Table of Content

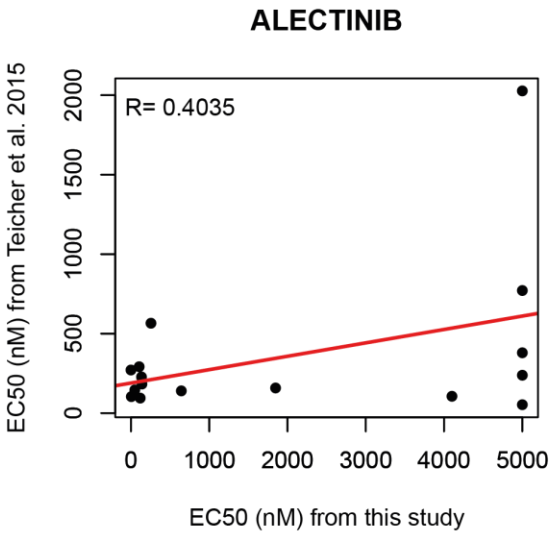
Appendix Table S1. Commercially or publicly available cell lines during cell line selection.

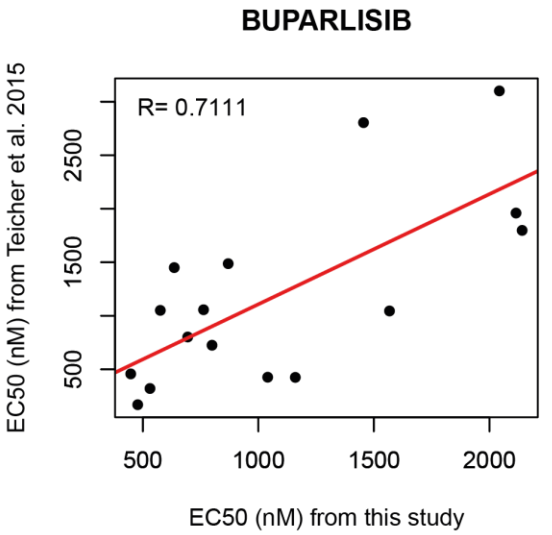
CELL LINE	SUBTYPES
A-204	Rhabdoid tumor
A-673	Ewing Sarcoma
G-401	Rhabdoid Tumor
HOS	Osteosarcoma
HS 706.T	Giant Cell Sarcoma
HS 729	Rhabdomyosarcoma
HS 913.T	Fibrosarcoma
HSSY-II	Synovial sarcoma
HT-1080	Fibrosarcoma
KHOS NP	Osteosarcoma
KHOS-240S	Osteosarcoma
KHOS-312H	Osteosarcoma
MES-SA	Uterine Sarcoma
RD	Rhabdomyosarcoma
RD-ES	Ewing Sarcoma
SAOS-2	Osteosarcoma
SJSA-1	Osteosarcoma
SK-ES-1	Ewing Sarcoma
SK-LMS-1	Leiomyosarcoma
SK-UT-1	Leiomyosarcoma
SK-UT-1B	Leiomyosarcoma
SW 1353	Chondrosarcoma
SW 684	Fibrosarcoma
SW 982	Atypical Synovial sarcoma
SYO-1	Synovial sarcoma
TC-71	Ewing Sarcoma
U-2 OS	Osteosarcoma
VA-ES-BJ	Epithelioid Sarcoma

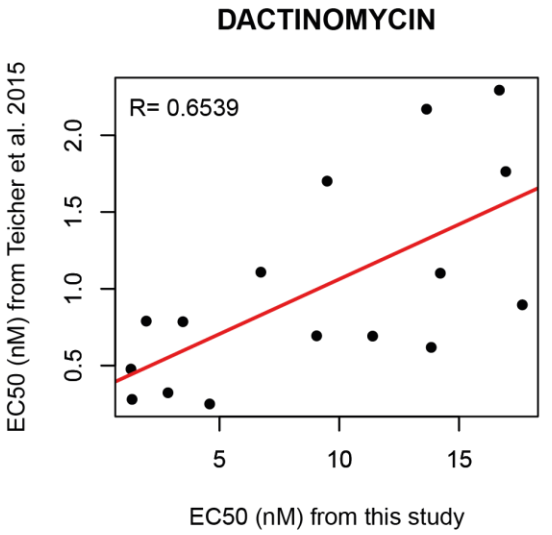
Appendix Table S2. EC50 values of Staurosporine in sarcoma lines.

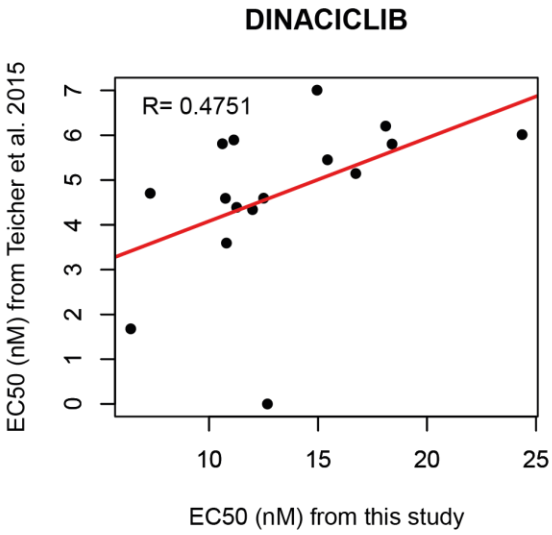
CELL LINE	MEAN EC50 (μM)	STDEV*
RD-ES	0.033	0.0016
MES-SA	0.028	0.0027
SW684	0.027	0.0038
SK-ES-1	0.024	0.0010
HS729	0.023	0.0073
SK-LMS-1	0.013	0.0029
KHOS-NP	0.012	0.0020
VA-ES-BJ	0.007	0.0006
HT1080	0.007	0.0005
G401	0.006	0.0011
RD	0.006	0.0006
A204	0.005	0.0012
SYO-1	0.003	0.0001
KHOS-240S	0.003	0.0002
SW872	0.003	0.0003
SW1353	0.003	0.0001
SW982	0.001	0.0001

*Standard deviation from triplicate viability assays.


ALECTINIB
R= 0.4035
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
0
500
1000
1500
2000
0
1000
2000
3000
4000
5000


BUPARLISIB
R= 0.7111
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
500
1500
2500
500
1000
1500
2000


DACTINOMYCIN
R= 0.6539
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
0.5
1.0
1.5
2.0
5
10
15


DINACICLIB
R= 0.4751
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
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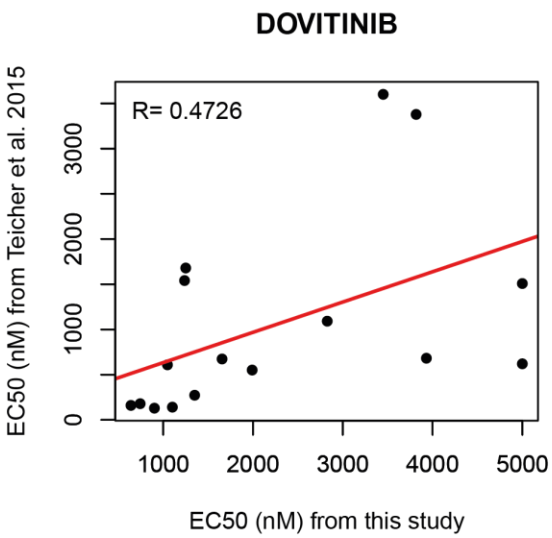
1
2
3
4
5
6
7
10
15
20
25


DOVITINIB
R= 0.4726
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
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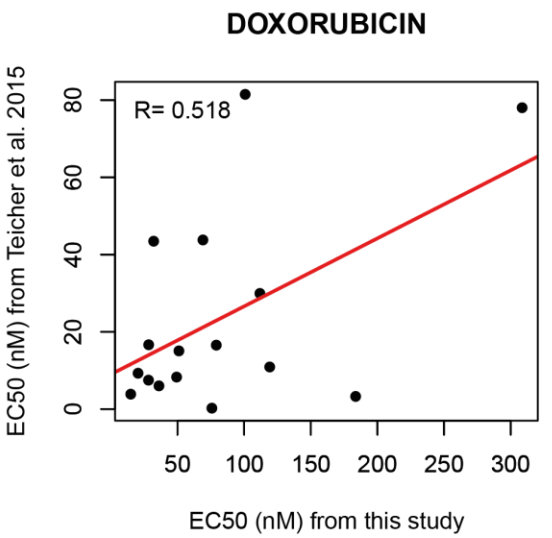
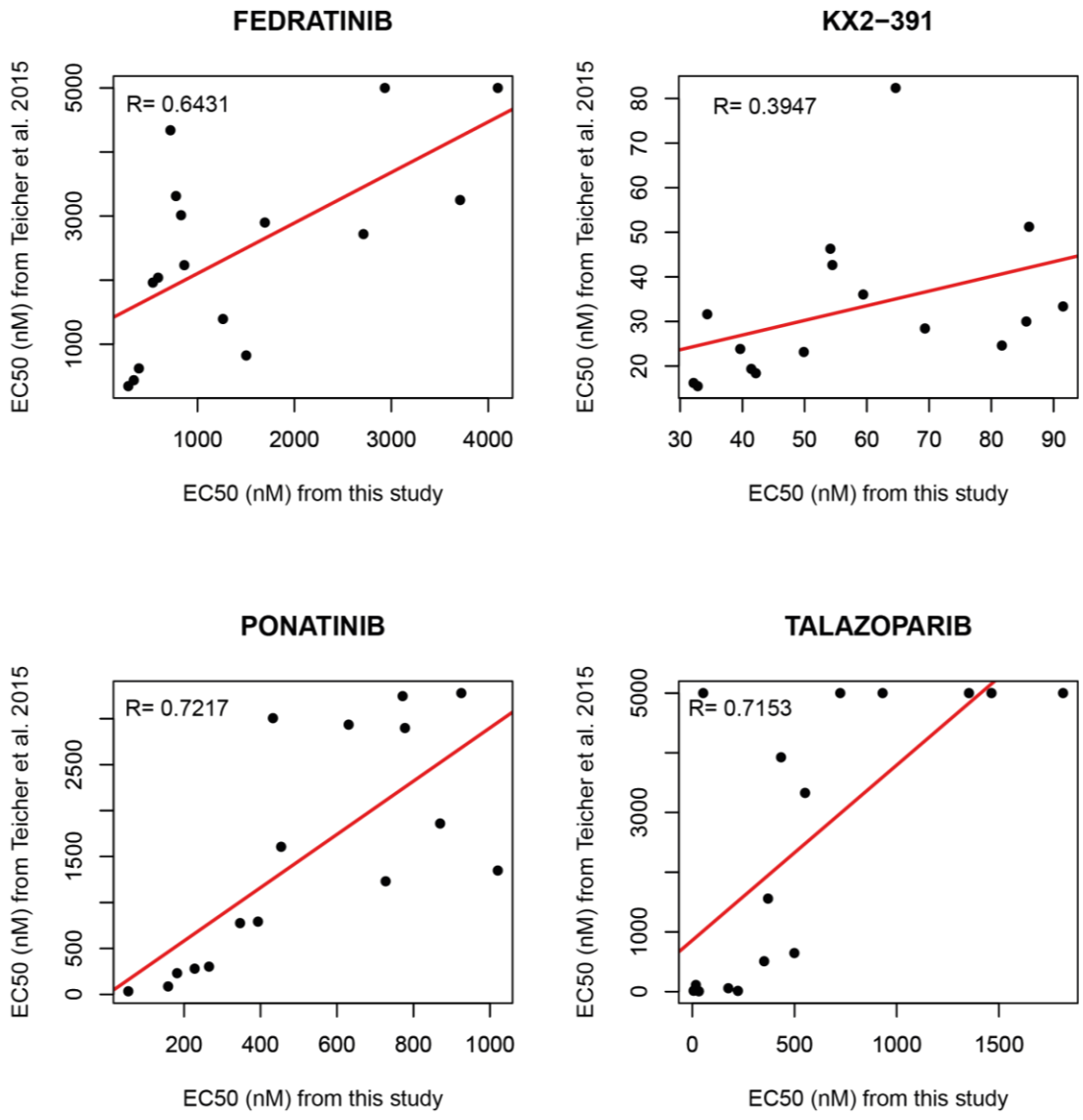
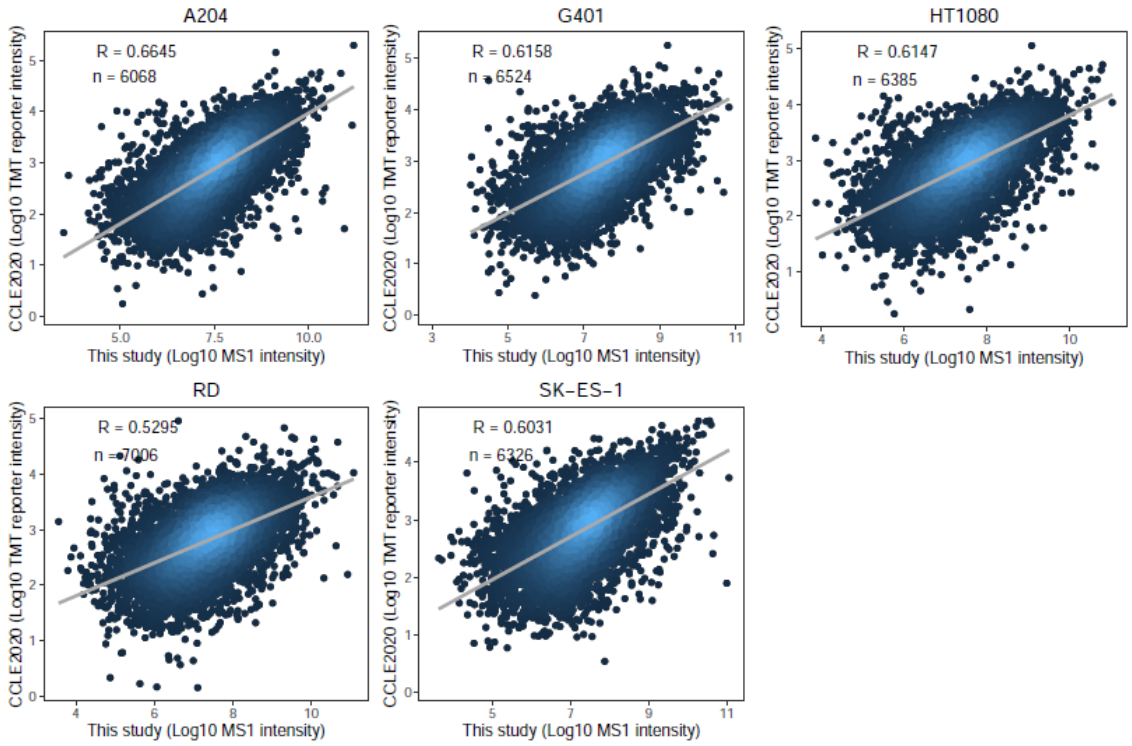
1000
2000
3000
1000
2000
3000
4000
5000


DOXORUBICIN
R= 0.518
EC50 (nM) from Teicher et al. 2015
EC50 (nM) from this study
0
20
40
60
80
50
100
150
200
250
300

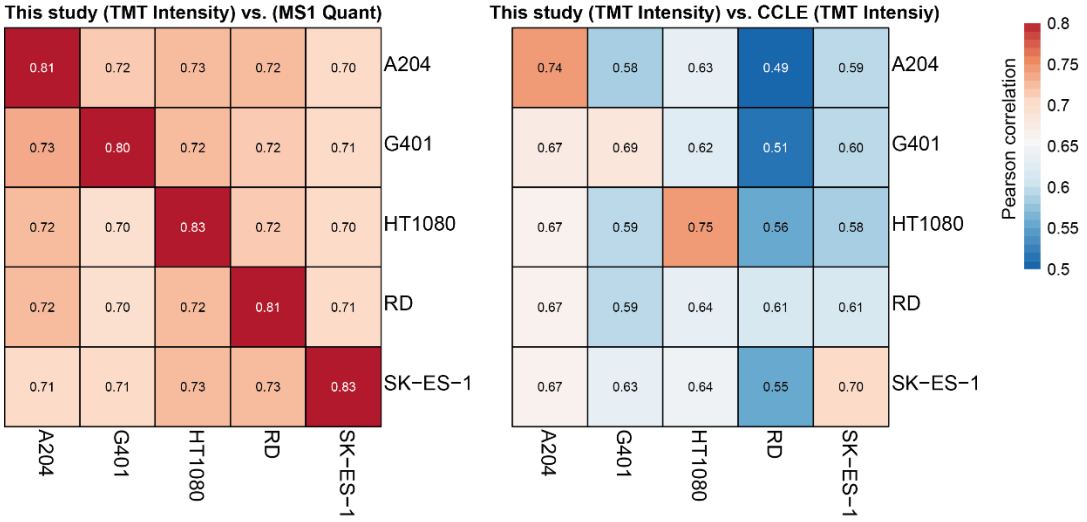


Appendix Figure S1. Correlation of EC50 values (nM) of effective drugs across sarcoma lines between previous study and this study. The drug screen dataset of 16 sarcoma lines was downloaded from precious study (Teicher *et al*, 2015) where 63 cell lines were screened with 445 compounds. In total, sixteen cell lines and 55 compound (52 KIs and 3 non-KIs) were shared with our screen library. Ten drugs shown here are the drugs with EC50 between 1 to 5000 nM across 16 cell lines in at least one of datasets. To make the plot clear, EC50 values > 5000 nM were plotted as 5000 nM.

A

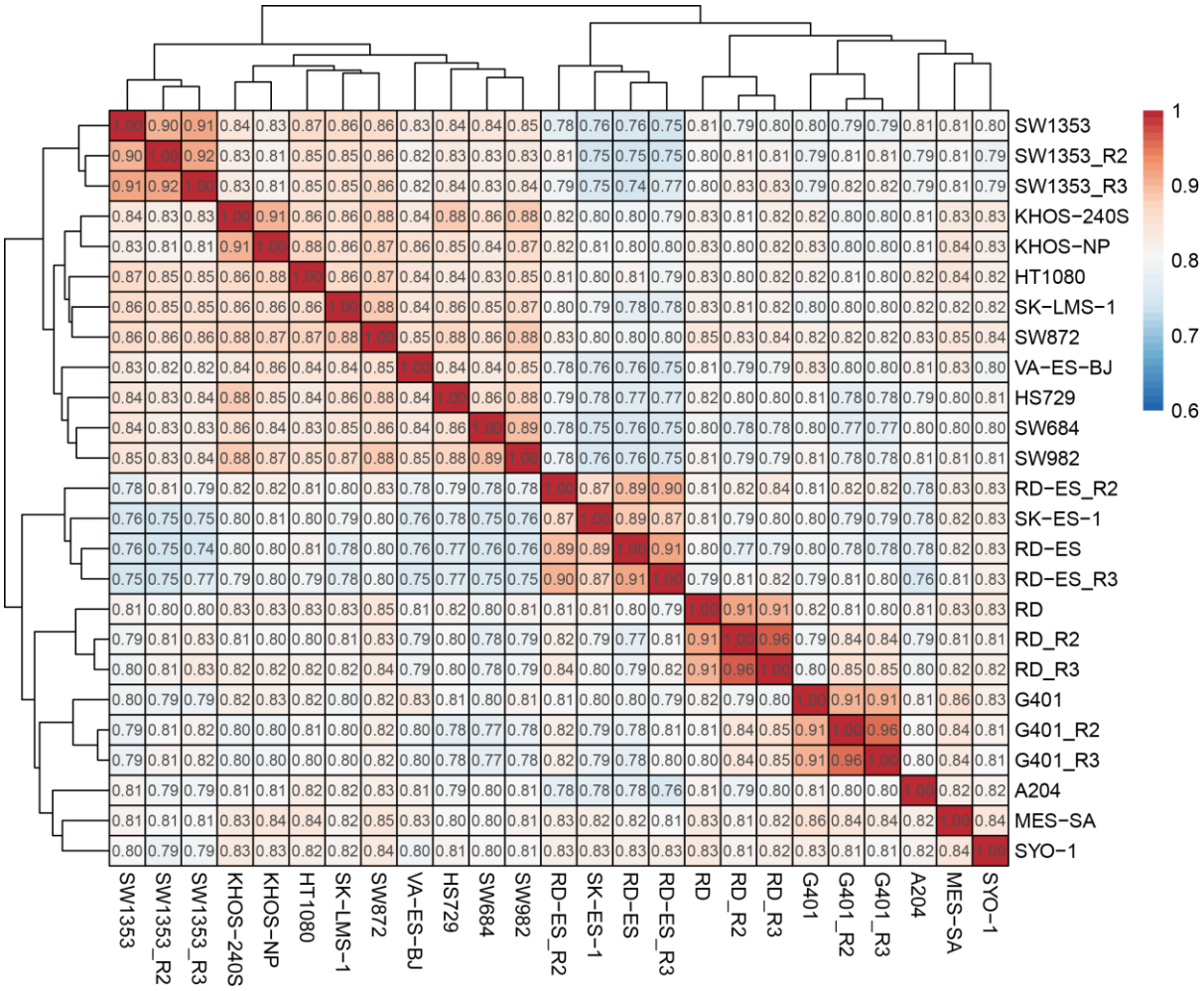


B



Appendix Figure S2. Correlation of intensity of the quantified proteins between CCLE proteomics analysis and this study. The proteomics dataset of CCLE 2020 was downloaded from precious study (Nusinow et al, 2020) where 375 cell lines from diverse lineages were multiplexed for proteomics analysis (TMT labelled). A. Five cell lines were shared between the two studies. The Pearson correlation and numbers of shared proteins were labelled on the plot. B. Comparison of correlations between matched and unmatched cell lines in our own datasets with MS1 quantification and TMT reporter intensity (left), as well as the datasets obtained from CCLE with TMT reporter intensity (right).

A



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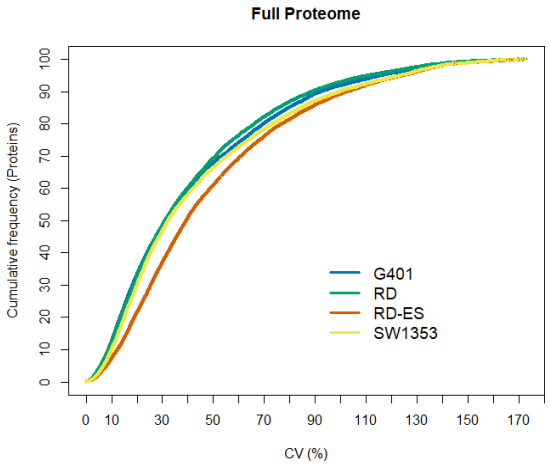
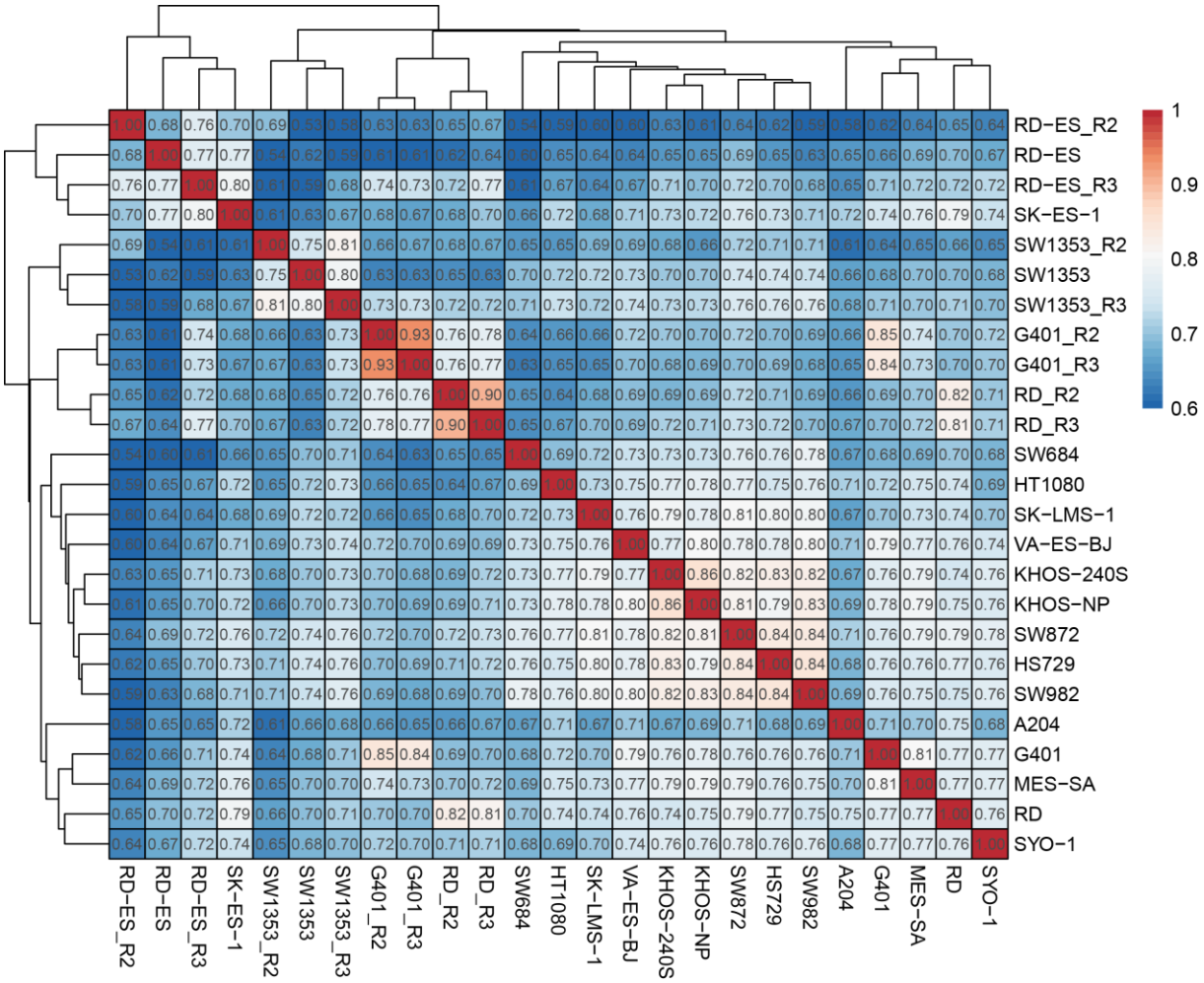
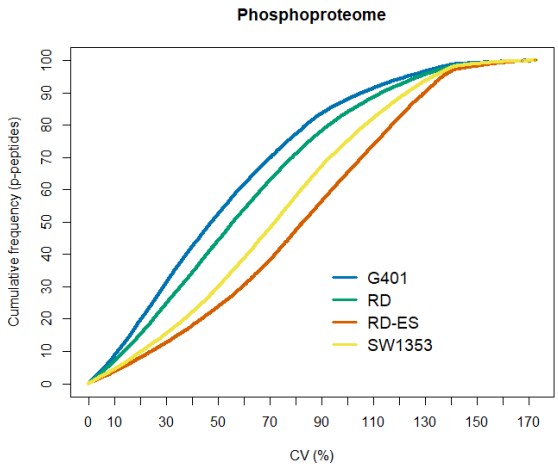


Appendix Figure S3. Reproducibility of proteomics analysis in biological triplicate. A. Unsupervised hierarchical clustering of 17 cell lines with 8 biological replicates cell lines. Pearson correlation was shown. R2, R3: biological replicates. B. Ranked protein coefficients of variation (CVs) of four triplicate cell lines.

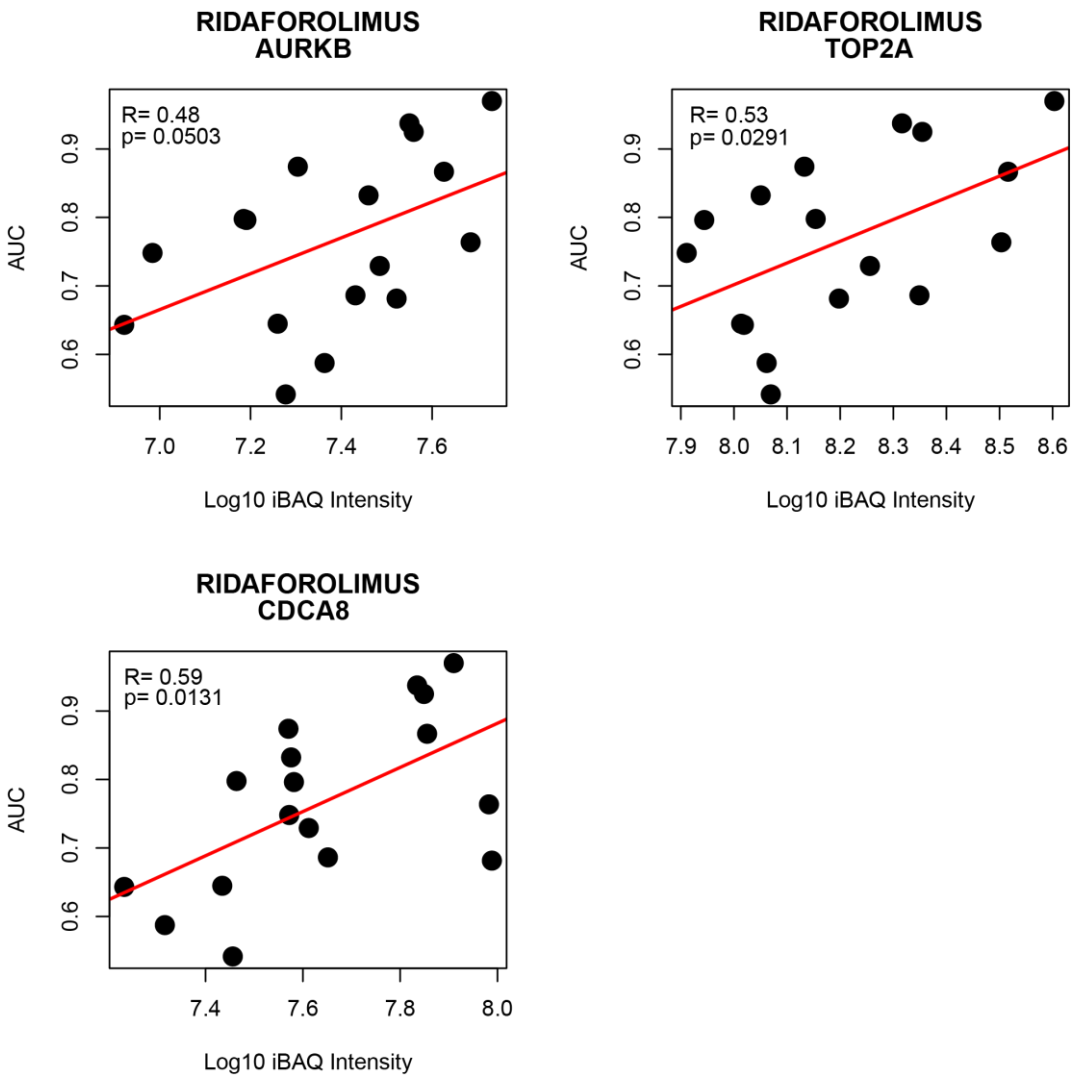
A



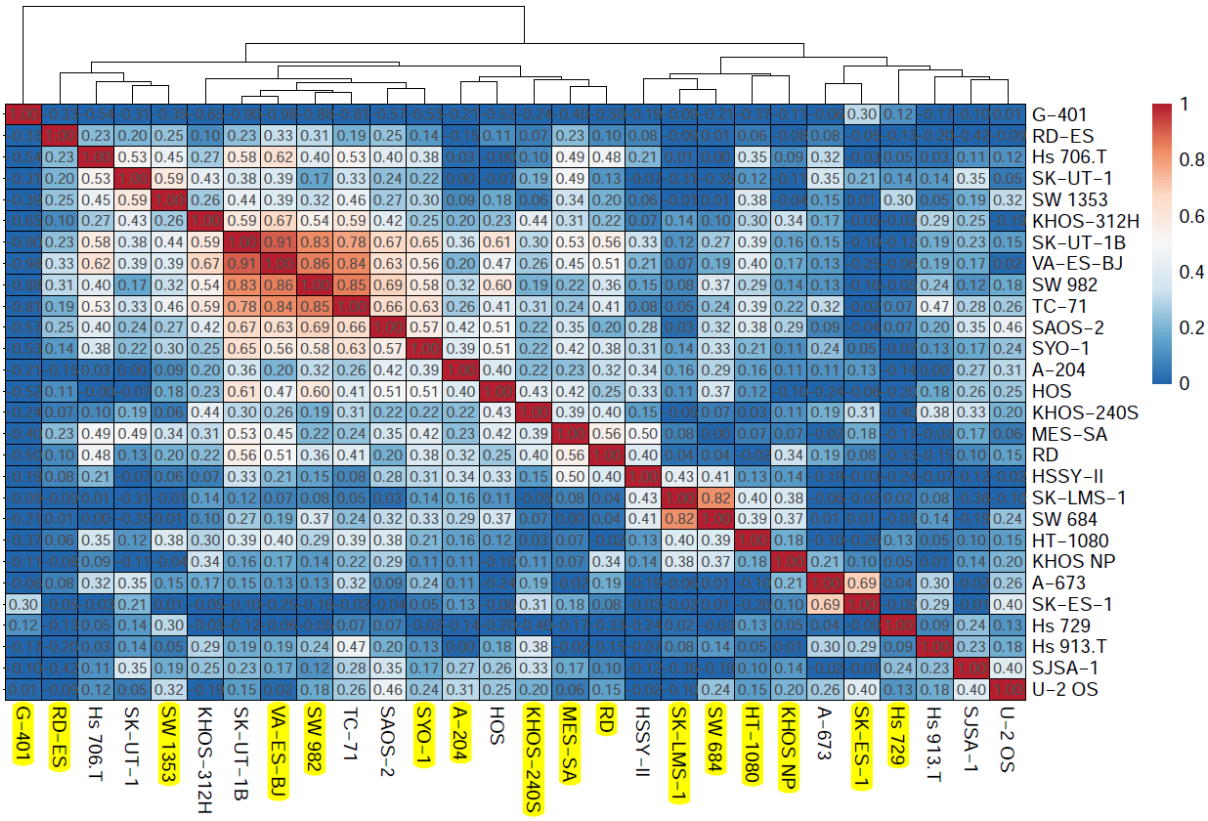
B



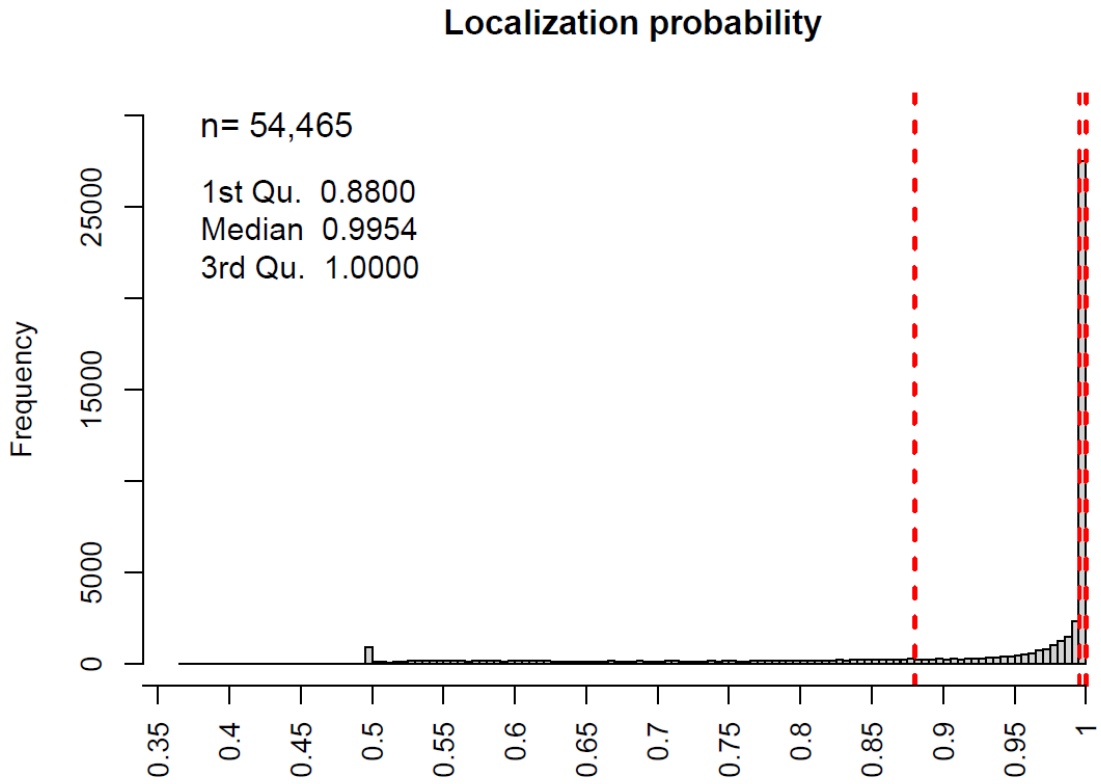
Appendix Figure S4. Reproducibility of phosphoproteomics analysis in biological triplicate. A. Unsupervised hierarchical clustering of 17 cell lines with eight biological replicates cell lines on phosphoprotein level. Pearson correlation was shown. R2, R3: biological replicates. B. Ranked phosphopeptides coefficients of variation (CVs) of four triplicate cell lines.



Appendix Figure S5. Correlation of the intensity several G2/M markers with the response of mTOR inhibitor Ridaforolimus.

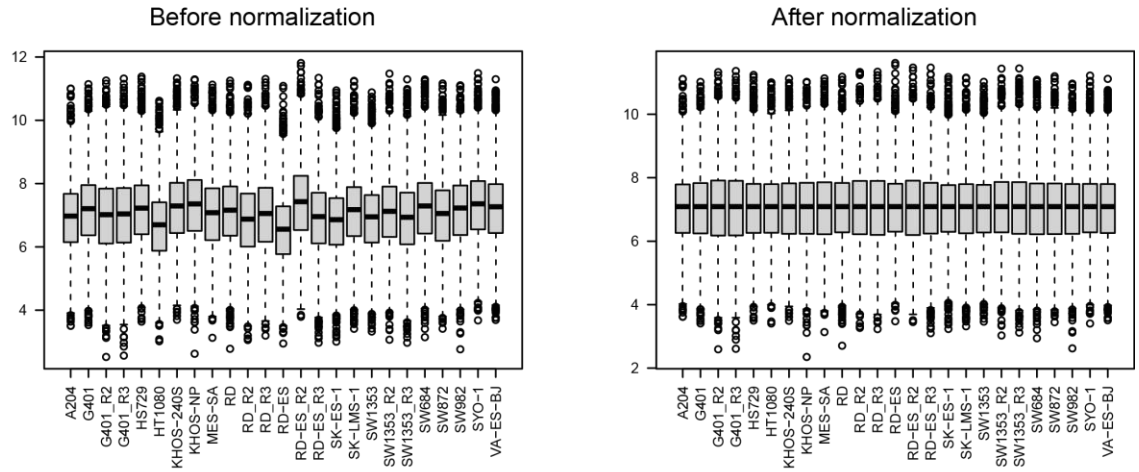


Appendix Figure S6. Clustering plot of correlations between drug responses among sarcoma cells. The Pearson correlation was calculated according to prior screen dataset (Teicher *et al.*, 2015). The cell lines chosen in this study were marked in yellow.

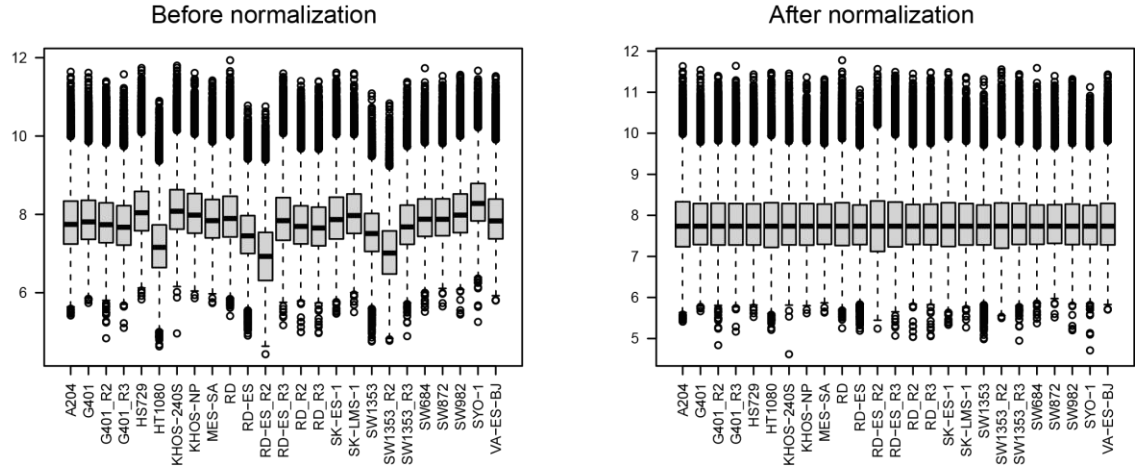


Appendix Figure S7. Localization probability of phosphorylation sites.

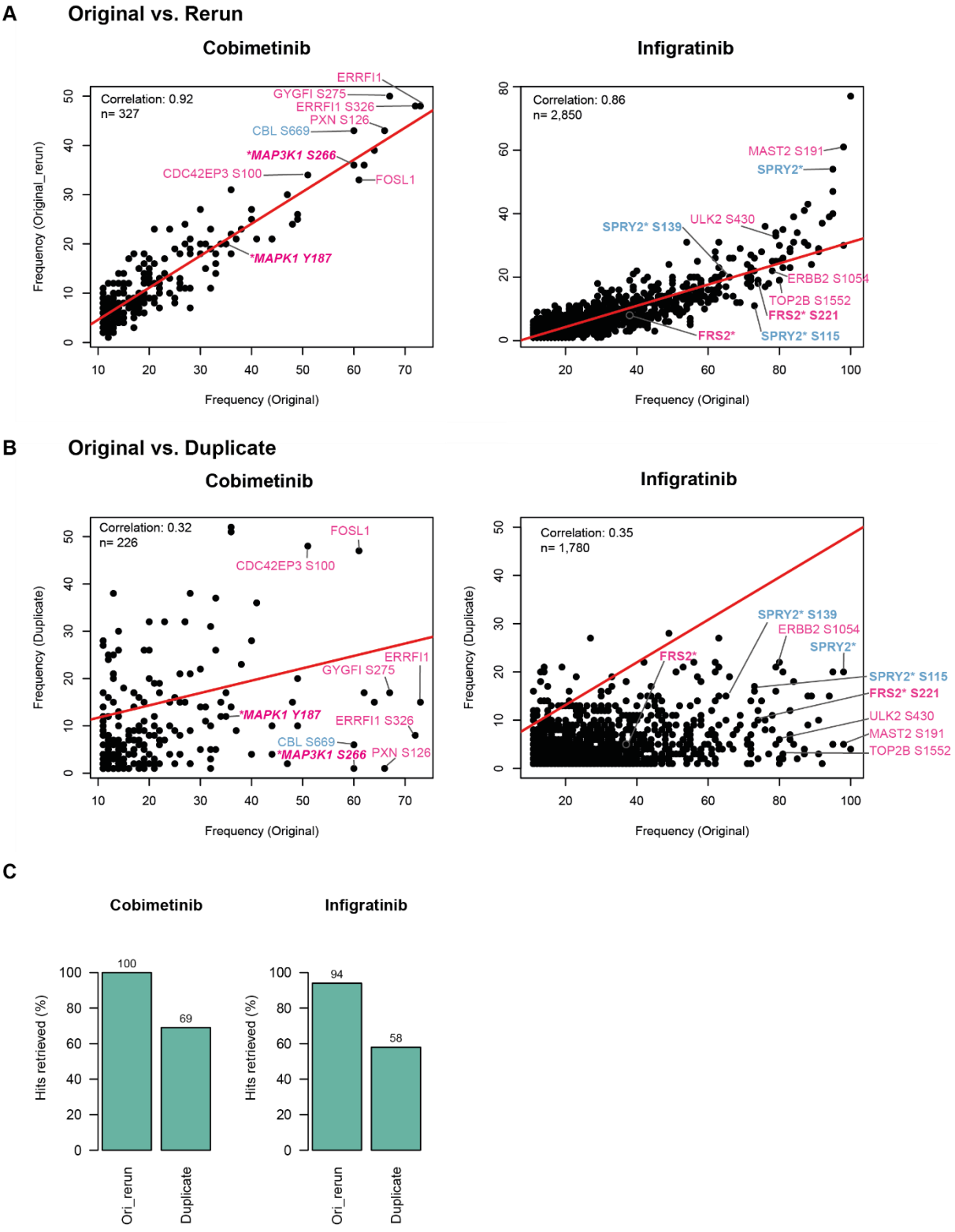
A Full Proteomes



B Phosphoproteomes



Appendix Figure S8. Boxplot of baseline proteomes and phosphoproteomes before and after median-centric normalization. A. Y-axis indicated log10-transformed iBAQ intensity. B. Y-axis indicated log10-transformed MS1 intensity. The central band represents the median, while the hinges denote the first and third quartiles with whiskers extending up to 1.5 times the interquartile range (IQR).



Appendix Figure S9. Reproducibility of elastic net regression in Cobimetinib and Infigratinib. A. The correlation of the frequencies of identified proteins and p-sites in original and rerun elastic net regression. B. The correlation of the frequencies of identified proteins and p-sites in original and duplicate datasets. The labels show the chosen example in main Figure 5. C. The percentage of retrieved proteins and p-sites compared to original analysis.

References

Nusinow DP, Szpyt J, Ghandi M, Rose CM, McDonald ER, 3rd, Kalocsay M, Jane-Valbuena J, Gelfand E, Schweppe DK, Jedrychowski M *et al* (2020) Quantitative Proteomics of the Cancer Cell Line Encyclopedia. *Cell* 180: 387-402 e316

Teicher BA, Polley E, Kunkel M, Evans D, Silvers T, Delosh R, Laudeman J, Ogle C, Reinhart R, Selby M *et al* (2015) Sarcoma Cell Line Screen of Oncology Drugs and Investigational Agents Identifies Patterns Associated with Gene and microRNA Expression. *Mol Cancer Ther* 14: 2452-2462