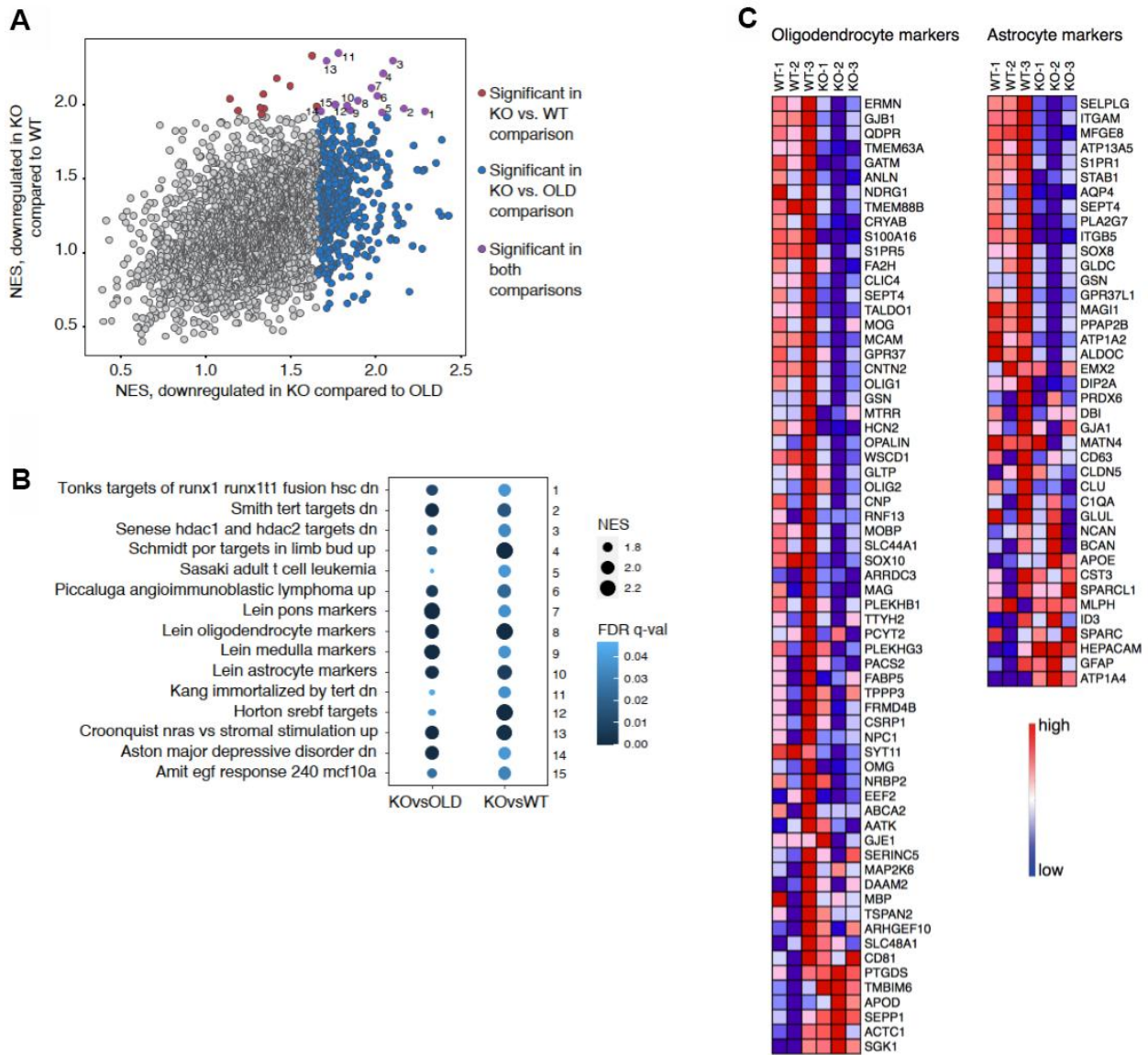
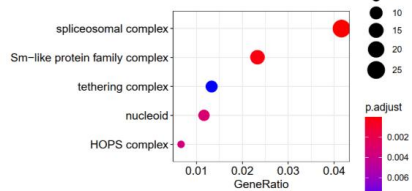


SUPPLEMENTARY FIGURES

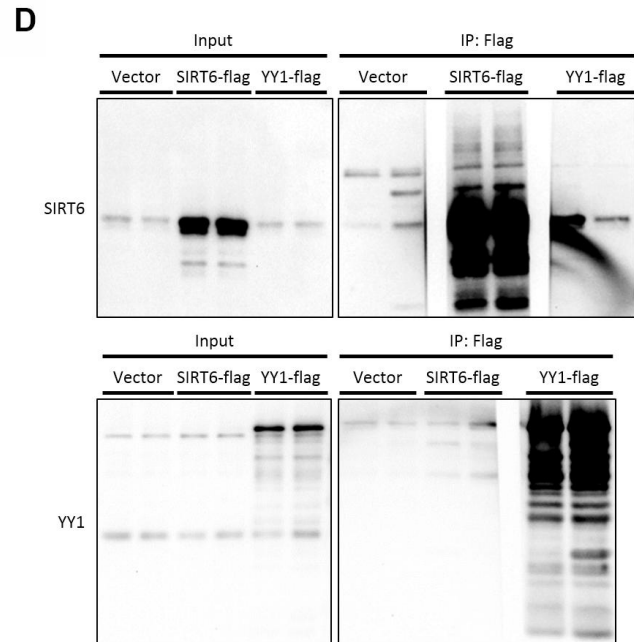
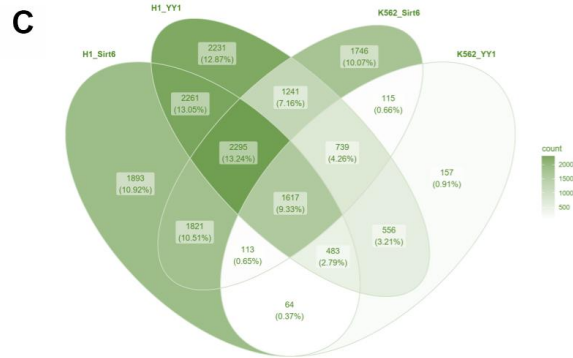
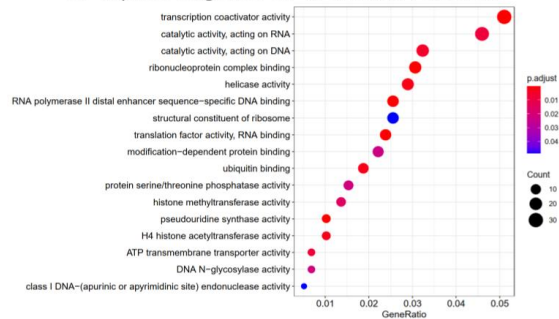


Supplementary Figure 1. SIRT6 deletion affects several unique gene categories. (A) Normalized Enrichment Scores (NES) calculated in Gene Set Enrichment Analysis (GSEA) for genes downregulated in SIRT6-KO compared to young WT mice (Y-axis) or to old WT mice (X-axis). Dots represent functional categories. Blue dots show significantly downregulated categories in a comparison between SIRT6-KO and old WT mice, while red dots correspond to a comparison between SIRT6-KO and young WT mice. Violet dots highlight categories significant in both comparisons. Significance cutoff: FDR < 0.05. (B) Significant categories in both comparisons. Colors represent FDR. Circle sizes are proportional to the NES. (C) Expression levels of genes in two significant categories: oligodendrocyte markers (left panel) and astrocyte markers (right panel). Red color corresponds to increased expression, while blue color corresponds to decreased expression.

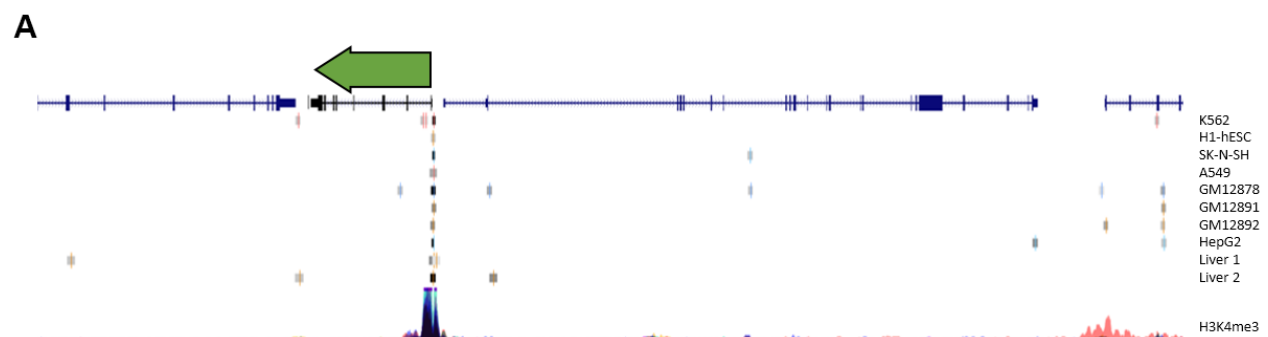
A Co-expressed genes GO Cellular Compartments



B Co-expressed genes GO Molecular Functions



Supplementary Figure 2. SIRT6 and YY1 present high similarity in targets. (A) Enriched GO Cellular Compartments categories the overlapping genes in Figure 4B are part of. (B) Enriched GO Molecular Functions categories the overlapping genes in figure 4B are part of. (C) A Venn diagram of SIRT6 and YY1 ChIP-seq genes, overlapping between the 4 used ChIP-seq datasets. Only genes that are shared among the 4 datasets were used in Figure 4D. (D) Western blots of SIRT6 and YY1 co-IP showing the transfection and IP efficiency.



Supplementary Figure 3. YY1 regulates SIRT6 promoter. (A) YY1 ChIP-seq data in a large region that flanks SIRT6 gene. *SIRT6* locus is marked with a green arrow; YY1 peaks are marked in black or grey shades; tested cell lines are marked on the right side of the panel.