

Title: Multi-omics delineate growth factor network underlying exercise effects in an Alzheimer's mouse model

SUPPLEMENTARY TABLES

Supplemental Table S1. RNA in excitatory neurons

Supplemental Table S2. RNA in inhibitory neurons.

Supplemental Table S3. RNA in oligodendrocytes.

Supplemental Table S4. RNA in oligodendrocyte progenitor cells.

Supplemental Table S5. RNA in astrocytes.

Supplemental Table S6. RNA in microglia.

Supplemental Table S7. GSEA results of DEGs for APP_RT vs. WT_RT

Supplemental Table S8. GSEA results of DEGs for APP_EX vs. APP_RT

Supplemental Table S9. GSEA results of DEGs for DEGs WT_EX vs. WT_RT

Supplemental Table S10. GSEA results of the EGFR signaling pathway.

Supplemental Table S11. GSEA results of the insulin signaling pathway.

Supplemental Table S12. Overlap of EGFR signaling with TFs targets genes in network analysis.

Supplemental Table S13. Overlap of Insulin signaling with TFs targets genes in network analysis.

SUPPLEMENTARY FIGURE LEGENDS

Supplemental Figure S1. Behavioral analysis of WT and APP^{NL-G-F} mice.

(a) Average daily exercise volume per mouse. n = 8 WT mice, n = 9 APP^{NL-G-F} mice. (b) Body weight, n = 12 mice for WT_RT, n = 8 mice for WT_EX; 10 mice for APP_RT; 9 mice for APP_EX. (c) Total distance in the standard 2-object OLT (n = 12 for WT_RT; 8 for WT_EX; 10 for APP_RT; and 9 for APP_EX). (d) Total distance in the Y-maze test (n = 12 for WT_RT; 8 for WT_EX; 10 for APP_RT; and 9 for APP_EX). Bar graphs show the mean with S.E.M. Asterisks indicate significant difference by two-way ANOVA. ns, not significant.

Supplemental Figure S2. Exercise activates growth factor signaling. (a) Proportions of major cell clusters based on snRNA-seq and snATAC-seq. (b) The number of DEGs from the indicated comparisons. (c) The number of significantly enriched pathways in DEGs from the indicated comparisons. (d) List of significantly enriched pathways in DEGs from the indicated comparisons.

Supplemental Figure S3. DEGs with the reversed pattern from snRNA-seq analysis.

(a) GSEA analyses of the EGFR signaling pathway, a top common enriched pathway in reversed DEGs in different cell types. (b) Heat map of reversed DEGs within the EGFR signaling in different cell types.

Supplemental Figure S4. DARs from snATAC-seq analysis.

(a) The number of DARs from the indicated comparisons. (b) Number of significantly enriched pathways in DARs from the indicated comparisons. (c) List of significantly enriched motifs in the indicated DARs. (d) Scatter plot of chromatin regions with negative correlations between the exercise-induced (APP_EX vs. APP_RT) and amyloid-induced (APP_RT vs. WT_RT) accessibility changes across different cell clusters.

Supplemental Figure S5. Transcriptional regulatory network in excitatory neurons.

Supplemental Figure S6. Transcriptional regulatory network in inhibitory neurons.

Supplemental Figure S7. Transcriptional regulatory network in oligodendrocytes.

Supplemental Figure S8. Transcriptional regulatory network in oligodendrocyte precursor cells.

Supplemental Figure S9. Transcriptional regulatory network in astrocytes.

Supplemental Figure S10. Transcriptional regulatory network in microglia.

Supplemental Figure S11. Spatial expression reconstruction.

Heat map of DG and CA1/2 landmark genes, Prox1 and Ociad2, in WT_RT mouse hippocampus after spatial expression reconstruction according to a previous spatial transcriptomics dataset.

Supplementary Figure S1

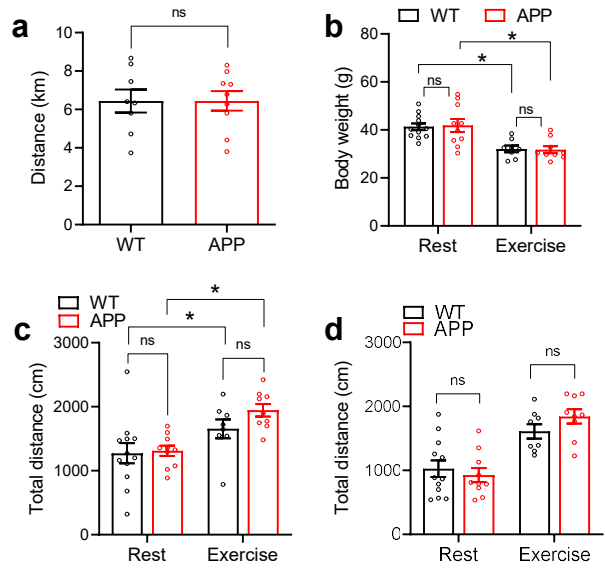
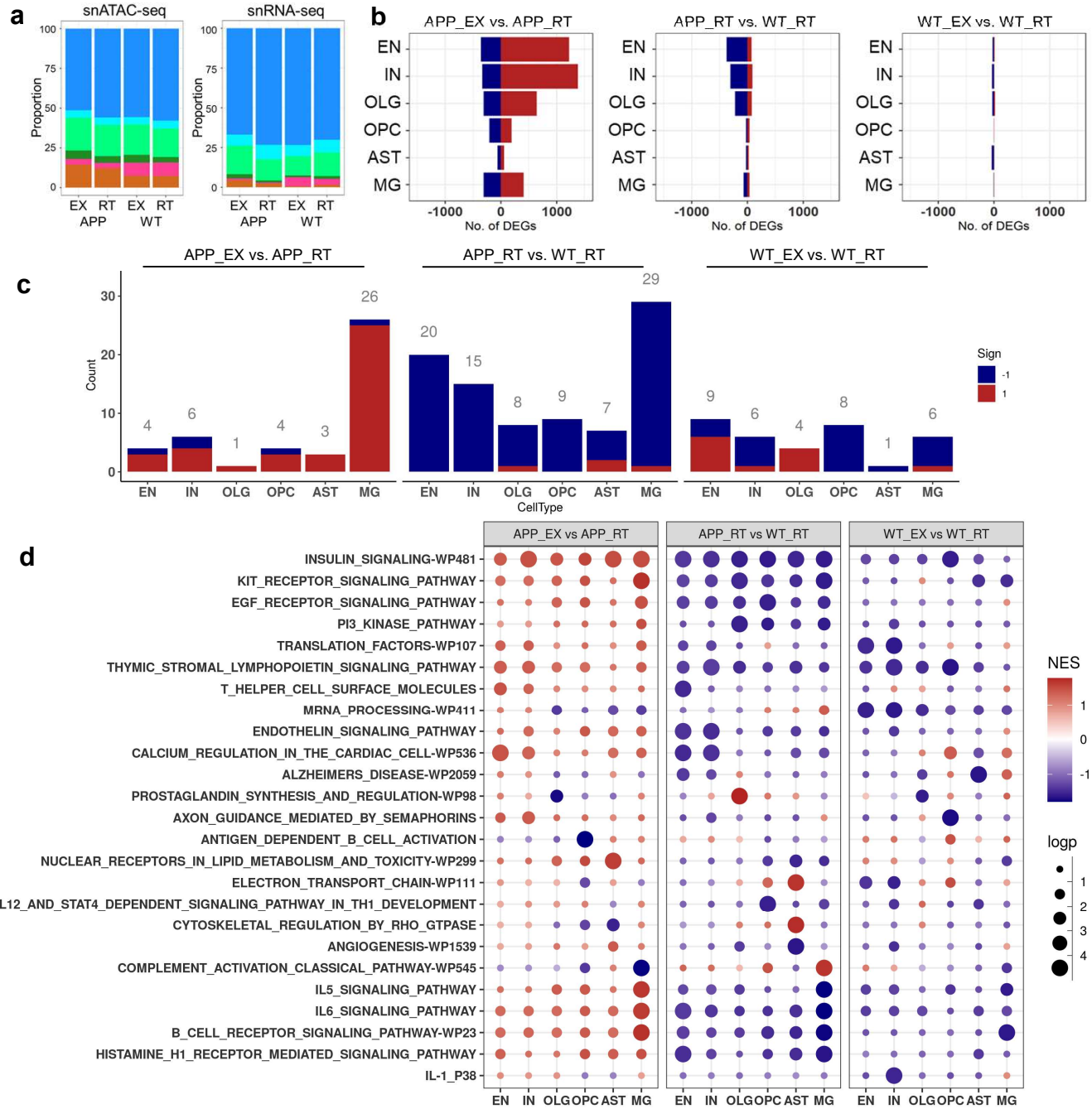
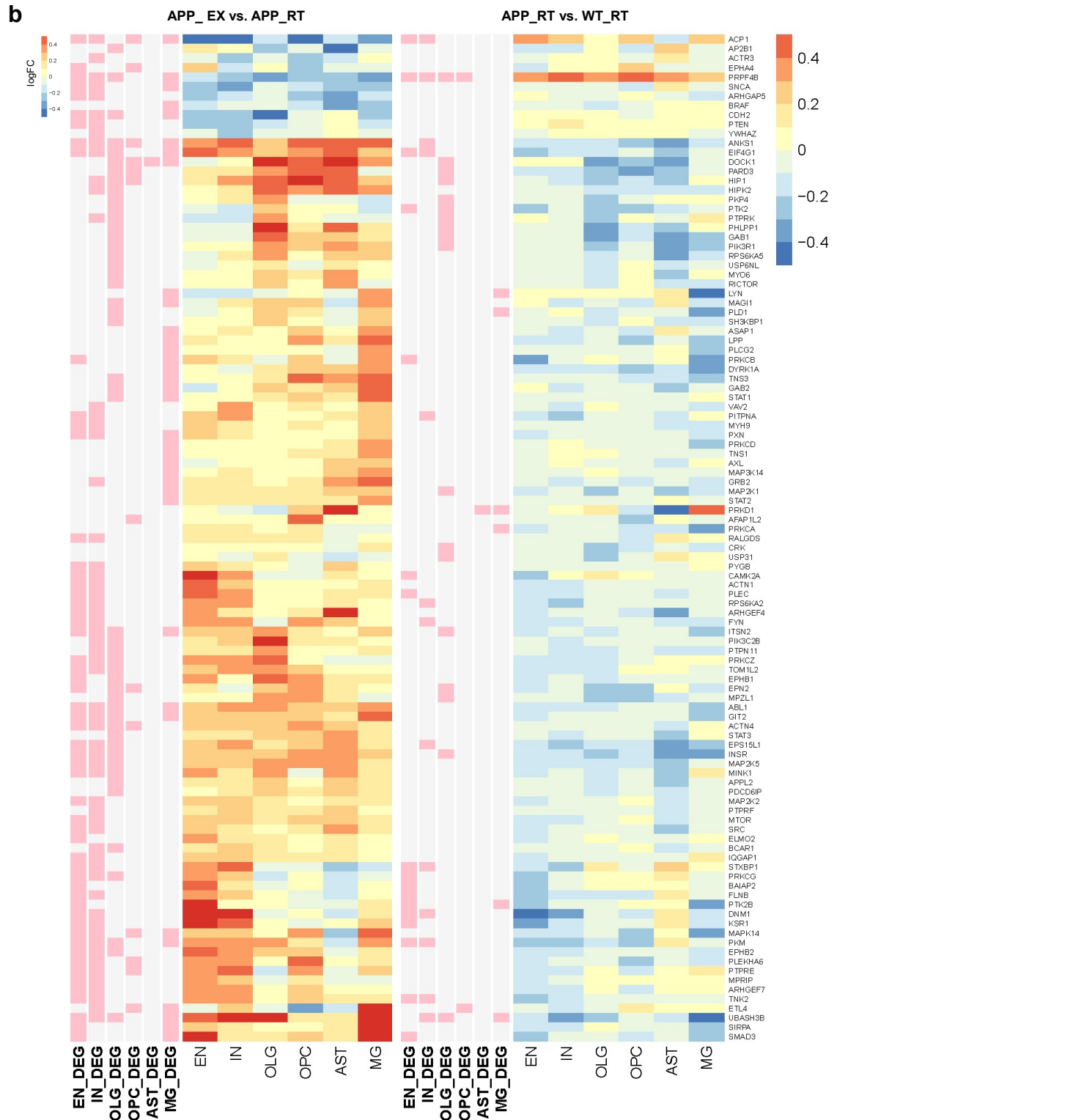
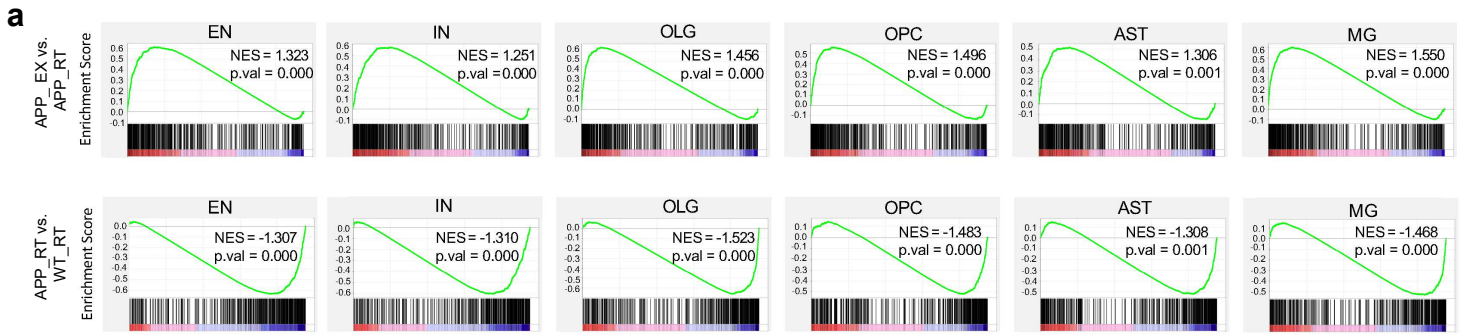


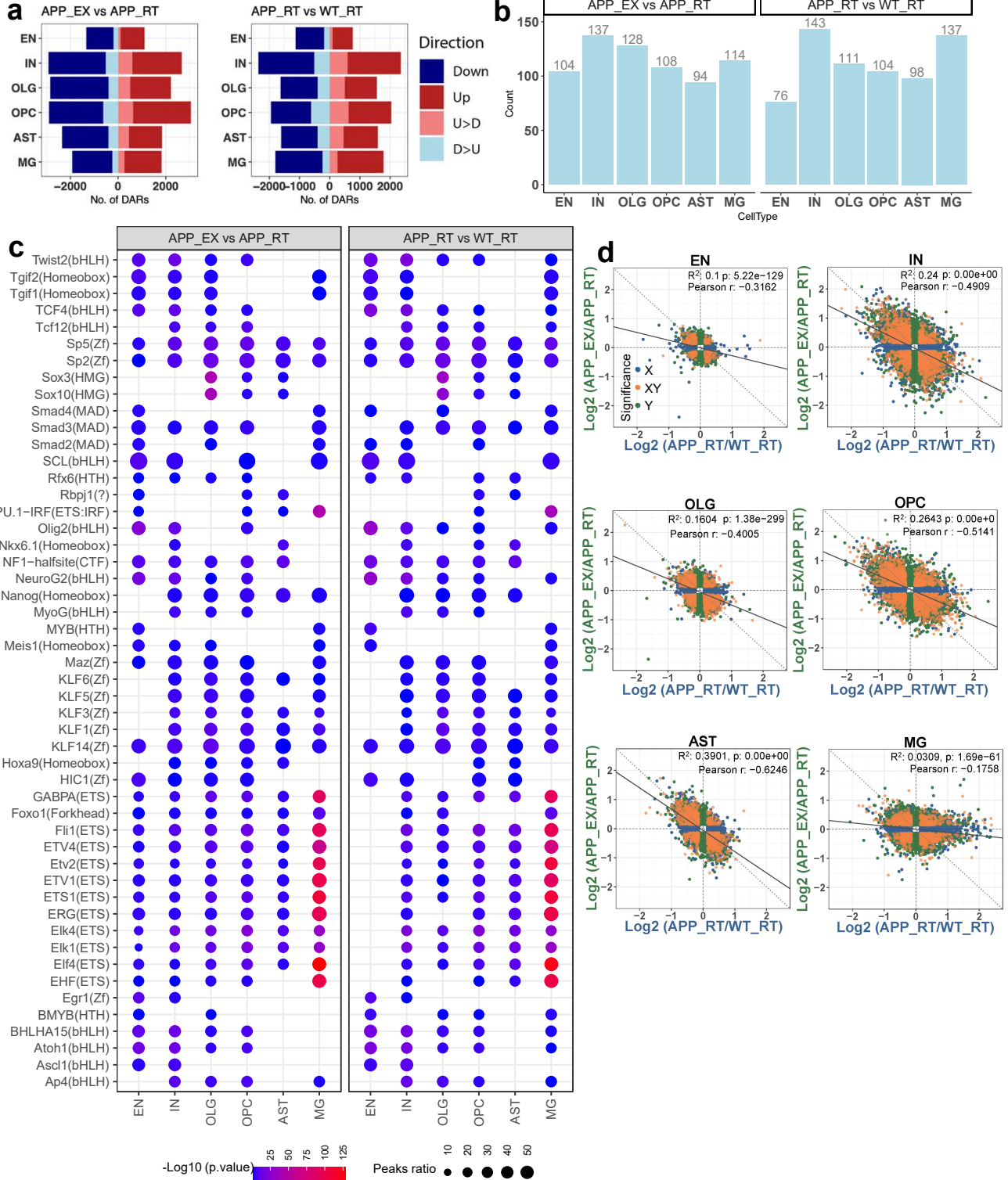
Figure S2



Supplementary Figure S3

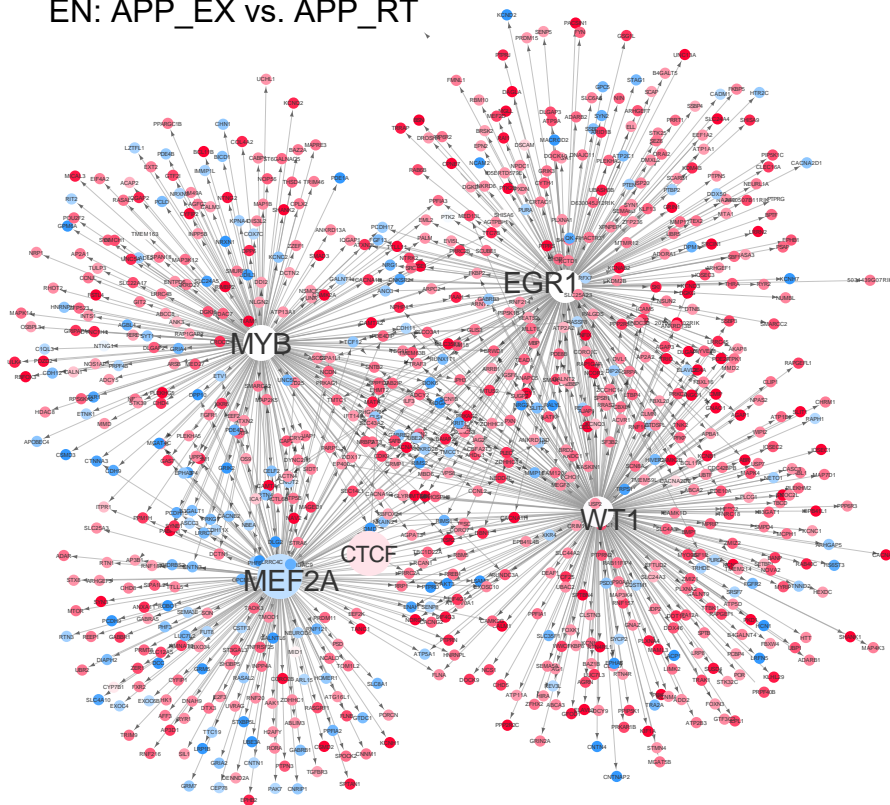


Supplementary Figure S4

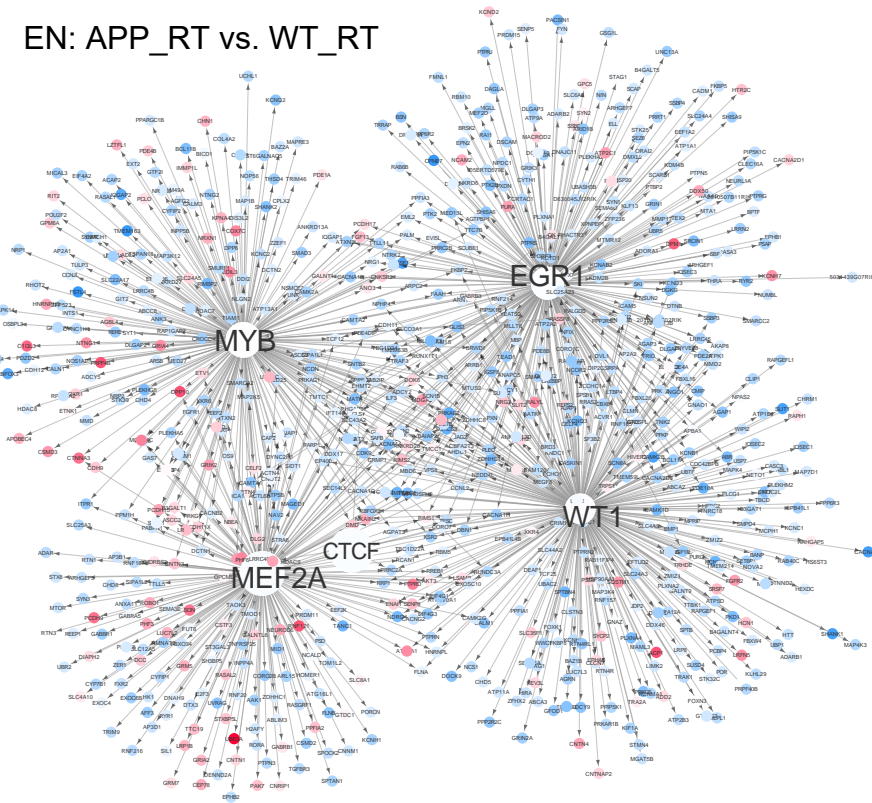


Supplementary Figure S5

EN: APP_EX vs. APP_RT

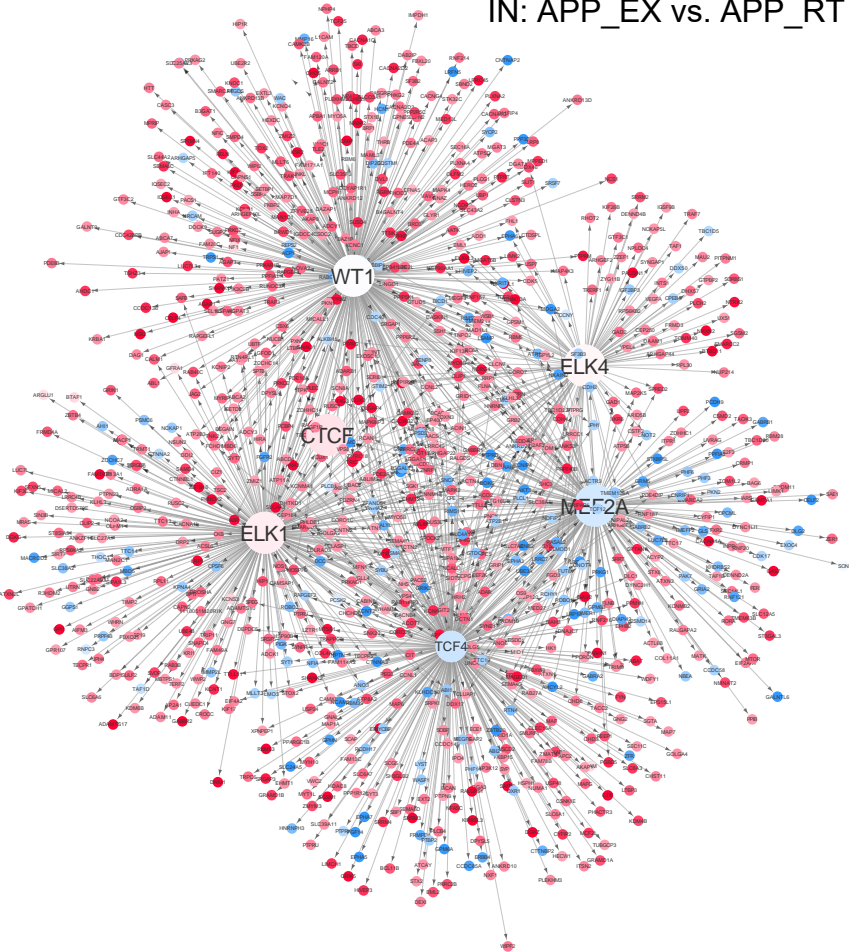


EN: APP_RT vs. WT_RT

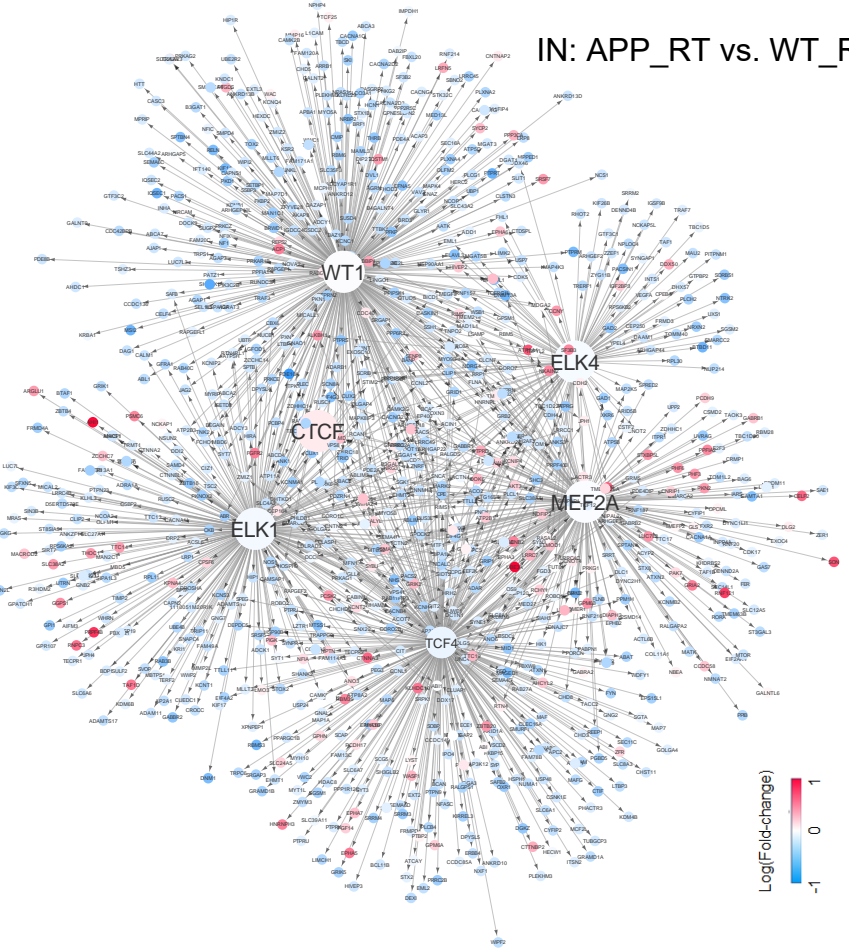


Supplementary Figure S6

IN: APP_EX vs. APP_RT



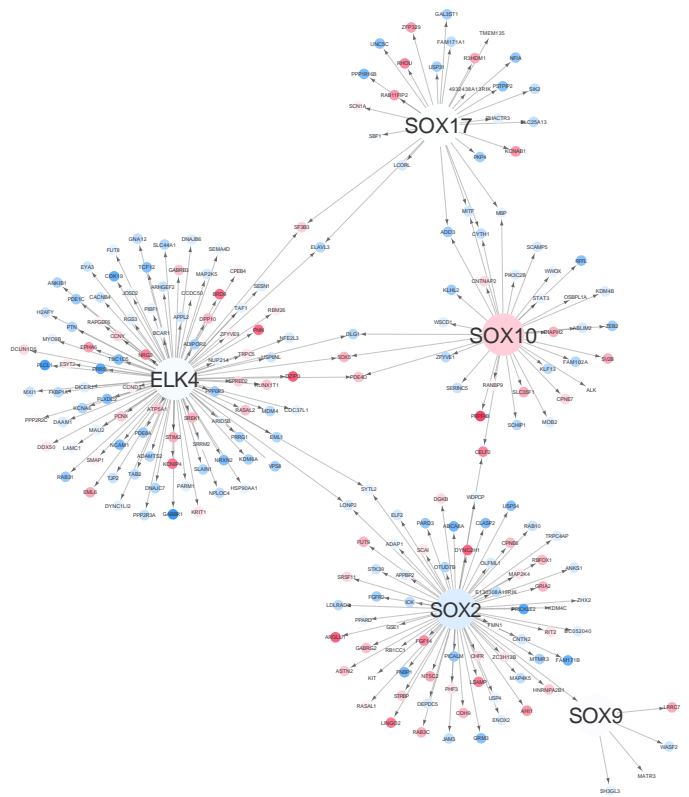
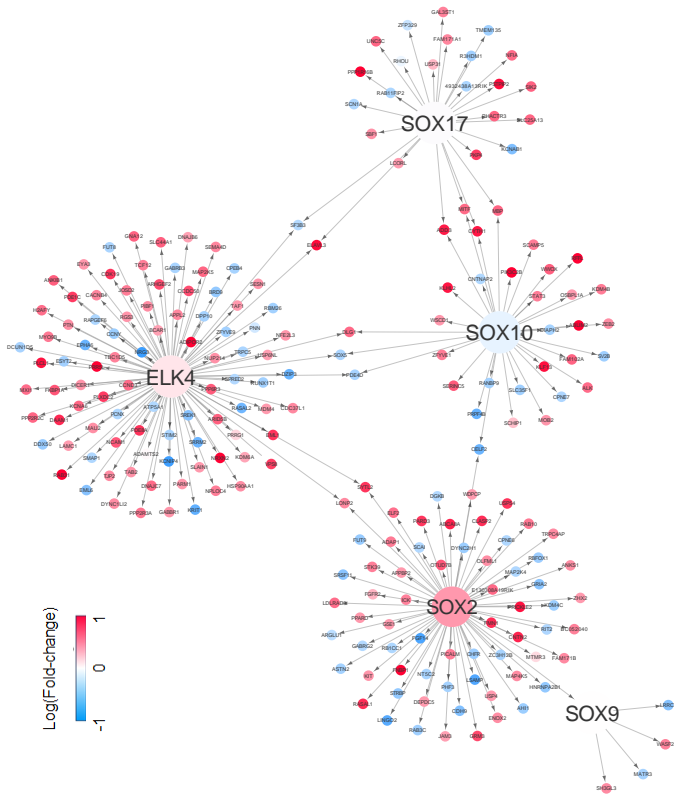
IN: APP_RT vs. WT_RT



Supplementary Figure S7

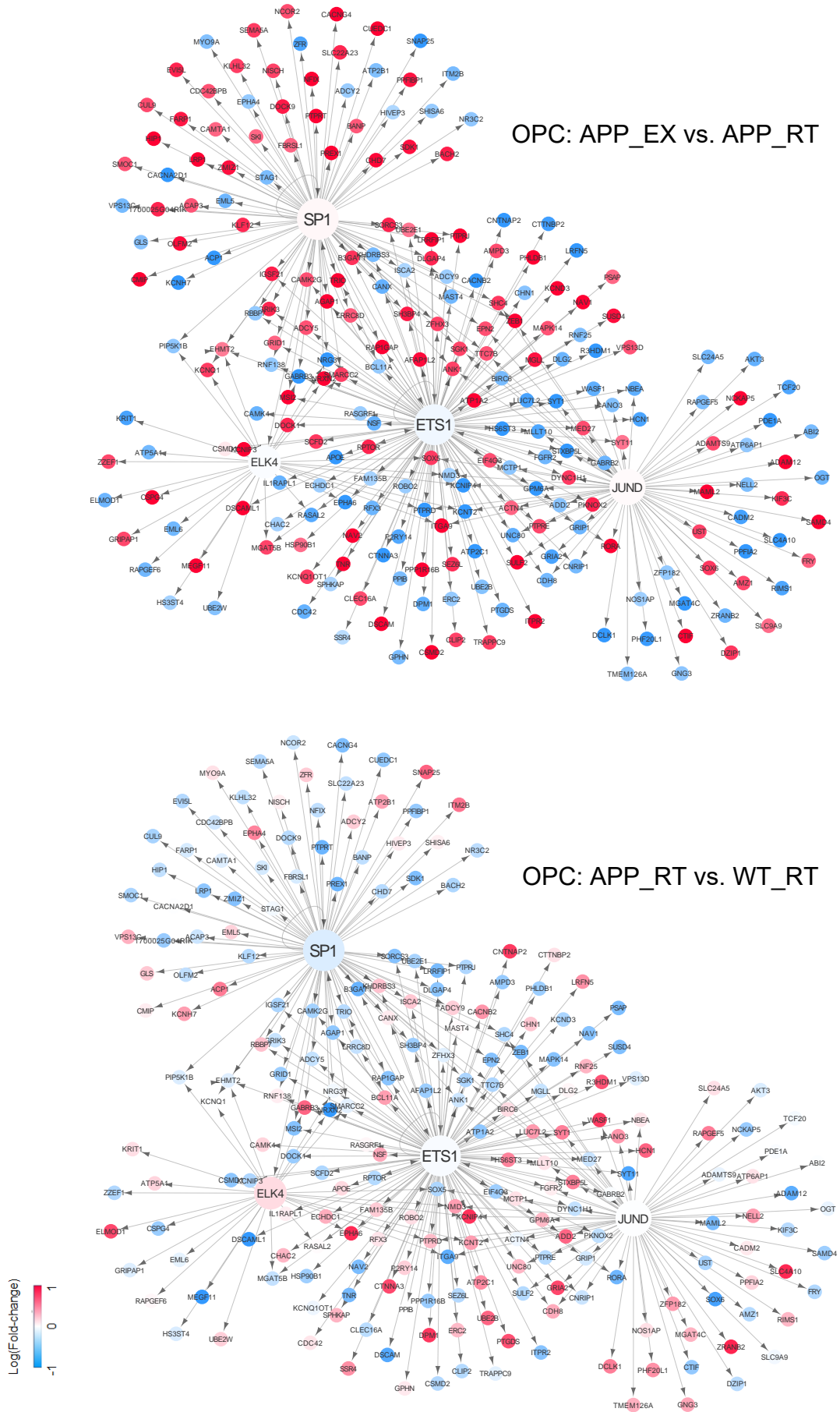
OLG: APP_EX vs. APP_RT

OLG: APP_RT vs. WT_RT



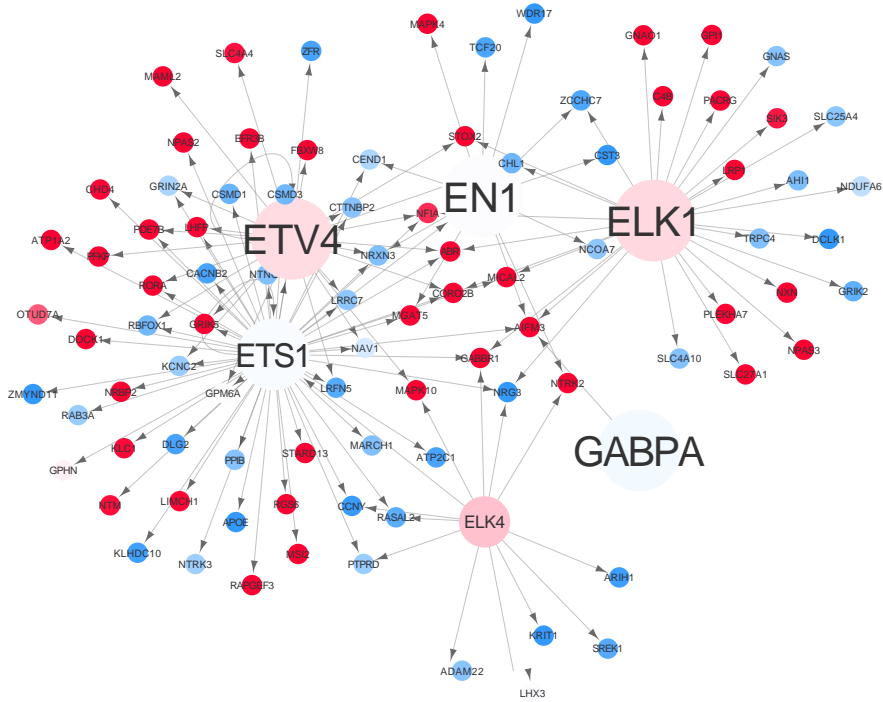
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Supplementar Figure S8

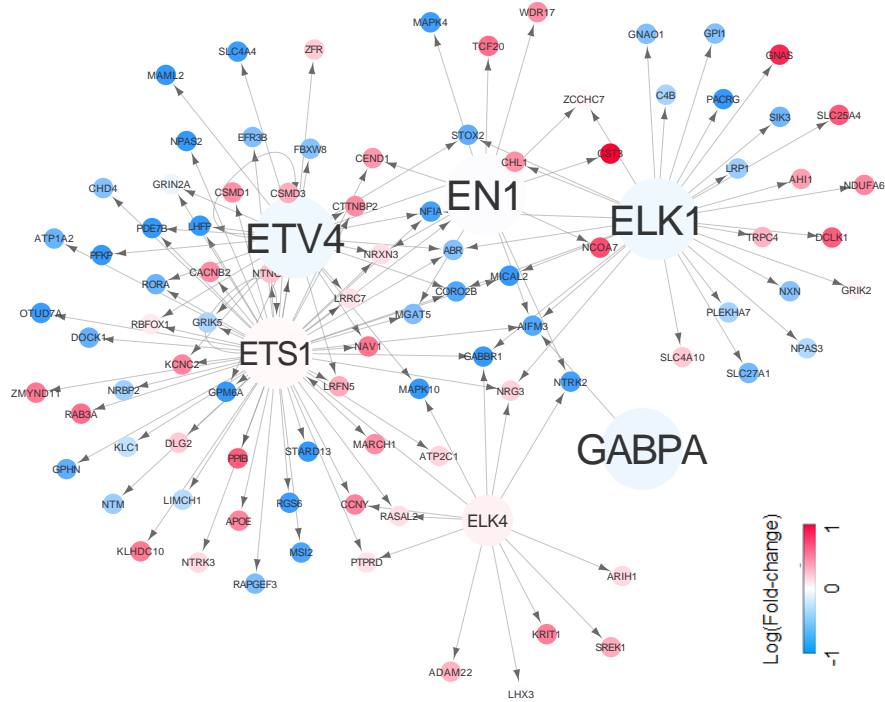


Supplementary Fig S9

AST: APP_EX vs. APP_RT

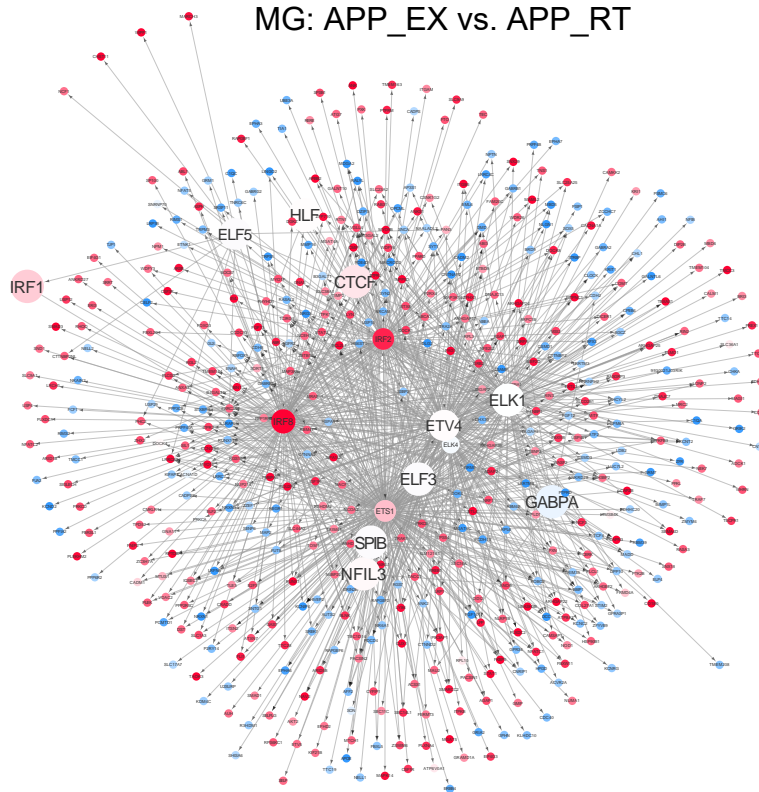


AST: APP_RT vs. WT_RT

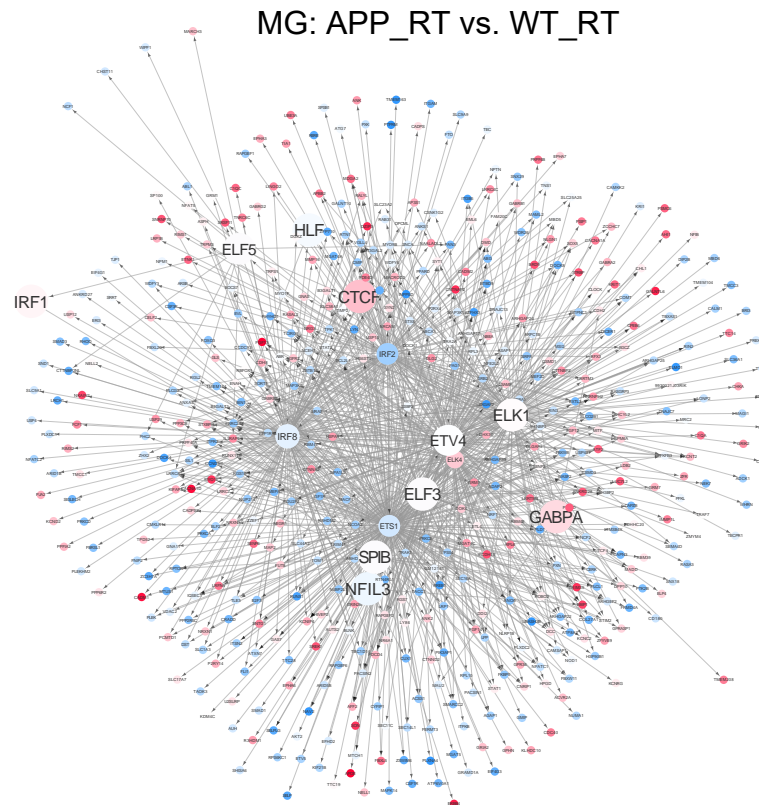


Supplementary Fig S10

MG: APP_EX vs. APP_RT



MG: APP_RT vs. WT_RT



Log(Fold-change)
-1 0 1

Supplementary Figure S11

