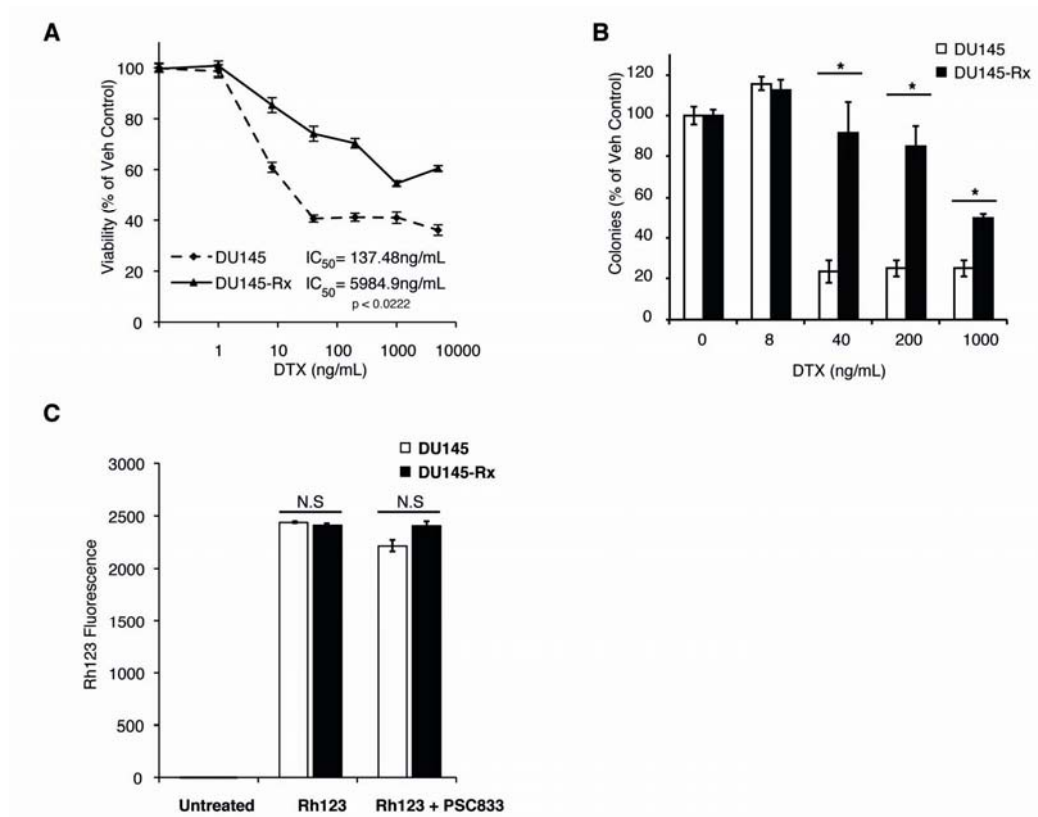


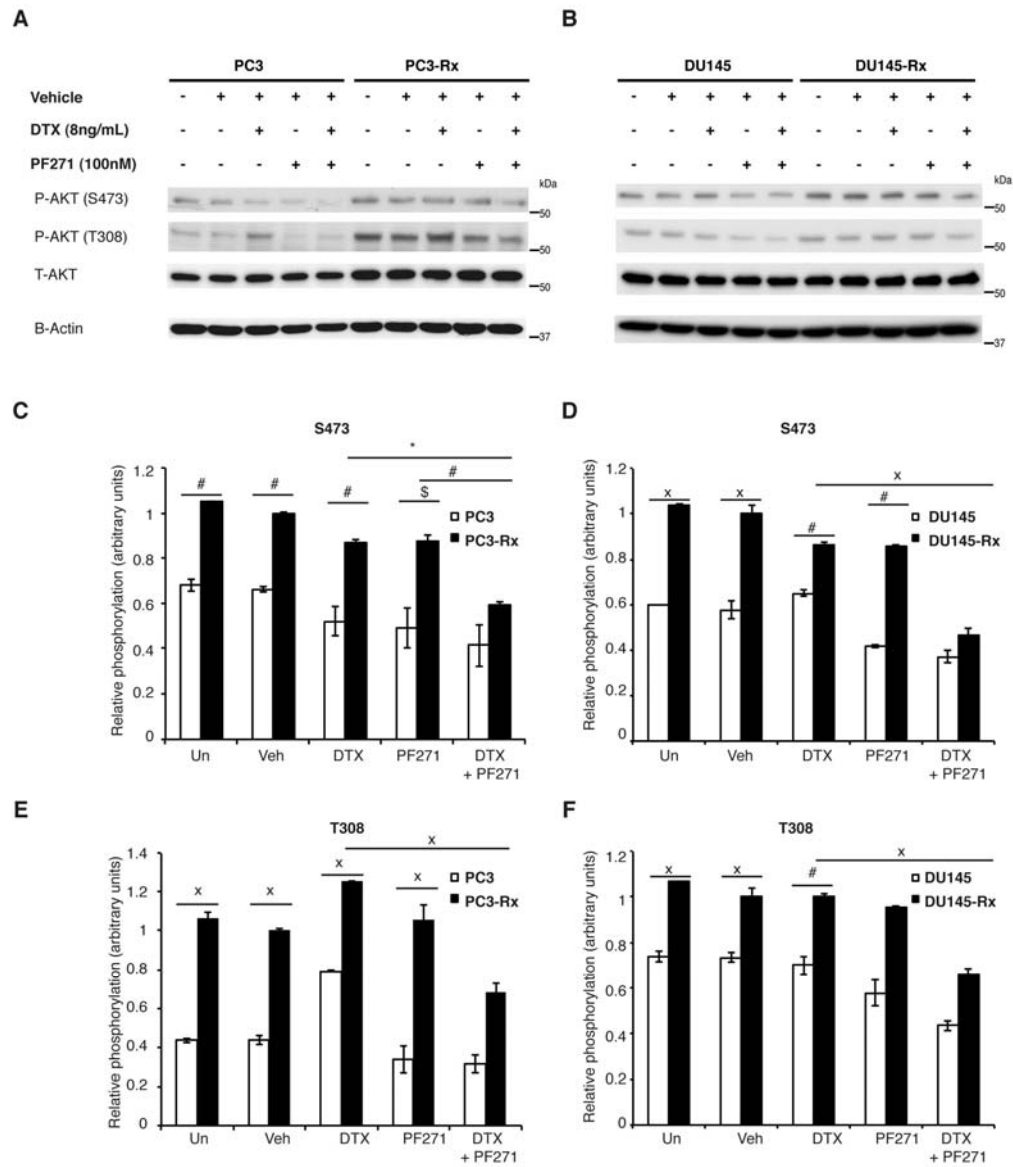
Supplementary Figure 1



Supplementary Figure 1. Validation of the Docetaxel-resistant prostate cancer cell line DU145-Rx. **A.** Dose-response curve assessing the effect of Docetaxel on cell viability. DU145 and DU145-Rx cells were treated with increasing doses of Docetaxel for 24 h. Cell viability was assessed using the trypan blue exclusion assay and is expressed relative to vehicle (saline) control. Results are shown as mean \pm SEM for each data point in three independent experiments with triplicate samples. IC_{50} values (Docetaxel concentration required to inhibit 50 % of viability) for DU145 and DU145-Rx cells are indicated. **B.** Effect of Docetaxel treatment on colony forming ability. Cells were treated with increasing doses of Docetaxel for 3h. Colonies were counted using crystal violet dye and are expressed relative to vehicle (saline). Results are shown as mean \pm SEM for each data point in three independent

experiments with triplicate samples. * indicates $p < 0.001$. C. P-glycoprotein activity. Rh123 fluorescence in DU145 and DU145-Rx cells was measured with/without P-glycoprotein inhibitor, PSC833, using a flow cytometer.

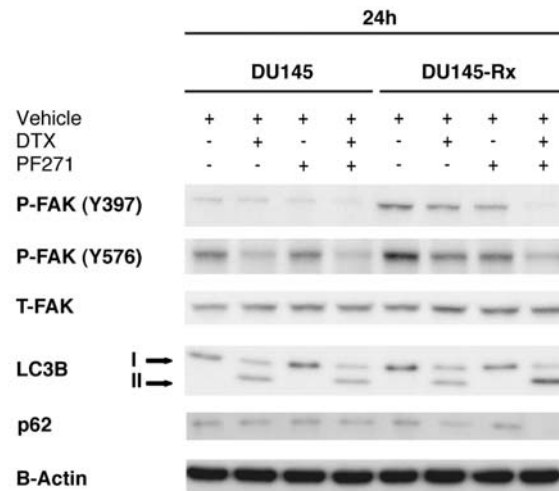
Supplementary Figure 2



Supplementary Figure 2. Regulation of Akt phosphorylation in Docetaxel-sensitive and -resistant prostate cancer cells. **A & B.** Immunoblotting analysis. PC3/PC3-Rx cells (A) and DU145/DU145-Rx cells (B) were treated with/without Docetaxel (DTX; 8 ng/mL) +/- PF-00562271 (PF271; 100 nM) for 24 h. Total cell lysates were immunoblotted for phospho-Akt (S473 and T308) and total-Akt, and β -Actin (loading control). Molecular size markers are indicated in kDa. **C-F.** Quantitative analysis of

the immunoblots described above using ImageJ software. Akt phosphorylation at S473 and T308 was normalized for total Akt levels and is expressed relative to vehicle (saline and DMSO) controls. Results are shown as mean \pm SEM for each data point in three independent experiments with triplicate samples. * indicates $p < 0.05$, \$ $p < 0.01$, # $p < 0.001$, x $p < 0.0001$.

Supplementary Figure 3



Supplementary Figure 3. Co-treatment-induced cell death in Docetaxel-resistant DU145-Rx cells is associated with enhanced autophagy. The effect of individual and combination treatments on the induction of autophagy. Cells were treated with Docetaxel (DTX; 8 ng/mL) +/- PF-00562271 (PF271; 100 nM) for 24 h. Total cell lysates were immunoblotted as indicated.

Supplementary Table 1

Tyrosine Phosphosites	PC3-Rx	DU145-Rx
ZDHHC5_533	3.76485	1.2198
ACTN1_246	3.5113	1.675
RIN1_36	3.3911	1.032145
PTPRA_798	2.73045	1.0337
PTPRE_696	2.526	1.06575
VIM_61	2.22265	1.2655
TYK2_292	2.0611	1.18995
AXL_702	2.0325	1.2889
ATP1A1_260	1.9732	1.234455
HIPK3_359	1.9453	1.375
VIM_53	1.9059	1.34105
FAK1_397	1.6519	1.87105
TNK2_518	1.83875	1.0778
FAK1_577	1.5129	1.7876
FAK1_576	1.41925	1.75895
ADAM9_815	1.7201	1.3251
PI3KR1_467	1.6804	1.1805
PDLIM5_251	1.6743	1.6274
ELMO2_48	1.5418	1.07755
FAK1_861	1.4032	1.0989
BCAR1_306	1.0114	1.4028
BCAR1_287	1.05632	1.32085
ANXA1_316	1.1139	1.30765
BCAR1_234	1.23415	1.29395
BCAR1_128	1.2938	1.0574
BCAR1_249	1.1481	1.2865
BCAR1_267	1.20205	1.2786
PKP4_478	1.25385	1.1502
MAPK12_185	1.2437	1.0776
PAX_88	1.23495	1.05035
PAX_118	1.21945	1.23105
RPS2_133	1.2165	1.031
CAV1_14	1.15535	1.21375
MAPK14_182	1.1416	1.20475
SNRNP70_126	1.11525	1.184
GSK3B_216	1.015415	1.1663
EPHA2_594	1.0408	1.03405
CDK1_15	0.991575	0.99219
DYRK1A_321	0.88669	0.872685
SHB_268	0.837915	0.996385
CAM1_100	0.794805	0.997585
YES_426	0.8605	0.761235
CRKL_132	0.7502	0.82728
MPZL1_263	0.75006	0.85452
EPHA2_772	0.737915	0.820075
YES_222	0.72536	0.77778

G6PD_401	0.72367	0.807545
PRP4_849	0.690765	0.89307
ERRFI1_394	0.67804	0.70489
ITGB1_783	0.663315	0.985495
EEF1A2_141	0.65913	0.77832
TLN1_25	0.65098	0.981715
YES_194	0.62353	0.9643
CBL_674	0.95626	0.60014
PTPN11_62	0.587415	0.745105
PTPN11_63	0.587415	0.74328
RPS10_12	0.56381	0.918455
ENO2_44	0.56039	0.900185
SHC1_428	0.49403	0.823045
ANXA1_39	0.45867	0.6746
CDK1_19	0.45554	0.86846
ANXA2_24	0.43508	0.97286
PTTG1IP_174	0.416035	0.621475
ANXA2_238	0.37715	0.93855
CTNND1_96	0.35895	0.82208
YES_446	0.3187	0.660515
GAB1_259	0.228745	0.923245
FLNB_2533	0.22776	0.87771
RFFL_34	0.218395	0.837535
LYN_194	0.15131	0.92987
LYN_397	0.12911	0.625395
PRKCD_334	0.10182	0.42766
CDCP1_707	0.088868	0.545705
PRKCD_313	0.0704005	0.796845
GAB1_689	0.03412	0.72159

Supplementary Table 1. SILAC ratios of up- or down-regulated tyrosine phosphorylation sites found in both PC3-Rx and DU145-Rx cell lines, in comparison to their parental cells, PC3 and DU145, respectively. SILAC ratio of 1 indicates no change, > 1 indicates upregulation and < 1 indicates downregulation.