Supplemental Figures

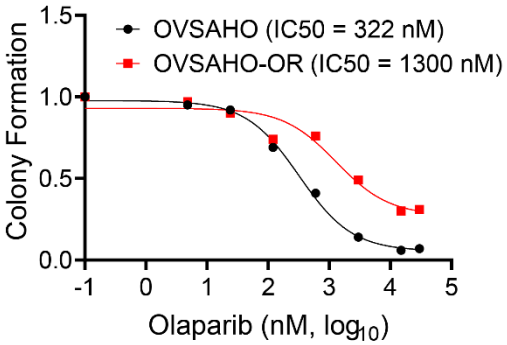


Fig. S1. OVSAHO cells selected in olaparib exhibit increased olaparib IC_{50} relative to the isogenic parental line. OVSAHO cells were subjected to stepwise dose escalation of olaparib to select for resistant cells. Elevated olaparib IC_{50} was confirmed in the olaparib-resistant (-OR) line by dose response colony formation assays. The proportion of colonies at each dose are shown relative to vehicle control. Olaparib IC_{50} values were calculated in GraphPad Prism.

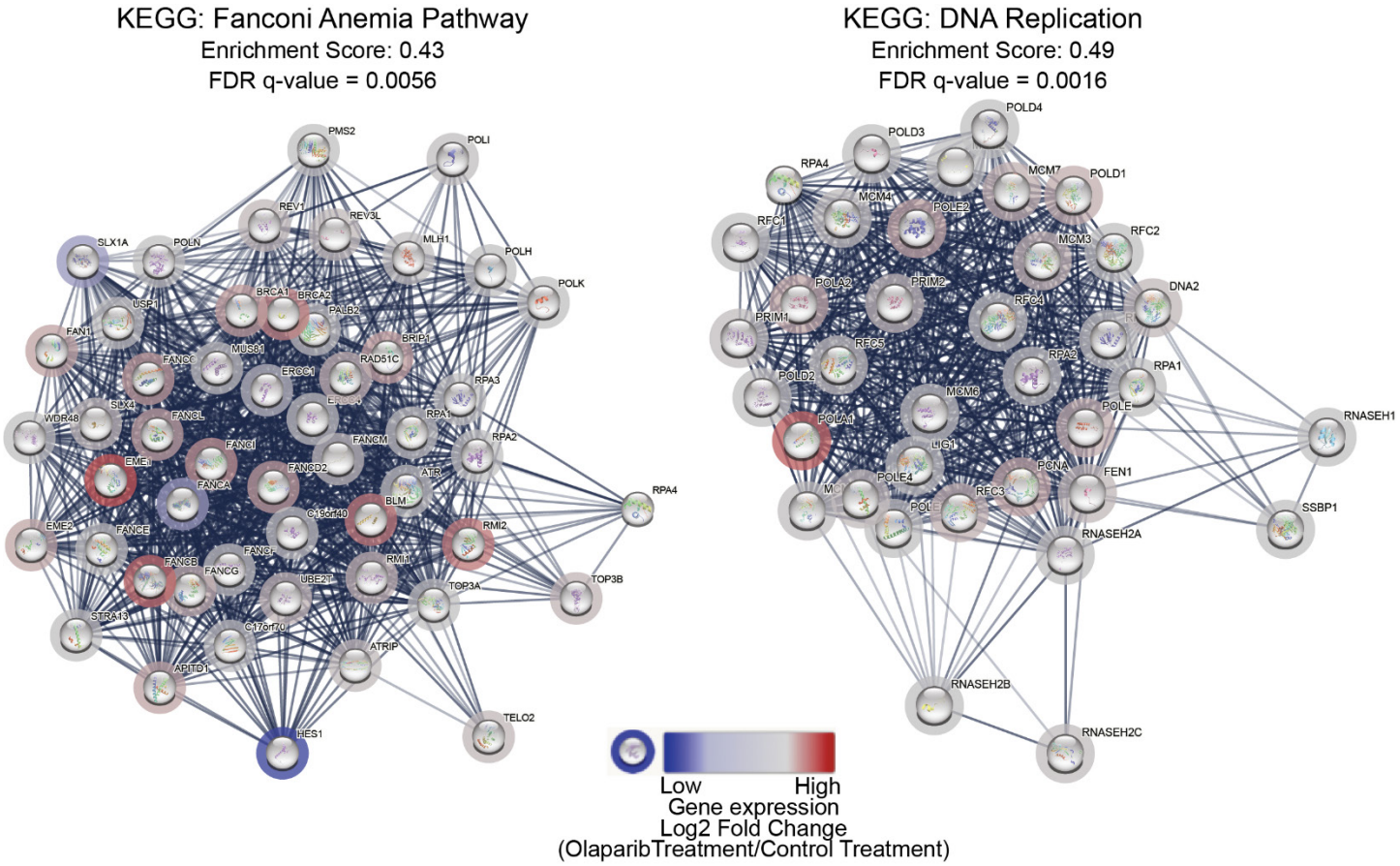


Fig. S2. Diagram of altered expression of KEGG pathways in olaparib-treated PDX vs control.

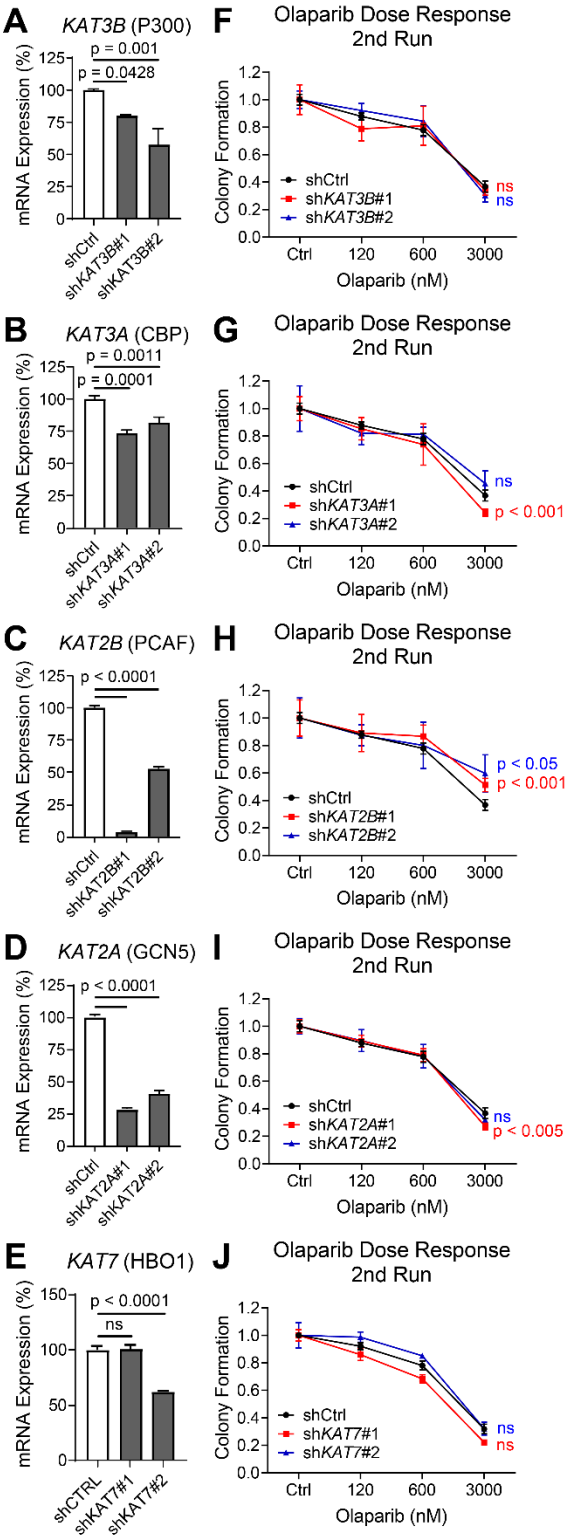


Fig. S3. Knockdown of specific HATs in PEO1-OR HGSOC cells moderately affects olaparib response.

(A-E) PEO1-OR cells were transduced with the indicated targeted shRNA or a non-targeting scrambled shRNA (shCTRL) and then selected in puromycin. The knockdown of each HAT was determined by RT-qPCR. mRNA expression was determined relative to *GAPDH* by ΔΔCt method, then normalized to shCTRL for each knockdown. Each bar represents the mean ± SD of three PCR reactions. p-value by t-test. Corresponding

immunoblots are shown in the main text **Fig. 2**. **(F-J)** Each shRNA line was seeded at 2500 cells per well in a 24-well plate and treated with vehicle control or the indicated doses of olaparib for eight days, after which colonies were fixed and stained with crystal violet. Stain was dissolved and the absorbance from each well was read by spectrophotometer, then normalized to vehicle control. Colony formation at each dose is shown normalized to vehicle control. Each data point represents the mean ± SD of six wells. p-value by t-test. ns = not significant.

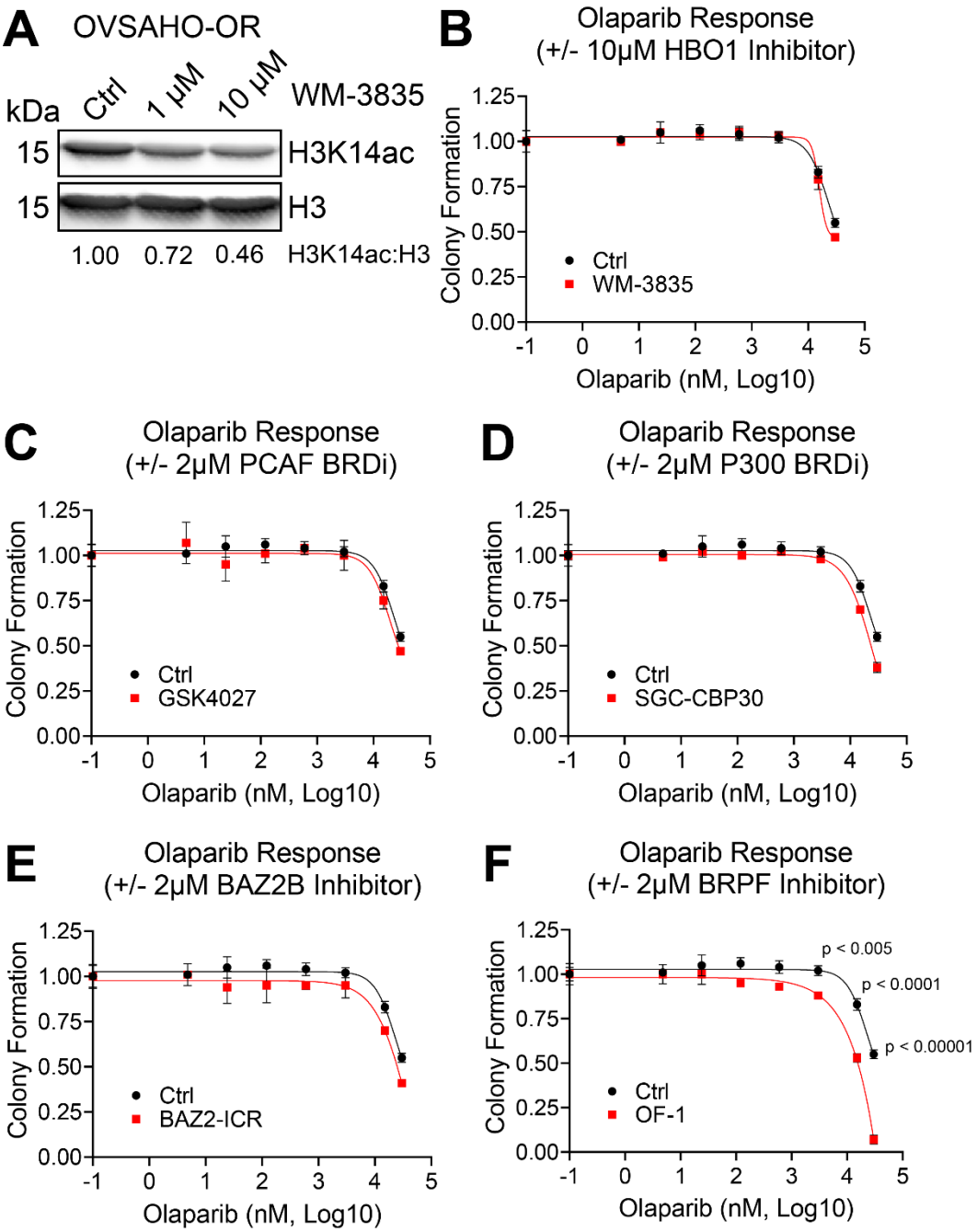
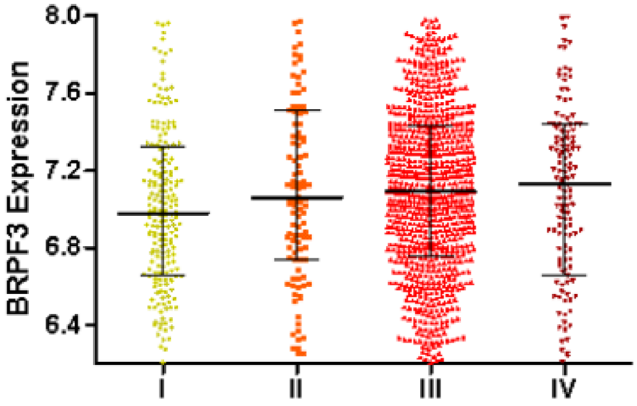


Fig. S4. Pharmacologic depletion of H3K14ac does not shift PARPi response, but BRPF-family inhibitor OF-1 moderately improves olaparib response in OVSAHO-OR. (A) OVSAHO-OR cells were treated with the indicated doses of HBO1 acetyltransferase inhibitor WM-3835 for 6 hours. Histone extracts were analyzed by immunoblot for H3K14ac and total H3. The H3K14ac:H3 ratio was calculated by densitometry to quantify H3K14ac depletion. **(B)** OVSAHO-OR were seeded at 7500 cells per well in a 96-well plate and treated with increasing doses of olaparib with or without 10 μM WM-3835. After six days, the colonies were fixed and stained with crystal violet. Stain was dissolved and the absorbance from each well was read by spectrophotometer, then normalized to vehicle control. Error bars, SEM. Olaparib IC_{50} for each treatment

condition was calculated in GraphPad Prism. **(C-F)** OVSAHO-OR cells in a 96-well plate were treated with increasing doses of olaparib with or without 2 μM of the indicated BRD inhibitors. Colony formation and olaparib IC_{50} were determined as described above. Error bars, SEM. p-value by t-test.

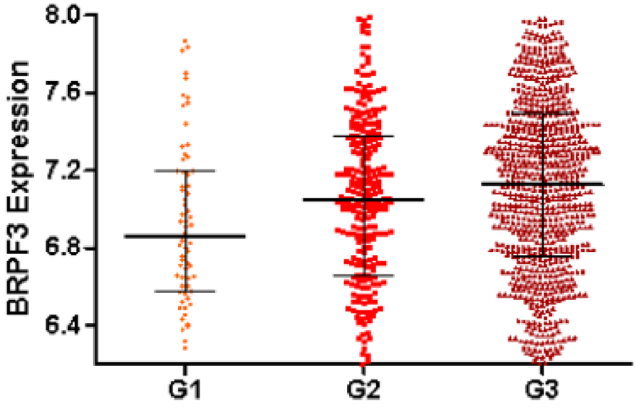
Stage



Mann Whitney Test	I	II	III	IV	Rest
I		1.13e-01	9.70e-03	1.24e-01	1.65e-02
II			9.50e-01	7.95e-01	6.39e-01
III				8.57e-01	1.40e-01
IV					8.10e-01

Description\Stage	I	II	III	IV
Mean	7.016	7.123	7.100	7.078
Quantile 1	6.656	6.742	6.757	6.667
Median	6.981	7.062	7.090	7.128
Quantile 4	7.324	7.513	7.436	7.440

Grade



Mann Whitney Test	Grade 1	Grade 2	Grade 3	Rest
Grade 1		5.07e-02	7.20e-04	3.76e-03
Grade 2			1.13e-02	1.45e-01
Grade 3				5.62e-04

Description\Grade	Grade 1	Grade 2	Grade 3
Mean	6.942	7.021	7.134
Quantile 1	6.576	6.662	6.754
Median	6.861	7.048	7.130
Quantile 4	7.196	7.375	7.493

Fig. S5. BRPF3 expression is positively correlated with higher HGSOC stage and grade. A meta-analysis of HGSOC microarray data was performed using CSIOVDB.

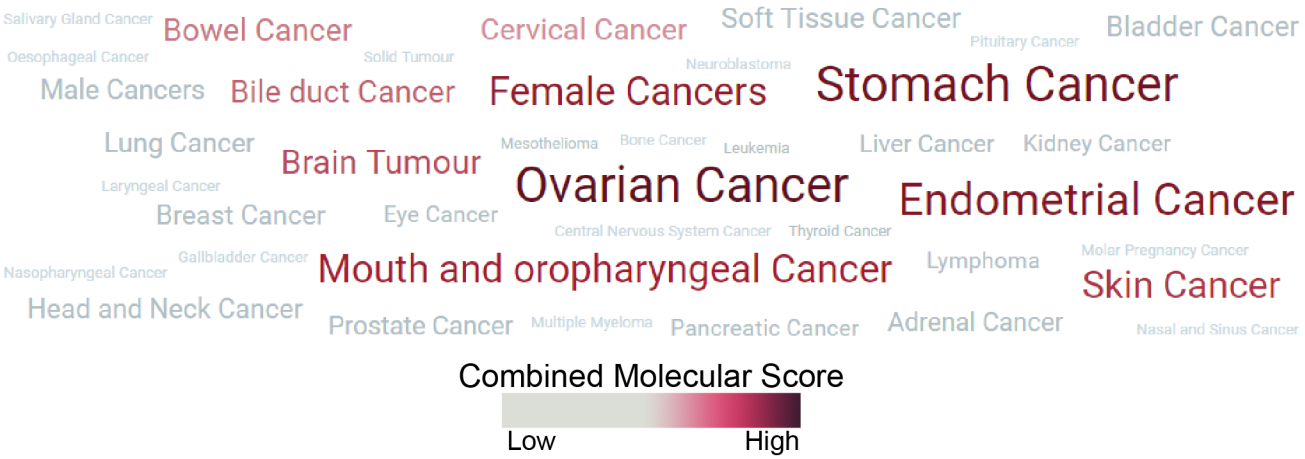


Fig. S6. BRPF3 is significantly associated with ovarian cancer in combined molecular score. Word cloud generated by canSAR Black by meta-analysis of cancer datasets. Combined molecular score includes mutation score, gene expression, and copy number variation.

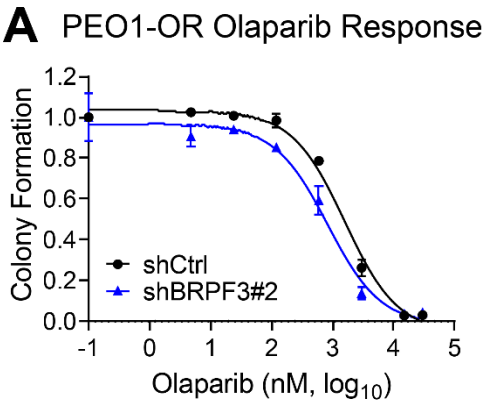


Fig. S7. shRNA-mediated knockdown of *BRPF3* sensitizes PEO1-OR cells to olaparib. PEO1-OR stably expressing the indicated shRNA were seeded at 2500 cells per well in a 24-well plate and treated with increasing doses of olaparib. Media and drug were changed every 2-3 days for eight days, after which colonies were fixed and stained with crystal violet. Stain was dissolved and the absorbance from each well was read by spectrophotometer, then normalized to vehicle control. Error bars, SEM. Olaparib IC_{50} for each treatment condition was calculated in GraphPad Prism.

Supplemental Tables

Gene (Protein)	TPM (834 Ctrl)	TPM (846 Ctrl)	TPM (827 Olap)	TPM (878 Olap)	logFC	P-value	FDR
KAT2A (GCN5)	6.35	5.98	15.09	13.61	1.093	5.11E-05	0.003
KAT2B (PCAF)	4.92	3.93	3.63	4.62	-0.149	0.593	1.000
KAT3A (CBP)	8.66	10.12	13.46	13.13	0.532	0.041	0.363
KAT3B (P300)	10.85	15.09	12.62	14.84	0.236	0.369	1.000
KAT7 (HBO1)	7.42	6.56	6.88	9.45	0.185	0.497	1.000
BRPF3 (BRPF3)	5	6.15	8.21	8.96	0.642	0.019	0.234

Table S1. RNA-Seq analysis of PDX-GTFB1009 olaparib-treated and -untreated ascites. For each of the indicated genes, the transcripts per million (TPM) are shown for the four indicated mice, as well as log fold change (logFC), P-value, and false discovery rate (FDR).

KEGG Pathway	# Genes Mapped	Enrichment Score	Direction	FDR (q-value)
Neuroactive ligand-receptor interaction	138	0.992824	Both	2.11E-11
Ribosome	128	0.446269	Inhibited	6.06E-10
Cytokine-cytokine receptor interaction	147	0.5105	Both	2.64E-07
Protein digestion and absorption	66	0.734508	Both	0.0002
Proteoglycans in cancer	175	0.376922	Inhibited	0.00057
Viral protein interaction with cytokine and	47	0.780212	Inhibited	0.00069
HIF-1 signaling pathway	89	0.544794	Inhibited	0.0011
Cell cycle	118	0.293541	Activated	0.0012
TNF signaling pathway	103	0.433002	Inhibited	0.0012
Kaposi sarcoma-associated herpesvirus	158	0.280737	Inhibited	0.0012
Inflammatory bowel disease	39	0.828738	Inhibited	0.0012
Th1 and Th2 cell differentiation	74	0.472015	Inhibited	0.0013
DNA replication	35	0.494633	Activated	0.0016
Autophagy - animal	127	0.243375	Inhibited	0.0016
Ferroptosis	36	0.748789	Inhibited	0.0018
Salmonella infection	195	0.297563	Inhibited	0.0018
Mitophagy - animal	63	0.41506	Inhibited	0.0024
Yersinia infection	115	0.424649	Inhibited	0.0035
Renal cell carcinoma	64	0.379247	Inhibited	0.0037
B cell receptor signaling pathway	61	0.470524	Inhibited	0.0048
C-type lectin receptor signaling pathway	84	0.247104	Inhibited	0.0053
Staphylococcus aureus infection	40	0.688738	Inhibited	0.0053
Insulin resistance	97	0.320517	Inhibited	0.0054
Fanconi anemia pathway	50	0.43917	Activated	0.0056
Sphingolipid signaling pathway	108	0.210381	Inhibited	0.0089
Systemic lupus erythematosus	57	0.773827	Activated	0.009
Type I diabetes mellitus	23	0.794405	Inhibited	0.0097

Table S2. Olaparib-resistant PDX exhibit altered KEGG pathways, including activated Cell Cycle, DNA Replication, and Fanconi Anemia.

shRNA	The RNAi Consortium Number	Target Sequence
shCTRL	N/A (Sigma-Aldrich #SHC016)	N/A
sh*KAT2A*#1	TRCN0000038879	GCTGAACTTTGTGCAGTACAA
sh*KAT2A*#2	TRCN0000286981	GCTGAACTTTGTGCAGTACAA
sh*KAT2B*#1	TRCN0000018528	GCAGACTTACAGCGAGTCTTT
sh*KAT2B*#2	TRCN0000364134	CCTAAACCGCATCAACTATTG
sh*KAT3A*#1	TRCN0000356081	ATCGCCACGTCCCTTAGTAAC
sh*KAT3A*#2	TRCN0000356082	CGTTTACCATGAGATCCTTAT
sh*KAT3B*#1	TRCN0000231133	TAACCAATGGTGGTGATATTA
sh*KAT3B*#2	TRCN0000009883	CAATTCCGAGACATCTTGAGA
sh*KAT7*#1	TRCN0000021630	CGGGATAAGCAGATAGAAGAA
sh*KAT7*#2	TRCN0000021632	CTCGTTCATCTGGTTCAGAAA
sh*BRPF3*#1	TRCN0000382105	AGGAGGACTTTAACCTTATAG
sh*BRPF3*#2	TRCN0000277697	TCACACTCTCTCCCGCTTATC

Table S3. shRNA

Name	Sequence	Usage
GAPDH_F	GTCTCCTCTGACTTCAACAGCG	Control (ΔΔCt)
GAPDH_R	ACCACCCTGTTGCTGTAGCCAA	Control (ΔΔCt)
KAT2A_GCN5_F	GCAGGTCAAGGGTTATGGGAC	Gene expression
KAT2A_GCN5_R	GCTCTTGGGCACCTTGATGT	Gene expression
KAT2B_PCAF_F	GGTGAAGAGCCATCAAAGCG	Gene expression
KAT2B_PCAF_R	GACTCGCTGTAAGTCTGCCA	Gene expression
KAT3A_CBP_F	GGCCTTCAGGTTTTGTGTGC	Gene expression
KAT3A_CBP_R	TTCCCAGTCTTGTGGTCTGC	Gene expression
KAT3B_P300_F	TGCCAAACCAGATGATGCCT	Gene expression
KAT3B_P300_R	ATAGCCCATAGGCGGGTTGA	Gene expression
KAT7_HBO1_F	CACCAACGGAGAGACAGCTT	Gene expression
KAT7_HBO1_R	GCAGCCTTAACTTCTCCAAATCC	Gene expression
BRPF3_F	CCCATCTGCAGTCCCAAAGA	Gene expression
BRPF3_R	GGACTTTGACCTGCTCTCGTT	Gene expression

Table S4. RT-qPCR Primers

Protein	Supplier & Catalog #	Species	RRID	Dilution
β-actin	Abcam #ab6276	Mouse	AB_2223210	1:10,000
BRPF3	Abcam #ab69410	Mouse	AB_1209613	1:1000
CBP	Cell Signaling #7389	Rabbit	AB_2616020	1:1000
GCN5	Cell Signaling #3305	Rabbit	AB_2128281	1:1000
H3	Cell Signaling #14269	Mouse	AB_2756816	1:1000
H3K14ac	Cell Signaling #7627	Rabbit	AB_10839410	1:1000
HBO1	Cell Signaling #58418	Rabbit	AB_2799547	1:1000
P300	Abcam #ab14984	Mouse	AB_301550	1:350
PCAF	Cell Signaling #3378	Rabbit	AB_2128409	1:1000

Table S5. Immunoblotting Antibodies