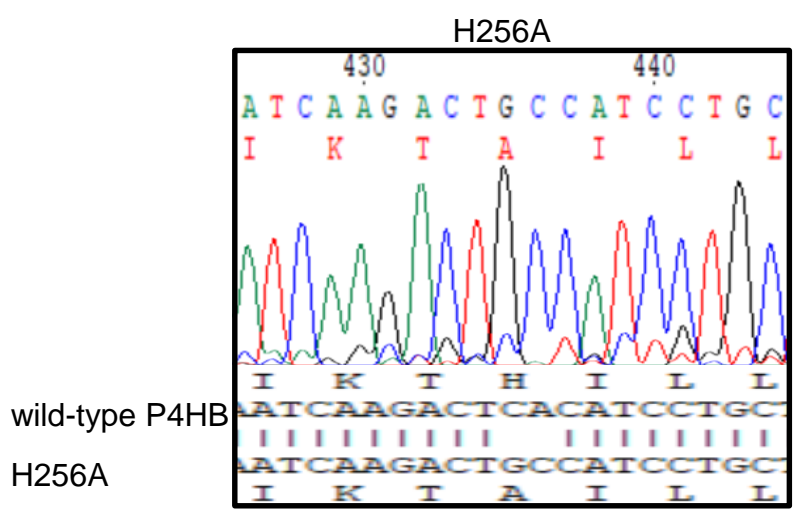
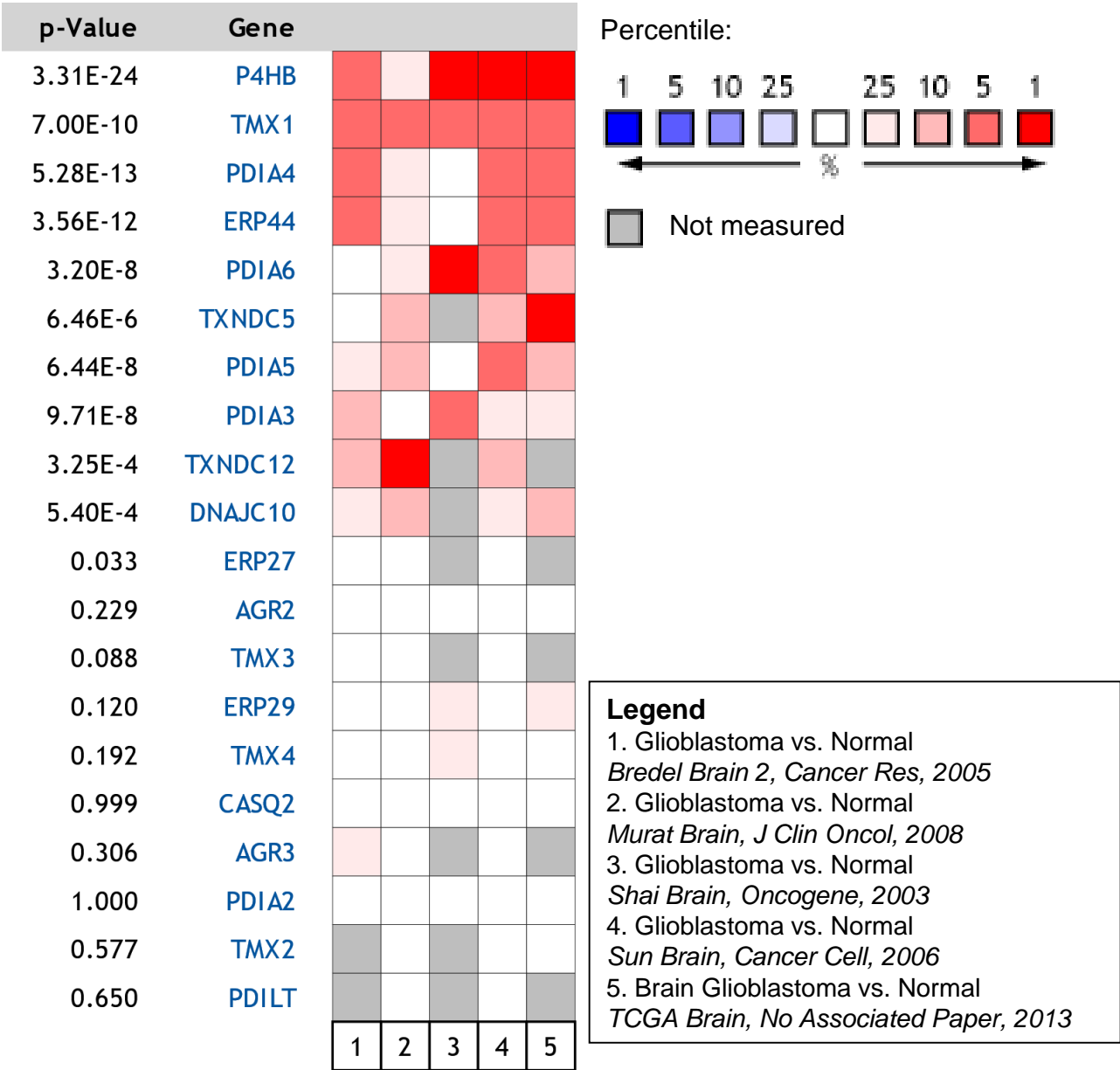


Fig. S1



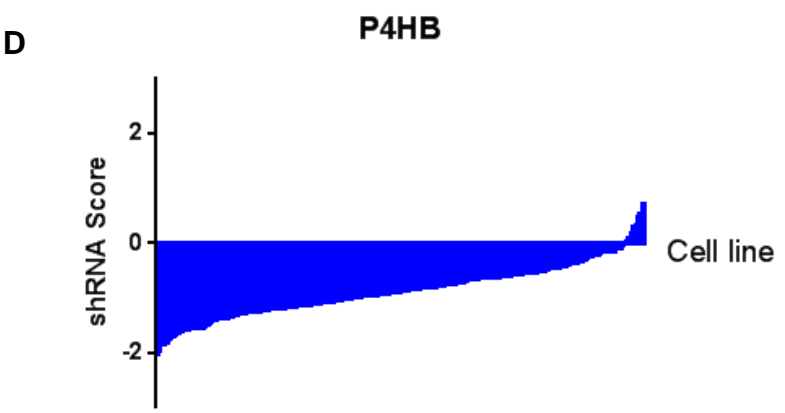
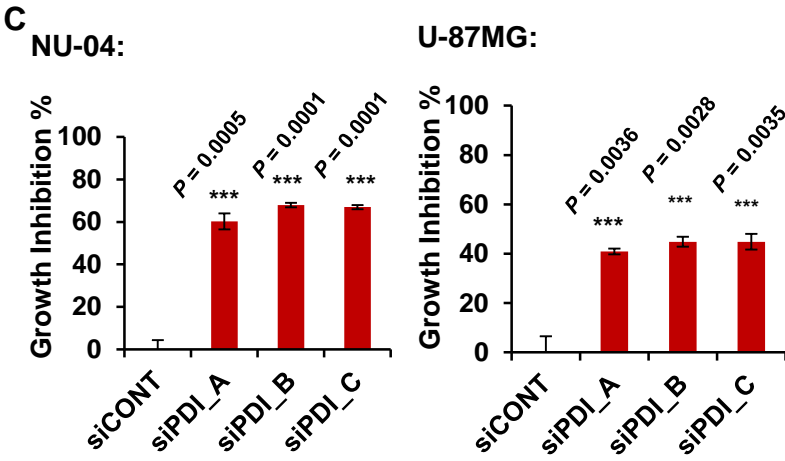
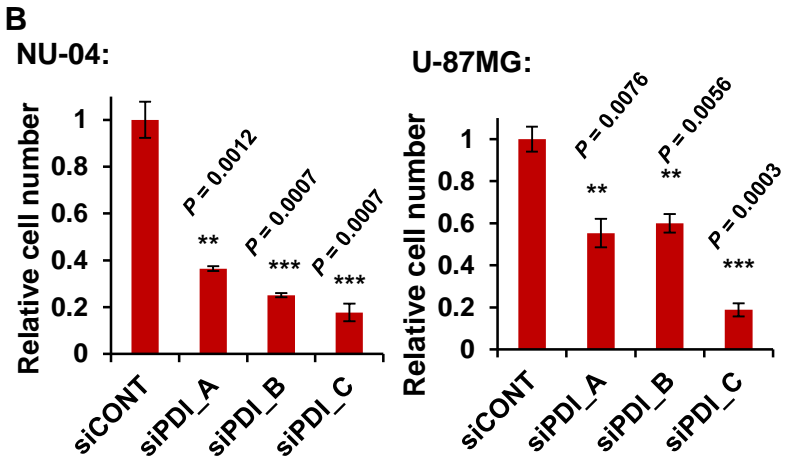
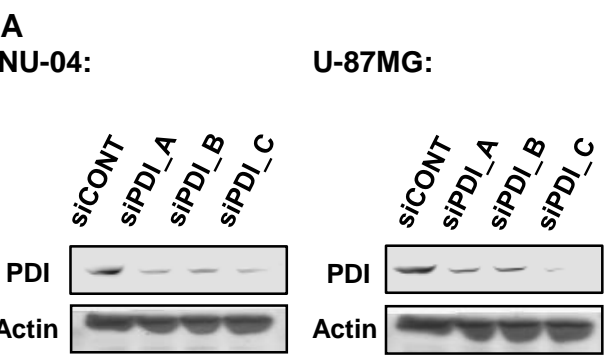
Supplementary Figure S1. Chromatogram confirming point mutation in tested PDI mutant.

Fig. S2



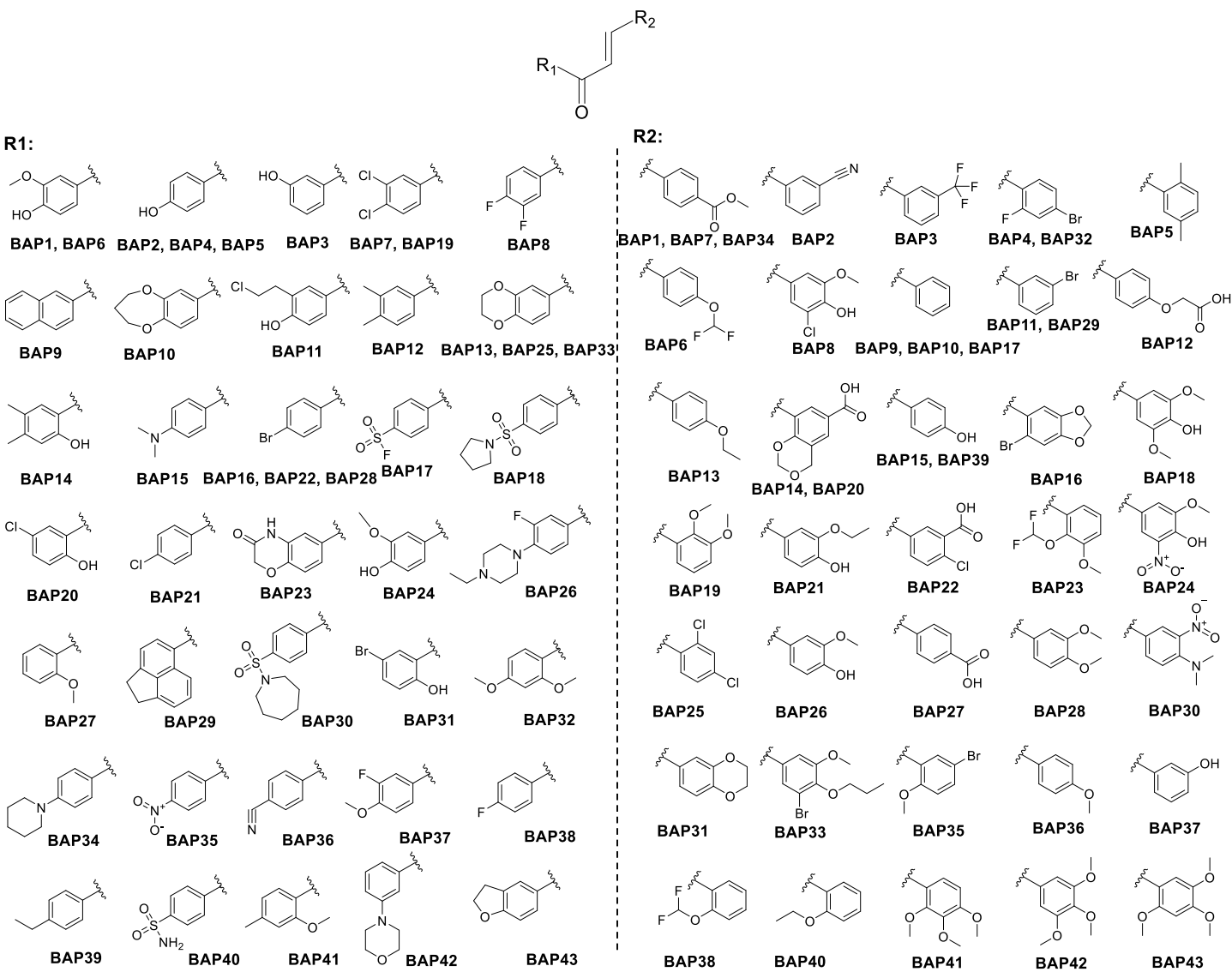
Supplementary Figure S2. mRNA expression of PDI isoforms in five GBM datasets from the Oncomine Platform (www.oncomine.org). The p-Value for a gene is its p-Value for the median-ranked analysis. Cell color is determined by the best gene rank percentile for the analyses within the cell.

Fig. S3

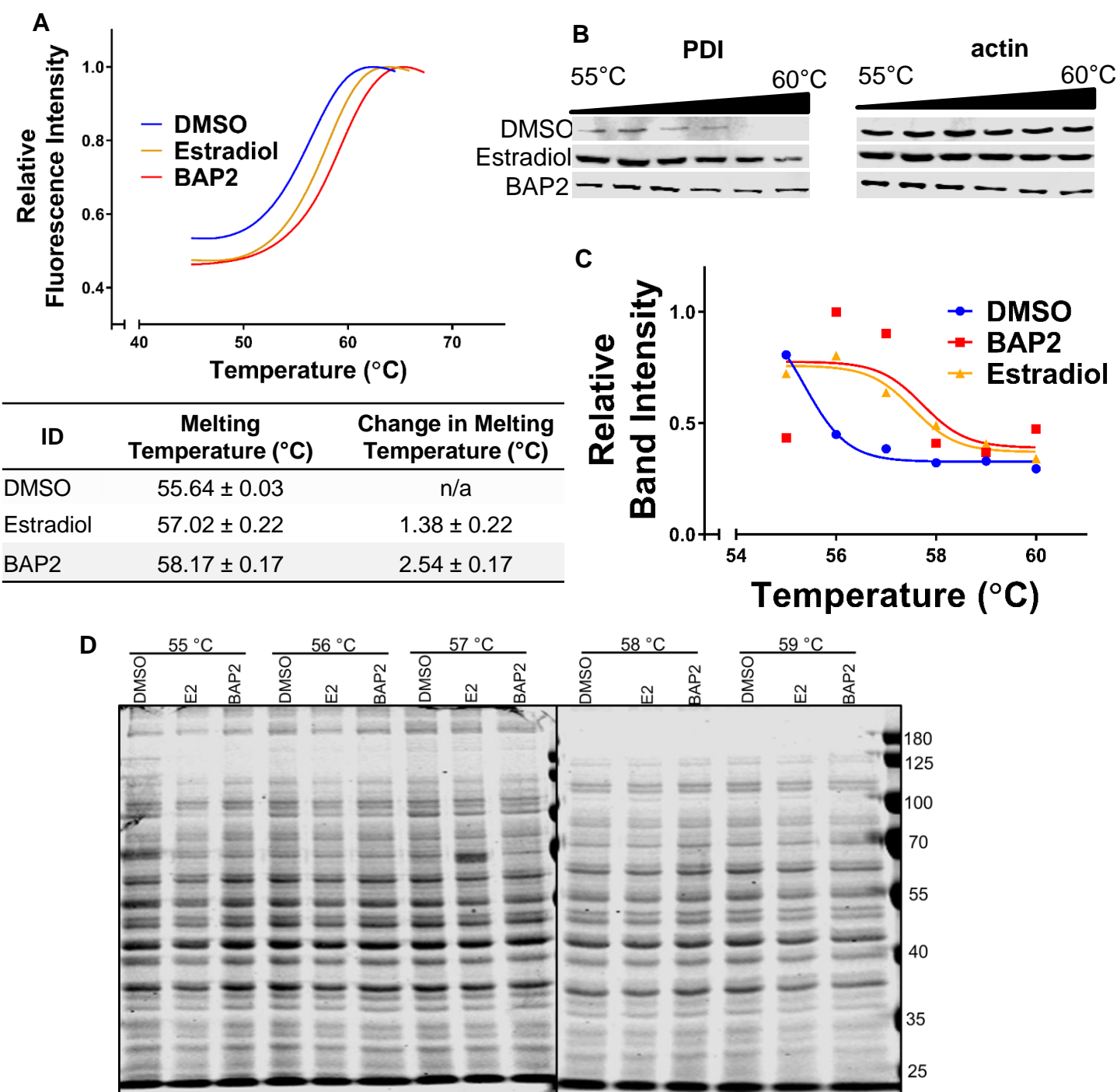


Supplementary Figure S3. PDI drives GBM progression and PDI knockdown inhibits cell proliferation. (a) PDI knockdown 72 h after PDI siRNA transfection in NU04 and U87MG cells. (b) Cell numbers counted under microscope and (c) cell growth and viability determined by the MTT assay were both significantly decreased. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$. (d) Waterfall plots of shRNA activities in a panel of cancer cell lines. shRNA score denotes the log₂-based decrease in PDI shRNA compared to pooled shRNA in 1002 cancer cell lines after several rounds of proliferation post-shRNA infection. A negative shRNA score indicates decreased cancer cell proliferation/survival after shRNA transfection.

Fig. S4



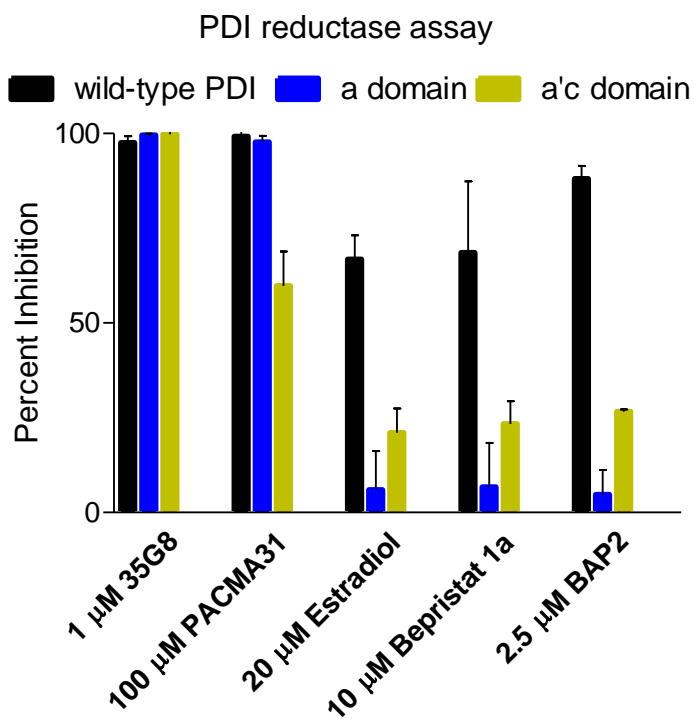
Supplementary Figure S4. Chemical structures of the chalcone derivatives.

Fig. S5

Supplementary Figure S5. BAP2 stabilizes intracellular PDI to thermal degradation. (a) Melt curve and Boltzmann melting temperature of PDI in the presence of DMSO (2.5%), estradiol (100 μM), or **BAP2** (100 μM). Experiment was repeated in triplicate. (b, c) PDI stability in the presence of 100 μM estradiol, 100 μM **BAP2**, or DMSO as a negative control. CETSA was performed in U87MG cells and cell lysate samples were probed by Western blotting with anti-PDI and actin antibodies. Actin was used as a loading control. (d) Coomassie-stained 10% acrylamide gel of intact A172 cells treated with DMSO, 100 μM estradiol (E2), or 100 μM **BAP2** and subjected to heat at indicated temperatures.

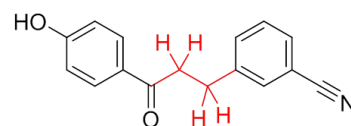
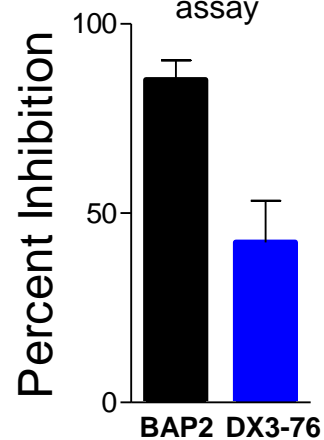
Fig. S6

A



B

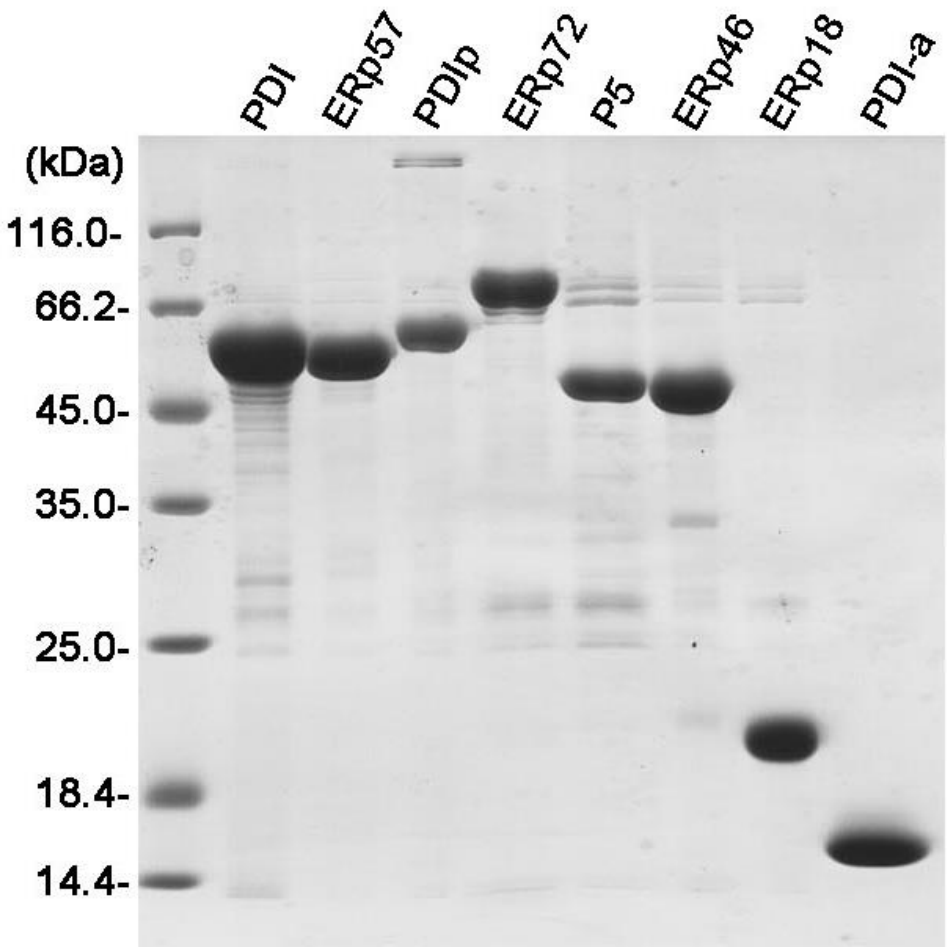
PDI reductase assay



DX3-76

Supplementary Figure S6. Activity of PDI inhibitors in the PDI reductase assay. (a) Percent inhibition of reductase activity of PDI or isolated **a** or **a'c** domains (1.6 μM) in the presence of inhibitors compared to DMSO control. (b) Percent inhibition of **BAP2** (100 μM) and saturated analog, **DX3-76** (100 μM), against wild-type PDI in the PDI reductase assay. Data expressed as means \pm S.D. (n = 3).

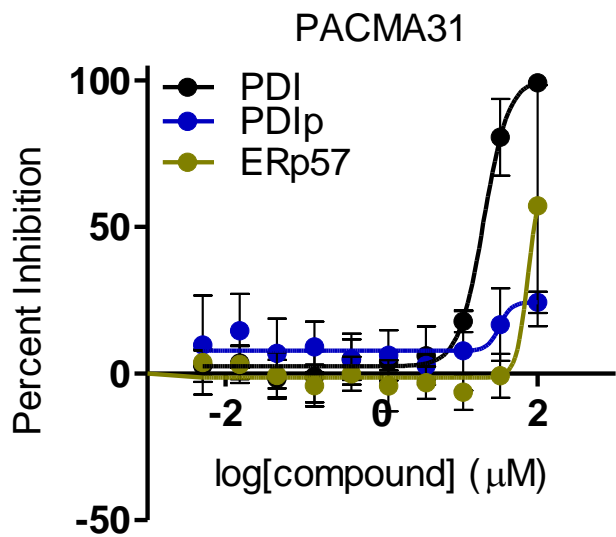
Fig. S7



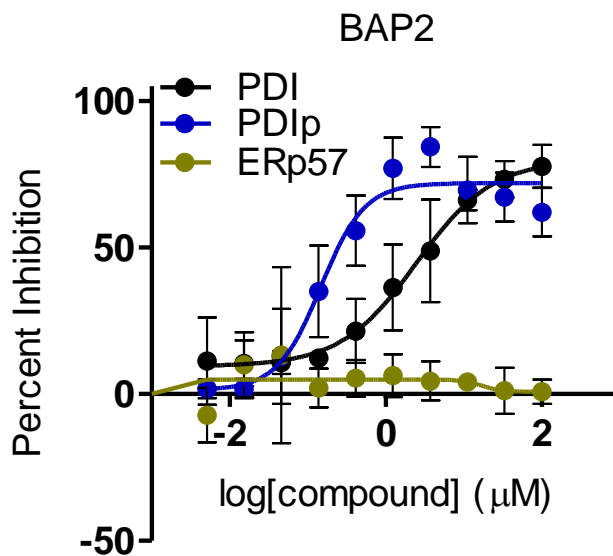
Supplementary Figure S7. Expression and purification of PDI family enzymes and the **a** domain of PDI. All the recombinant proteins contain an N-terminal His tag, and were purified using a nickel-nitrilotriacetic acid column, examined by 12% SDS-PAGE.

Fig. S8

A

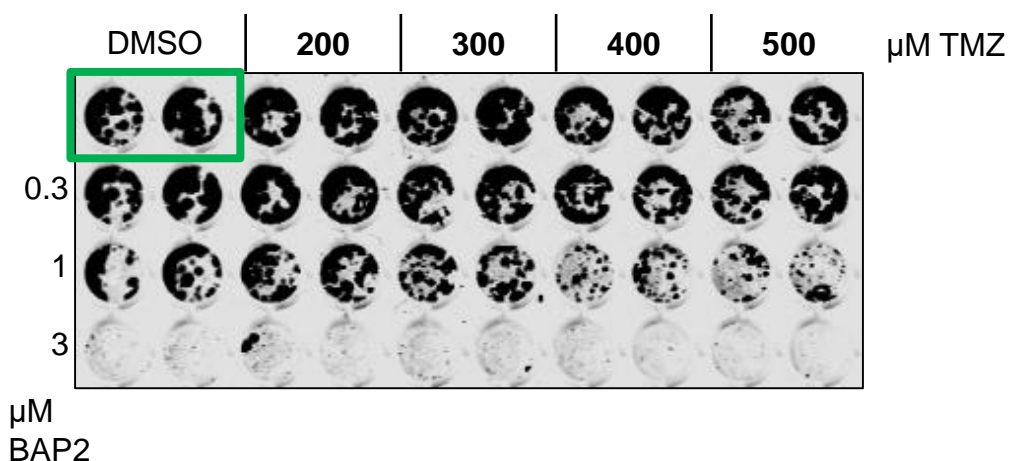


B



Supplementary Figure S8. Activity of PDI inhibitors **PACMA31** (a) and **BAP2** (b) against PDI, PDIp, and Erp57 in the PDI reductase assay. PDI was tested at 0.4 μM , PDIp was tested at 0.8 μM and ERp57 was tested at 1.6 μM . Data expressed as mean \pm S.D. ($n = 3$).

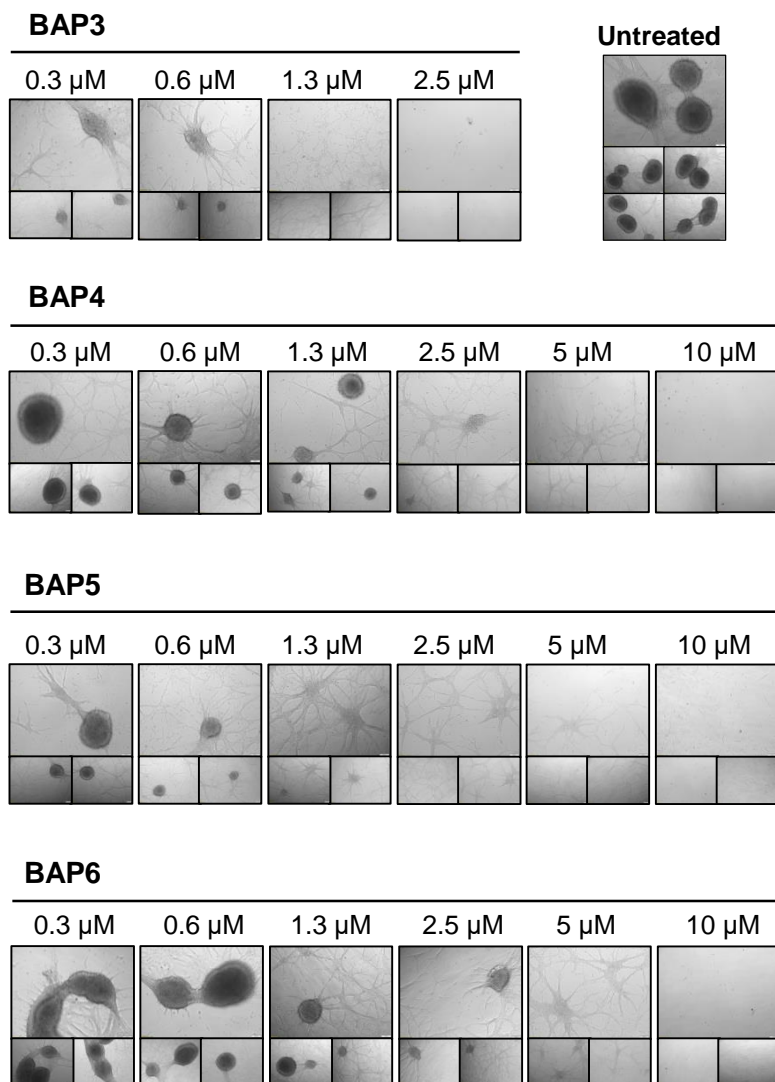
Fig. S9



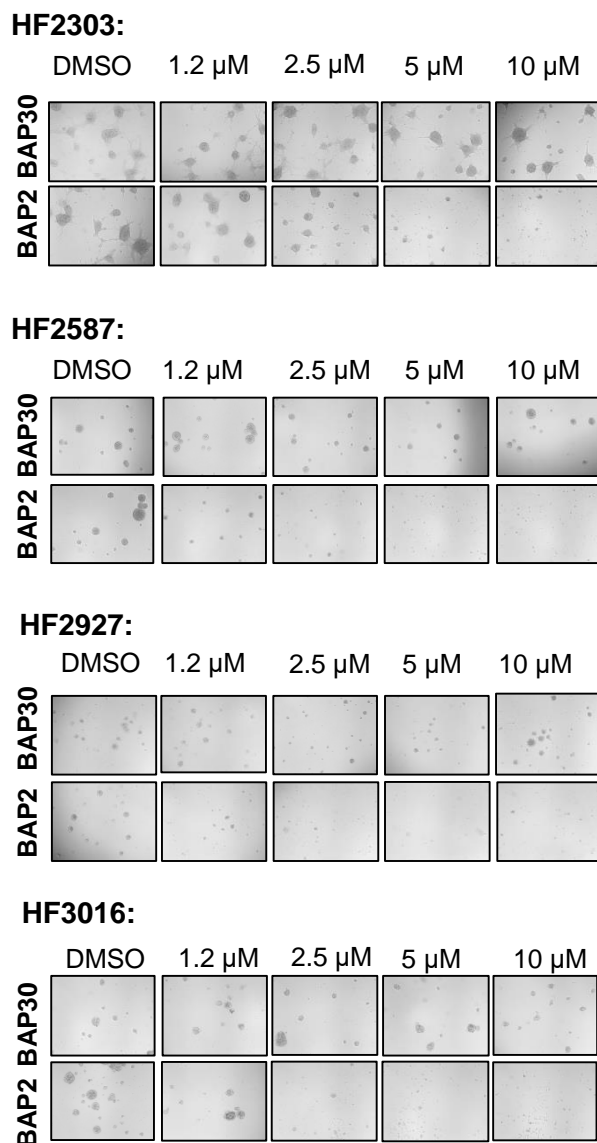
Supplementary Figure S9. Colony formation assay of TMZ and **BAP2** in combination in HCT116 cells. Cells treated for 7 days before staining. Result is representative of three independent experiments.

Fig. S10

A

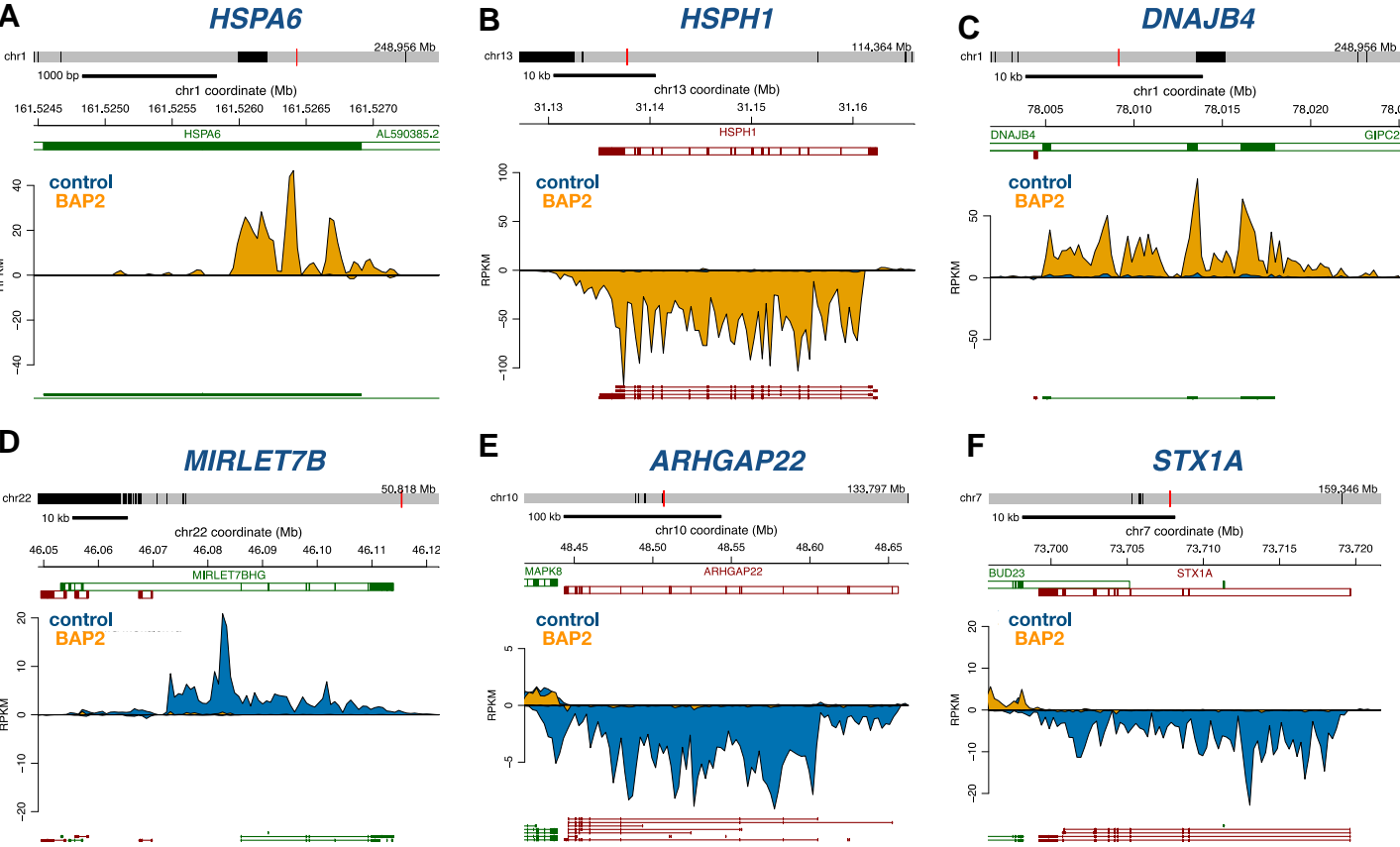


B



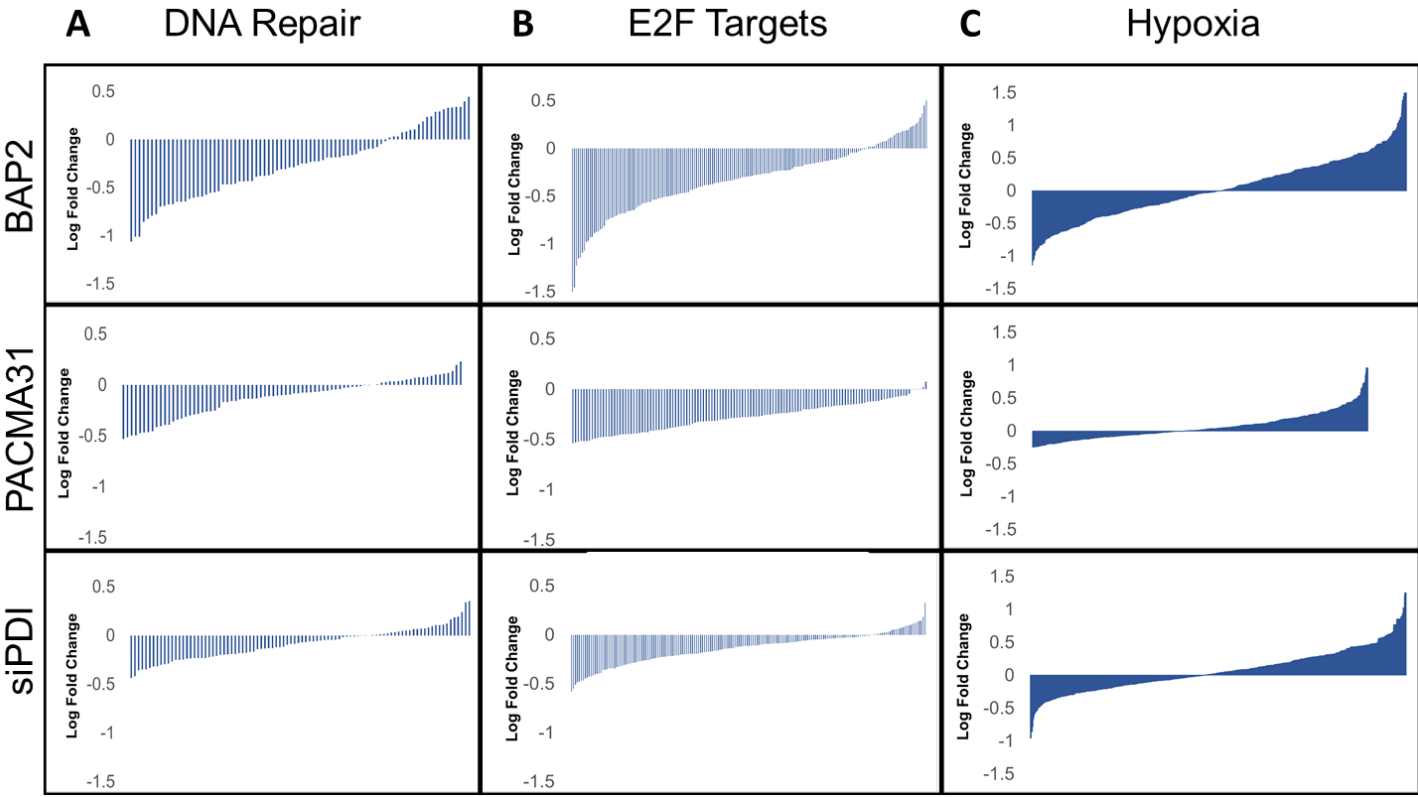
Supplementary Figure S10. Active chalcone derivatives inhibit the neurosphere formation in GBM cells. (a) **BAP2** analogues inhibit neurosphere formation in a dose-dependent manner in U87MG cells. Cells were exposed to chalcones for 24 h, and allowed to form neurospheres in fresh medium. Three representative images are shown for each condition ten days after the drug treatment. (b) **BAP2** impaired neurosphere formation in HF2303, HF2587, HF2927, and HF3016 GBM cells, whereas the inactive **BAP30** showed no significant inhibition. Cells were treated with **BAP2** or **BAP30** at indicated concentrations for 24 h. Representative images show sphere formation in the indicated conditions seven days after drug treatment.

Fig. S11

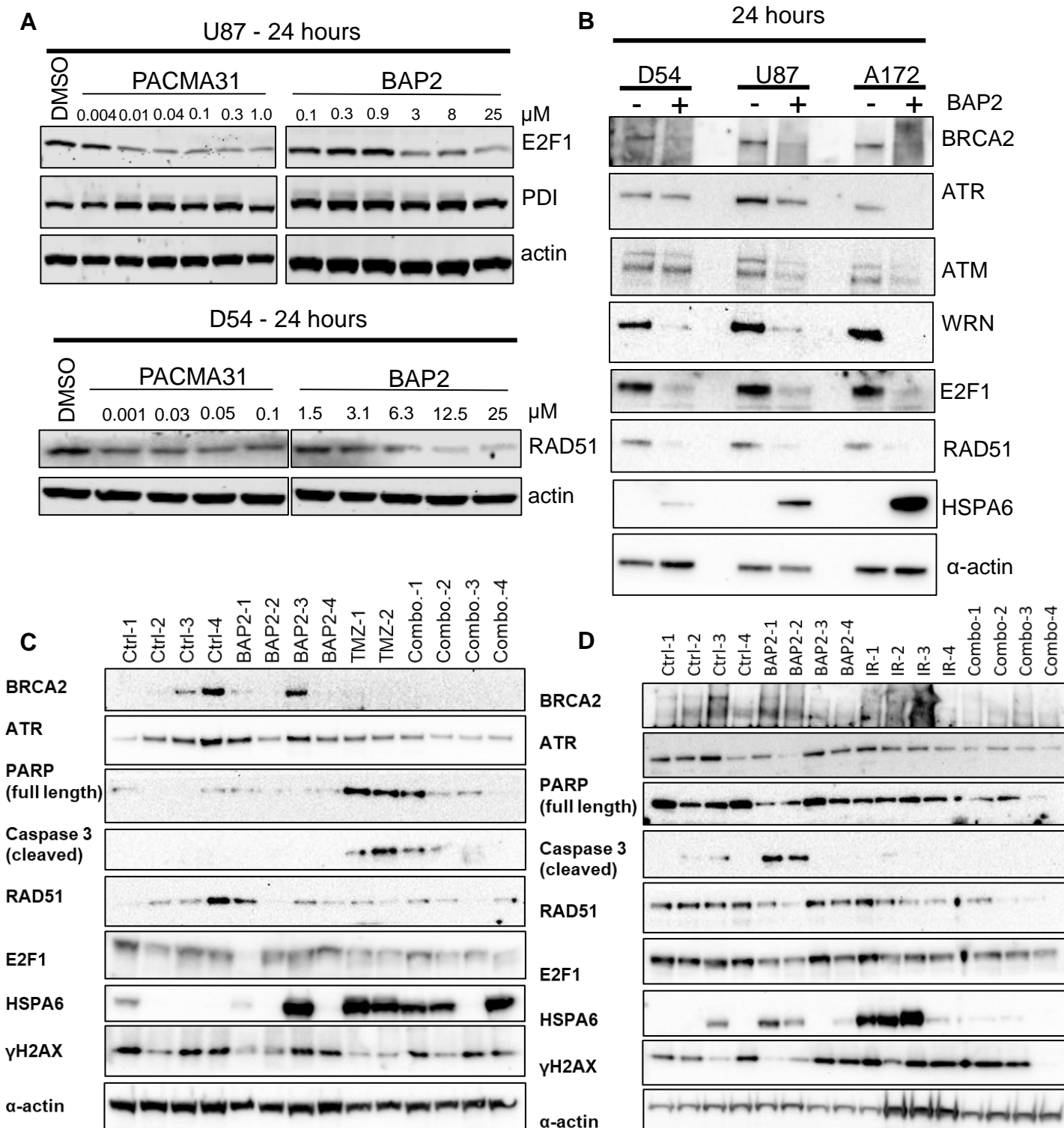


Supplementary Figure S11. BAP2 increases expression of genes involved in UPR. BAP2 significantly upregulates *HSPA6* (a), *HSPH1* (b), and *DNAJB4* (c) expression. BAP2 significantly downregulates *MIRLET7B* (d), *ARHGAP22* (e), and *STX1A* (f) expression levels.

Fig. S12



Supplementary Figure S12. Inhibition of PDI in GBM causes downregulation of DNA repair genes and E2F targets and promotes a hypoxic response. Waterfall plots of DNA repair (a), E2F target (b), and hypoxia (c) gene transcription in response to PDI inhibition by **BAP2**, **PACMA31**, and siRNA-mediated knockdown in U87MG cells.

Fig. S13

Supplementary Figure S13. PDI inhibitors decrease the expression of DNA damage markers and DNA repair genes. (a) U87MG or D54 cells were treated with DMSO, **PACMA31**, or **BAP2** at indicated doses for 24 hours. (b) D54, U87, and A172 cells were treated with DMSO or **BAP2** at 15 μM (D54 and A172) or 30 μM (U87MG) for 24 hours. (c) Western blot of mouse tissue from *in vivo* experiment. Conditions: BL030216 U87MG xenografts with TMZ (5mg/kg, 5 days/wk, oral); **BAP2** (20mg/kg, 5 days/wk, i.p. injection in 5% DMSO / 65% 1,2-Propanediol / 30% saline); vehicle control (i.p. saline) for 2 weeks. (d) Western blot of mouse tissue from *in vivo* experiment. Conditions: BL062216 D54MG xenografts with IR (2Gy/day, 5 days a week); **BAP2** (20mg/kg, 5 days/wk, i.p. injection in 5% DMSO / 65% 1,2-Propanediol / 30% saline); vehicle control (i.p. saline) for 2 weeks.

Table S1. Biological activities and molecular properties of inactive chalcone derivatives studied in the present study

Chalcone	IC ₅₀ ^a (μM)	MW	No. Rotatable Bonds	No. H Donors	No. H Acceptors	LogP	PSA
BAP1	0.83 ± 0.20 ^b	312.32	6	1	5	3.30	72.83
BAP2	0.93 ± 0.09	249.26	3	1	3	3.34	61.09
BAP3	0.97 ± 0.12	292.25	4	1	2	4.40	37.29
BAP4	1.07 ± 0.12	321.14	3	1	2	4.41	37.29
BAP5	1.97 ± 0.12	252.31	3	1	2	4.43	37.29
BAP7	5.20 ± 0.97	335.18	5	0	3	4.89	43.37
BAP8	6.52 ± 1.38	324.71	4	1	3	4.52	46.53
BAP9	8.40 ± 0.69	258.31	3	0	1	4.61	17.07
BAP10	24	280.32	3	0	3	3.55	35.53
BAP11	32	365.65	5	1	2	5.13	37.29
BAP12	39	310.34	6	1	4	4.14	63.60
BAP13	52	310.34	5	0	4	3.82	44.76
BAP14	64	354.35	4	2	6	3.65	93.06
BAP15	64	267.32	4	1	3	3.62	40.54
BAP16	66	410.06	3	0	3	4.97	35.53
BAP17	66	290.31	4	0	3	3.32	59.59
BAP18	74	417.48	7	1	6	3.01	101.52
BAP19	78	337.20	5	0	3	5.00	35.53
BAP20	79	360.75	4	2	6	3.34	93.06
BAP21	88	302.75	5	1	3	4.46	46.53
BAP22	90	366.59	4	0	3	5.01	62.89
BAP23	96	375.32	6	1	5	3.28	73.86
BAP24	98	345.30	6	2	7	3.08	121.81
BAP25	> 10	335.18	3	0	3	4.82	35.53
BAP26	> 10	384.44	6	1	5	4.12	53.01
BAP27	> 10	282.29	5	1	4	3.32	63.60
BAP28	> 100	347.20	5	0	3	4.42	35.53
BAP29	> 100	363.25	3	0	1	5.96	17.07
BAP30	> 100	457.54	7	0	6	4.25	111.89
BAP31	> 100	361.19	3	1	4	3.99	55.76
BAP32	> 100	365.19	5	0	3	4.62	35.53
BAP33	> 100	433.29	7	0	5	5.08	53.99
BAP34	> 100	349.42	6	0	4	4.64	46.61
BAP35	> 100	362.17	5	0	4	4.33	72.12
BAP36	> 100	263.29	4	0	3	3.56	50.09
BAP37	> 100	272.27	4	1	3	3.65	46.53
BAP38	> 100	292.25	5	0	2	4.71	26.30
BAP39	> 100	252.31	4	1	2	4.40	37.29
BAP40	> 100	345.41	7	1	4	2.95	80.85

BAP41	> 100	342.39	7	0	5	4.12	53.99
BAP42	> 100	383.44	7	0	6	3.50	57.23
BAP43	> 100	340.37	6	0	5	3.71	53.99

^a IC₅₀ is defined as the drug concentration causing a 50% decrease in PDI activity.

^b Values (mean ± SD) are calculated from three independent experiments.

Table S2. Cytotoxicity of active compounds in GBM cell lines

Chalcone	IC ₅₀ ^a (μM)		
	NU04	U87MG	U118MG
BAP1	8.13 ± 0.55 ^b	9.63 ± 0.27	17.69 ± 1.93
BAP2	5.33 ± 1.75	5.97 ± 1.50	4.29 ± 1.42
BAP3	7.46 ± 2.03	7.53 ± 1.00	10.13 ± 1.75
BAP4	14.21 ± 0.43	15.41 ± 0.32	16.99 ± 2.67
BAP5	> 20	> 20	> 20
BAP6	15.82 ± 0.83	15.06 ± 0.09	15.08 ± 0.76
TMZ	549 ± 225	596 ± 178	944 ± 127

^aIC₅₀ is defined as the drug concentration causing a 50% decrease in the cell population.

^bValues (mean ± SD) are calculated from three independent experiments.

Table S3. The top 20 genes upregulated after **BAP2** treatment

Gene Symbol	Description	Fold Change
ANKRD1	ankyrin repeat domain 1	1164.883
HSPA6	heat shock 70kDa protein 7 (HSP70B); heat shock 70kDa protein 6 (HSP70B')	875.728
HSPA4L	heat shock 70kDa protein 4-like	175.279
HSPH1	heat shock 105kDa/110kDa protein 1	99.493
MAP2	microtubule-associated protein 2	94.301
TRIB3	tribbles homolog 3 (Drosophila)	81.200
ARAP2	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 2	53.228
KLHL24	kelch-like 24 (Drosophila)	45.567
CTH	cystathionase (cystathionine gamma-lyase)	41.895
SORBS1	sorbin and SH3 domain containing 1	41.456
RNF103	vacuolar protein sorting 24 homolog (S. cerevisiae); ring finger protein 103	41.324
FBXO32	F-box protein 32	40.778
SLC7A11	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	40.163
RUNDC3B	RUN domain containing 3B	36.265
OTUD1	OTU domain containing 1	34.522
JHDM1D	jumonji C domain containing histone demethylase 1 homolog D (S. cerevisiae)	34.293
ALOXE3	arachidonate lipoxygenase 3	31.022
GPR137C	G protein-coupled receptor 137C	29.713
DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	28.393
ZFAND2A	zinc finger, AN1-type domain 2A	27.559

Table S4. The top 20 genes downregulated after **BAP2** treatment

Gene Symbol	Description	Fold Change
METTL12	methyltransferase like 12	0.008
ARHGAP22	Rho GTPase activating protein 22	0.027
CENPM	centromere protein M	0.031
KY	kyphoscoliosis peptidase	0.033
SLC10A5	solute carrier family 10 (sodium/bile acid cotransporter family), member 5	0.033
TUBB	Beta Tubulin	0.035
STX1A	syntaxin 1A (brain)	0.037
SIVA1	SIVA1, apoptosis-inducing factor	0.038
HLA-DRA	major histocompatibility complex, class II, DR alpha	0.041
	ribosomal protein S18 pseudogene 12; ribosomal protein S18 pseudogene 5;	
RPS18	ribosomal protein S18	0.043
DUS3L	dihydrouridine synthase 3-like (<i>S. cerevisiae</i>)	0.050
SNHG3	small nucleolar RNA host gene 3 (non-protein coding)	0.051
ATOH8	atonal homolog 8 (<i>Drosophila</i>)	0.054
ABT1	activator of basal transcription 1	0.055
CDCA7	cell division cycle associated 7	0.056
LMNB1	lamin B1	0.059
SNHG11	small nucleolar RNA host gene 11 (non-protein coding)	0.059
PPAN	peter pan homolog (<i>Drosophila</i>)	0.062
C6orf48	chromosome 6 open reading frame 48; small nucleolar RNA, C/D box 52	0.066
C19orf48	chromosome 19 open reading frame 48	0.067
SCARNA2	small Cajal body-specific RNA 2	0.068

Table S5. The top 10 Ingenuity canonical pathways involving genes influenced by **BAP2** treatment

Canonical pathway	P-value	Ratio
Protein ubiquitination pathway	1.12E-10	63 out of 263
NRF2-mediated oxidative stress response	2.40E-09	47 out of 187
Aldosterone signaling in epithelial cells	3.63E-07	38 out of 156
ERK5 signaling	2.00E-05	19 out of 64
tRNA charging	2.00E-05	14 out of 38
Hereditary breast cancer signaling	3.89E-05	27 out of 119
Hypoxia signaling in the cardiovascular system	7.24E-05	18 out of 64
Role of BRCA1 in DNA damage response	1.26E-04	17 out of 63
p53 signaling	2.19E-04	23 out of 100
Prostate cancer signaling	2.24E-04	20 out of 91

Table S6. The top 20 gene sets for genes upregulated by **BAP2** treatment

Gene set ^a	Size	ES ^b	NES ^c
PODAR_RESPONSE_TO_ADAPHOSTIN_UP	111	0.663	2.871
GSE9988_ANTI_TREM1_AND_LPS_VS_CTRL_TREATED_MONOCYTES_UP	130	0.621	2.751
GARGALOVIC_RESPONSE_TO_OXIDIZED_PHOSPHOLIPIDS_BLUE_UP	106	0.620	2.660
GSE9988_ANTI_TREM1_VS_CTRL_TREATED_MONOCYTES_UP	135	0.588	2.646
GERY_CEBP_TARGETS	57	0.678	2.633
GSE9988_ANTI_TREM1_VS_VEHICLE_TREATED_MONOCYTES_UP	129	0.592	2.630
GSE9988_ANTI_TREM1_AND_LPS_VS_VEHICLE_TREATED_MONOCYTES_UP	117	0.594	2.624
AMUNDSON_RESPONSE_TO_ARSENITE	147	0.572	2.575
CONCANNON_APOPTOSIS_BY_EPOXOMICIN_UP	149	0.556	2.539
HELLER_SILENCED_BY_METHYLATION_DN	59	0.636	2.481
PICCALUGA_ANGIOIMMUNOBLASTIC_LYMPHOMA_DN	100	0.580	2.465
GSE9988_LOW_LPS_VS_ANTI_TREM1_AND_LPS_MONOCYTE_DN	122	0.542	2.425
BLUM_RESPONSE_TO_SALIRASIB_UP	193	0.512	2.400
GSE9988_LPS_VS_LPS_AND_ANTI_TREM1_MONOCYTE_DN	129	0.537	2.398
KRIGE_AMINO_ACID_DEPRIVATION	22	0.754	2.361
GARGALOVIC_RESPONSE_TO_OXIDIZED_PHOSPHOLIPIDS_MAGENTA_UP	23	0.728	2.322
GSE29617_CTRL_VS_DAY7_TIV_FLU_VACCINE_PBMC_2008_UP	105	0.536	2.321
GSE22886_NAIVE_TCELL_VS_DC_DN	114	0.529	2.303
GROSS_HYPOXIA_VIA_ELK3_DN	103	0.535	2.299
MODULE_355	21	0.750	2.293

^aThe criteria for the GSEA analysis was $P < 0.05$ and $FDR < 25\%$.

^bES: enrichment score.

^cNES: normalized enrichment score.

Table S7. The top 20 gene sets for genes downregulated by **BAP2** treatment

Gene set ^a	Size	ES ^b	NES ^c
DUTERTRE_ESTRADIOL_RESPONSE_24HR_UP	217	-0.608	-3.020
MANALO_HYPOXIA_DN	231	-0.600	-2.994
GOBERT_OLIGODENDROCYTE_DIFFERENTIATION_UP	394	-0.552	-2.936
ZHANG_TLX_TARGETS_60HR_DN	227	-0.579	-2.905
KOBAYASHI_EGFR_SIGNALING_24HR_DN	221	-0.575	-2.887
ROSTY_CERVICAL_CANCER_PROLIFERATION_CLUSTER	120	-0.628	-2.822
GNF2_PCNA	65	-0.697	-2.820
GSE15750_DAY6_VS_DAY10_TRAF6KO_EFF_CD8_TCELL_UP	153	-0.592	-2.802
LEE_EARLY_T_LYMPHOCYTE_UP	75	-0.668	-2.799
GNF2_CCNA2	65	-0.672	-2.761
KONG_E2F3_TARGETS	77	-0.654	-2.753
GRAHAM_CML_DIVIDING_VS_NORMAL QUIESCENT_UP	127	-0.595	-2.746
GARGALOVIC_RESPONSE_TO_OXIDIZED_PHOSPHOLIPIDS_TURQUOISE_DN	30	-0.790	-2.736
GSE24634_TEFF_VS_TCONV_DAY7_IN_CULTURE_UP	132	-0.588	-2.723
REN_BOUND_BY_E2F	55	-0.689	-2.706
GRAHAM_NORMAL QUIESCENT_VS_NORMAL_DIVIDING_DN	69	-0.650	-2.693
GNF2_SMC4L1	82	-0.629	-2.688
GNF2_MCM4	50	-0.690	-2.679
ZHOU_CELL_CYCLE_GENES_IN_IR_RESPONSE_6HR	73	-0.646	-2.679
CHANG_CYCLING_GENES	122	-0.592	-2.678

^aThe criteria for the GSEA analysis was $P < 0.05$ and $FDR < 25\%$.

^bES: enrichment score.

^cNES: normalized enrichment score.

Table S8. Fold change values of DNA repair genes for **BAP2**, **PACMA31** and siPDI 48 hr treatments.

DNA Repair Genes (Wood Laboratory)	Activity	FC (BAP2)	FC (PACMA31)	FC (siPDI_48hr)
Base excision repair (BER)	DNA glycosylases: major altered base released			
UNG	U	0.342	0.405	0.382
SMUG1	U	0.342	1.133	1.555
MBD4	U or T opposite G at CpG sequences	1.54	0.969	1.07
TDG	U, T or ethenoC opposite G	1.078	1.067	0.816
OGG1	8-oxoG opposite C	NA	1.367	1.013
MUTYH	A opposite 8-oxoG	NA	NA	NA
NTHL1	Ring-saturated or fragmented pyrimidines	NA	NA	NA
MPG	3-meA, ethenoA, hypoxanthine	NA	NA	NA
NEIL1	Removes thymine glycol	NA	NA	NA
NEIL2	Removes oxidative products of pyrimidines	1.216	0.791	2.184
NEIL3	Removes oxidative products of pyrimidines	0.098	NA	0.979
APEX1	AP endonuclease	NA	NA	NA
APEX2	AP endonuclease	0.278	0.73	0.639
LIG3	DNA Ligase III	0.593	0.752	0.735
XRCC1	LIG3 accessory factor	0.098	0.695	0.68
PNKP	Converts some DNA breaks to ligatable ends	NA	0.855	0.482
APEX1	Accessory factor for DNA end-joining	0.898	0.825	0.849
PARP1	Protects strand interruptions	NA	NA	NA
PARP2	PARP-like enzyme	NA	NA	NA
PARP3	PARP-like enzyme	NA	NA	NA
Direct reversal of damage				
MGMT	O6-meG alkyltransferase	NA	NA	NA
ALKBH2	1-meA dioxygenase	NA	NA	NA
ALKBH3	1-meA dioxygenase	NA	NA	NA
Repair of DNA-topoisomerase crosslinks				
TDP1	Removes 3'-tyrosylphosphate and 3'-phosphoglycolate from DNA; human disorder SCAN1	0.493	0.341	0.994
TDP2	5'- and 3'-tyrosyl DNA phosphodiesterase	0.694	1.57	1.456
Mismatch excision repair (MMR)				
MSH2	Mismatch (MSH2-MSH6) and loop (MSH2-MSH3) recognition	0.29	0.456	0.645
MSH3		0.283	0.94	0.801

MSH6	MSH2, MSH3, MSH6	0.565	0.465	0.618
MLH1	MutL homologs, forming heterodimer	1.045	0.681	0.87
PMS2	MLH1, PMS2	NA	NA	NA
MSH4	MutS homologs specialized for meiosis	NA	NA	NA
MSH5	MSH4, MSH5	NA	NA	0.643
MLH3	MutL homologs of unknown function	0.342	1.089	1.328
PMS1		0.168	0.806	0.821
PMS2L3	MLH3, PMS1, PMS2L3	NA	NA	NA
Nucleotide excision repair (NER)	(XP = xeroderma pigmentosum)			
XPC	Binds DNA distortions	0.65	1.013	1.024
RAD23B		1.079	0.8	1.206
CETN2	XPC, RAD23B, CETN2	2.773	1.191	1.048
RAD23A	Substitutes for RAD23B	0.512	1.261	0.9
XPA	Binds damaged DNA in preincision complex	0.424	1.055	1.161
DDB1	Complex defective in XP group E	1.26	0.837	1.097
DDB2	DDB1, DDB2	NA	NA	NA
RPA1	Binds DNA in preincision complex	0.586	0.598	0.837
RPA2		0.37	0.51	0.756
RPA3	RPA1, RPA2, RPA3	NA	NA	NA
TFIIH	<i>Catalyzes unwinding in preincision complex</i>	NA	NA	NA
ERCC3	3' to 5' DNA helicase	NA	NA	NA
ERCC2	5' to 3' DNA helicase	NA	NA	NA
GTF2H1	Core TFIIH subunit p62	1.714	1.097	0.976
GTF2H2	Core TFIIH subunit p44	NA	NA	NA
GTF2H3	Core TFIIH subunit p34	2.067	0.849	0.896
GTF2H4	Core TFIIH subunit p52	NA	NA	NA
GTF2H5	Core TFIIH subunit p8	NA	NA	NA
CDK7	Kinase subunits of TFIIH	2.187	0.871	1.163
CCNH		1.438	0.734	0.915
MNAT1	CDK7, CCNH, MNAT1	2.14	0.904	0.976
ERCC5	3' incision	NA	NA	NA
ERCC1	5' incision DNA binding subunit	0.959	0.909	0.681
ERCC4	5' incision catalytic subunit	NA	NA	NA
LIG1	DNA ligase	NA	NA	NA
NER-related		NA	NA	NA
ERCC8	Cockayne syndrome and UV-Sensitive Syndrome; Needed for transcription-coupled NER	NA	NA	NA
ERCC6		NA	NA	NA
UVSSA	ERCC8, ERCC6, UV-sensitive	NA	NA	NA

	syndrome			
XAB2	XAB2	NA	NA	NA
MMS19	Iron-sulfur cluster loading and transport	0.409	0.768	1.29
Homologous recombination				
RAD51	Homologous pairing	0.087	NA	0.437
RAD51B	Rad51 homolog	NA	NA	1.037
RAD51D	Rad51 homolog	0.161	0.729	0.585
DMC1	Rad51 homolog, meiosis	NA	NA	NA
XRCC2	DNA break and crosslink repair	0.241	NA	0.446
XRCC3	XRCC2, XRCC3	NA	NA	NA
RAD52	Accessory factors for recombination	NA	0.939	NA
RAD54L		0.15	NA	0.56
RAD54B	RAD52, RAD54L, RAD54B	0.836	0.385	0.969
BRCA1	Accessory factor for transcription and recombination, E3 Ubiquitin ligase	0.763	NA	0.507
SHFM1	BRCA2 associated	NA	NA	NA
RAD50	ATPase in complex with MRE11A, NBS1	0.613	0.993	1.119
MRE11A	3' exonuclease, defective in ATLD (ataxia-telangiectasia-like disorder)	NA	0.485	0.577
NBN	Mutated in Nijmegen breakage syndrome	NA	NA	NA
RBBP8	Promotes DNA end resection	NA	NA	NA
MUS81	Subunits of structure-specific DNA nuclease	NA	0.843	0.657
EME1		NA	NA	NA
EME2	MUS81, EME1, EME2	NA	NA	NA
GIYD1	subunit of SLX1-SLX4 structure-specific nuclease, two identical tandem genes in the human genome	NA	NA	NA
GIYD2		NA	NA	NA
GEN1	Nuclease cleaving Holliday junctions	0.808	0.536	1.01
Fanconi anemia				
FANCA	FANCA	0.201	0.32	0.365
FANCB	FANCB	0.779	NA	0.564
FANCC	FANCC	0.439	0.295	0.754
BRCA2	Cooperation with RAD51, essential function	NA	NA	NA
FANCD2	target for monoubiquitination	0.479	NA	0.727
FANCE	FANCE	NA	NA	NA
FANCF	FANCF	0.255	1.142	0.987
FANCG	FANCG	NA	NA	NA
FANCI	target for monoubiquitination	NA	NA	NA
BRIP1	DNA helicase, BRCA1-interacting	NA	NA	NA
FANCL	FANCL	0.248	0.52	0.586

FANCM	helicase/translocase	0.367	0.35	0.903
PALB2	co-localizes with BRCA2 (FANCD1)	0.267	0.775	0.607
RAD51C	Rad51 homolog FANCO	NA	NA	0.769
BTBD12 (SLX4)	nuclease subunit/scaffold BTBD12 (SLX4) FANCP			
FAAP20	FANCA - associated	NA	NA	NA
FAAP24	FAAP24	NA	NA	NA
Non-homologous end-joining				
XRCC6	DNA end binding subunit	NA	NA	NA
XRCC5	DNA end binding subunit	NA	NA	NA
PRKDC	DNA-dependent protein kinase catalytic subunit	0.253	0.56	0.481
LIG4	Ligase	2.181	0.876	1.276
XRCC4	Ligase accessory factor	2.148	0.549	0.875
DCLRE1C	Nuclease	NA	NA	NA
NHEJ1	End-joining factor	NA	NA	NA
Modulation of nucleotide pools				
NUDT1	8-oxoGTPase	NA	NA	NA
DUT	dUTPase	0.226	0.344	0.54
RRM2B	p53-inducible ribonucleotide reductase small subunit 2 homolog	1.275	0.954	1.737
DNA polymerases				
POLB	BER in nuclear DNA	NA	NA	NA
POLG	BER in mitochondrial DNA	0.368	1.261	0.857
POLD1	NER and MMR	NA	NA	NA
POLE	POLD1, POLE1	0.418	0.318	0.446
PCNA	Sliding clamp for pol delta and pol epsilon	0.204	0.305	0.597
REV3L	DNA pol zeta catalytic subunit, essential function	1.188	0.721	1.272
MAD2L2	DNA pol zeta subunit	NA	NA	NA
REV1L	dCMP transferase	NA	NA	NA
POLH	xeroderma pigmentosum (XP) variant	0.679	0.772	1.115
POLI	Lesion bypass	NA	1.174	2.25
POLQ	Sensitivity to ionizing radiation	0.54	NA	0.583
POLK	Lesion bypass and NER	1.745	0.839	1.174
POLL	Gap-filling during non-homologous end-joining	NA	1.308	1.534
POLM	Gap filling during non-homologous end-joining	NA	1.286	NA
POLN	DNA crosslink repair?	NA	NA	NA
Editing and processing nucleases				
FEN1	5' nuclease	NA	NA	NA

FAN1	5' nuclease interacting with FANCD2	0.346	1.086	0.741
TREX1	3' exonuclease	NA	NA	NA
TREX2	3' exonuclease	NA	NA	NA
EXO1	5' exonuclease	0.226	NA	0.5
APTX	Processing of DNA single-strand interruptions	NA	NA	NA
SPO11	endonuclease	NA	NA	NA
ENDOV	incision 3' of hypoxanthine and uracil in DNA and inosine in RNA	NA	NA	NA
Ubiquitination and modification				
UBE2A	Ubiquitin-conjugating enzyme	1.963	1	0.897
UBE2B	Ubiquitin-conjugating enzyme	NA	NA	NA
RAD18	E3 ubiquitin ligase	2.488	0.336	0.584
SHPRH	E3 ubiquitin ligase, SWI/SNF related, homolog of <i>S. cerevisiae</i> Rad5	0.37	1.225	1.077
HLTF	E3 ubiquitin ligase, SWI/SNF related, homolog of S. cerevisiae Rad5	NA	NA	NA
RNF168	E3 ubiquitin ligase for DSB repair; ATM-like and RIDDLE syndrome	0.595	0.695	0.665
SPRTN	Reads ubiquitylation	NA	NA	NA
RNF8	E3 ubiquitin ligase for DSB repair	NA	NA	NA
RNF4	E3 ubiquitin ligase	0.566	0.682	0.963
UBE2V2	Ubiquitin-conjugating complex	0.68	0.993	1.239
UBE2N	UBE2V2, UBE2N	0.709	0.828	1
Chromatin Structure and Modification				
H2AFX	Histone, phosphorylated after DNA damage	NA	NA	NA
CHAF1A	Chromatin assembly factor	0.213	NA	0.513
SETMAR	DNA damage-associated histone methylase and nuclease	NA	NA	NA
Genes defective in diseases associated with sensitivity to DNA damaging agents				
BLM	Bloom syndrome helicase	0.228	NA	0.463
WRN	Werner syndrome helicase / 3' - exonuclease	0.648	0.73	0.562
RECQL4	Rothmund-Thompson syndrome	NA	NA	NA
ATM	ataxia telangiectasia	NA	0.787	0.869
TTDN1	non-photosensitive form of trichothiodystrophy	NA	NA	NA
Other identified genes with known or suspected DNA repair				

function				
DCLRE1A	DNA crosslink repair	NA	NA	NA
DCLRE1B	Related to SNM1	NA	NA	NA
RPA4	Similar to RPA2	NA	1.699	NA
PRPF19	DNA crosslink repair; binding to SETMAR	NA	NA	NA
RECQL	DNA helicase	NA	NA	NA
RECQL5	DNA helicase	NA	1.197	NA
HELQ	DNA helicase	NA	NA	NA
RDM1	Similar to RAD52	NA	NA	NA
OBFC2B	Single-stranded DNA binding protein	1.949	0.897	0.885
Other conserved DNA damage response genes				
ATR	ATM- and PI-3K-like essential kinase	0.211	0.96	0.632
ATRIP	ATR-interacting protein	0.14	0.436	0.585
MDC1	Mediator of DNA damage checkpoint	NA	NA	NA
RAD1	subunits of PCNA-like sensor of damaged DNA	0.653	0.502	0.726
RAD9A		NA	NA	NA
HUS1	RAD1, RAD9, HUS1	0.8	1.186	1.131
RAD17	RFC-like DNA damage sensor	NA	NA	NA
CHEK1	Effector kinases	0.513	0.394	0.657
CHEK2	CHEK1, CHEK2	NA	NA	NA
TP53	Regulation of the cell cycle	NA	NA	NA
TP53BP1	chromatin-binding checkpoint protein	NA	NA	NA
RIF1	suppressor of 5'-end-resection	0.652	0.545	0.738
TOPBP1	DNA damage checkpoint control	0.491	0.406	0.636
CLK2	S-phase check point and biological clock protein	0.419	1.083	1.18
PER1	S-phase check point and biological clock protein	NA	NA	NA

Table S9. Fold change values of E2F genes for **BAP2**, **PACMA31** and siPDI 48 hr treatments

Gene	FC (BAP2)	FC (PACMA31)	FC (siPDI_48hr)
AK2	0.951	0.863	1.533
ANP32E	1.203	0.291	1.177
ASF1A	0.744	0.63	1.236
ASF1B	0.487	NA	0.575
ATAD2	0.689	NA	0.548
AURKA	0.238	0.419	1.238
AURKB	0.072	NA	0.545
BARD1	0.105	NA	0.765
BIRC5	0.33	NA	0.718
BRCA1	0.763	NA	0.507
BRCA2	0.785	NA	0.615
BRMS1L	0.9	0.803	0.897
BUB1B	0.222	NA	0.775
CBX5	0.505	0.478	0.82
CCNB2	0.548	0.362	1.388
CCNE1	2.098	NA	NA
CCP110	0.322	0.366	1.067
CDC20	0.314	0.304	0.78
CDC25A	0.208	NA	0.343
CDC25B	0.458	0.674	0.912
CDCA3	0.338	NA	0.932
CDCA8	0.195	NA	0.935
CDK1	0.188	NA	0.974
CDK4	1.097	0.719	0.675
CDKN1A	1.194	0.812	0.898
CDKN1B	0.901	0.635	2.107
CDKN2A	NA	NA	NA
CDKN2C	NA	NA	NA
CDKN3	0.572	0.295	1.357
CENPE	0.453	NA	1
CENPM	0.031	NA	0.309
CHEK1	0.513	0.394	0.657
CHEK2	NA	NA	NA
CIT	0.188	NA	0.943
CKS1B	0.673	NA	0.917
CKS2	1.818	0.334	0.869
CSE1L	0.475	0.567	0.722
CTCF	0.305	0.643	0.942
CTPS	0.399	0.59	0.357
DCK	0.906	0.481	0.604
DCLRE1B	0.527	0.503	0.706

DCTPP1	NA	NA	NA
DDX39A	1.528	0.543	0.639
DEK	0.736	0.372	0.78
DEPDC1	0.641	NA	1.159
DIAPH3	1.042	NA	0.795
DLGAP5	0.343	NA	1.304
DNMT1	0.181	0.412	0.525
DONSON	0.8	0.373	0.629
DSCC1	0.117	NA	0.397
DUT	0.226	0.344	0.54
E2F	NA	NA	NA
E2F8	0.142	NA	0.76
EED	1.266	0.759	0.922
EIF2S1	0.723	0.857	0.818
ESPL1	NA	NA	0.879
EXOSC8	1.558	0.515	1.034
EZH2	4.316	0.394	0.818
GINS1	0.085	NA	0.617
GINS3	0.716	0.482	0.407
GINS4	0.679	0.499	0.567
GSPT1	1.737	0.779	0.729
H2AFX	NA	NA	NA
H2AFZ	1.544	0.431	0.891
HELLS	0.314	NA	0.453
HMGA1	0.516	0.577	0.327
HMGB2	0.642	NA	1.135
HMGB3	1.899	0.358	1.251
HMMR	0.59	NA	1.397
HN1	0.449	0.694	1.267
HNRNPD	0.46	0.556	0.876
HUS1	0.8	1.186	1.131
ILF3	0.761	0.761	0.753
ING3	0.855	0.845	0.977
IPO7	0.416	0.588	0.473
KIF18B	0.07	NA	0.882
KIF22	NA	NA	NA
KIF2C	0.422	0.301	1.198
KIF4A	0.144	NA	0.813
KPNA2	0.542	0.353	0.836
LBR	1.177	0.356	0.765
LIG1	NA	NA	NA
LMNB1	0.059	NA	0.836
LUC7L3	0.824	0.701	0.945
LYAR	0.414	0.706	0.64

MAD2L1	0.366	NA	0.727
MCM2	0.274	0.385	0.402
MCM3	0.129	NA	0.376
MCM4	0.394	0.337	0.398
MCM5	0.198	NA	0.341
MCM6	0.209	0.34	0.482
MCM7	0.291	0.337	0.365
MELK	0.222	NA	0.667
MKI67	0.647	NA	0.973
MLH1	1.045	0.681	0.87
MMS22L	NA	NA	NA
MRE11A	NA	0.485	0.577
MSH2	0.29	0.456	0.645
MTHFD2	1.29	0.671	0.928
MXD3	NA	NA	NA
MYBL2	0.225	NA	0.437
MYC	1.308	0.836	0.375
NAA38	0.535	0.733	0.94
NAP1L1	1.003	0.56	0.639
NASP	0.581	0.323	0.517
NBN	0.311	1.009	0.895
NCAPD2	0.265	NA	0.829
NME1	0.587	0.53	0.639
NOLC1	0.461	0.567	0.336
NOP56	0.302	0.534	0.281
NUDT21	0.551	0.72	1.077
NUP107	0.513	0.517	0.81
NUP153	1.149	0.465	0.597
NUP205	0.698	0.414	0.732
ORC2	1.037	0.713	0.973
ORC6	0.472	NA	0.499
PA2G4	0.76	0.59	0.619
PAICS	0.686	0.522	0.973
PAN2	NA	NA	NA
PCNA	0.204	0.305	0.597
PDS5B	2.313	0.529	0.94
PHF5A	0.266	0.75	0.823
PLK1	0.206	0.426	0.895
PLK4	0.25	NA	0.82
PMS2	NA	NA	NA
PNN	0.596	0.526	0.629
POLA2	0.154	NA	0.454
POLD1	NA	NA	NA
POLD2	0.502	0.863	0.808

POLD3	0.134	0.373	0.608
POLE	0.418	0.318	0.446
POLE4	0.348	0.826	0.814
POP7	0.443	0.536	0.264
PPM1D	2.805	0.603	0.925
PPP1R8	0.398	1.05	1.021
PRDX4	0.735	0.996	1.32
PRIM2	0.439	NA	0.505
PRKDC	0.253	0.56	0.481
PRPS1	0.924	0.529	0.439
PSIP1	1.661	0.435	1.075
PSMC3IP	0.216	NA	0.456
PTTG1	0.59	0.305	1.031
RACGAP1	0.327	NA	0.984
RAD1	0.653	0.502	0.726
RAD21	0.979	0.397	1.147
RAD50	0.613	0.993	1.119
RAD51AP1	0.338	NA	0.585
RAD51C	NA	NA	0.769
RAN	1.44	0.687	0.774
RANBP1	0.55	0.481	0.513
RBBP7	1.445	0.697	0.915
RFC1	0.696	0.537	0.809
RFC2	0.578	0.356	0.608
RFC3	0.134	NA	0.469
RNASEH2A	NA	0.63	0.924
RPA1	0.586	0.598	0.837
RPA2	0.37	0.51	0.756
RPA3	NA	NA	NA
RQCD1	0.432	0.767	0.817
RRM2	0.378	NA	0.539
SHMT1	NA	NA	NA
SLBP	1.375	0.522	0.552
SMC1A	0.328	0.483	0.607
SMC3	0.483	0.39	0.943
SMC4	0.815	NA	0.958
SMC6	0.436	0.658	0.898
SNRPB	0.302	0.575	0.551
SPAG5	0.548	0.346	1.013
SPC24	0.119	NA	0.629
SPC25	0.723	0.474	0.855
SRSF1	0.528	0.666	0.778
SRSF2	0.535	0.756	0.668
SSRP1	1.476	0.665	0.855

STAG1	1.123	0.579	0.85
STMN1	0.765	NA	1.04
SUV39H1	NA	NA	0.585
SYNCRIP	0.712	0.701	0.789
TACC3	0.276	0.328	0.692
TBRG4	0.081	0.997	0.634
TCF19	NA	NA	NA
TFRC	0.972	0.797	0.823
TIMELESS	0.383	0.359	0.532
TIPIN	0.271	0.361	0.455
TK1	0.176	NA	0.493
TMPO	0.291	NA	0.71
TOP2A	0.32	NA	1.048
TP53	NA	NA	NA
TRA2B	1.716	0.685	0.797
TRIP13	0.449	0.387	0.687
TUBB	0.035	0.477	0.639
TUBG1	0.651	0.578	0.598
UBE2S	0.413	0.639	0.687
UBE2T	0.108	NA	0.663
UBR7	1.04	0.429	0.677
UNG	0.342	0.405	0.382
USP1	0.502	0.333	0.763
WDR90	NA	NA	NA
WEE1	0.58	0.307	0.652
XPO1	1.517	0.439	0.925
XRCC6	0.592	0.632	0.908
ZW10	0.902	0.901	0.896