



Supplemental Figure 8. Core molecular features of human ANNUBP and MPNST are retained in two independent genetically engineered mouse models driven by combined inactivation of *Nf1* and *Ink4a/Arf*. (A) Unsupervised clustering of murine PNF (*Nf1^{fl/fl}* NF), ANF (*Ink4a/Arf^{+/−};Nf1^{flox/flox};DhhCre⁺* PST), and MPNST (*Ink4a/Arf^{+/−};Nf1^{flox/flox};DhhCre⁺* GEM-PST) by t-stochastic neighbor embedding (t-SNE) of RNAseq data generated by Cheney et al. ¹⁸. (B) Heatmap showing gene expression of the top 50 variably expressed features across all samples sorted by two-way hierarchical clustering. Red corresponds to increased expression, and blue to decreased expression of a gene. Four distinct gene modules (S1-4) emerged, with functional enrichments annotated against Hallmark gene sets at the right. The top enriched signatures ranked by correlation coefficient (R) for each gene module are shown. (C) t-SNA plots for cell proliferation, DNA damage repair, and apoptosis signature scores where dots corresponding to sample are colored based on the upregulation (red) or downregulation (blue) of each signature score. Gene set enrichment plots of cell proliferation, DNA damage repair and apoptosis gene signatures in GEM-PNST vs NF and GEM-PNST vs PST are shown below. Black vertical bars indicate the rank of genes comprising each signature. The green curve corresponds to the “running statistics” of the enrichment score. Q-values are as shown comparing NF (n=12), PST (n=4) and GEM-PNST (n=4) samples. (D) Barplot of *Birc5* expression (RNAseq normalized counts) in normal nerve (*Nf1^{flox/flox};PostnCre[−]*, n=6), PNF (*Nf1^{flox/flox};PostnCre⁺*, n=6), ANNUBP (*Nf1^{flox/flox};Arf^{flox/flox};PostnCre⁺*, n=6), and MPNST (*Nf1^{flox/flox};Arf^{flox/flox};PostnCre⁺*, n=6). Dots represent individual samples. Error bars represent the standard error of the mean (SEM). Data were analyzed by one-way ANOVA and p-values represent Tukey’s multiple comparisons tests between groups. (E) Barplot of *Birc5* expression (RNAseq normalized counts) in NF (n=12), PST (n=4), and GEM-PNST (n=4) arising in *DhhCre* mice. Data were analyzed by one-way ANOVA and p-values represent Tukey’s multiple comparisons tests between groups. (F) Barplot of *Cenpf* expression (RNAseq normalized counts) in normal nerve (n=6), PNF (n=6), ANNUBP (n=6), and MPNST (n=6) arising in *PostnCre* mice. Data were analyzed by one-way ANOVA and p-values represent Tukey’s multiple comparisons tests between groups. (G) Barplot of *Cenpf* expression (RNAseq normalized counts) in NF (n=12), PST (n=4), and GEM-PNST (n=4) arising in *DhhCre* mice. Data were analyzed by one-way ANOVA and p-values represent Tukey’s multiple comparisons tests between groups.