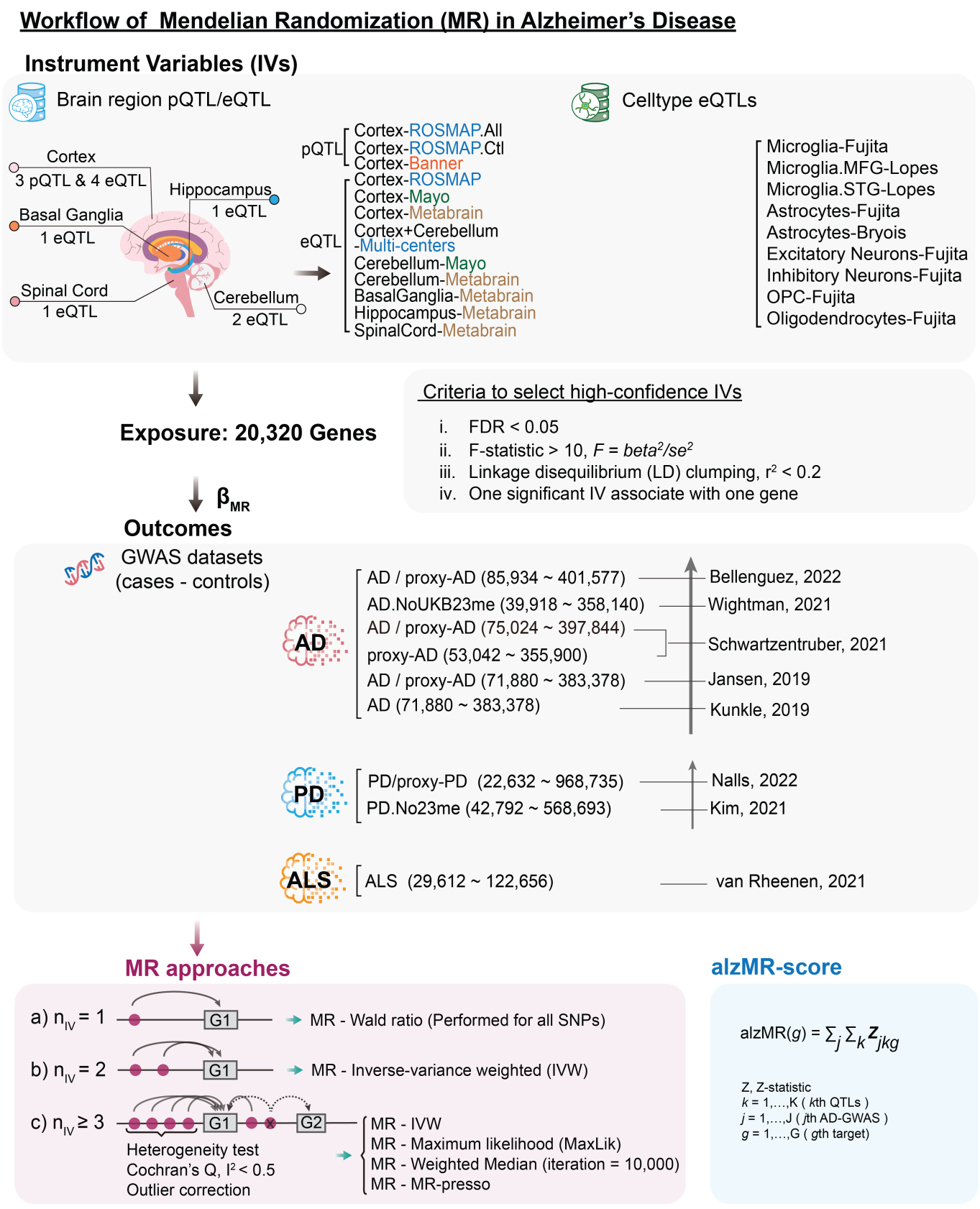
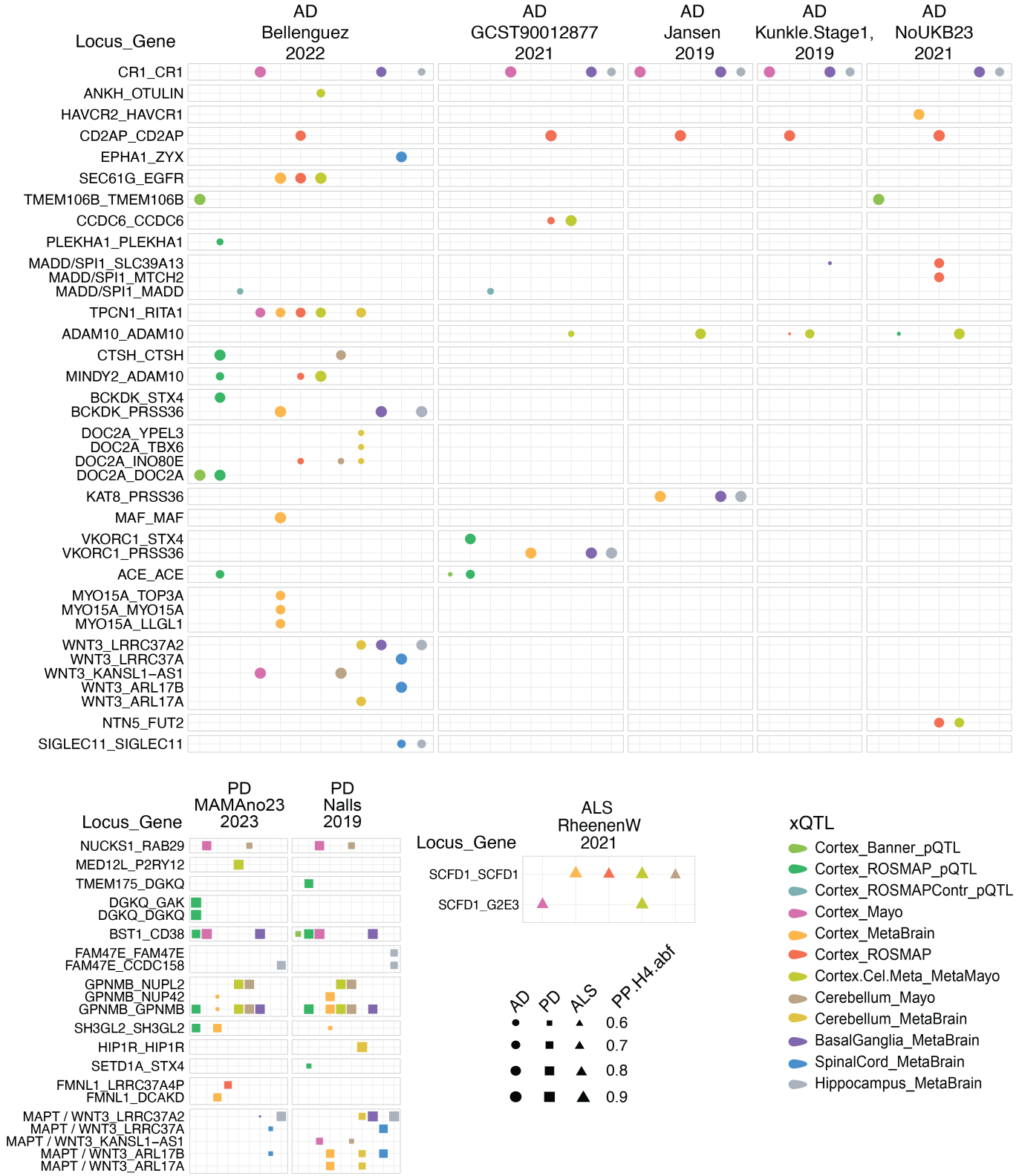
Supplementary Figure 1



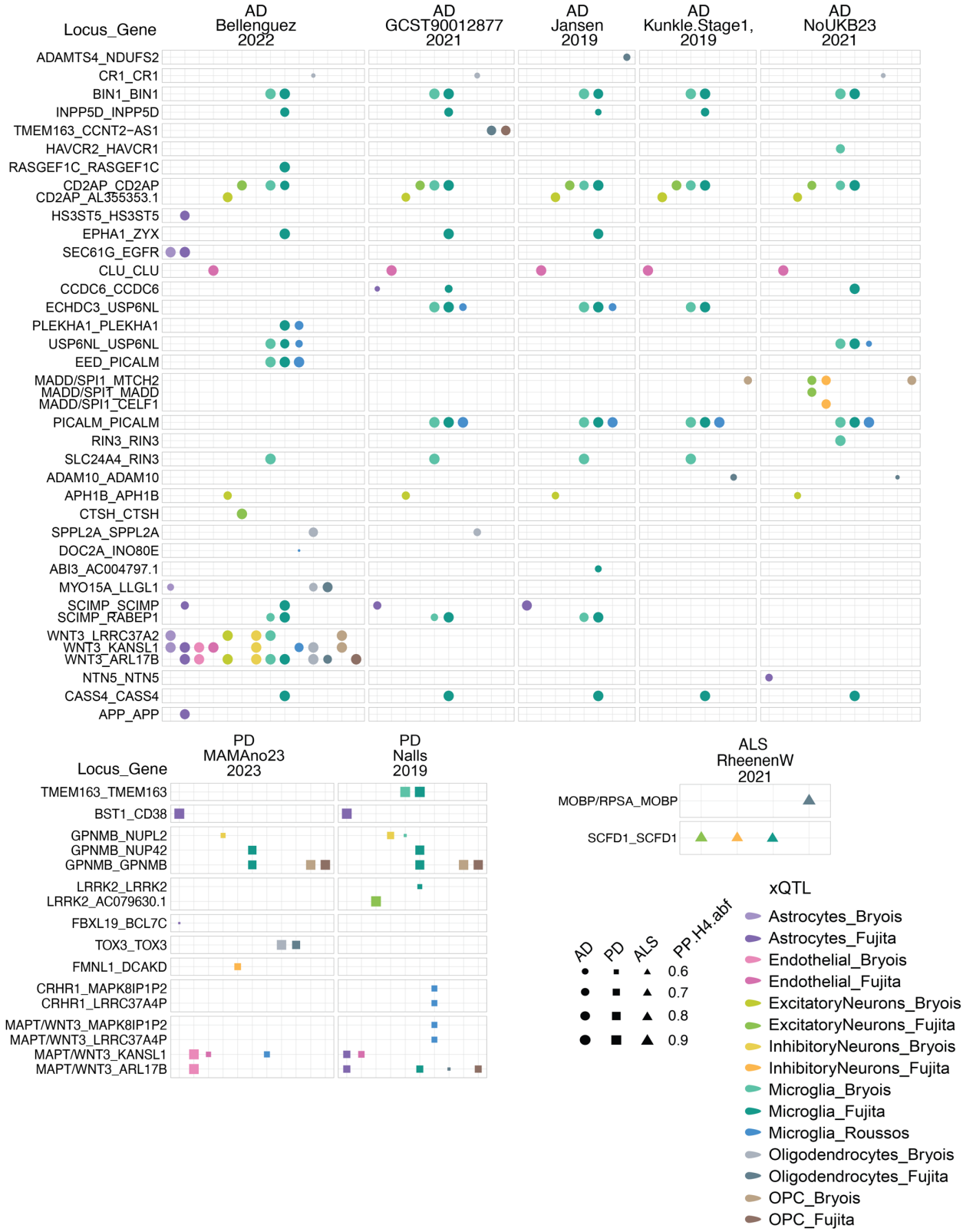
Supplementary Figure 1. Workflow of Mendelian Randomization (MR) analysis across Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS).

Supplementary Figure 2



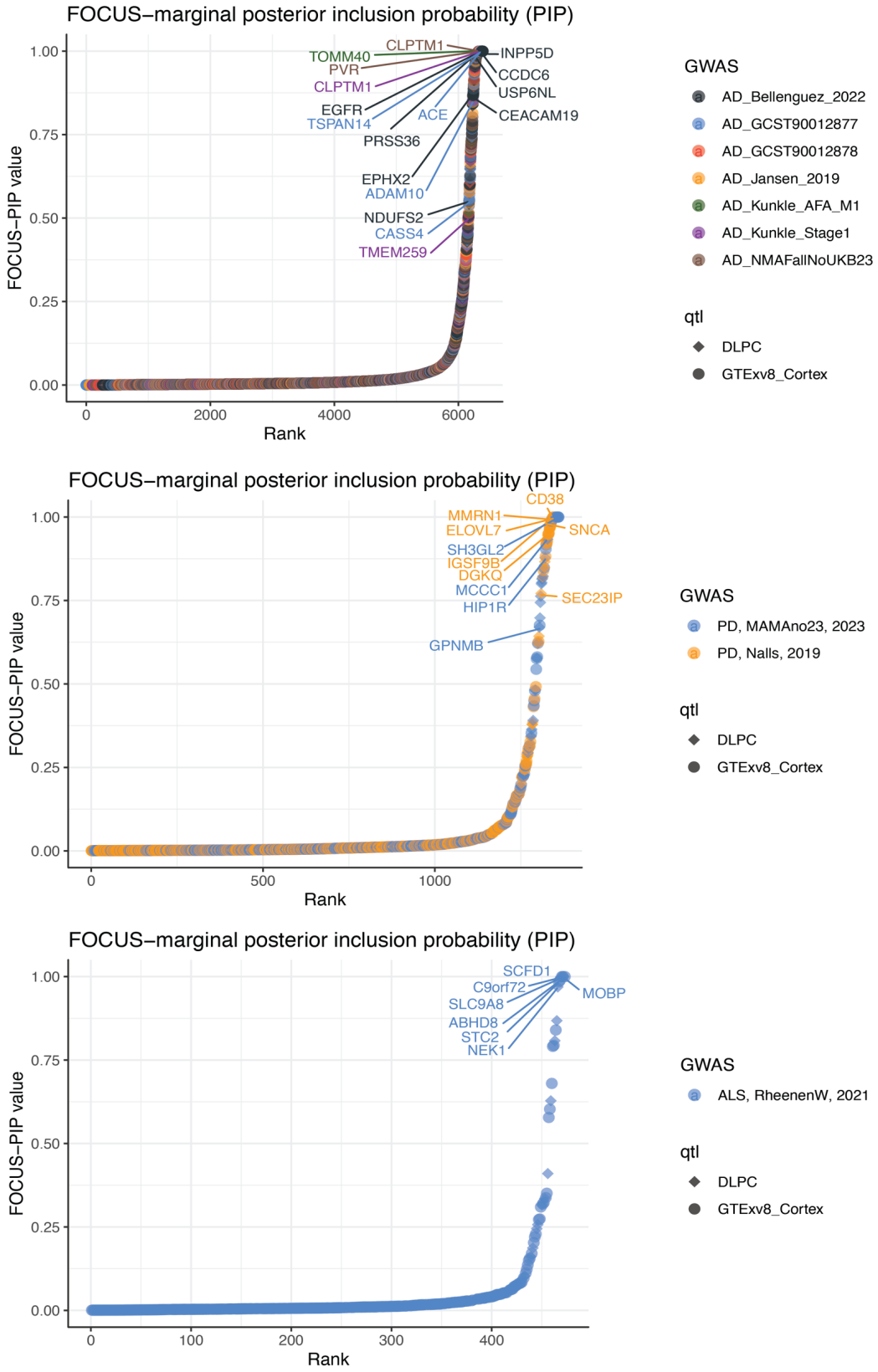
Supplementary Figure 2. Colocalization of brain region eQTLs with Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) GWAS signals. Three different shapes represent AD, PD, and ALS GWAS data sources. Twelve colors denote eQTL data sources from different brain regions.

Supplementary Figure 3



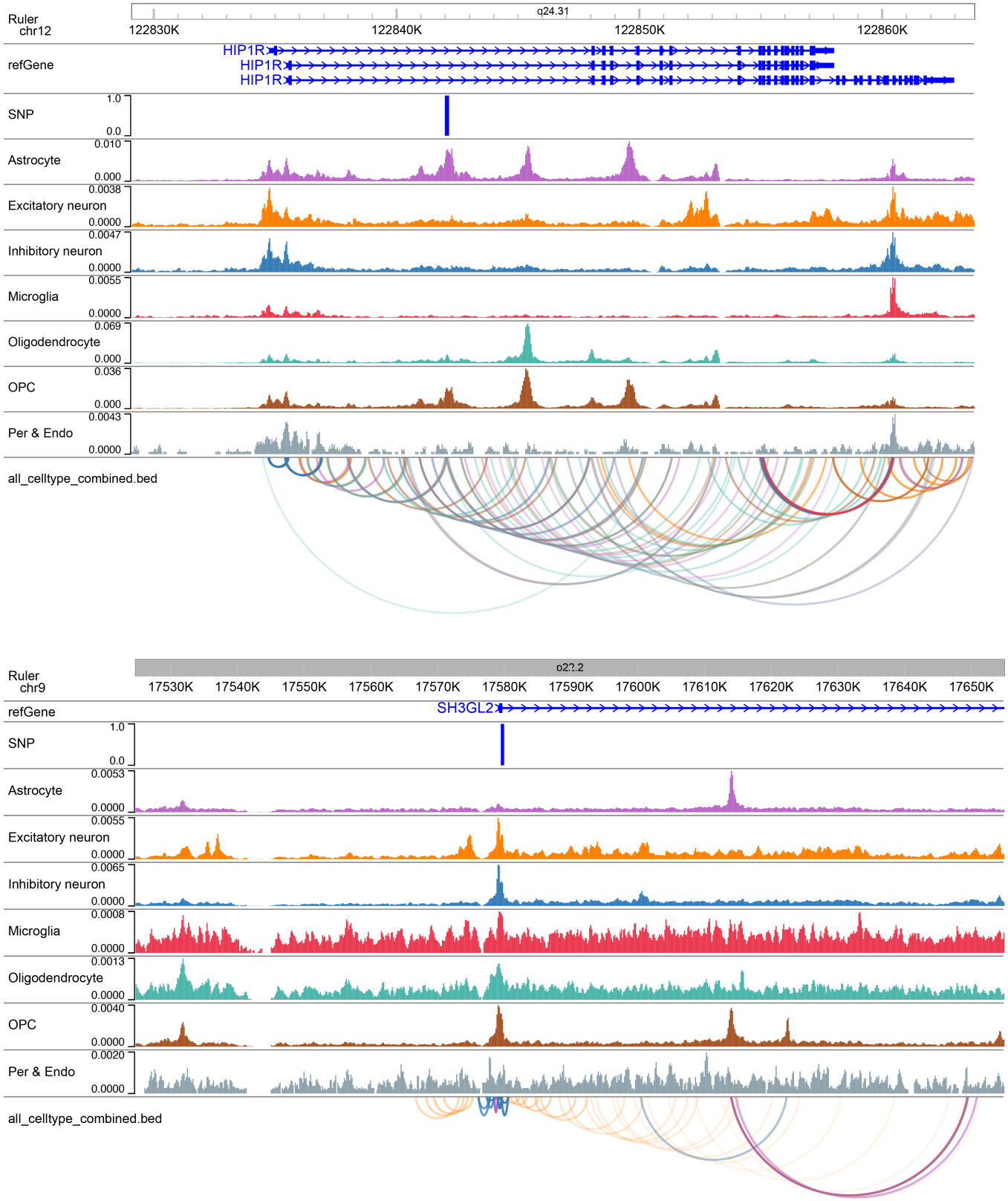
Supplementary Figure 3. Colocalization of brain cell type specific eQTLs with Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS) GWAS signals. Three different shapes represent AD, PD, and ALS GWAS data sources. Colors denote eQTL data sources from different cell types.

Supplementary Figure 4



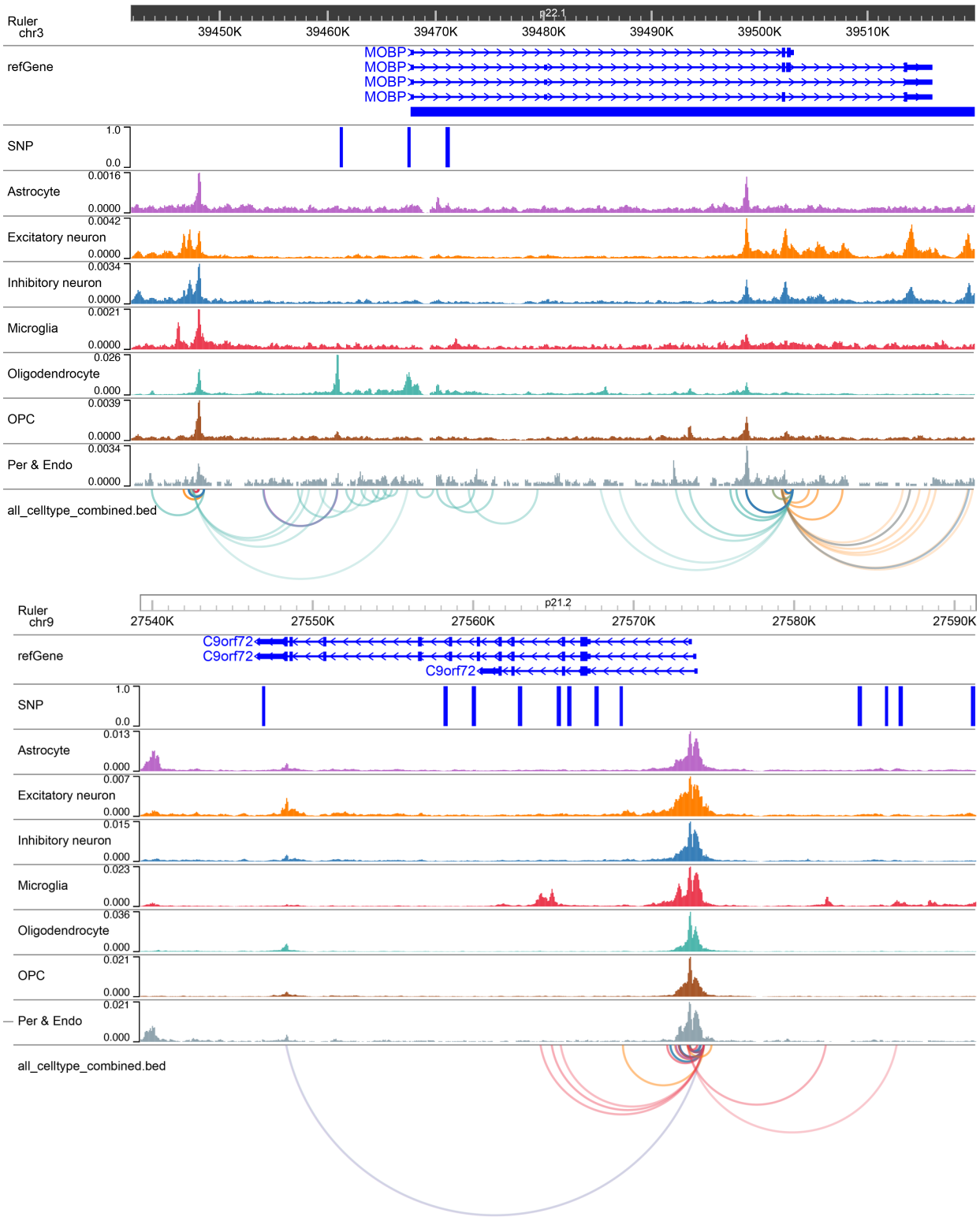
Supplementary Figure 4. FOCUS fine-mapping analysis for Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS). Colors indicate different GWAS datasets and shapes indicate the QTL data used for analysis.

Supplementary Figure 5



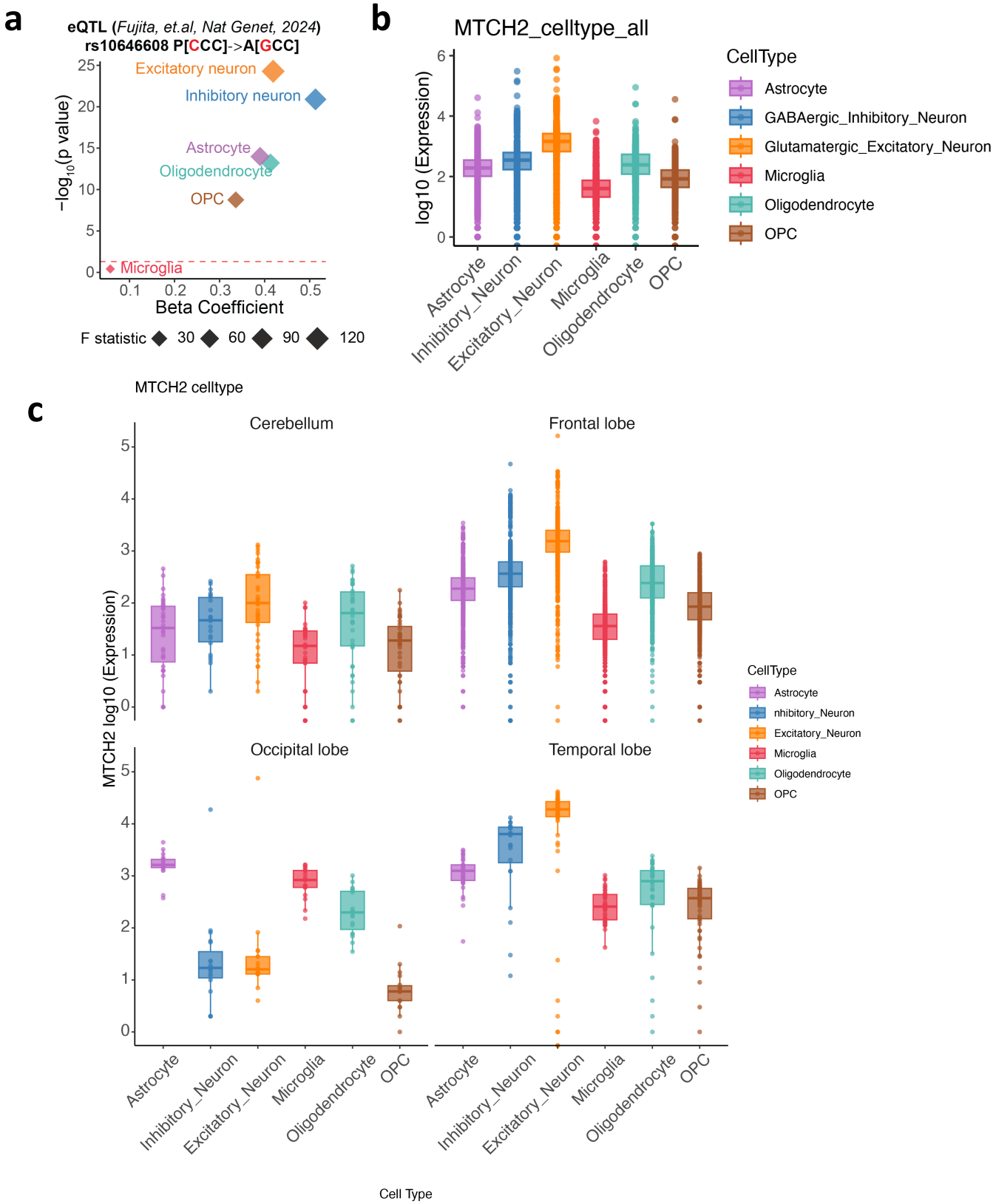
Supplementary Figure 5. The case studies of SNP-gene pairs validated by peak-to-gene analysis for Parkinson's disease (PD). a. snATAC-seq and peak-to-gene loop validated SNP-gene association pairs across PD. Different colored arch lines denote cell type specific significant peak-to-gene associations and the colorful peaks indicate chromatin accessibility in snATAC-seq data.

Supplementary Figure 6



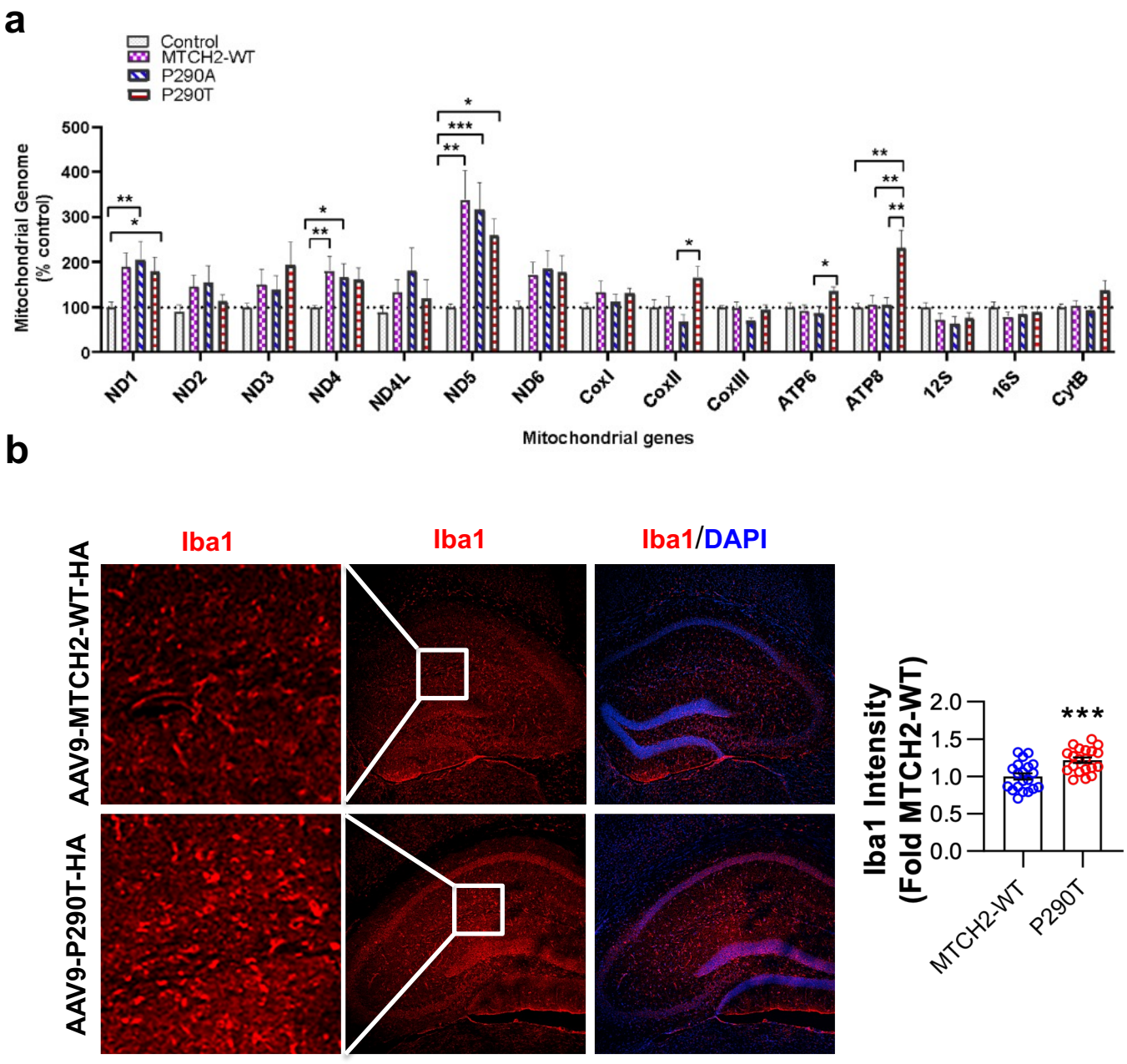
Supplementary Figure 6. The case studies of SNP-gene pairs validated by peak-to-gene analysis for amyotrophic lateral sclerosis (ALS). a. snATAC-seq and peak-to-gene loop validated SNP-gene association pairs across ALS. Different colored arch lines denote cell type specific significant peak-to-gene associations, and the colorful peaks indicate chromatin accessibility in snATAC-seq data.

Supplementary Figure 7



Supplementary Figure 7. *MTCH2* eQTL data and expression level across different human brain cell types. a, Cell type specific eQTL of *MTCH2* nonsynonymous mutation rs10646608 p.P290A (C>G). OPC: oligodendrocyte precursor cells. **b-c,** *MTCH2* expression levels across cell types (**b**) and brain regions (**c**).

Supplementary Figure 8



Supplementary Figure 8. *MTCH2* shows strong genetic evidence in vivo in mouse brains by AAV experiments. a, The mitochondrial genome expression comparing in the groups of MTCH-WT, P290A, P290T and controls. **b,** Representative images of IBA1 in the brains of C57BL6/J mice injected with rAAV9-*MTCH2*^{WT}-HA and rAAV9-*MTCH2*$^{p.P290T}$-HA. Quantification of IBA1 intensity (t-test, ***P < 0.001, n = 4 mice/group).