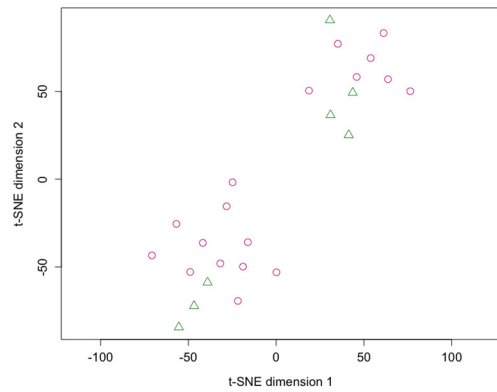
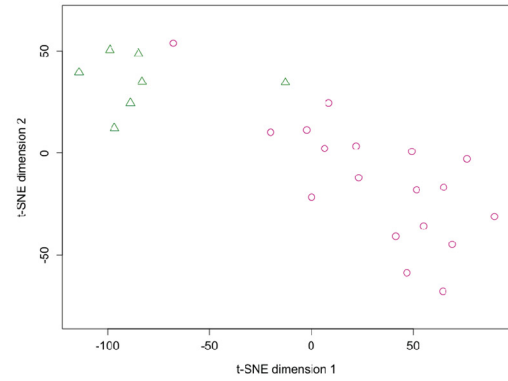


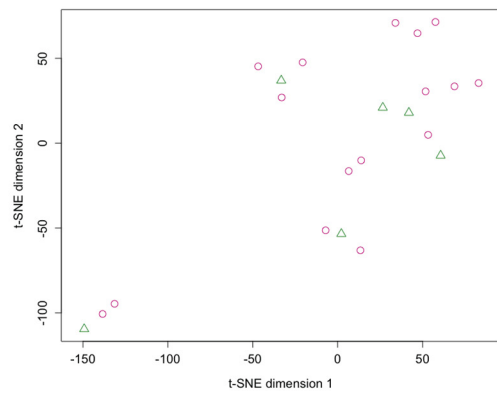
A) t-SNE of circRNAs in Spinal Cord Cervical ALS and control samples



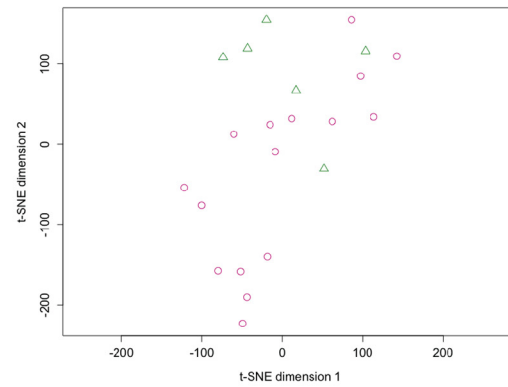
B) t-SNE of linear RNAs in Spinal Cord Cervical ALS and control samples



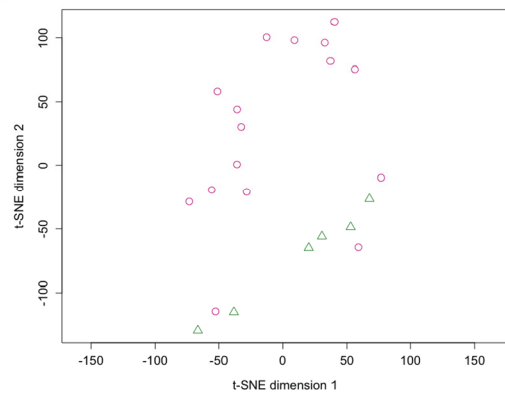
C) t-SNE of circRNAs in Spinal Cord Lumbar ALS and control samples



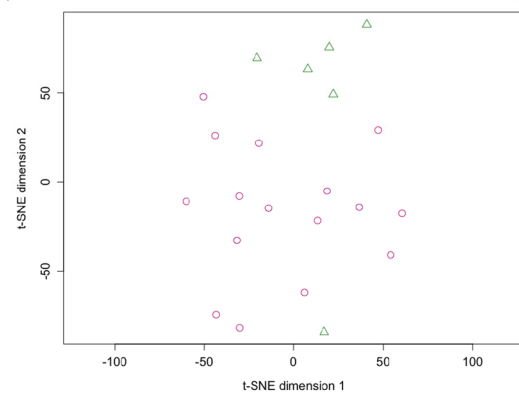
D) t-SNE of linear RNAs in Spinal Cord Lumbar ALS and control samples



E) t-SNE of circRNAs in Spinal Cord Thoracic ALS and control samples



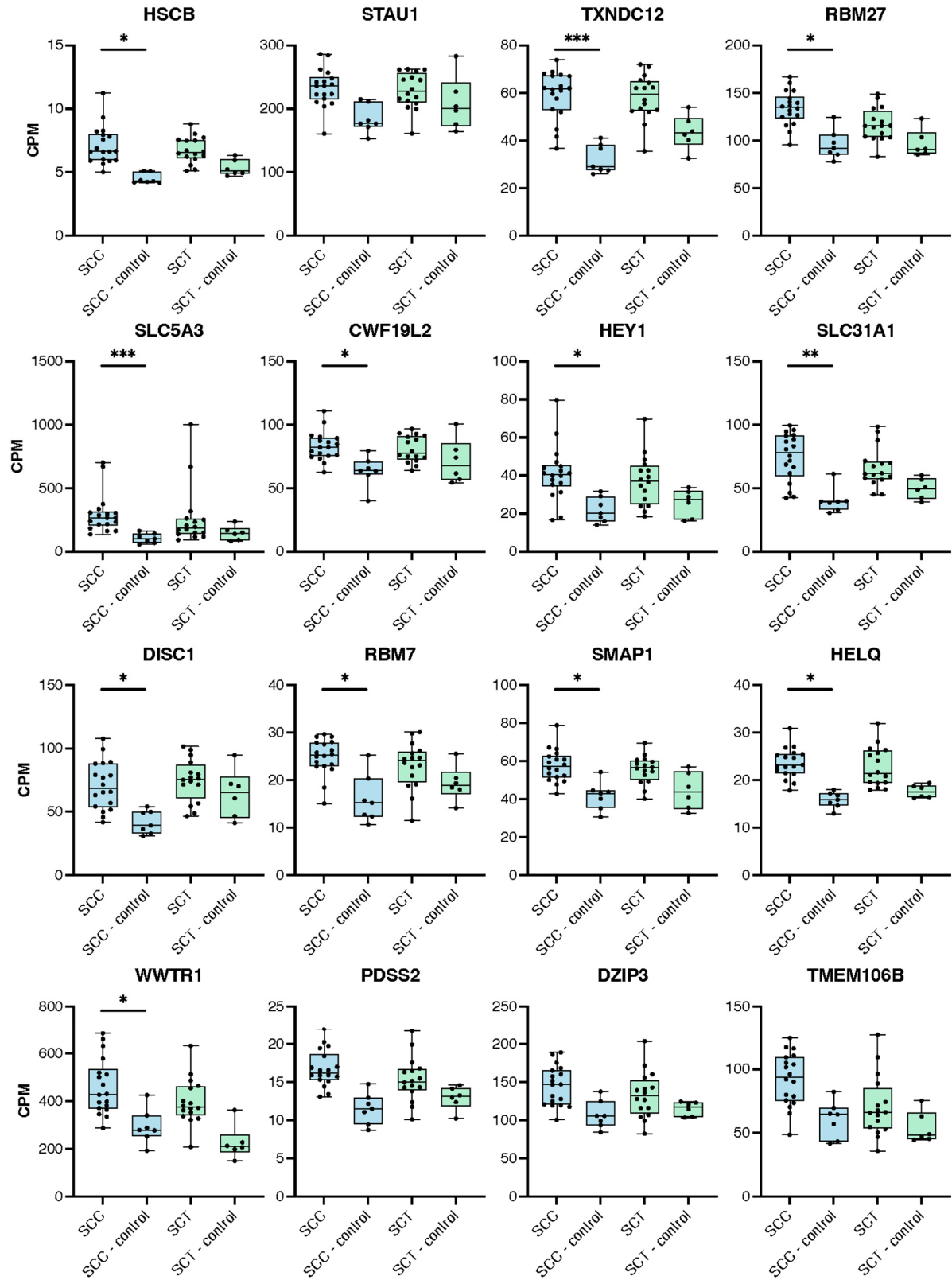
F) t-SNE of linear RNAs in Spinal Cord Thoracic ALS and control samples

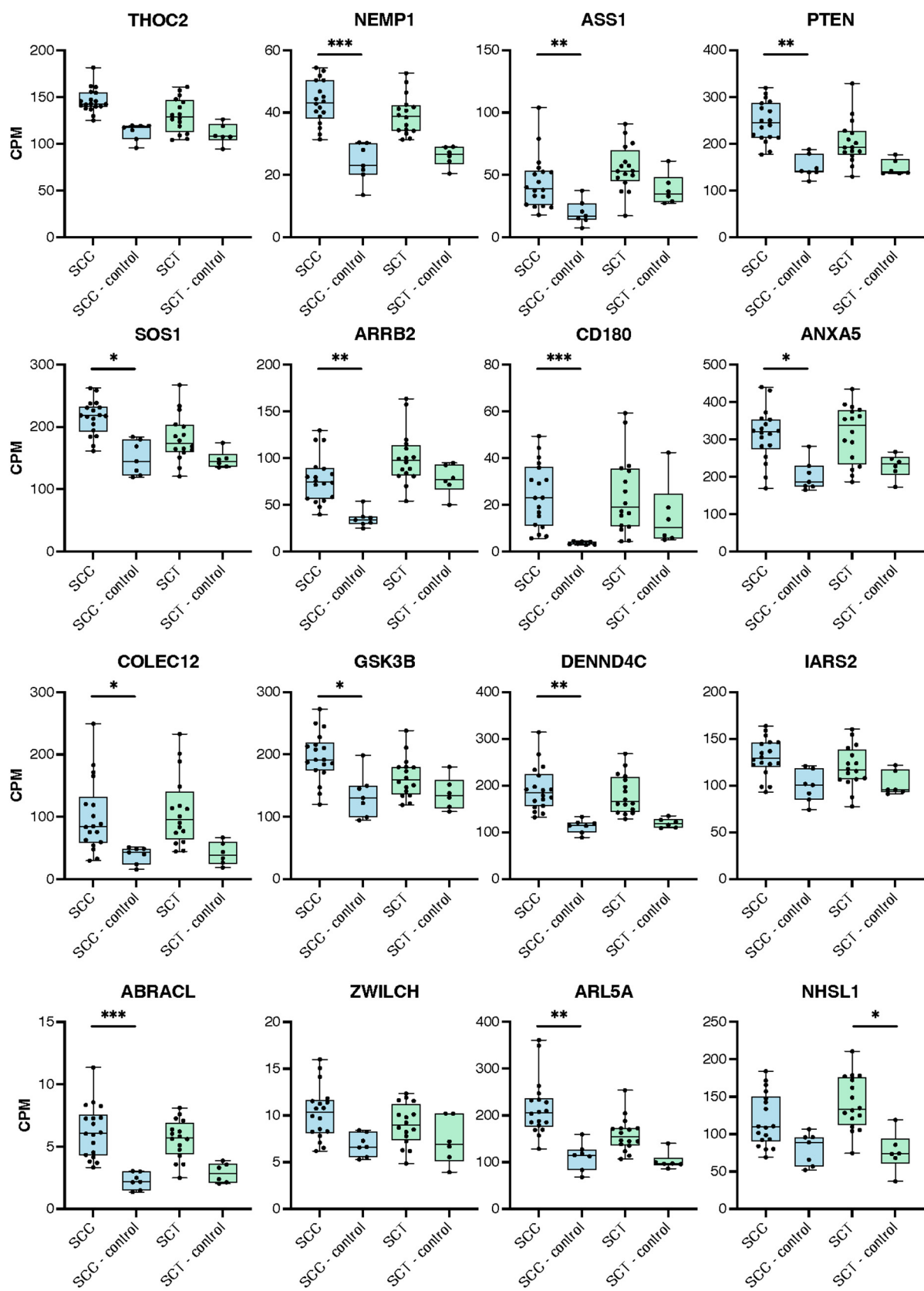


Legend



Figure S1. t-SNE plots of the circular transcriptome (A,C,E) and linear transcriptome (B,D,F). Distinct clusters can be seen in both sets of plots, and control and ALS samples appear in clusters together. However, in some plots, the control samples are closer together within a general area. The clustering within ALS samples indicates the variability of the disease.





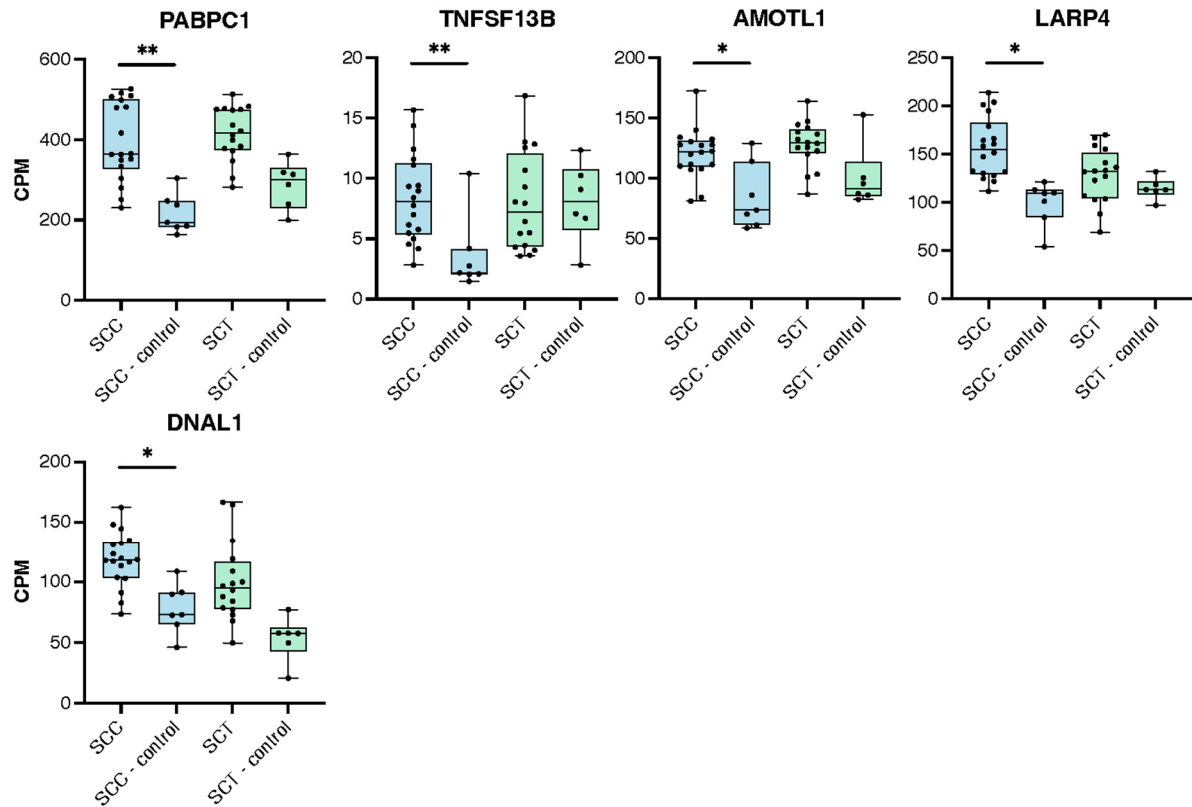


Figure S2. Differential expression of genes identified in the circRNA-miRNA-mRNA interaction network in SCC and SCT. Differential gene expression in SCC and SCT samples in ALS and control cohorts indicates lower expression in control cohorts for all genes identified in this interaction network and included in Figure 2. Upregulation of candidate gene expression in the ALS samples is suggestive of the hypothesized circRNA sequestering of candidate miRNAs which would otherwise be involved in genetic regulation as shown in the control samples. Blue: SCC; Green: SCT; * < 0.05, ** < 0.01, *** < 0.001.

Table S1. Median proportion of variance explained across all genes by each variable.

Tissue	Group	Sex	RIN	PMI	Residuals
SCC	0	0	0.035	0.018	0.89
SCL	0	0	0.026	0.022	0.906
SCT	0	0	0.044	0.021	0.885