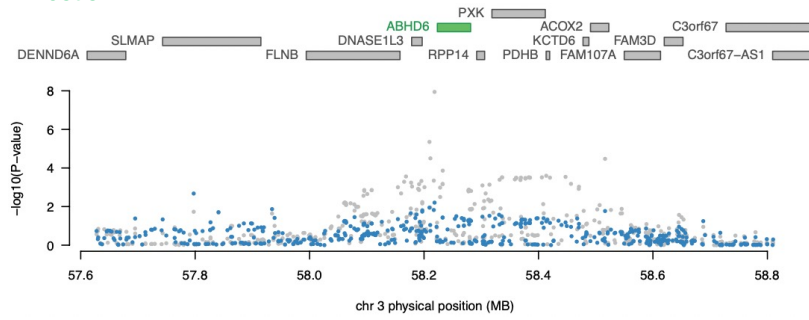
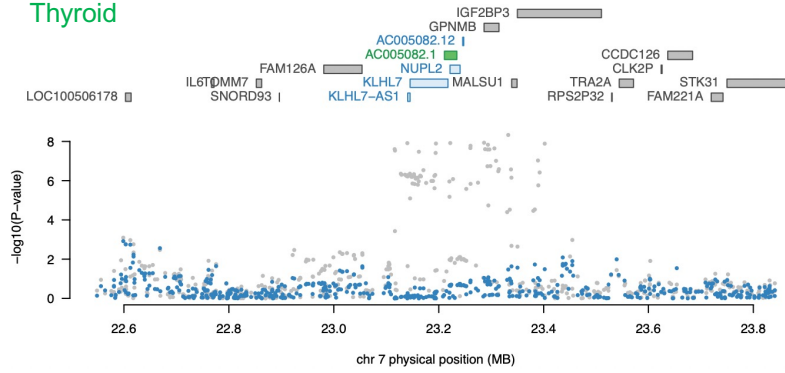


(Supplementary Fig. 1.) Prediction accuracy across three linear models: BLUP (best linear unbiased predictor) , Elastic Net, LASSO regression. BSLMM (Bayesian sparse linear mixed model) was dropped due to poor convergence during cross validation. The model with the best prediction accuracy was used for imputing gene expression onto GWAS cohort.

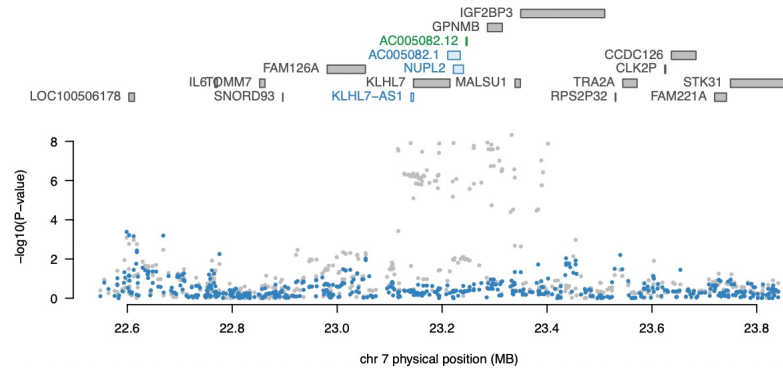
Testis



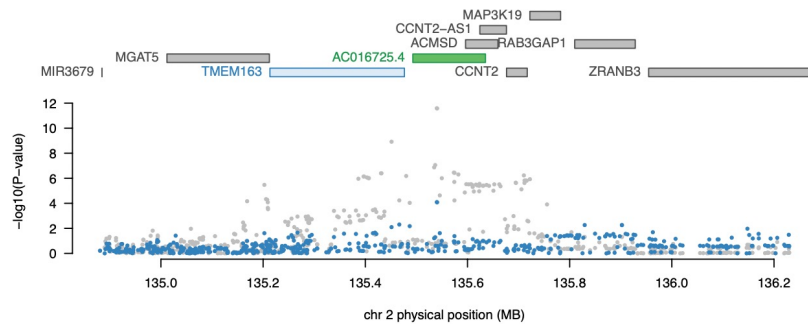
Thyroid



Breast mammary

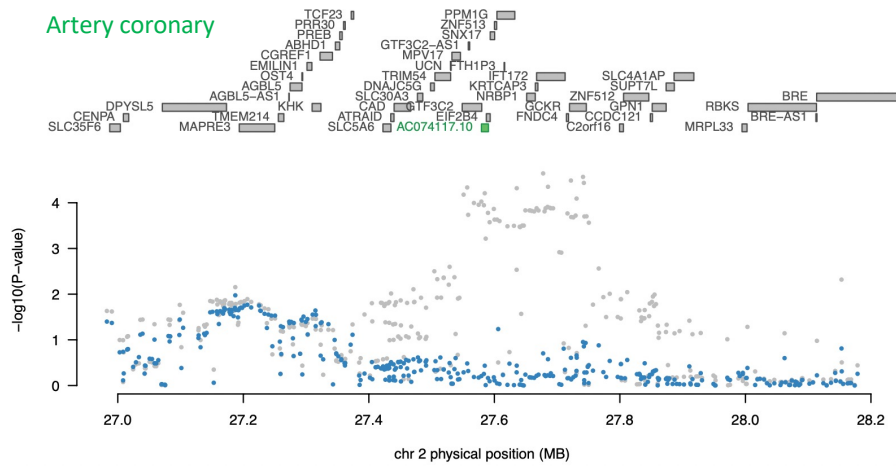


Testis

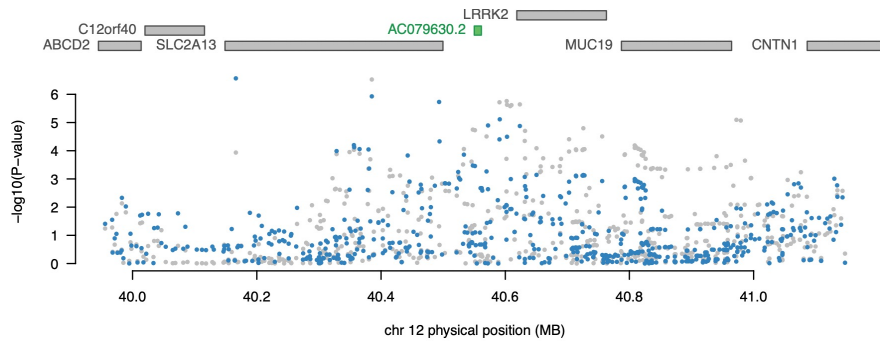


(Supplementary Fig. 2.1) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

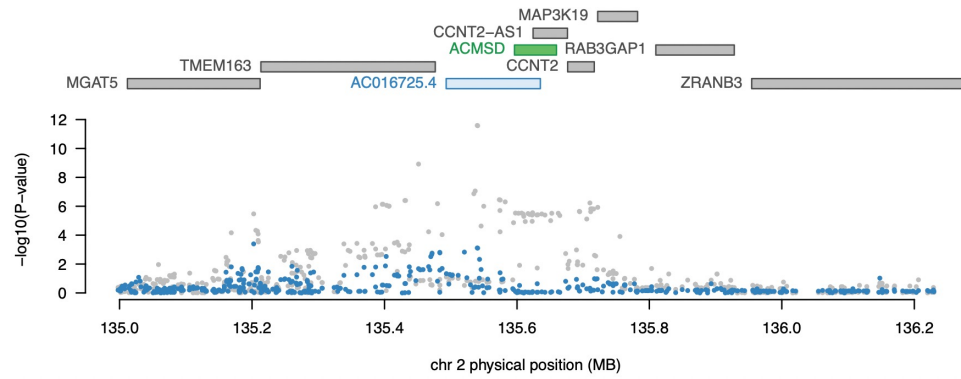
Artery coronary



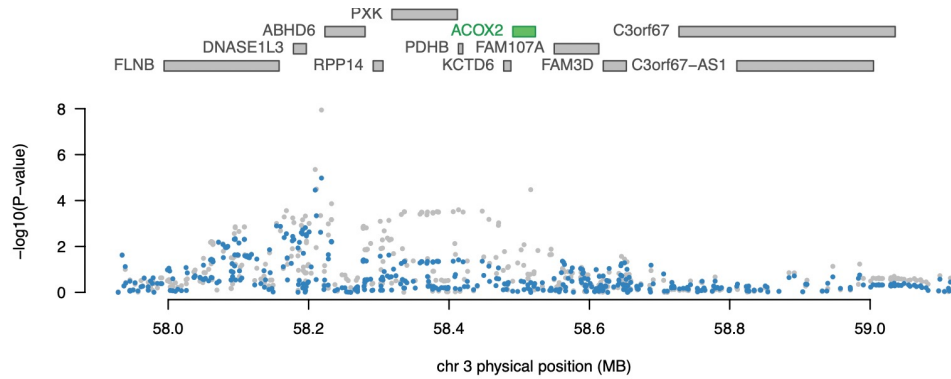
Pituitary



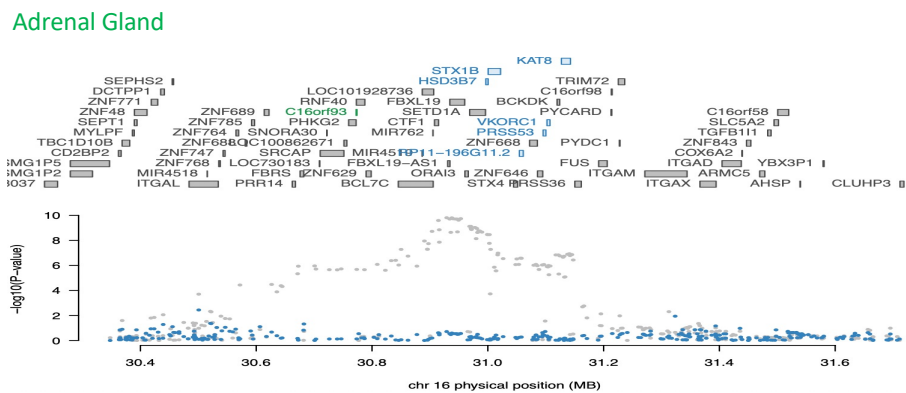
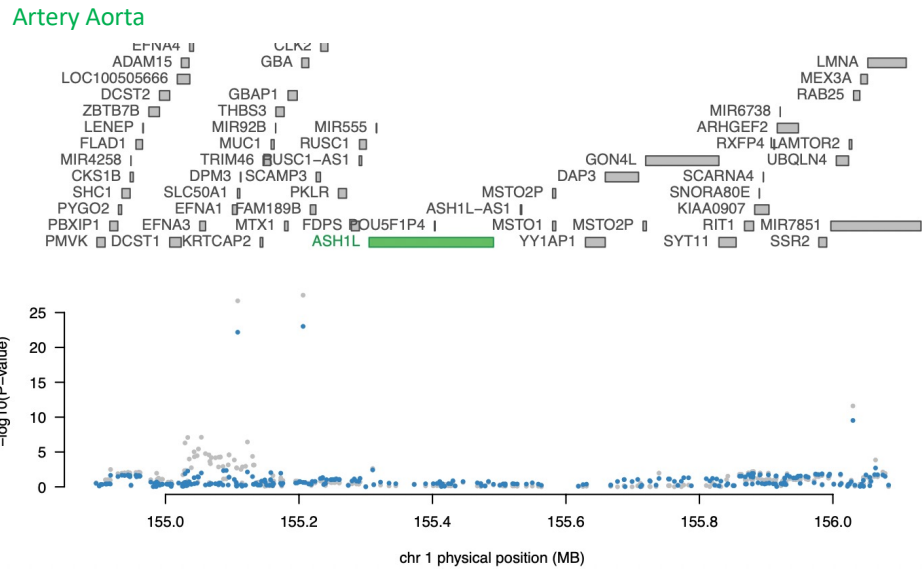
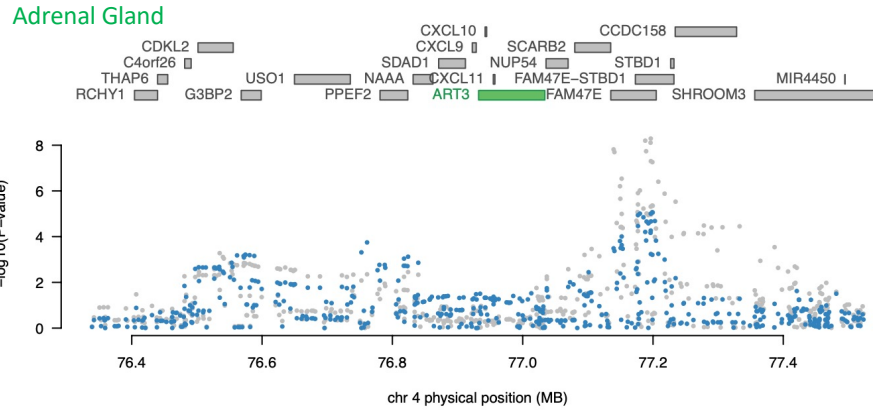
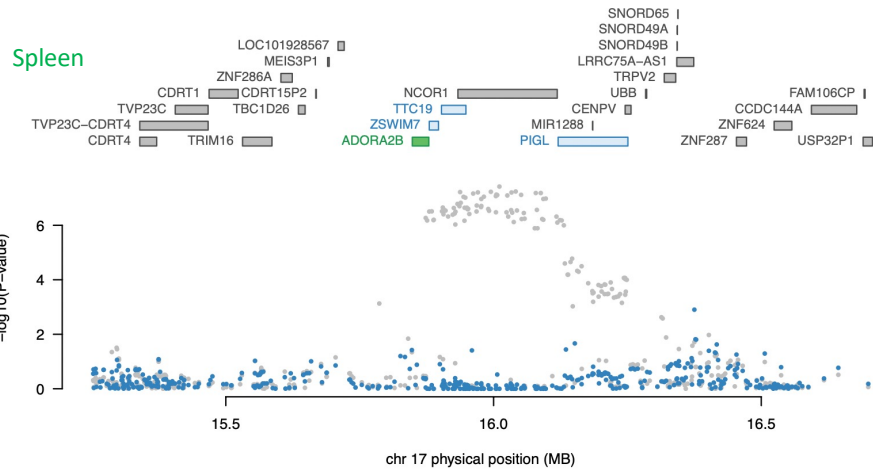
Pancreas



Heart_atrial_appendage

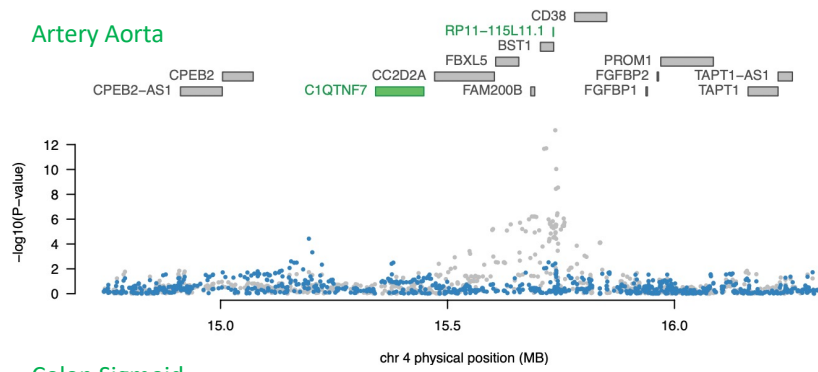


(Supplementary Fig. 2.2) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

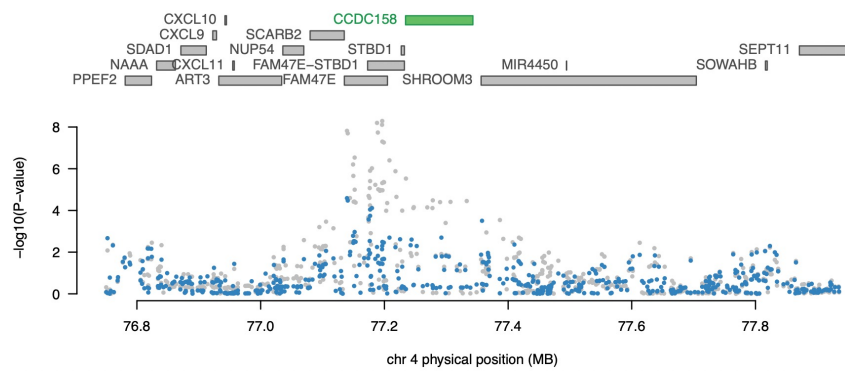


(Supplementary Fig. 2.3) FUSION plots of PD TWAS locus. Reference panel(GTex tissues) are shown for each plot.

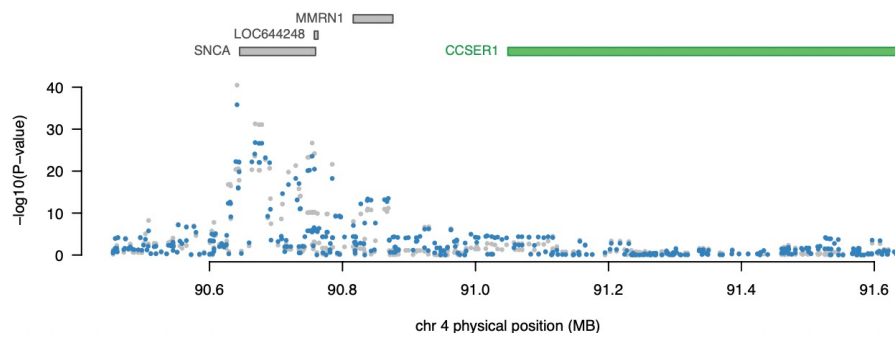
Artery Aorta



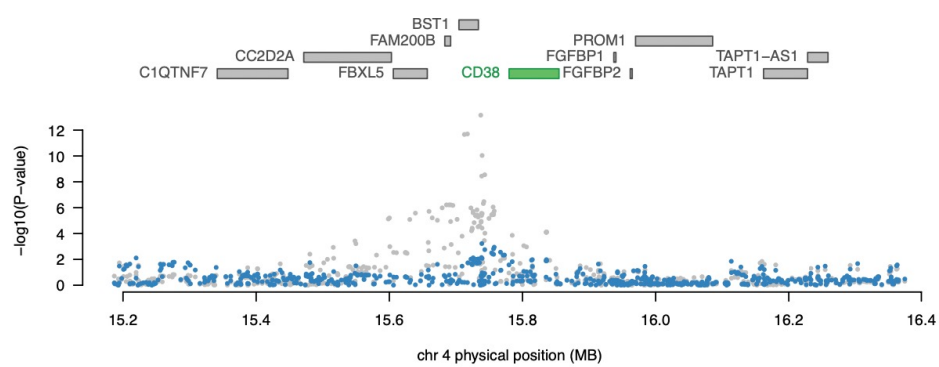
Colon Sigmoid



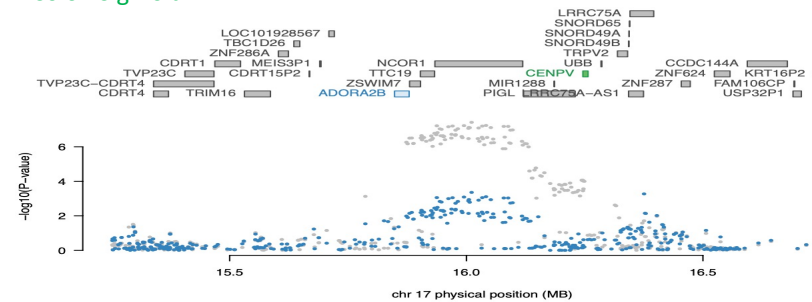
Testis



Brain_Caudate_basal_ganglia

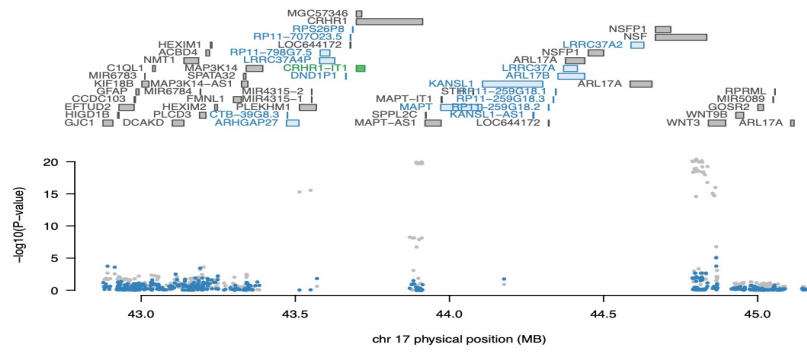


Colon Sigmoid

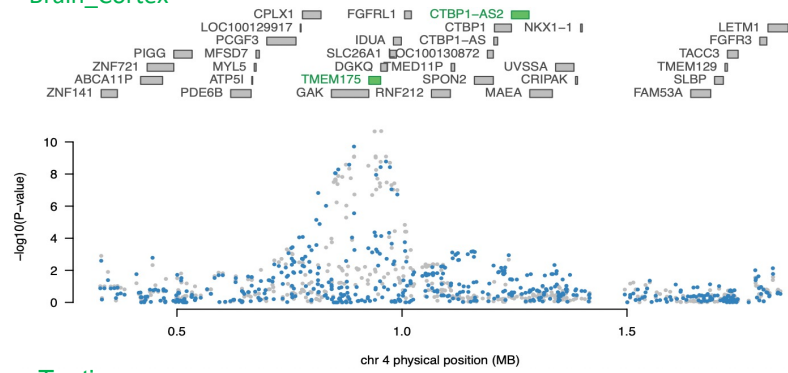


(Supplementary Figure 2.4) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

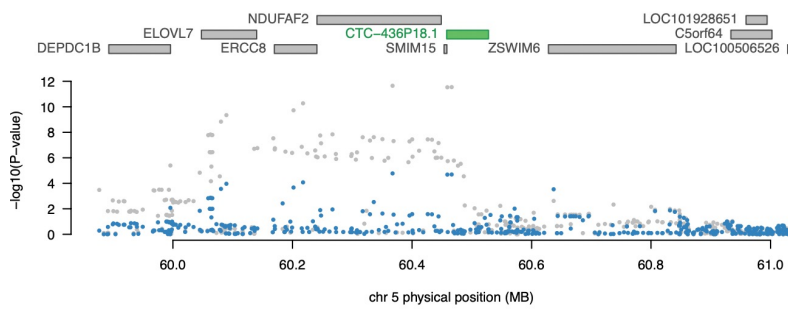
Skin_Not_Sun_Exposed_Suprapubic



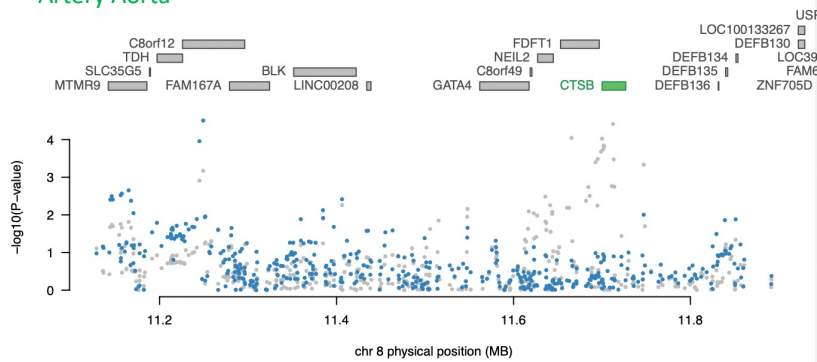
Brain_Cortex



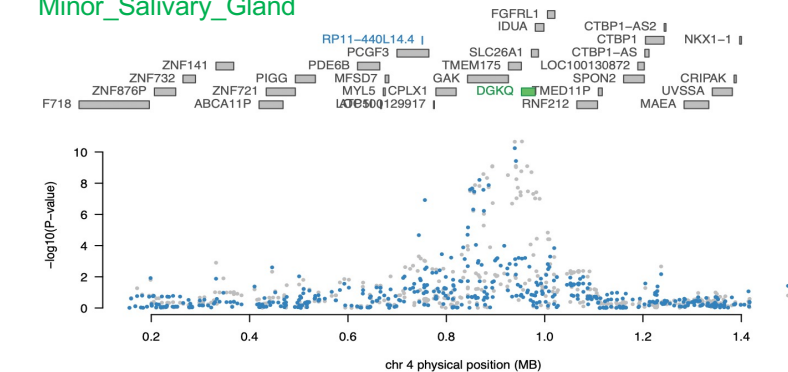
Testis



Artery Aorta

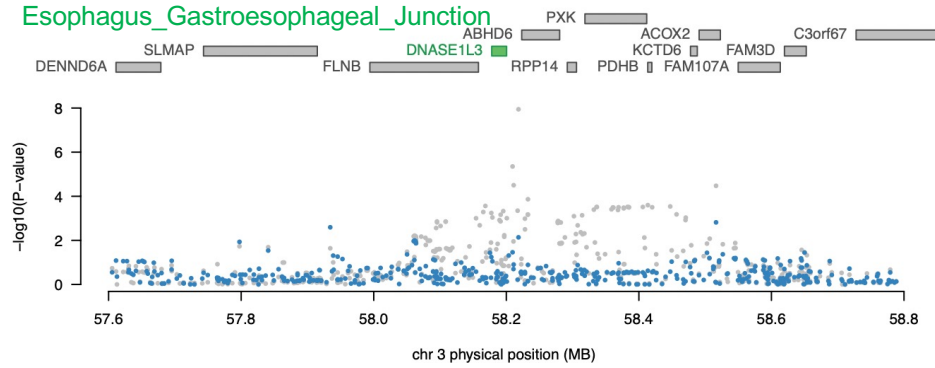


Minor_Salivary_Gland

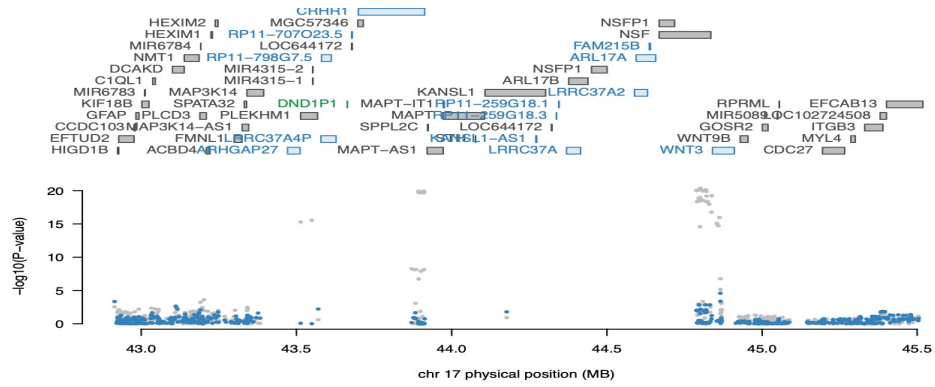


(Supplementary Fig. 2.5) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

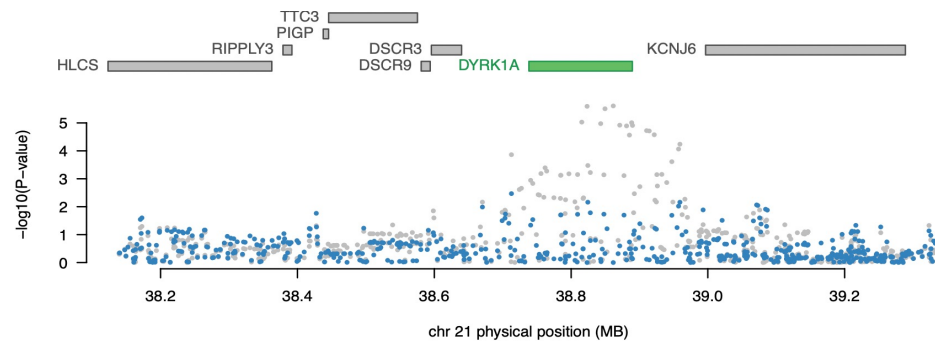
Esophagus_Gastroesophageal_Junction



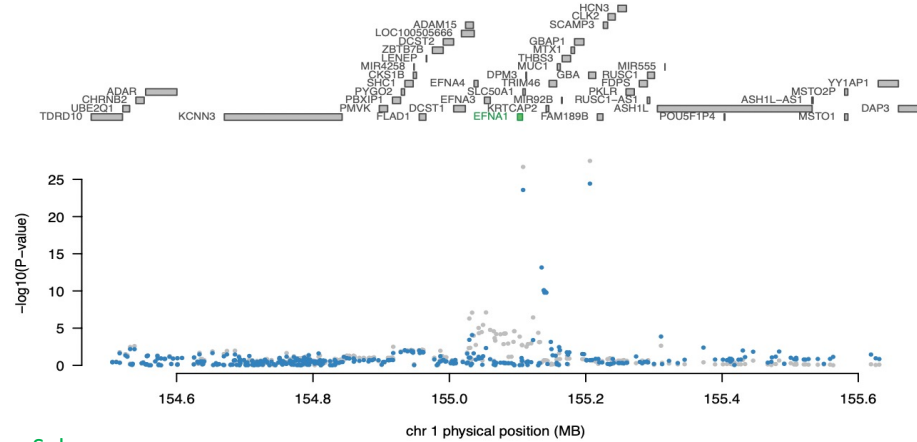
Adipose_Visceral_Omentum



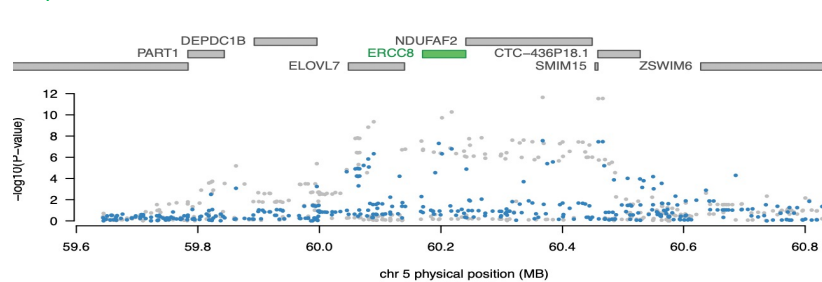
Skin_Not_Sun_Exposed_Suprapubic



Heart_Left_Ventricle

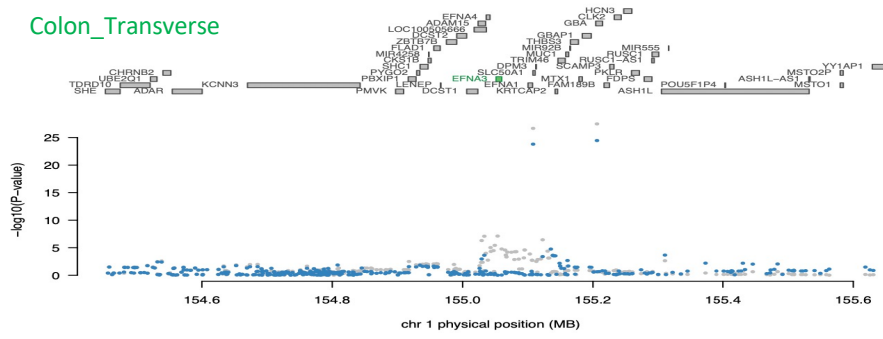


Spleen

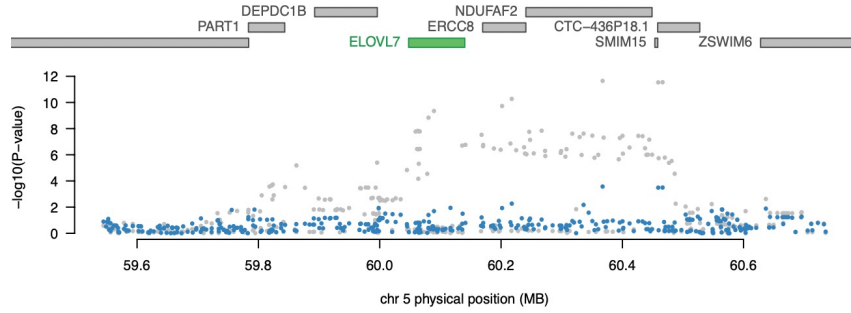


(Supplementary Fig. 2.6) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

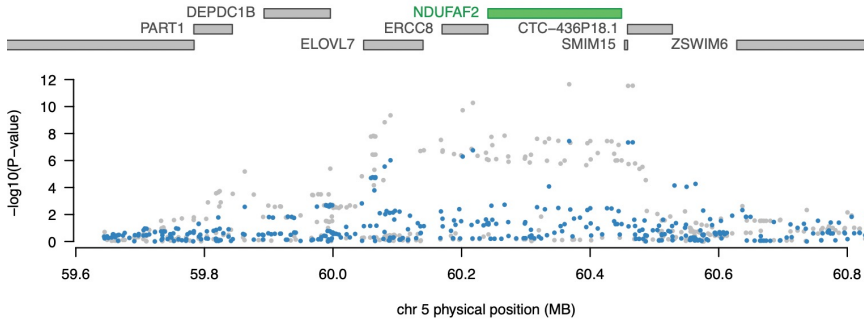
Colon_Transverse



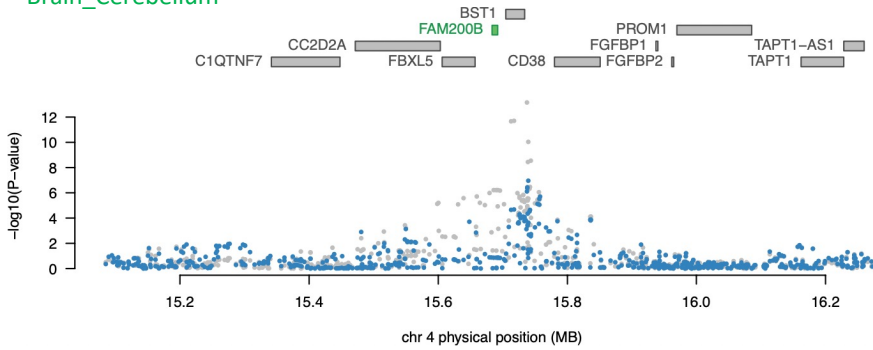
Lung



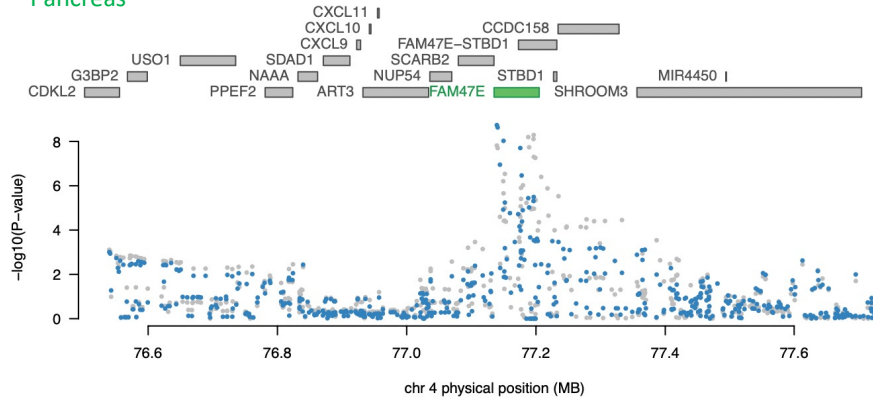
Brain_Nucleus_accumbens_basal_ganglia



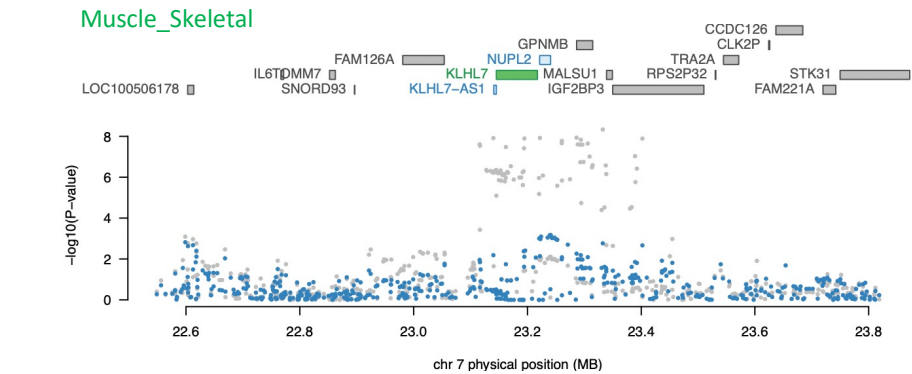
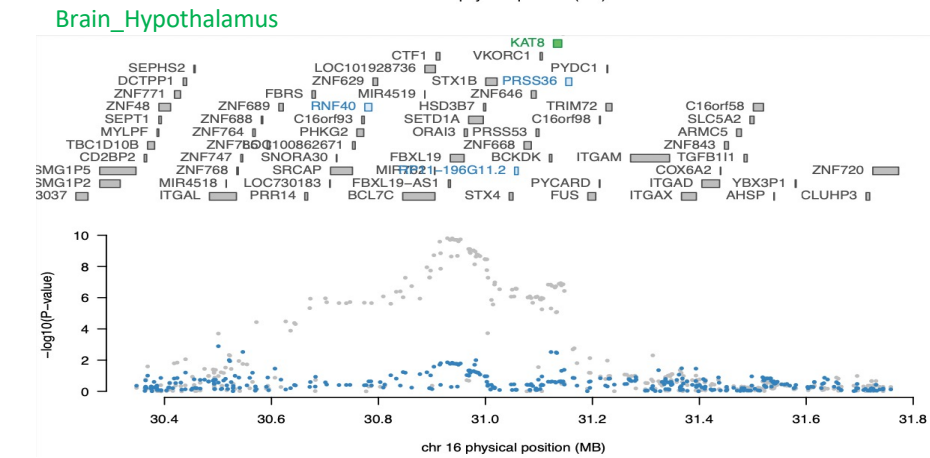
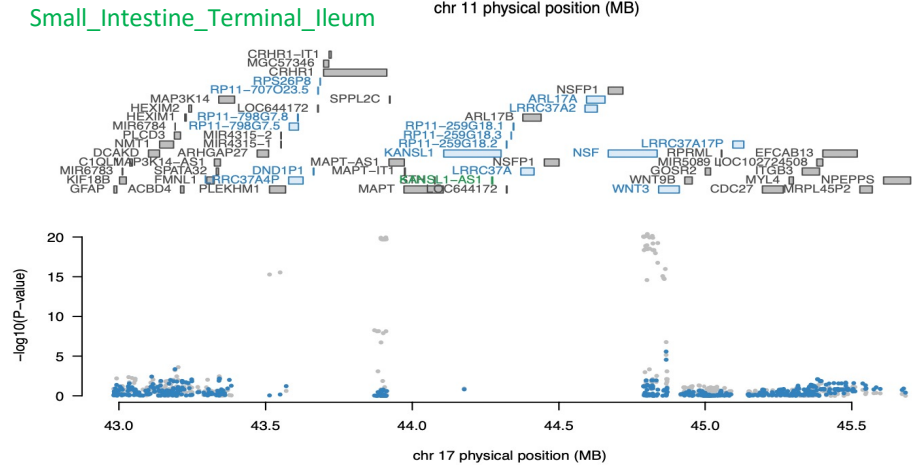
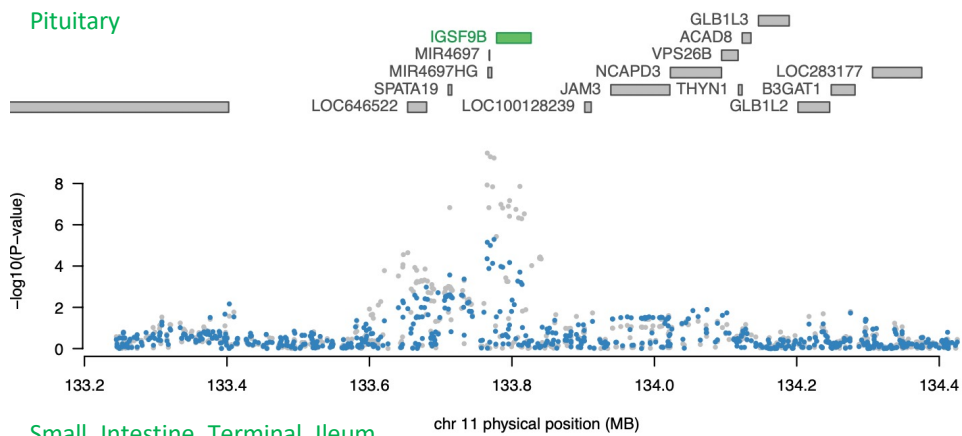
Brain_Cerebellum



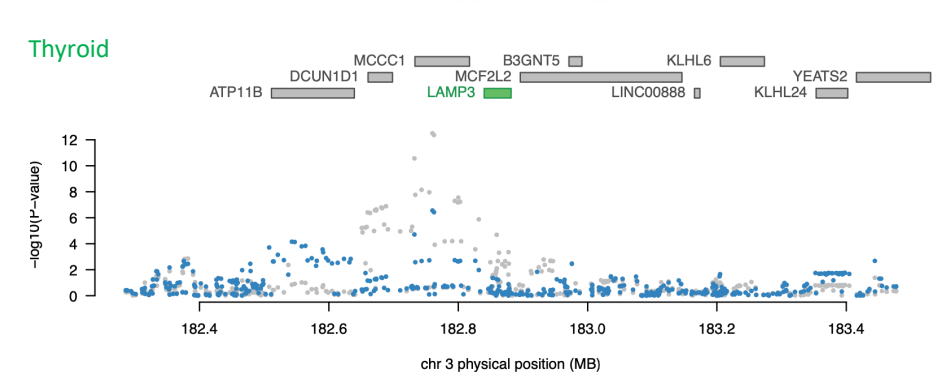
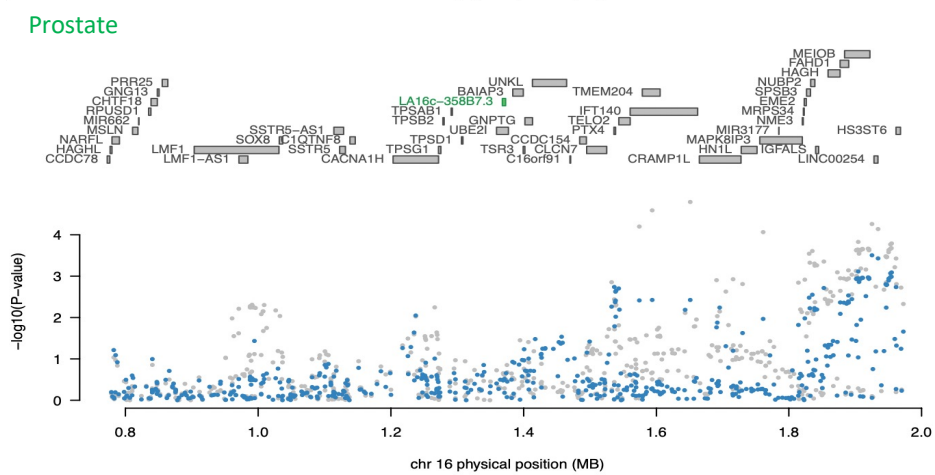
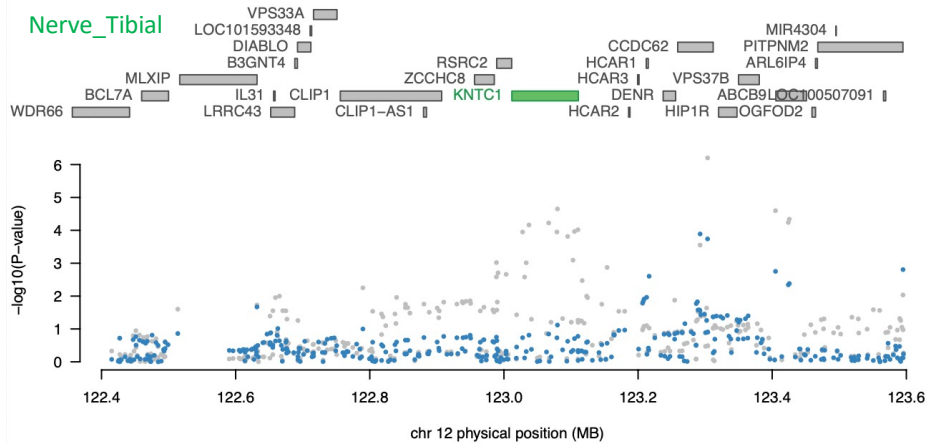
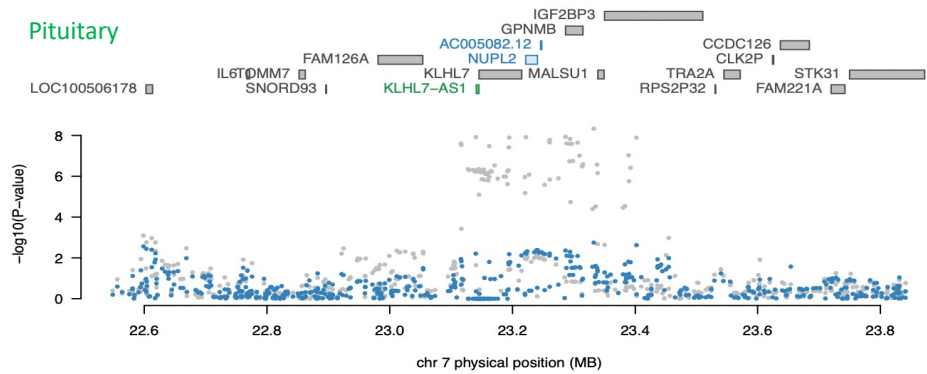
Pancreas



(Supplementary Fig. 2.7) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

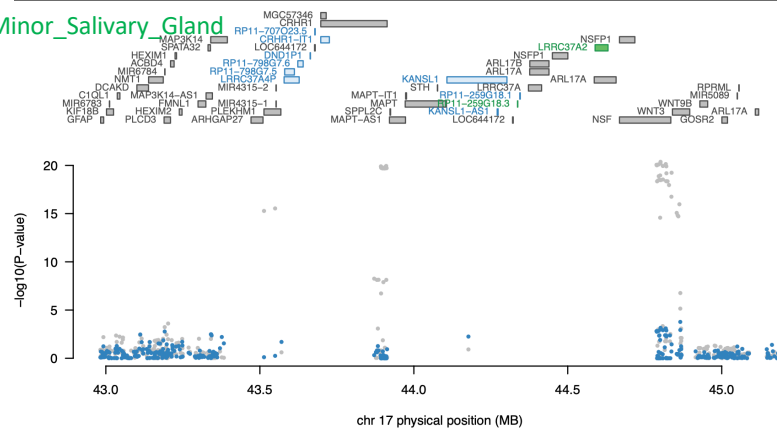


(Supplementary Fig. 2.10) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

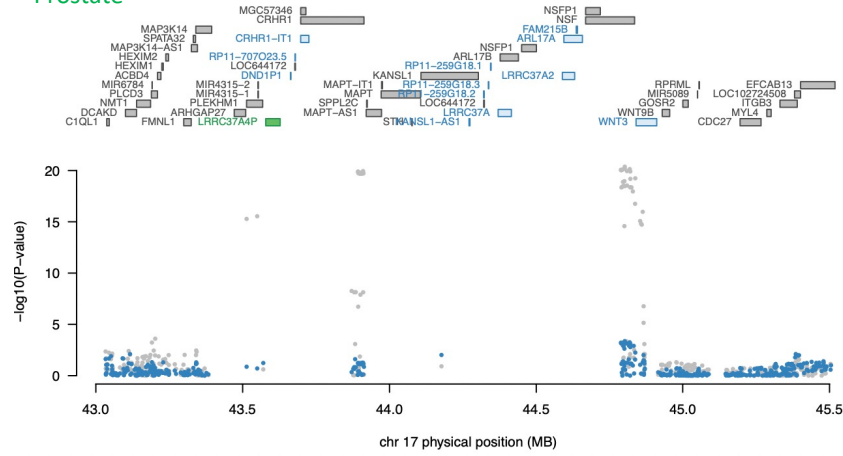


(Supplementary Fig. 2.11) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

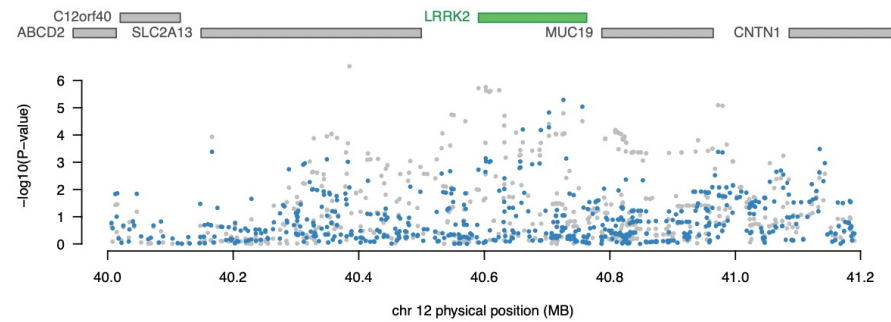
Minor_Salivary_Gland



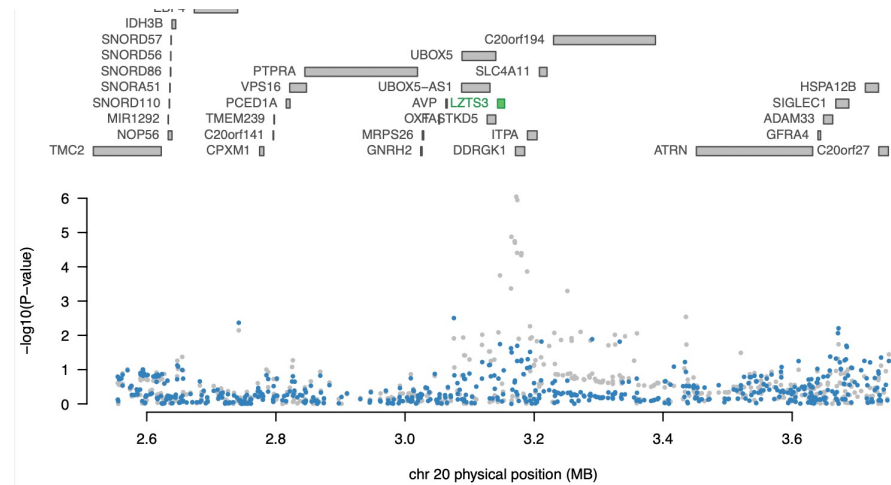
Prostate



Artery_Coronary

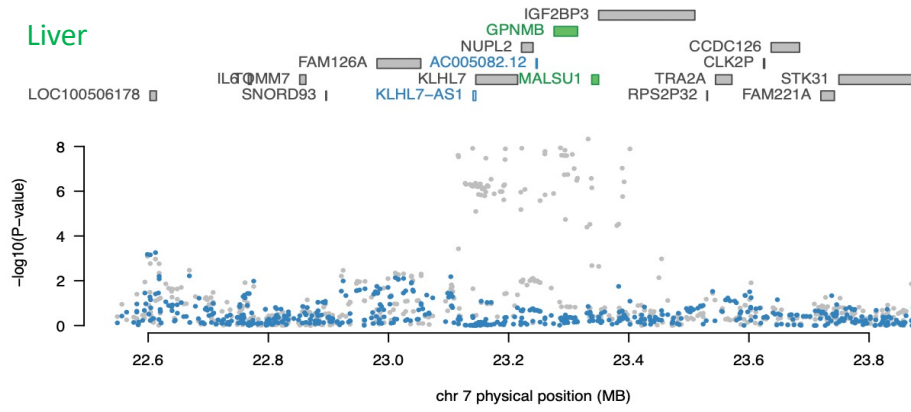


Cells_Transformed_fibroblasts

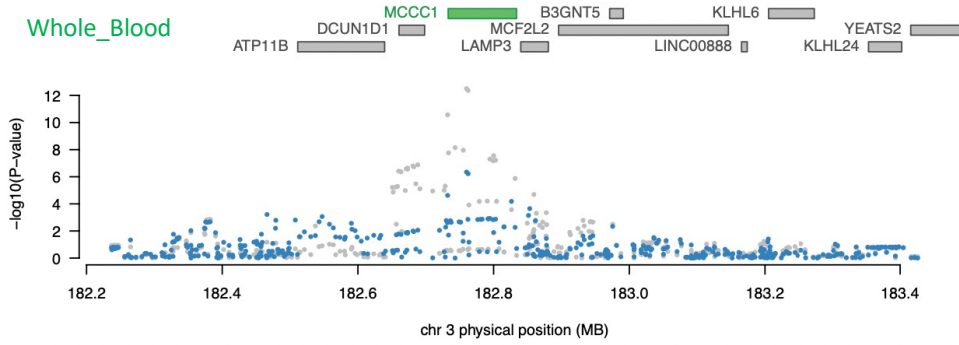


(Supplementary Fig. 2.12) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

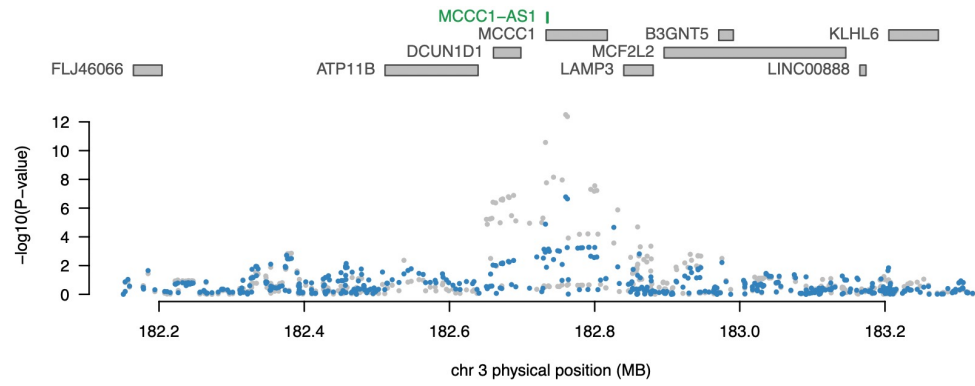
Liver



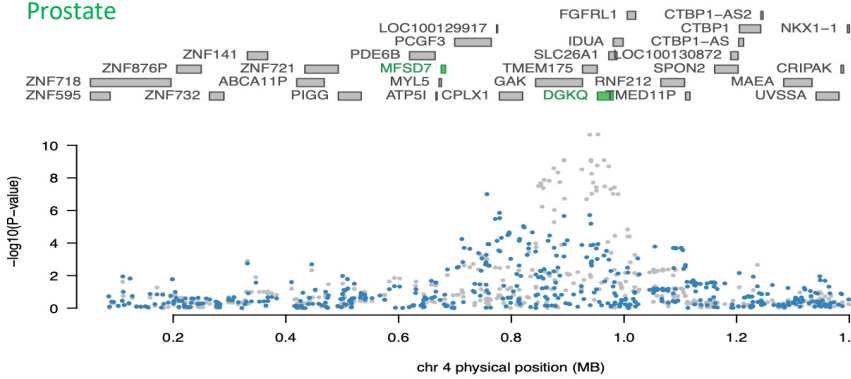
Whole_Blood



Skin_Sun_Exposed_Lower_leg

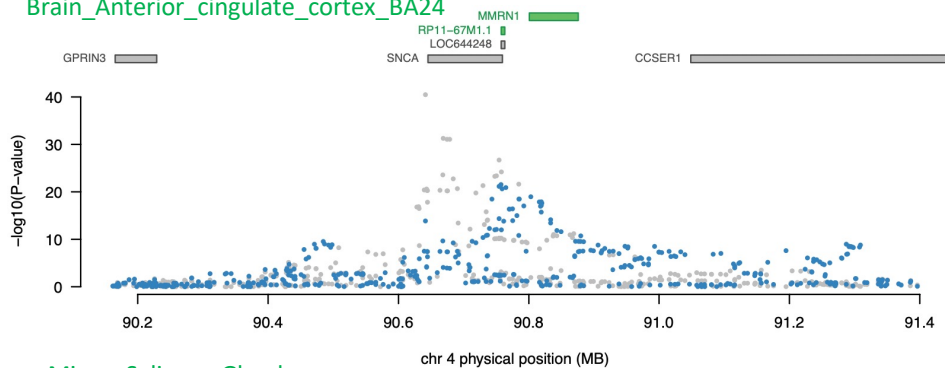


Prostate

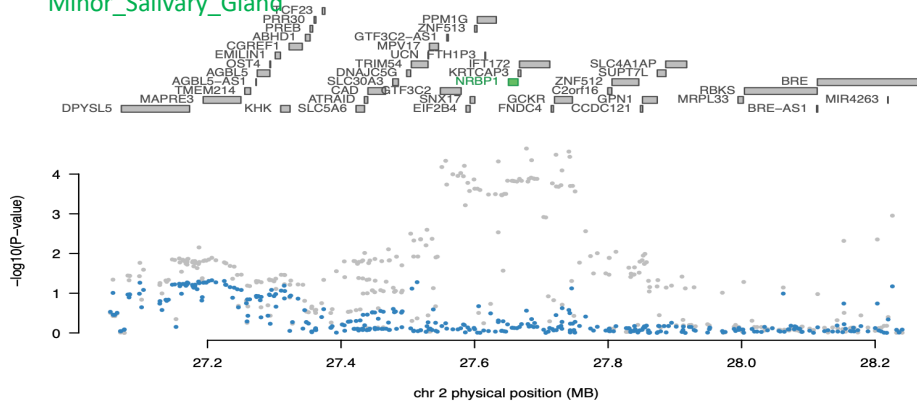


(Supplementary Fig. 2.13) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

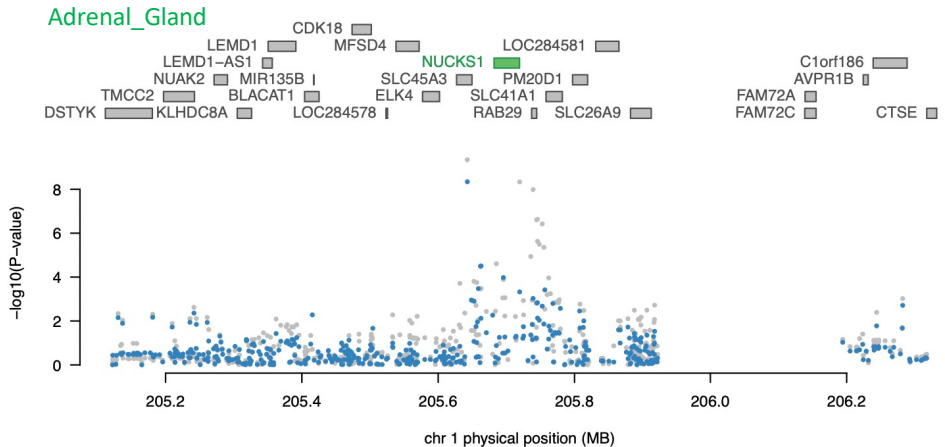
Brain_Anterior_cingulate_cortex_BA24



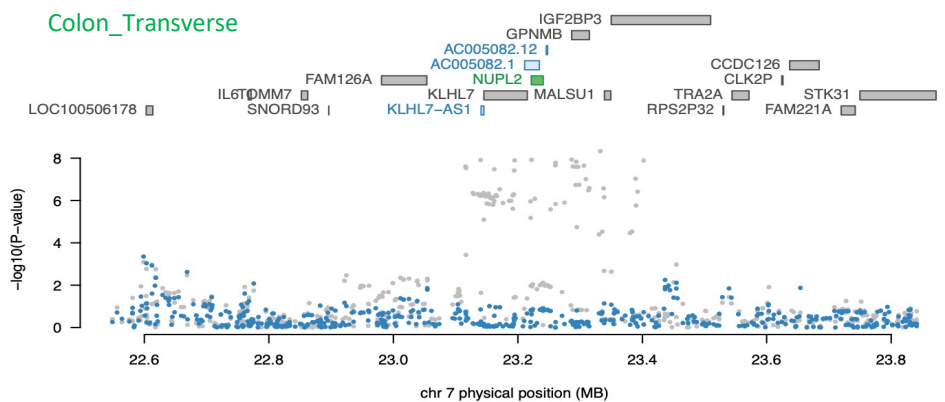
Minor_Salivary_Gland



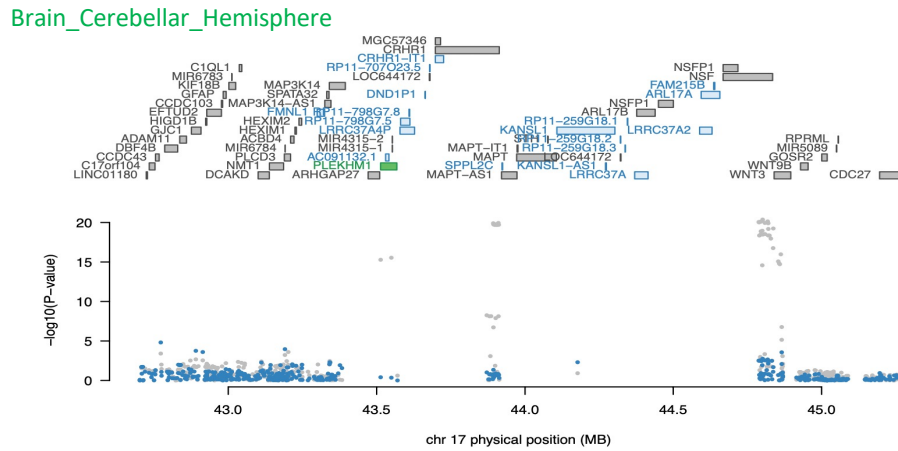
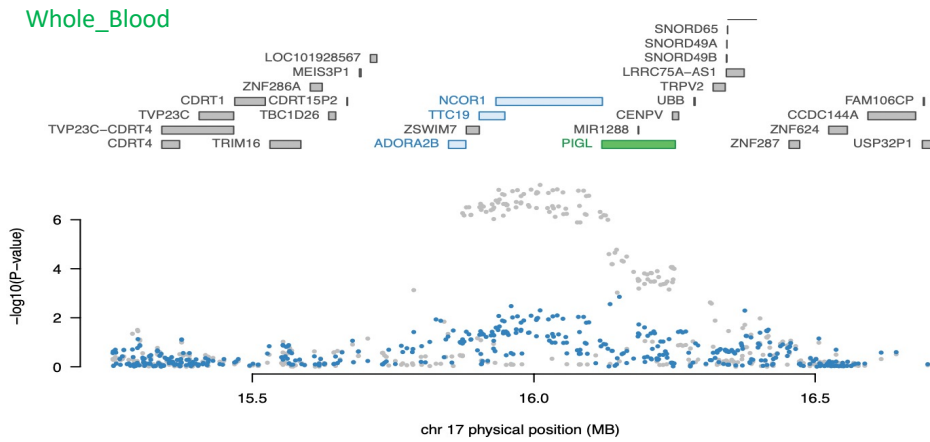
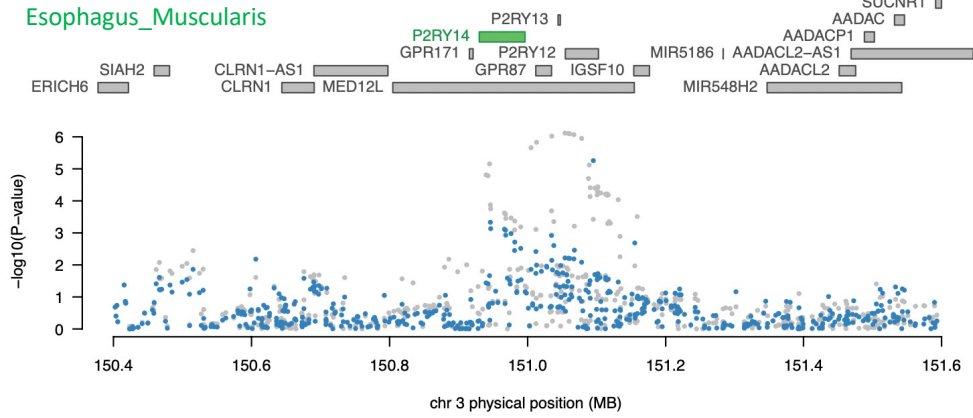
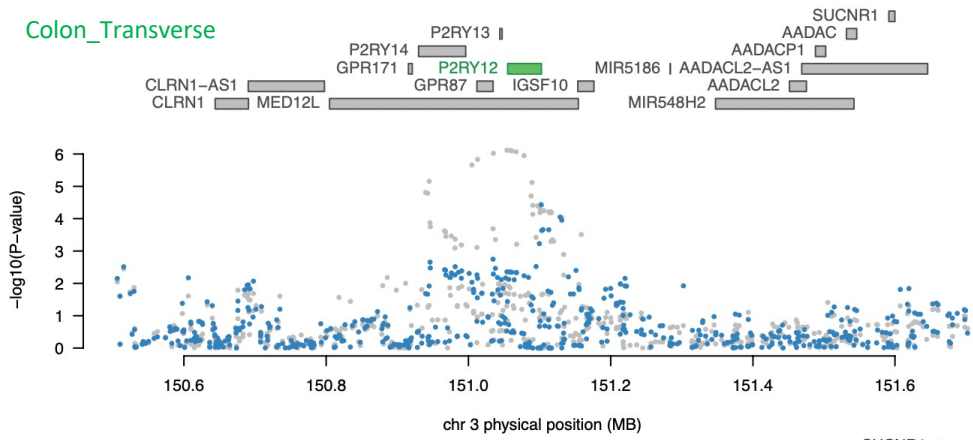
Adrenal_Gland



Colon_Transverse

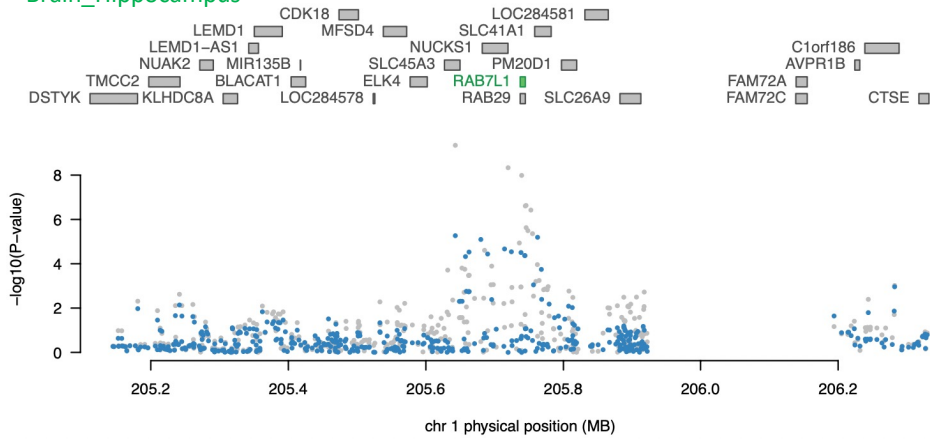


(Supplementary Fig. 2.14) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

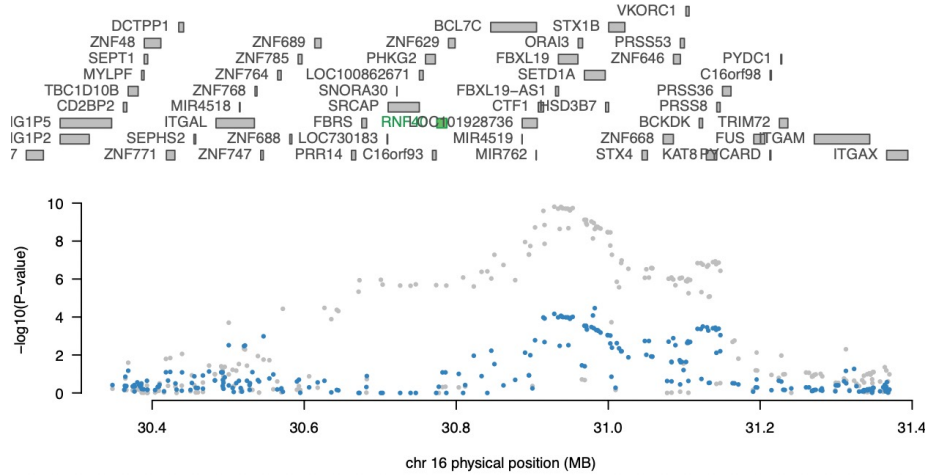


(Supplementary Fig. 2.15) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

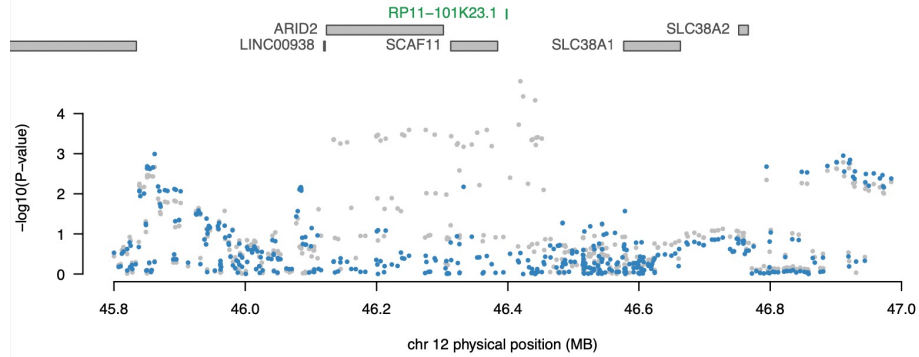
Brain_Hippocampus



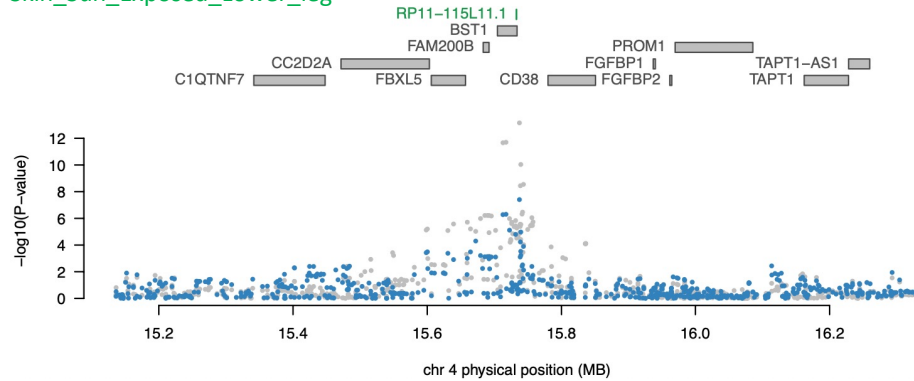
Brain_Substantia_nigra



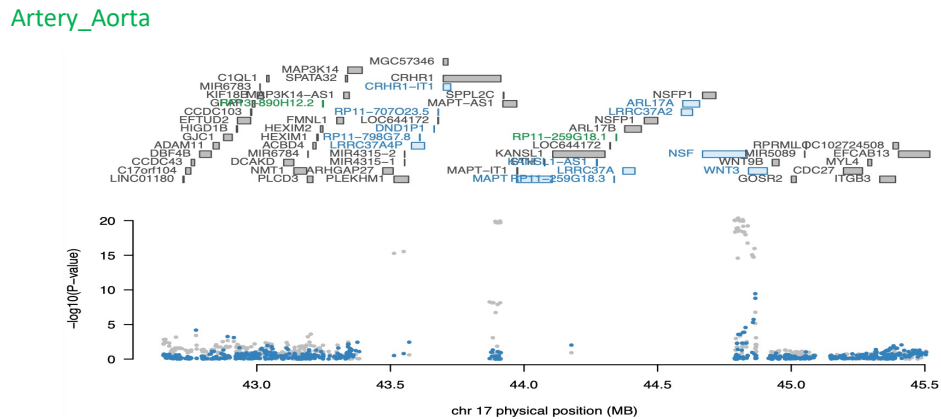
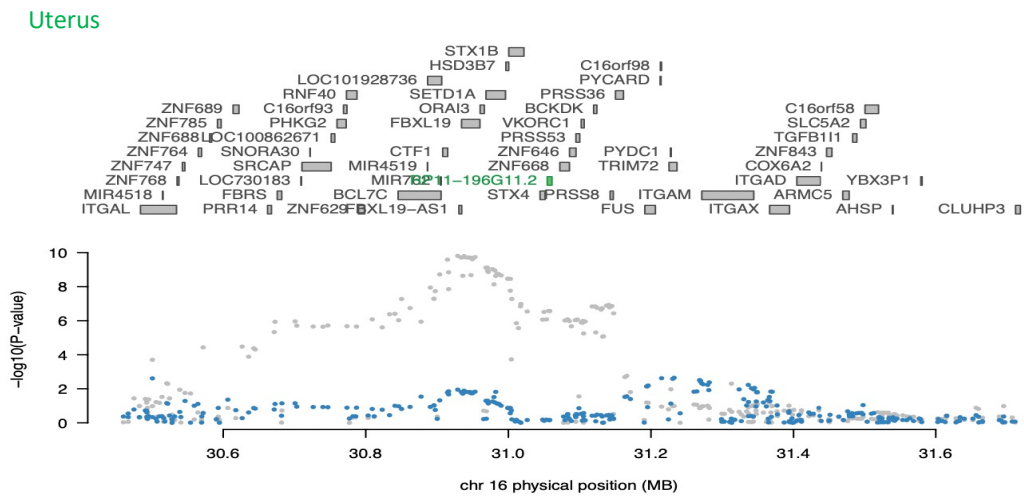
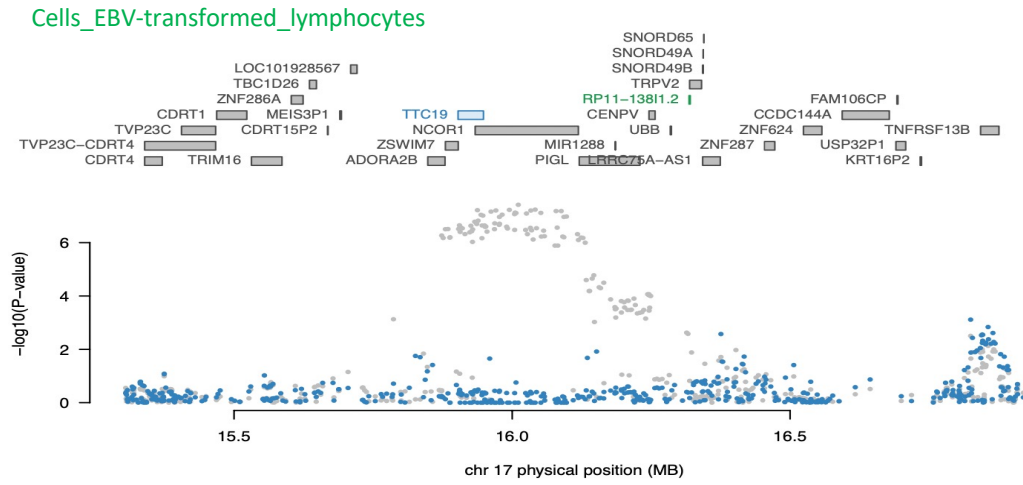
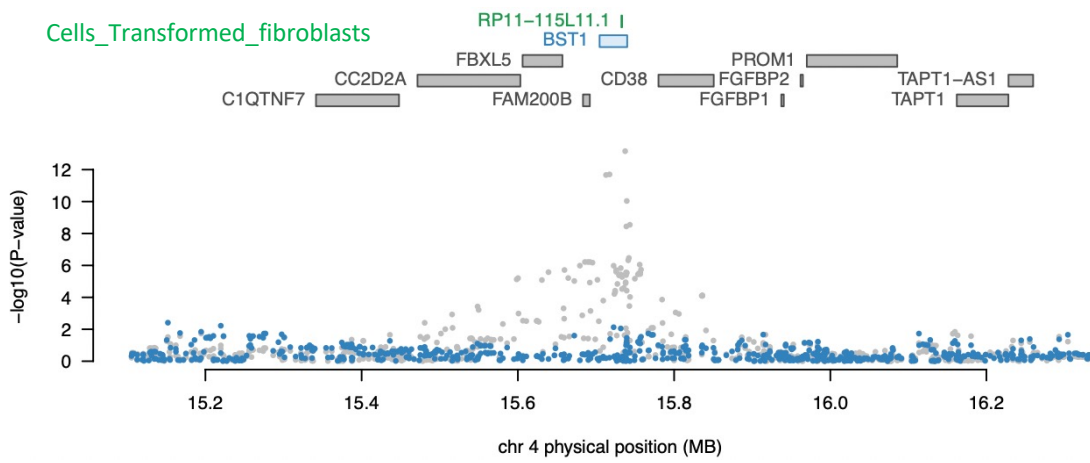
Testis



Skin_Sun_Exposed_Lower_leg

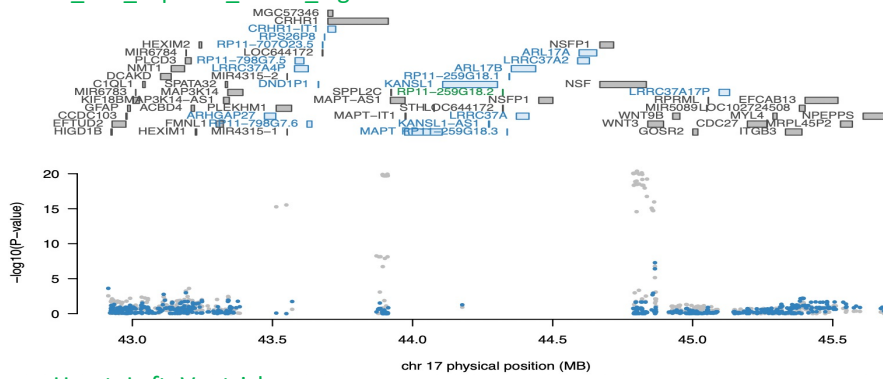


(Supplementary Fig. 2.17) FUSION plots of PD TWAS locus. Reference panel(GTEx tissues) are shown for each plot.

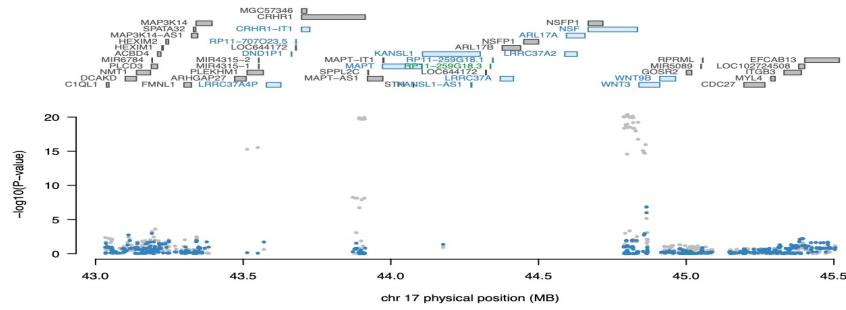


(Supplementary Fig. 2.18) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

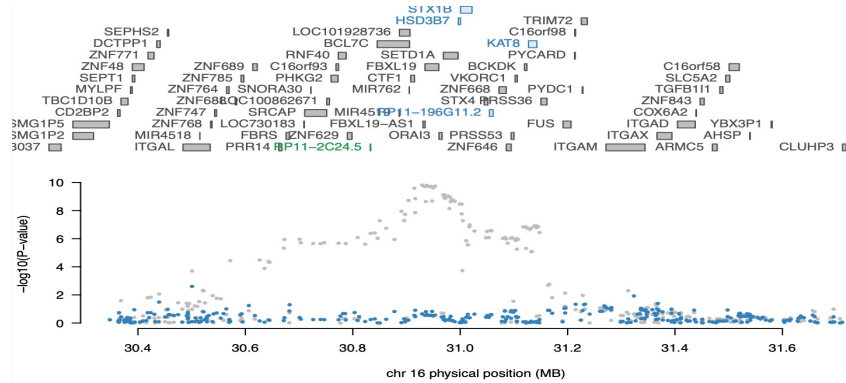
Skin_Sun_Exposed_Lower_leg



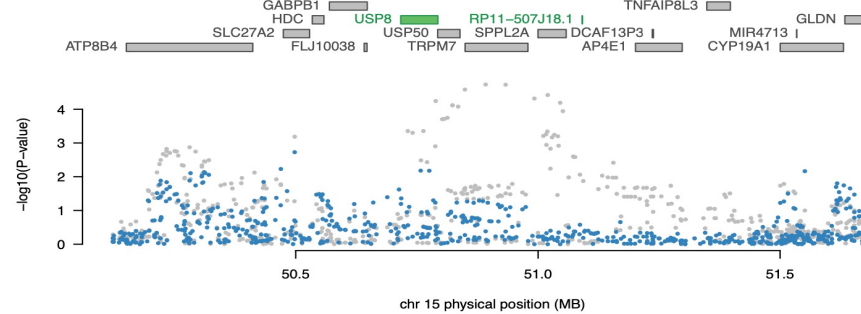
Heart_Left_Ventricle



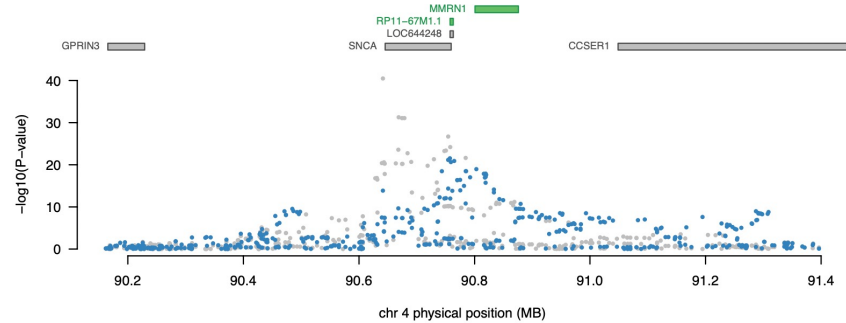
Artery_Aorta



Muscle_Skeletal

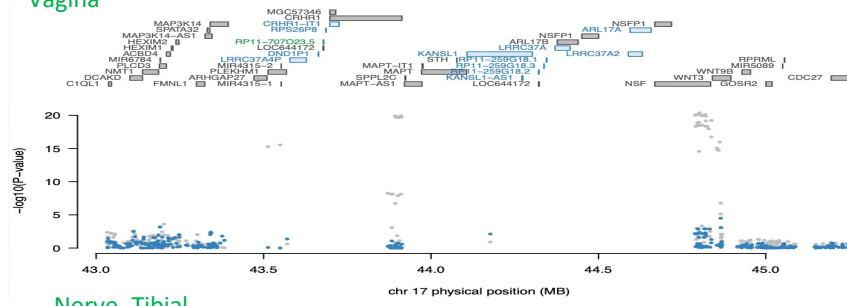


Brain_Anterior_cingulate_cortex_BA24

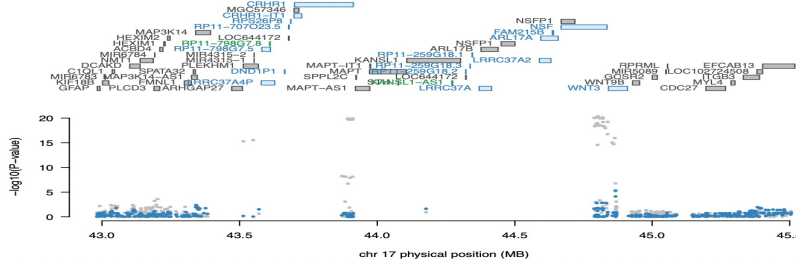


(Supplementary Fig. 2.19) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

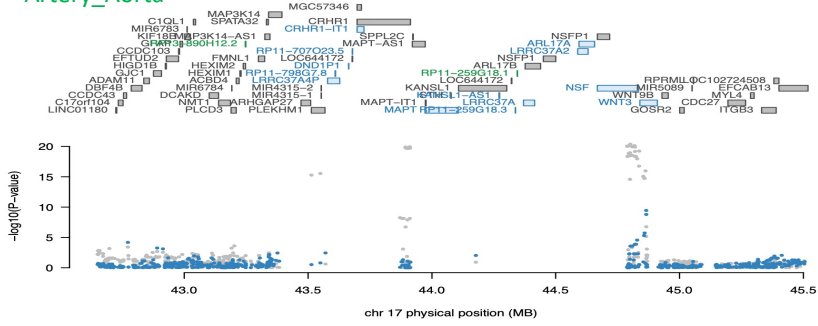
Vagina



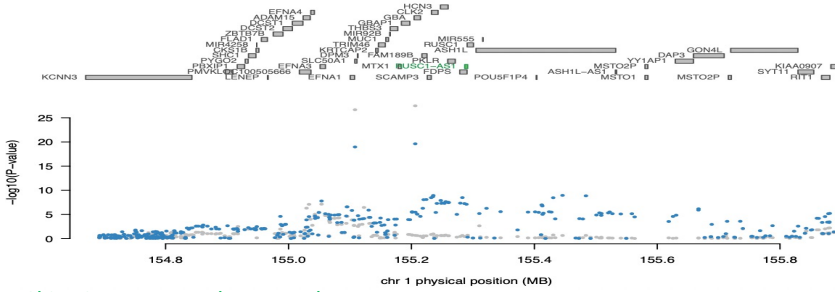
Nerve_Tibial



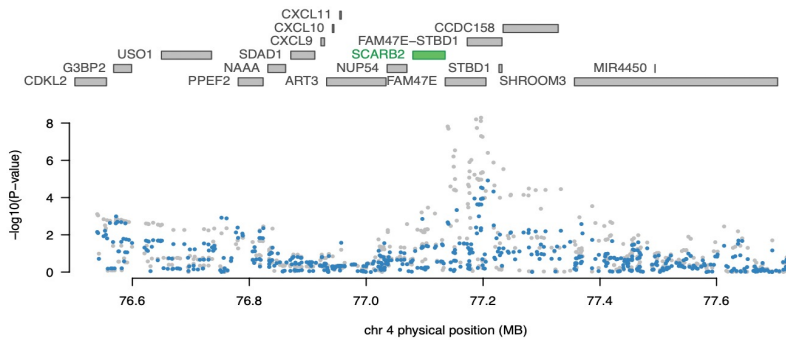
Artery_Aorta



Brain_Putamen_basal_ganglia

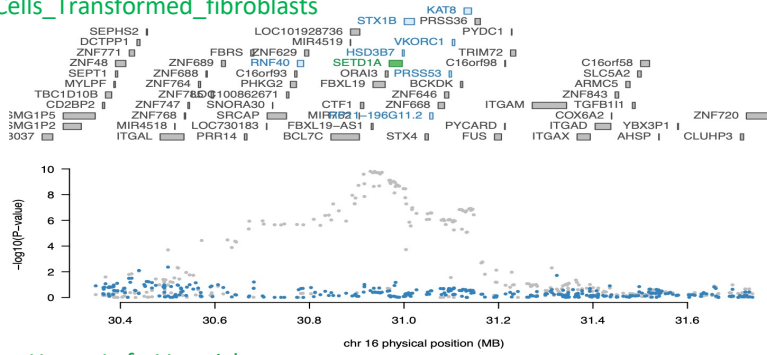


Skin_Sun_Exposed_Lower_leg

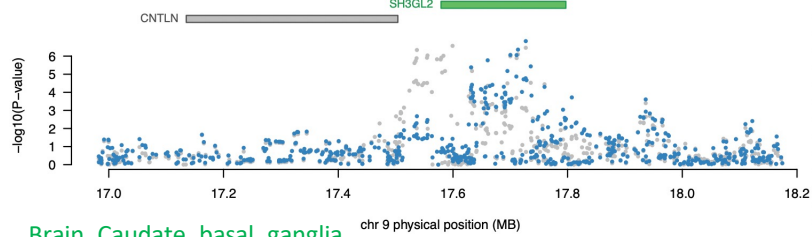


(Supplementary Fig. 2.20) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.

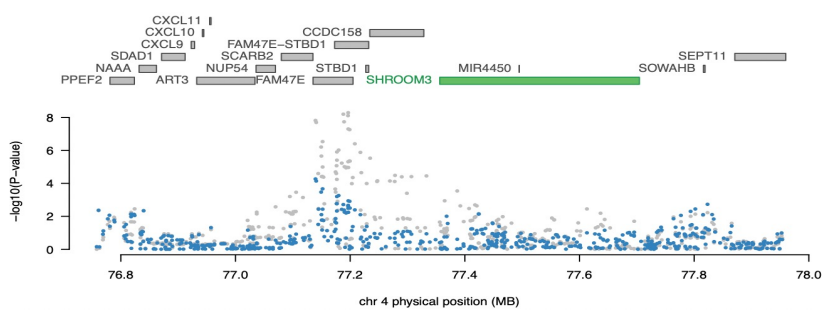
Cells_Transformed_fibroblasts



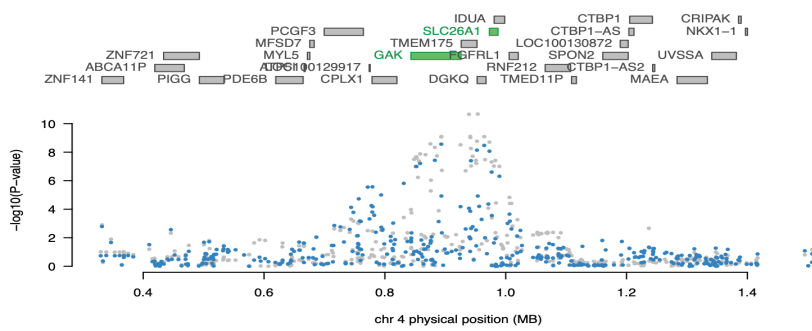
Heart_Left_Ventricle



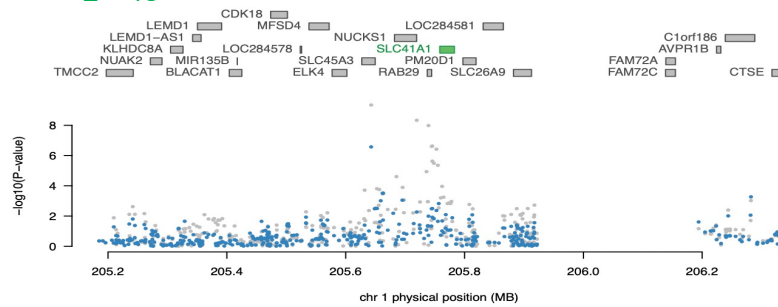
Brain_Caudate_basal_ganglia



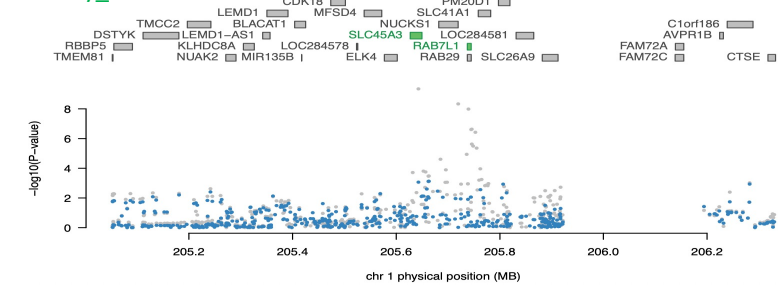
Brain_Cerebellar_Hemisphere



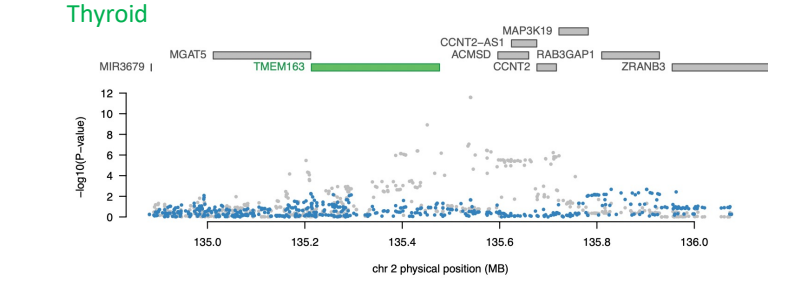
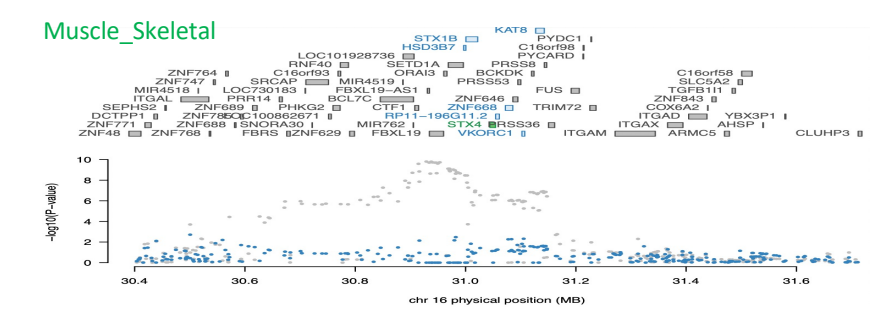
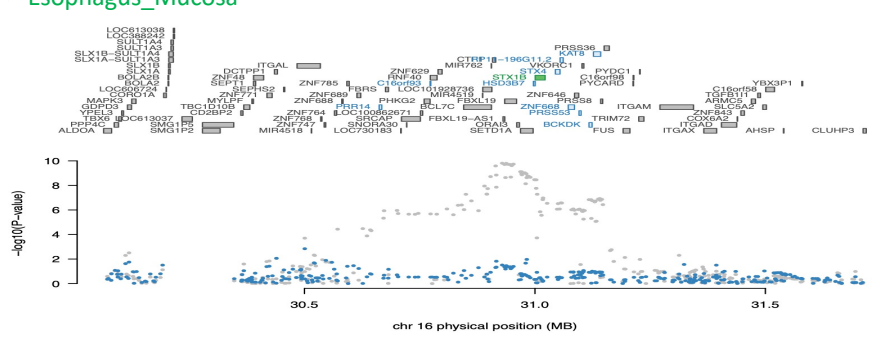
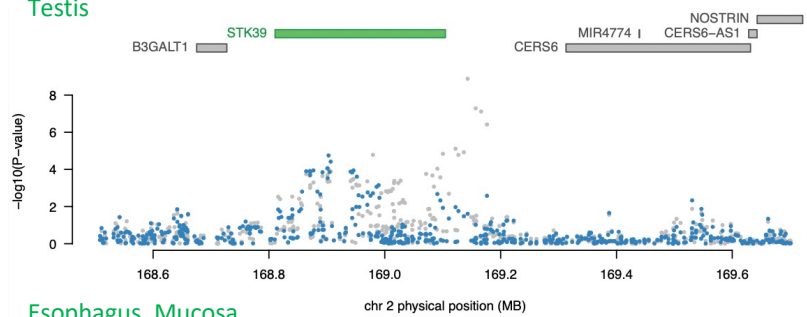
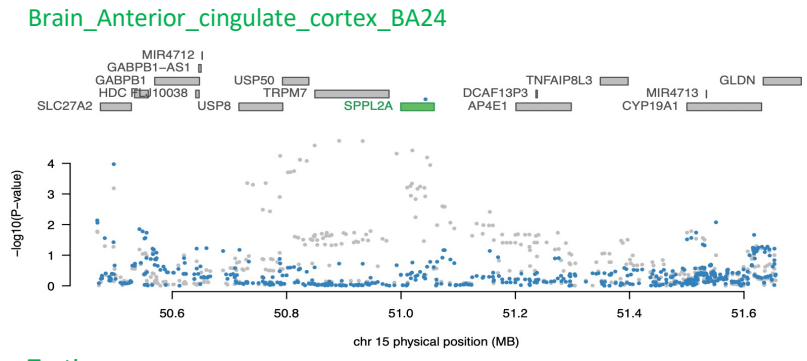
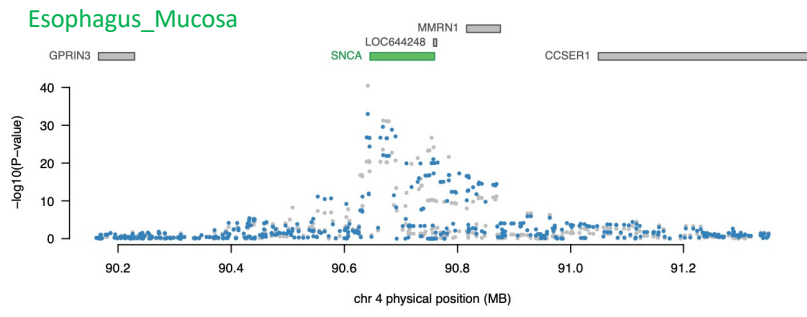
Brain_Amygdala



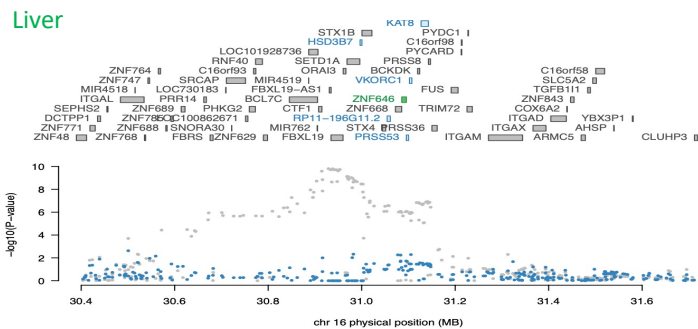
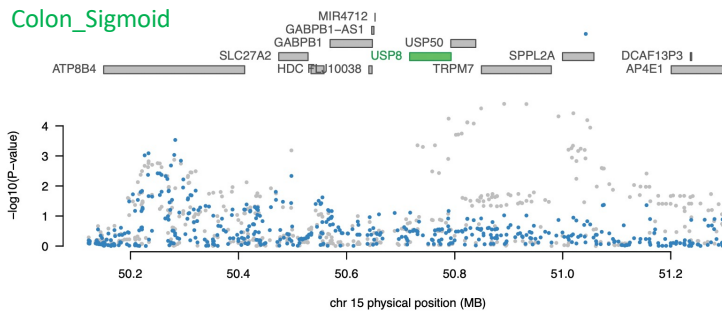
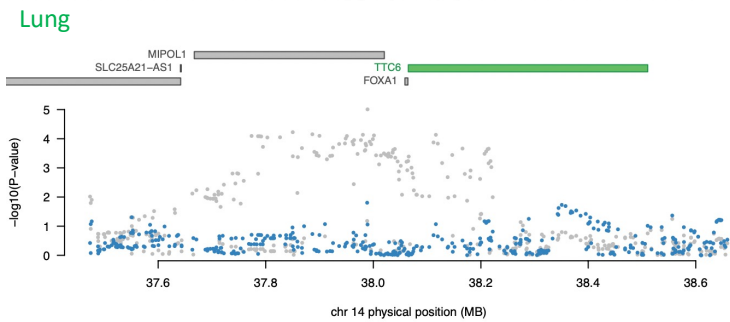
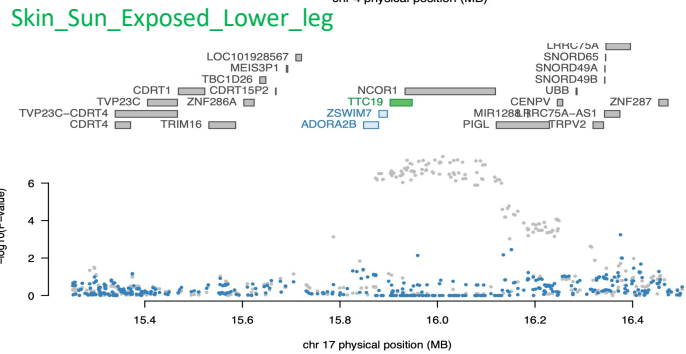
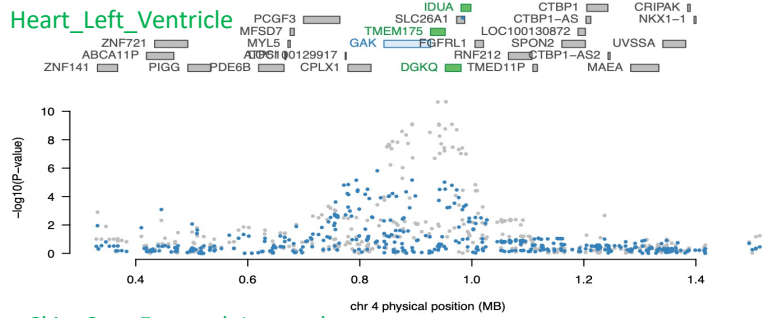
Artery_Tibial



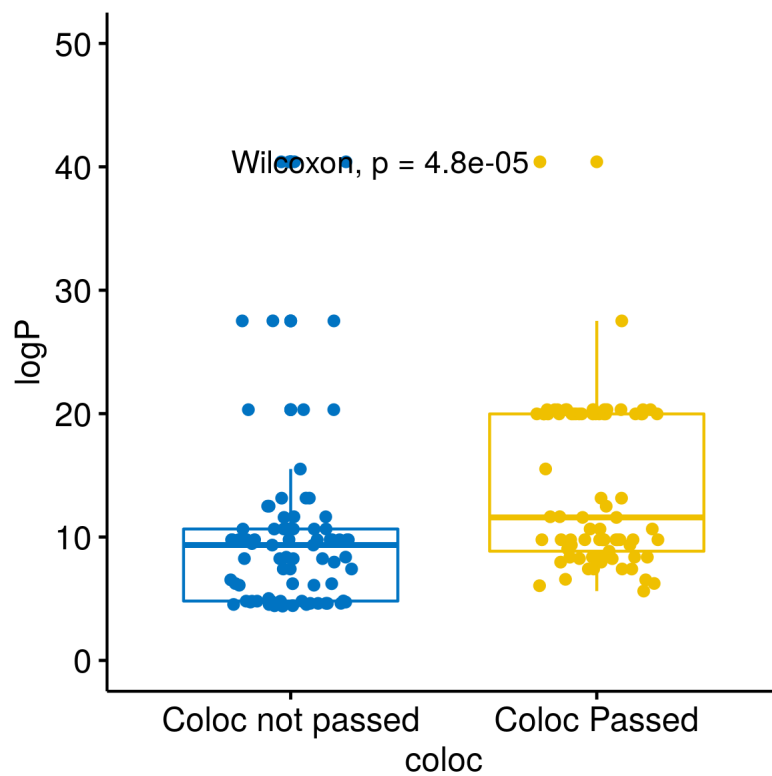
(Supplementary Fig. 2.21) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.



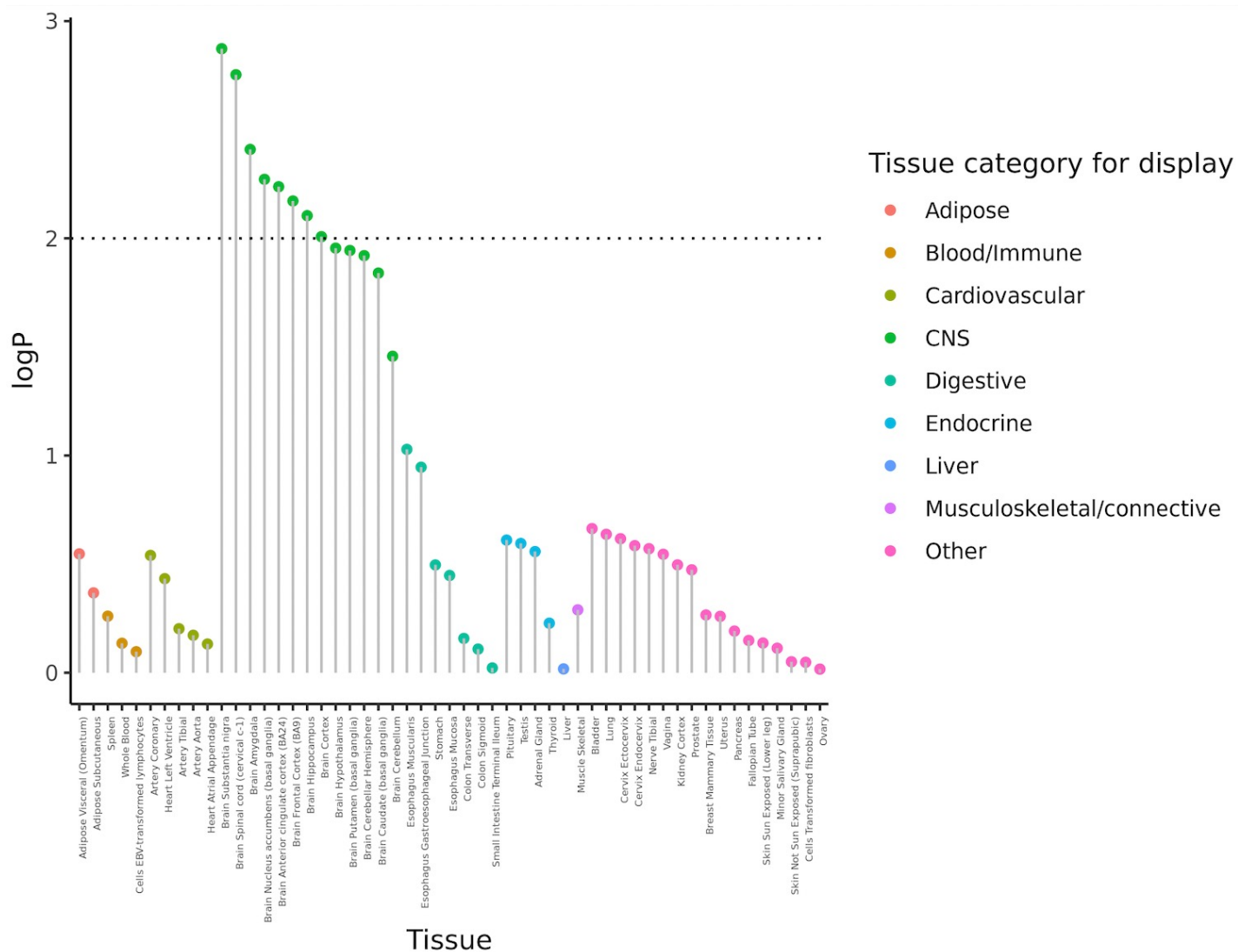
(Supplementary Fig. 2.22) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.



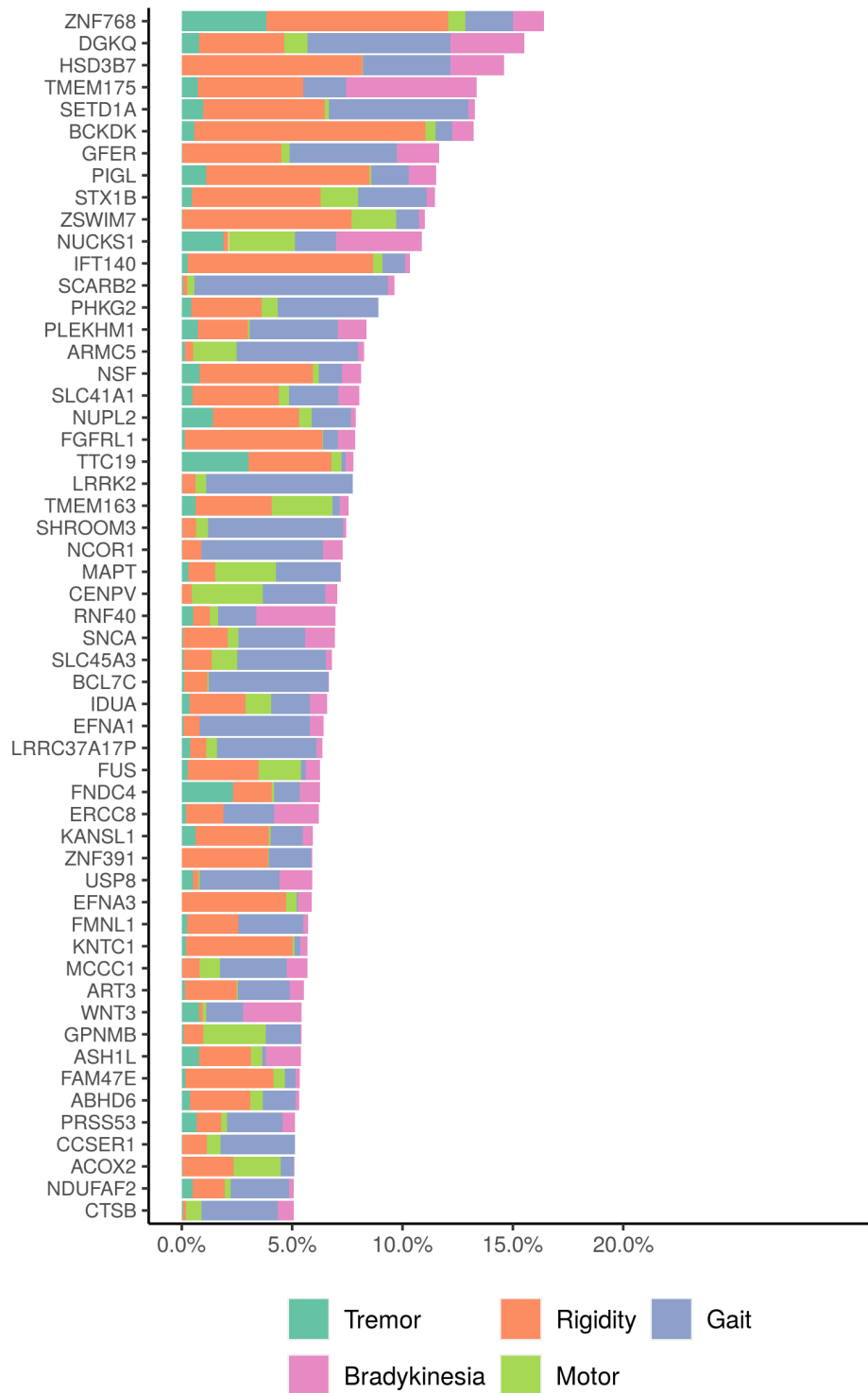
(Supplementary Fig. 2.23) FUSION plots of PD TWAS locus. Reference panel(GTEX tissues) are shown for each plot.



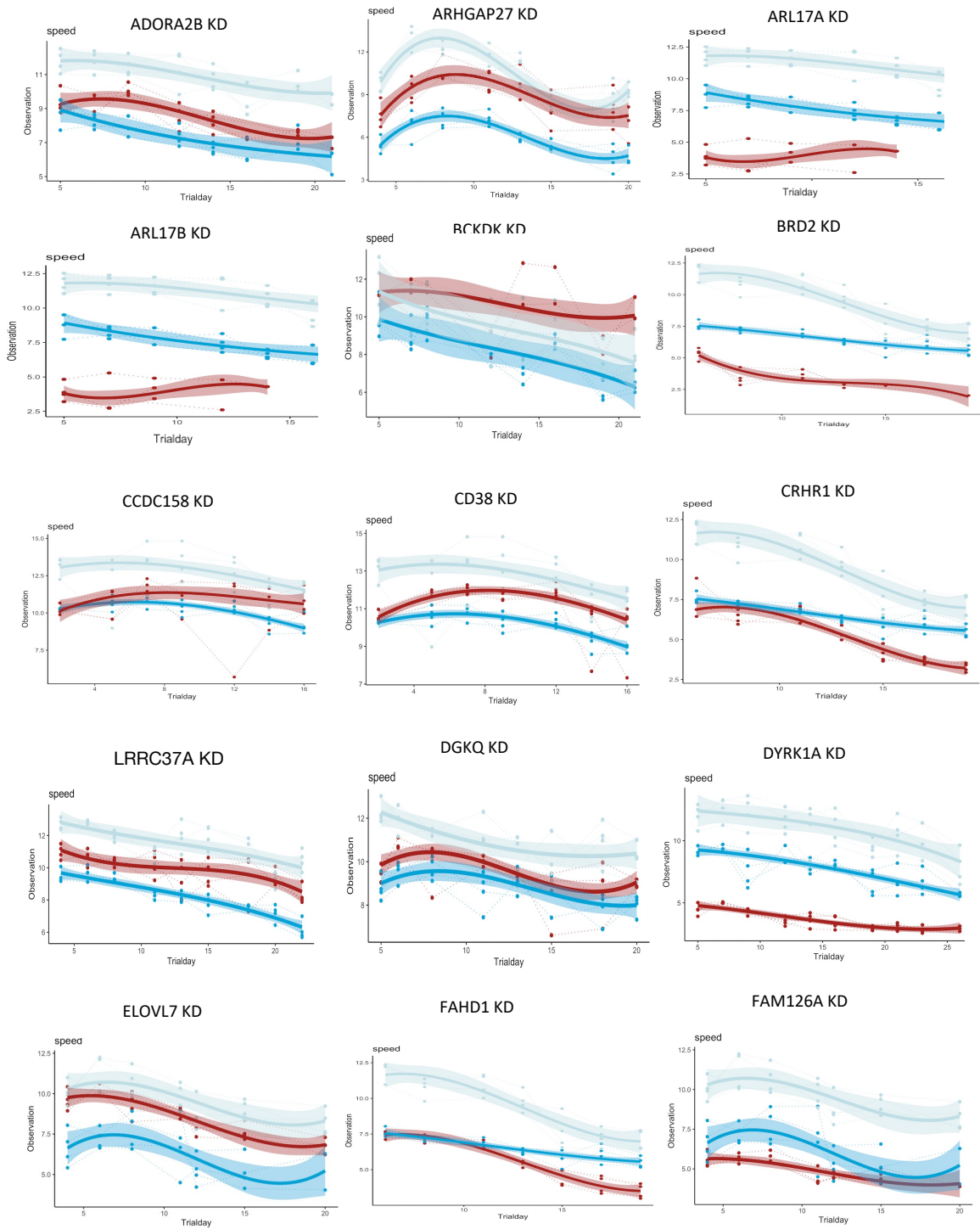
(Supplementary Fig. 3.) TWAS-prioritized genes whose GWAS signals colocalized with eQTL signals have more GWAS significance compared to genes that do not show colocalize with eQTLs. Wilcoxon test was used to access the difference.



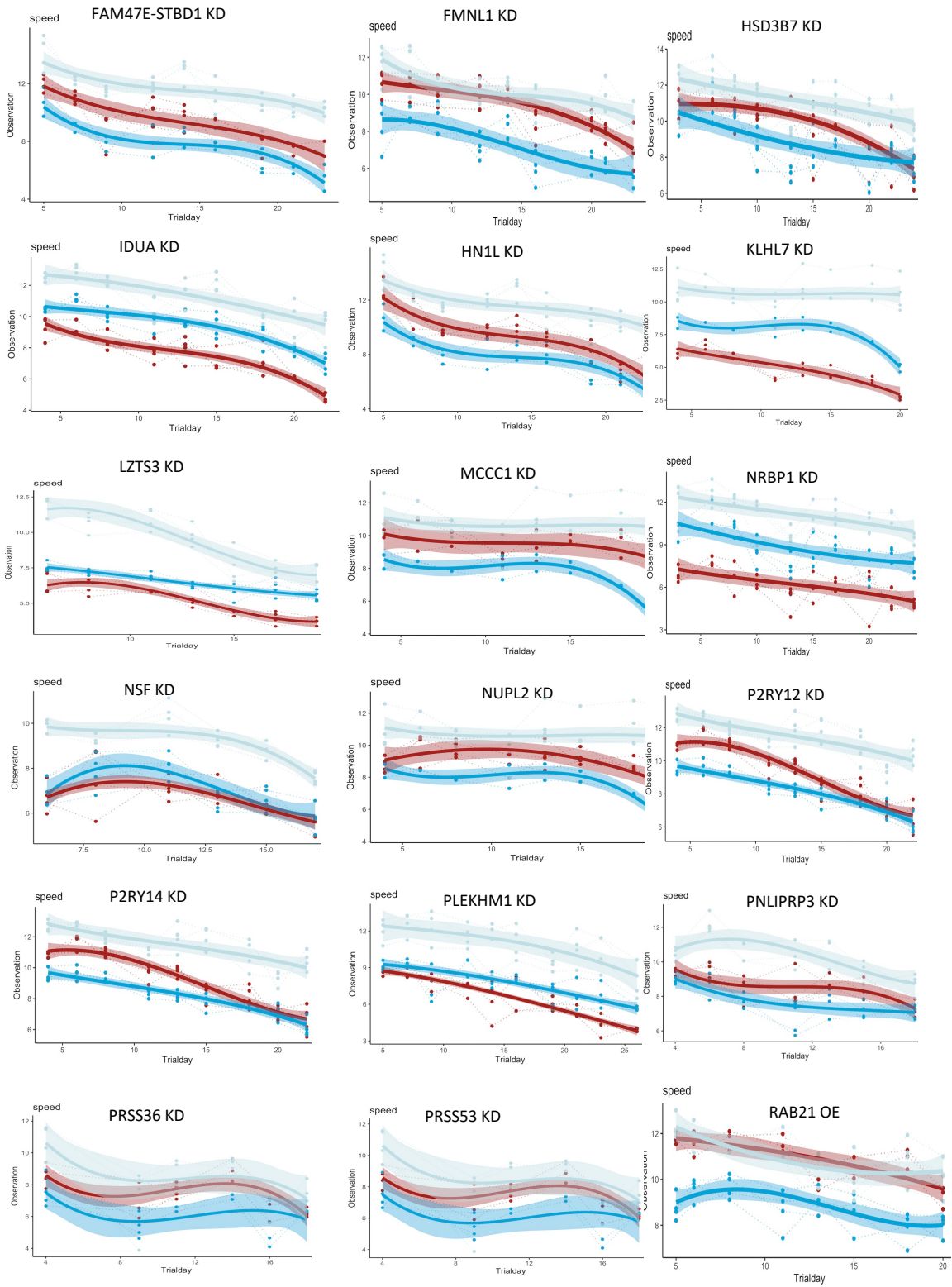
(Supplementary Fig. 4.) Multi-tissue analysis to select PD-relevant tissues via linkage disequilibrium (LD) score regression in specifically expressed genes. Among 53 tissues accessed in the GTEx project, 8 brain-derived tissues were significantly enriched ($p < 0.05$) for PD heritability in regions surrounding specifically expressed genes.



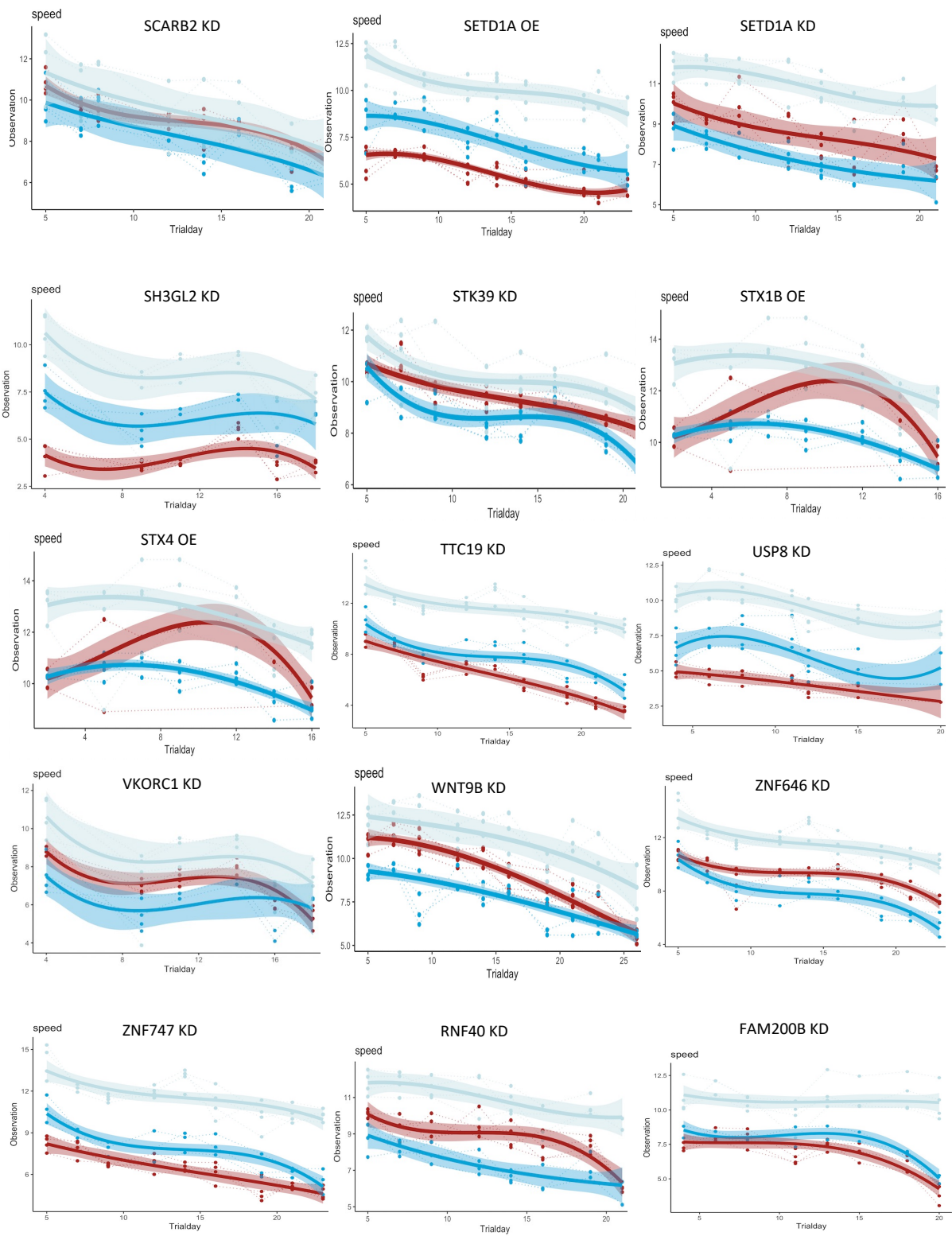
Supplementary Fig. 5. Result of applying a linear mixed model to correlate genes expression with clinical traits. The 55 shown PD candidates correspond to genes whose differences in expression are correlated with 5% or more of the summed variance of the indicated clinical traits among defined PD cases and controls.



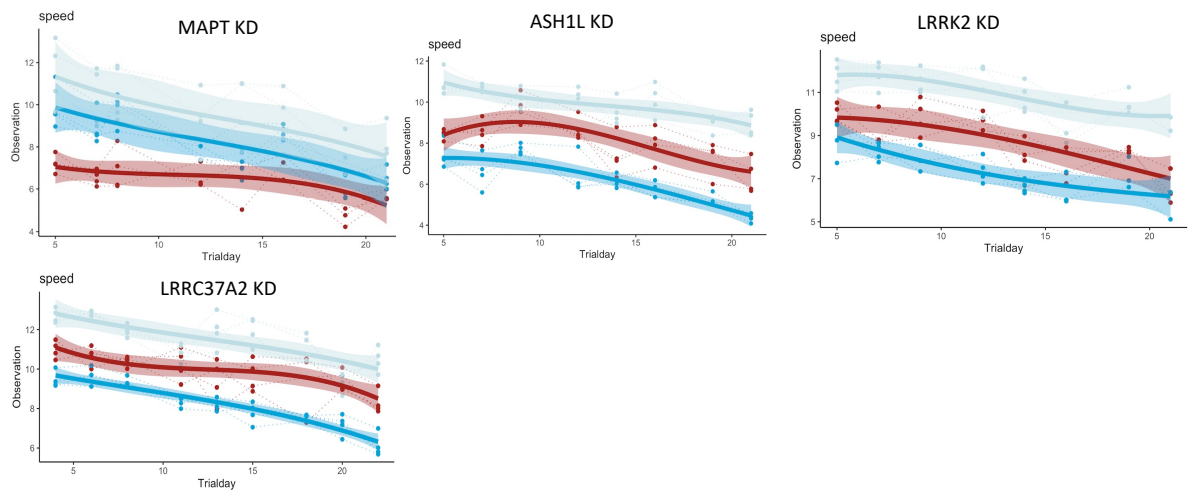
Supplementary figure 6.1



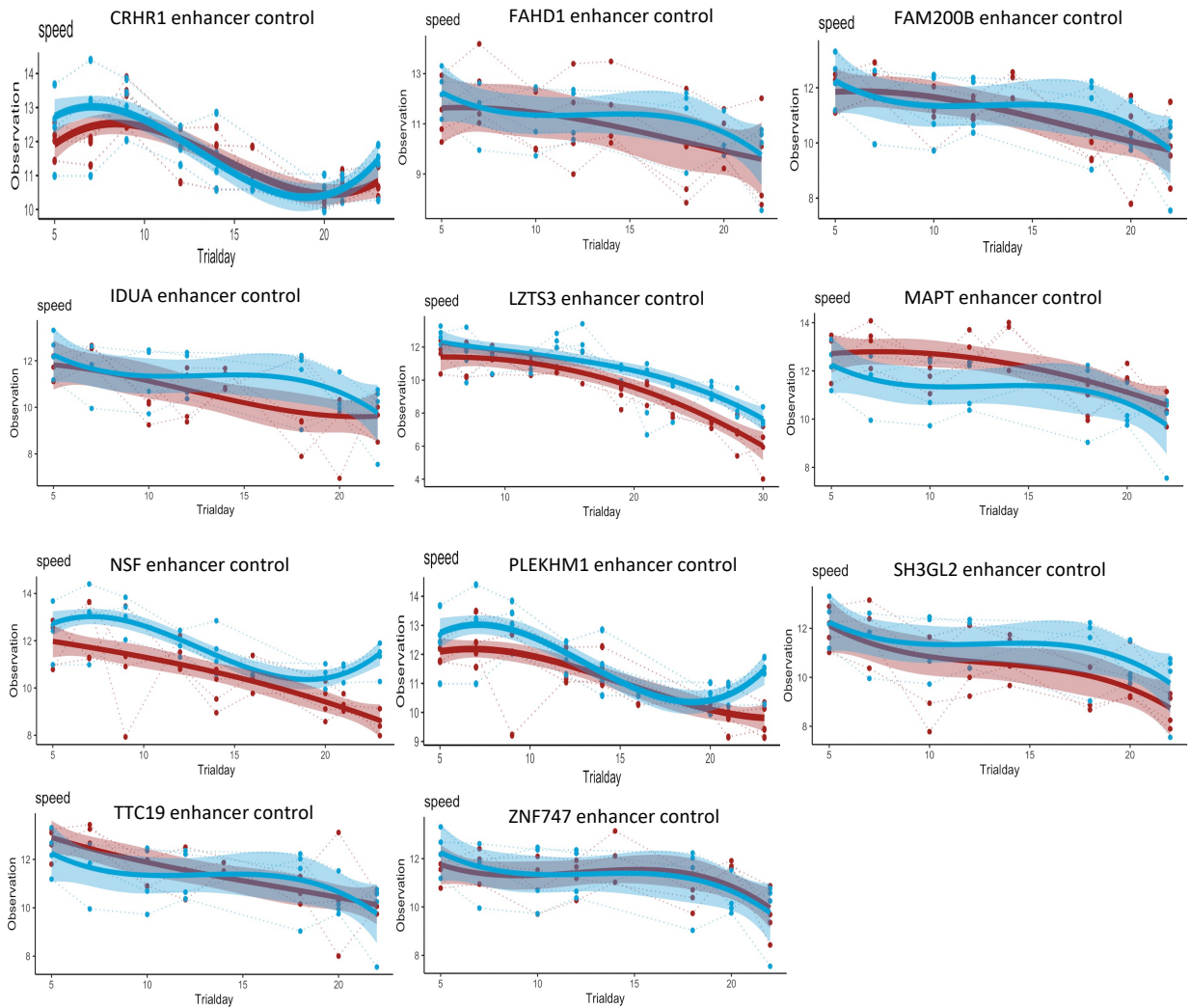
Supplementary figure 6.2



Supplementary figure 6.3



Supplementary figure 6.1-6.4. Specific graphs depicting speed as a function of age for the alleles listed in Figure 4B, which match to the modifiers. Negative controls with scrambled hp-RNA are shown in grey. Blue depicts the age-related performance of α -syn/scramble. The performance of animals harboring the allele indicated on top and α -syn is shown in red. Third degree polynomial regressions (lines), confidence intervals (shaded area), and individual data are shown in the graphs (dots). When examined using the linear mixed effect model ANOVA, all studies shown are statistically substantially different ($p < 0.05$).



Supplementary figure 6.5. Specific graphs depicting speed as a function of age for the alleles listed in Figure 4B, which match to the enhancers. Blue lines indicate the motor performance of negative controls (*elav_{C155}/w¹¹¹⁸*). Red line shows motor performance of animals carrying the indicated modifier alleles but not expressing human α -syn. Note that some modifiers impair motor performance of both the negative controls (*elav_{C155}/w¹¹¹⁸*) and the PD animals