Description of Additional Supplementary Files

Supplementary Data 1. Tumor sample annotation table. Provided as an Excel file. By tumor, sample annotation, with corresponding molecular data and comparisons for gene features of interest, is provided for the CBTN cohort of 2417 tumors representing 2127 patients, with data on at least one data platform for WGS, RNA-seq, or DNA methylation. Also provided in a separate tab are TCGA cases analyzed by RNA or DNA methylation signature for association with patient survival.

Supplementary Data 2. Gene-level associations between RNA expression and nearby SV breakpoint. Provided as an Excel file. All gene-level associations between gene expression by RNA-seq and nearby somatic SV breakpoint in the CBTN cohort, according to region examined (e.g., 0–100 kb upstream, 0–100 kb downstream, within the gene body, or 1 Mb upstream or downstream). Also included as a separate tab are the somatic SV breakpoint enrichment patterns by brain tumor histologic type for the 2277 genes with significant patterns for at least one histologic type (from Figure 1b).

Supplementary Data 3. By histologic type, gene-level associations between RNA expression and nearby SV breakpoint. Provided as an Excel file. All gene-level correlations between expression and nearby somatic SV breakpoint for each histology-based tumor type (using linear regression models with corrections for gene-level copy, with 1Mb region upstream or downstream of the gene using weighted relative distance). In all, 13 pediatric brain tumor types were analyzed separately: ATRT, CPP, CRANIO, DIPG, DNT, EPMT, GNG, MBL, MNG, NFIB, PHGG, PLGG, and SCHW.

Supplementary Data 4. Data involving SV-mediated mechanisms of altered expression or DNA methylation. Provided as an Excel file. Provided are all potential enhancer hijacking and enhancer duplication events (from Figure 2e), events involving the translocation of a region with lower methylation (from Figures 2f and 2g), and enhancer-level associations with altered DNA methylation (from Figure 4).

Supplementary Data 5. Probe-level CpG Island (CGI) associations between DNA methylation and nearby SV breakpoint. Provided as an Excel file. Complete set of CGI probe-level associations between methylation and nearby somatic SV breakpoint in the compendium cohort (CPTAC tumors), according to region examined (e.g., 0–100 kb upstream, 0–100 kb downstream, within the gene body, or 1 Mb upstream or downstream).

Supplementary Data 6. Top gene-level associations between expression or methylation and nearby SV breakpoint for each histologic type. Provided as an Excel file. Data for top genes and CGI probes showing both expression and DNA methylation associations with SV breakpoints for one or more histology-based cancer types ($p<0.05$ by linear model for 1Mb region with covariates).

Supplementary Data 7. Gene-level and CGI probe-level correlations with patient overall survival. Provided as an Excel file. By stratified Cox, correcting for cancer type, survival associations with both nearby SV breakpoints and expression are provided. For expression, positive Cox beta indicates that higher expression is associated with worse outcomes; negative Cox beta, associated with better outcomes. For SV breakpoints, positive Cox beta indicates that nearby breakpoints are associated with

worse outcomes; negative Cox beta, associated with better outcomes. A separate tab provides the CGI methylation associations with patient survival. Also provided are GO term enrichment results for the set of genes for which there was both an RNA-level association with worse patient survival and a negative association between CGI methylation and nearby SV breakpoints (from Figure 5b). Another tab provides gene-level or CGI probe-level survival associations in TCGA pan-cancer datasets for the signatures derived from CBTN datasets (Figures 5a and 5b).

Supplementary Data 8. Gene-level and CGI probe-level associations with progressive or recurrent tumors versus initial tumors. Provided as an Excel file. Also provided are GO term enrichment results for the following sets of genes: 1) genes with RNA higher in progressive-recurrent tumors versus paired initial tumor (from Figure 6c); 2) genes with RNA lower in progressive-recurrent tumors versus paired initial tumor (from Figure 6c); 3) genes for which CGI methylation was higher in progressive-recurrent tumors versus paired initial tumor (from Figure 6c). Another tab provides CGI probe-level survival associations in TCGA pan-cancer datasets for the progressive-recurrent CGI methylation derived from CBTN dataset (Figure 6c).