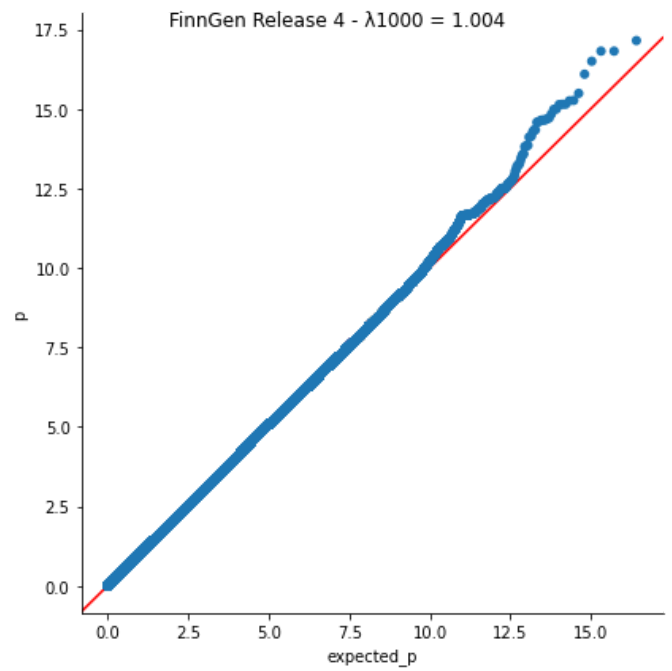
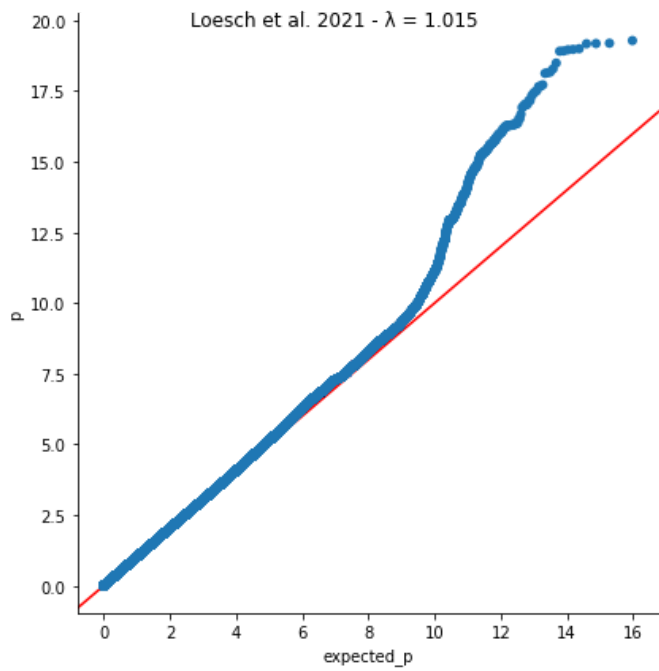
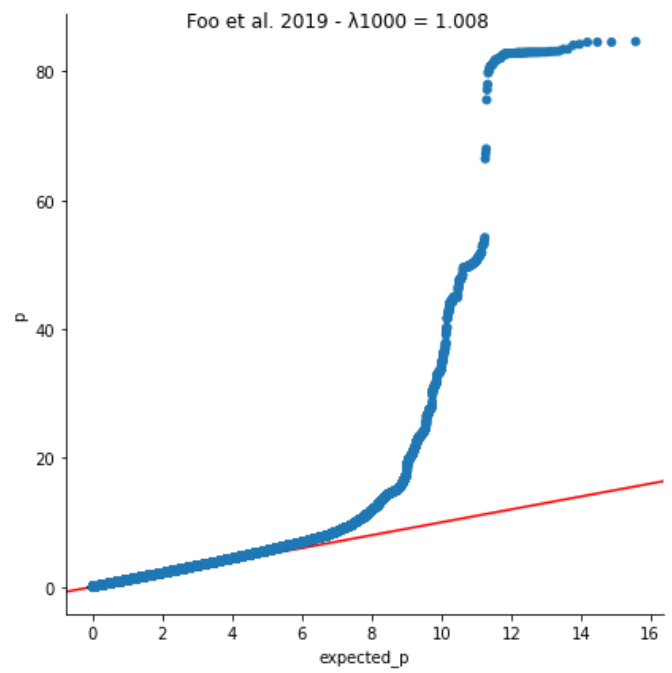
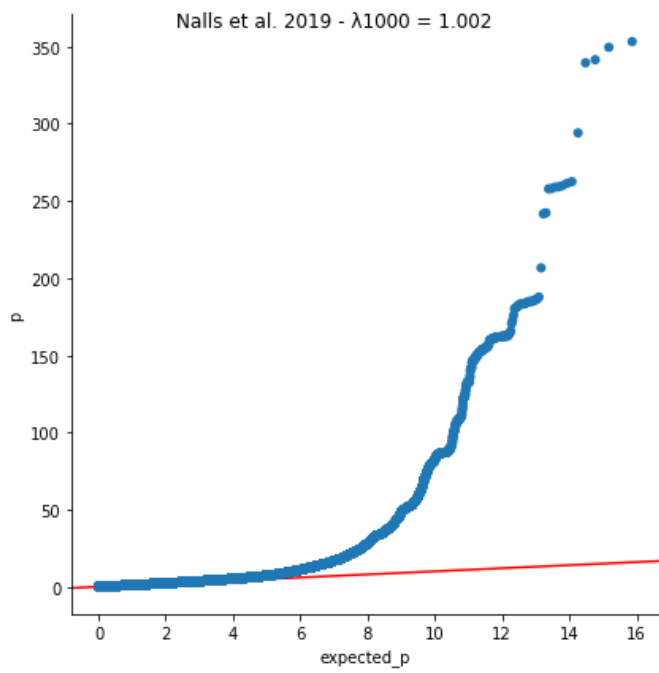


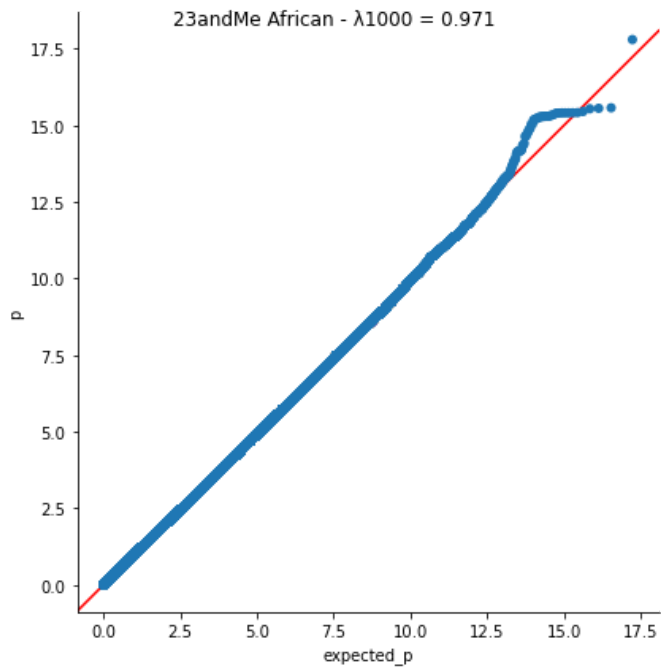
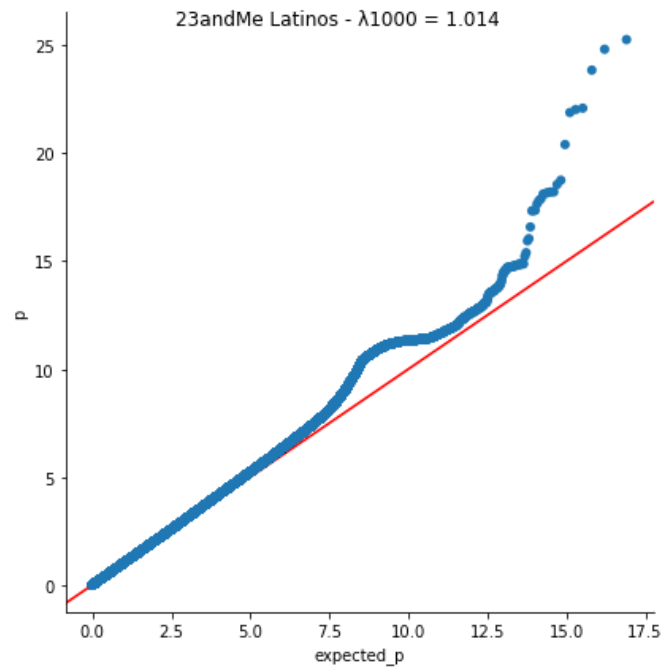
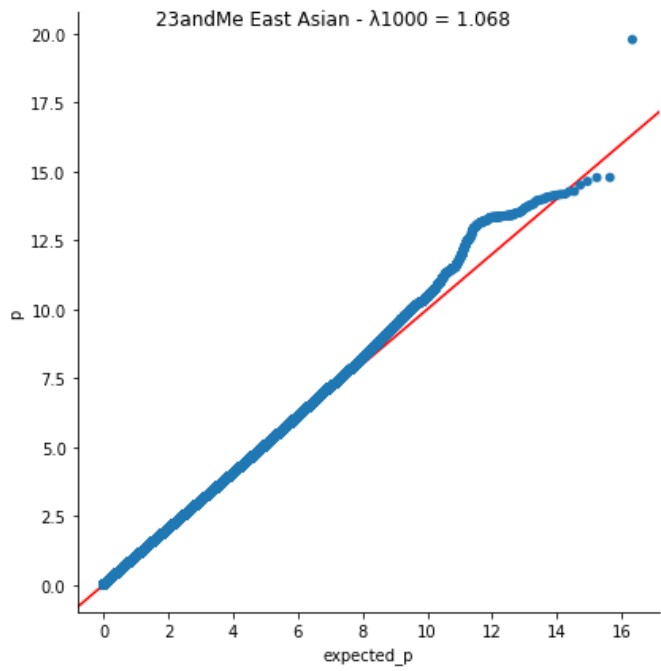


Multi-ancestry genome-wide association meta-analysis of Parkinson's disease

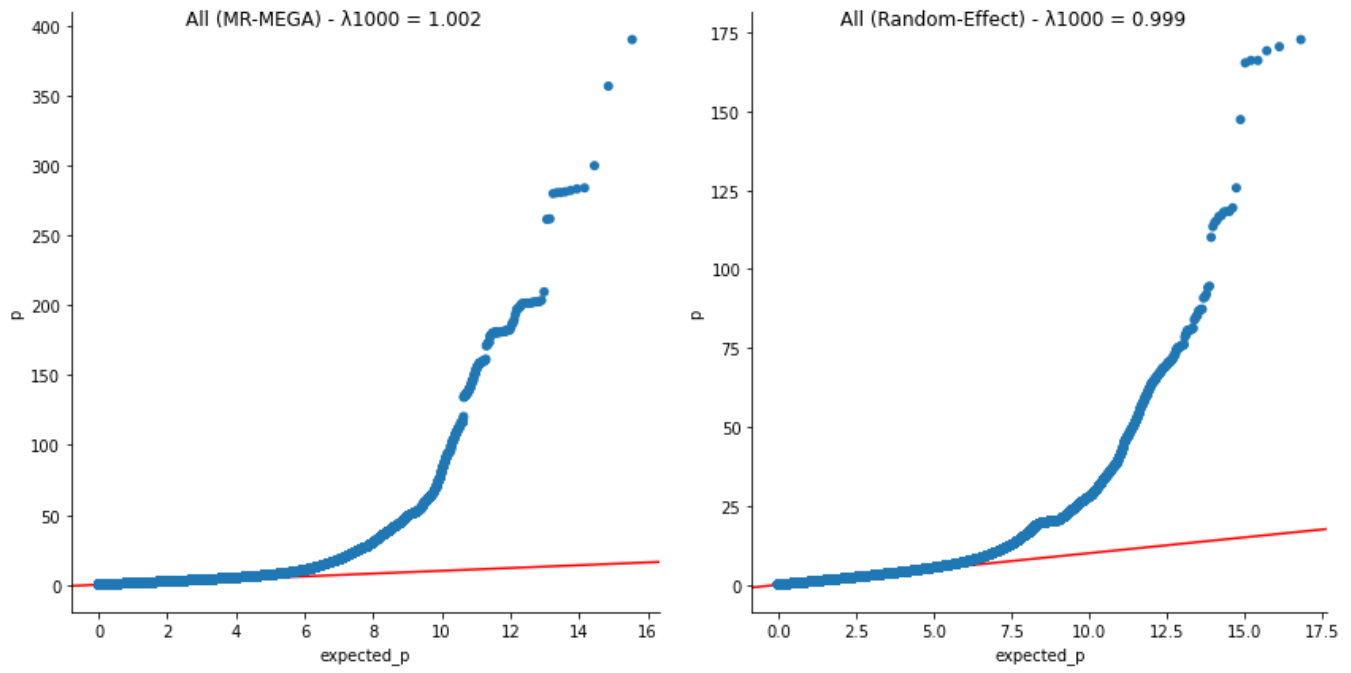
In the format provided by the authors and unedited

Supplementary Figures

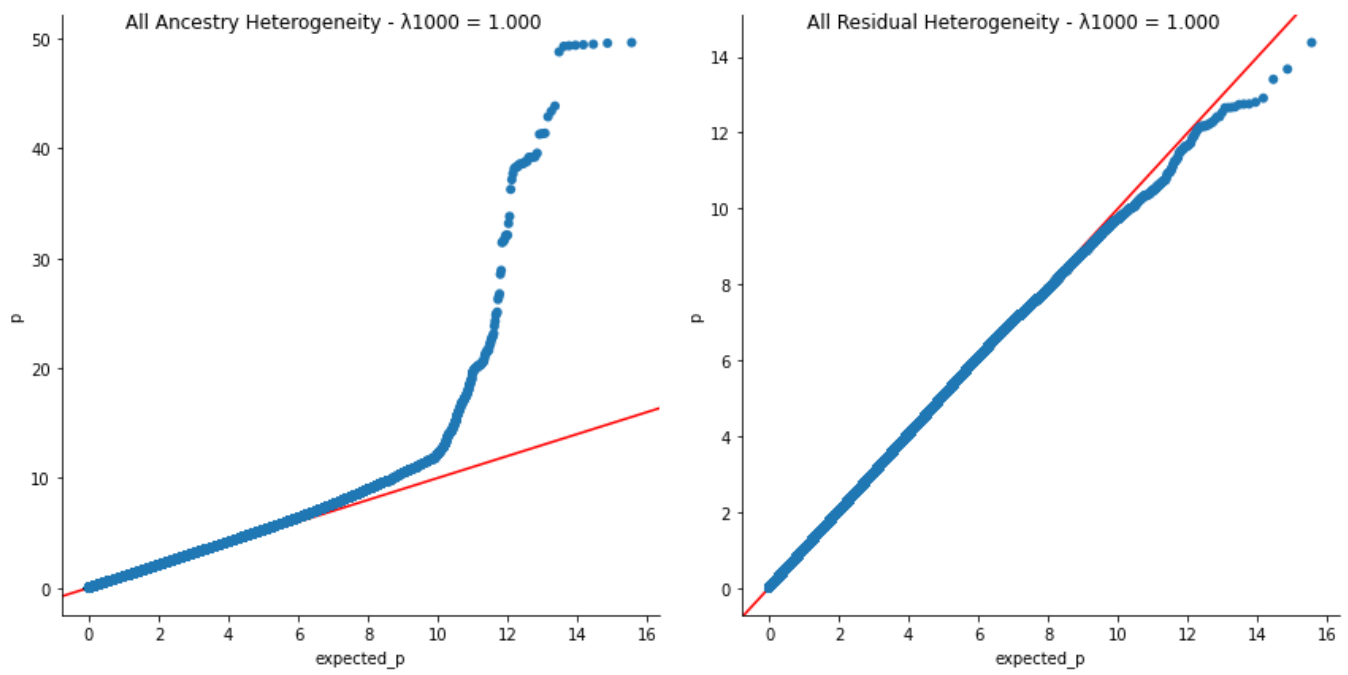




Supplementary Figure 1 – QQ Plots and Genomic Inflation (λ) of each ancestry cohort. Genomic inflation was normalized to 1000 cases and 1000 controls for all datasets outside of Loesch et al 2021 due to large discrepancy between number of cases and controls.

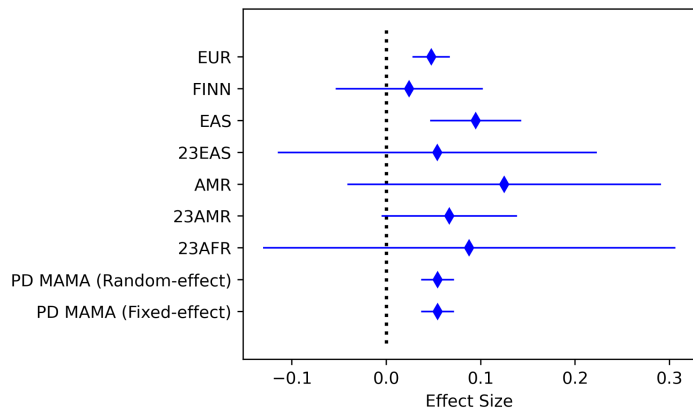


Supplementary Figure 2 – QQ Plots and normalized Genomic Inflation (λ) of the two meta-analyses. Genomic inflation was normalized to 1000 cases and 1000 controls for all datasets due to large discrepancy between number of cases and controls.

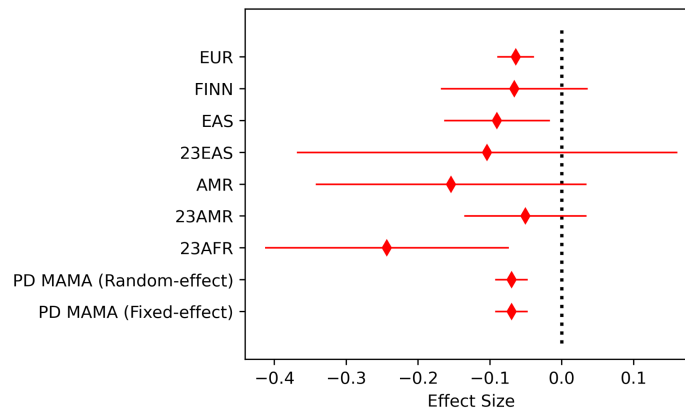


Supplementary Figure 3 - QQ Plot and Genomic Inflation of MR-MEGA ancestry heterogeneity and residual heterogeneity. Genomic inflation was normalized to 1000 cases and 1000 controls.

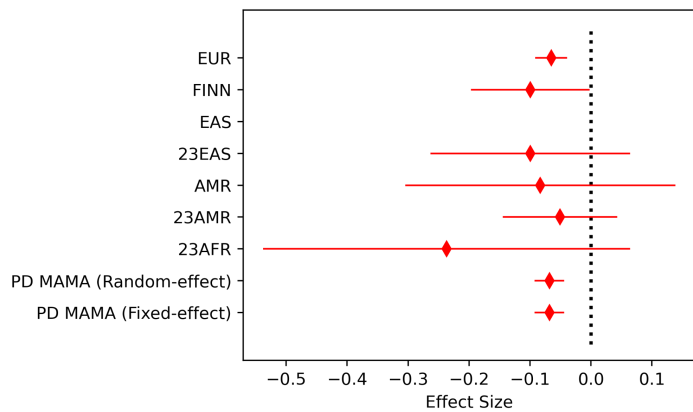
Forest Plot of Random-effect Locus 1 (rs11164870, *MTF2*)



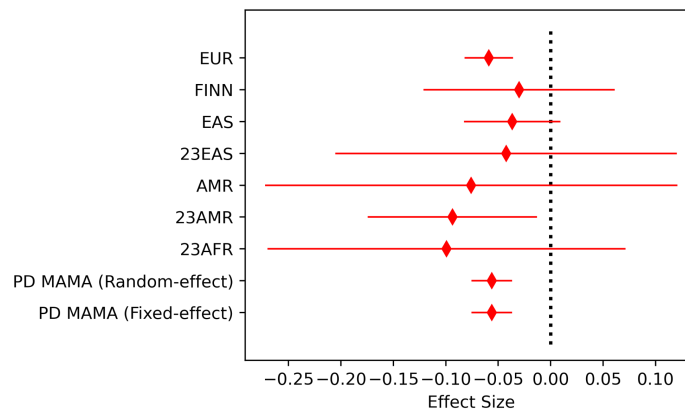
Forest Plot of Random-effect Locus 15 (rs6806917, *PIK3CA*)



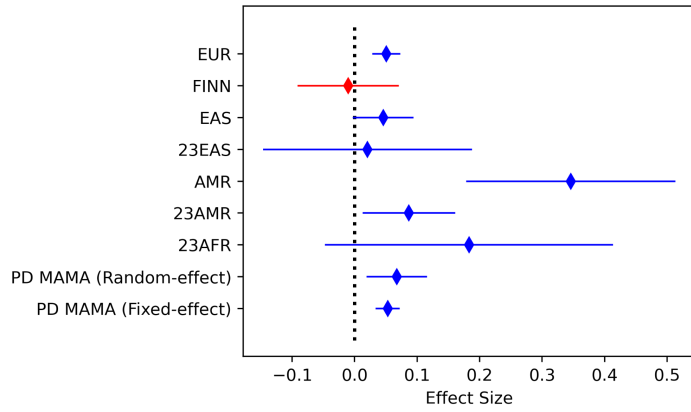
Forest Plot of Random-effect Locus 18 (rs16843452, *ADD1*)



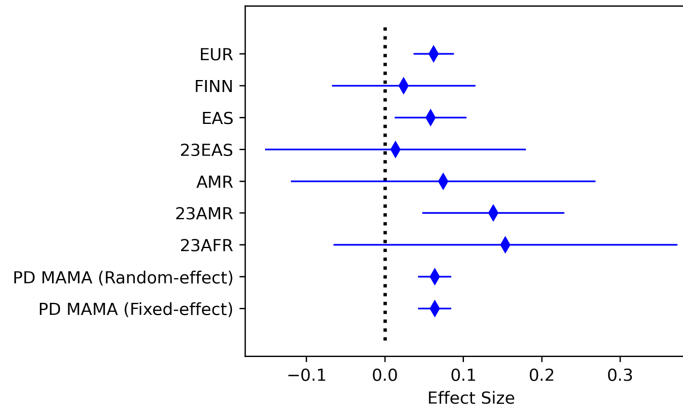
Forest Plot of Random-effect Locus 36 (rs6469271, *SYBU*)



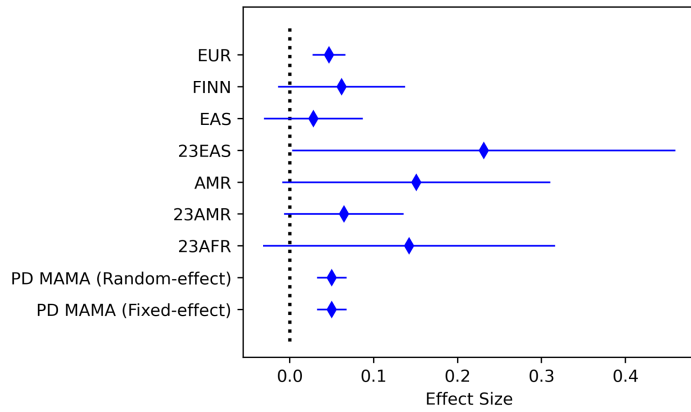
Forest Plot of MR-MEGA Locus 47 (rs1078514, *IRS2*)



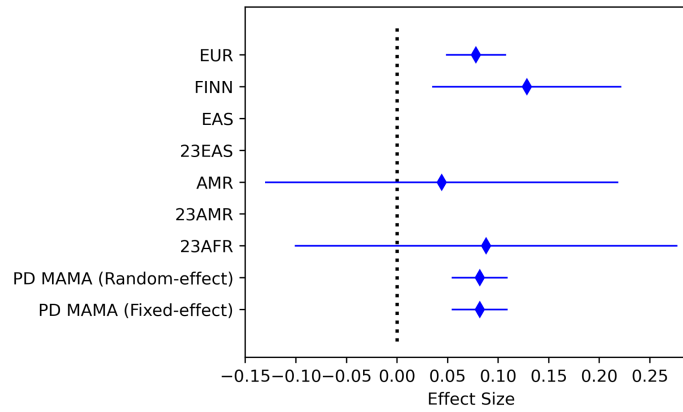
Forest Plot of Random-effect Locus 54 (rs28648524, *USP8*)



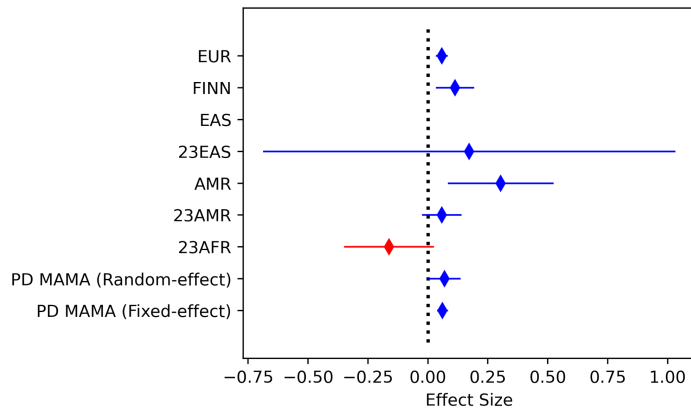
Forest Plot of Random-effect Locus 60 (rs11650438, *PIGL*)



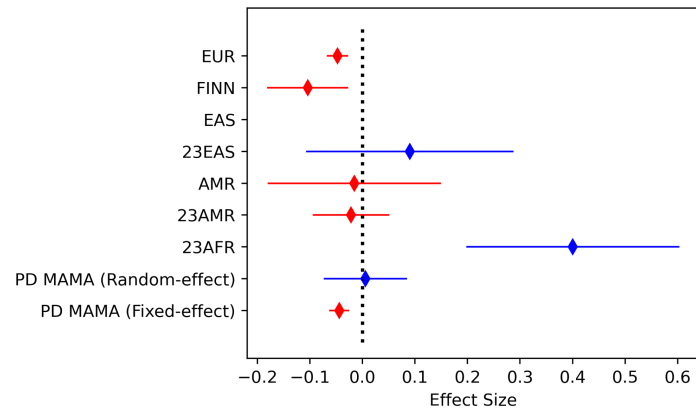
Forest Plot of Random-effect Locus 65 (rs4485435, *FASN*)



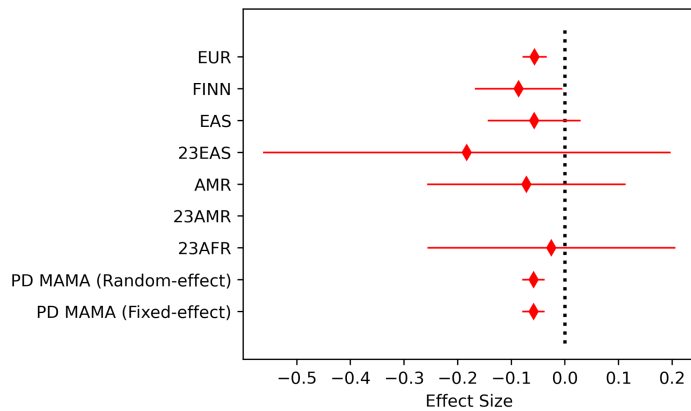
Forest Plot of MR-MEGA Locus 61 (rs6060983, MYLK2)



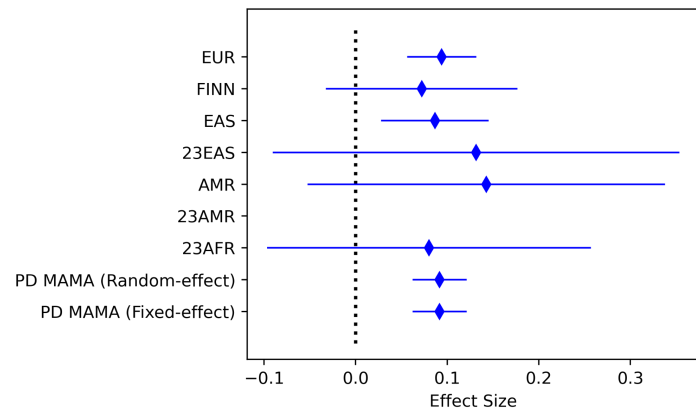
Forest Plot of MR-MEGA Locus 62 (rs1736020, USP25)



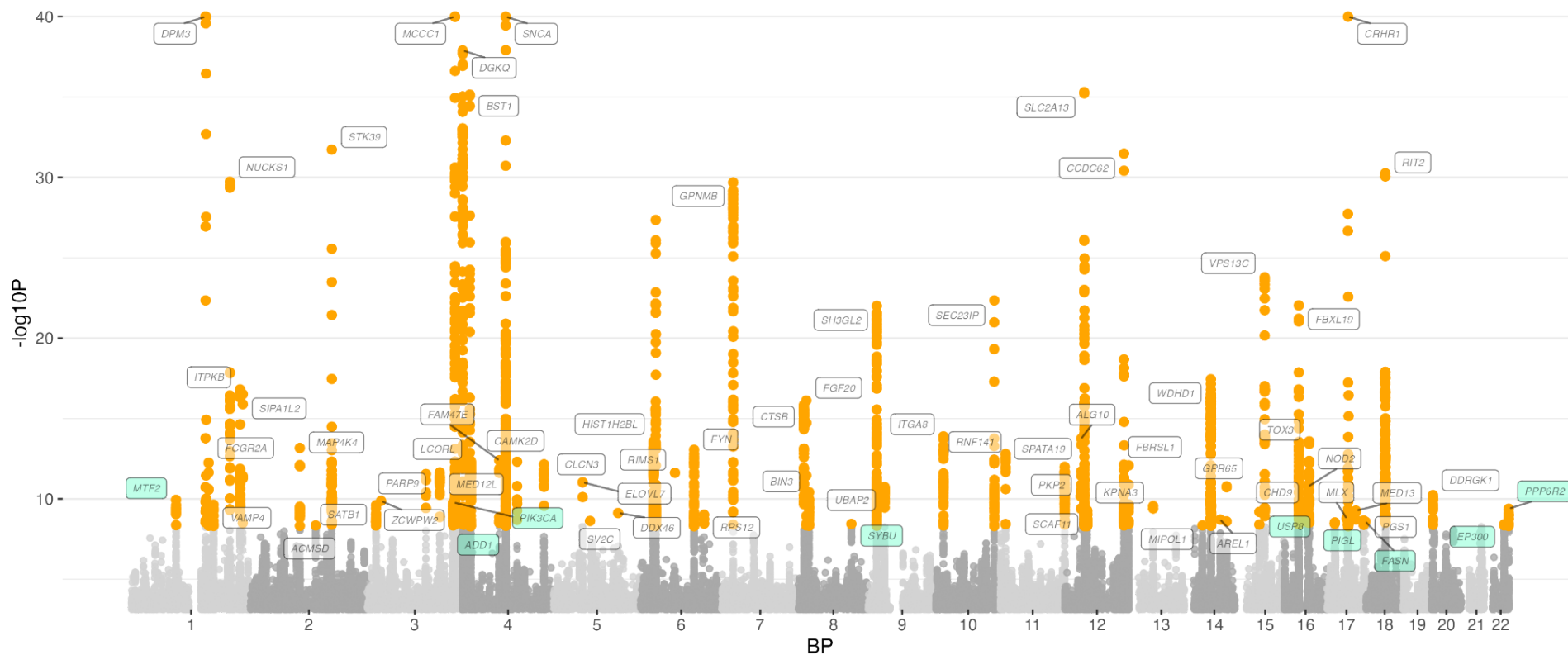
Forest Plot of Random-effect Locus 68 (rs73174657, EP300)



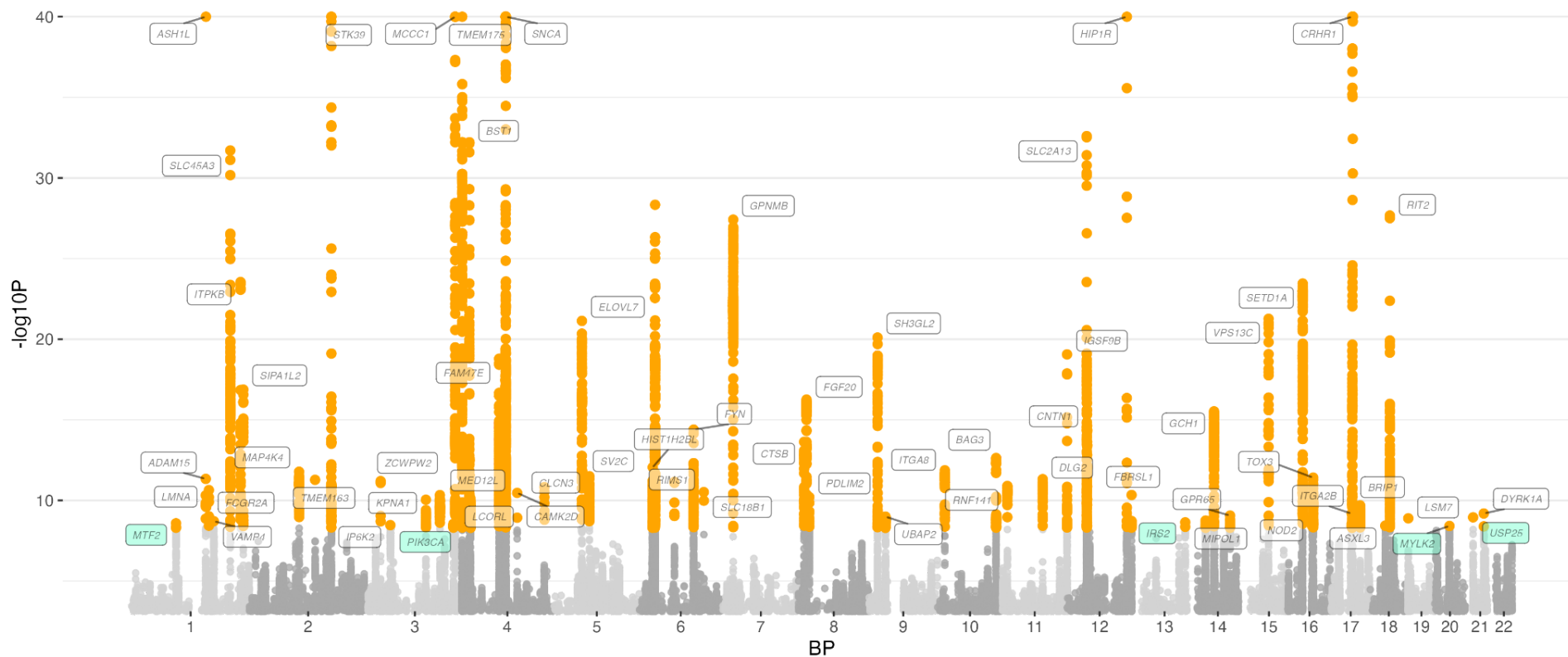
Forest Plot of Random-effect Locus 69 (rs10775809, PPP6R2)



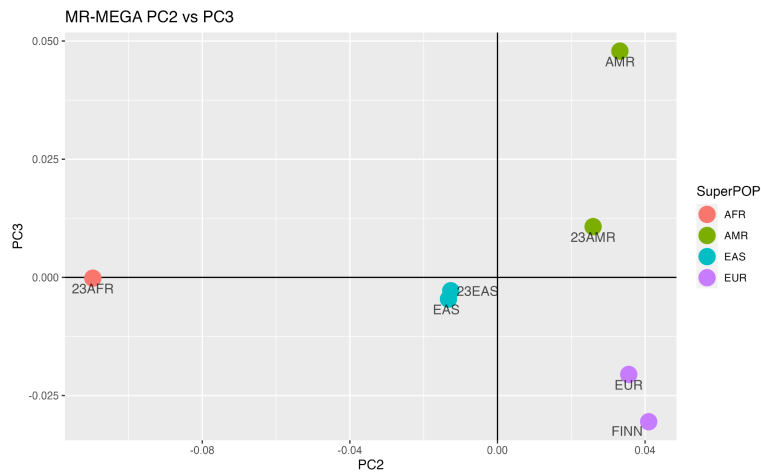
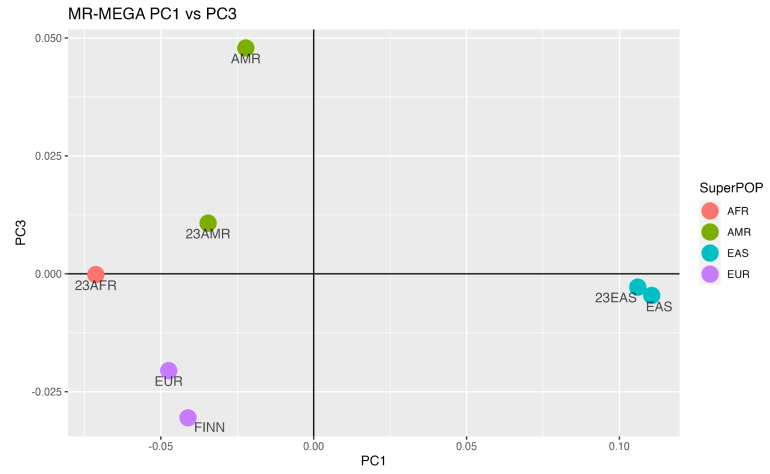
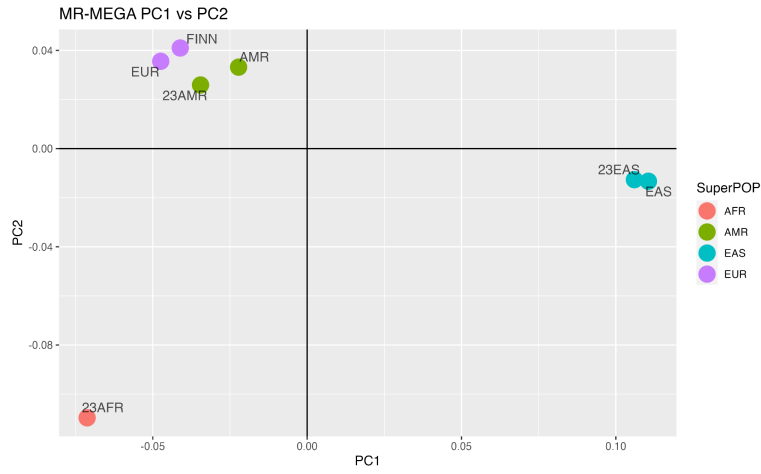
Supplementary Figure 4 - Forest plots of the lead SNPs of novel loci in the ancestrally distinct cohorts and the random effect meta-analysis results. The error bar indicates the 95% confidence interval for the SNP effect size in log odds ratio. MR-MEGA results were not represented as they do not provide effect direction or size. Red represents negative effect direction and blue represents positive effect direction. EUR: Nalls et al. 2019 (n = 1,467,312), FINN: FinnGen R4 (n = 95,683), EAS: Foo et al. 2020 (n= 31,575), 23EAS: 23andMe East Asians (n = 152,227), AMR: Loesch et al. 2021 (n = 1,497), 23AMR: 23andMe Latino (n = 583,163), 23AFR: 23andMe African (n = 194,273), PD MAMA: Multi-ancestry Meta-Analysis (n = 2,525,730)



Supplementary Figure 5 - Manhattan plot of the random effect meta-analysis result. The x-axis shows chromosome and base pair positions of each variant tested in the meta-analyses. The y-axis shows the two-sided P value in the $-\log_{10}$ scale. Orange points indicate a significant variant at $P < 5 \times 10^{-9}$. The genomic risk loci are annotated with the nearest protein coding gene, with novel loci highlighted in green.

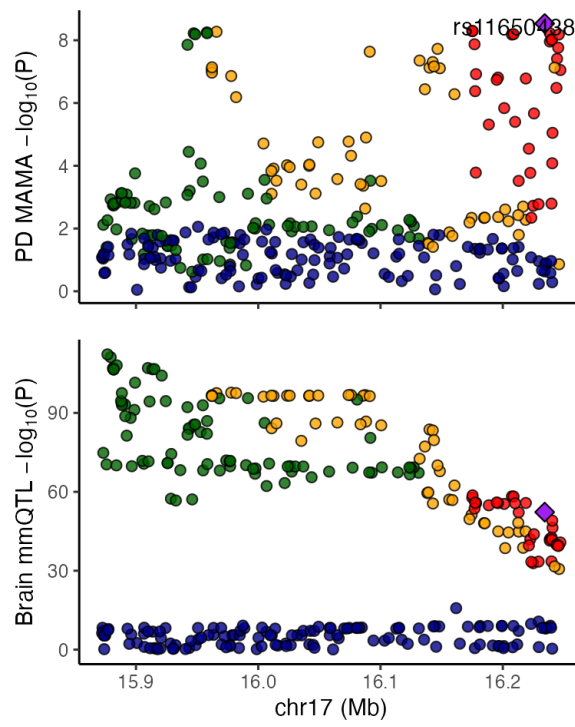
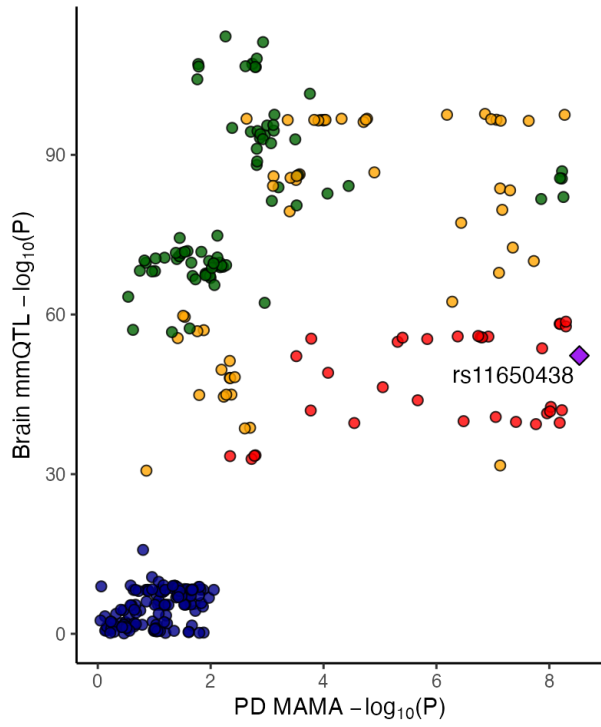


Supplementary Figure 6 - Manhattan plot of the MR-MEGA meta-analysis result. The x-axis shows chromosome and base pair positions of each variant tested in the meta-analyses. The y-axis shows the two-sided P value in the $-\log_{10}$ scale. Orange points indicate a significant variant at $P < 5 \times 10^{-9}$. The genomic risk loci are annotated with the nearest protein coding gene, with novel loci highlighted in green.

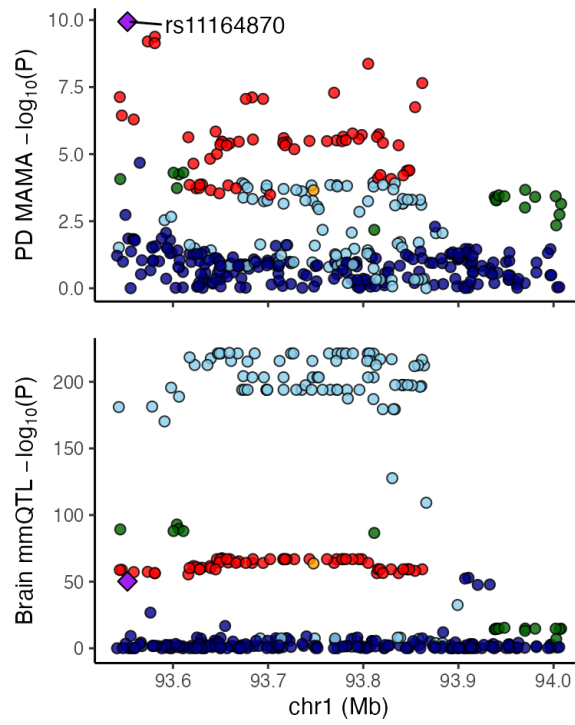
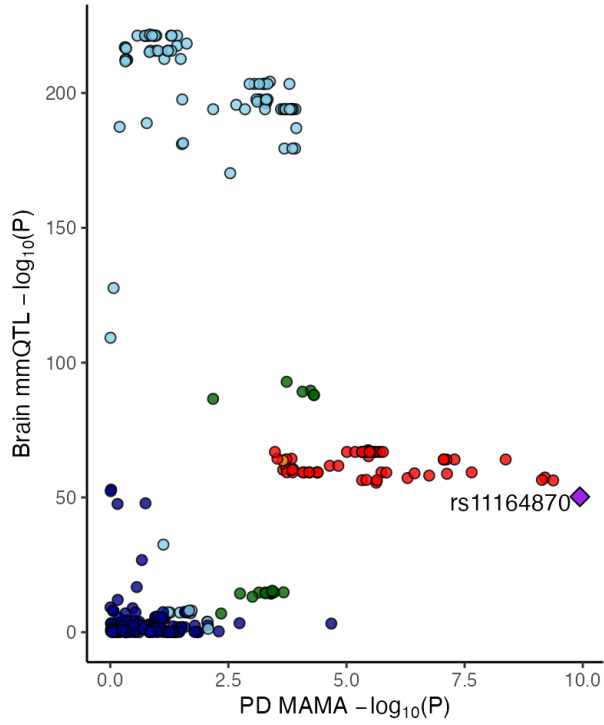


Supplementary Figure 7 - Principal Component of Ancestry Heterogeneity from MR-MEGA.

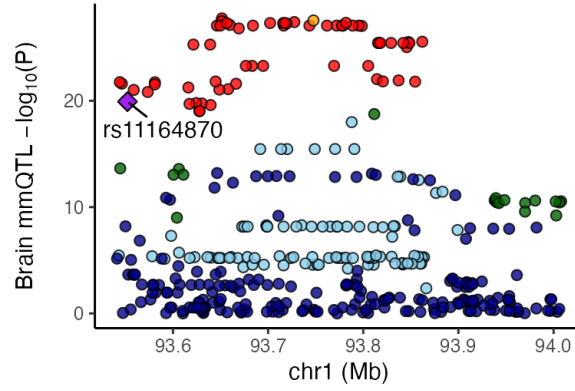
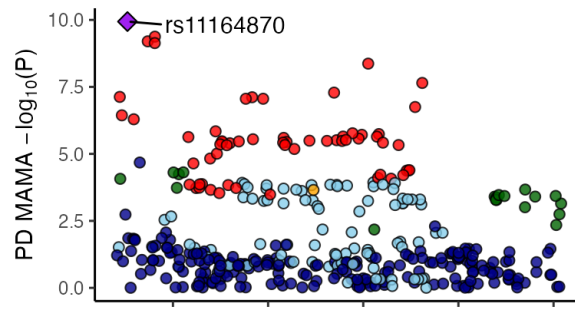
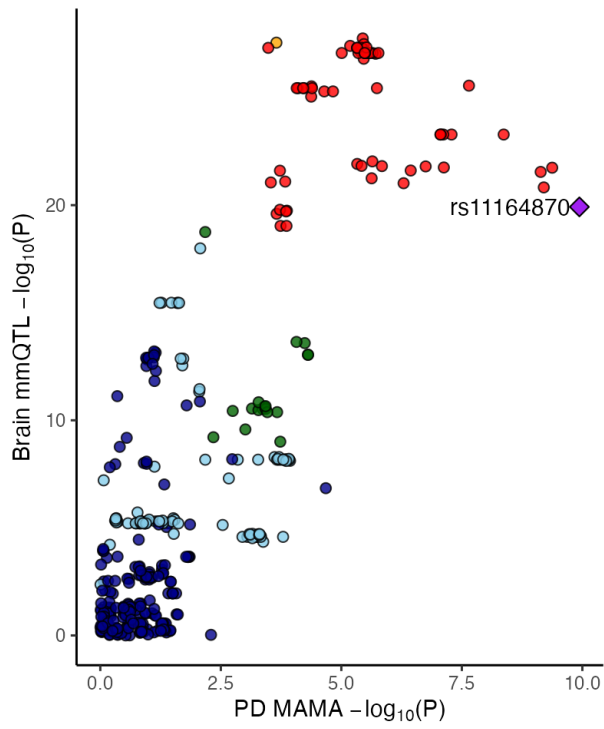
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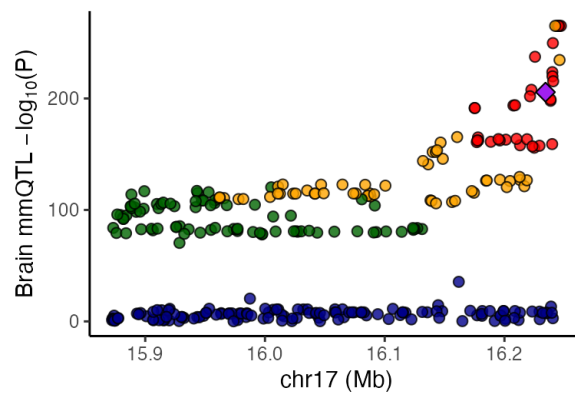
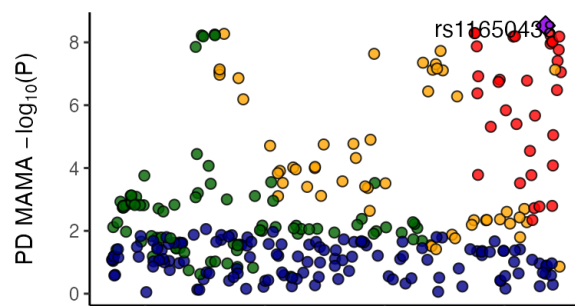
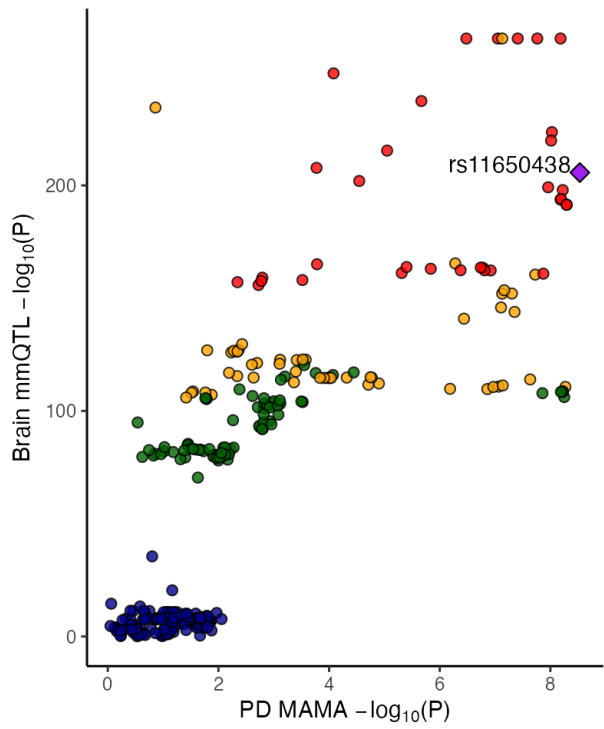
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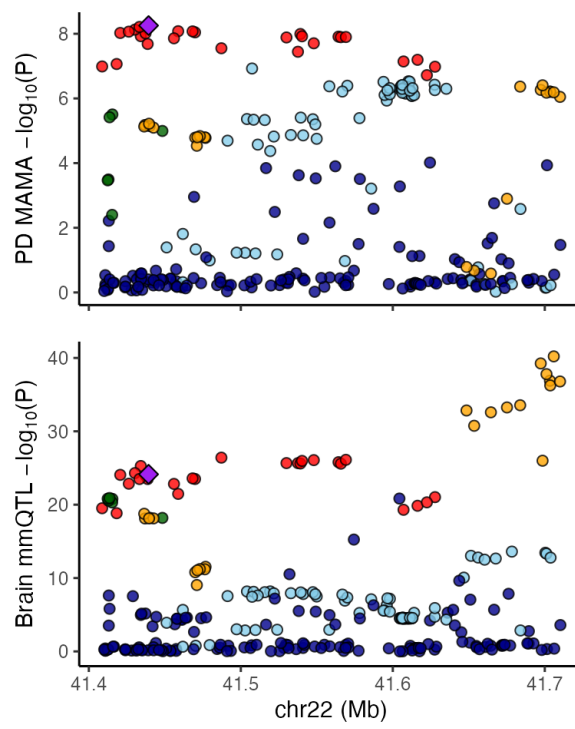
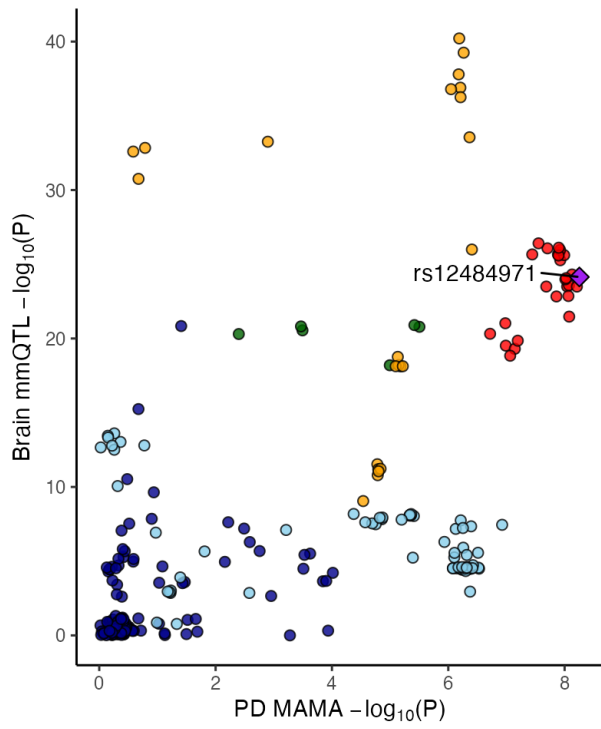
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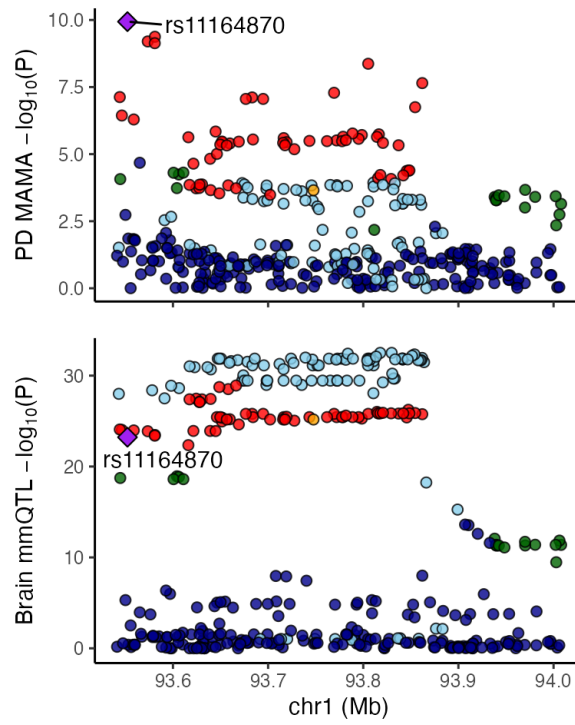
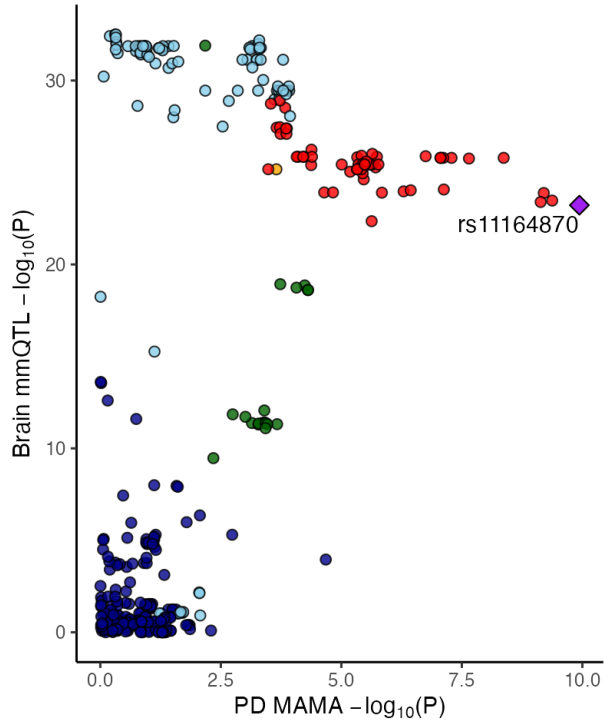
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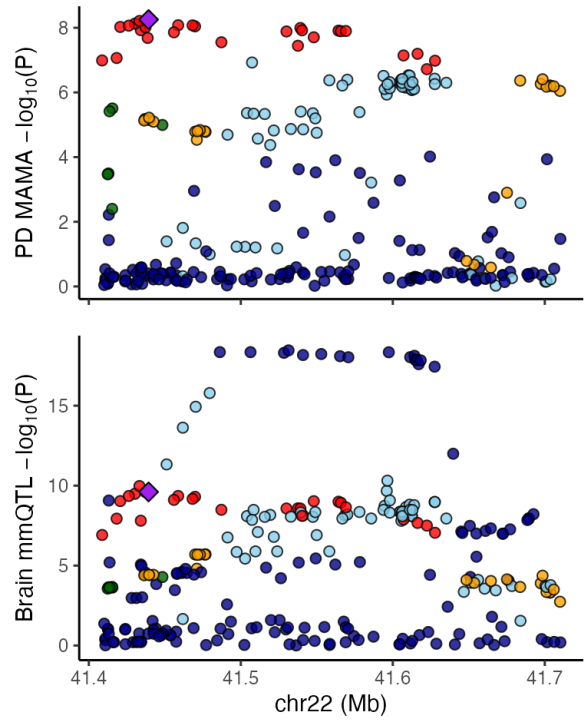
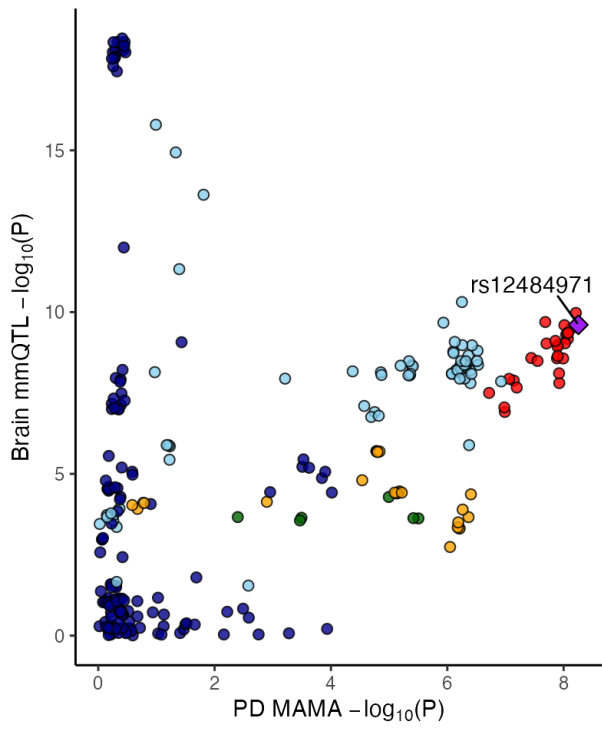
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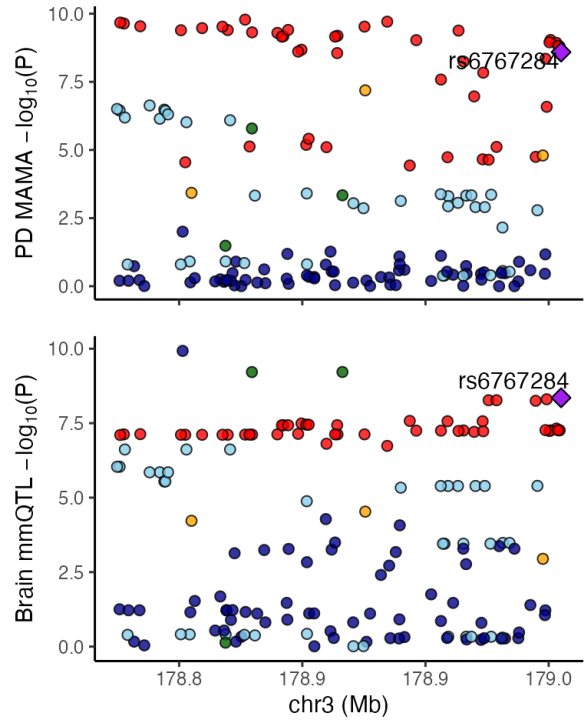
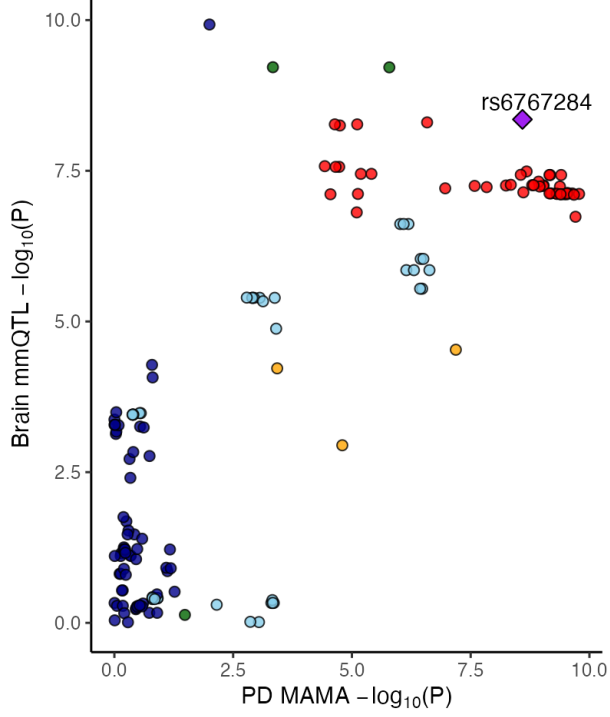
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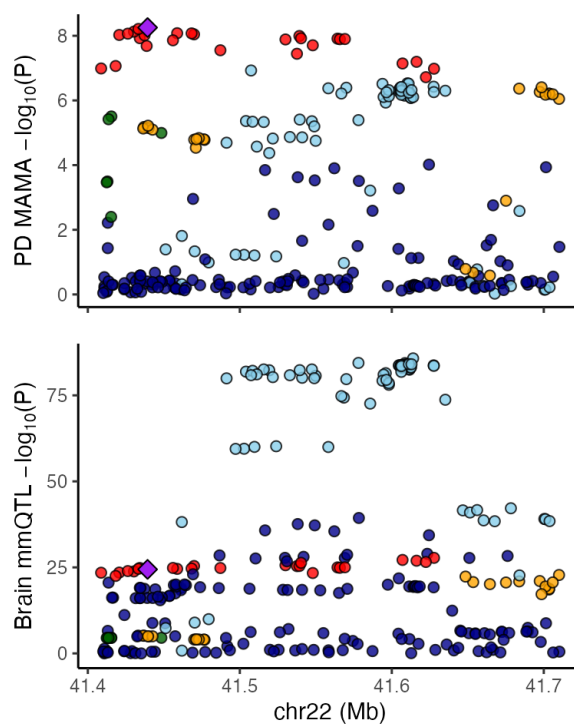
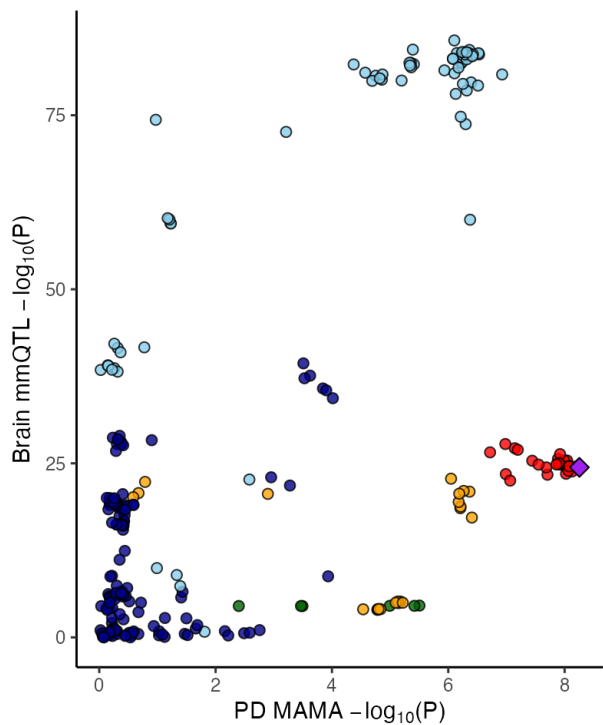
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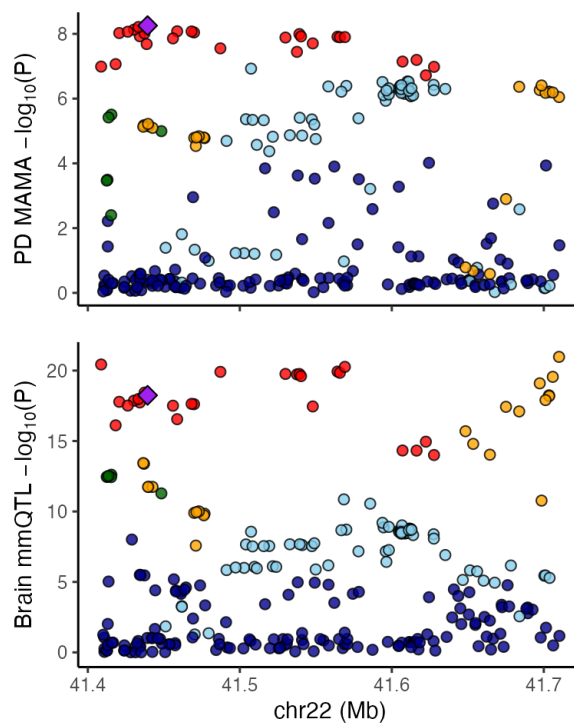
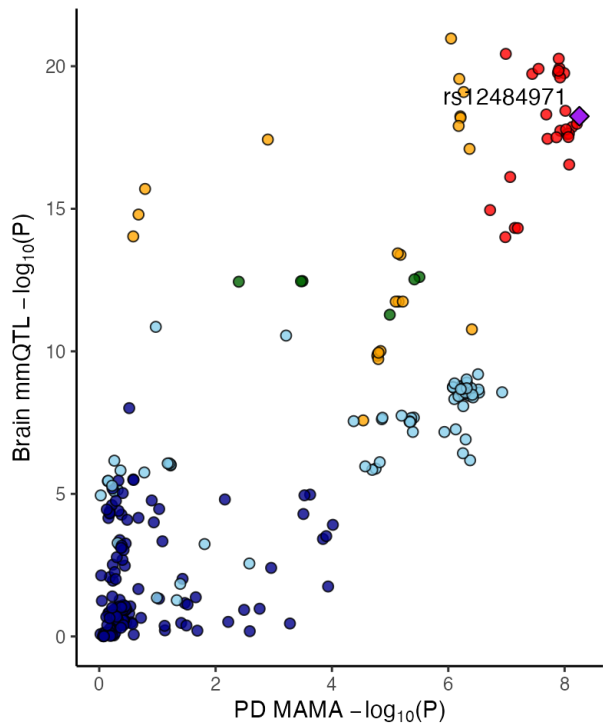
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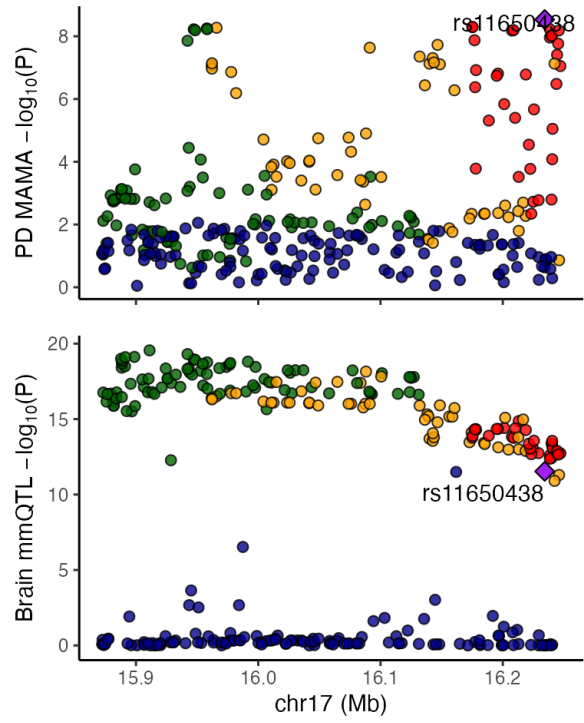
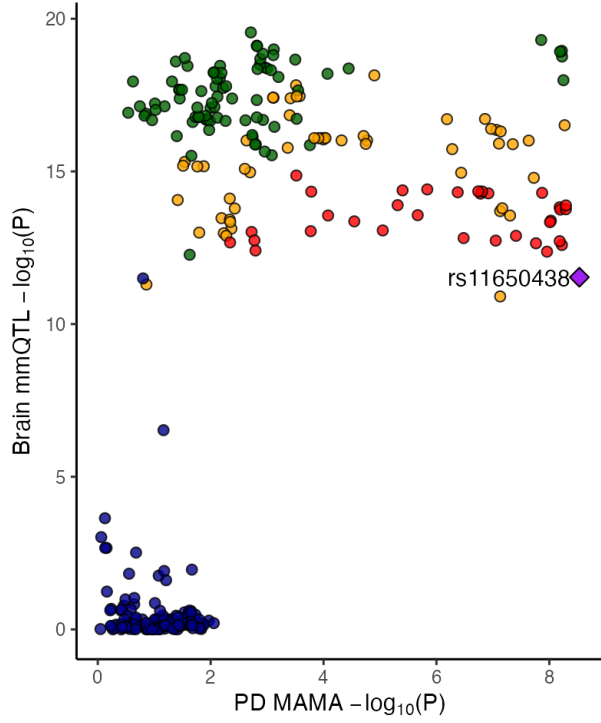
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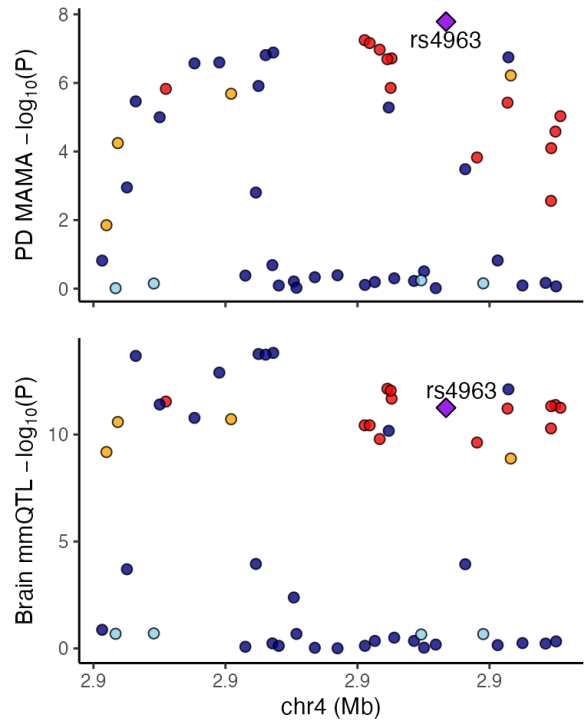
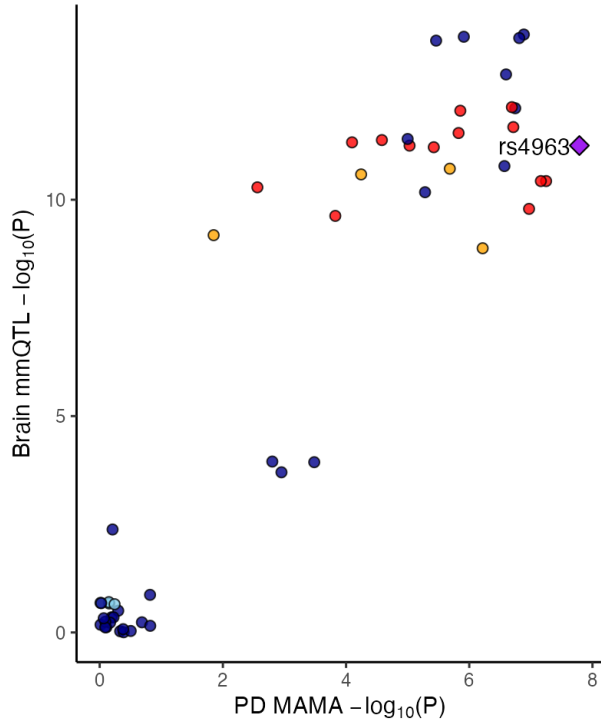
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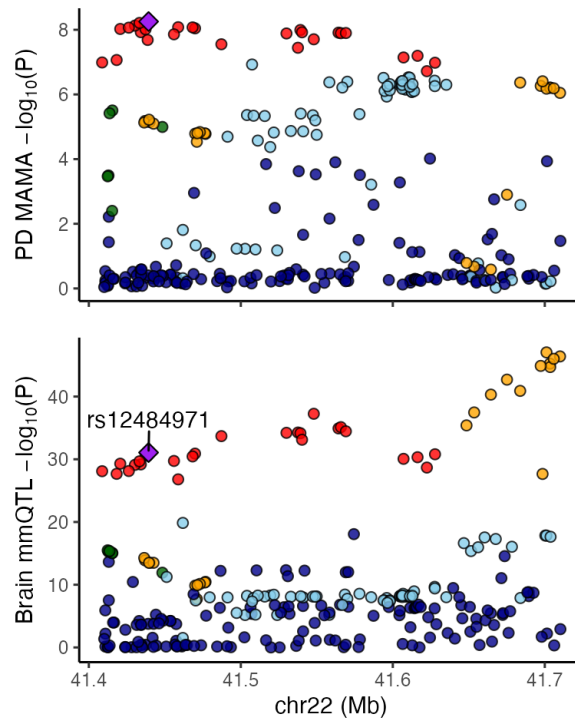
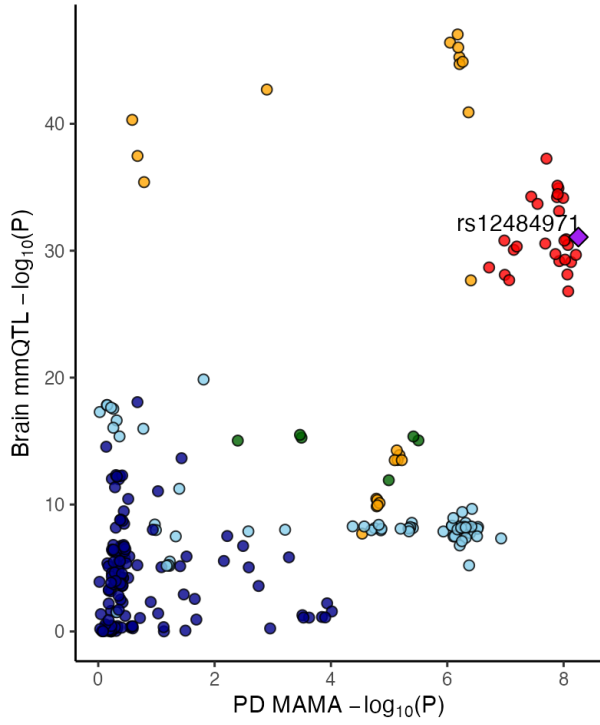
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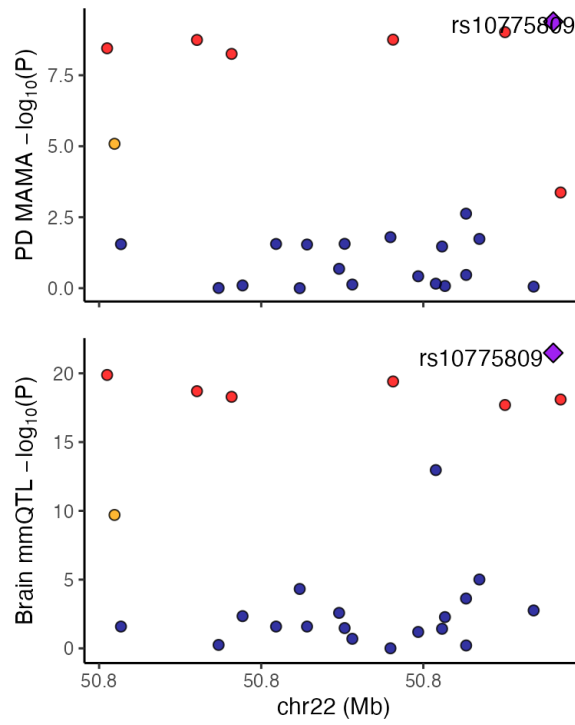
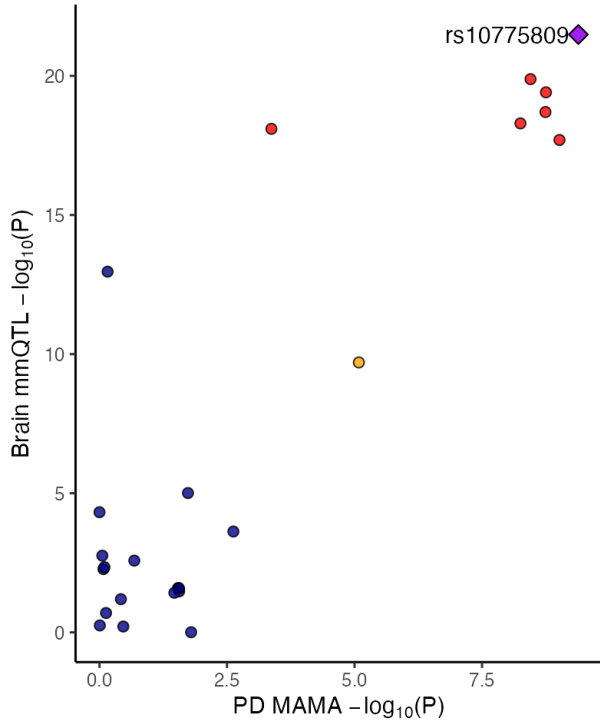
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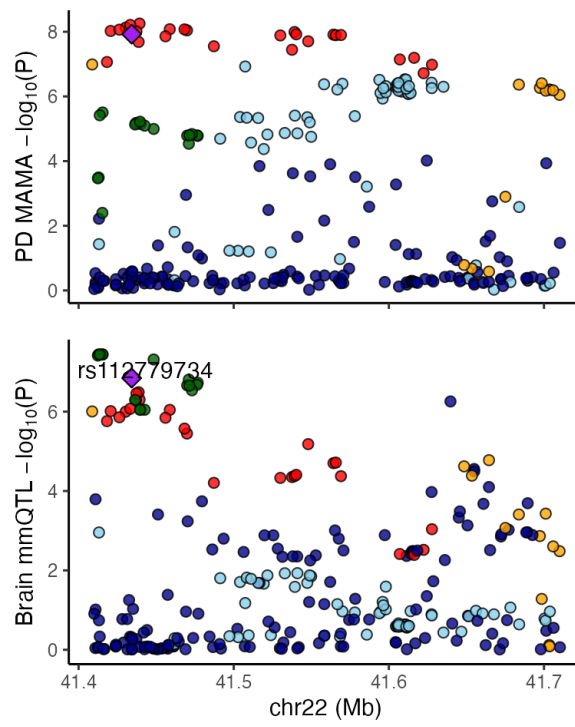
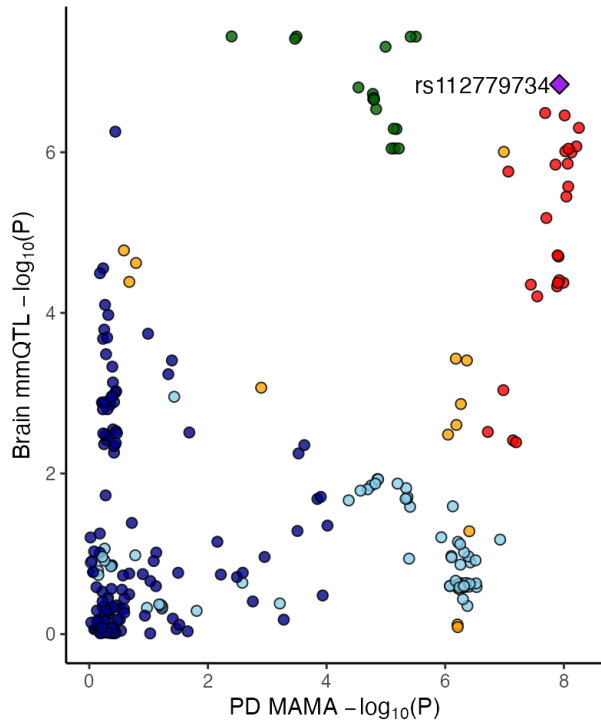
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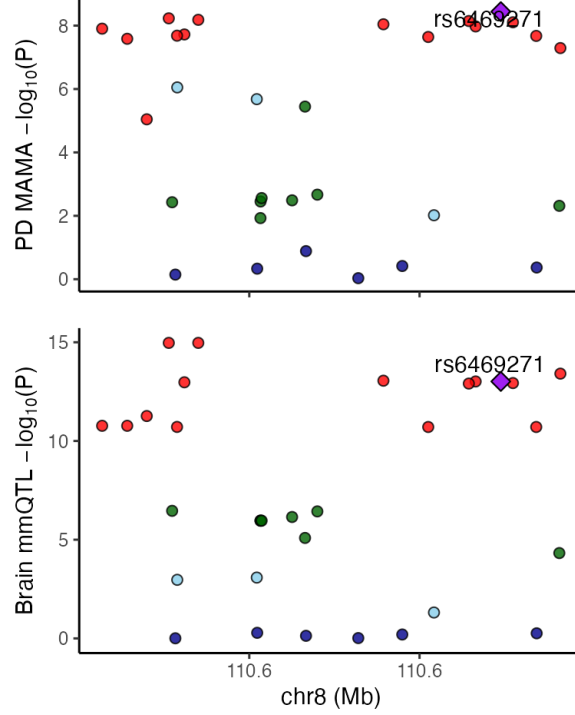
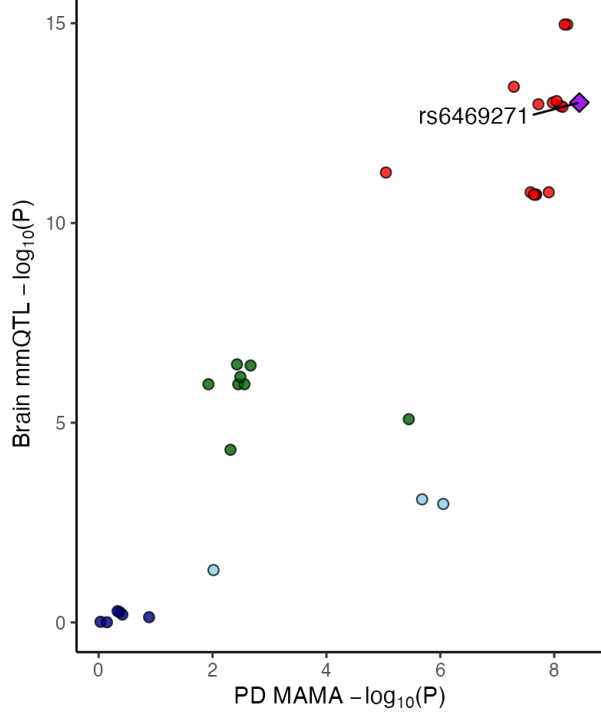
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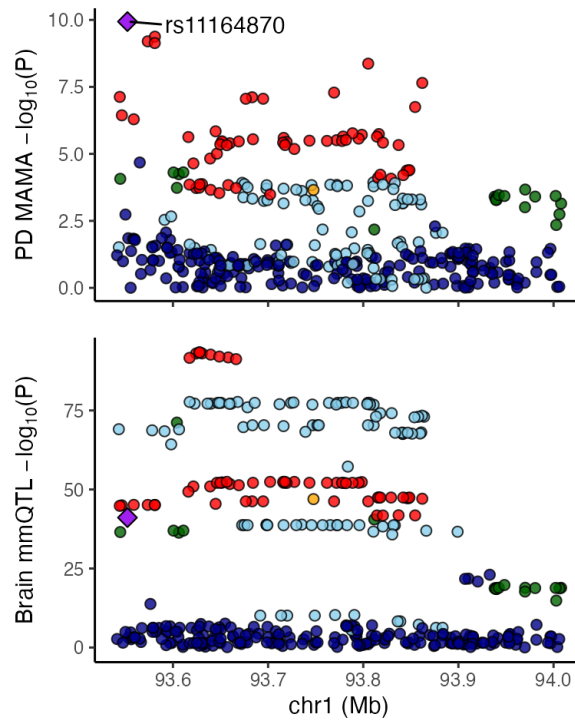
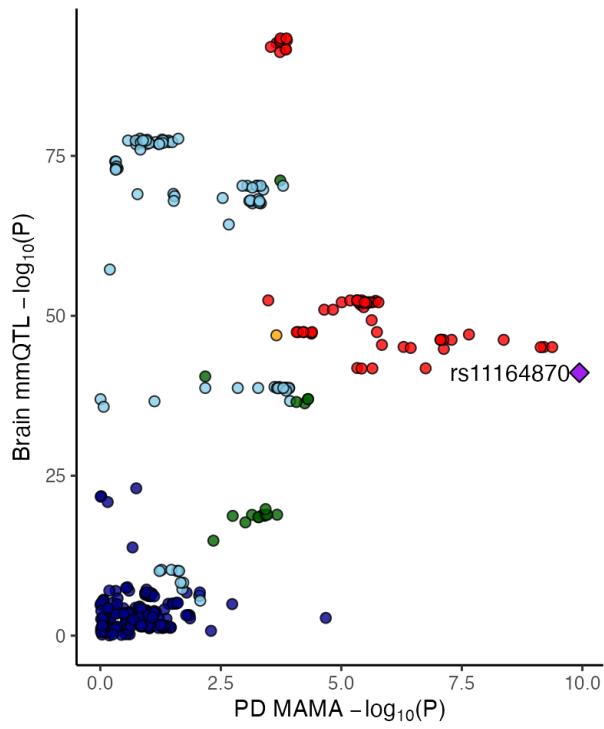
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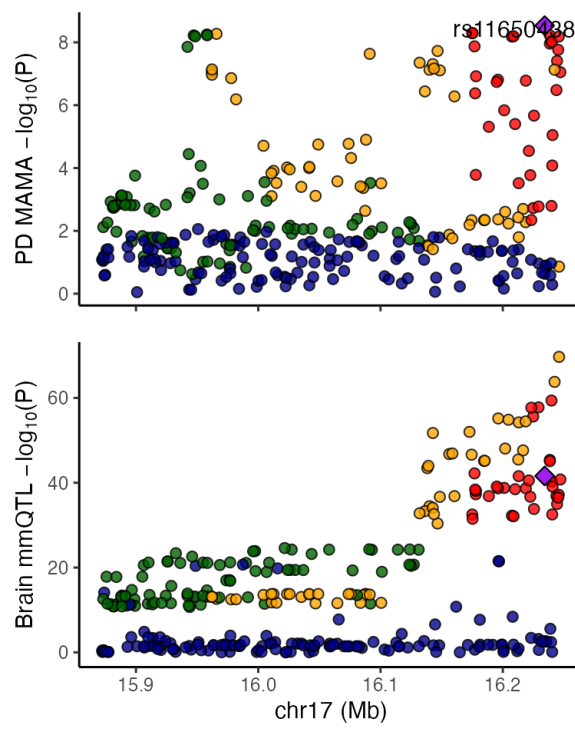
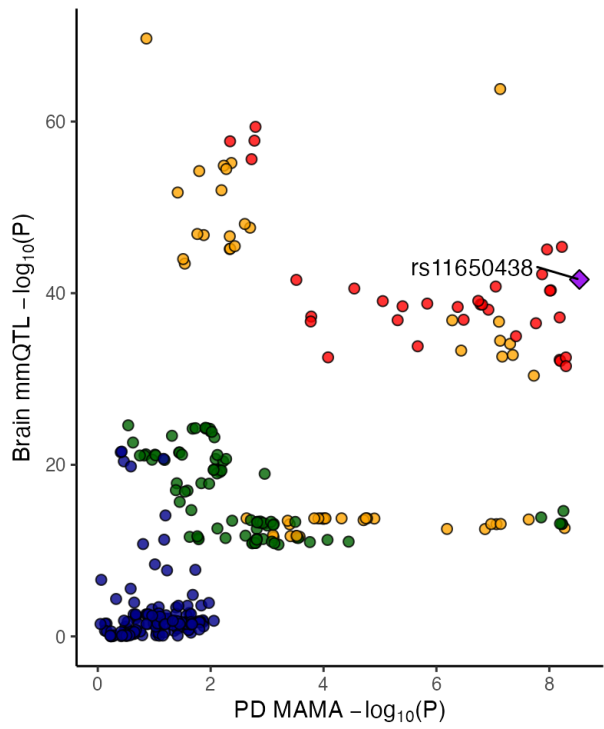
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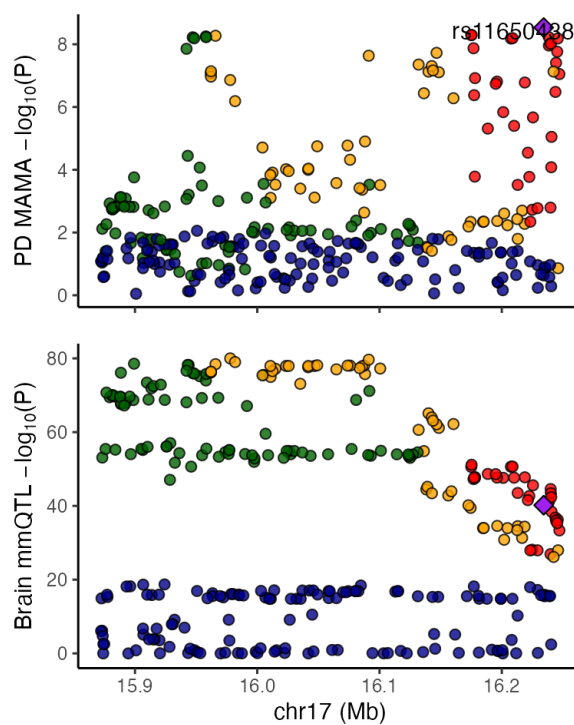
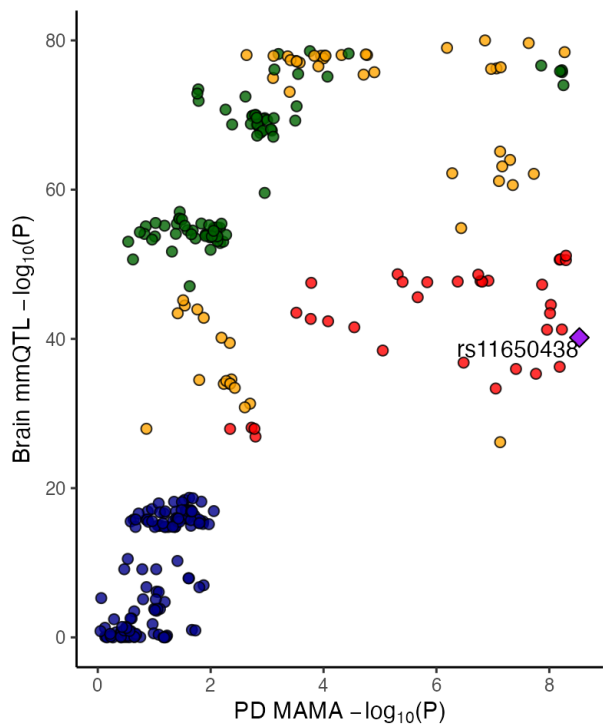
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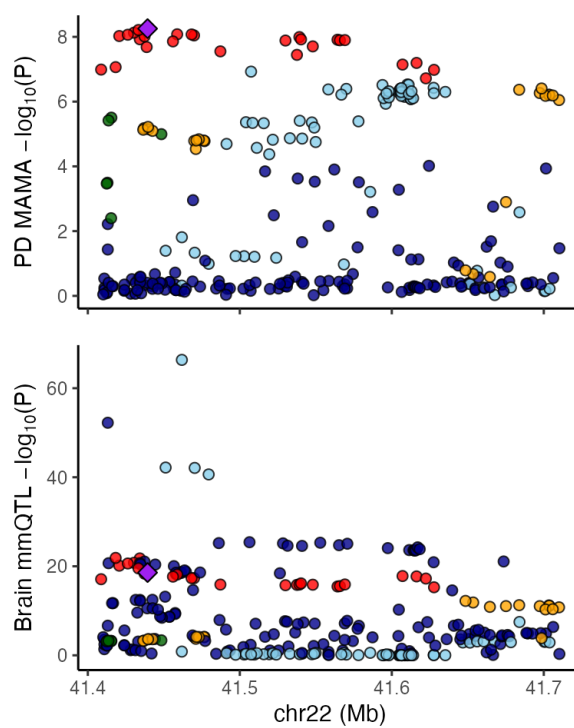
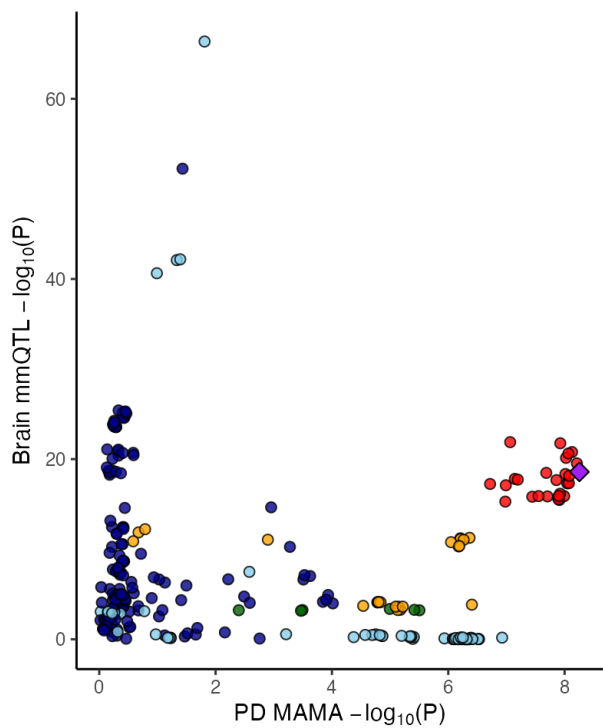
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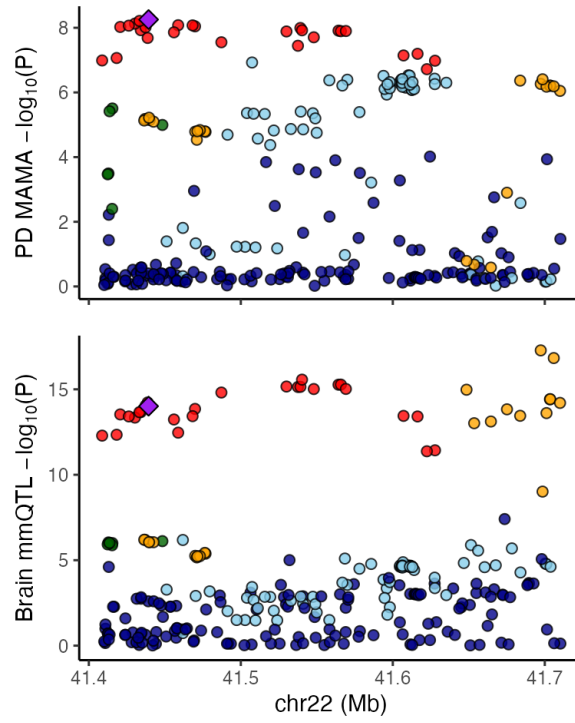
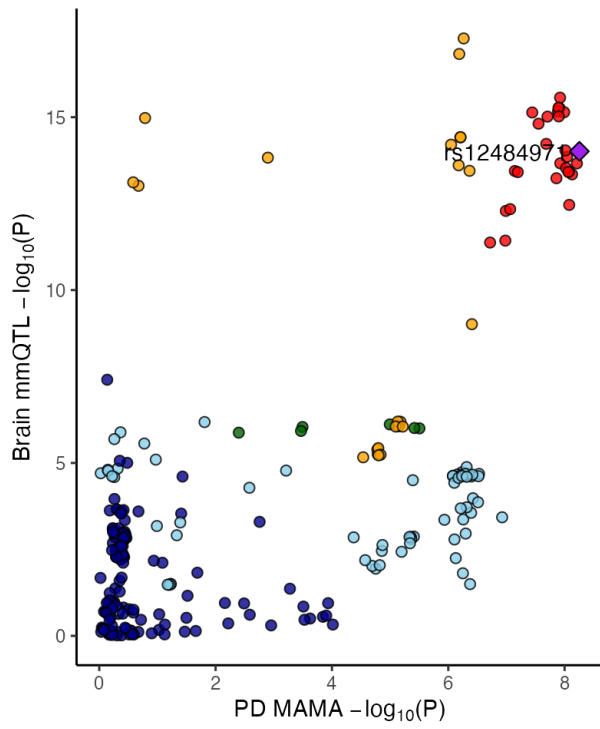
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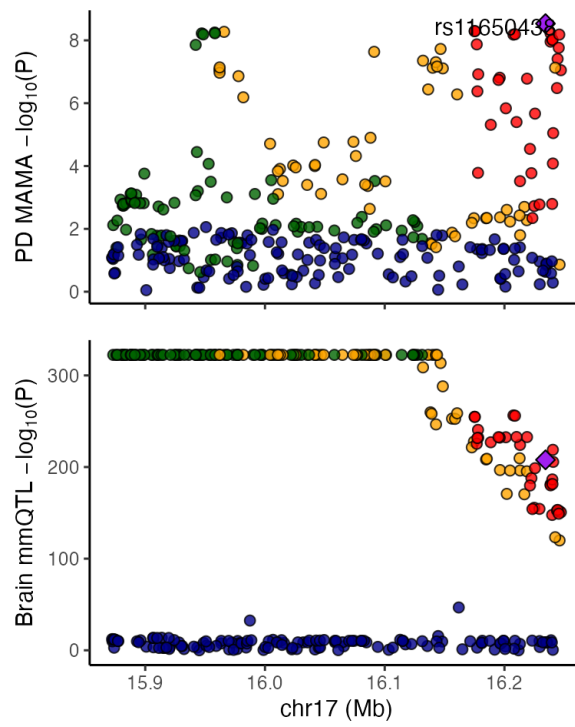
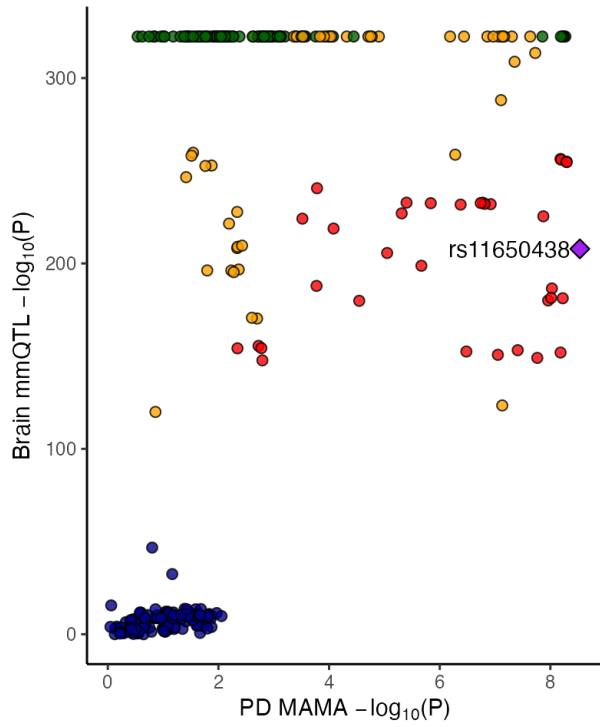
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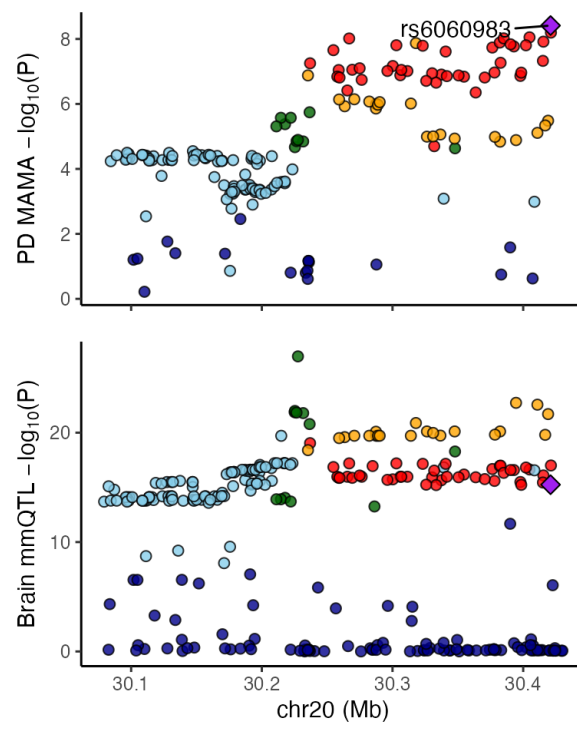
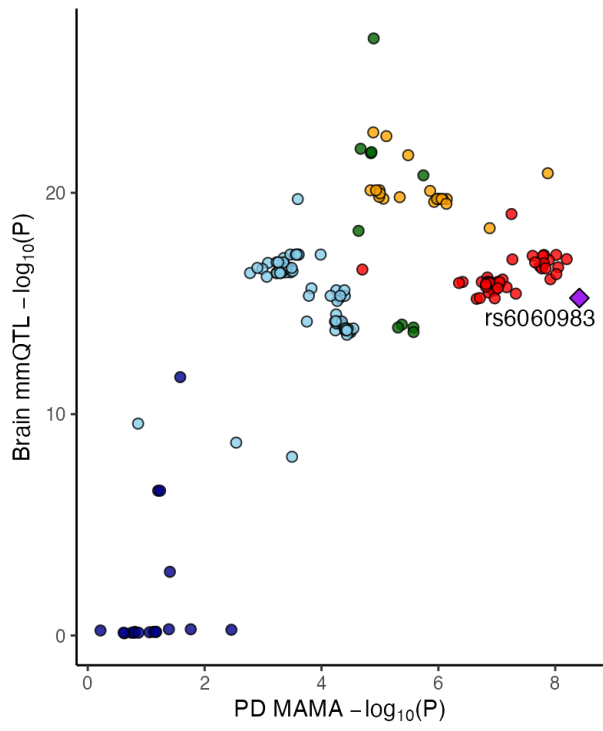
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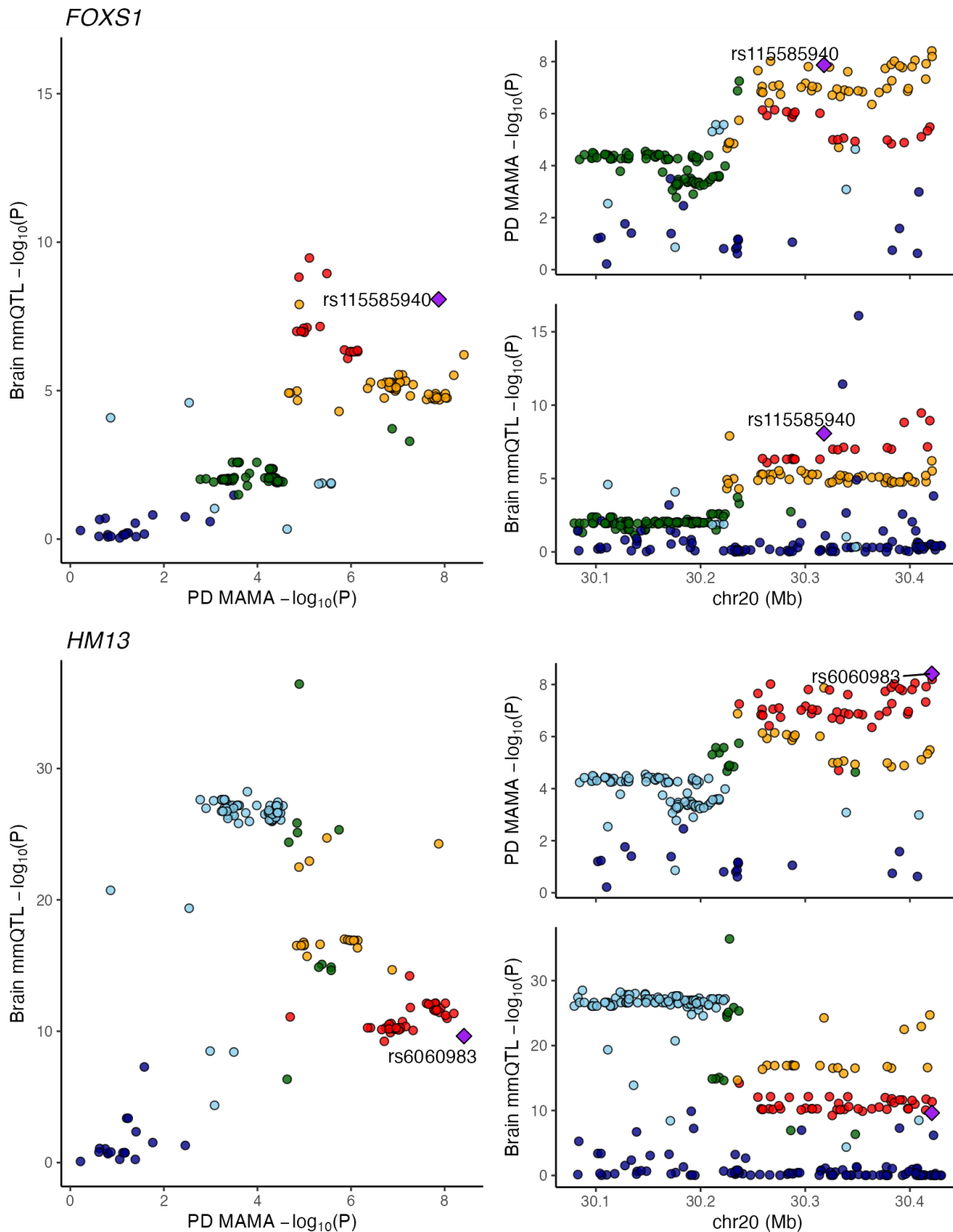


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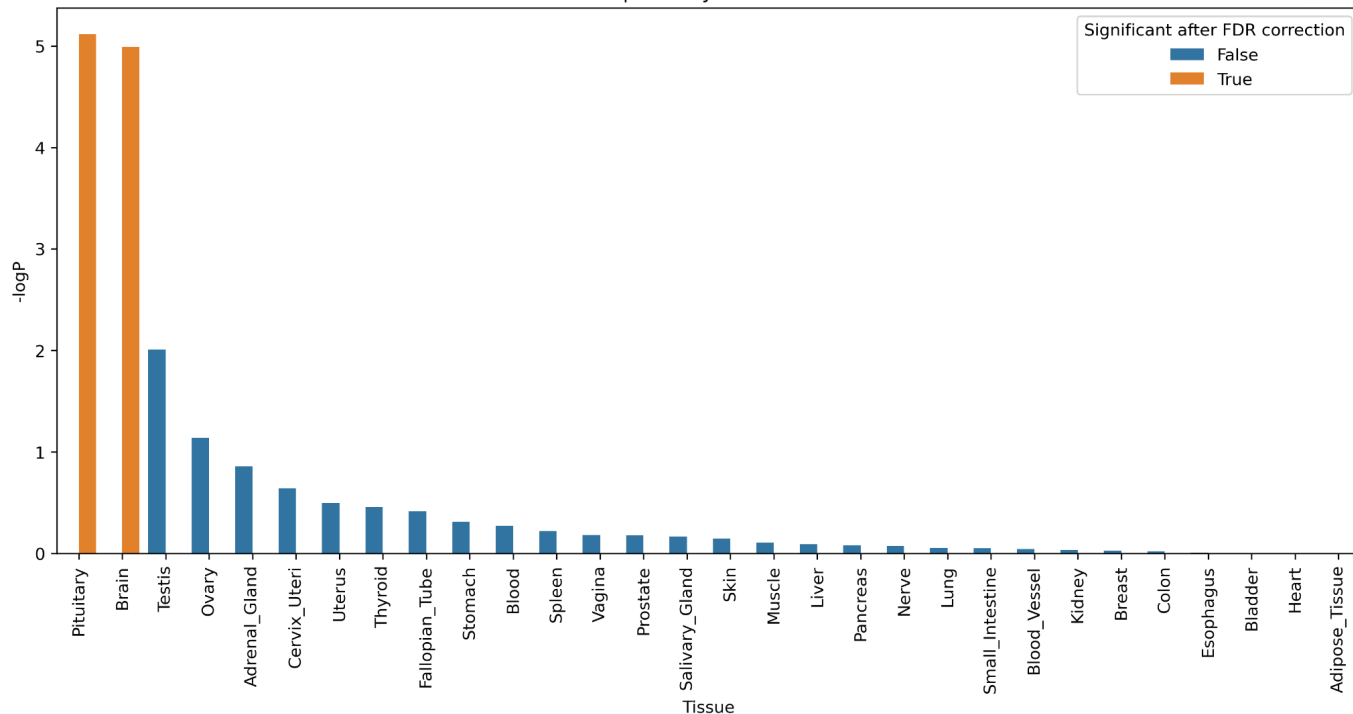
COX4I2



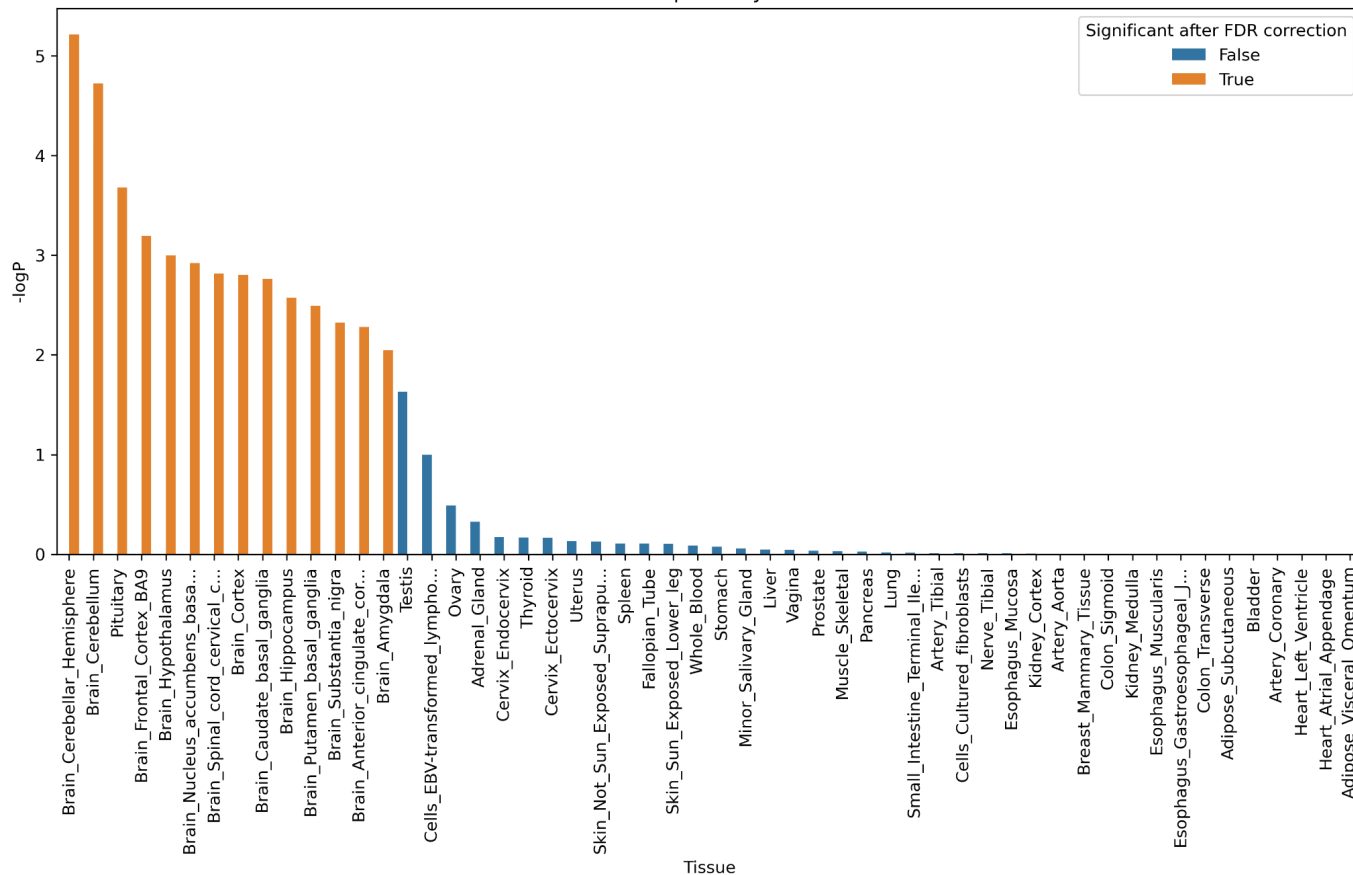


Supplementary Figure 8 - LocusCompare Plots of novel loci comparing PD MAMA association and brain eQTL results. Left is the LocusCompare plot between the PD MAMA GWAS results and eQTL results, where x-axis is the $-\log_{10}$ two-sided P value of the meta-analysis GWAS result and y-axis is the $-\log_{10}$ two-sided P value of the multi-ancestry brain eQTL. Right are two locuszoom plots, with the GWAS results on top and eQTL results on the bottom. The x-axis represents the basepair-position in hg19 while the y-axis represents the $-\log_{10}$ two-sided P value of the GWAS or eQTL results. Violet diamond denotes the lead SNP determined by the highest $-\log_{10}$ p-value. Linkage disequilibrium reference is based on the 1000 Genome dataset, EUR populations. Brain eQTL data is from the meta-analysis study by Zeng et. al 2022. Lead SNP was determined by summing the p-values of the two studies and selecting the lowest sum. All GWAS P values are from random-effects tests with the exception of *COX4I2*, *FOXS1*, and *HM13*, which are from MR-MEGA as the relevant locus were only identified in MR-MEGA. The plots only include eQTL order 1 to improve visibility.

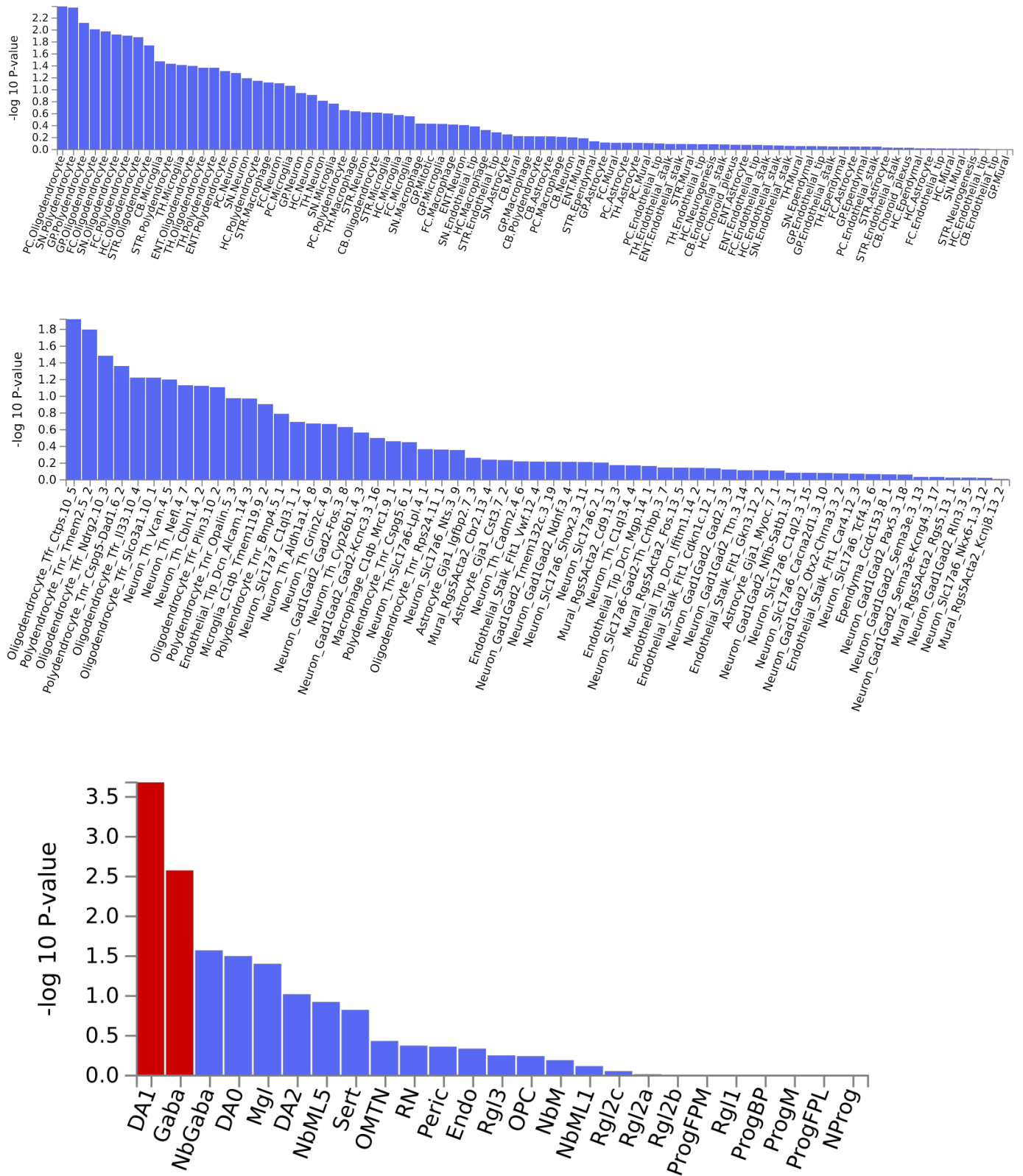
GTEx Tissue Specificity Enrichment - General



GTEx Tissue Specificity Enrichment



Supplementary Figure 9 - MAGMA GTEx tissue expression enrichment by tissue from FUMA. The x-axis shows the different GTEx tissues while the y-axis shows the two-sided p value of MAGMA gene-property analyses in $-\log_{10}P$ scale. P values were not corrected for multiple tests but tissues significant after false-discovery rate correction are highlighted as orange. Top is the 30 general tissue level. Bottom is the 53 detailed tissue level.

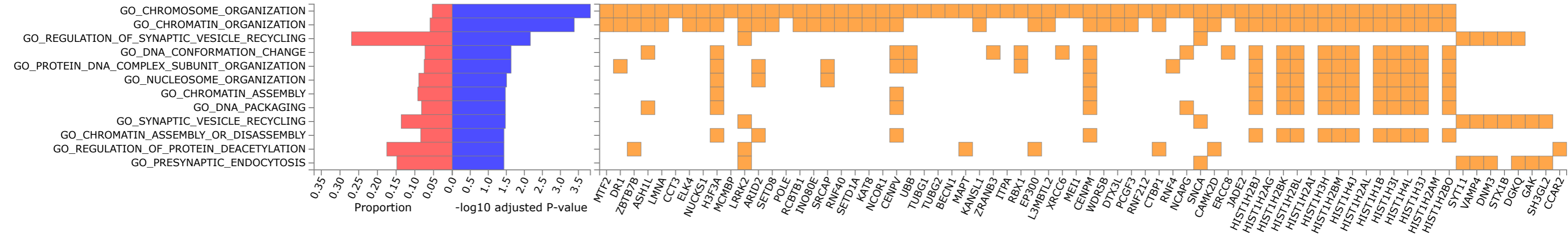


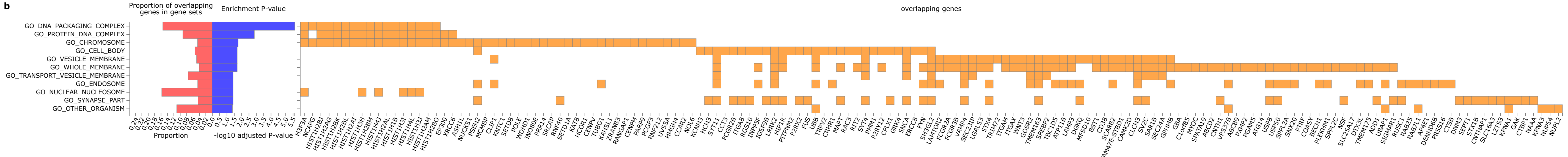
Supplementary Figure 10 - MAGMA expression enrichment from single cell RNAseq data. The x-axis shows the different cell types while the y-axis shows the $-\log_{10}$ two-tailed p-value for the MAGMA enrichment test. Top: murine cells from DropViz - all level 1 cell type class; center: murine substantia nigra cells from DropViz - level 2 cell type subcluster; Bottom: human midbrain cells (La Manno et al. 2016. GEO: GSE76381)

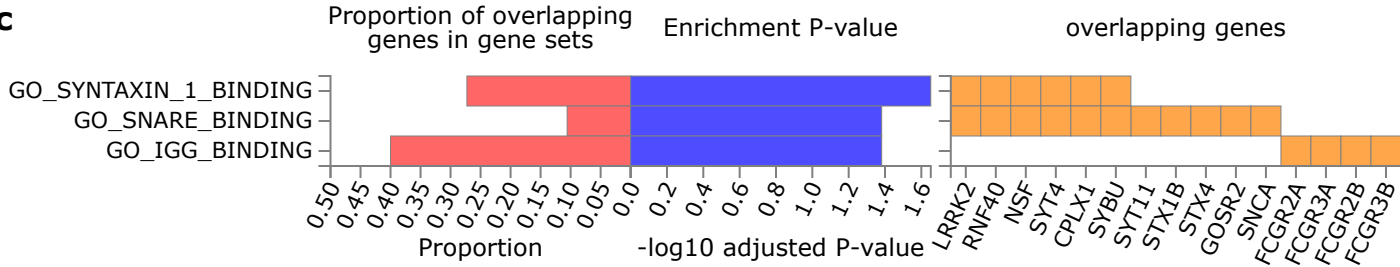
a

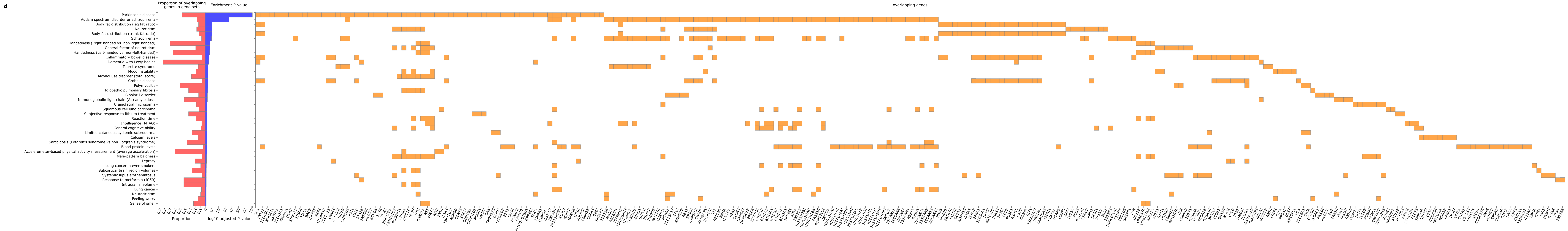
Proportion of overlapping genes in gene sets Enrichment P-value

overlapping genes

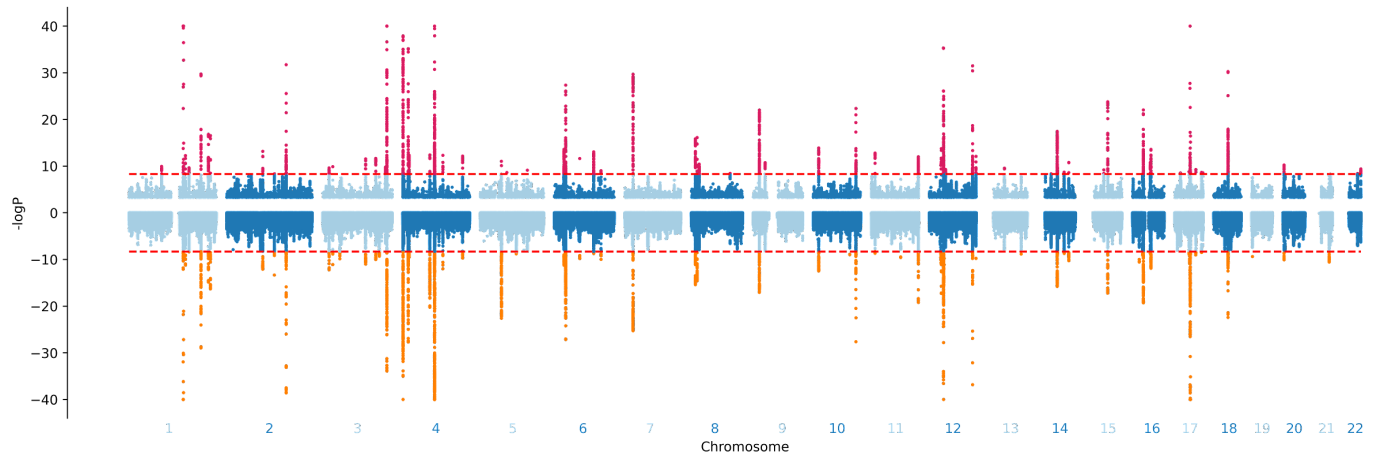




C



Supplementary Figure 11 - FUMA GENE2FUNC analysis of FUMA SNP2GENE mapped genes. The plots show enrichment analysis in a. biological processes b. cellular components c. molecular function d. GWAS Catalog



Supplementary Figure 12 - Miami plot of multi-ancestry random-effect meta-analysis (top) and Nalls et al. 2019 European single ancestry meta-analysis (bottom). The x-axis shows chromosome and base pair positions of each variant tested. The y-axis shows the two-sided P value in the $-\log_{10}$ scale, above 0 showing the $-\log_{10}$ value of the multi-ancestry random-effect meta-analysis while below 0 showing \log_{10} value of the European-only meta-analysis. Significant variants in multi-ancestry and European-only analyses are highlighted in red and orange respectively.