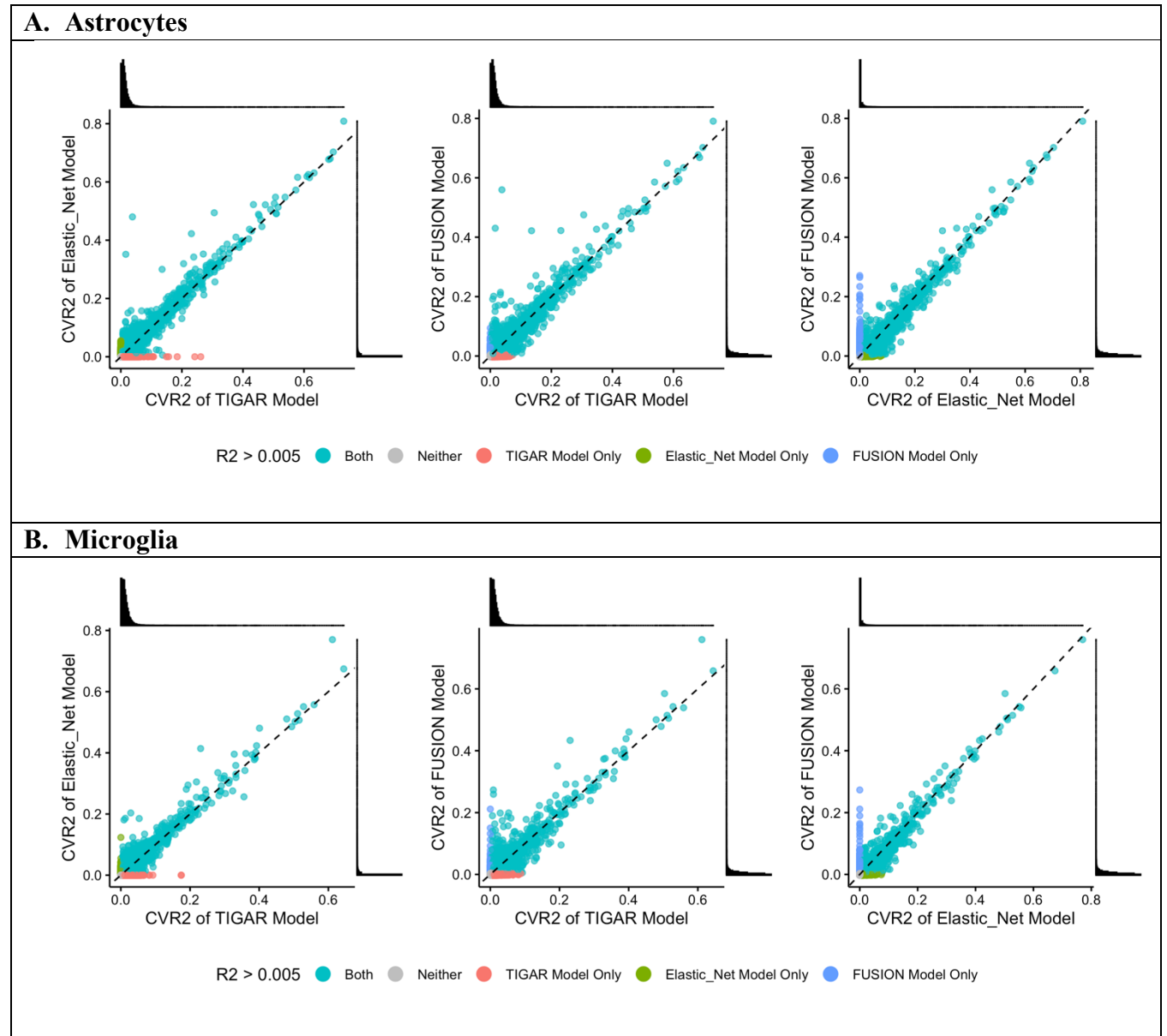


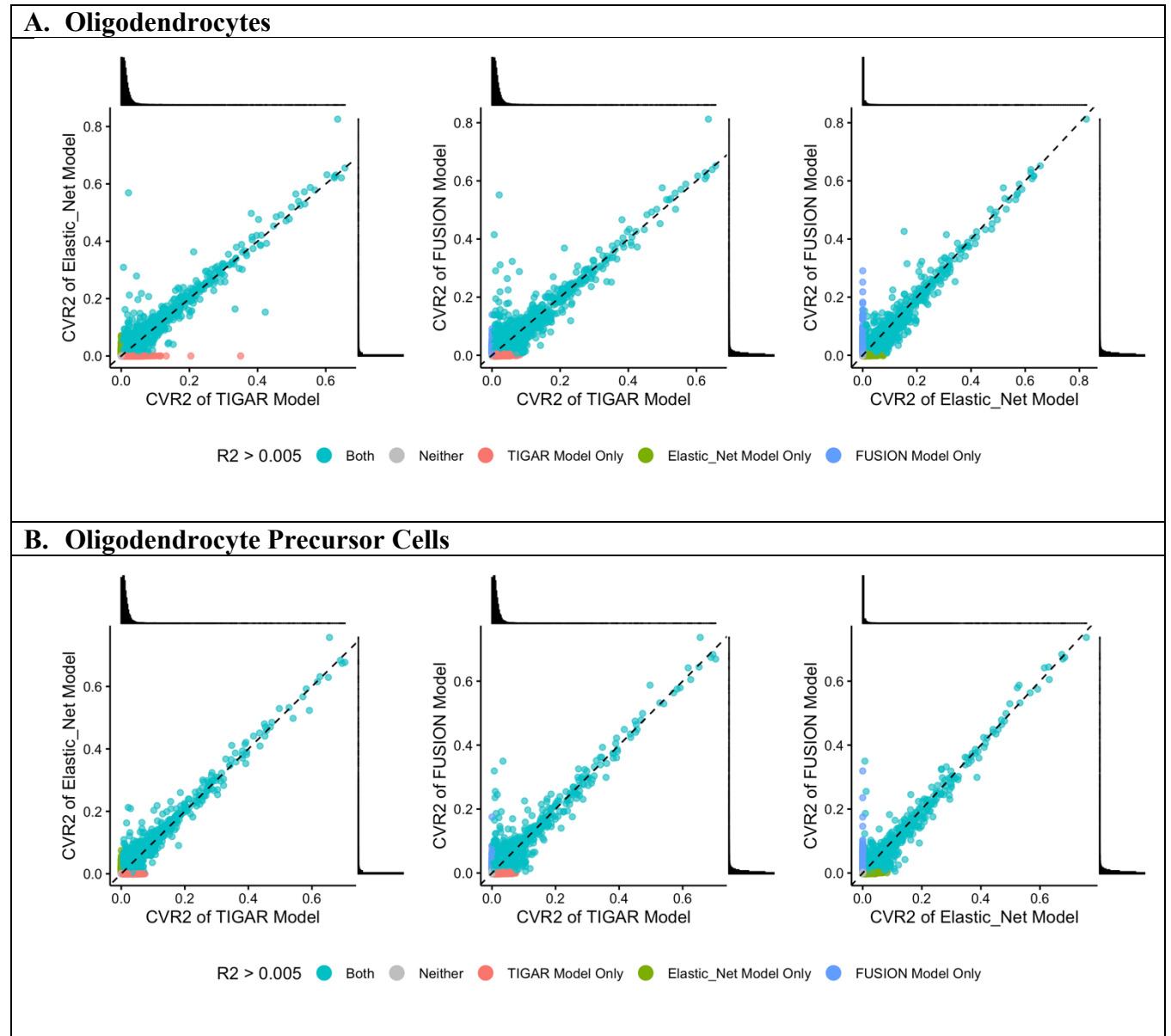
Supplementary Figure 1. Pairwise comparison of CV R^2 of cell-type-specific gene expression imputation models by TIGAR/DPR, PrediXcan/EN, and FUSION/BestModel in astrocytes and microglia.

Each panel presents scatter plots comparing CV R^2 between pair-wise models, with each dot representing a gene. Colors indicate different gene groups: genes with CV $R^2 > 0.5\%$ in both compared models (Both:teal), in only one of the two compared models (TIGAR-only:red, Elastic Net-only:green, or FUSION-only:blue), or in neither models (Neither:gray).



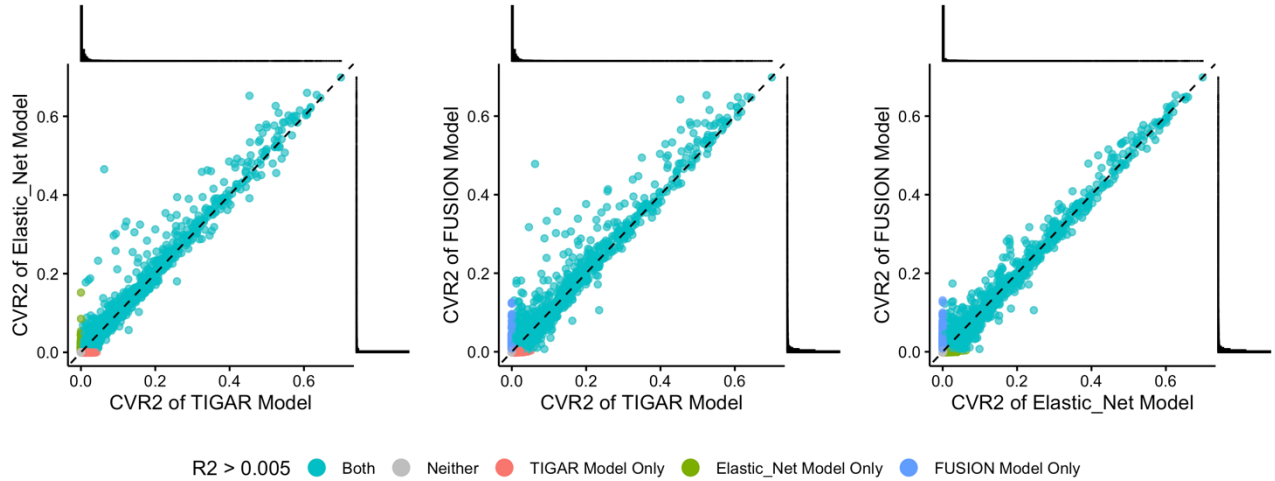
Supplementary Figure 3. Pairwise comparison of CV R^2 of cell-type-specific gene expression imputation models by TIGAR/DPR, PrediXcan/EN, and FUSION/BestModel in Oligodendrocytes and Oligodendrocyte Precursor Cells.

Each panel presents scatter plots comparing CV R^2 between pair-wise models, with each dot representing a gene. Colors indicate different gene groups: genes with CV $R^2 > 0.5\%$ in both compared models (Both:teal), in only one of the two compared models (TIGAR-only:red, Elastic Net-only:green, or FUSION-only:blue), or in neither model (Neither:gray).



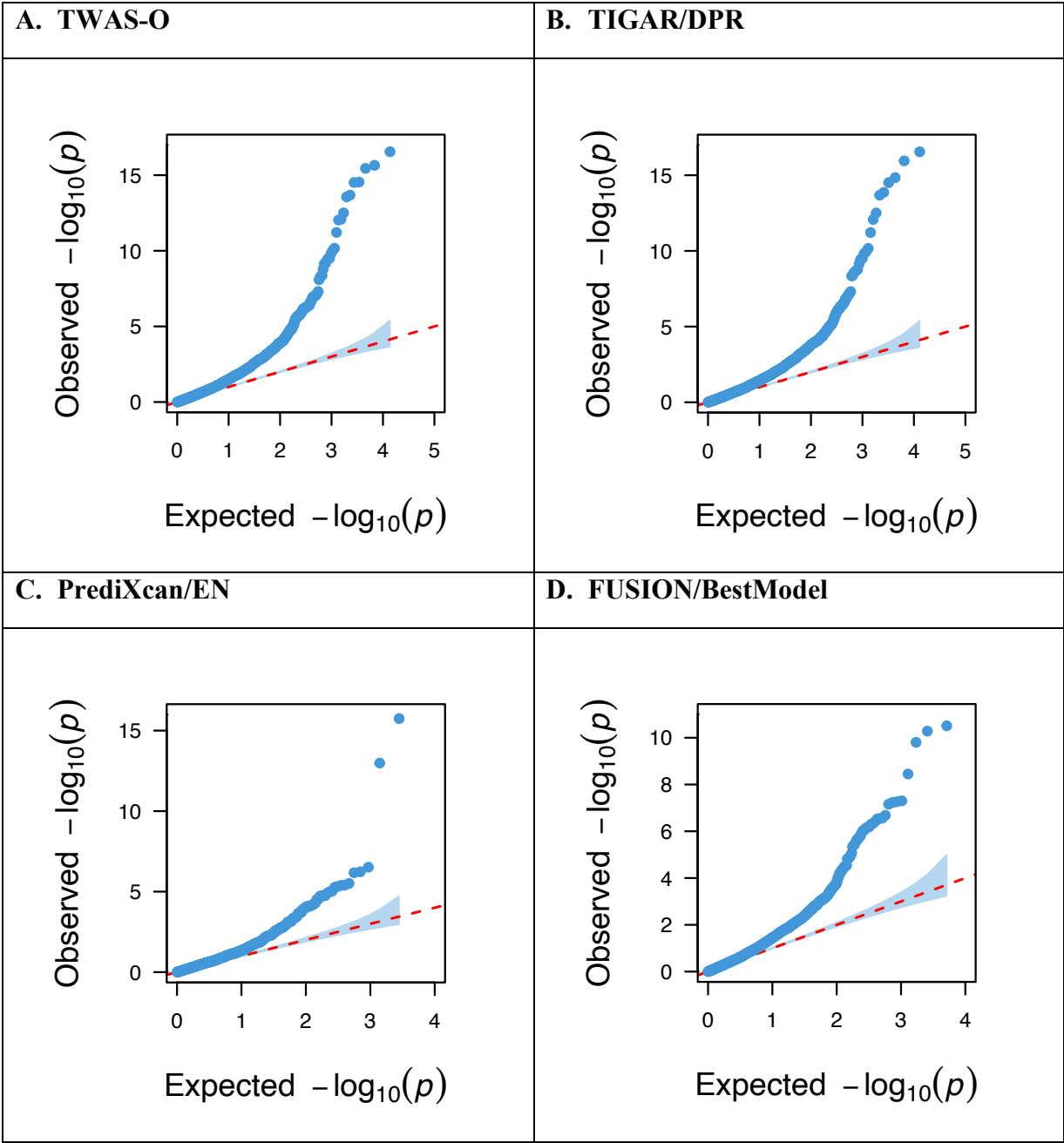
Supplementary Figure 4. Pairwise comparison of CV R^2 of protein abundance imputation models by TIGAR/DPR, PrediXcan/EN, and FUSION/BestModel.

Each panel presents scatter plots comparing CV R^2 between pair-wise models, with each dot representing a gene. Colors indicate different gene groups: genes with CV $R^2 > 0.5\%$ in both compared models (Both:teal), in only one of the two compared models (TIGAR-only:red, Elastic Net-only:green, or FUSION-only:blue), or in neither model (Neither:gray).



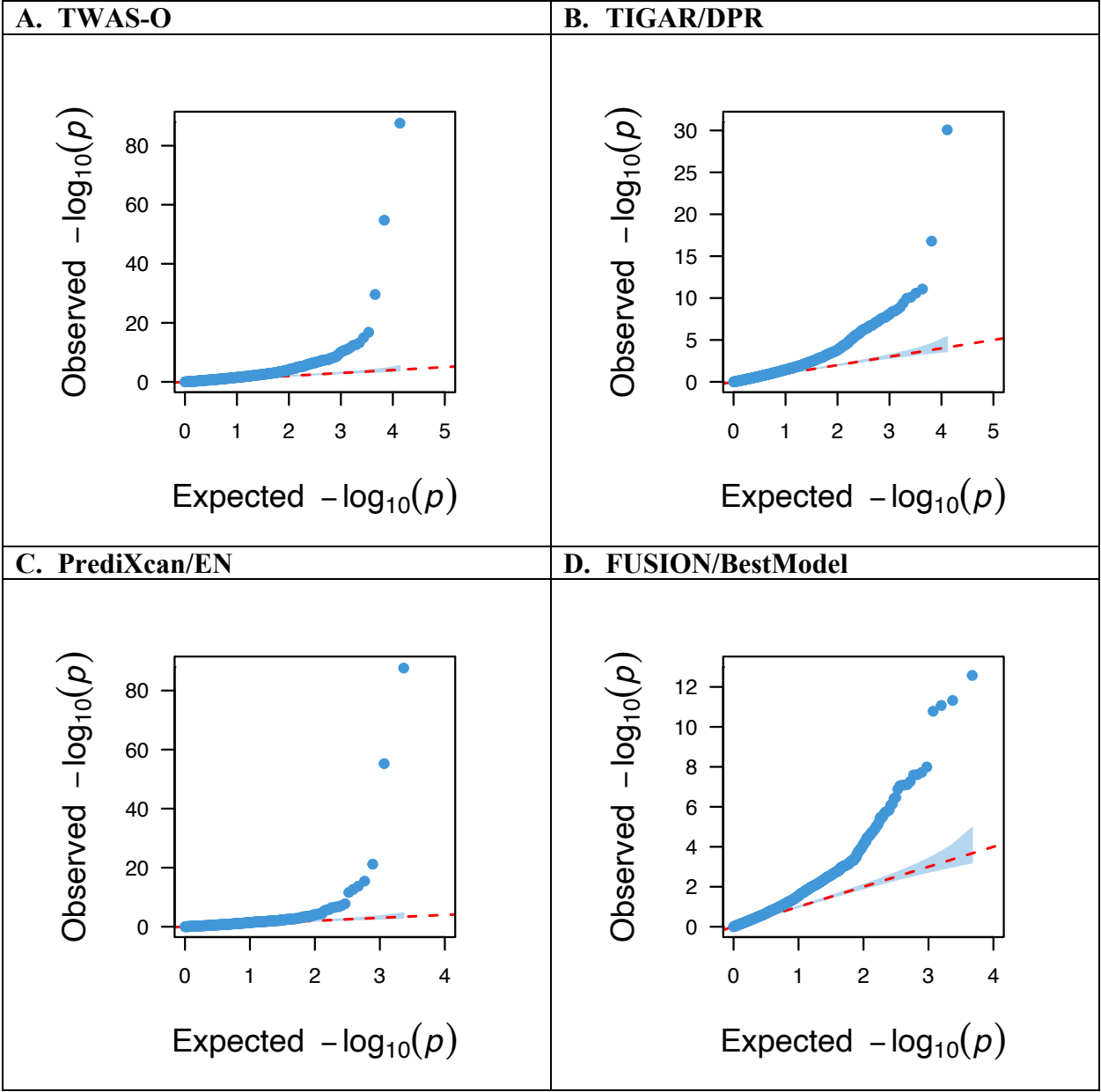
Supplementary Figure 5. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in astrocytes.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.45$ for TWAS-O p-values.



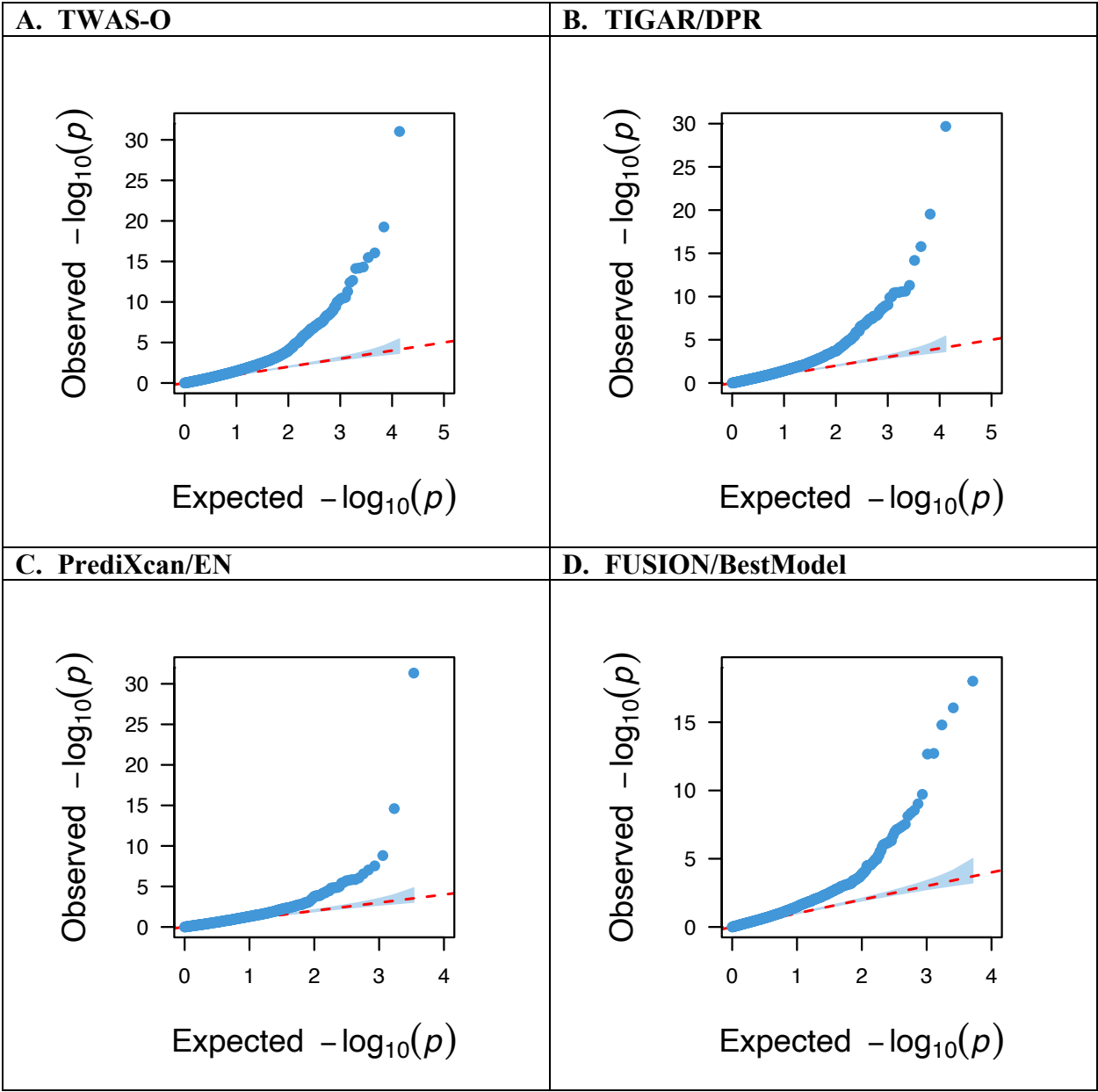
Supplementary Figure 6. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in microglia.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.48$ for TWAS-O p-values.



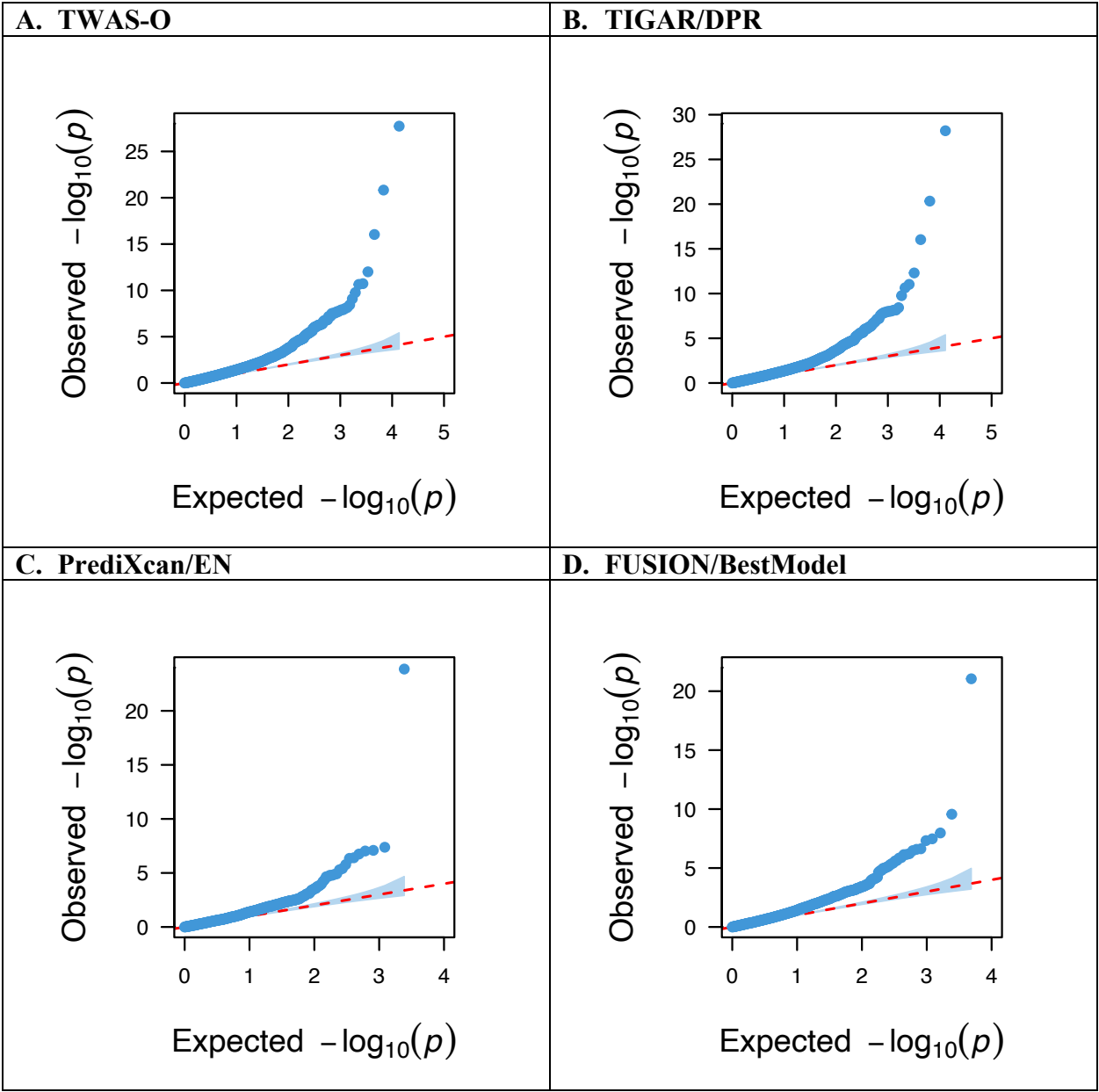
Supplementary Figure 7. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in excitatory neurons.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.45$ for TWAS-O p-values.



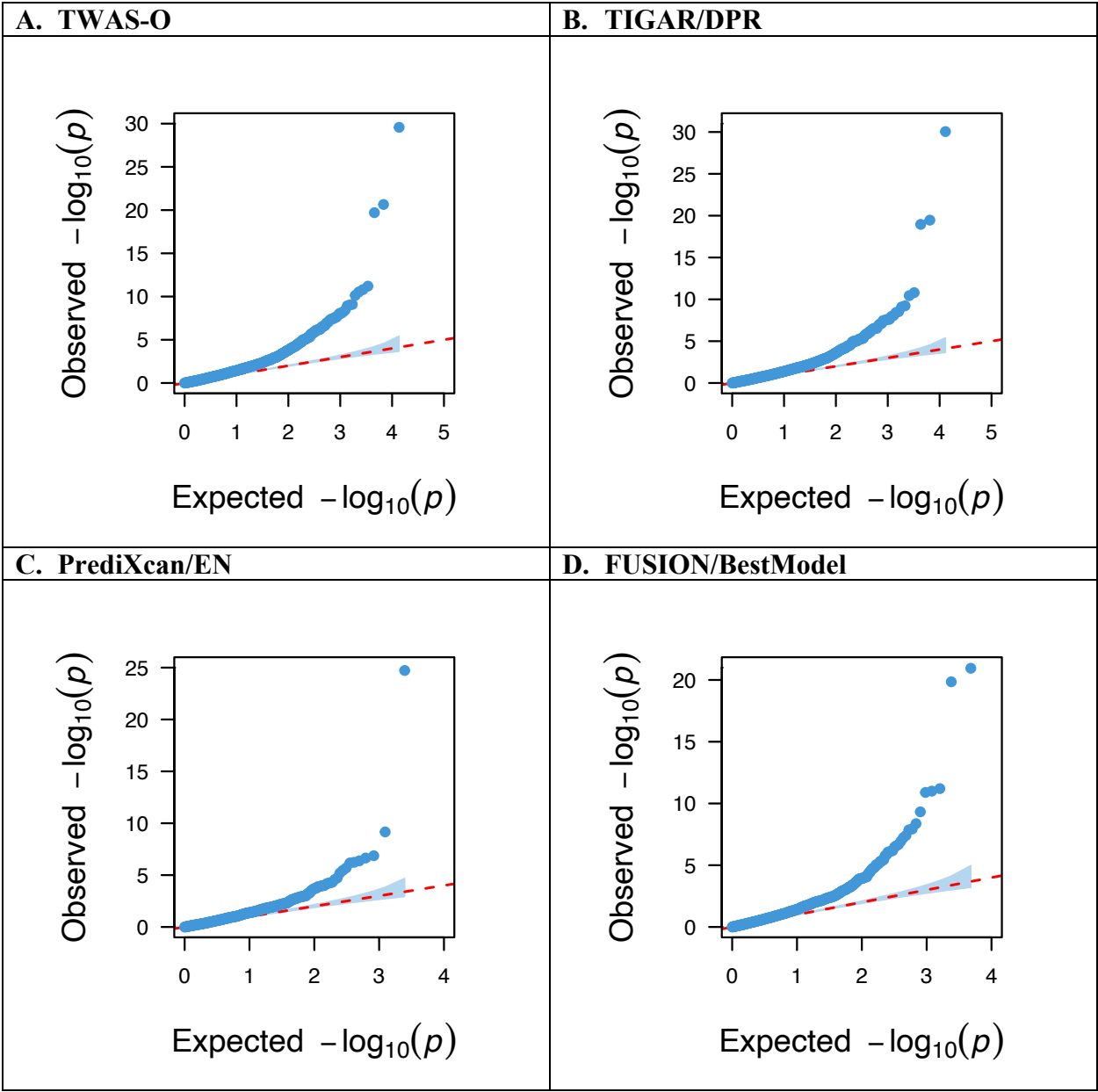
Supplementary Figure 8. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in inhibitory neurons.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.41$ for TWAS-O p-values.



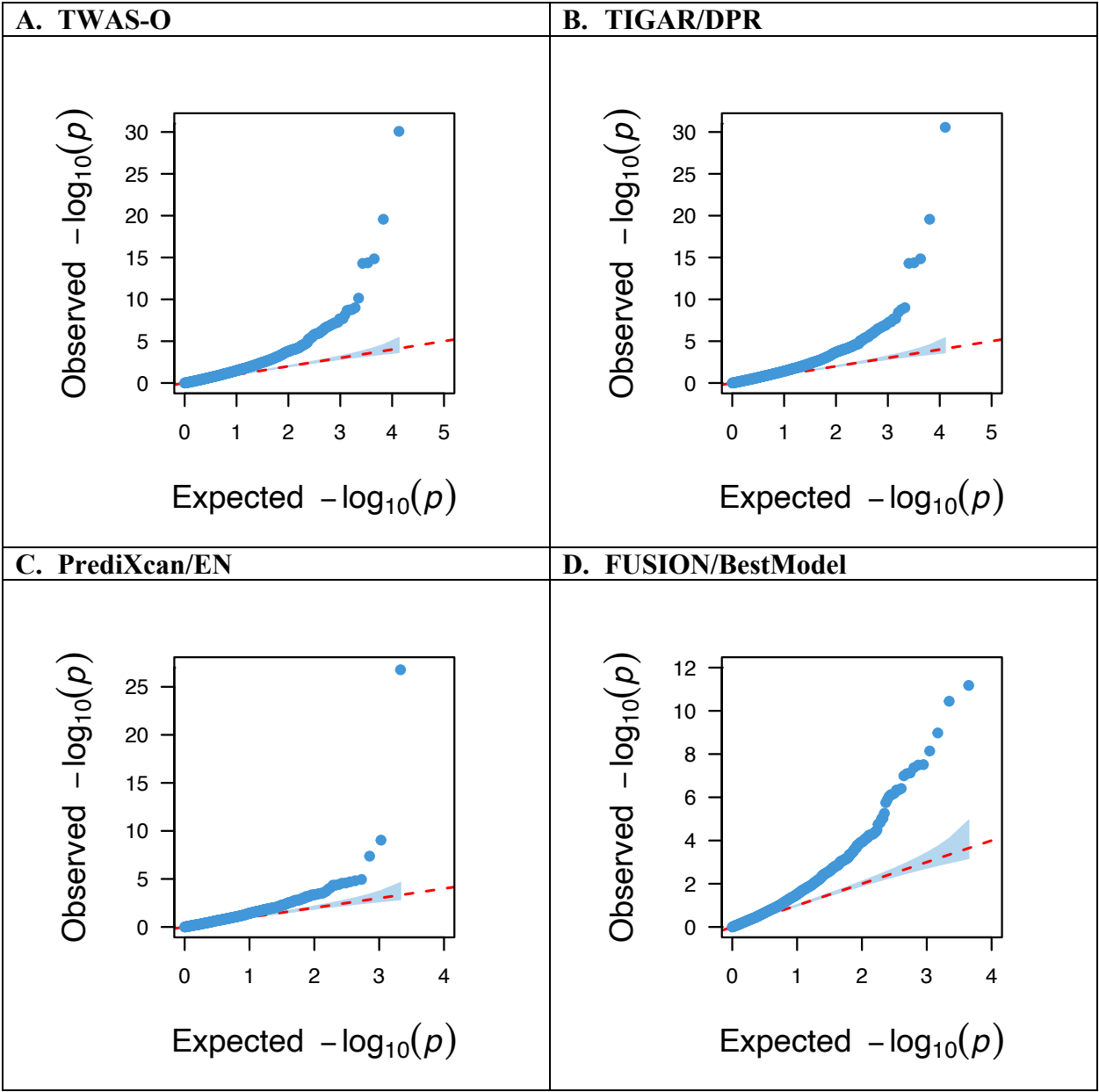
Supplementary Figure 9. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in oligodendrocytes.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.40$ for TWAS-O p-values.

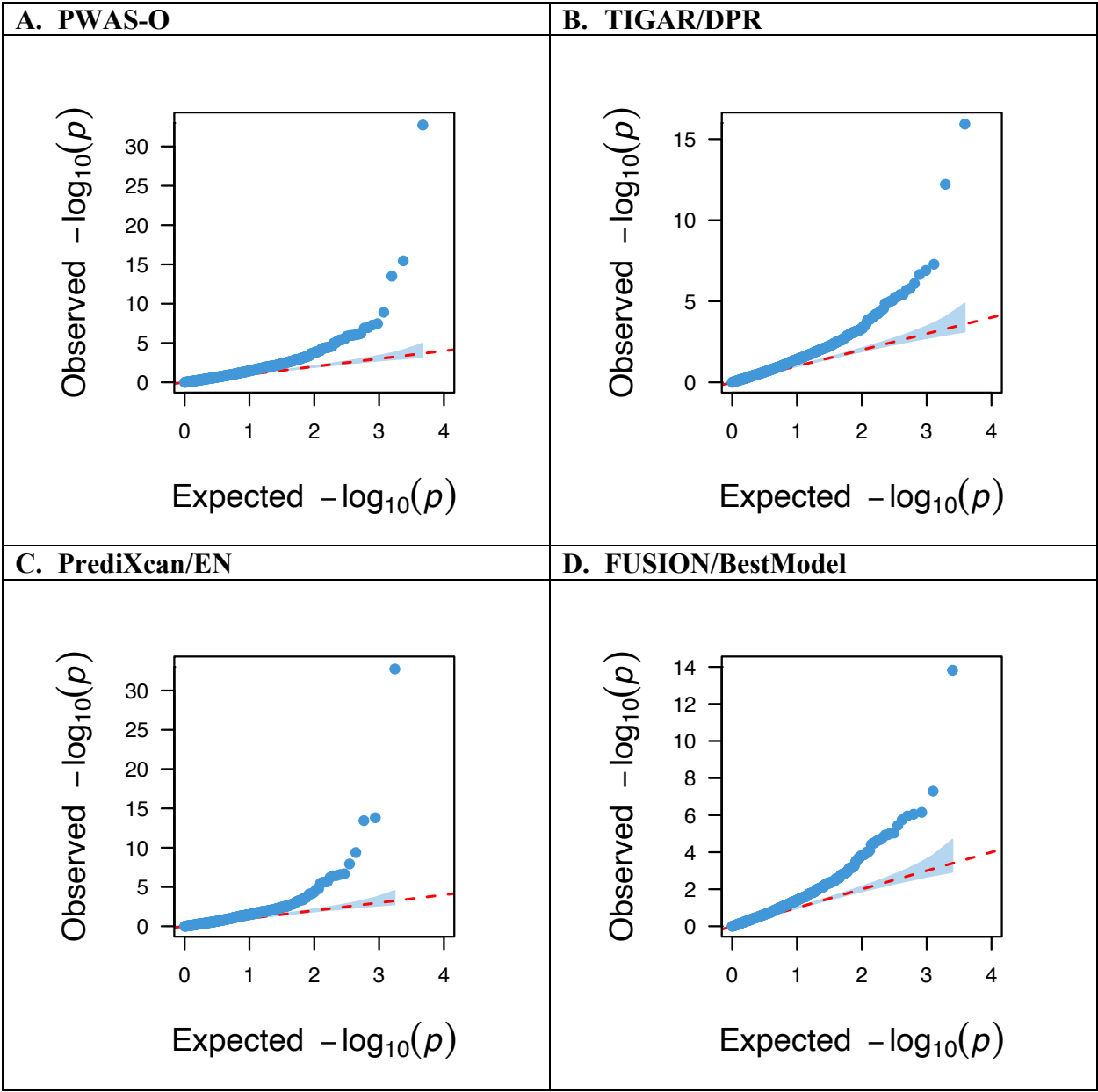


Supplementary Figure 10. Quantile-Quantile (Q-Q) plots of transcriptome-wide $-\log_{10}(p)$ -values obtained by TWAS-O and three individual tools for studying AD dementia in oligodendrocyte precursor cells.

Inflated false positive rates are observed in all TWAS results. Genomic control factor was obtained as $\lambda = 1.47$ for TWAS-O p-values.

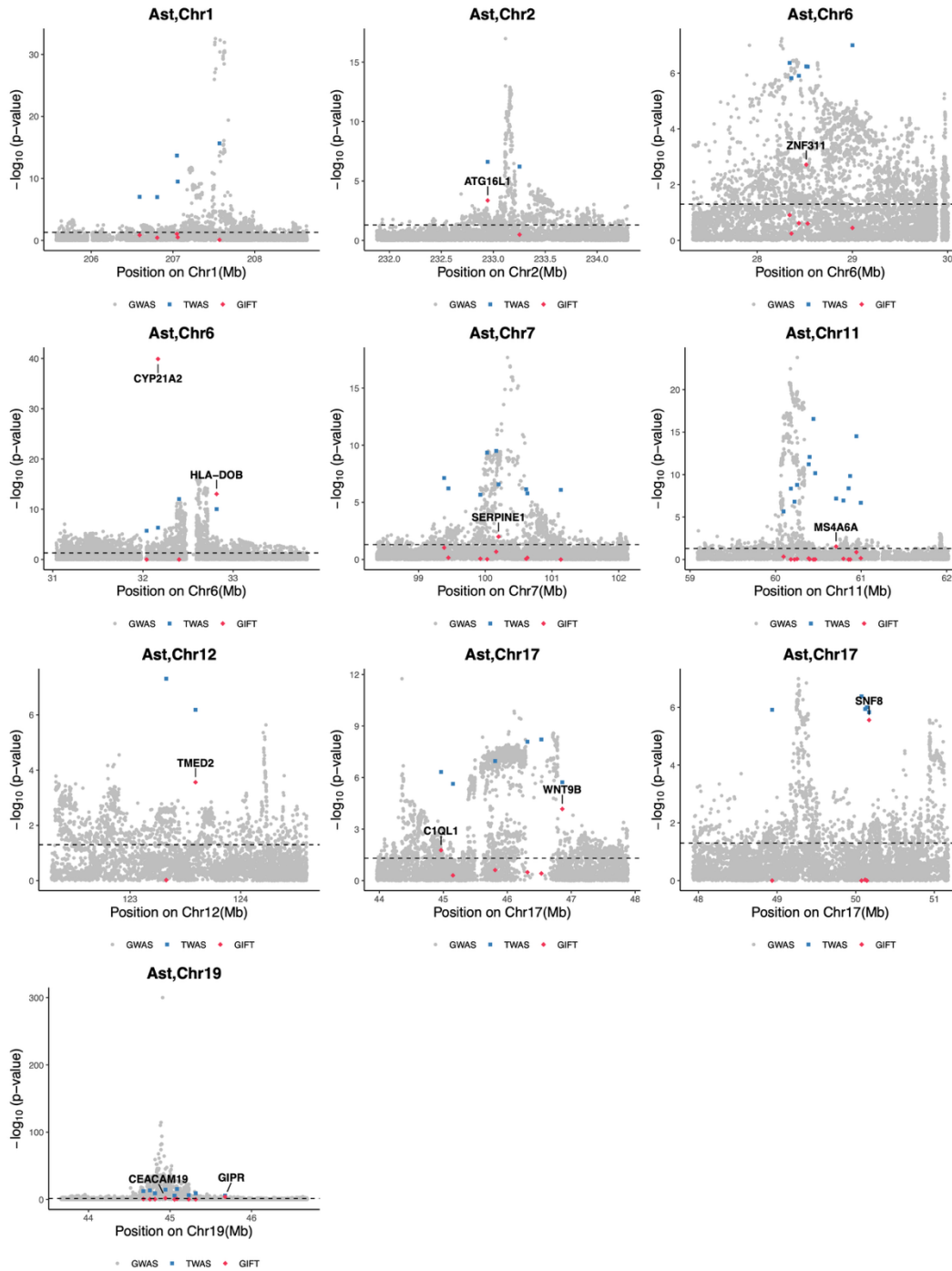


Supplementary Figure 11. Quantile-Quantile (Q-Q) plots of proteome-wide $-\log_{10}(p)$ -values obtained by PWAS-O and three individual tools for studying AD dementia. Inflated false positive rates are observed in all PWAS results. Genomic control factor was obtained as $\lambda = 1.47$ for PWAS-O p-values.



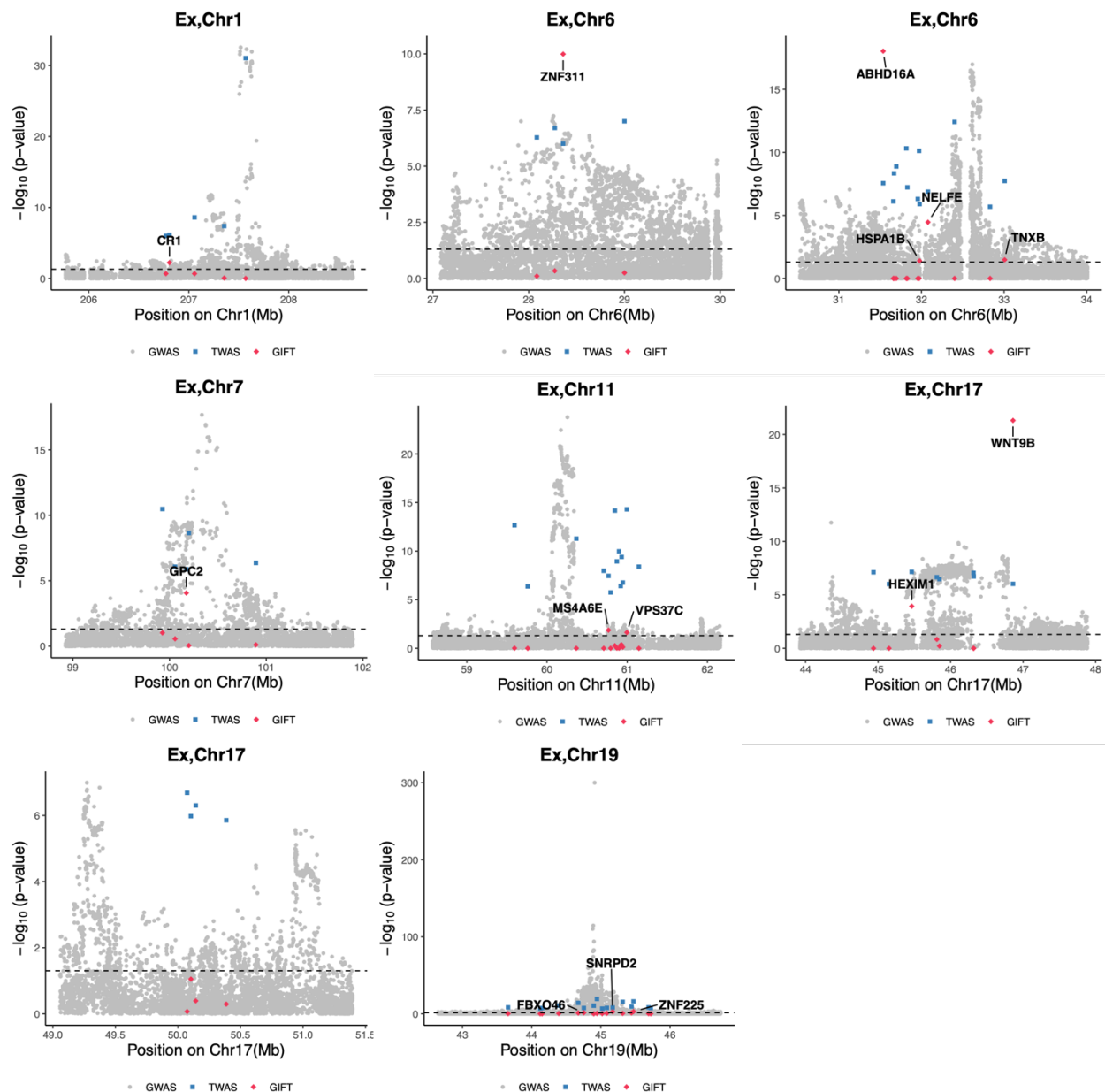
Supplementary Figure 12. Locus plots of the fine-mapped results by GIFT of TWAS-O results in astrocytes (Ast).

Each panel represents the fine-mapped results by GIFT within one genomic region (± 1 Mb around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-values})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



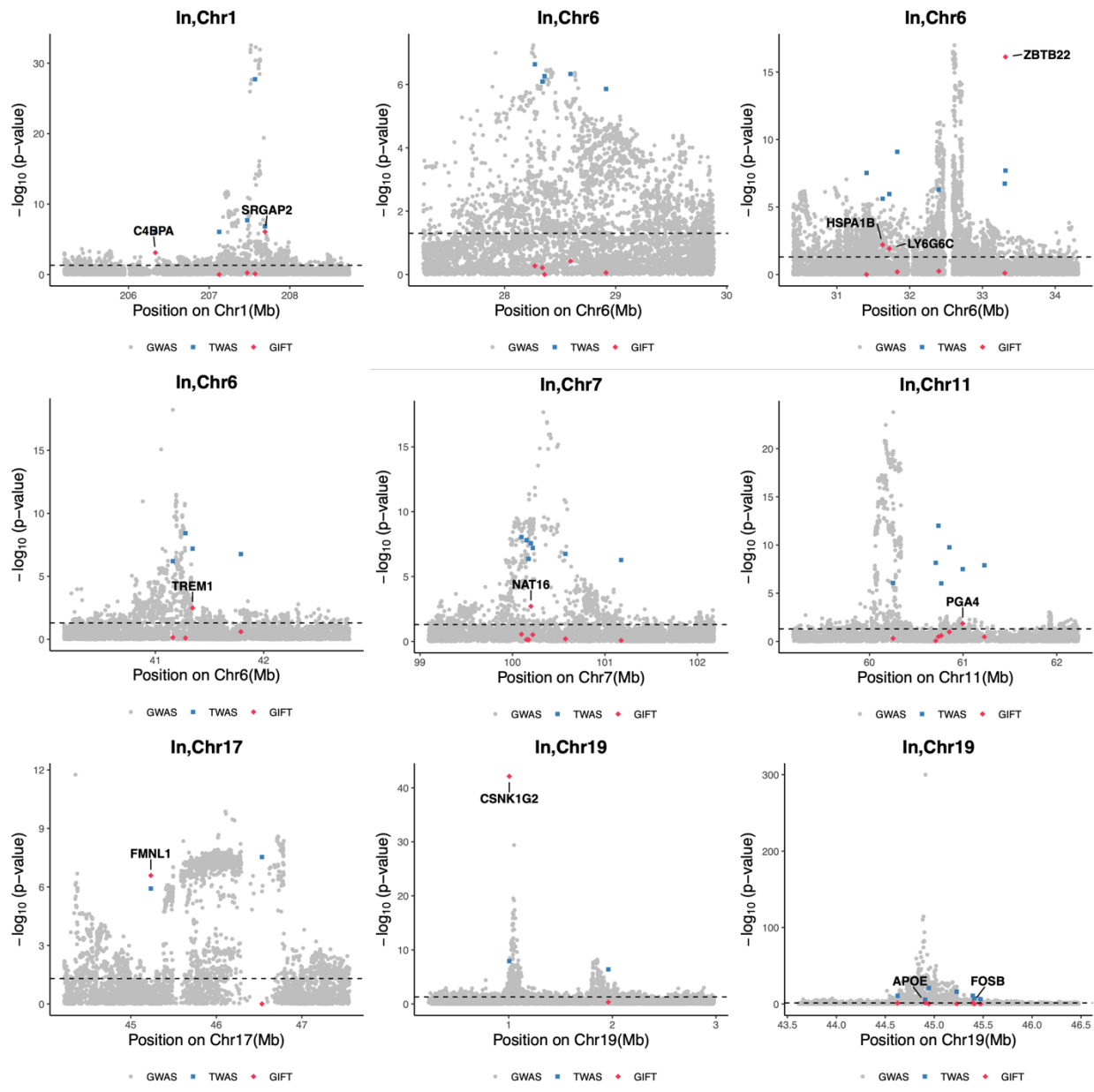
Supplementary Figure 13. Locus plots of the fine-mapped results by GIFT of TWAS-O results in excitatory neurons (Ex).

Each panel represents the fine-mapped results by GIFT within one genomic region (± 1 Mb around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-value})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



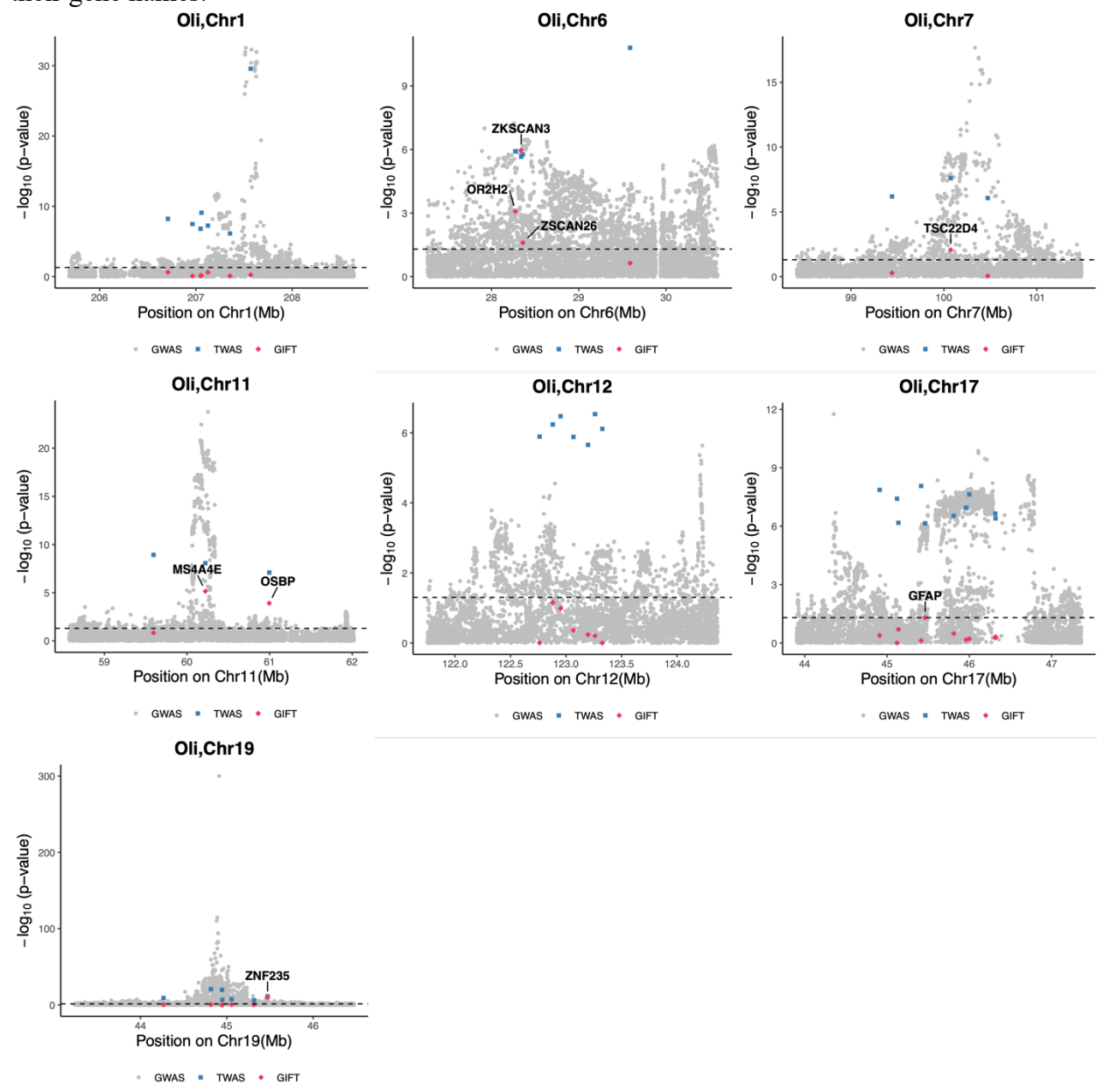
Supplementary Figure 14. Locus plots of the fine-mapped results by GIFT of TWAS-O results in inhibitory neurons (In).

Each panel represents the fine-mapped results by GIFT within one genomic region ($\pm 1\text{Mb}$ around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-value})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



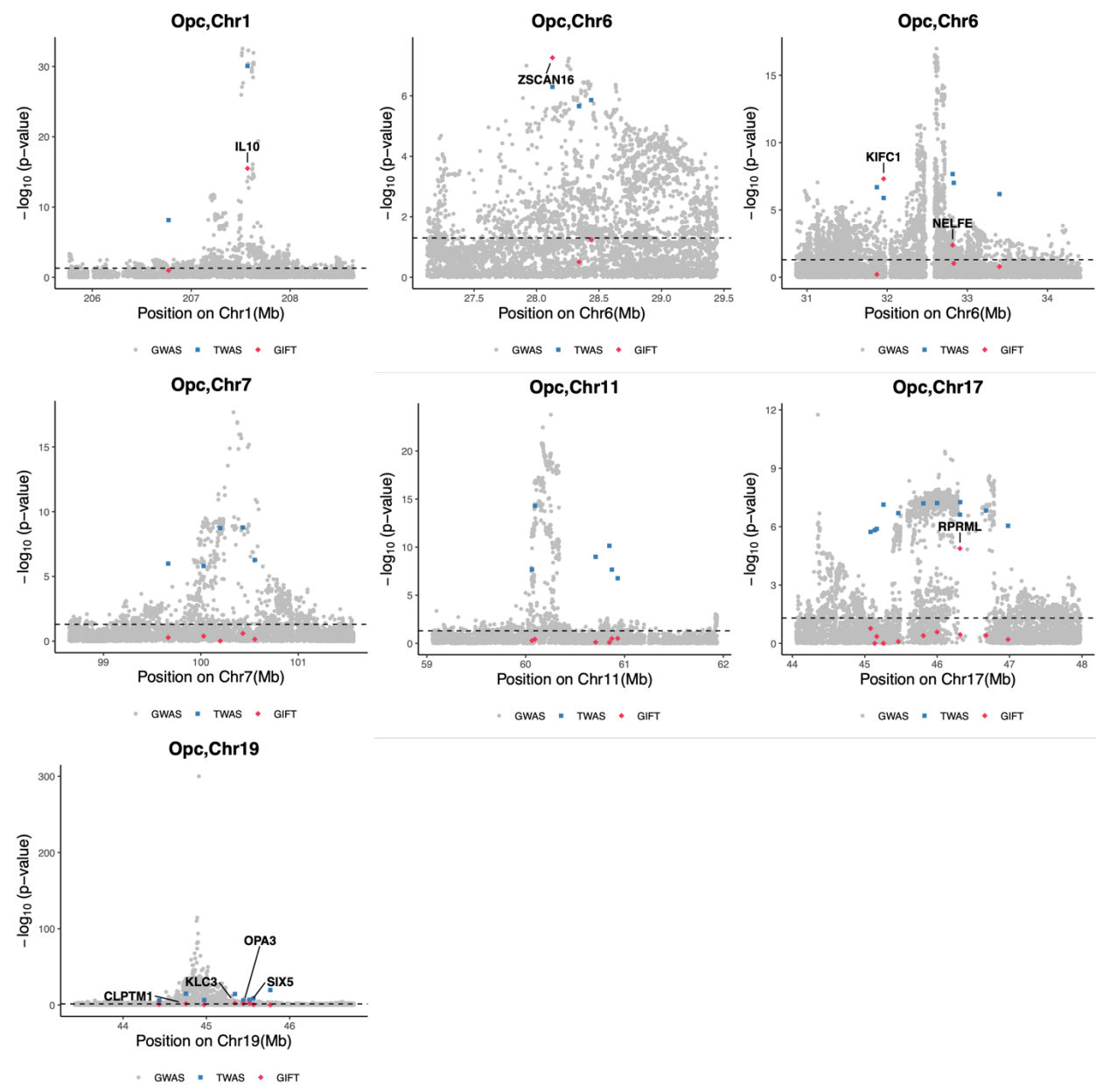
Supplementary Figure 15. Locus plots of the fine-mapped results by GIFT of TWAS-O results in oligodendrocytes (Oli).

Each panel represents the fine-mapped results by GIFT within one genomic region (± 1 Mb around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-values})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



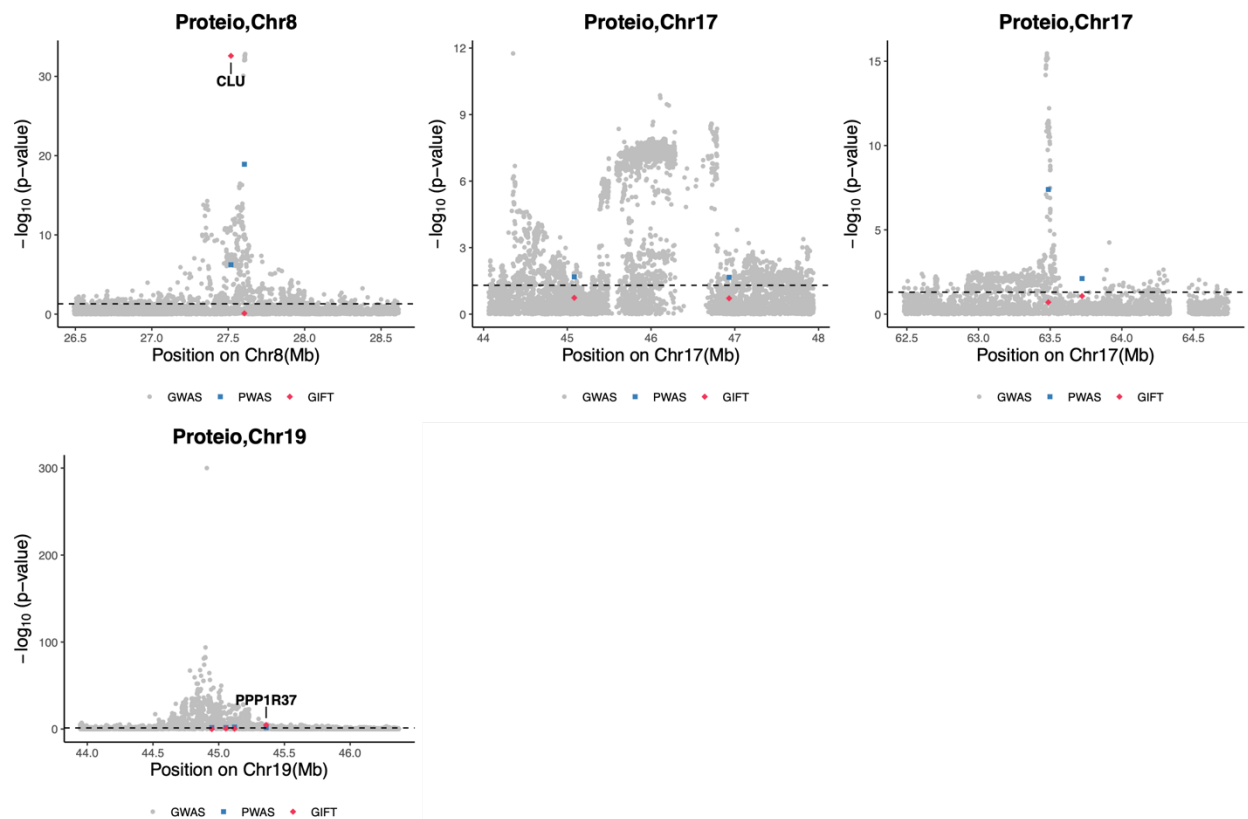
Supplementary Figure 16. Locus plots of the fine-mapped results by GIFT of TWAS-O results in oligodendrocyte precursor cells (OPCs).

Each panel represents the fine-mapped results by GIFT within one genomic region (± 1 Mb around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-value})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



Supplementary Figure 17. Locus plots of the fine-mapped results by GIFT of PWAS-O results in proteomics (Proteome).

Each panel represents the fine-mapped results by GIFT within one genomic region (± 1 Mb around the top significant TWAS-O risk genes) that contains multiple significant TWAS-O risk genes. X-axis: chromosomal position (Mb); Y-axis: $-\log_{10}(\text{p-values})$ by GWAS (gray dots), TWAS-O (blue squares), and GIFT (red diamonds); Dashed horizontal line: the significance threshold of 0.05 for GIFT p-value. Genes with significant GIFT p-values < 0.05 are labeled with their gene names.



Supplementary Figure 18. Jaccard similarity indexes of overlapped transcriptome-wide and proteome-wide significant TWAS-O/PWAS-O risk genes by pair-wise comparisons. Jaccard similarity index is the proportion of overlapped significant risk genes among the union of unique significant risk genes detected by both compared analyses. Only genes with the same names are considered overlapped in the calculation of Jaccard similarity indexes. Higher Jaccard Index value represents higher proportions of overlapped findings.

