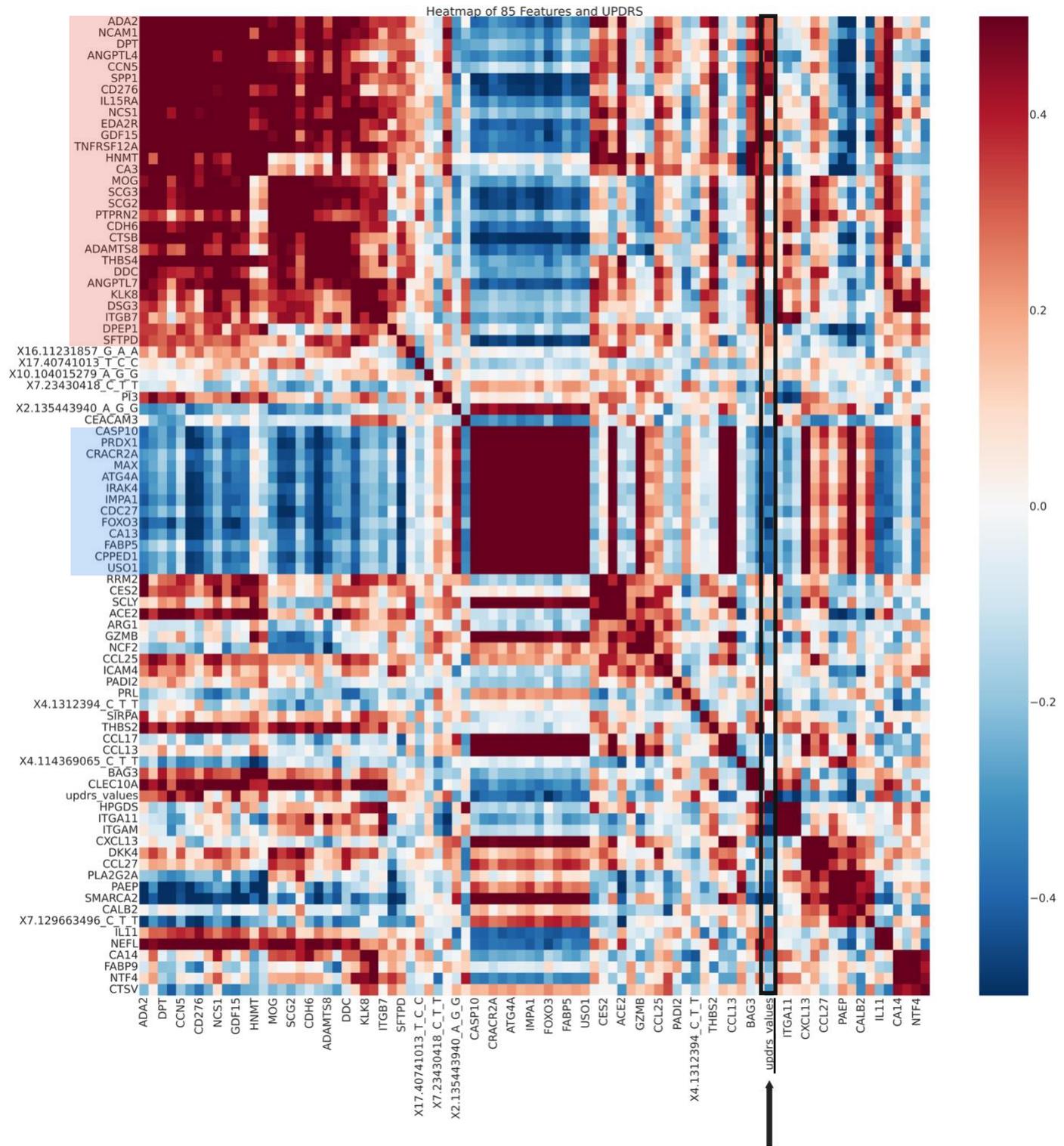


Supplementary Material

Supplement Table 1: Performances of PD prediction models using genetic variants and demographic data. Like table 1, the performance of the three models using SNPs variants was evaluated by AUC, sensitivity, specificity measures for PD classification performance on the UK biobank held-out data as well as AUC performance on the PPMI external validation set.

	Ridge Regression	SVM	Neural Network
<u>AUROC</u> Test	0.70	0.70	0.62
Sensitivity	0.72	0.59	0.37
Specificity	0.55	0.68	0.78
AUROC PPMI	0.55	0.45	0.51

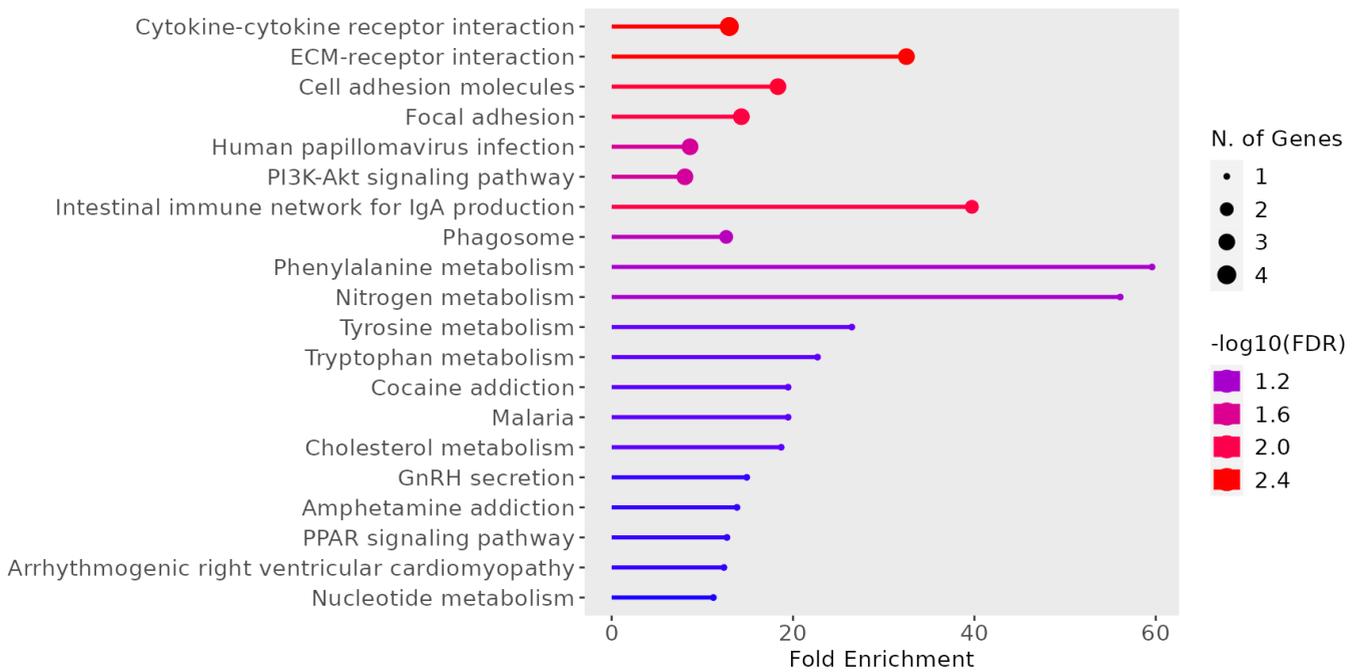
It is made available under a [CC-BY-NC 4.0 International license](https://creativecommons.org/licenses/by-nc/4.0/).



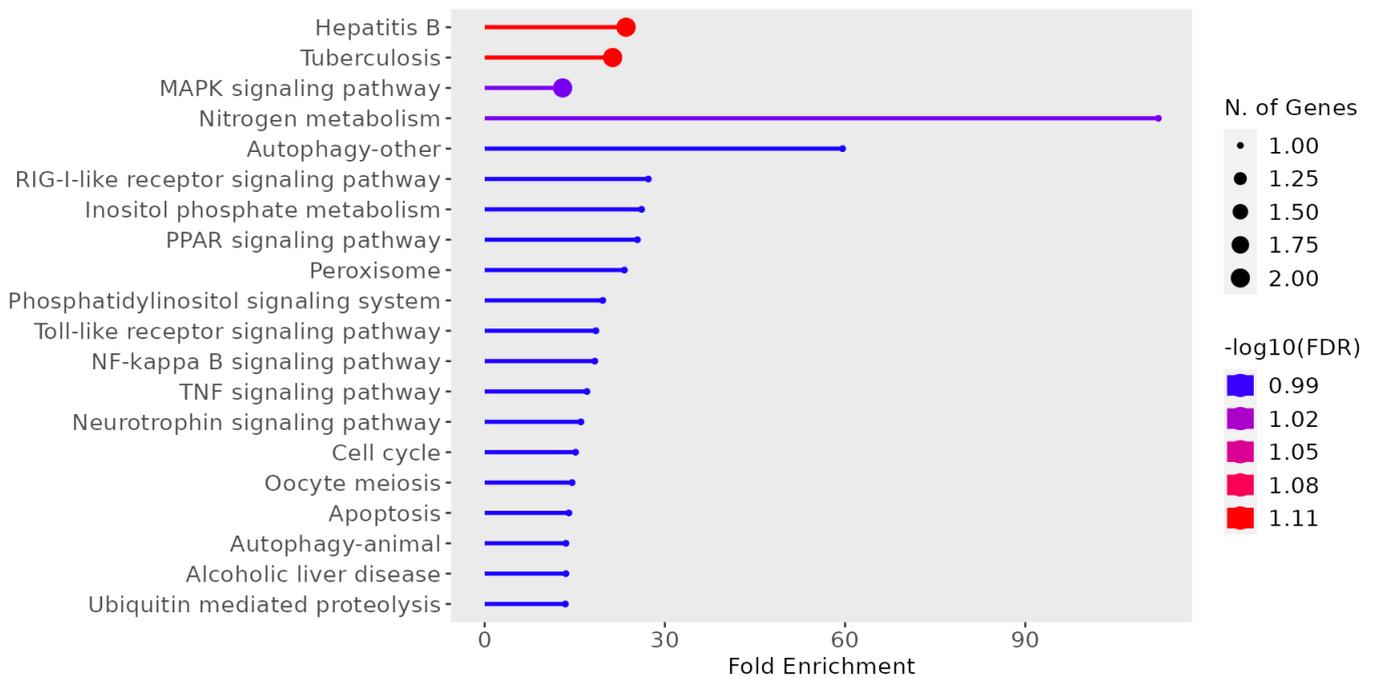
Supplement Figure 1: Feature correlation. The Pearson correlation heatmap between 85 selected features and the UPDRS score, with color intensity indicating the strength and direction of the correlations. Strong correlations are marked by darker shades, while lighter shades represent weaker correlations, highlighting potential patterns and associations relevant to Parkinson's severity. Two main feature groups are strongly correlated (in red) and anticorrelated (in blue) with UPDRS scores (marked by black arrow). Note that due to space constraints every second feature is labeled on the vertical axis.

A)

It is made available under a [CC-BY-NC 4.0 International license](https://creativecommons.org/licenses/by-nc/4.0/).



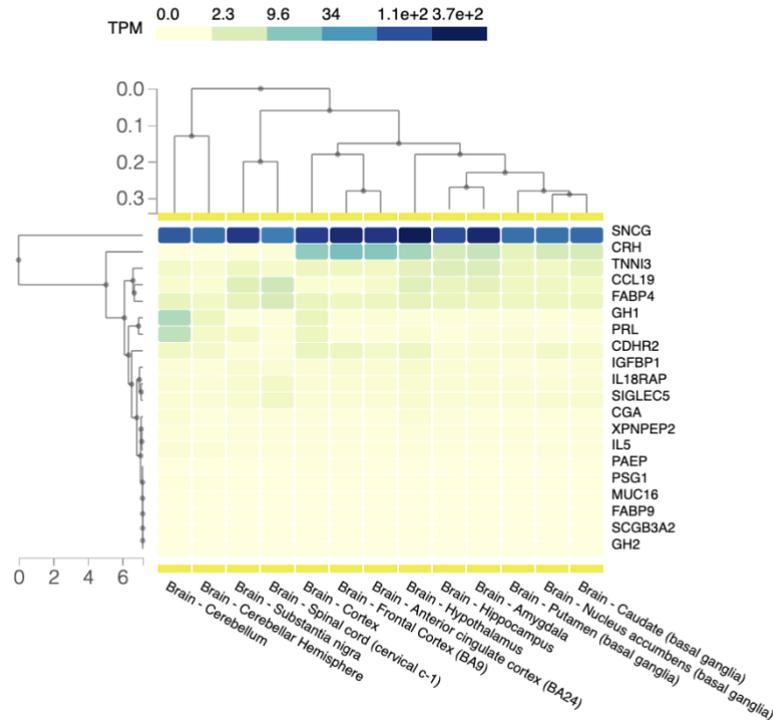
B)



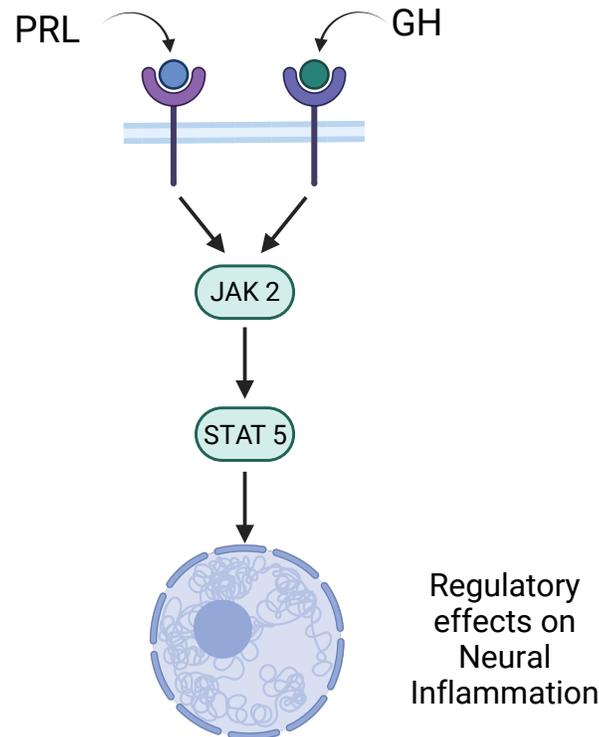
Supplementary Figure 2: Pathway enrichment of UPDRS correlated features. A) KEGG analysis of top UPDRS correlated features (red in group in Supplementary Figure 1) highlight enrichment in the cytokine-cytokine receptor interaction and PI3K-AKT signaling pathways. B) Similarly, enrichment analysis of top UPDRS anticorrelated features highlights the MAPK signaling pathway and apoptotic pathways.

It is made available under a [CC-BY-NC 4.0 International license](https://creativecommons.org/licenses/by-nc/4.0/).

A

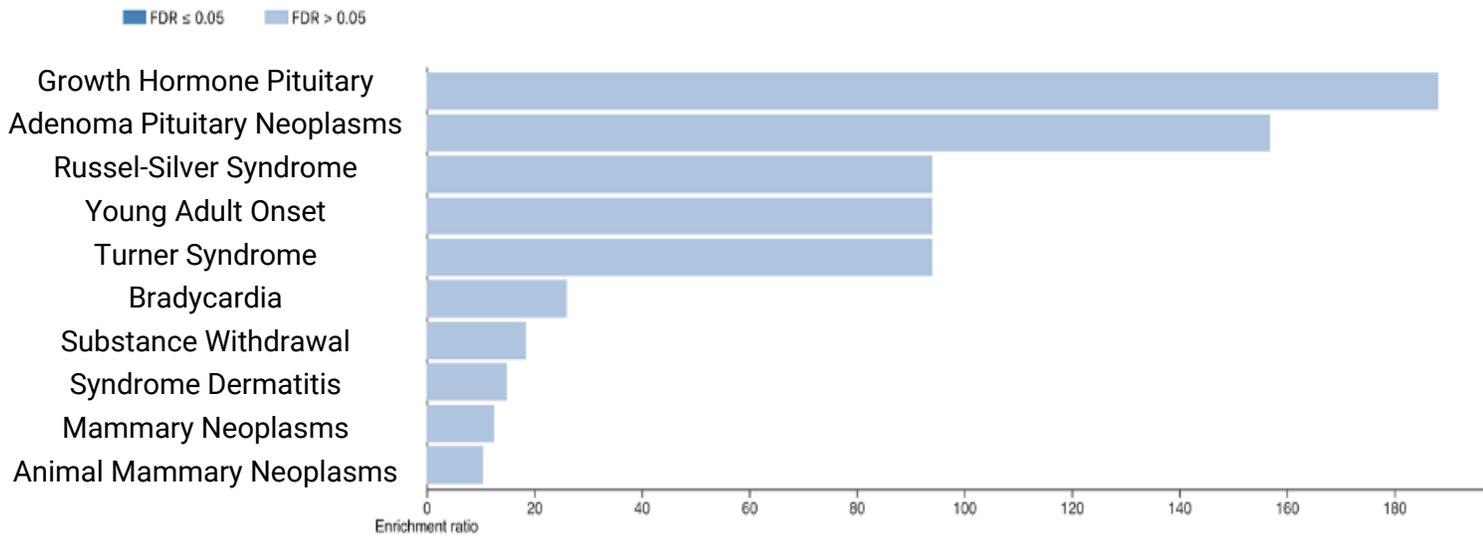


B



Supplementary figure 3: (A) Gene expression levels across different brain tissues from the GTEx study [50], highlighting the differential expression patterns relevant to the pathway including, GH1 and PRL expression in the Cerebellum. (B) The PRL pathway depicting the JAK2-STAT5 signaling cascade, illustrating key molecular interactions and activation steps.

It is made available under a [CC-BY-NC 4.0 International license](https://creativecommons.org/licenses/by-nc/4.0/) .



Supplementary Figure 4: Phenotype-gene enrichment analysis of the top 20 features identified by the neural network model, conducted using the WEB-based GENE SeT AnaLysis Toolkit. The enrichment analysis highlights significant associations between these features and relevant gene sets, providing insights into potential biological pathways linked to the observed phenotypes.