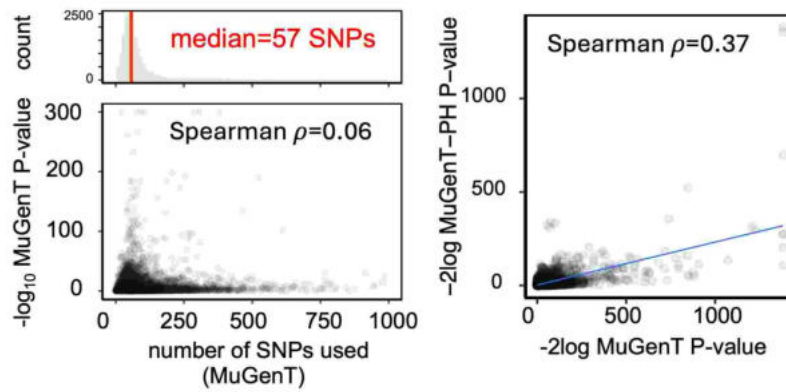**Figure S1: Summary metrics of MuGenT and MuGenT-PH performance with T2D**

Summary statistics from MuGenT testing of T2D. The top left panel displays the distribution of the number of SNPs used in MuGenT testing and their median, 57. The bottom left panel displays the association between the number of SNPs used in MuGenT and the MuGenT P-value. The right panel displays the association between transformed MuenT P-values and MuGenT-PH P-values.

Figure S2: Replication of Suzuki et al. (2024) T2D-associated genes

MuGenT, MuGenT-PH, and GenT P-values are displayed in each square. The selected genes are the top associated genes from T2D association testing from Suzuki et al. (2024).

Figure S3: Demonstration of mixture deconvolution of MuGenT-Sel
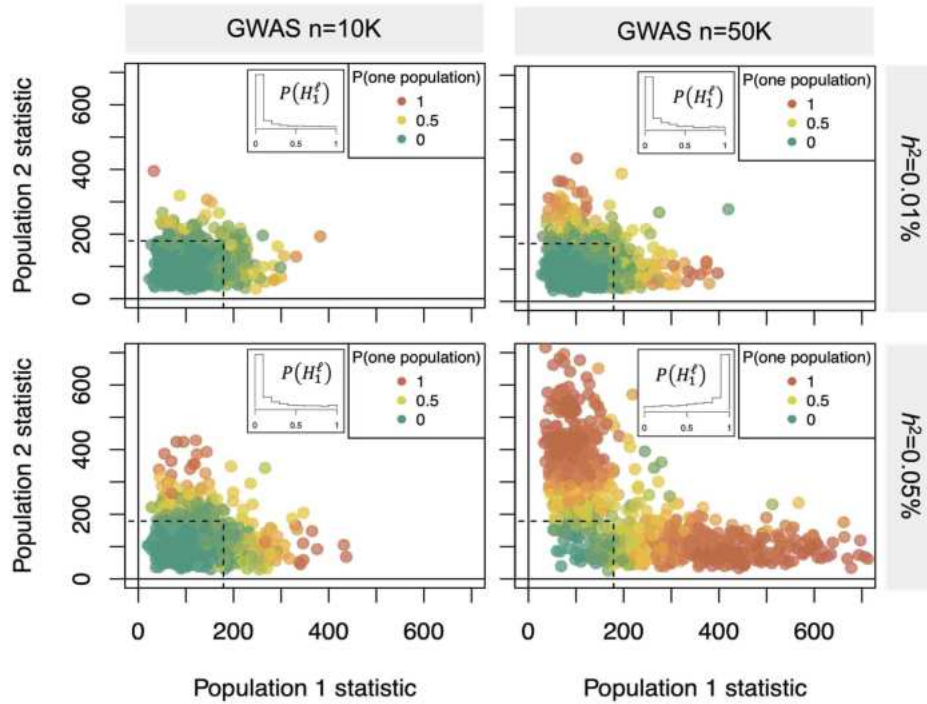
Demonstration of how MuGenT-Sel performs inference using simulation. Scatterplots display GenT statistics for multiple simulated genes and two traits, with fixed heritability explained by the gene annotated on right panel of the plot and the GWAS sample size annotated on the top panel. Histograms embedded within the plots display the distribution of MuGenT-Sel posterior probabilities. Full code to reproduce these results is available at
https://github.com/noahlorinczcomi/gent_analysis/tree/main/simulations/mugent_sel.

**Figure S4: Top AD genes detected using xGenT with brain eQTLs by chromosome**
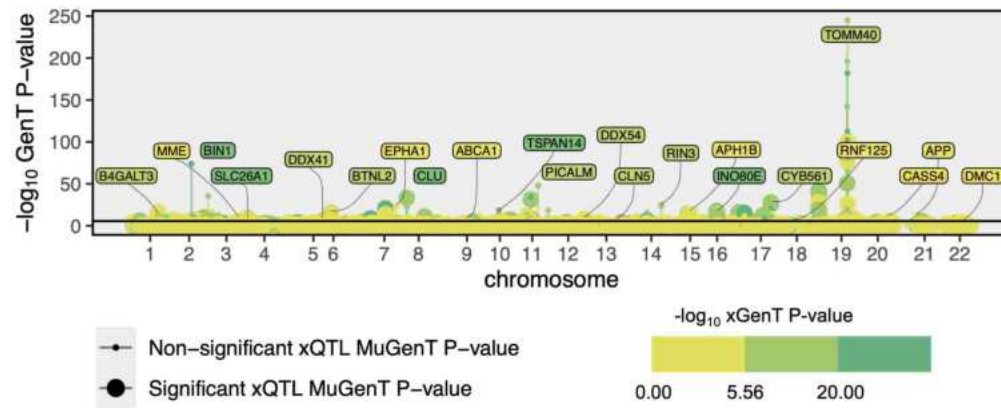
Manhattan plot of GenT P-values for association with AD. Colors represent the level of significance of testing with brain eQTLs and xGenT, and sizes represent the state of significance of MuGenT testing across the multiple brain eQTL types (see Methods in main text).

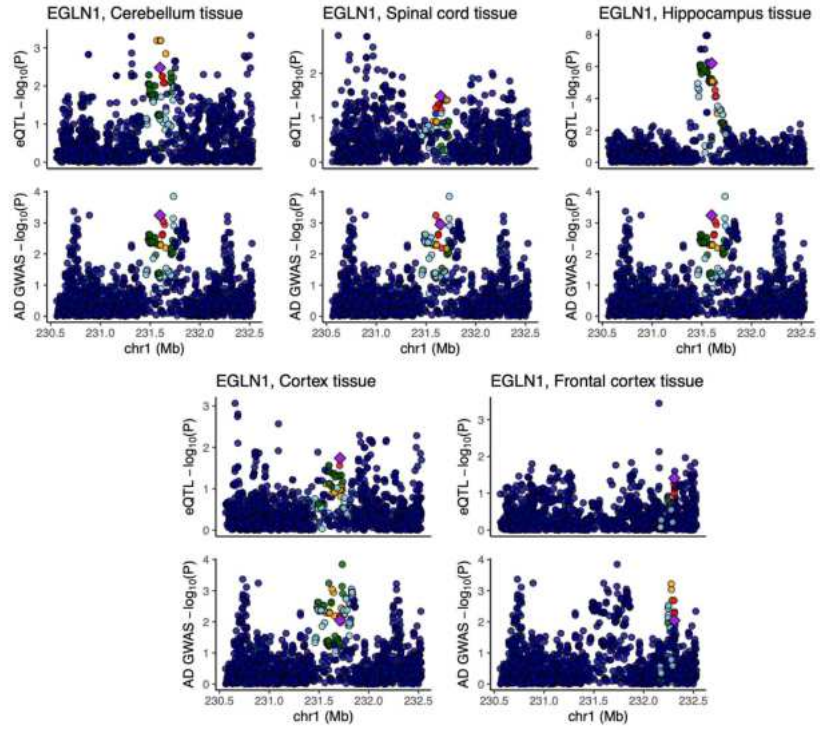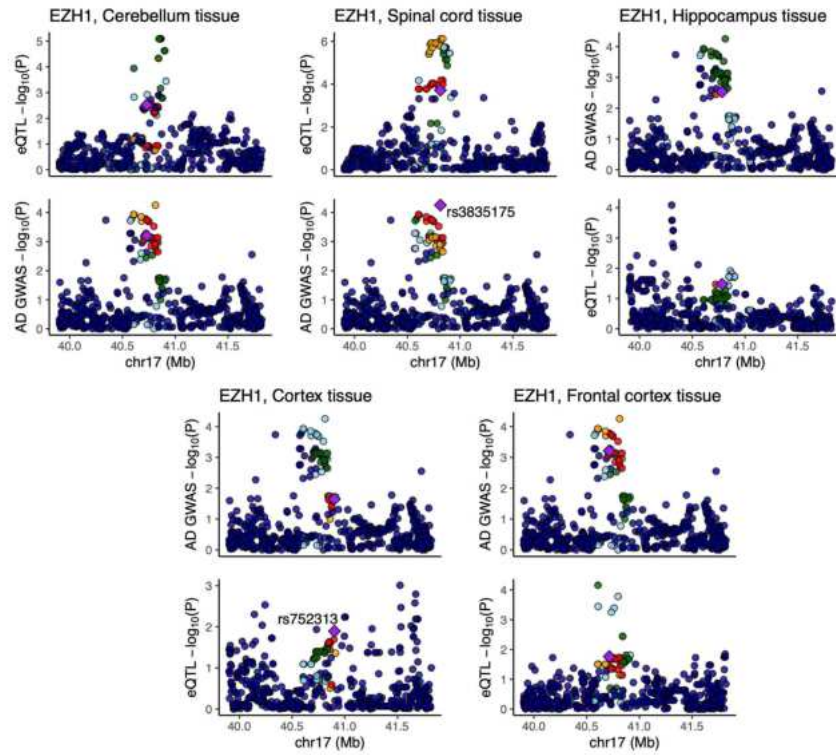## Figure S5: DNMT3B AD GWAS and brain tissue eQTL locus comparison
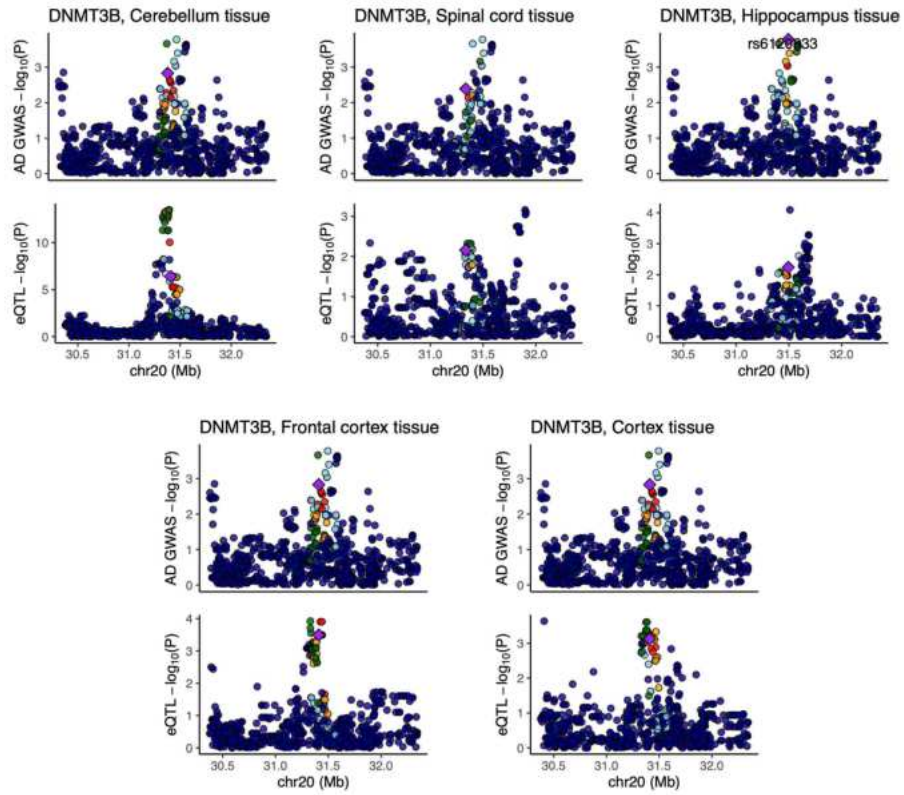
Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

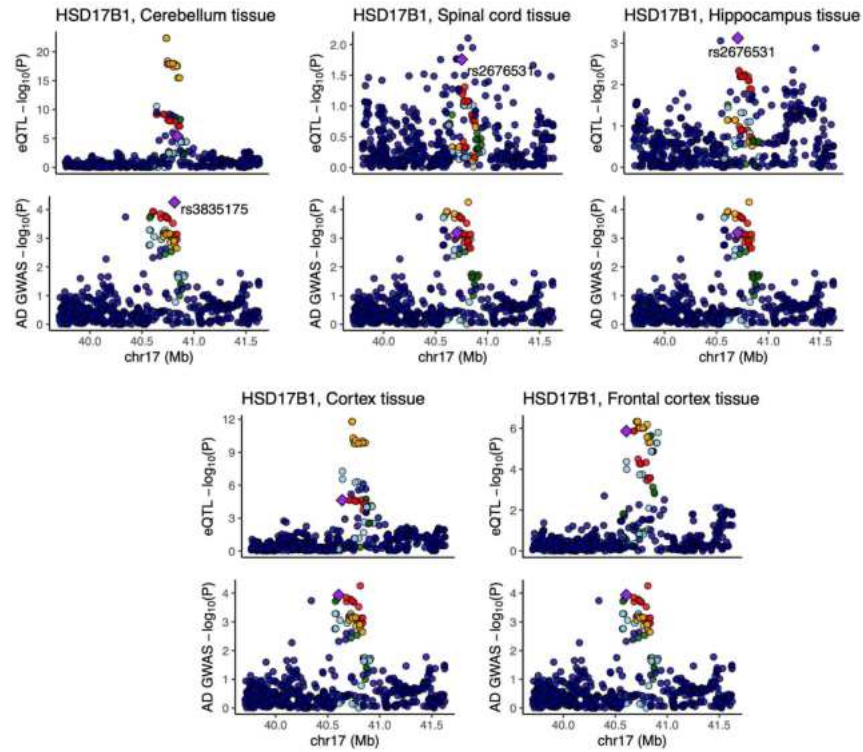**Figure S6: DSTYK AD GWAS and brain tissue eQTL locus comparison**
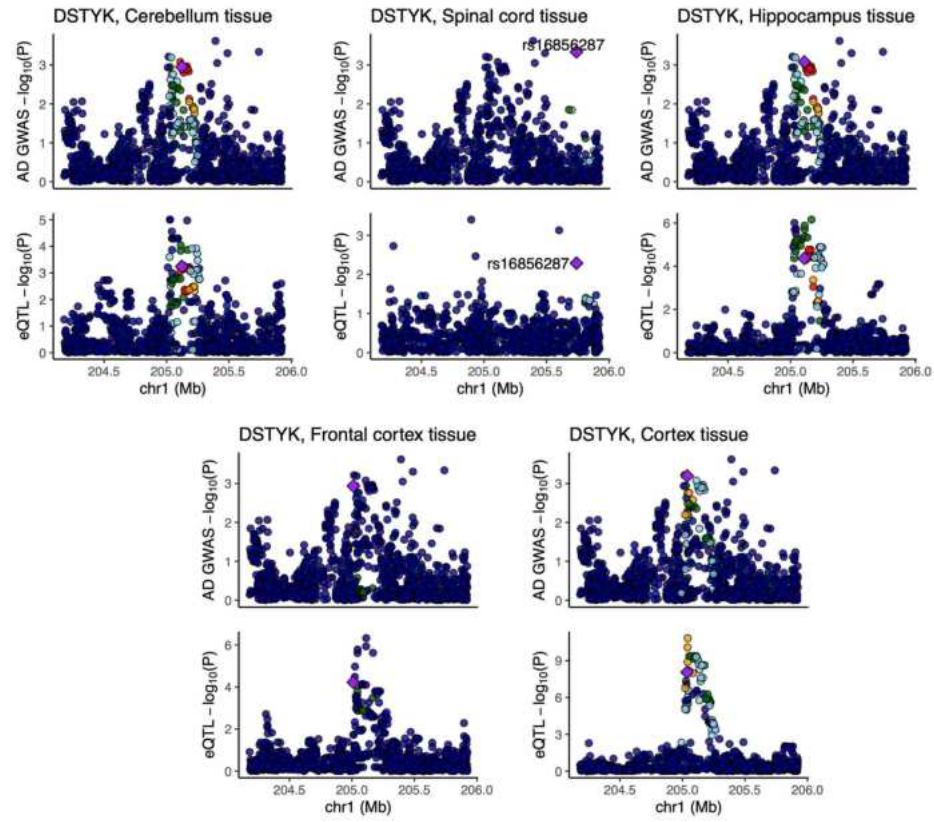
Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

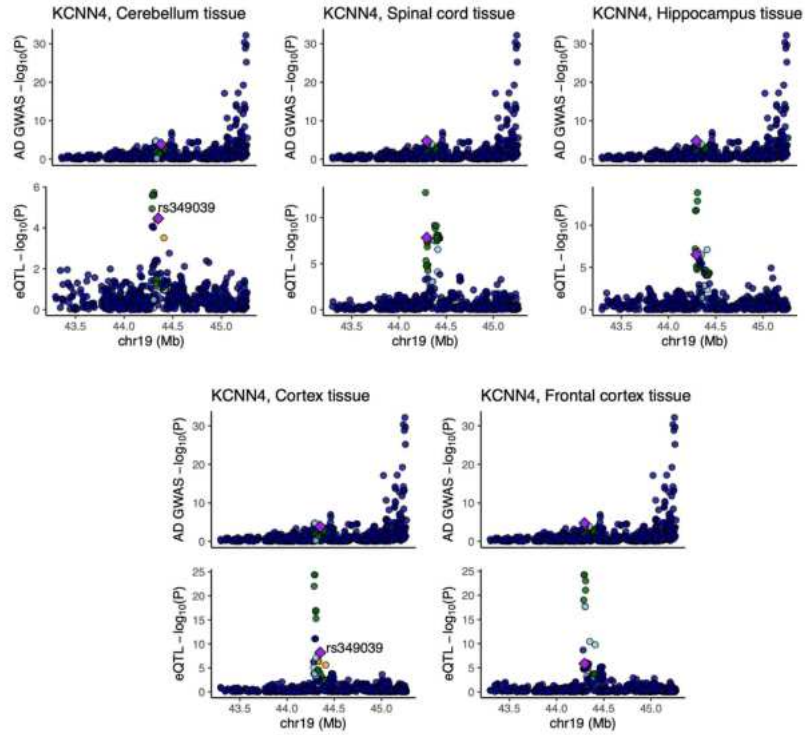**Figure S7: EGLN1 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

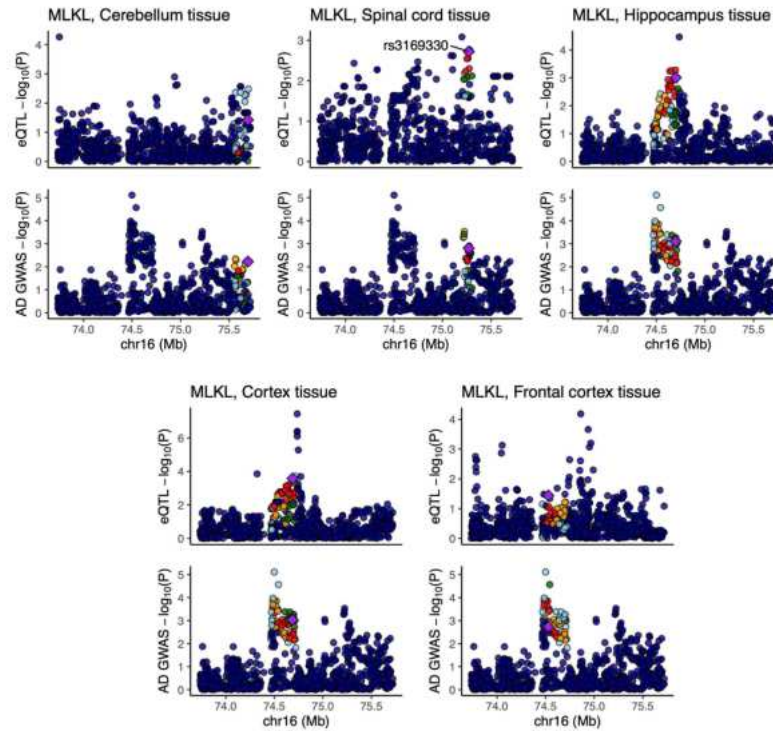**Figure S8: EZH1 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.
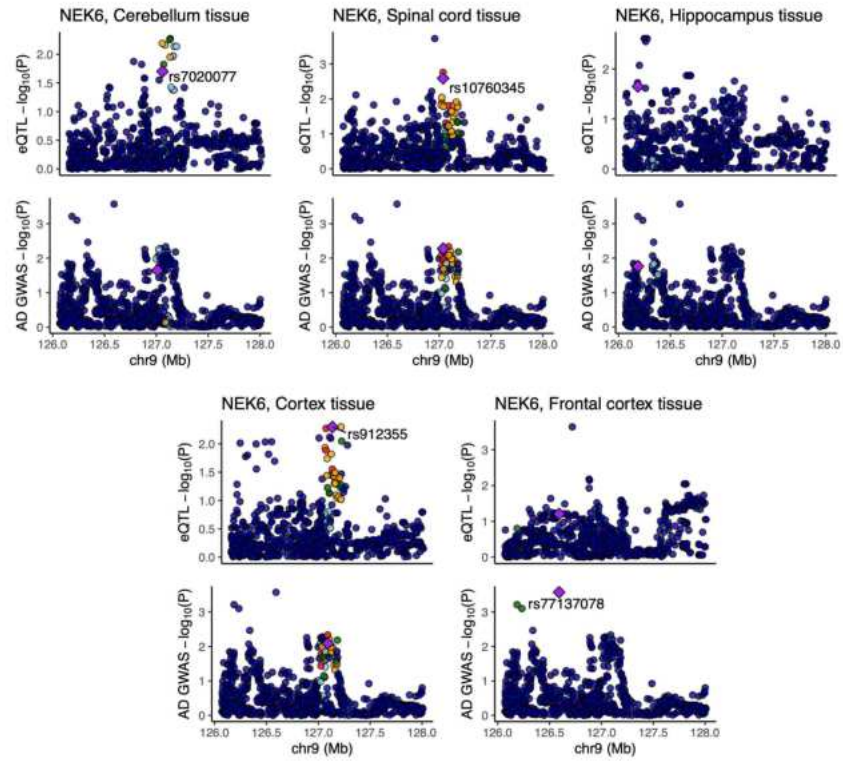
Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

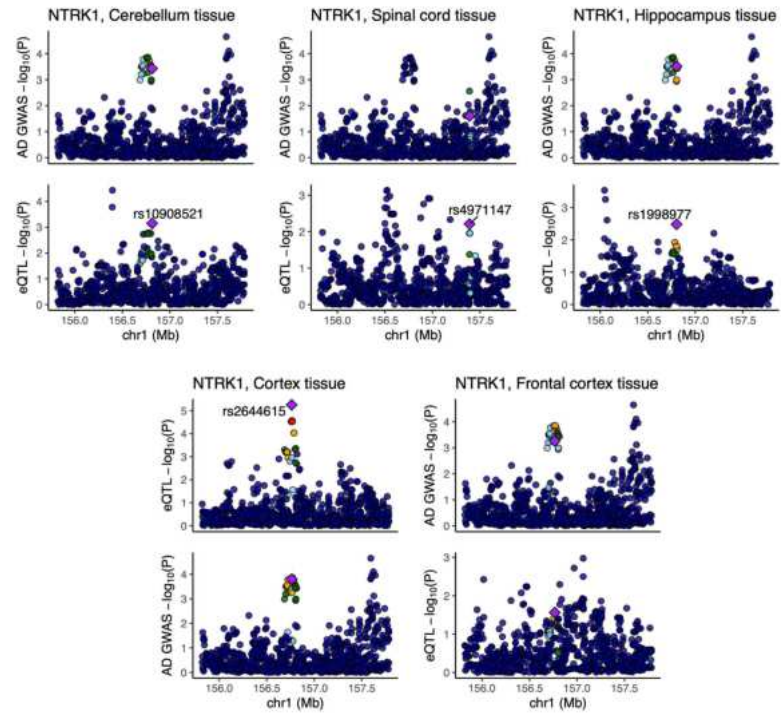**Figure S10: KCNN4 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

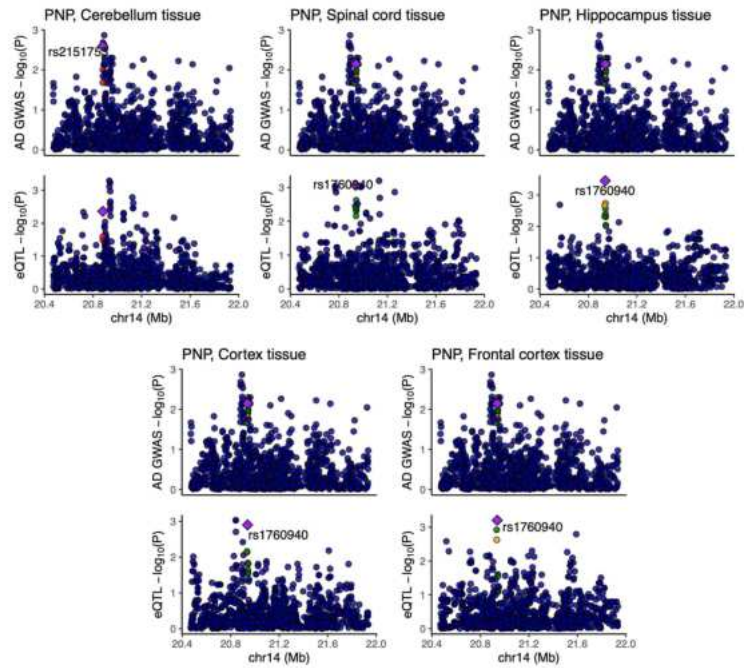**Figure S11: MLKL AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

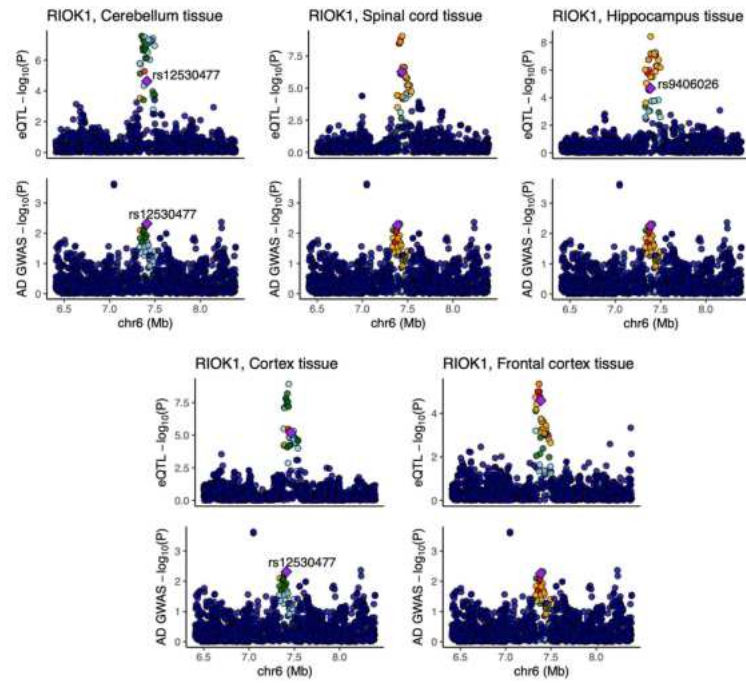**Figure S12: NEK6 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

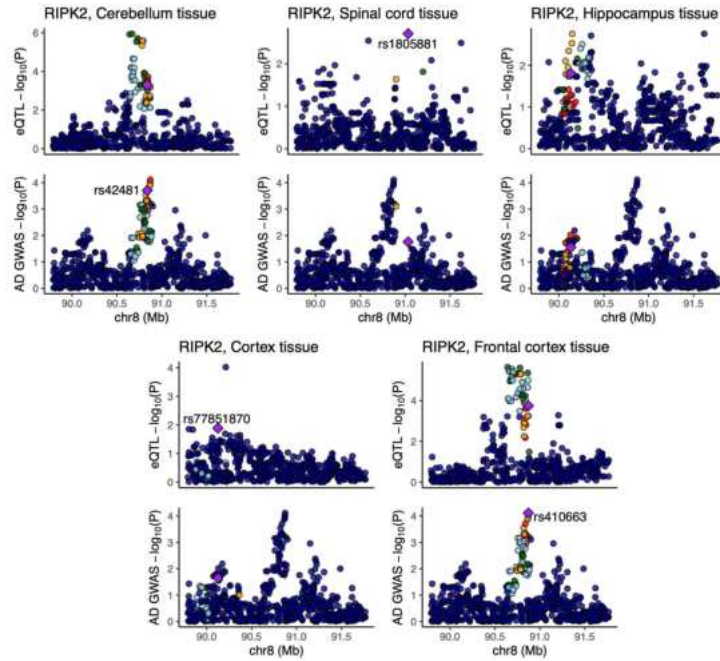**Figure S13: NTRK1 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

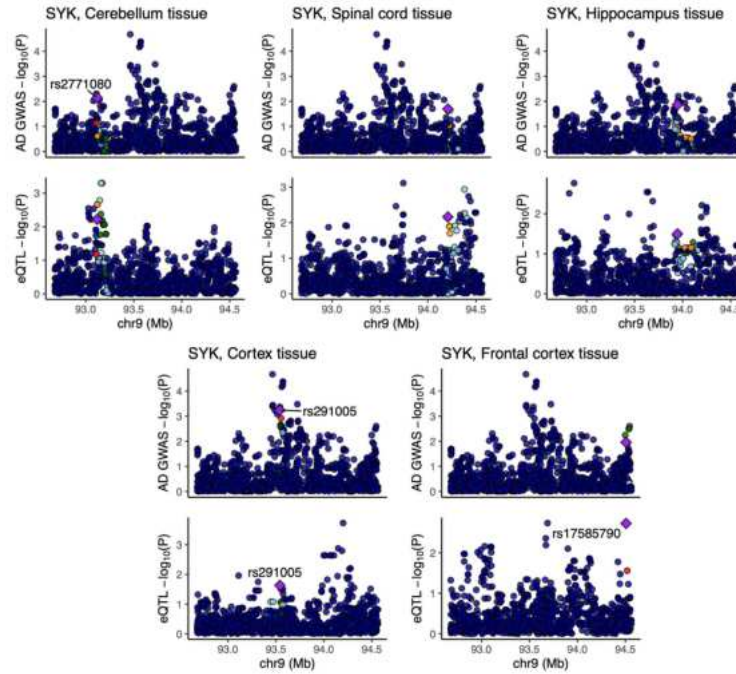**Figure S14: PNP AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

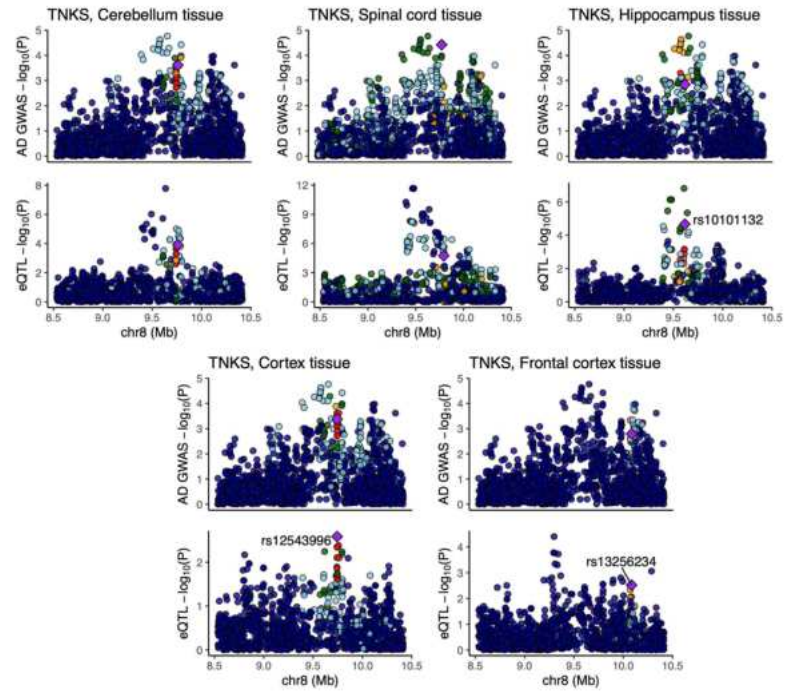**Figure S15: RIOK1 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

**Figure S16: RIPK2 AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

**Figure S17: SYK AD GWAS and brain tissue eQTL locus comparison**

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

Figure S18: TNKS AD GWAS and brain tissue eQTL locus comparison

Locus-specific plots of SNP P-values and their eQTL/AD GWAS P-values. Colors represent strength of absolute LD with the SNP with the smallest joint P-value (purple diamond). Red indicates stronger LD; blue indicates weaker LD.

Figure S19: BMPR1B genetic correlations across eQTL tissues and disease phenotypes
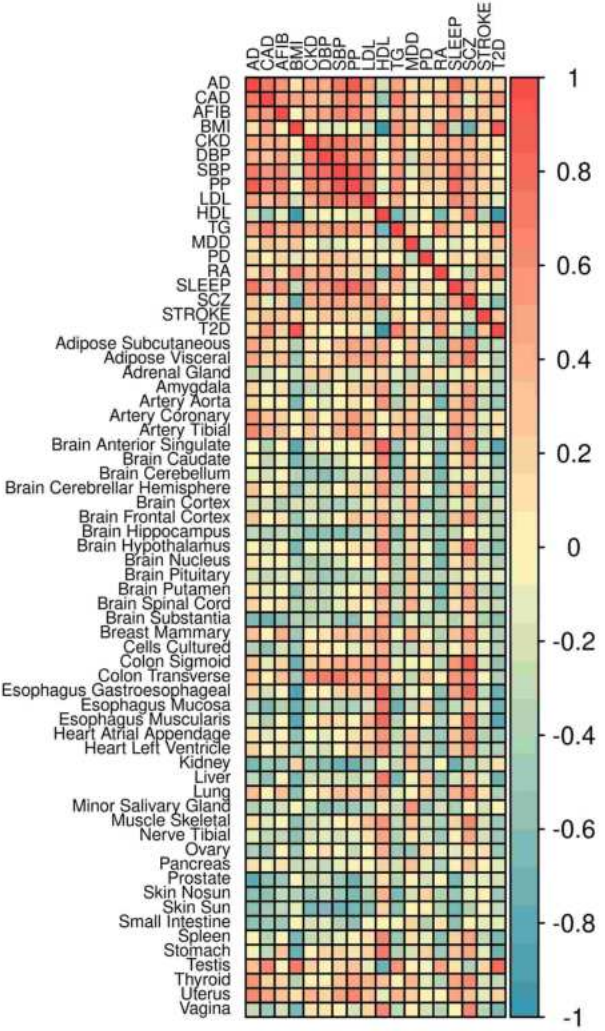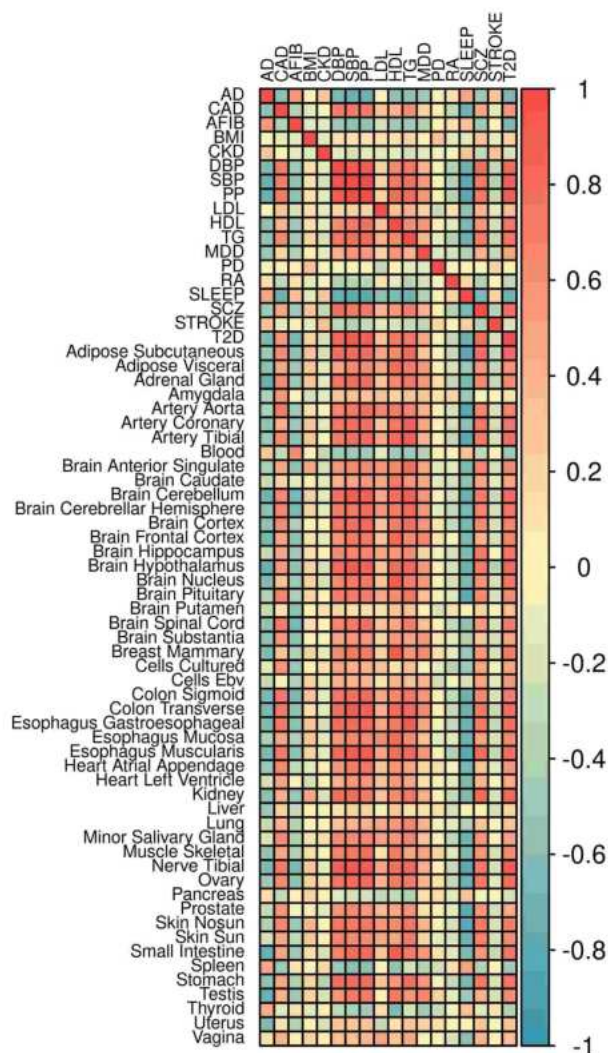

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

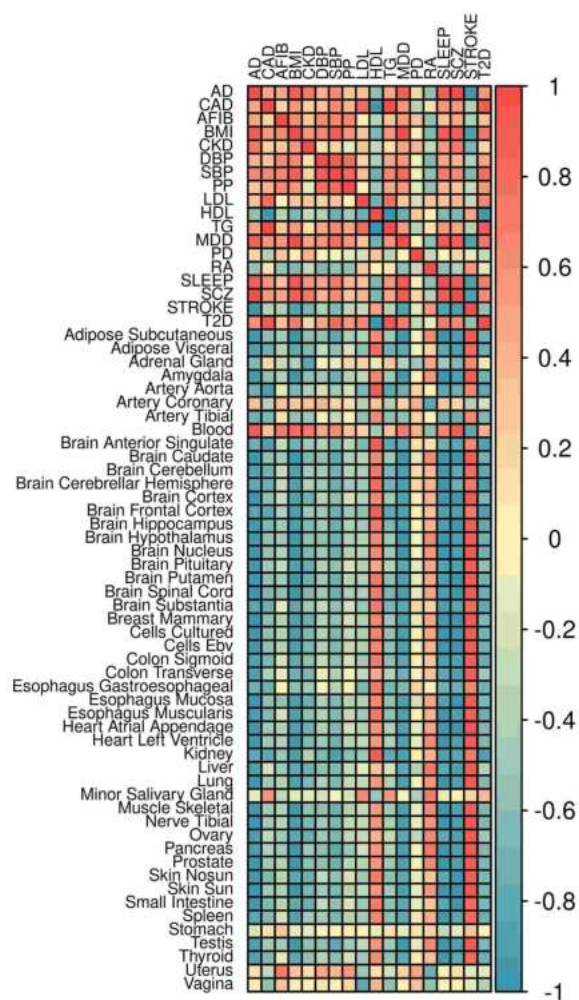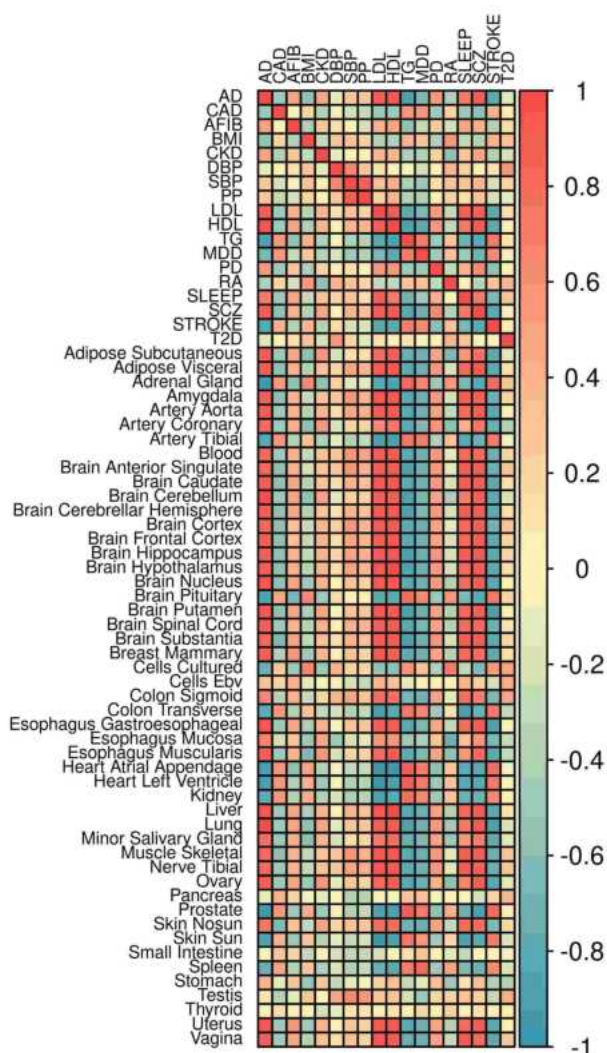# Figure S20: CHRM5 genetic correlations across eQTL tissues and disease phenotypes
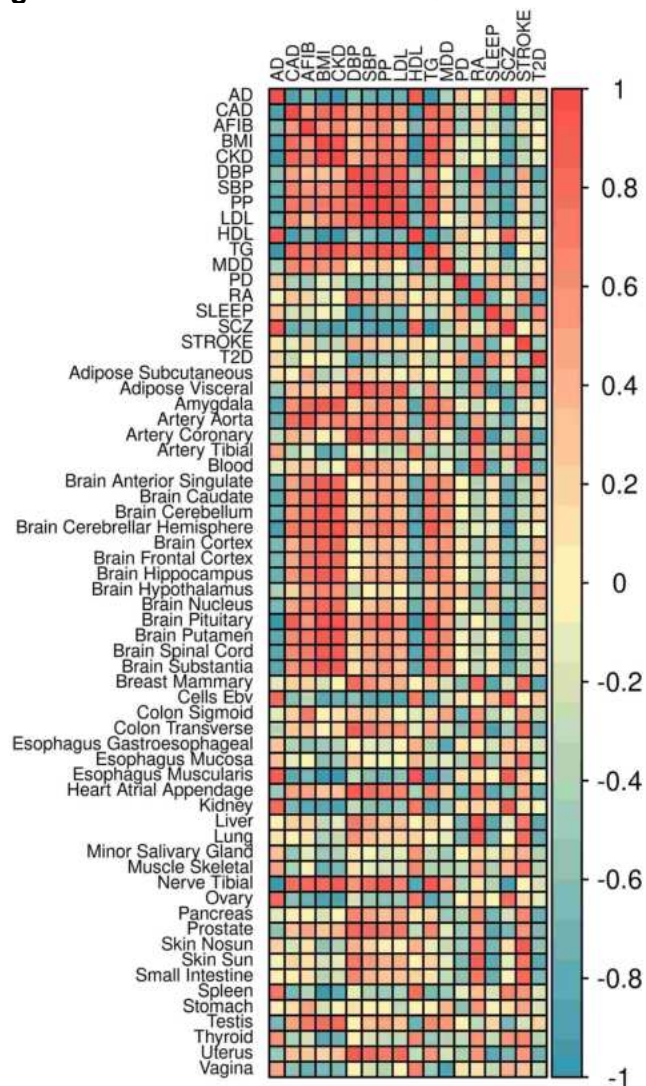
Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

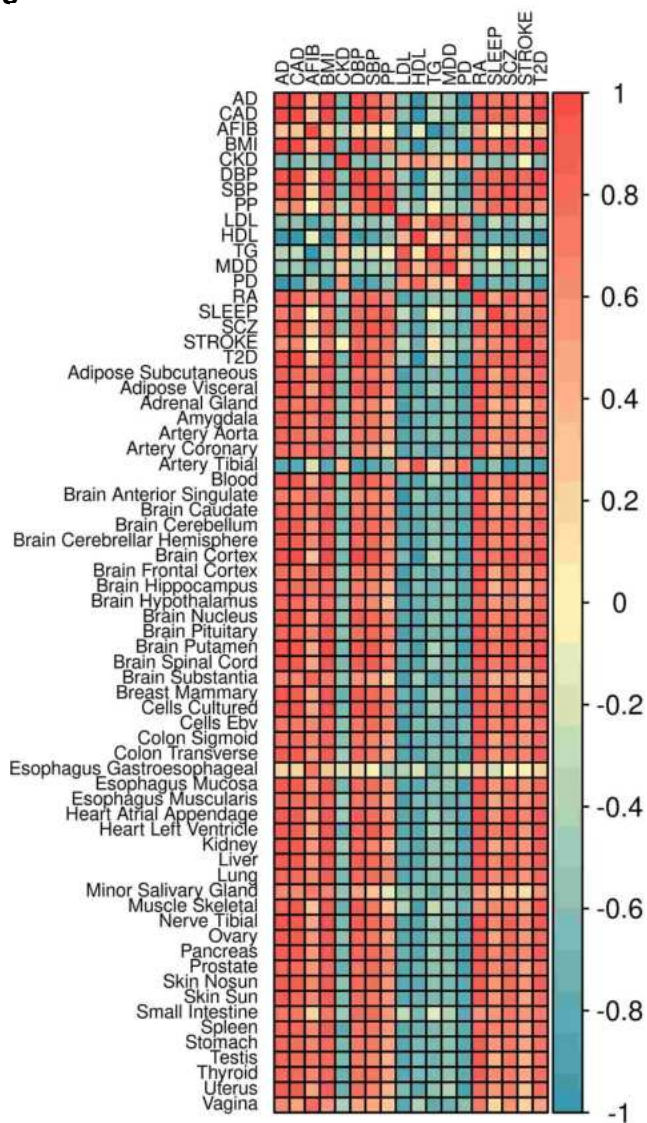# Figure S21: DNMT3B genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

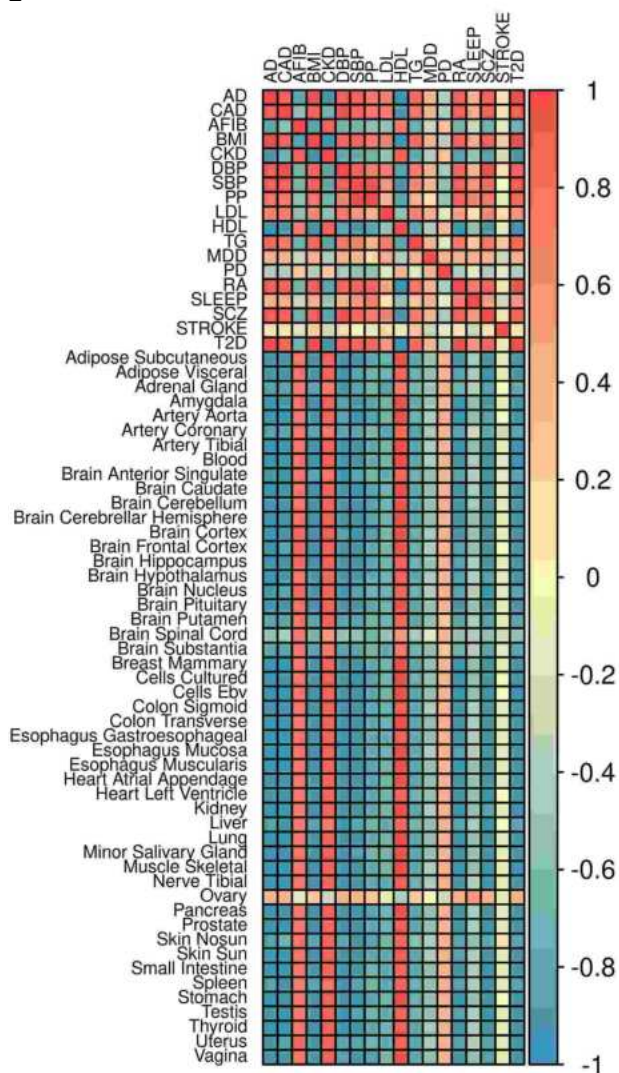# Figure S22: DSTYK genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

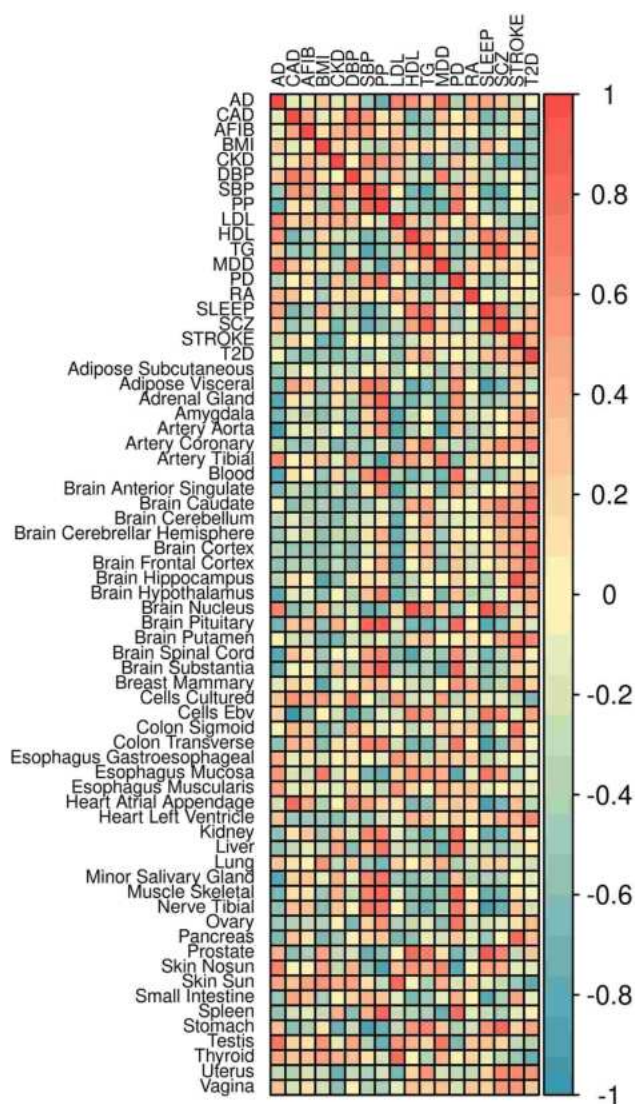## Figure S23: EGLN1 genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

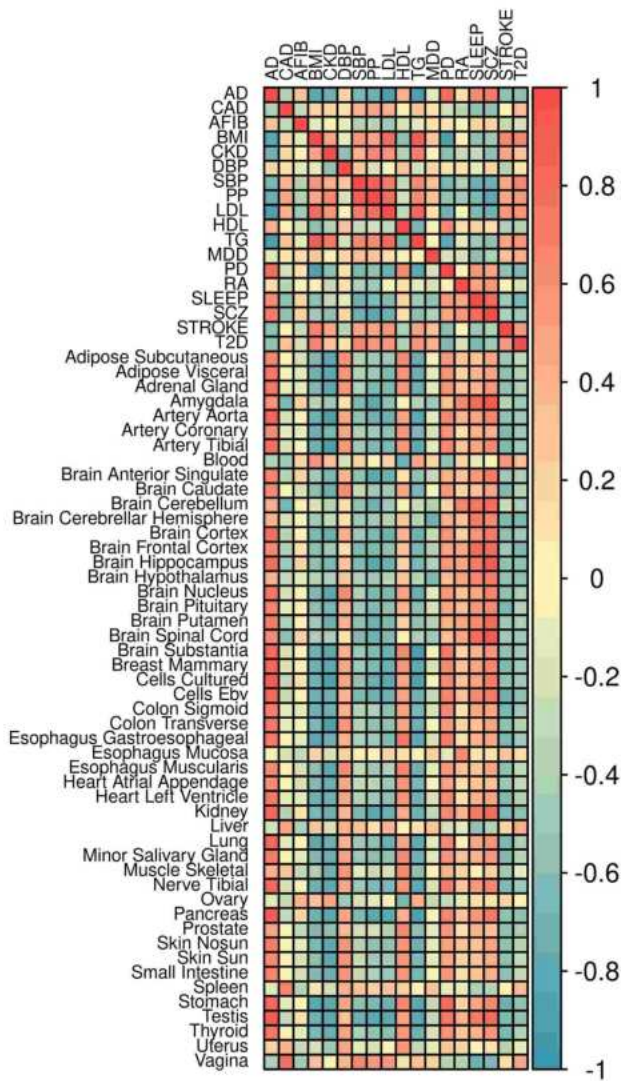# Figure S24: EZH1 genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S25: HSD17B1 genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

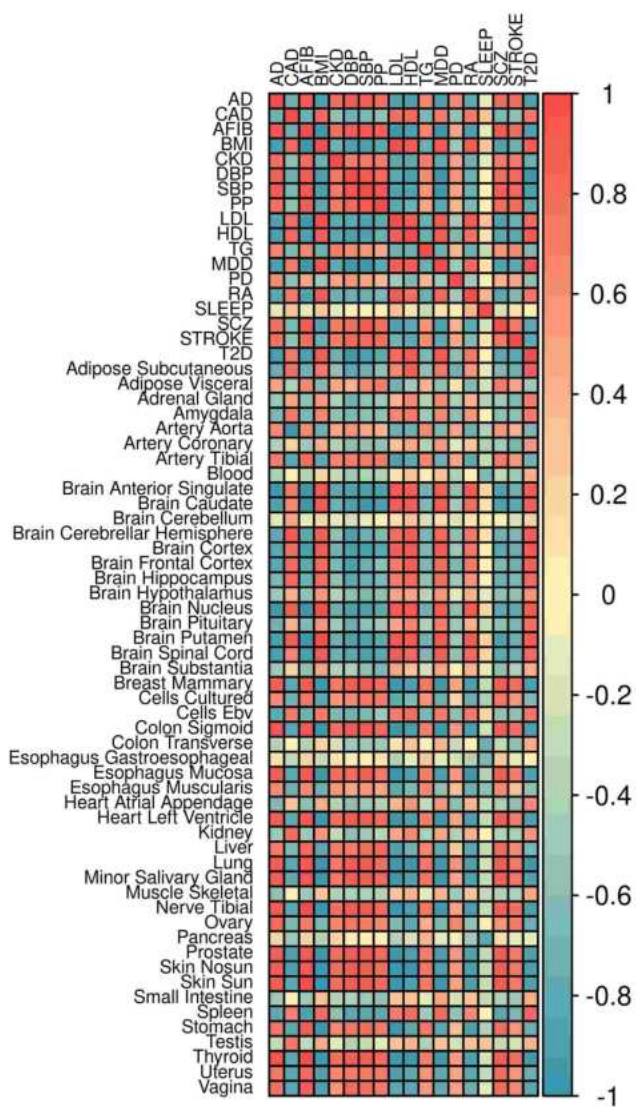# Figure S26: KCNN4 genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

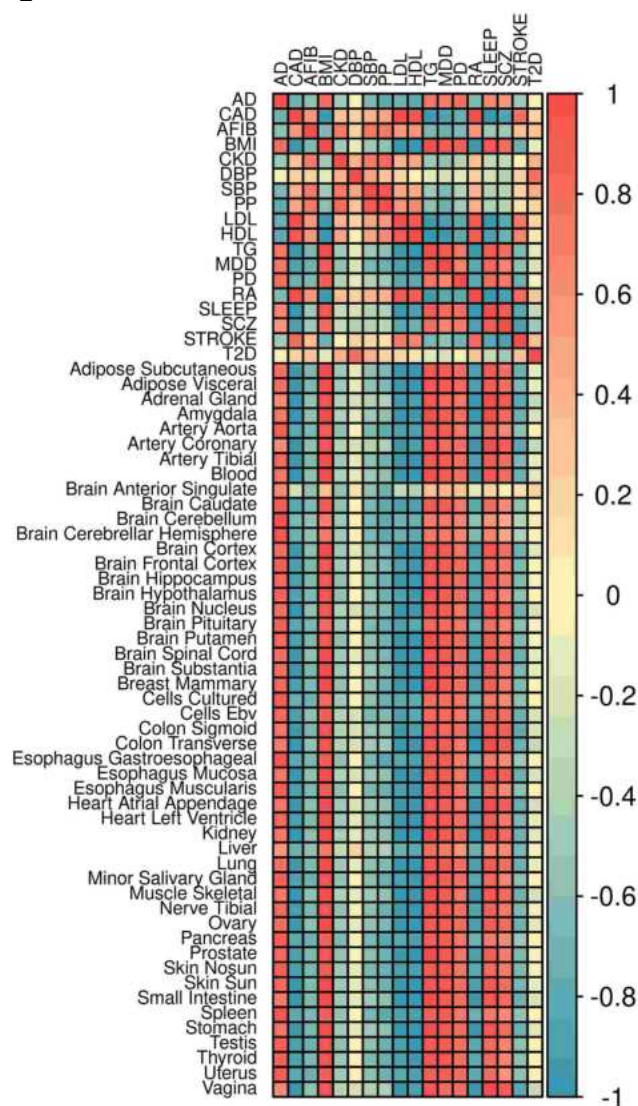**Figure S27: MLKL genetic correlations across eQTL tissues and disease phenotypes**

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

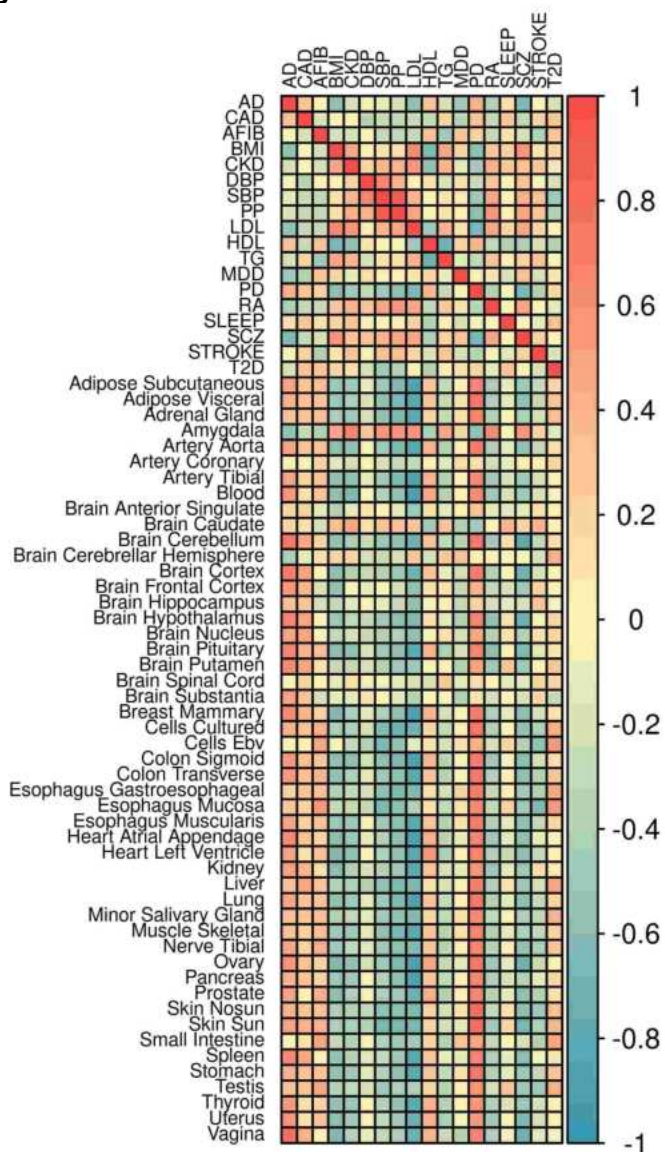# Figure S28: NEK6 genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

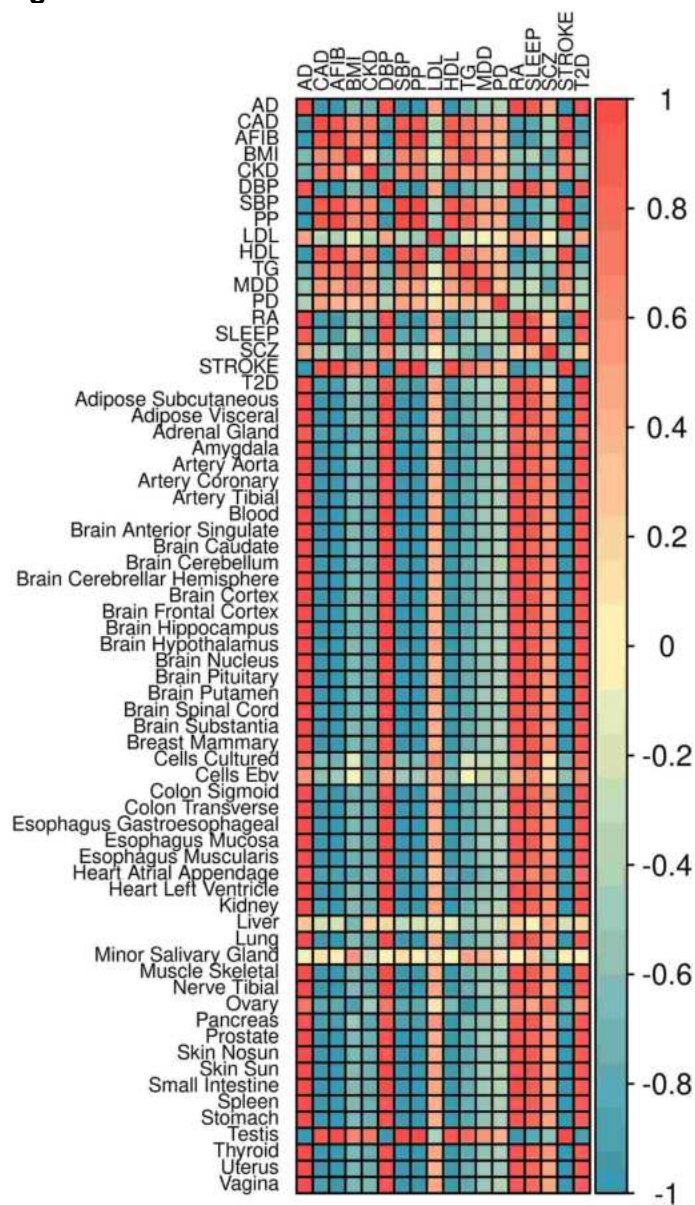## Figure S29: NPEPPS genetic correlations across eQTL tissues and disease phenotypes
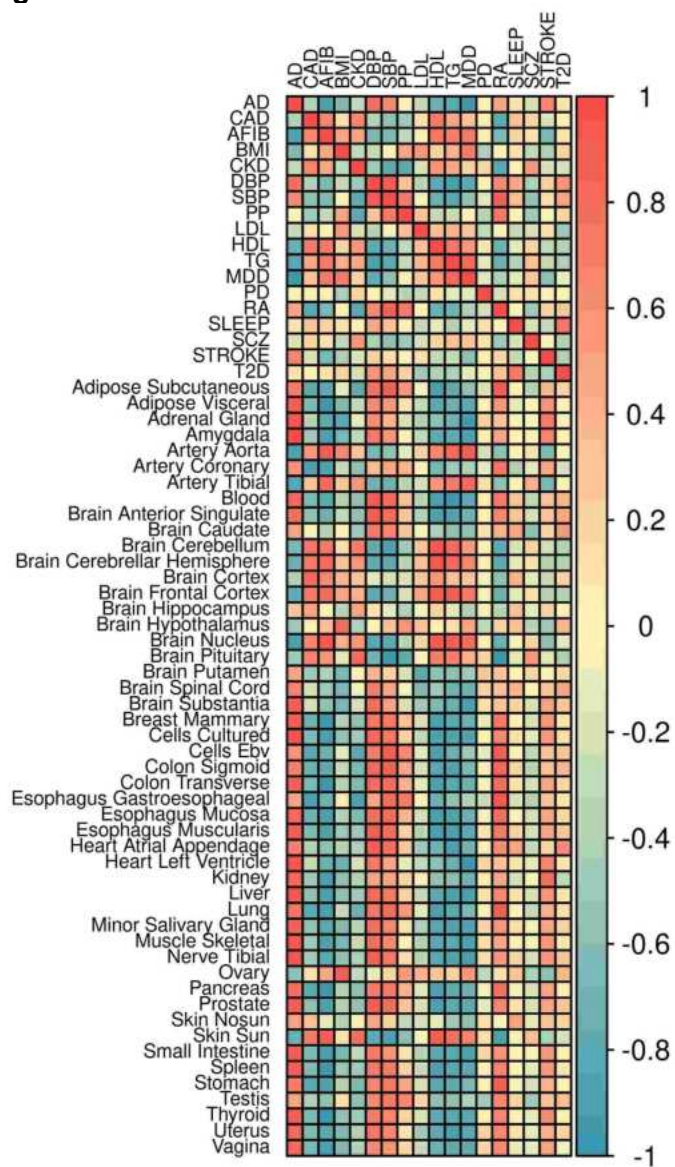

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S30: NTRK1 genetic correlations across eQTL tissues and disease phenotypes
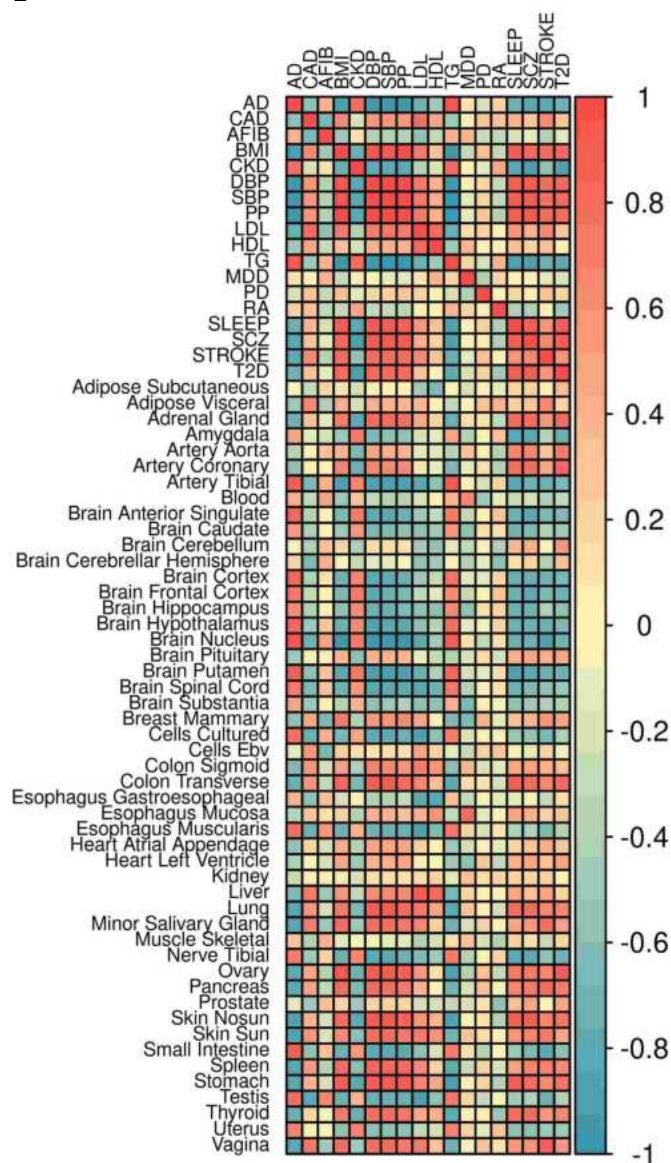

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S31: PNP genetic correlations across eQTL tissues and disease phenotypes
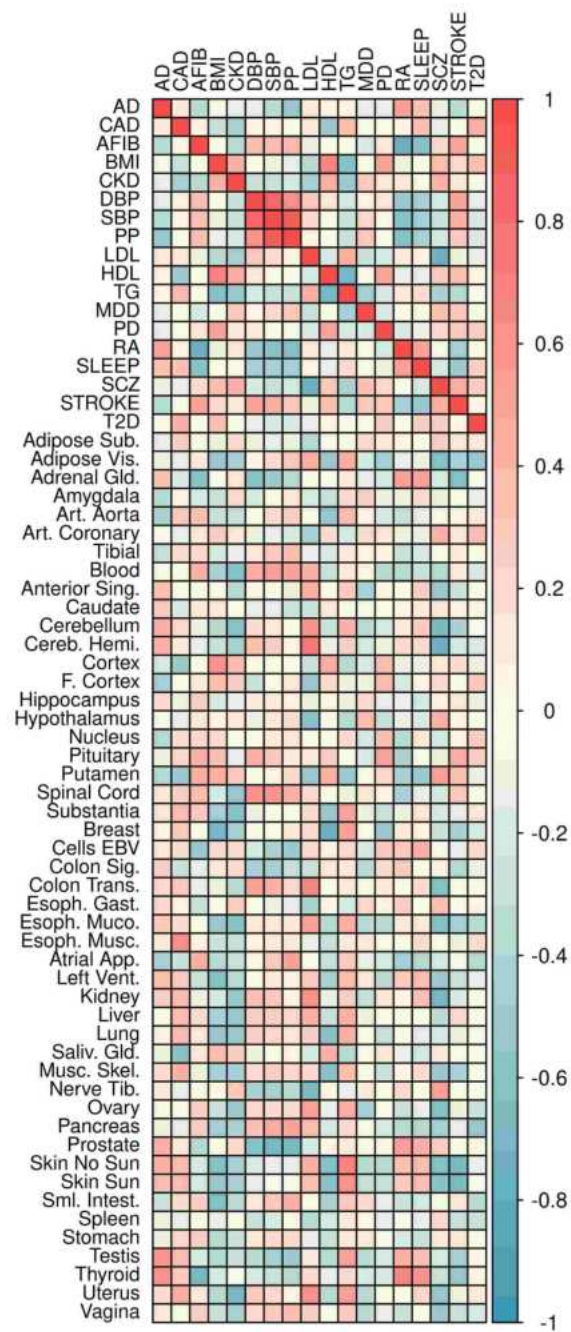

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S32: RIOK1 genetic correlations across eQTL tissues and disease phenotypes


Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S33: RIPK2 genetic correlations across eQTL tissues and disease phenotypes


Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S34: TNKS genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).

Figure S35: SYK genetic correlations across eQTL tissues and disease phenotypes

Matrix of genetic estimated local correlations between multiple phenotypes and eQTLs from all GTEx v8 tissues (see Methods in main text).
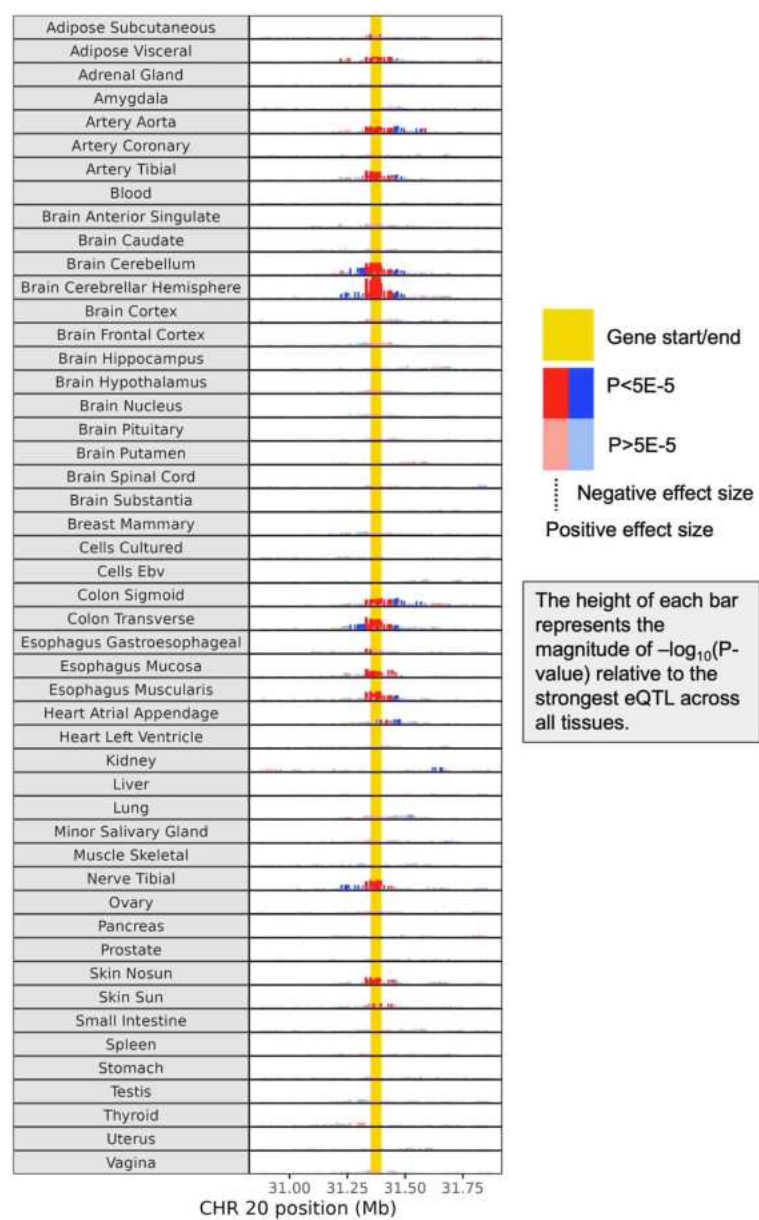
Figure S36: BMPR1B eQTLs across tissues
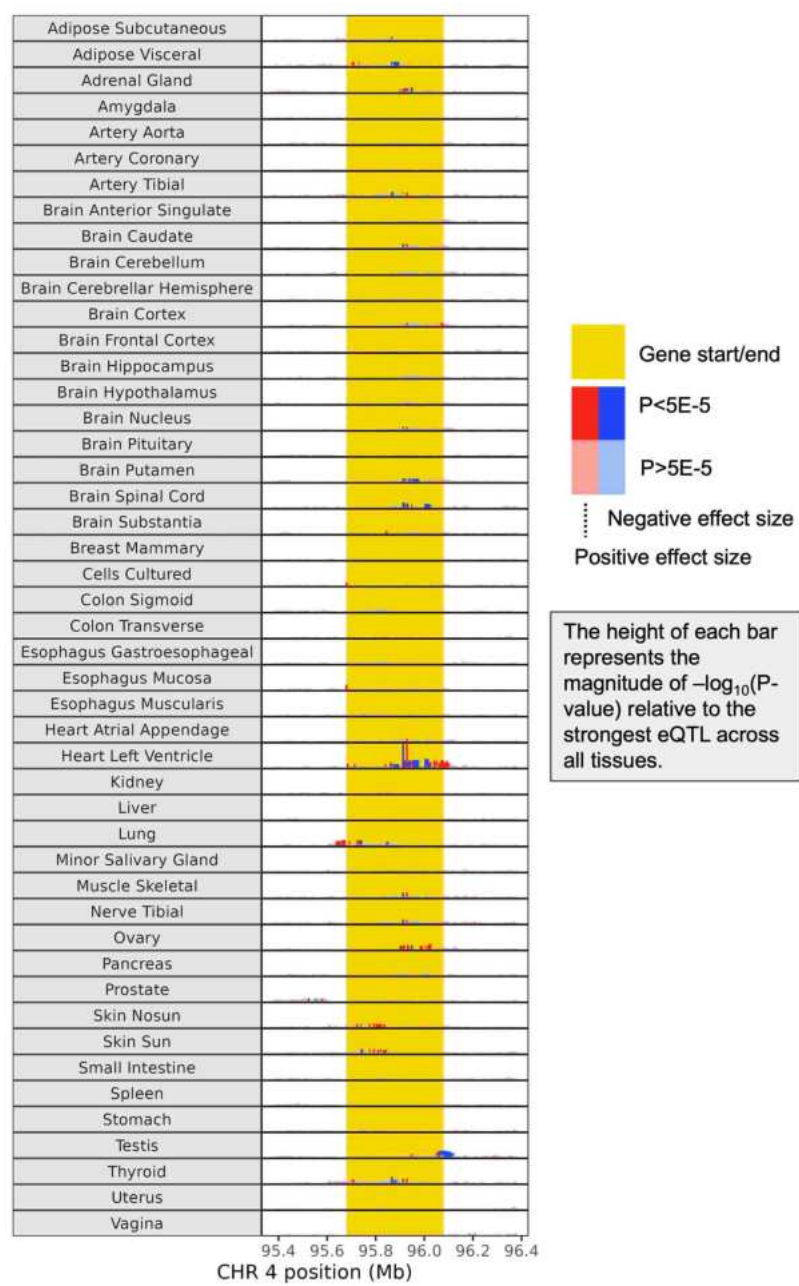
Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels

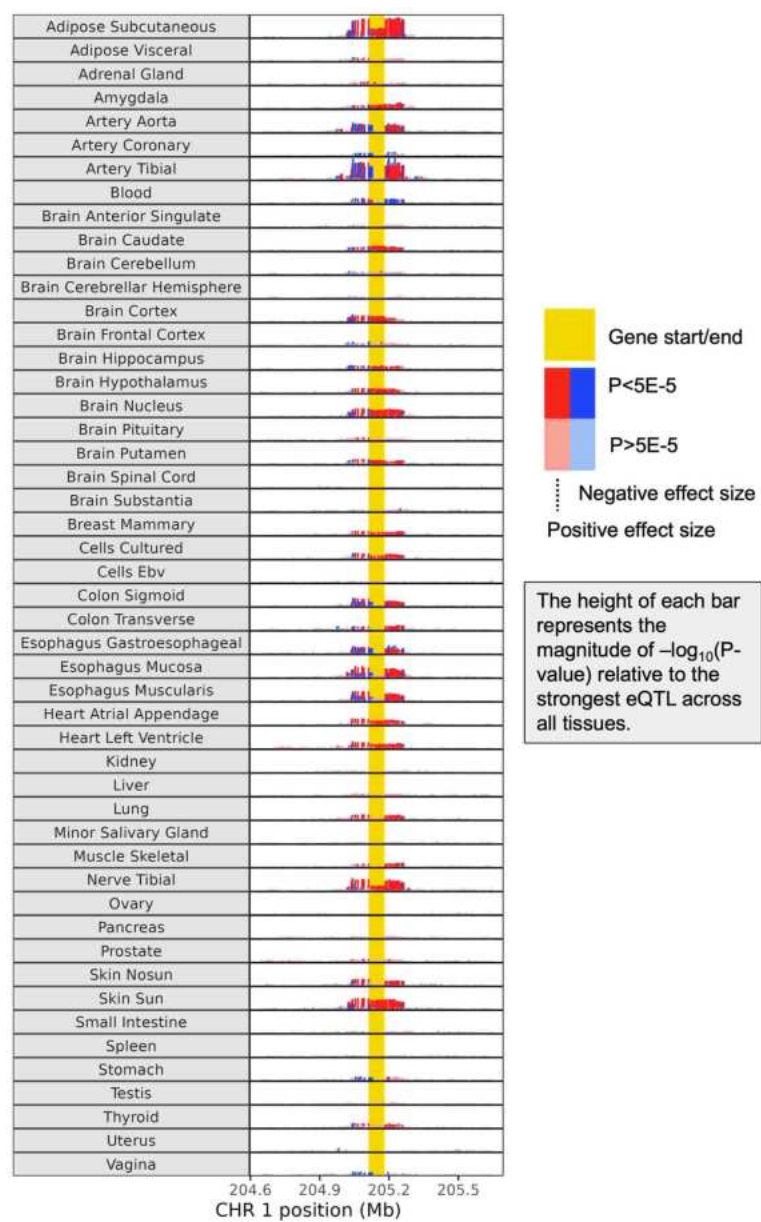**Figure S37: CHRM5 eQTLs across tissues**
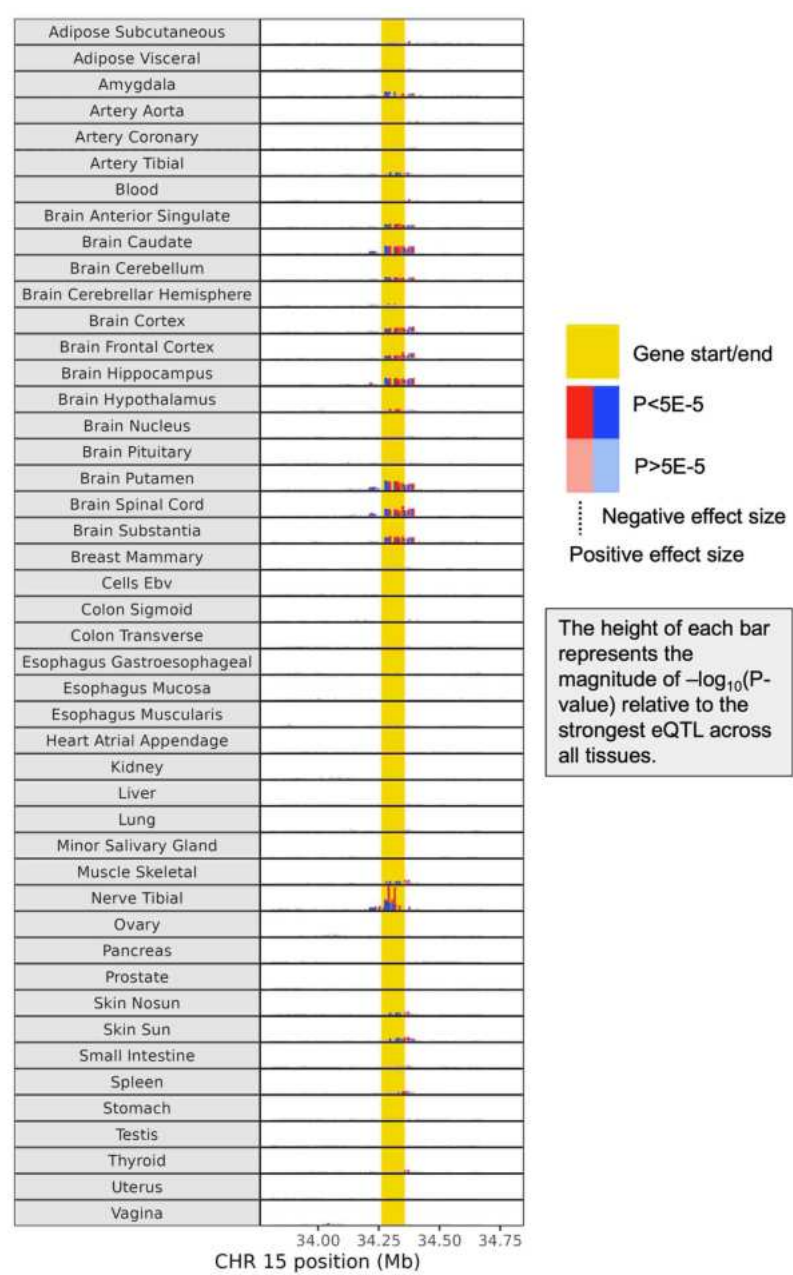
Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
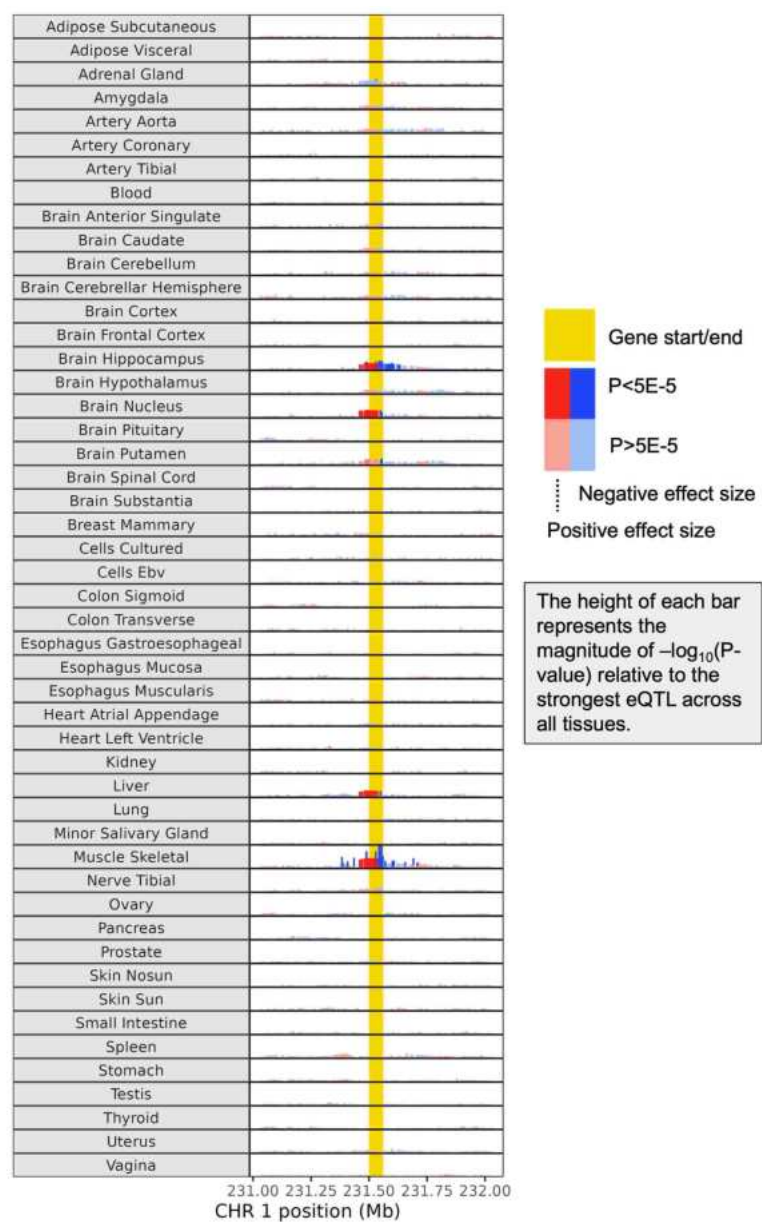
Figure S38: DNMT3B eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
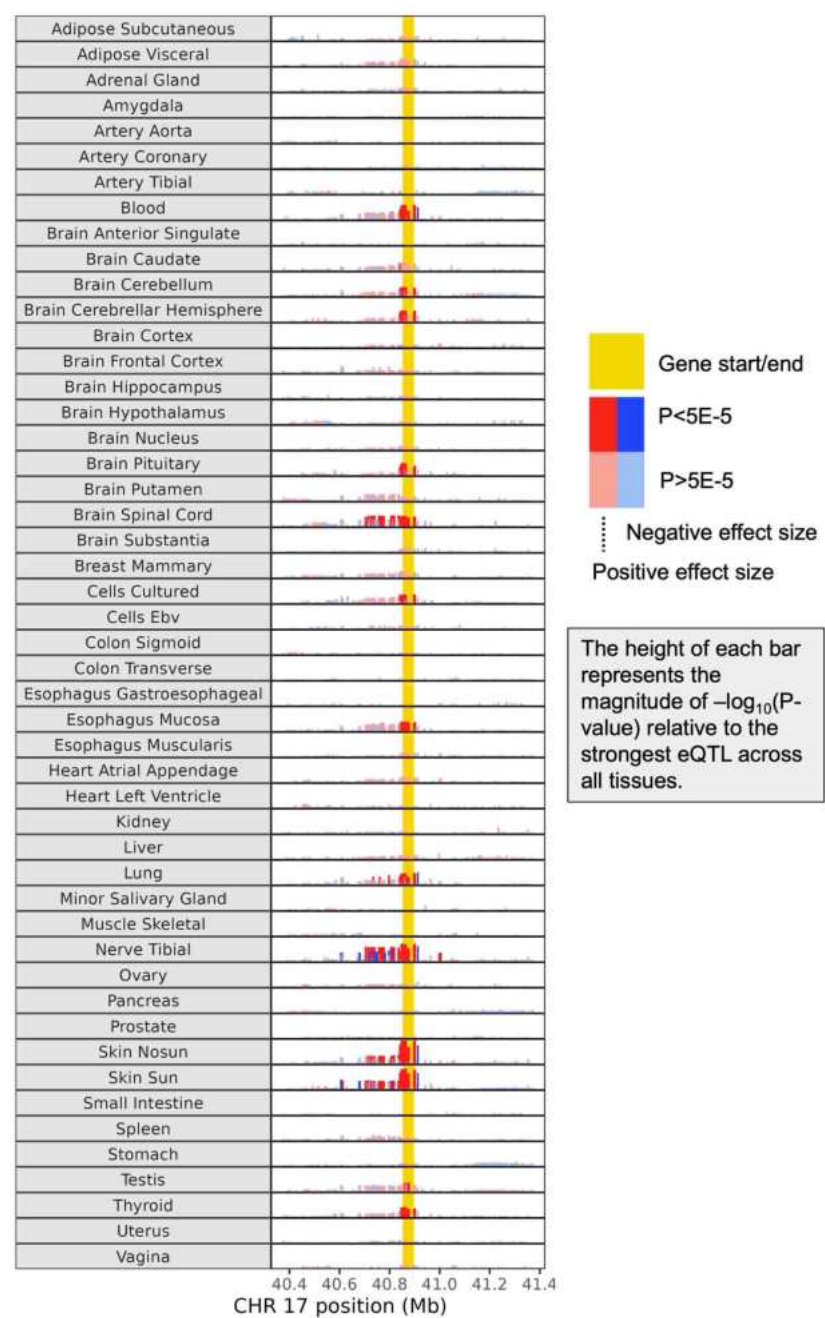
Figure S39: DSTYK eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
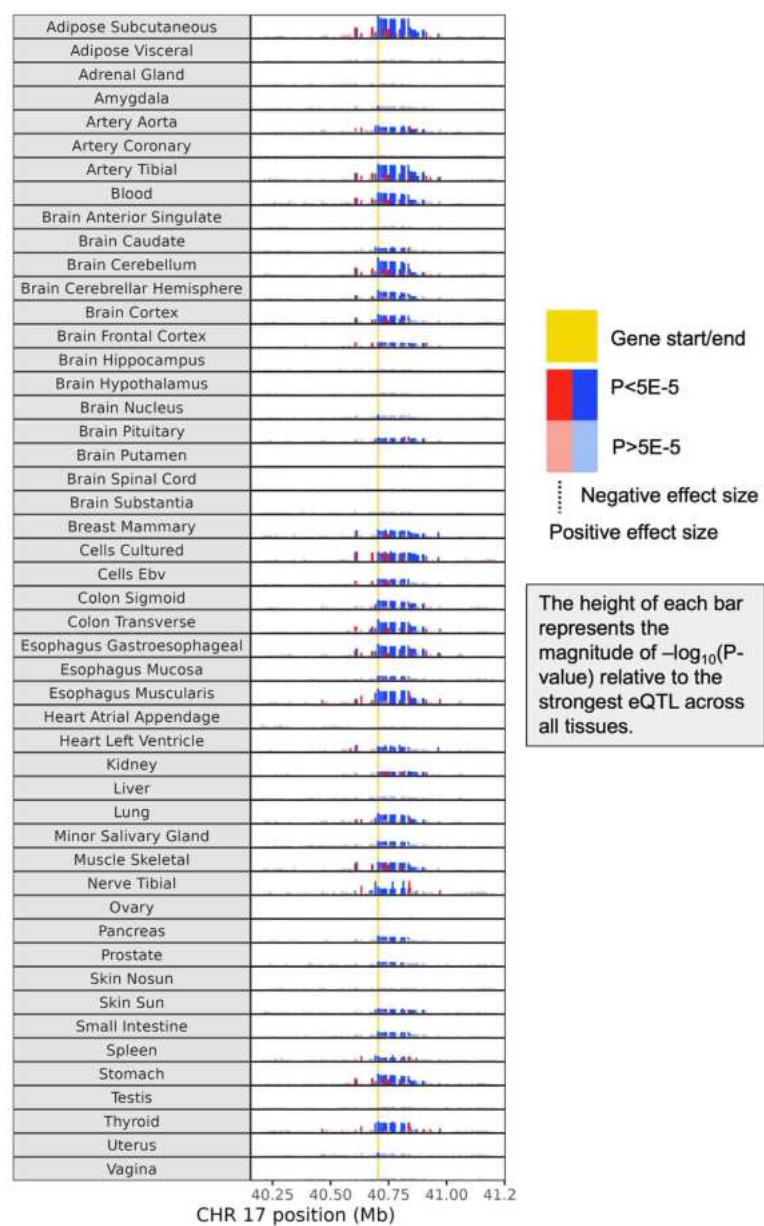
Figure S40: EGLN1 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
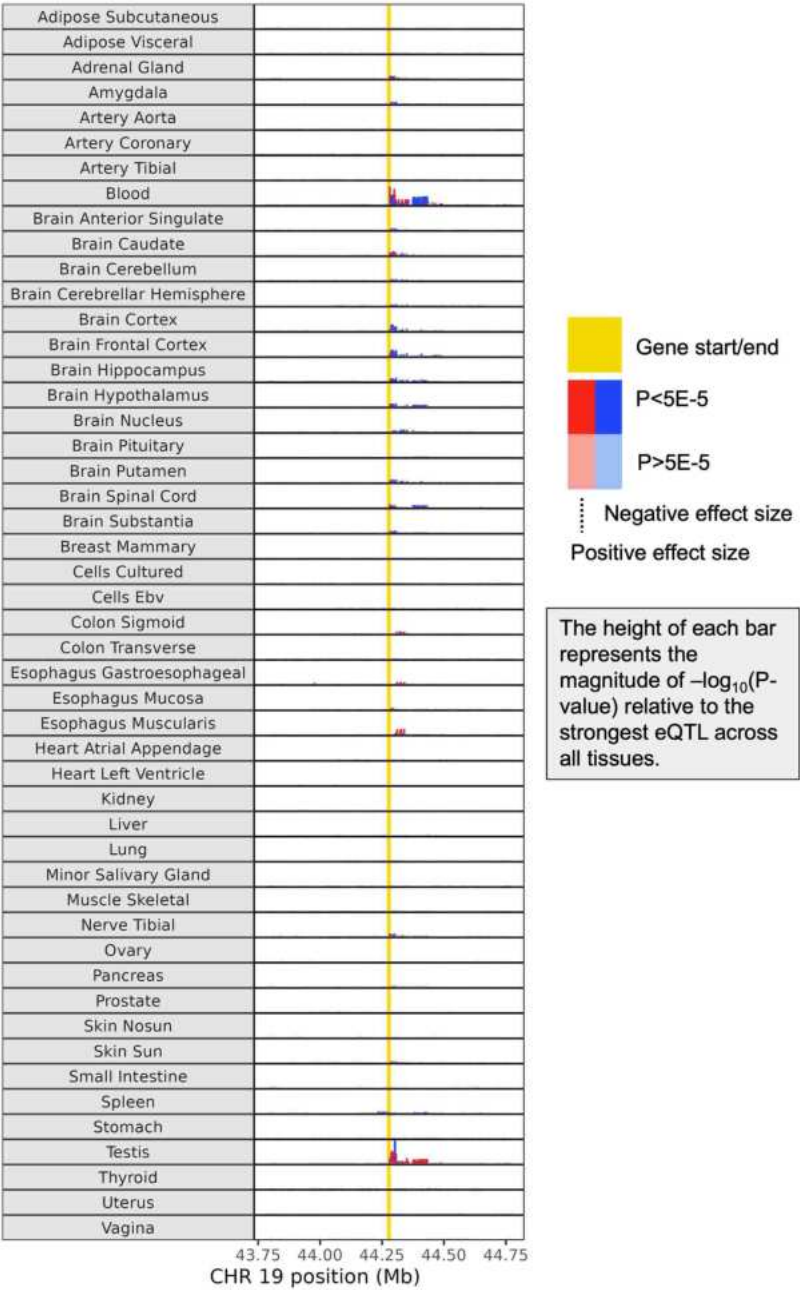
Figure S41: EZH1 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
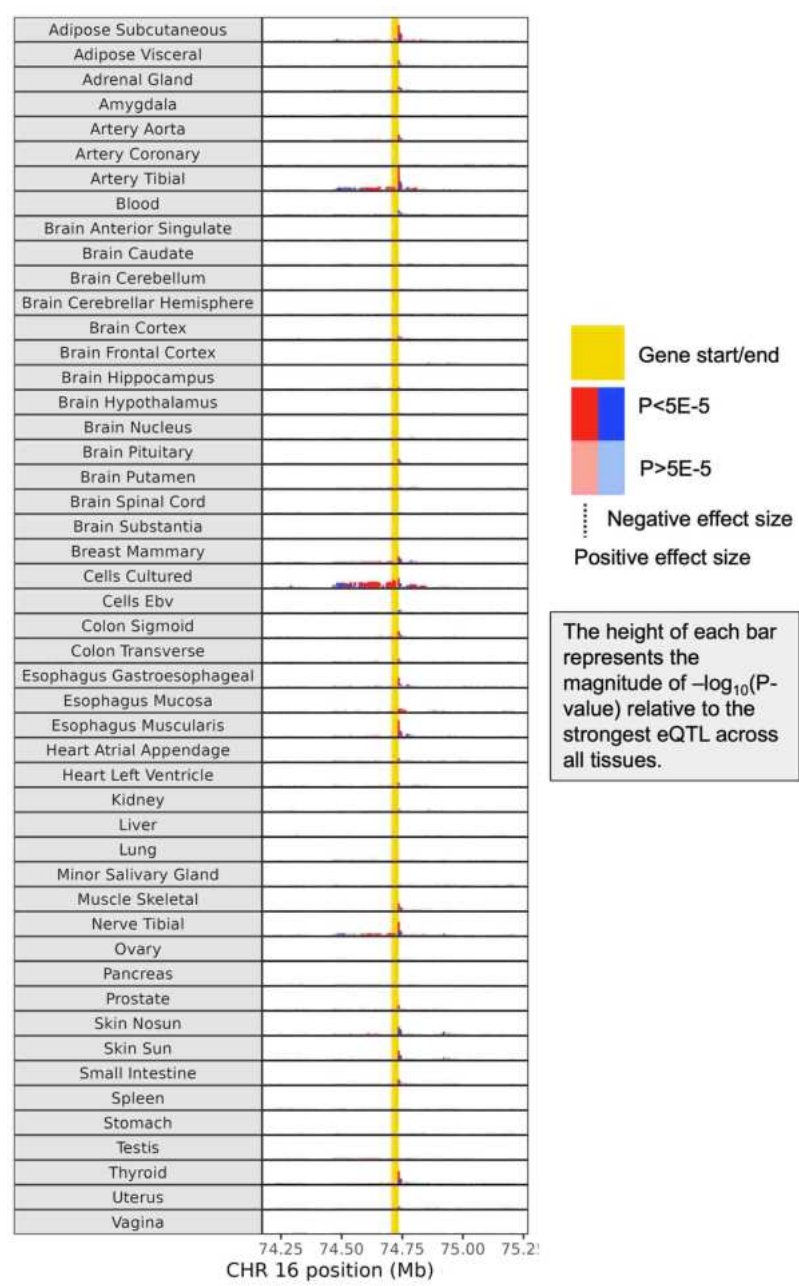
Figure S42: HSD17B1 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
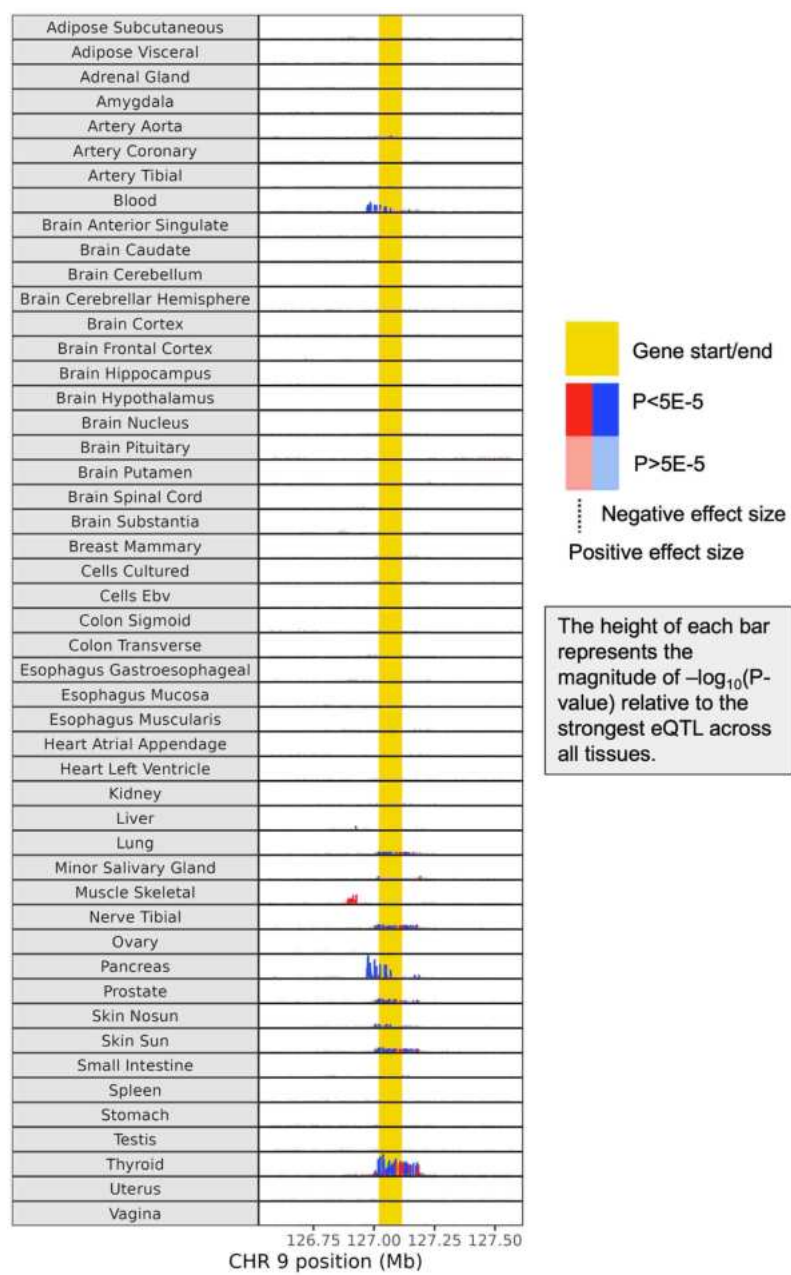
Figure S43: KCNN4 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
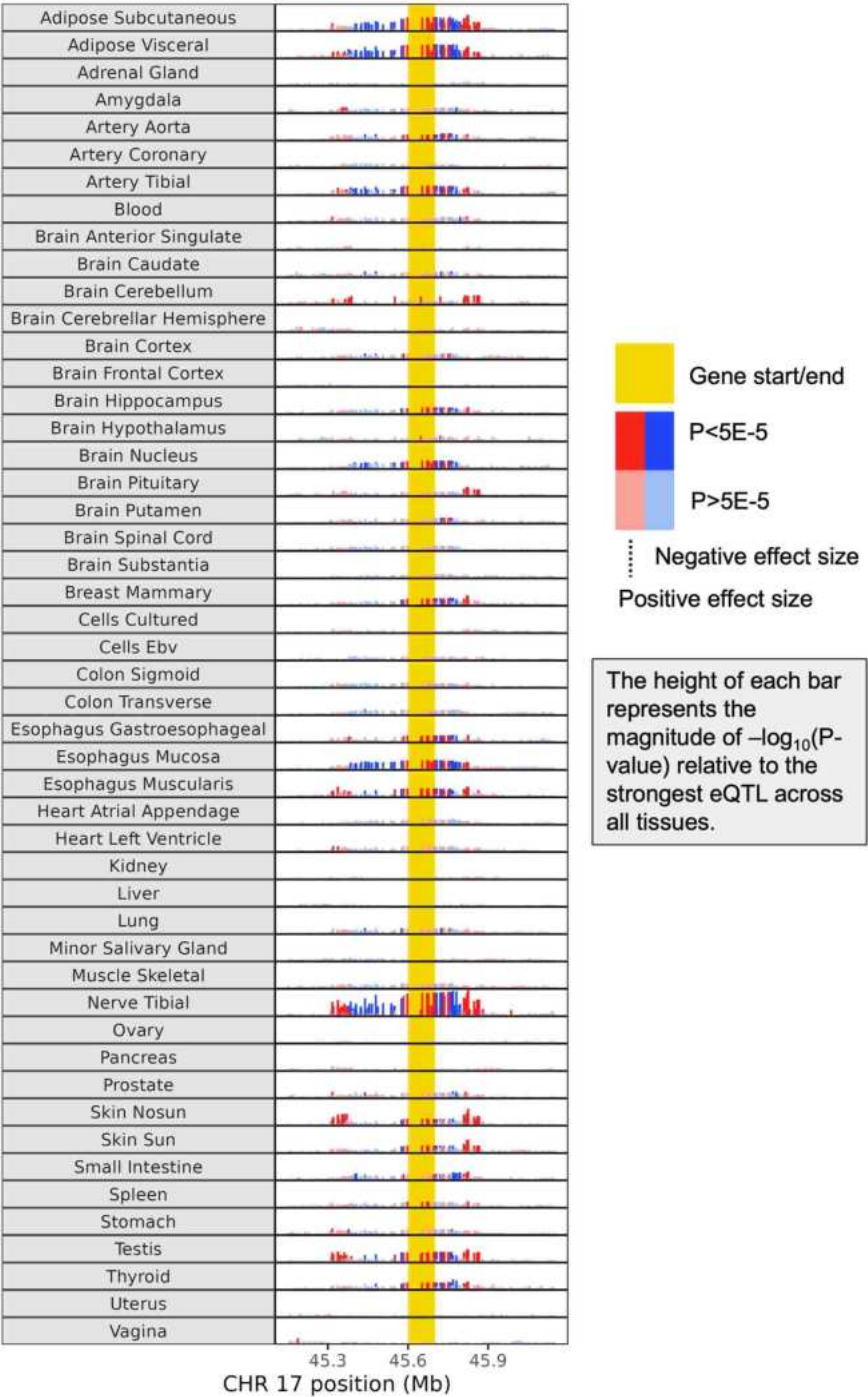
Figure S44: MLKL eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
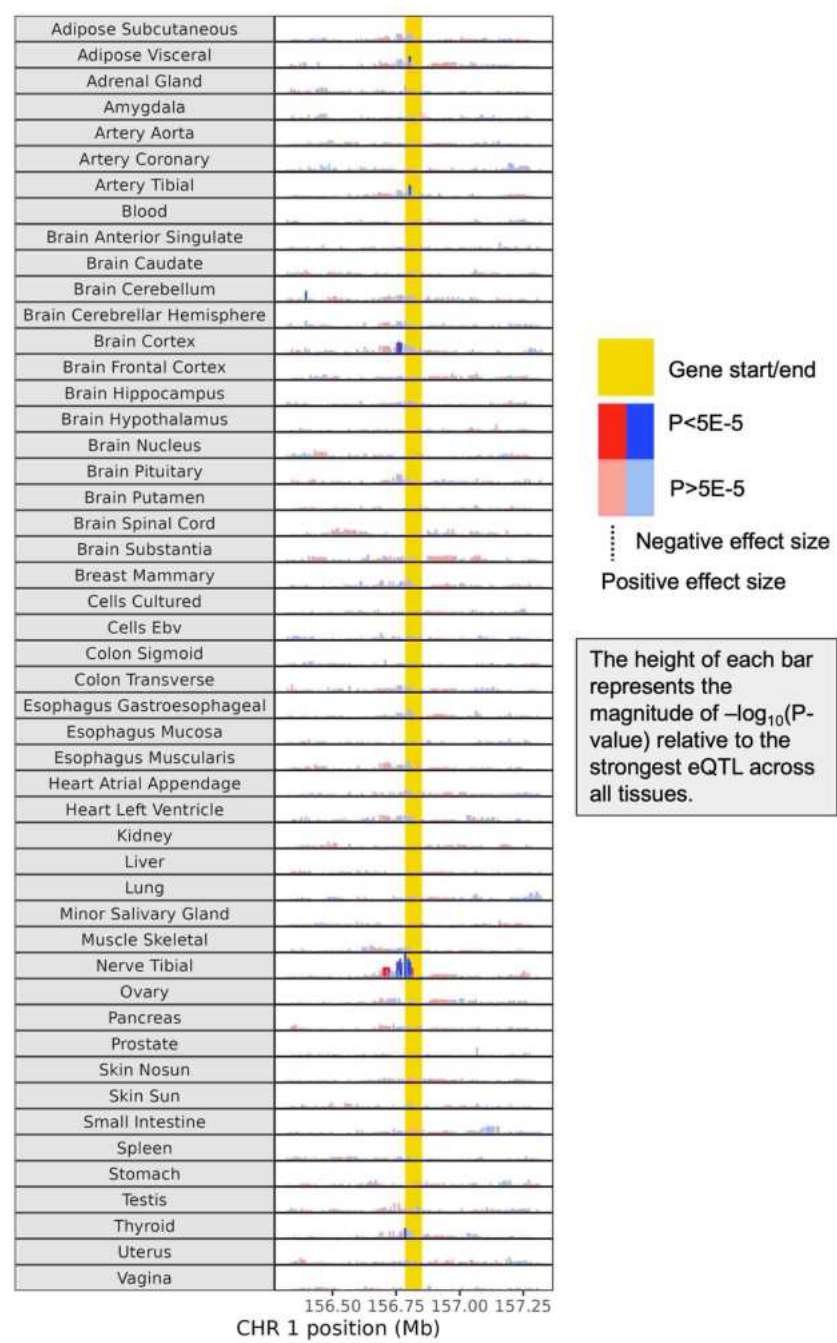
Figure S45: NEK6 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
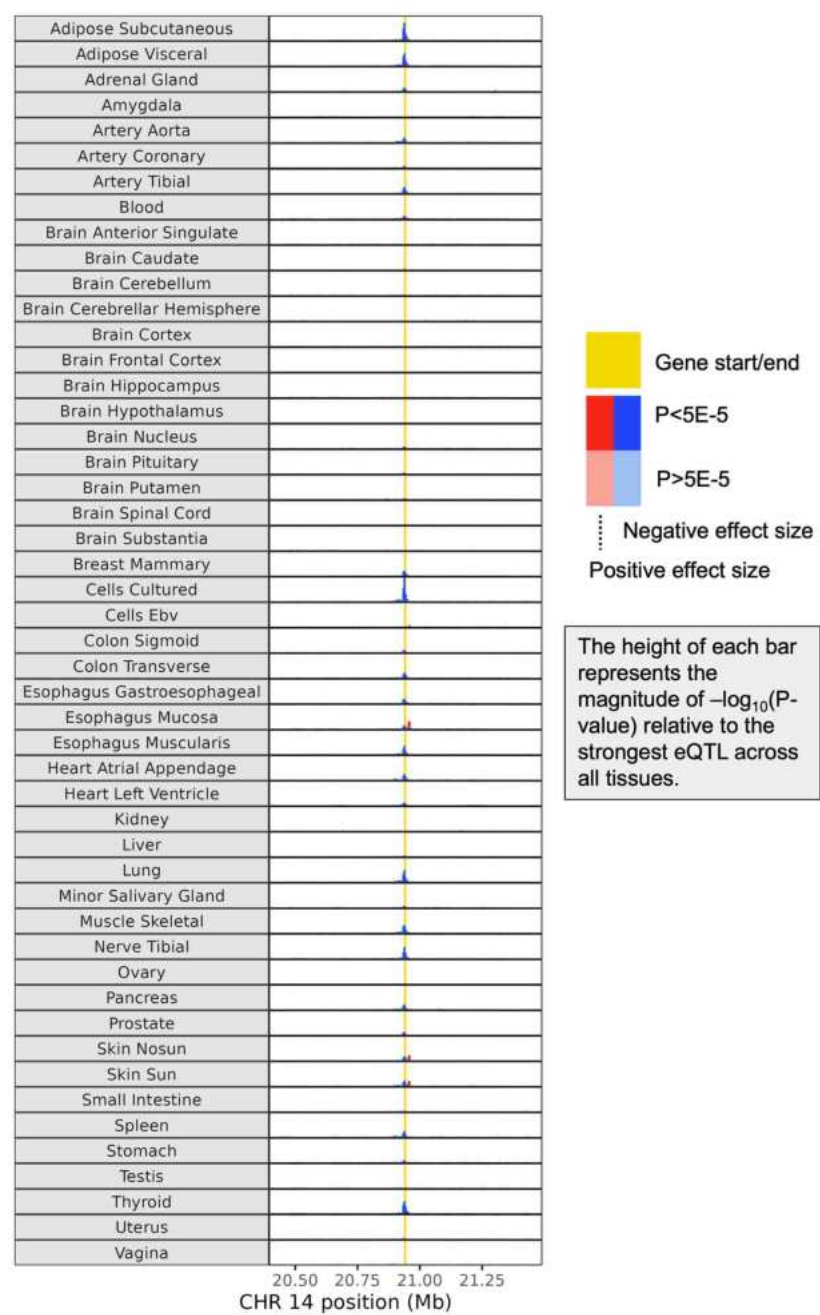
Figure S46: NPEPPS eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
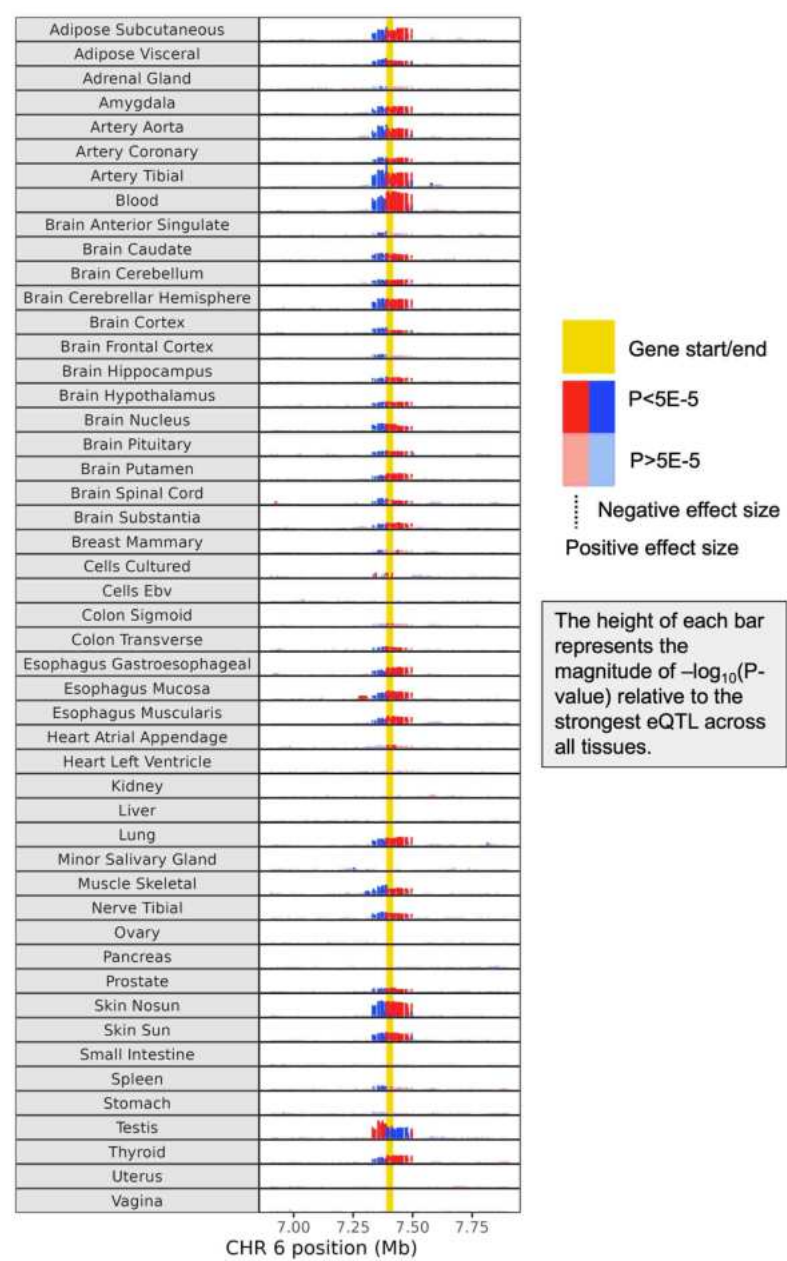
Figure S47: NTRK1 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
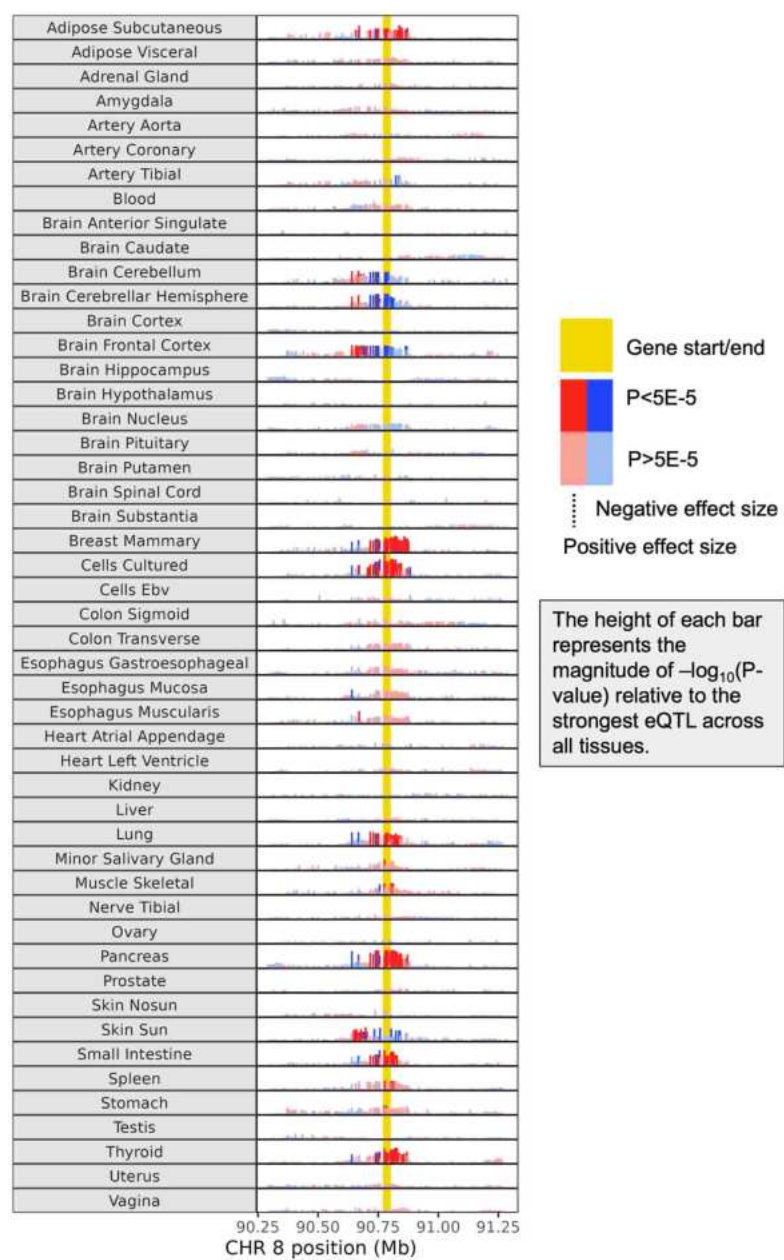
Figure S48: PNP eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels

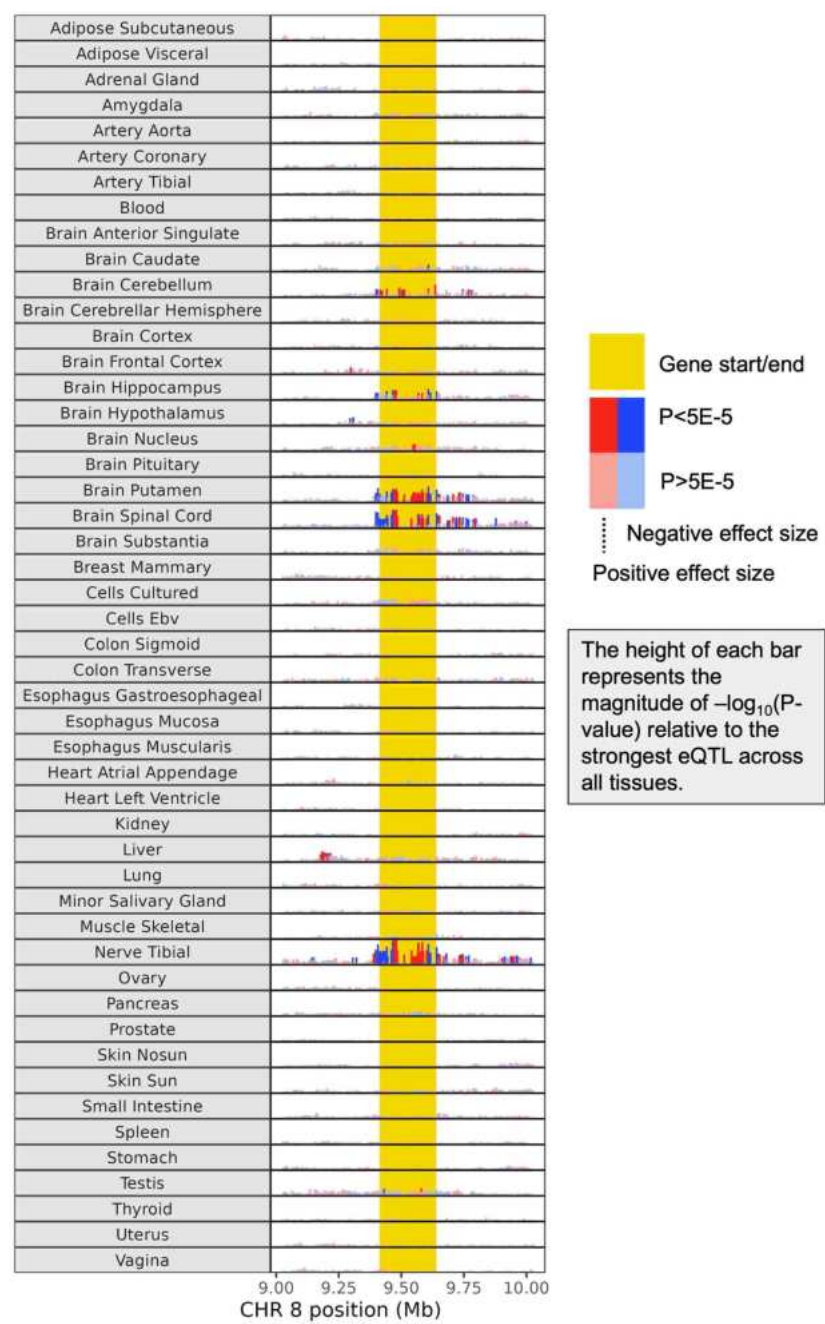## Figure S49: RIOK1 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels
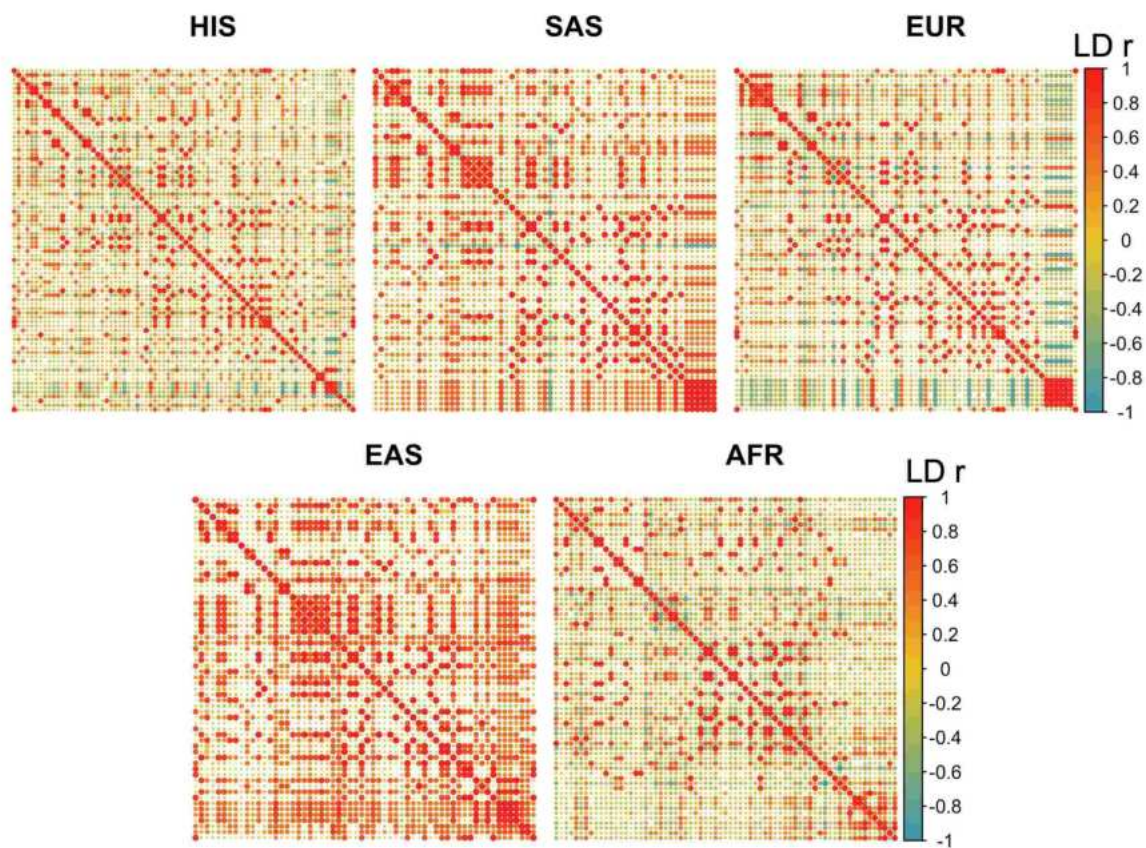
Figure S50: RIPK2 eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels

Figure S51: TNKS eQTLs across tissues

Manhattan plot of eQTLs across all GTEx v8 tissues and indications of the nominal significance levels

Figure S52: LD correlations in the KIF11 locus across populations


Matrices of LD correlations in the *KIF11* (±1Mb) locus using 1000 Genomes Phase 3 sample (see Methods in the main text).

Figure S53: RIPK2 multi-tissue eQTL genetic correlation network
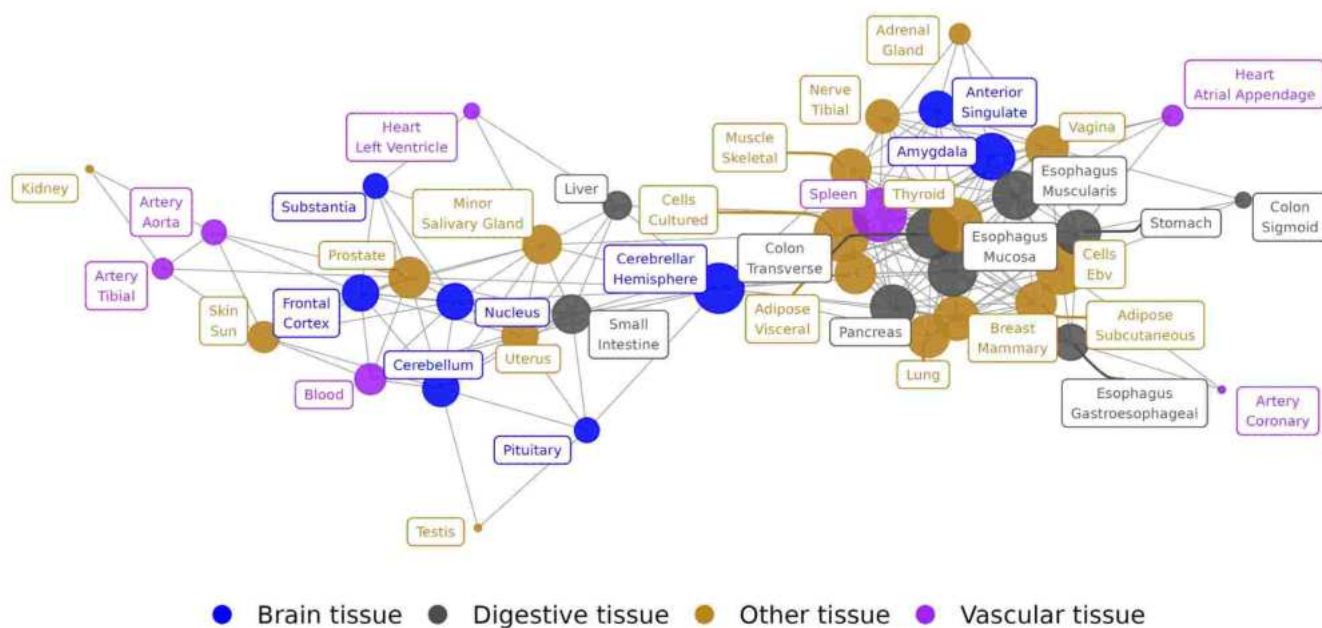

Sparse network of genetic correlations between eQTLs from all GTEx v8 tissues in the *RIPK2* locus and their meta categories (see Methods in the main text).

Figure S54: Cell type-specific expression of 3 novel druggable AD genes in cortex tissue
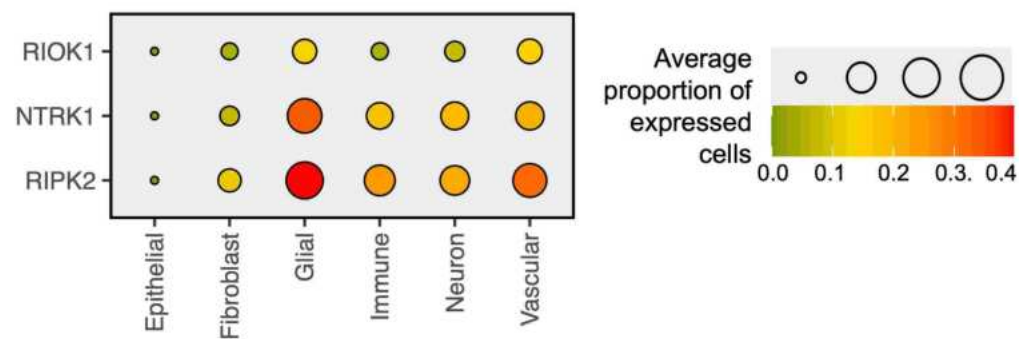
Average levels of expression in six major cell types for three select AD-associated genes with xGenT evidence from analyses with brain eQTLs (see Methods in the main text).

Figure S55: NTRK1 physical protein-protein interactions with Bonferroni significant AD genes

GenT evidence: AD-associated Not AD-associated
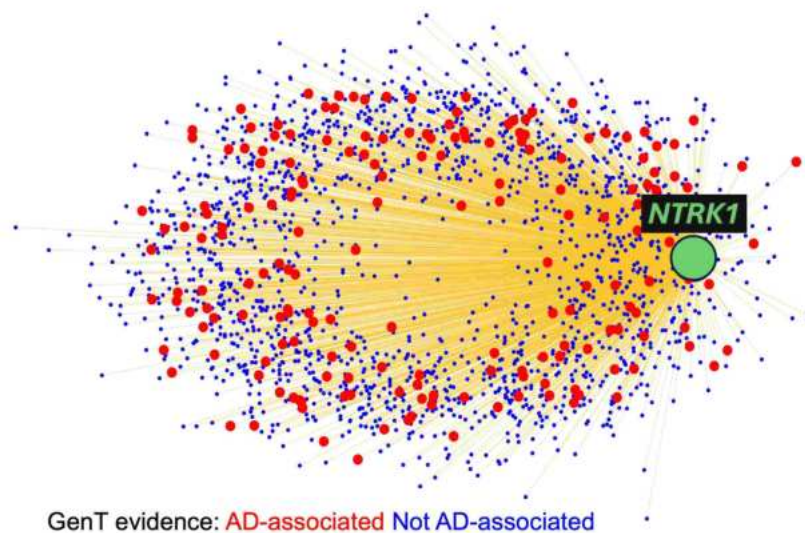
Physical protein-protein interactions between interaction pairs with *NTRK1* and indications of their significance in gene-based association testing with GenT. Genes significant at the 0.05/18,257 Bonferroni level are colored in red and others are colored in blue.