

Figure S1

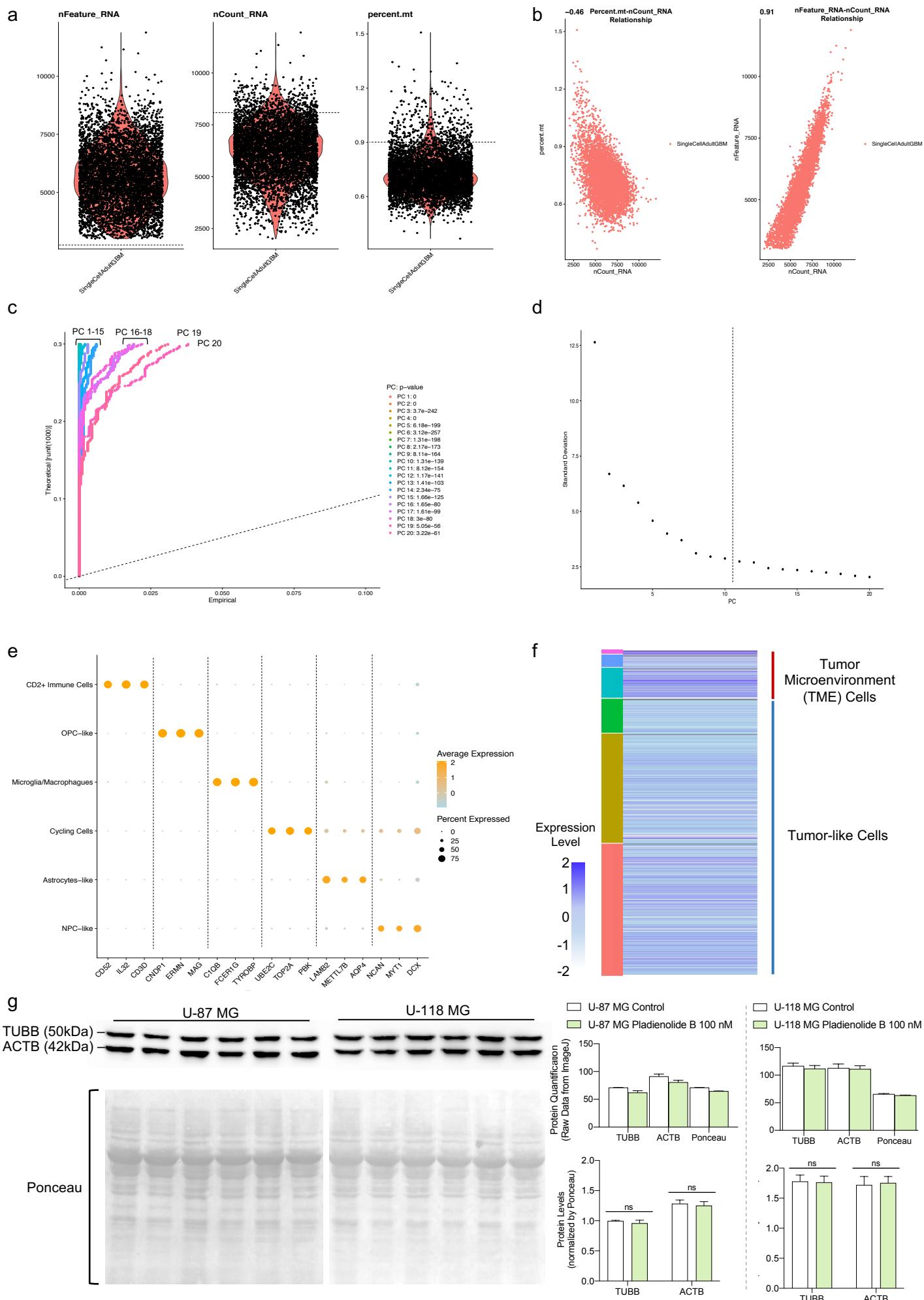
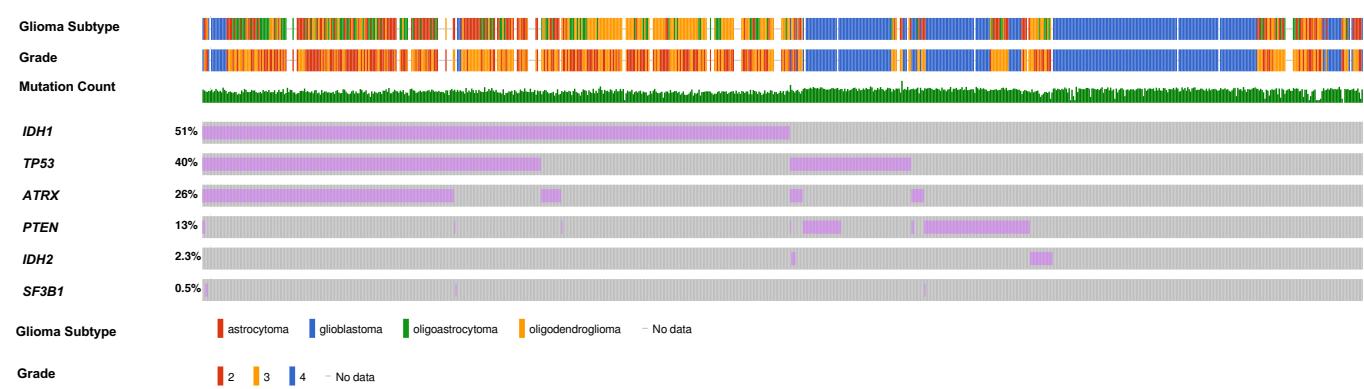
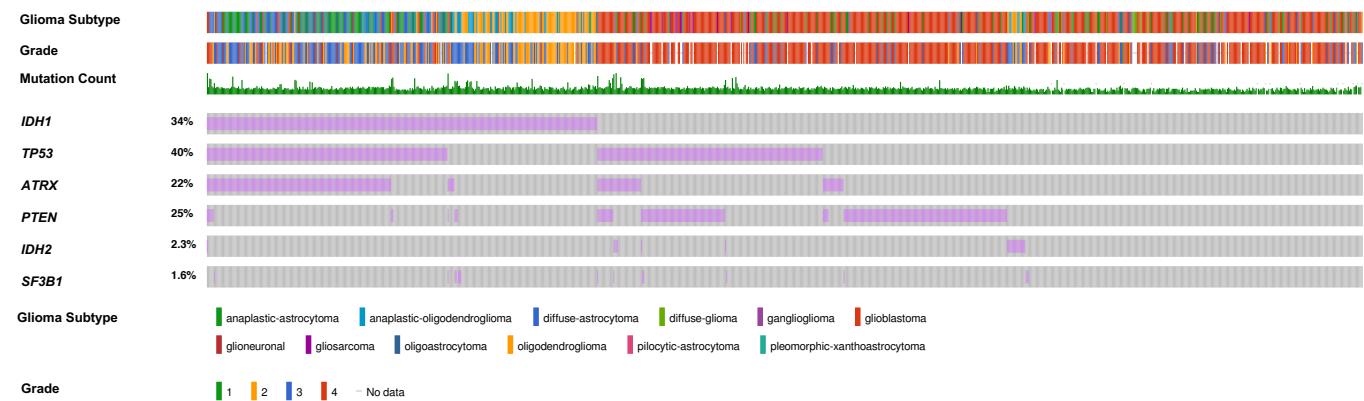


Figure S2

a TCGA dataset

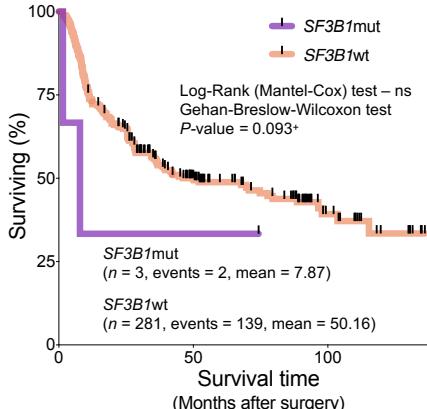


b MSKCC dataset



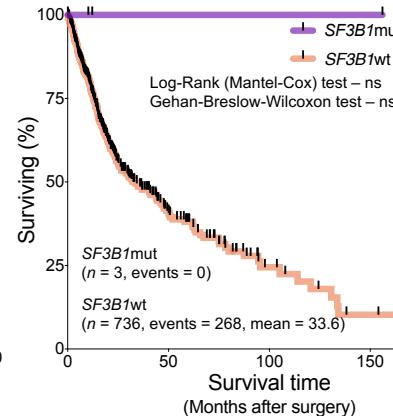
c

SF3B1mut - CGGA



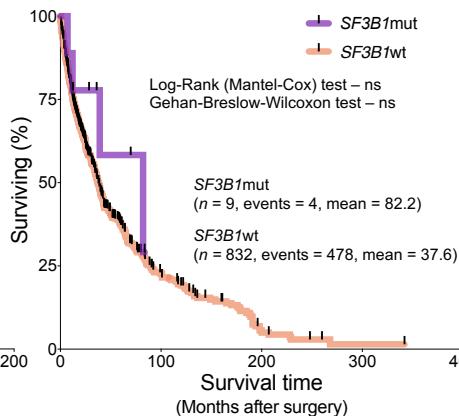
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SF3B1mut - TCGA



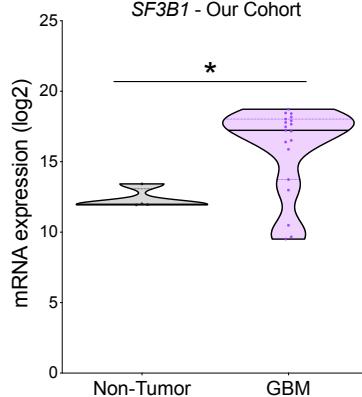
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SF3B1mut - MSKCC



f

SF3B1 - Our Cohort



SF3B1 - Rembrandt

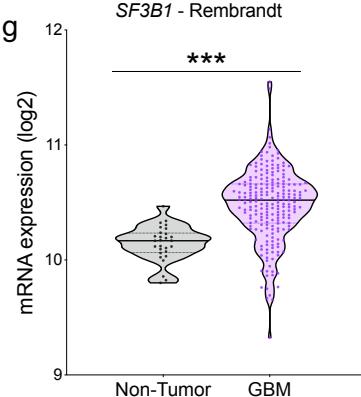


Figure S3

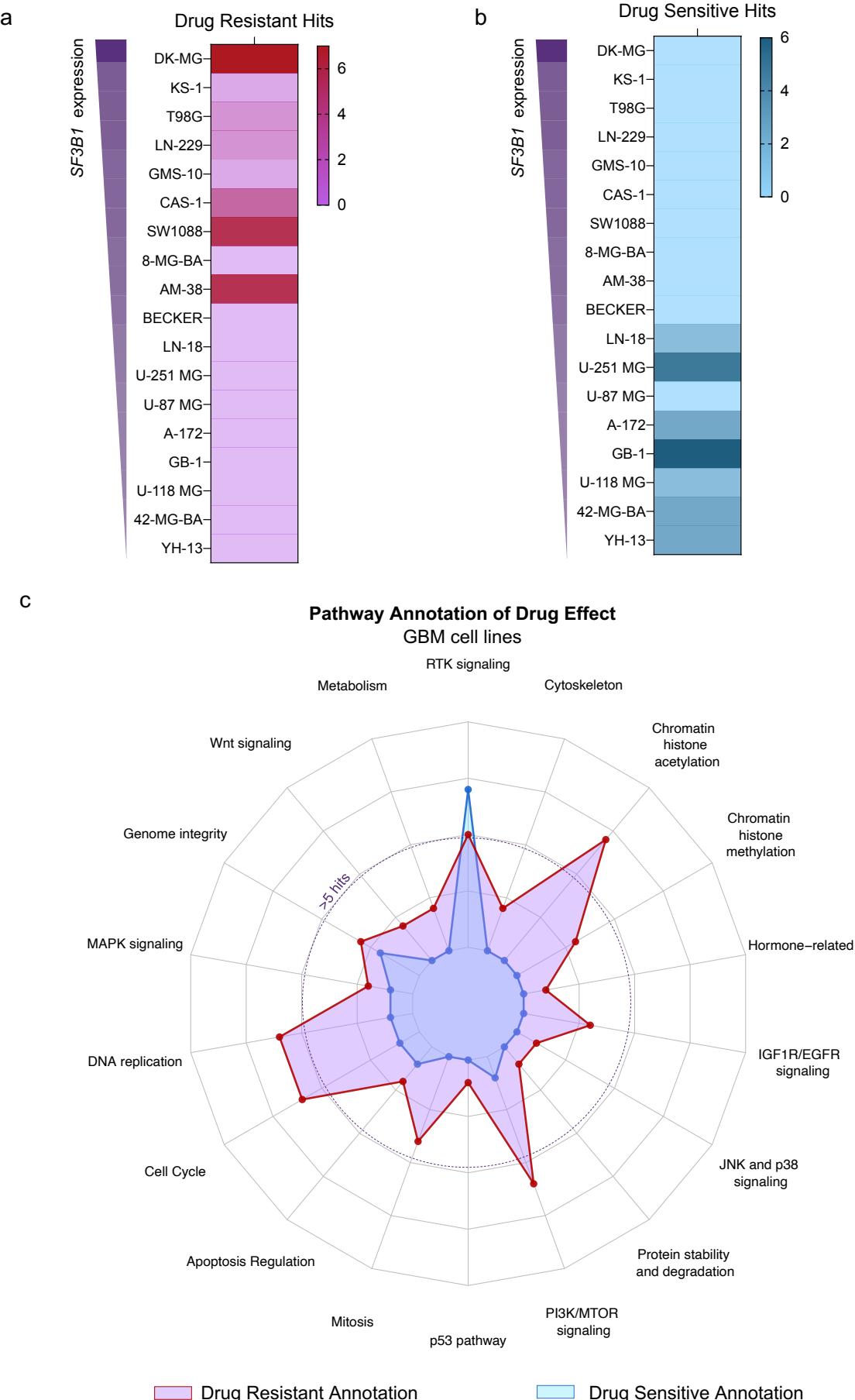


Figure S4

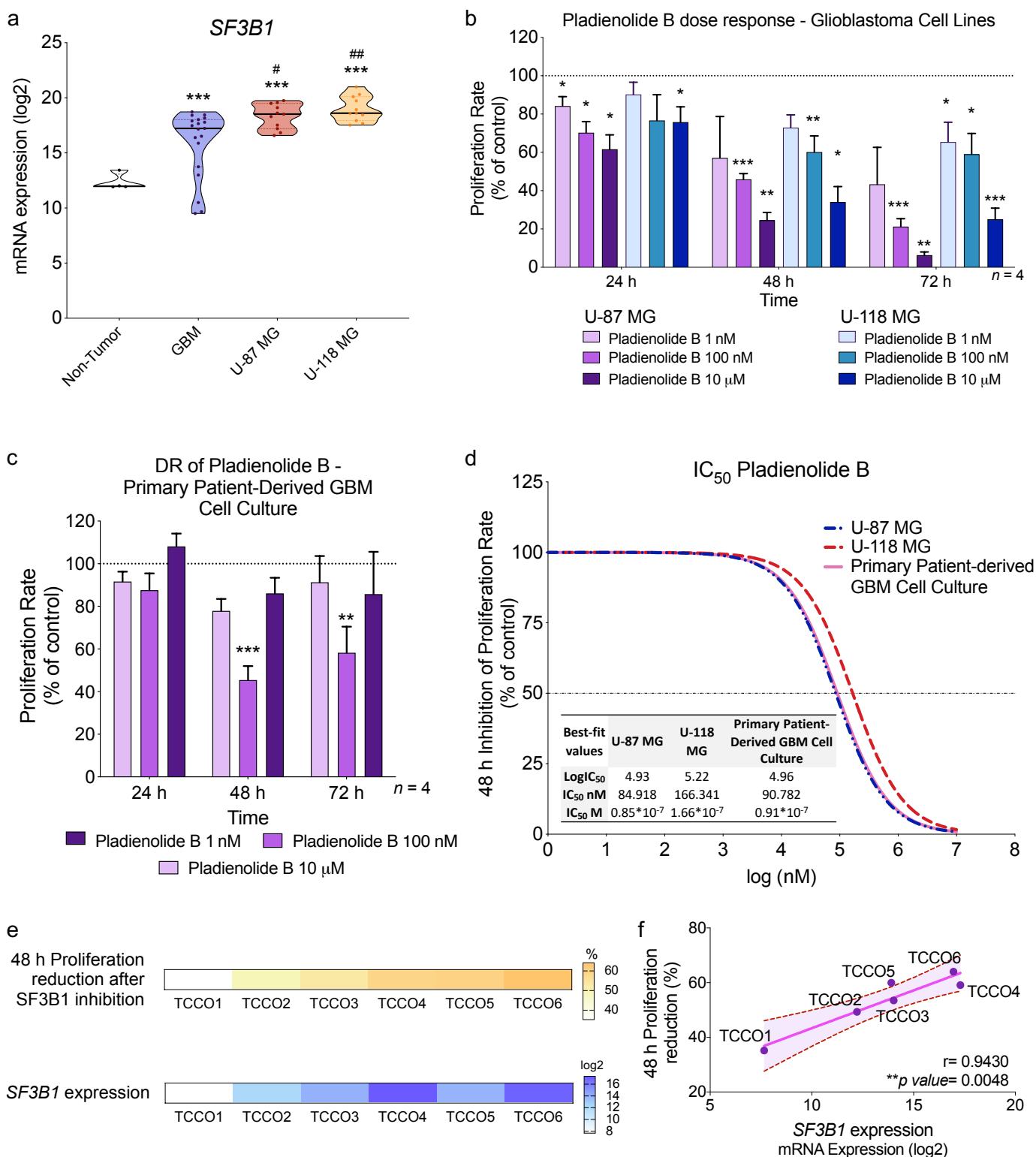


Figure S5

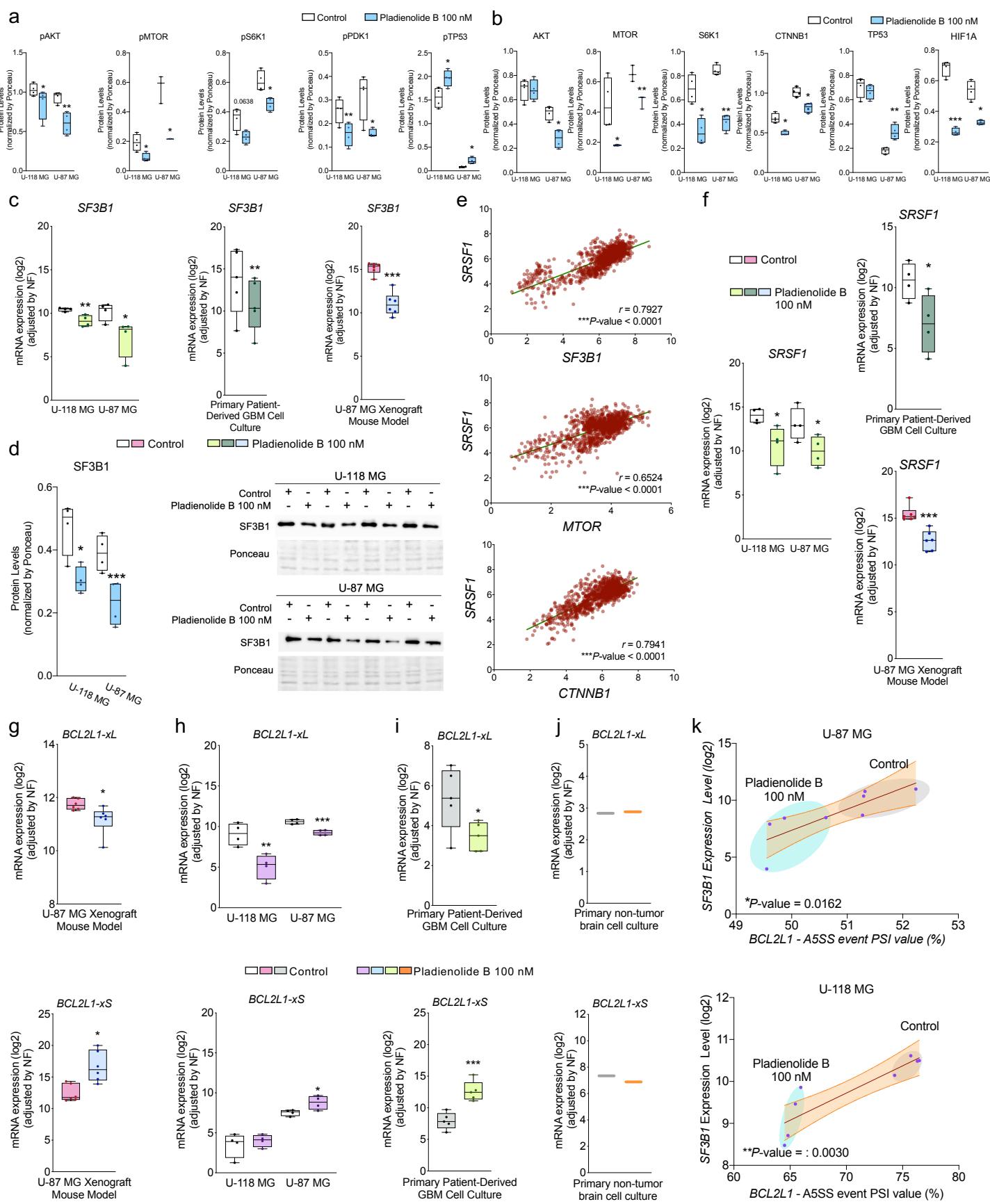


Table S1

Parameters	Glioma patients
<hr/>	
CGGA WEsq	
Patients (n)	284
Gender (M/F)	168 (59.15 %) / 116 (40.85 %)
Primary LGG	124 (43.67 %)
Recurrent LGG	58 (20.42 %)
Primary GBM	54 (19.01 %)
Recurrent GBM	48 (16.90 %)
Age at surgical intervention (mean±desvest)	41.97 ± 12.34
Grade II	91 (32.04 %)
Grade III	91 (32.04 %)
Grade IV	102 (35.92 %)
GBM IDH1 status (wt/mut)	151 (53.17 %) / 133 (46.83 %)
GBM survival rate (Mean - Months)	42.03 ± 34.89
<hr/>	
TCGA	
Patients (n)	746
Gender (M/F)	441 (59.11 %) / 305 (40.88 %)
Primary LGG	451 (60.46 %)
Recurrent LGG	N/A
Primary GBM	295 (39.54 %)
Recurrent GBM	N/A
Age at surgical intervention (mean±desvest)	50.26 ± 15.91
Grade II	212 (28.42 %)
Grade III	239 (32.04 %)
Grade IV	295 (39.54 %)
GBM IDH1 status (wt/mut)	315 (50.97 %) / 303 (49.03 %)
GBM survival rate (Mean - Months)	19.08 ± 24.57
<hr/>	
MSKCC	
Patients (n)	923
Gender (M/F)	557 (60.35 %) / 366 (39.65 %)
Primary LGG	273 (29.58 %)
Recurrent LGG	123 (13.33 %)
Primary GBM	431 (46.70 %)
Recurrent GBM	118 (12.78 %)
Age at surgical intervention (mean±desvest)	49.49 ± 16.06
Grade II	145 (15.71 %)
Grade III	251 (27.19 %)
Grade IV	549 (59.48 %)
GBM IDH1 status (wt/mut)	584 (63.27 %) / 339 (33.8 %)
GBM survival rate (Mean - Months)	40.61 ± 48.49

Table S2

Parameters	Control patients	GBM patients
Our Cohort		
Patients (n)	4	22
Gender (M/F)	1(25 %) / 3(75 %)	17(77.27%) / 5(23.73%)
Age at surgical intervention (mean±desvest)	51.2 ± 5.38	59.81 ± 12.77
Grade IV	-	22
%KI67 (mean±desvest)	-	33.9 ± 14.76
% of P53 positive	-	72.73 %
% of PAGF positive	-	72.73 %
% of IDH1 positive	-	18.18 %
GBM survival rate (Mean - Months)	-	14.92
Rembrandt		
Patients (n)	28	219
Gender (M/F)	N/A	N/A
Age at surgical intervention (mean±desvest)	N/A	N/A
Grade IV	-	219
Molecular subtype:Classical	-	99 (45.21 %)
Molecular subtype:Mesenchymal	-	37 (16.89 %)
Molecular subtype:Proneural	-	39 (17.81 %)
G-CIMP status (Positive/Negative)	-	11 (5.02 %) / 208 (94.98 %)
GBM survival rate (Mean - Months)	-	19.83
CGGA		
Patients (n)	-	388
Gender (M/F)	-	236 (60.82 %) / 152 (29.18 %)
Age at surgical intervention (mean±desvest)	-	48.01 ± 13.30
Grade IV	-	388
Molecular GBM subtype:Classical	-	107 (25.58 %)
Molecular GBM subtype:Mesenchymal	-	89 (30.90 %)
Molecular GBM subtype:Proneural	-	83 (21.39 %)
Primary GBM	-	225 (57.99 %)
Secondary GBM	-	30 (6.15 %)
Recurrent GBM	-	133 (35.86 %)
GBM IDH1 status (wt/mut)	-	288 (74.23 %) / 100 (25.77 %)
GBM survival rate (Mean - Months)	-	17.15

Table S3

P-value	pct.1	pct.2	p_val_adj	cluster	gene	
0	0.819	0.429	0	0	DCX	NPC-like
0	0.612	0.132	0		MYT1	
8.55E-276	0.675	0.183	1.87E-270		NCAN	
3.22E-267	0.61	0.159	7.04E-263		MIAT	
9.94E-261	0.845	0.611	2.17E-256		CD24	
1.10E-253	0.565	0.126	2.40E-249		ELAVL4	
4.36E-220	0.583	0.175	9.53E-216		TAGLN3	
1.08E-217	0.415	0.055	2.35E-213		STMN2	
2.16E-200	0.606	0.209	4.73E-196		B4GALNT1	
6.80E-138	0.363	0.079	1.49E-132		NNAT	
0	0.733	0.147	0	1	AQP4	Astrocytes-like
0	0.645	0.126	0	1	METTL7B	
0	0.85	0.246	0	1	LAMB2	
0	0.856	0.331	0	1	TNC	
0	0.62	0.121	0	1	EMP1	
2.66E-289	0.716	0.186	5.82E-285	1	HOPX	
9.51E-288	0.811	0.262	2.08E-282	1	S100A16	
3.06E-274	0.813	0.27	6.69E-270	1	LGALS3	
2.82E-256	0.844	0.488	6.17E-252	1	F3	
3.09E-183	0.387	0.063	6.76E-179	1	CHI3L1	
0	0.836	0.044	0	2	PBK	Cycling Cells
0	0.887	0.073	0	2	TOP2A	
0	0.808	0.071	0	2	UBE2C	
0	0.882	0.073	0	2	BIRC5	
0	0.895	0.102	0	2	UBE2T	
0	0.753	0.054	0	2	FAM64A	
0	0.863	0.078	0	2	TPX2	
0	0.886	0.112	0	2	NUSAP1	
0	0.803	0.07	0	2	CDK1	
0	0.799	0.044	0	2	NUF2	
0	0.983	0.007	0	3	TYROBP	Microglia/Macrophages
0	0.977	0.018	0	3	FCER1G	
0	0.924	0.008	0	3	C1QB	
0	0.968	0.031	0	3	RGS1	
0	0.971	0.026	0	3	SRGN	
0	0.947	0.005	0	3	C1QA	
0	0.935	0.007	0	3	C1QC	
0	0.947	0.006	0	3	FCGR3A	
0	0.996	0.031	0	3	LAPTM5	
0	0.996	0.071	0	3	HLA.DRA	
0	0.99	0.009	0	4	MAG	OPC-like
0	0.995	0.022	0	4	ERMN	
0	0.97	0.013	0	4	CNDP1	
0	1	0.031	0	4	ENPP2	
0	0.98	0.011	0	4	KLK6	
0	0.98	0.013	0	4	SPOCK3	
0	1	0.074	0	4	PTGDS	
0	1	0.091	0	4	TF	
0	0.985	0.043	0	4	RNASE1	
0	1	0.08	0	4	TMEM144	
0	0.91	0.001	0	5	CD3D	CD2+ Immune Cells
0	0.955	0.021	0	5	IL32	
0	0.866	0.006	0	5	CD52	
0	0.866	0.003	0	5	CD2	
0	0.97	0.002	0	5	CD3E	
0	0.866	0.019	0	5	IL2RG	
2.33E-230	0.896	0.038	5.10E-225	5	CYTIP	
1.74E-186	0.881	0.048	3.80E-182	5	PTPRCAP	
8.28E-180	0.761	0.035	1.81E-175	5	IFITM1	
2.03E-141	1	0.09	4.43E-137	5	LCP1	

Table S4

Parameters	Non-tumor patients	GBMs patients
CPTAC		
Patients (n)	10	100
Gender (M/F)	5(50 %) / 5(50 %)	56(56 %) / 44(44 %)
Age at surgical intervention (mean±desvest)	57.5 ± 9.10	57.93 ± 12.44
Grade IV	-	100
GBM survival rate (Mean - Months)	-	11.26

Table S5

#term ID	term description	observed gene count	background gene count	P-value FDR <0.01
HSA-8953854	Metabolism of RNA	126	652	1.68E-28
HSA-72172	mRNA Splicing	66	186	2.64E-26
HSA-72203	Processing of Capped Intron-Containing Pre-mRNA	73	234	2.64E-26
HSA-72163	mRNA Splicing - Major Pathway	64	178	5.75E-26
HSA-74160	Gene expression (Transcription)	143	1366	6.95E-11
HSA-73857	RNA Polymerase II Transcription	125	1233	1.52E-08
HSA-392499	Metabolism of proteins	166	1948	1.65E-06
HSA-72187	mRNA 3'-end processing	18	56	3.52E-06
HSA-109688	Cleavage of Growing Transcript in the Termination Region	19	65	4.60E-06
HSA-162599	Late Phase of HIV Life Cycle	27	135	5.92E-06
HSA-3700989	Transcriptional Regulation by TP53	48	359	6.39E-06
HSA-162587	HIV Life Cycle	28	148	7.95E-06
HSA-162906	HIV Infection	35	224	1.29E-05
HSA-1640170	Cell Cycle	65	586	1.59E-05
HSA-674695	RNA Polymerase II Pre-transcription Events	20	84	1.98E-05
HSA-69620	Cell Cycle Checkpoints	38	265	2.24E-05
HSA-72202	Transport of Mature Transcript to Cytoplasm	19	77	2.24E-05
HSA-5696398	Nucleotide Excision Repair	22	109	5.00E-05
HSA-112382	Formation of RNA Pol II elongation complex	16	61	7.93E-05
HSA-159236	Transport of Mature mRNA derived from an Intron-Containing Transcript	17	69	7.93E-05
HSA-6781823	Formation of TC-NER Pre-Incision Complex	15	53	7.93E-05
HSA-73894	DNA Repair	38	290	0.00011
HSA-167172	Transcription of the HIV genome	17	73	0.00013
HSA-68886	M Phase	42	343	0.00015
HSA-212436	Generic Transcription Pathway	98	1112	0.00017
HSA-68882	Mitotic Anaphase	28	186	0.00021
HSA-72165	mRNA Splicing - Minor Pathway	14	52	0.00021
HSA-199991	Membrane Trafficking	62	612	0.00022
HSA-2467813	Separation of Sister Chromatids	27	178	0.00024
HSA-597592	Post-translational protein modification	114	1366	0.00024
HSA-167152	Formation of HIV elongation complex in the absence of HIV Tat	13	48	0.00035
HSA-5663205	Infectious disease	42	363	0.00039
HSA-1632852	Macroautophagy	15	66	0.00043
HSA-5653656	Vesicle-mediated transport	63	649	0.00053
HSA-69618	Mitotic Spindle Checkpoint	19	105	0.00054
HSA-380972	Energy dependent regulation of mTOR by LKB1-AMPK	10	29	0.00058
HSA-6781827	Transcription-Coupled Nucleotide Excision Repair (TC-NER)	16	78	0.00062
HSA-69278	Cell Cycle Mitotic	50	483	0.00080
HSA-983168	Antigen processing: Ubiquitination & Proteasome degradation	36	303	0.00082
HSA-8953897	Cellular responses to external stimuli	48	459	0.00087
HSA-165159	mTOR signalling	11	39	0.00094
HSA-5633007	Regulation of TP53 Activity	23	159	0.0015
HSA-5696395	Formation of Incision Complex in GG-NER	11	42	0.0016
HSA-3108232	SUMO E3 ligases SUMOylate target proteins	22	154	0.0025
HSA-167200	Formation of HIV-1 elongation complex containing HIV-1 Tat	11	46	0.0031
HSA-5696399	Global Genome Nucleotide Excision Repair (GG-NER)	15	83	0.0031
HSA-6782210	Gap-filling DNA repair synthesis and ligation in TC-NER	13	64	0.0031
HSA-6782135	Dual incision in TC-NER	13	65	0.0034
HSA-983169	Class I MHC mediated antigen processing & presentation	38	365	0.0048
HSA-141430	Inactivation of APC/C via direct inhibition of the APC/C complex	7	19	0.0052
HSA-68877	Mitotic Prometaphase	24	190	0.0054
HSA-6807070	PTEN Regulation	19	135	0.0068
HSA-6804756	Regulation of TP53 Activity through Phosphorylation	15	92	0.0070
HSA-6807505	RNA polymerase II transcribes snRNA genes	13	74	0.0089
HSA-72086	mRNA Capping	8	29	0.0089
HSA-429914	Deadenylation-dependent mRNA decay	11	55	0.0090
HSA-72766	Translation	31	288	0.0090
HSA-166208	mTORC1-mediated signalling	7	22	0.0092
HSA-6796648	TP53 Regulates Transcription of DNA Repair Genes	12	65	0.0092
HSA-3214847	HATs acetylate histones	16	107	0.0095
HSA-167161	HIV Transcription Initiation	10	47	0.0097
HSA-167162	RNA Polymerase II HIV Promoter Escape	10	47	0.0097
HSA-176408	Regulation of APC/C activators between G1/S and early anaphase	13	76	0.0097
HSA-69052	Switching of origins to a post-replicative state	14	86	0.0097
HSA-73776	RNA Polymerase II Promoter Escape	10	47	0.0097
HSA-73779	RNA Polymerase II Transcription Pre-Initiation And Promoter Opening	10	47	0.0097
HSA-75953	RNA Polymerase II Transcription Initiation	10	47	0.0097

Table S6

Gene	Accession Number	Sense Primer Sequence	AntiSense Primer Sequence	Product Size
ACTB	NM_001101	ACTCTTCAGCCTCCCTCCT	CAGTGATCTCCTCTGCATCCT	176
GAPDH	NM_002046	AATCCCACCATCACCATTTCCA	AAATGAGCCCCAGCCTTC	122
HPRT	NM_000194.2	CTGAGGATTGGAAAGGGTGT	TAATCCAGCAGGTCAAGCAAAG	157
SF3B1	NM_012433.3	CAGTTCCGTCTGTGTGTTCG	GCTGCCTTCTTGCCTTGA	101
VEGFA	NM_001171623.1	GGGCAGAACATCACGAAGT	ATCTGCATGGTGTGTTGGA	218
MKI67	NM_002417.5	GACATCCGTATCCAGCTTCCT	GCCGTACAGGCTCATCAATAAC	139
EGFR	NM_005228.5	CCTTGCCGCAAAGTGTGTA	TGTGAAGGAGTCACCCCTAAAT	153
CDK4	NM_000075.4	ACAGTTCGTGAGGTGGCTTT	TACCTTGATCTCCGGTCAG	111
PDGFRA	NM_006206.6	CAGGCCCATTTACATCATC	CATAGCTCGTGTGCTTC	162
PDGFRB	NM_002609.4	AGCTTGCCTCAATGTCTCCA	GGGATCTGGCACAAAGATGTA	248
SRSF3	NM_003017.4	TAACCCTAGATCTCGAAATGCATC	CATAGTAGCCAAAAGCCCGTT	117
RBM22	NM_018047.2	CTCTGGGTTCCAACACCTACA	GGCACAGATTTGCATTCT	137
PTBP1	NM_002819.4	TGGGTCGGTTCTGCTATT	CAGATCCCCGCTTGTAC	111
RBM3	NM_006743.4	AAGCTTCTCGTGGAGGG	TTGACAACGACCACCTCAGA	98
MYC	NM_002467.6	CTCGGATTCTCTGCTCTCCTC	TTCCTCATCTTCTTGTTCCTCCT	124
CCND1	NM_053056.3	CCTCGGTGTCCTACTTCAAAT	TCCTCCTCGCACTTGTTC	109
SRSF1	NM_006924.5	TGTCTCTGGACTGCCTCCA	TGCCATCTCGTAAACATCA	98
BCL2L1	NM_138578.3	TCCCCATGGCAGCAGTAAAG	GGTGGGAGGGTAGAGTGGAT	494 BCL2L1-xS 305 BCL2L1-xL
BCL2-xS	NM_001191.4	GAGCTTGAACAGGATACTTTGTG	GAAGAGTGAGCCCAGCAGAA	97
BCL2-xL	NM_001317919.2			
	NM_001317920.2			
	NM_001317921.2			
	NM_001322239.2	GATGGCCACTTACCTGAATGA	TGCTGCATTGTTCCCATAGA	94
	NM_001322240.2			
KLF6	NM_001322242.2			
	NM_138578.3			
	NM_001300.6			585 KLF6a
CRK	NM_001160124.2	CATCTCTCCGGAACTGAGC	GCTATGCCGCTTCTTACAGG	459 KLF6b
	NM_001160125.2			461 KLF6c
MCL1	NM_005206.5	GCAAGAGAGGGATGATTCCA	ATGGGAAGTGACCTCGTTG	333 CRKsvI
	NM_016823.4			163 CRKsvII
CASP2	NM_182763.3	AGACCTTACGACGGTTGG	ACCAGCTCTACTCCAGCAA	401 MCL1L
	NM_021960.5			153 MCL1S
RAC1	NM_001224.5	AACTGCCAAGCCTACAGAA	CTGCGTGGTTCTTCCATCT	167 CASP2S
	NM_032982.4			106 CASP2L
BIRC5	NM_018890.4	CCCTATCCTATCCGCAAACA	GGACTCACAGGGAAAAGCA	55 RAC1
	NM_006908.5			112 RAC1b
	NM_001012270.2			516 BIRC5
MST1R	NM_001012271.2	CCACTGAGAACGCCAGA	GAGAGAACGCCACTGTTACC	585 BIRC5-2b
	NM_001168.3			398 BIRC5-ΔEx3
SPP1	NM_002447.4	GATGGAGCTGCTGGCTTAC	ATCTACGCAGACCTGCAATG	270 RON
	XM_011533739.2			150 RONlack11
	NM_001251830.2			390 SPP1
	NM_001040058.2	GCATCACCTGTGCCATACC	TGGACTTACTTGGAAAGGGTCTC	201 SPP1a
	NM_000582.3			159 SPP1b
	NM_001040060.2			120 SPP1c

Table S7

Name	3'-5' ASO sequence	5'-3' <i>BCL2L1</i> Targeted Region	Oligo Size
ASO1_BCL2L1	TGTTCAAAGCTCTGATATGCTGTC	GACAGCATATCAGAGCTTGAAACA	24 bases
ASO2_BCL2L1	CCCCATCCCAGGAAGAGTTC	GAACCTTCCGGGATGGGG	19 bases
ASO3_BCL2L1	ACAATGCGACCCAGTTA	TAAACTGGGTGCATTGT	19 bases
ASO4_BCL2L1	CGCCGAAGGAGAAAAAGGCC	GGCCTTTTCTCCTCGGCG	20 bases
ASO5_BCL2L1	TTTCCACGCACAGTGCC	GGGCACTGTGCGTGGAAA	18 bases

Table S8

Drug Name	Drug Target	Target Pathway Annotation
Wnt-C59	PORCN	WNT signaling
IWP-2	PORCN	WNT signaling
Staurosporine	Broad spectrum kinase inhibitor	RTK signaling
GSK1904529A	IGF1R, IR	RTK signaling
Crizotinib	MET, ALK, ROS1	RTK signaling
Foretinib	MET, KDR, TIE2, VEGFR3/FLT4, RON, PDGFR, FGFR1, EGFR	RTK signaling
Cediranib	VEGFR, FLT1, FLT2, FLT3, FLT4, KIT, PDGFRB	RTK signaling
ML323	USP1, UAF1	Protein stability and degradation
MK-2206	AKT1, AKT2	PI3K/MTOR signaling
Rapamycin	MTORC1	PI3K/MTOR signaling
Pilaralisib	PI3K	PI3K/MTOR signaling
Dactolisib	PI3K (class 1), MTORC1, MTORC2	PI3K/MTOR signaling
Alpelisib	PI3Kalpha	PI3K/MTOR signaling
CZC24832	PI3Kgamma	PI3K/MTOR signaling
PRIMA-1MET	TP53 activation	p53 pathway
Vinorelbine	Microtubule destabiliser	Mitosis
Docetaxel	Microtubule stabiliser	Mitosis
Paclitaxel	Microtubule stabiliser	Mitosis
TTK_3146	TTK	Mitosis
AICA Ribonucleotide	AMPK agonist	Metabolism
GSK2606414	PERK	Metabolism
TAK-715	p38alpha, p38beta	JNK and p38 signaling
Linsitinib	IGF1R	IGF1R signaling
NVP-ADW742	IGF1R	IGF1R signaling
Fulvestrant	ESR	Hormone-related
VE-822	ATR	Genome integrity
Mirin	MRE11	Genome integrity
BIBR-1532	TERT	Genome integrity
VX-11e	ERK2	ERK MAPK signaling
KRAS (G12C) Inhibitor-12	KRAS (G12C)	ERK MAPK signaling
Lapatinib	EGFR, ERBB2	EGFR signaling
Cyclophosphamide	Alkylating agent	DNA replication
Doxorubicin	Anthracycline	DNA replication
Mitomycin-C	DNA crosslinker	DNA replication
Pyridostatin	G-quadruplex stabiliser	DNA replication
Etoposide	TOP2	DNA replication
Carmustine		DNA replication
BDP-00009066	MRCKB_HUMAN	Cytoskeleton
PAK_5339	PAK1, PAK2	Cytoskeleton
I-BET-762	BRD2, BRD3, BRD4	Chromatin other
JQ1	BRD2, BRD3, BRD4, BRDT	Chromatin other
PFI-1	BRD4	Chromatin other
PFI3	Polybromo 1, SMARCA4, SMARCA2	Chromatin other
EPZ5676	DOT1L	Chromatin histone methylation
GSK343	EZH2	Chromatin histone methylation
GSK591	PMRT5	Chromatin histone methylation
OF-1	BRPF1B, BRPF2	Chromatin histone acetylation
Vorinostat	HDAC inhibitor Class I, IIa, IIb, IV	Chromatin histone acetylation
Dacinostat	HDAC1	Chromatin histone acetylation
JQ12	HDAC1, HDAC2	Chromatin histone acetylation
Entinostat	HDAC1, HDAC3	Chromatin histone acetylation
ACY-1215	HDAC6	Chromatin histone acetylation
PCI-34051	HDAC8, HDAC6, HDAC1	Chromatin histone acetylation
Flavopiridol	CDK	Cell cycle
RO-3306	CDK1	Cell cycle
AZD5438	CDK2	Cell cycle
Palbociclib	CDK4, CDK6	Cell cycle
THZ-2-102-1	CDK7	Cell cycle
Wee1 Inhibitor	WEE1, CHEK1	Cell cycle
Embelin	XIAP	Apoptosis regulation
AZD5582	XIAP, ciAP	Apoptosis regulation

Table S9

Drug Name	Drug Target	Target Pathway Annotation
Staurosporine	Broad spectrum kinase inhibitor	RTK signaling
Motesanib	VEGFR, RET, KIT, PDGFR	RTK signaling
SB505124	TGFBR1, ACVR1B, ACVR1C	RTK signaling
PD173074	FGFR1, FGFR2, FGFR3	RTK signaling
Tivozanib	VEGFR1, VEGFR2, VEGFR3	RTK signaling
Pazopanib	CSF1R, KIT, PDGFRA, PDGFRB	RTK signaling
PD173074	FGFR1, FGFR2, FGFR3	RTK signaling