

Supplemental Table 1: Cell line characteristics

Name	Derivation	Classification	Genetic Features
BT 145	Adult resection	Glioblastoma	<i>MYC</i> overexpressed, <i>CDKN2A/B</i> homozygous deletion, <i>PTEN/RB1</i> underexpressed
BT 159	Adult resection	Glioblastoma	<i>EGFR</i> overexpressed, <i>PIK3C2B</i> overexpressed
DIPG 4	Pediatric autopsy	DIPG	<i>HIST1H3B</i> mutant, <i>ACVR1</i> mutant
DIPG 6	Pediatric autopsy	DIPG	<i>H3F3A</i> mutant, <i>TP53</i> mutant
SF7761	Pediatric biopsy	DIPG	<i>H3F3A</i> mutant, exogenous hTERT
GBM1	Pediatric resection	Glioblastoma	H3K27 WT
DIPG 7	Pediatric autopsy	DIPG	<i>H3F3A</i> mutant, <i>ACVR1</i> mutant
DIPG 33	Pediatric autopsy	DIPG	
T3691	Adult resection	Glioblastoma	
T387	Adult resection	Glioblastoma	

Supplemental Table 2: Most overexpressed genesets with *BPTF* KD by GSEA

NAME	SIZE	ES	NES	FDR q-val
GO_CELL_MORPHOGENESIS_INVOLVED_IN_NEURON_DIFFERENTIATION	361	0.415601	9.3597	0
GO_NEURON_PROJECTION_MORPHOGENESIS	393	0.400031	9.172595	0
GO_REGULATION_OF_SYSTEM_PROCESS	498	0.353762	8.910024	0
GO_SKELETAL_SYSTEM_DEVELOPMENT	451	0.344876	8.543805	0
GO_TAXIS	451	0.339593	8.357675	0
GO_SENSORY_ORGAN_DEVELOPMENT	490	0.316914	8.07137	0
GO_SYNAPTIC_SIGNALING	417	0.332879	7.801979	0
GO_MUSCLE_STRUCTURE_DEVELOPMENT	421	0.320035	7.762128	0
GO_EXTRACELLULAR_STRUCTURE_ORGANIZATION	301	0.375465	7.641332	0
GO_REGULATION_OF_BLOOD_CIRCULATION	290	0.385971	7.564449	0
GO_HEART_DEVELOPMENT	456	0.303947	7.553804	0
GO_FOREBRAIN_DEVELOPMENT	354	0.344524	7.511221	0
GO_EMBRYONIC_ORGAN_DEVELOPMENT	404	0.326681	7.505429	0
GO_EPITHELIAL_CELL_DIFFERENTIATION	486	0.29093	7.401311	0
GO_VASCULATURE_DEVELOPMENT	462	0.303339	7.380436	0
GO_CIRCULATORY_SYSTEM_PROCESS	359	0.340834	7.30921	0
GO_ANION_TRANSPORT	495	0.278589	7.214427	0
GO_REGULATION_OF_TRANSMEMBRANE_TRANSPORT	415	0.30337	7.187595	0
GO_REGULATION_OF_NEURON_PROJECTION_DEVELOPMENT	398	0.307157	7.092272	0
GO_POSITIVE_REGULATION_OF_NERVOUS_SYSTEM_DEVELOPMENT	418	0.300016	7.033771	0

Supplemental Table 3: Most underexpressed genesets with *BPTF* KD by GSEA

NAME	SIZE	ES	NES	FDR q-val
GO_RIBONUCLEOPROTEIN_COMPLEX_BIOGENESIS	426	-0.44033	-10.6926	0
GO_NCRNA_PROCESSING	372	-0.45012	-9.98928	0
GO_RIBOSOME_BIOGENESIS	302	-0.47571	-9.53313	0
GO_MRNA_PROCESSING	418	-0.39262	-9.11744	0
GO_AMIDE_BIOSYNTHETIC_PROCESS	497	-0.3502	-9.09894	0
GO_POSTTRANSCRIPTIONAL_REGULATION_OF_GENE_EXPRESSION	432	-0.37365	-8.97247	0
GO_RNA_SPLICING	355	-0.39724	-8.68594	0
GO_PROTEASOMAL_PROTEIN_CATABOLIC_PROCESS	266	-0.42809	-8.19792	0
GO_RNA_SPLICING_VIA_TRANSESTERIFICATION_REACTIONS	261	-0.42362	-8.08109	0
GO_REGULATION_OF_PROTEIN_CATABOLIC_PROCESS	383	-0.35543	-8.0554	0
GO_RRNA_METABOLIC_PROCESS	251	-0.43527	-7.98752	0
GO_POSITIVE_REGULATION_OF_CATABOLIC_PROCESS	389	-0.33797	-7.81993	0
GO_MITOCHONDRIAL_TRANSLATION	105	-0.62389	-7.55179	0
GO_REGULATION_OF_CELLULAR_PROTEIN_CATABOLIC_PROCESS	267	-0.39145	-7.54257	0
GO_RESPONSE_TO_ENDOPLASMIC_RETICULUM_STRESS	227	-0.42001	-7.50055	0
GO_TRNA_METABOLIC_PROCESS	168	-0.5021	-7.49502	0
GO_PROTEIN_POLYUBIQUITINATION	238	-0.41364	-7.44369	0
GO_REGULATION_OF_PROTEIN_MODIFICATION_BY_SMALL_PROTEIN_CONJUGATION_OR_REMOVAL	274	-0.39349	-7.41669	0
GO_POSITIVE_REGULATION_OF_PROTEOLYSIS	359	-0.33297	-7.28157	0
GO_DNA_REPAIR	456	-0.28877	-7.19827	0
GO_POSITIVE_REGULATION_OF_PROTEIN_CATABOLIC_PROCESS	258	-0.38321	-7.17706	0
GO_MACROMOLECULAR_COMPLEX_DISASSEMBLY	180	-0.44485	-7.06967	0

Supplemental Table 5: HDAC inhibitor dose-response results

IC₅₀ (nM) (95% CI)

	BT 145		DIPG 4	
	shNull	shBPTF	shNull	shBPTF
Apicidin	833.3 (485-1431)	255.3 (186-351)	77.18 (72-83)	39.68 (35-45)
Oxamflatin	2348 (1940-2483)	892.4 (524-1520)	638.1 (460-885)	226.9 (149-345)
SAHA	1646 (1238-2188)	956.9 (625-1464)	1142 (973-1341)	966.7 (833-1122)