

**Supplementary Figure 1.** Effects of the drug combination on the proliferation of B16F10. The parental (B16F10C) and resistant melanoma (B16F10R) cells were treated with the drug combination at various concentrations (0.62-80  $\mu$ M). This figure is the results of the MTT assay- parental (dark bars) and resistant (light bars).Data shown are means ± SEM of three replicate wells. Graphs were plotted with concentration of the inhibitor (X-axis) Vs cell viability % (Y-axis) and the IC<sub>50</sub> values were calculated using the formula y = b + ax. IC<sub>50</sub> values are the concentration of the drug combination which results in 50% cell death.

## HDAC2 phosphorylation in drug-resistant melanoma

SR NO	GENE ID	DESCRIPTION	PHOSPOSITES
1	Bclaf1	bcl-2-associated transcription factor 1 isoform 1	S395(100); T400(100)]
2	Map4k4	Mitogen-activated protein kinase kinase kinase kinase 4 isoform X1	S787(98.7)]
	Psip1	PC4 and SFRS1-interacting protein isoform 1	S272(99.9); S274(100)]
	lws1	protein IWS1 homolog [Mus musculus]	S343(100); S345(100)]
	Eif5b	eukaryotic translation initiation factor 5B	S184(100); S187(100); S191(100)]
	Pnn	pinin	S701(100); S704(99)]
	Nvl	nuclear valosin-containing protein-like	S190(100)]
	Ctr9	RNA polymerase-associated protein CTR9 homolog	S1079(100); S1083(98)]
	Larp1	la-related protein 1	S826(96.1); S828(95.4)]
0	Top2b	DNA topoisomerase 2-beta	S1539(100)]
1	Psip1	PC4 and SFRS1-interacting protein isoform 1	S272(99.9); S274(100)]
2	Ubap2I	PREDICTED: ubiquitin-associated protein 2-like isoform X1	S644(95.8); S/Y/T]
3	Eif4g1	PREDICTED: eukaryotic translation initiation factor 4 gamma 1 isoform X2	S708(100)]
4	Rcc2	protein RCC2	S48(99.9); S49(99.9)]
5	Cdc42bpb	PREDICTED: serine/threonine-protein kinase MRCK beta isoform X1	S1705(100); S1709(100)]
6	Safb	scaffold attachment factor B1 isoform X1	S577(98.7)
7	Chd4	chromodomain-helicase-DNA-binding protein 4 isoform X1 [Mus musculus]	S1563(100)]
8	Acin1	apoptotic chromatin condensation inducer in the nucleus isoform 2	S1003(100)]
9	Gatad2b	transcriptional repressor p66-beta	T121(100); S123(100); S130(100); S136(96.6)]
0	Ddx46	probable ATP-dependent RNA helicase DDX46	S102(100); S104(98.8); S106(100)
1	Scrib	protein scribble homolog isoform 2	S1292(100)]
2	Nop2	PREDICTED: probable 28S rRNA (cytosine-C(5))-methyltransferase isoform X1	T169(100)]
3	Ppig	PREDICTED: peptidyl-prolyl cis-trans isomerase G isoform X1	S354(100); T356(100)]
4	MIIt4	PREDICTED: afadin isoform X1	S1180(97.9); S1190(100)]
5	Eif3b	eukaryotic translation initiation factor 3 subunit B	S68(100); S79(96.9); S84(97)]
6	Hmga2	high mobility group protein HMGI-C	S104(99.9)]
7	Hirip3	HIRA-interacting protein 3	S205(100); S207(100); S208(100)]
8	Fip1l1	PREDICTED: pre-mRNA 3'-end-processing factor FIP1 isoform X1	S502(100)]
9	Ythdc1	PREDICTED: YTH domain-containing protein 1 isoform X1	S528(100)]
0	Lrrc47	leucine-rich repeat-containing protein 47	S430(100)]
1	Casc3	protein CASC3	S145(100)]
2	Rbm17	splicing factor 45	S155(100)]
3	Gigyf2	PERQ amino acid-rich with GYF domain-containing protein 2 isoform b	S237(100)]; 159032016 1xPhospho
4	Stim1	PREDICTED: stromal interaction molecule 1 isoform X2	S550(100)]
5	Map2	PREDICTED: microtubule-associated protein 2 isoform X1	S1814(96.6); S1819(98.3); S1822(100); S/T]
6	Chchd6	MICOS complex subunit Mic25 isoform 1	S164(100)]
7	Dnaja2	dnaJ homolog subfamily A member 2	S394(99.6); S395(99.6)]
8	Ppfia1	PREDICTED: liprin-alpha-1 isoform X1	\$797(98.8)]
9	Srrm1	serine/arginine repetitive matrix protein 1 isoform 1	T600(100); S602(100)]
0	Tjp2	PREDICTED: tight junction protein ZO-2 isoform X1	S188(100)]
1	Map4	PREDICTED: microtubule-associated protein 4 isoform X1	S1250(98.3)]
2	Nedd4l	PREDICTED: E3 ubiquitin-protein ligase NEDD4-like isoform X1	S502(100)]
3	Larp7	la-related protein 7	S253(99.9); S256(99.9)]
4	Pum2	pumilio homolog 2 isoform 1	S177(100); S181(100)]
5	Rrbp1	ribosome-binding protein 1 isoform a	S625(98.8)]
.6	Srrm2	PREDICTED: serine/arginine repetitive matrix protein 2 isoform X1	S2681(99)]
-	011112	myc box-dependent-interacting protein 1 isoform 1	S332(98.1); S/T]

## **Supplementary Table 1.** List of novel phosposites (n=74) on 47 proteins identified in 95 proteins from LC-MS and bioinformatic analyses