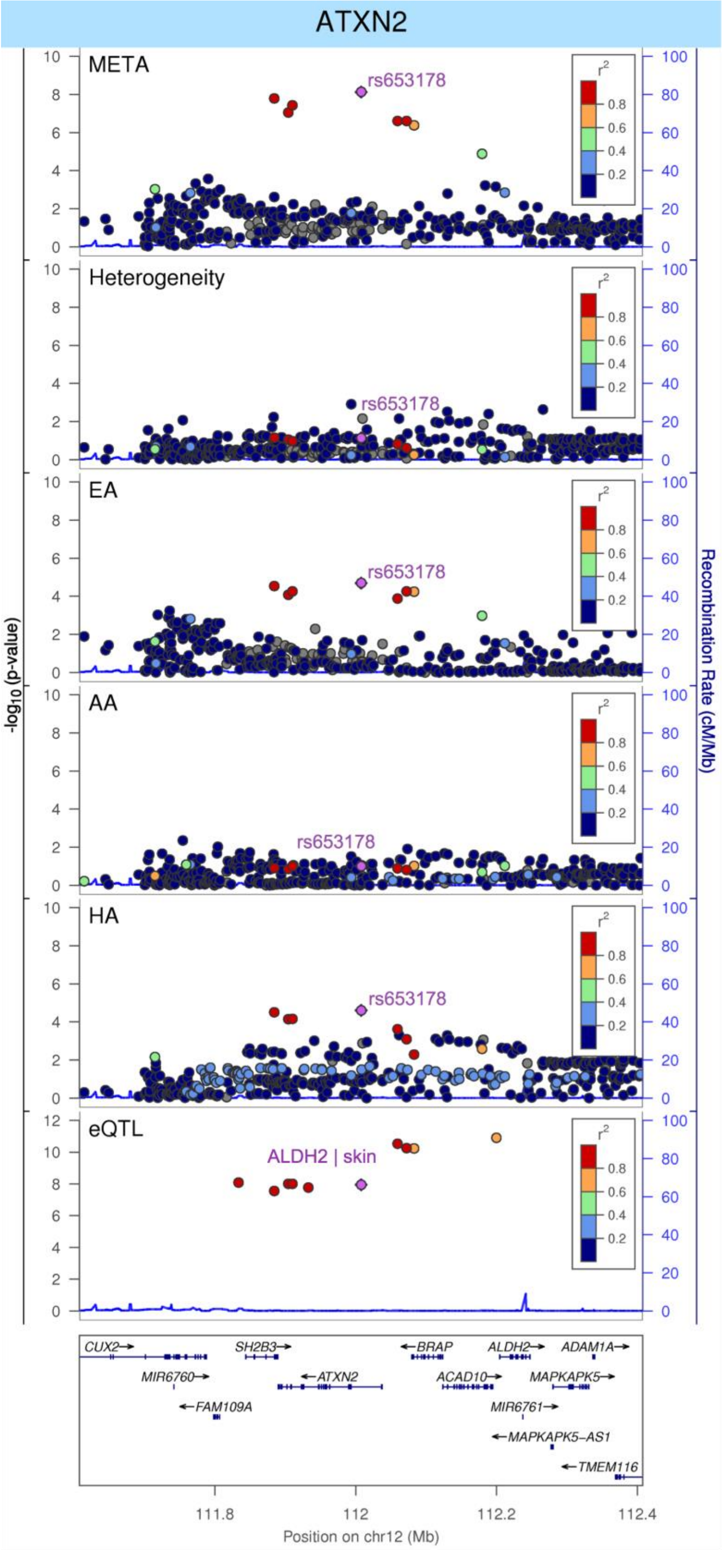
o. WDFY4


WDFY4
META
rs10857635
Heterogeneity
EA
AA
HA
eQTL
WDFY4 | whole blood
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
MAPK8
ARHGAP22
WDFY4
LRRC18
MIR4294
VSTM4
FAM170B-AS1
FAM170B
C10orf128
49.6
49.8
50
50.2
Position on chr10 (Mb)

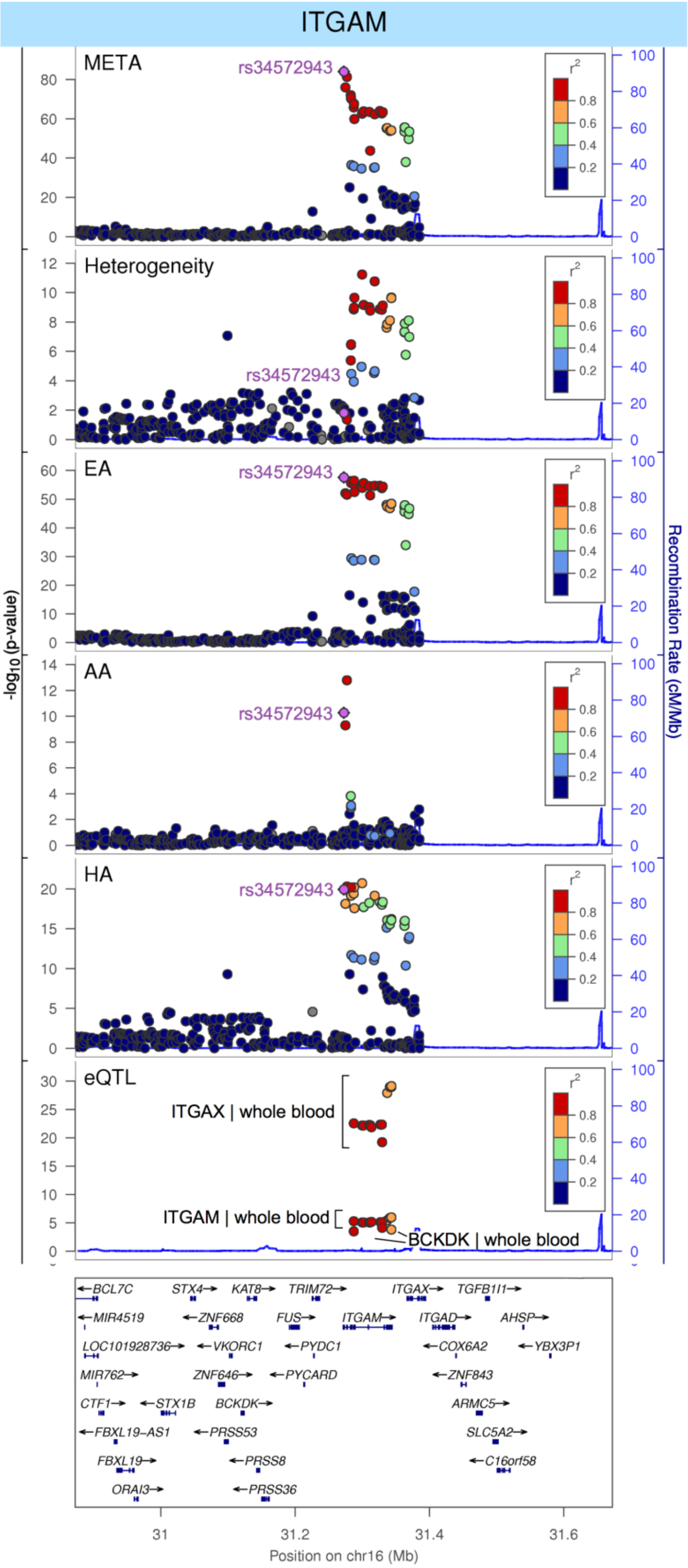
p. ETS1


ETS1
META
Heterogeneity
EA
AA
HA
rs12574073
-log10 (p-value)
Recombination Rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
15
10
5
0
8
6
4
2
100
80
60
40
20
ETS1
MIR6090
LOC101929517
FLI1
SENCR
KCNJ1
128
128.2
128.4
128.6
Position on chr11 (Mb)

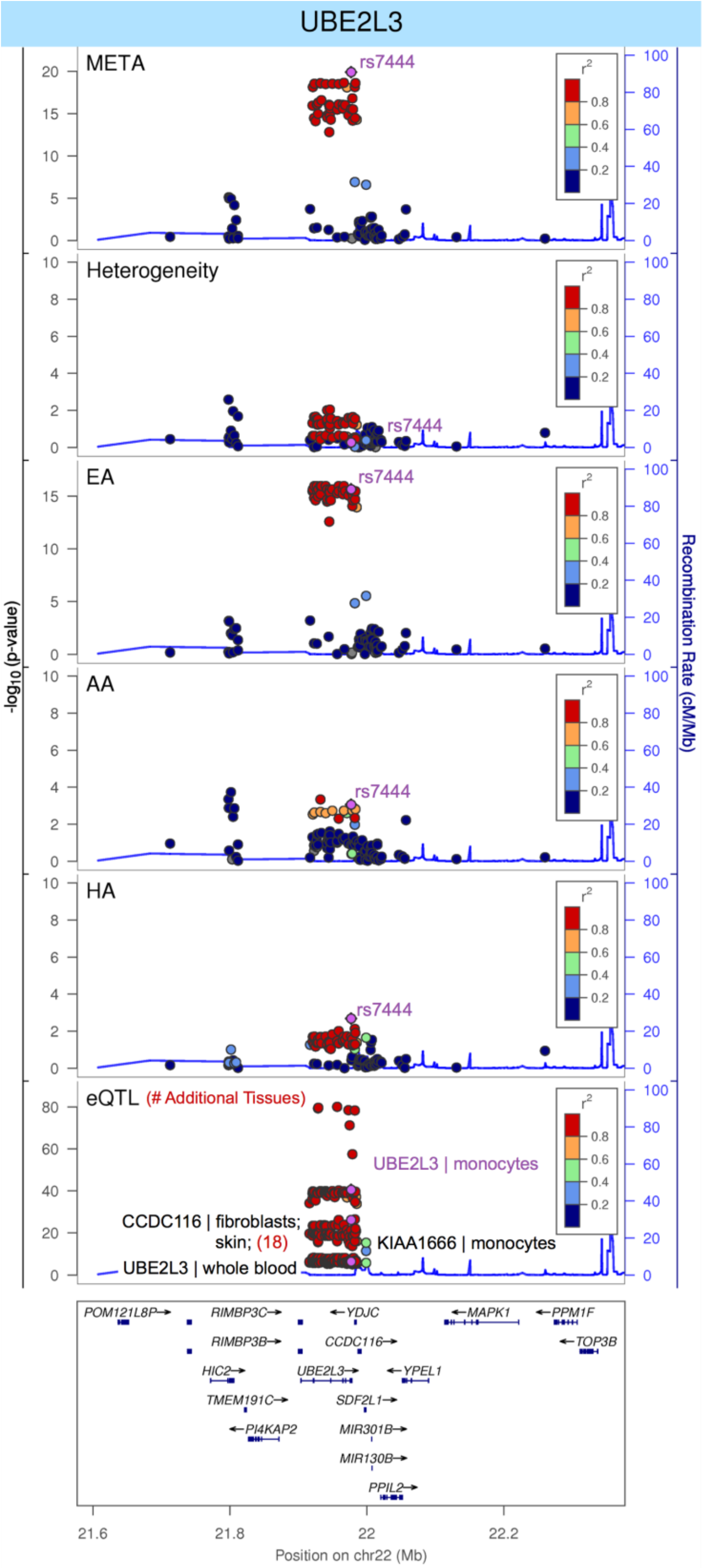
q. ATXN2


ATXN2
META
Heterogeneity
EA
AA
HA
eQTL
rs653178
ALDH2 | skin
r²
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
CUX2→
SH2B3→
←BRAP
ALDH2→
ADAM1A→
MIR6760→
←ATXN2
ACAD10→
MAPKAPK5→
←FAM109A
MIR6761→
←MAPKAPK5-AS1
←TMEM116
111.8
112
112.2
112.4
Position on chr12 (Mb)

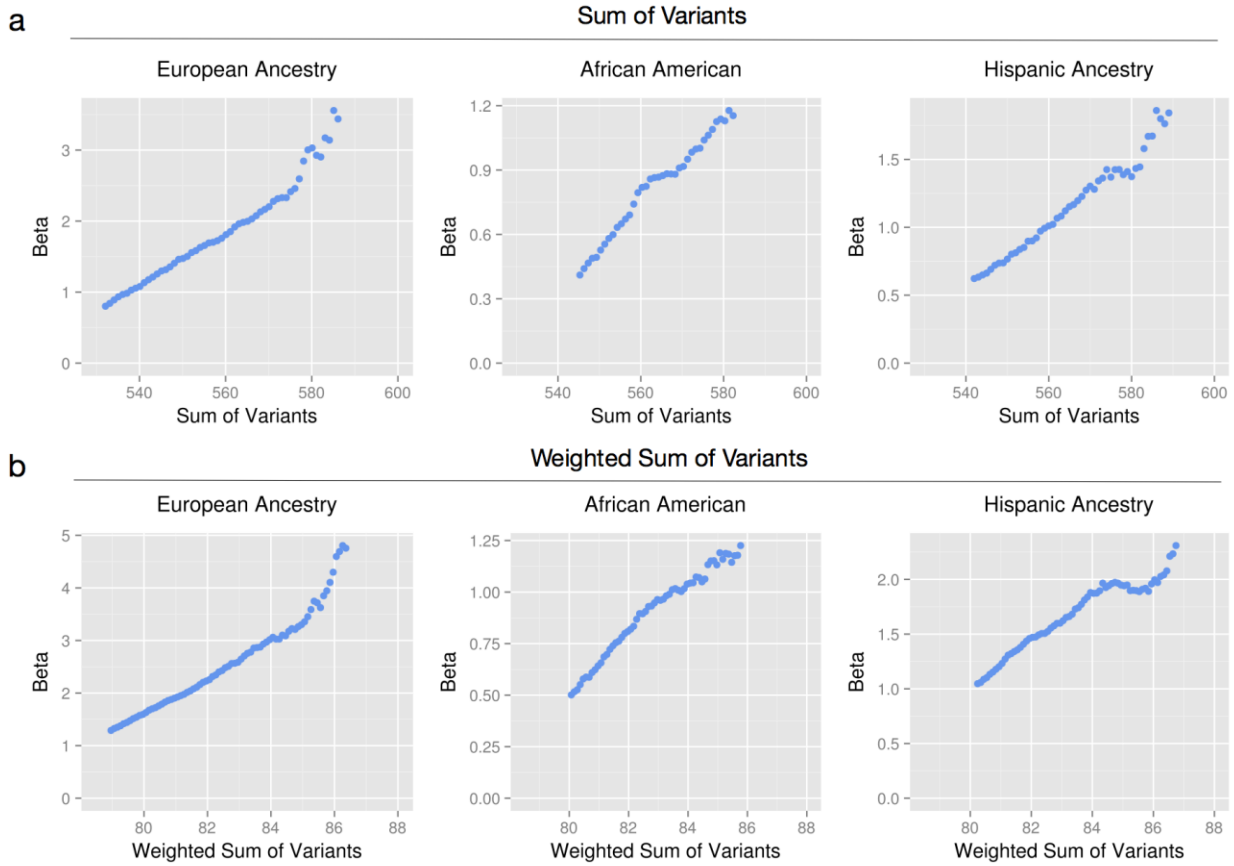
r. ITGAM


ITGAM
META
Heterogeneity
EA
AA
HA
eQTL
rs34572943
ITGAX | whole blood
ITGAM | whole blood
BCKDK | whole blood
-log10(p-value)
Recombination Rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
BCL7C
STX4
KAT8
TRIM72
ITGAX
TGFB1I1
MIR4519
ZNF668
FUS
ITGAM
ITGAD
AHSP
LOC101928736
VKORC1
PYDC1
COX6A2
YBX3P1
MIR762
ZNF646
PYCARD
ZNF843
CTF1
STX1B
BCKDK
ARMC5
FBXL19-AS1
PRSS53
SLC5A2
FBXL19
PRSS8
C16orf58
ORAI3
PRSS36
31
31.2
31.4
31.6
Position on chr16 (Mb)

s. UBE2L3


UBE2L3
META
rs7444
Heterogeneity
EA
AA
HA
eQTL (# Additional Tissues)
UBE2L3 | monocytes
CCDC116 | fibroblasts; skin; (18)
KIAA1666 | monocytes
UBE2L3 | whole blood
r2
0.8
0.6
0.4
0.2
-log10 (p-value)
Recombination Rate (cM/Mb)
POM121L8P
RIMBP3C
YDJC
MAPK1
PPM1F
RIMBP3B
CCDC116
TOP3B
HIC2
UBE2L3
YPEL1
TMEM191C
SDF2L1
PI4KAP2
MIR301B
MIR130B
PPIL2
21.6
21.8
22
22.2
Position on chr22 (Mb)

Supplementary Figure 17. The non-additive effect of EA risk-allele genetic load on SLE risk (beta values). Plots of the beta (natural logarithm of the odds ratio), instead of the odds ratios, as found in **Figure 5**.



Supplementary Figure 18. Kaplan-Meier curve for age at SLE diagnosis.