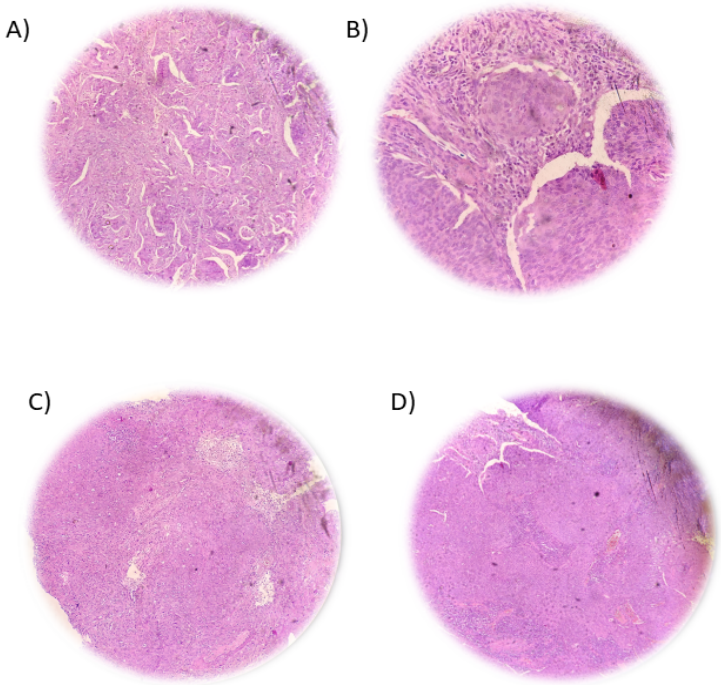
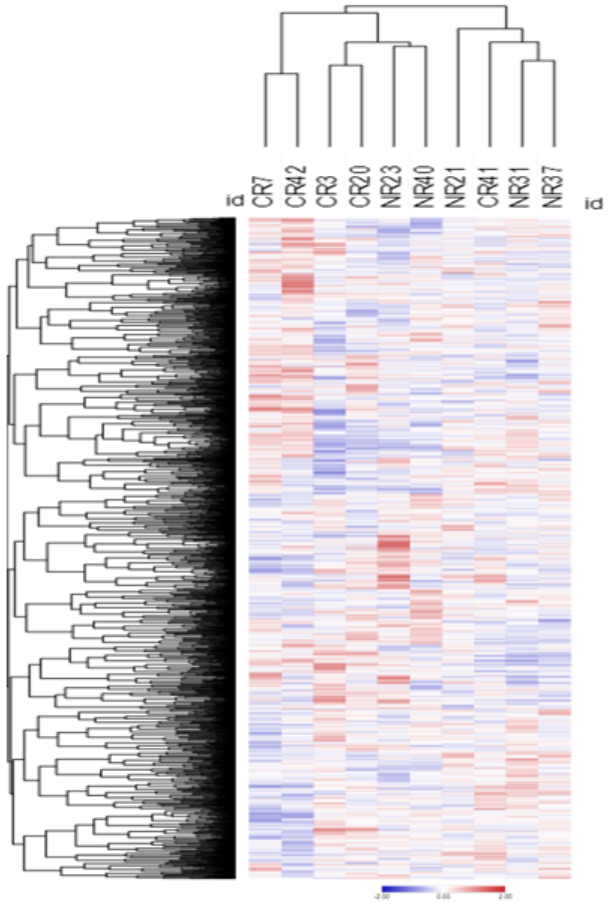
Phosphoproteomics guides low dose drug combination of cisplatin and silmitasertib against concurrent chemoradiation resistant cervical cancer

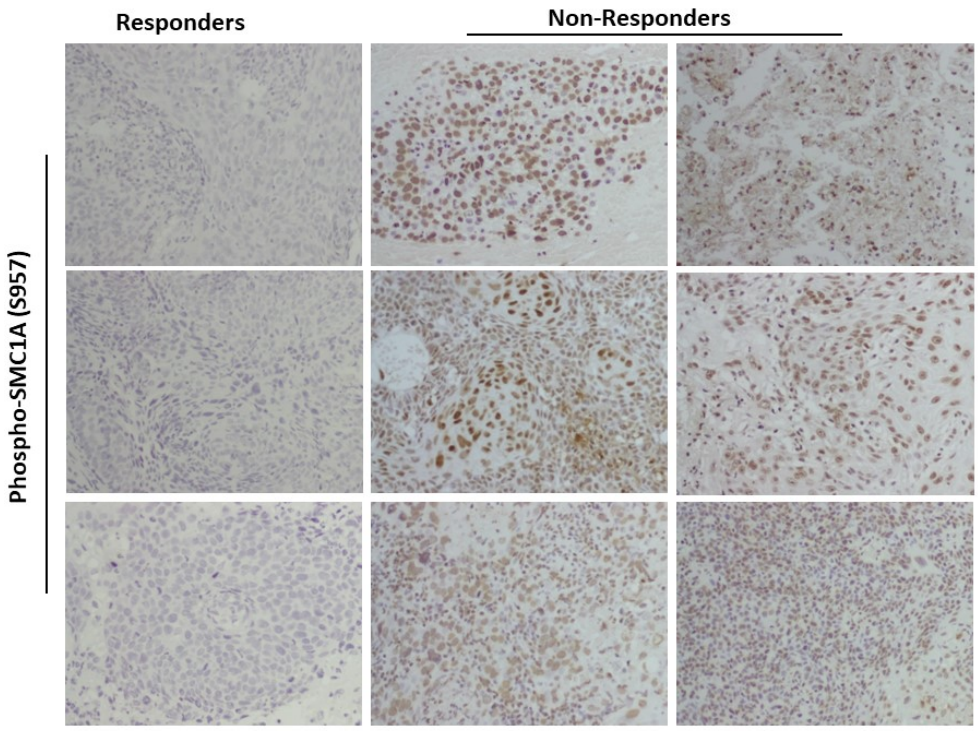
Supplementaary figure 1: Hematoxylin and eosin (H&E) staining was performed on the tissue biopsy samples to confirm their histological classification as cervical squamous cell carcinoma. Sections show infiltrating tumor cells arranged in sheets and cluster. Tumor cells are oval to polygonal with abundant eosinophilc cytoplasm. Nuclei are showing moderate pleomorphism with prominent nucleoliImages A and B correspond to samples from patients who were sensitive to concurrent chemoradiotherapy (CCRT), while images C and D are from patients resistant to CCRT.



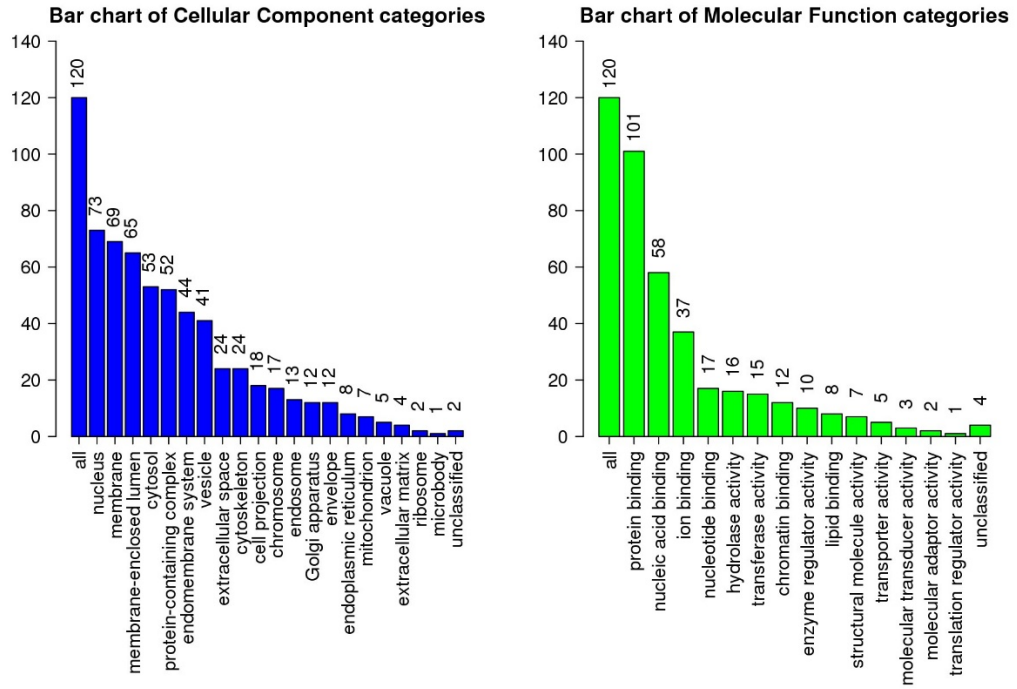
Supplementary figure 2: Hierarchial clustering of quantified phosphopeptides in CCRT resistant and sensitive cohort.



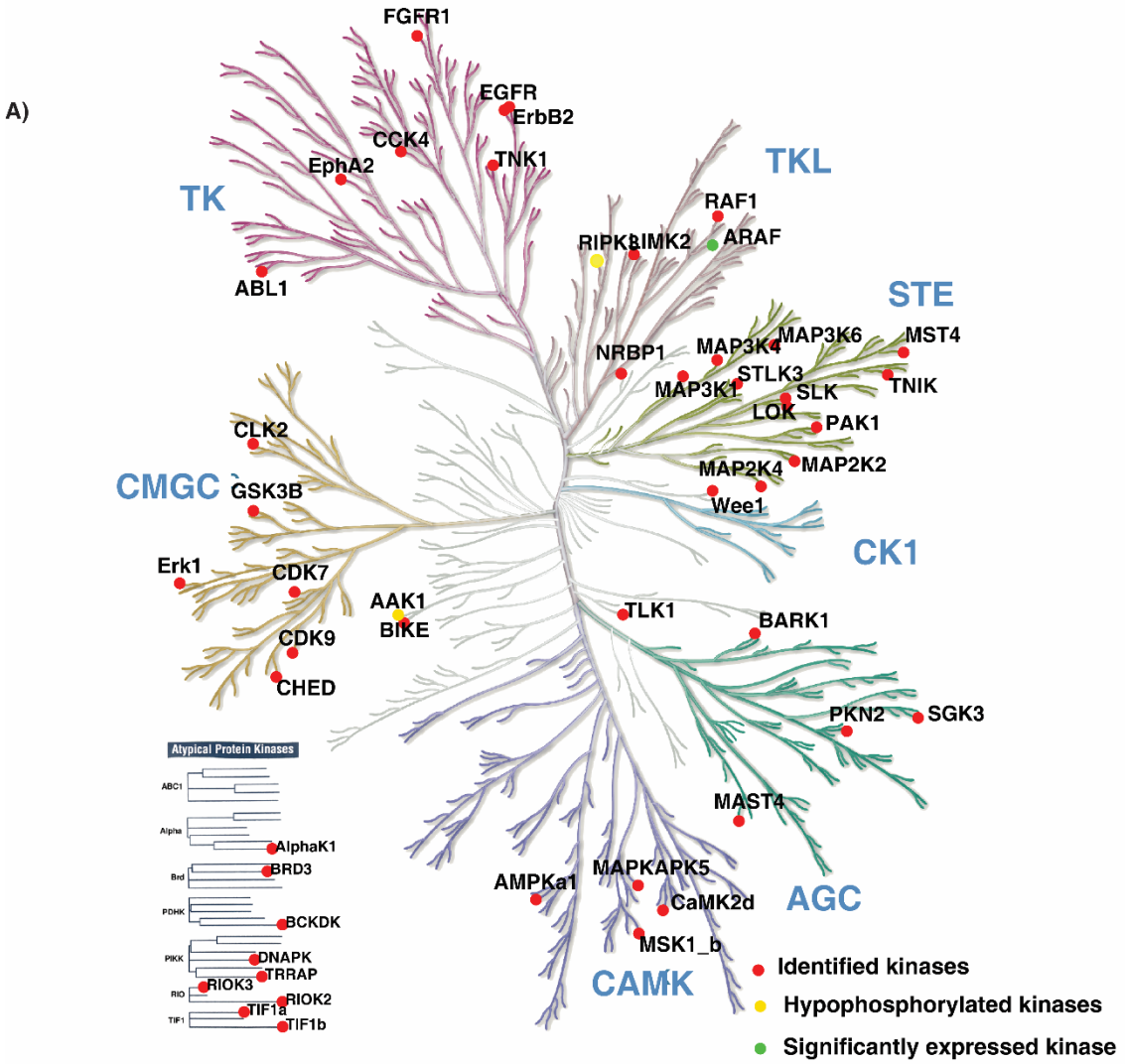
Supplementary figure 3: Immunohistochemitry of phosphorylated SMC1A in repsonders and non responders. Non-repsonders showing hyperphosphorylation of SMC1A.

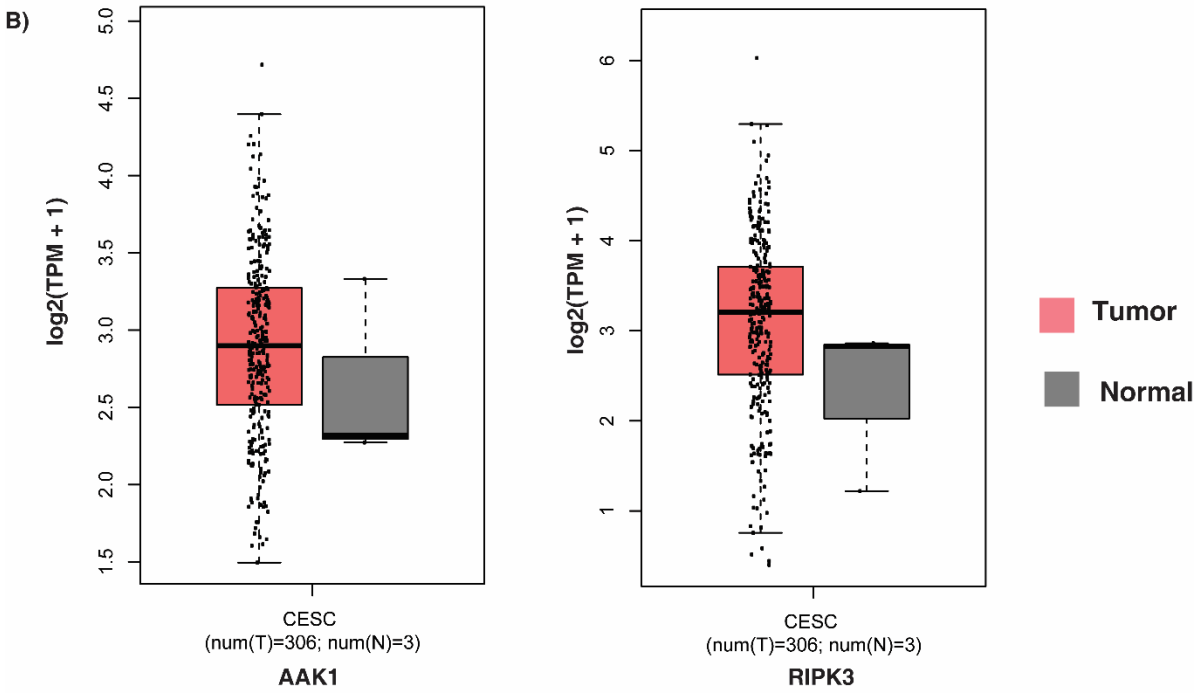


Supplementary Figure 4: GO-term of differentially phosphorylated proteins in non-repsonders. Data was analysed using webgestalt.

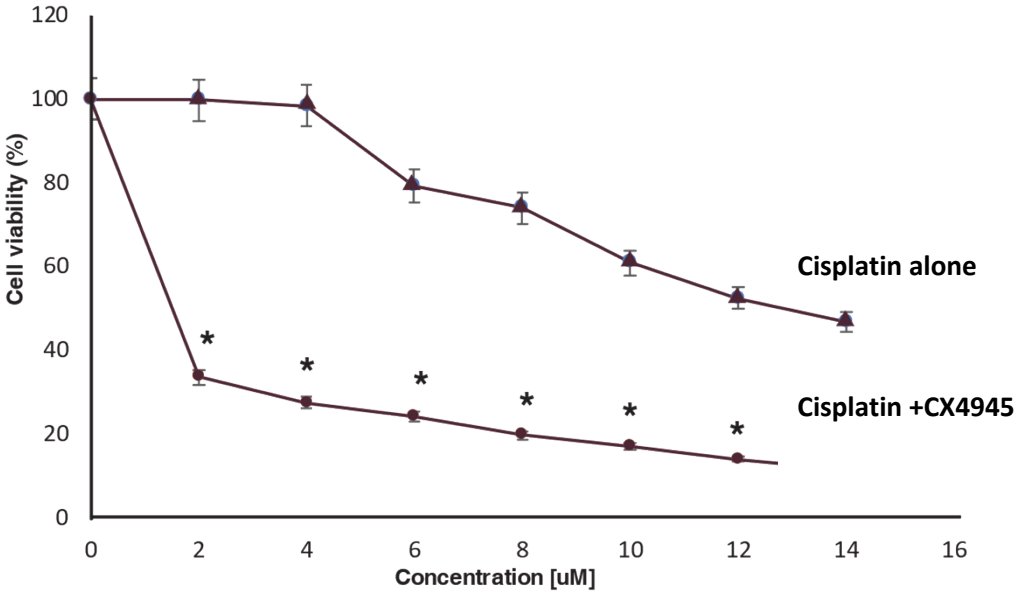


Supplementary Figure 5: (A) Kinome map of kinases identified in our data. Identified kinases are highlighted in red. Kinasses which are significantly phosphorylated in non-repsonders are highlighted in green. Kinases which are hypophosphorylated in non-responders are highlighted in yellow. (B) Box plot representing the differential expression of RIPK3 and AAK1 in tumor and normal samples in cervical TCGA data.


A)
FGFR1
EGFR
ErbB2
CCK4
EphA2
TNK1
TK
TKL
RAF1
RIPK3
IMK2
ARAF
ABL1
STE
NRBP1
MAP3K4
MAP3K6
MST4
STLK3
MAP3K1
TNIK
SLK
LOK
PAK1
CLK2
MAP2K4
MAP2K2
CMGC
GSK3B
Wee1
CK1
Erk1
CDK7
AAK1
TLK1
BARK1
BIKE
CDK9
CHED
PKN2
SGK3
Atypical Protein Kinases
ABC1
Alpha
AlphaK1
Brd
BRD3
PDHK
BCKDK
PIKK
DNAPK
TRRAP
RIO
RIOK3
RIOK2
TIF1
TIF1a
TIF1b
MAST4
AMPKa1
MAPKAPK5
CaMK2d
AGC
MSK1_b
CAMK
Identified kinases
Hypophosphorylated kinases
Significantly expressed kinase


B)
log2(TPM + 1)
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
CESC
(num(T)=306; num(N)=3)
AAK1
log2(TPM + 1)
1
2
3
4
5
6
CESC
(num(T)=306; num(N)=3)
RIPK3
Tumor
Normal

Supplementary figure 6: CaSki treated with varying dose of cisplatin alone and varying concentration of cisplatin in combination with constant dose of CX4945.



Supplementary table 7: The Fraction of affected and corresponding CI values.

Fa	CI Value
0.05	25.3488
0.1	8.96973
0.15	4.81645
0.2	3.07936
0.25	2.17294
0.3	1.63645
0.35	1.29213
0.4	1.05849
0.45	0.89354
0.5	0.77370
0.55	0.68489
0.6	0.61826
0.65	0.56805
0.7	0.53041
0.75	0.50279
0.8	0.48359
0.85	0.47209
0.9	0.46887
0.95	0.47836
0.97	0.49029