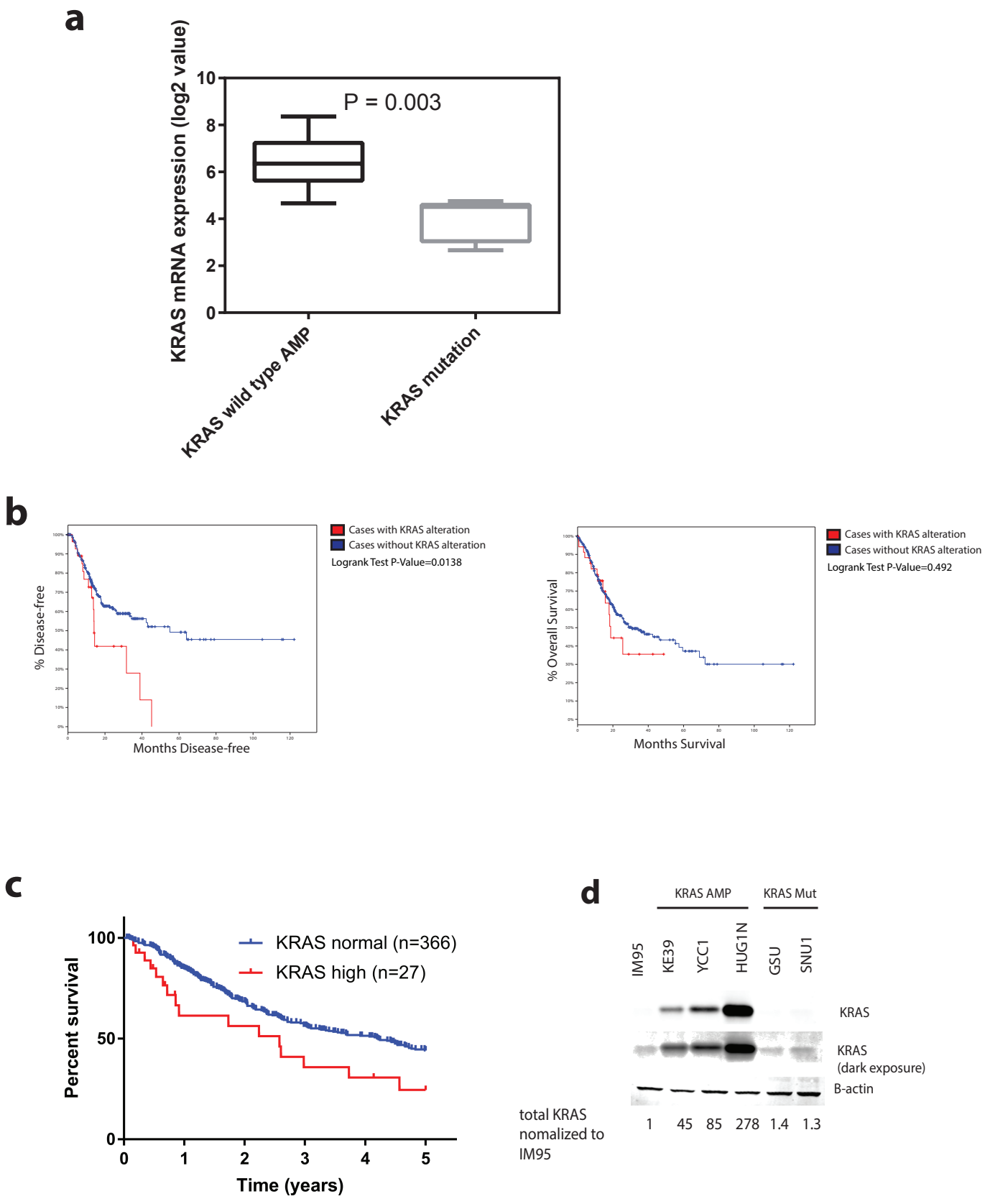
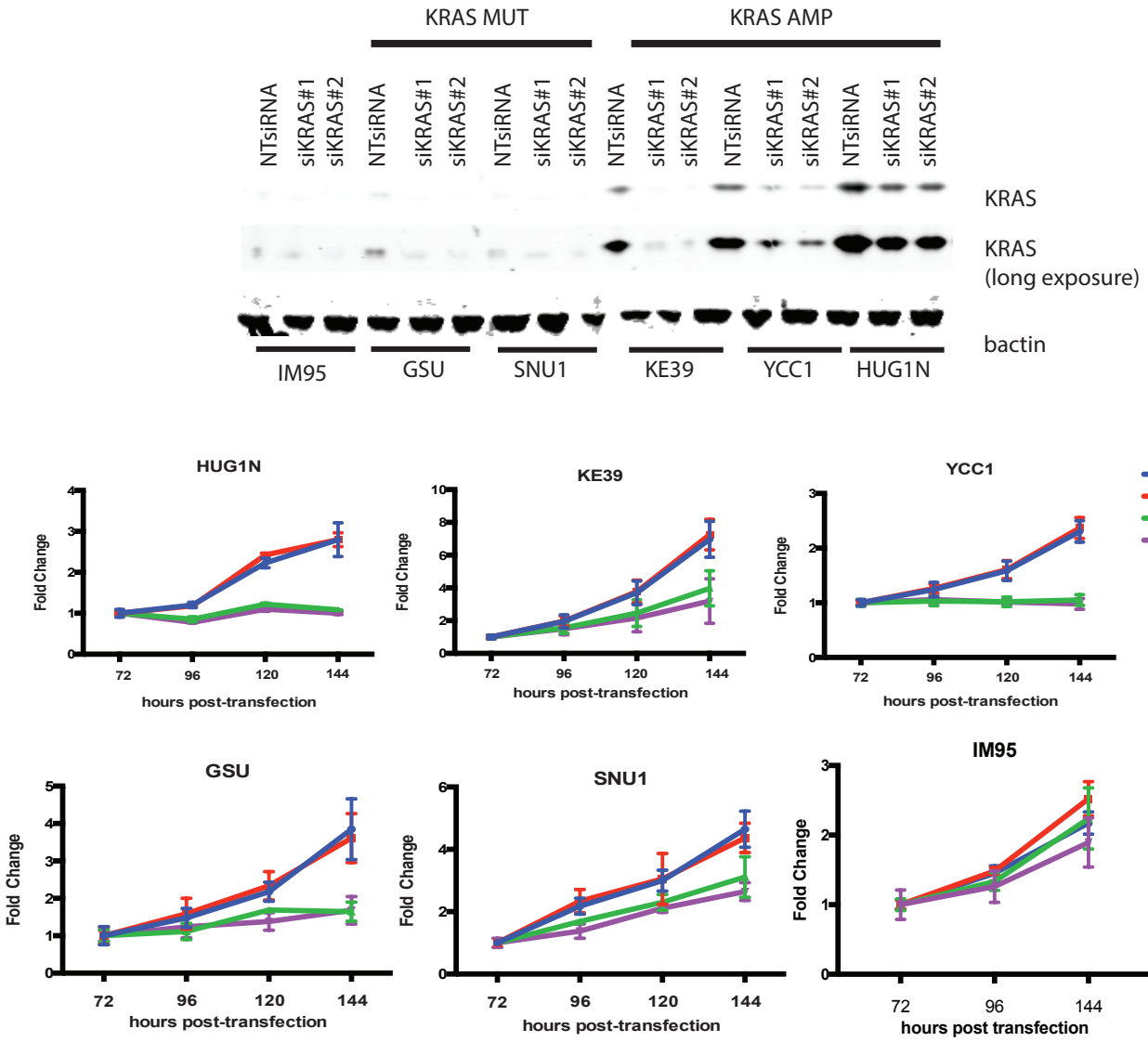
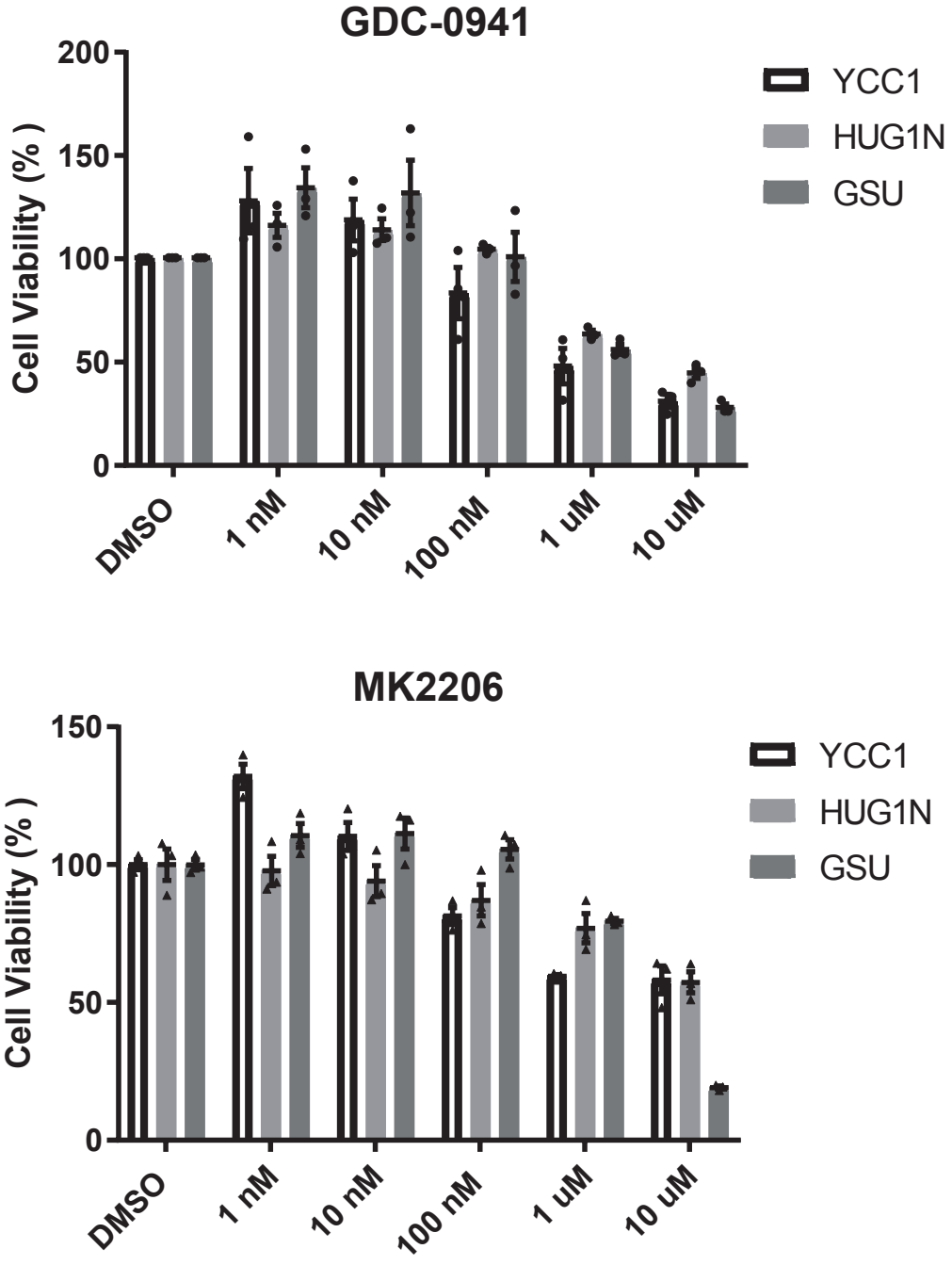
Supplementary Figure 1



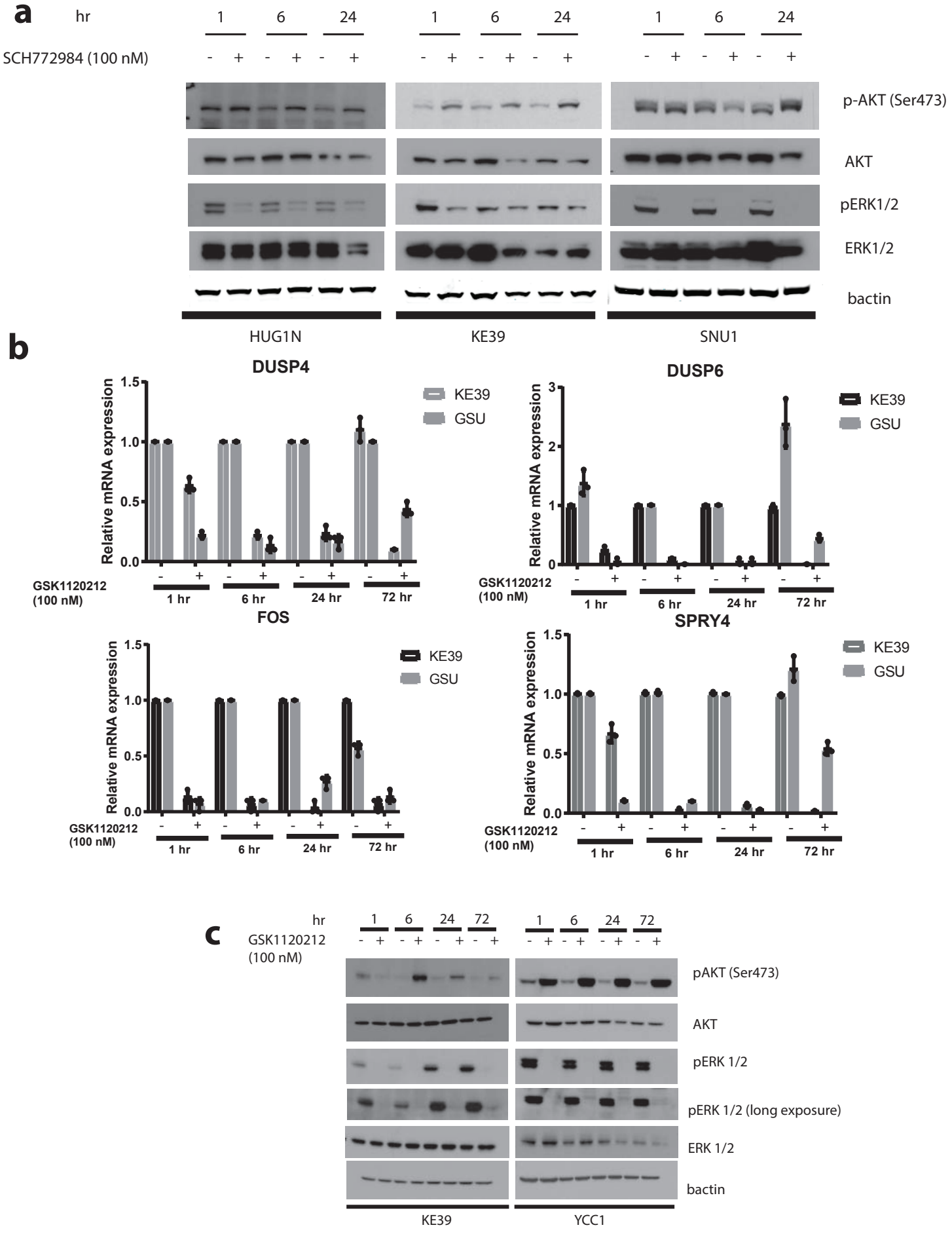
Supplementary Figure 2



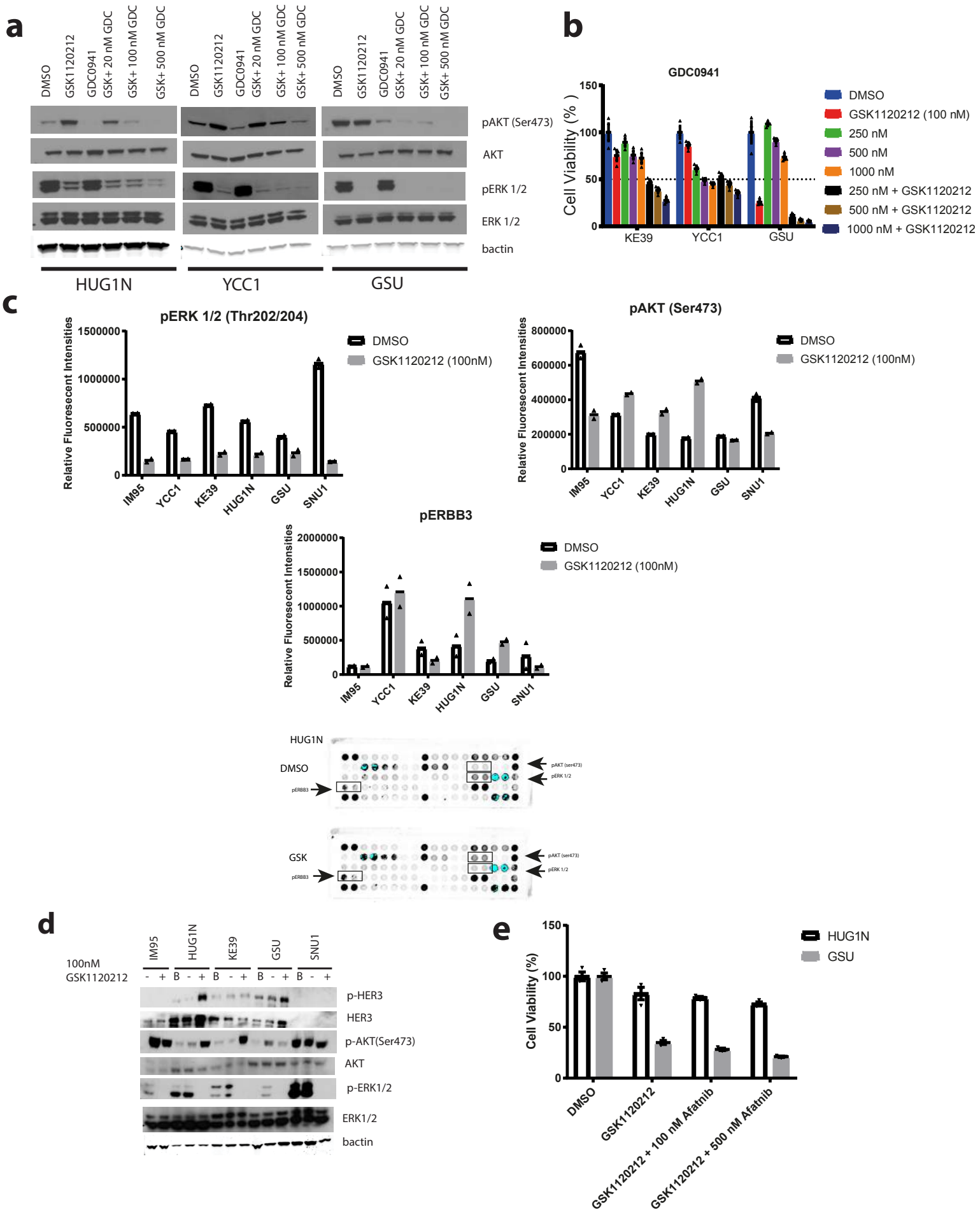
SUPPLEMENTARY FIGURE 3



Supplementary Figure 4



Supplementary Figure 5



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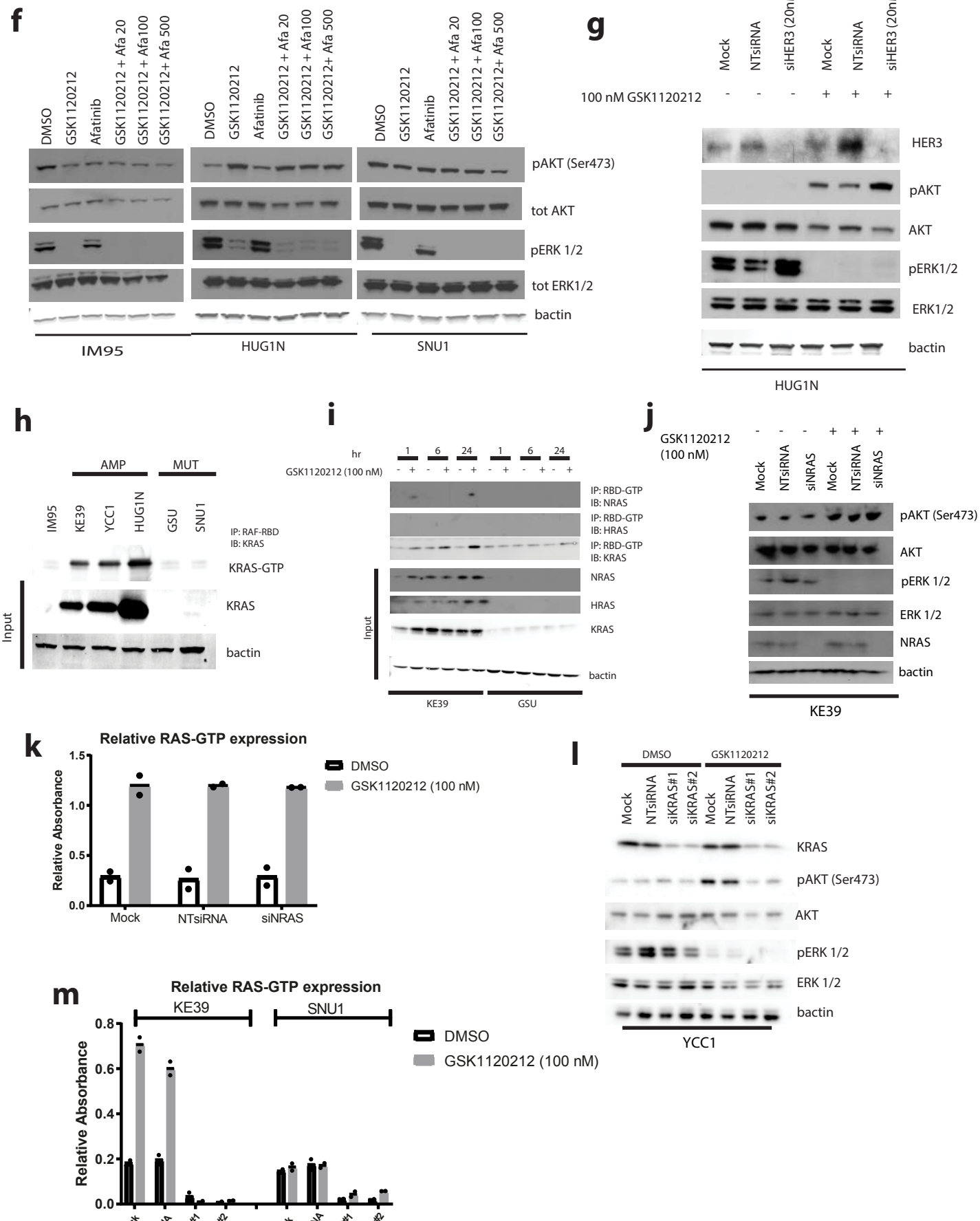
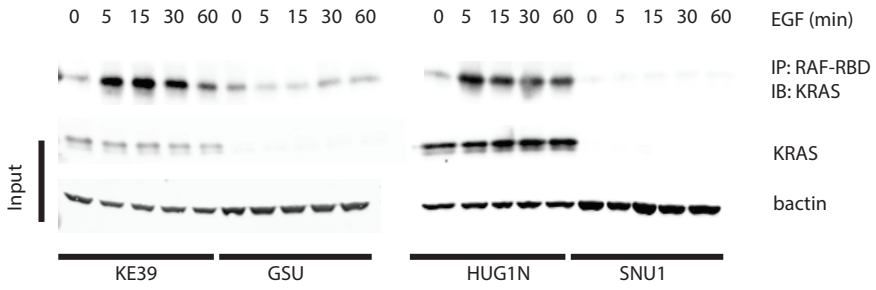


SUPPLEMENTARY FIGURE 6

a



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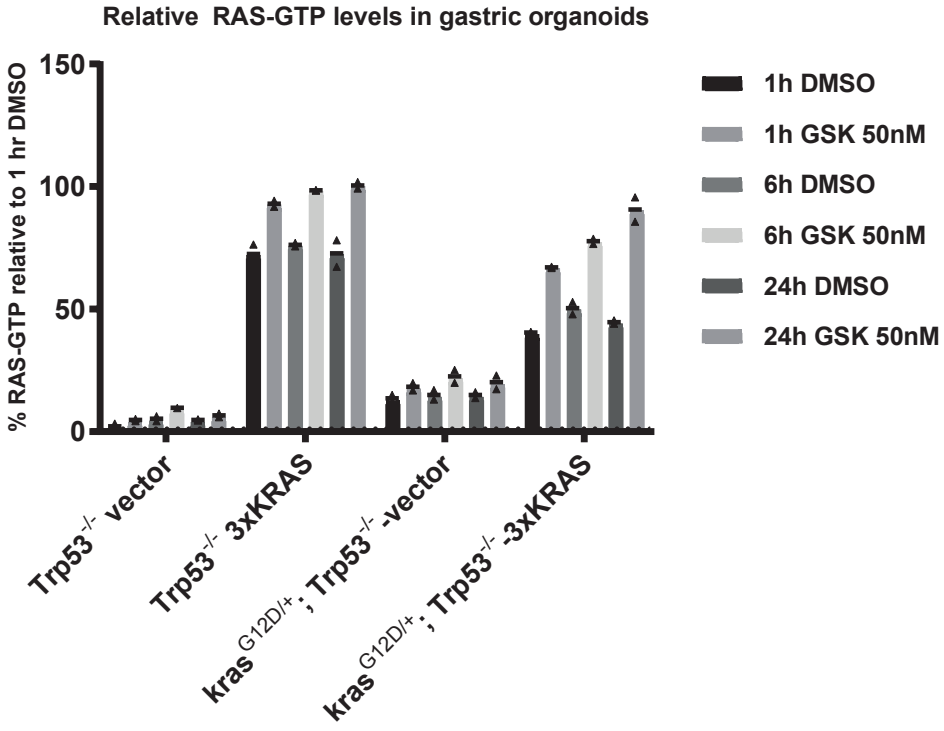
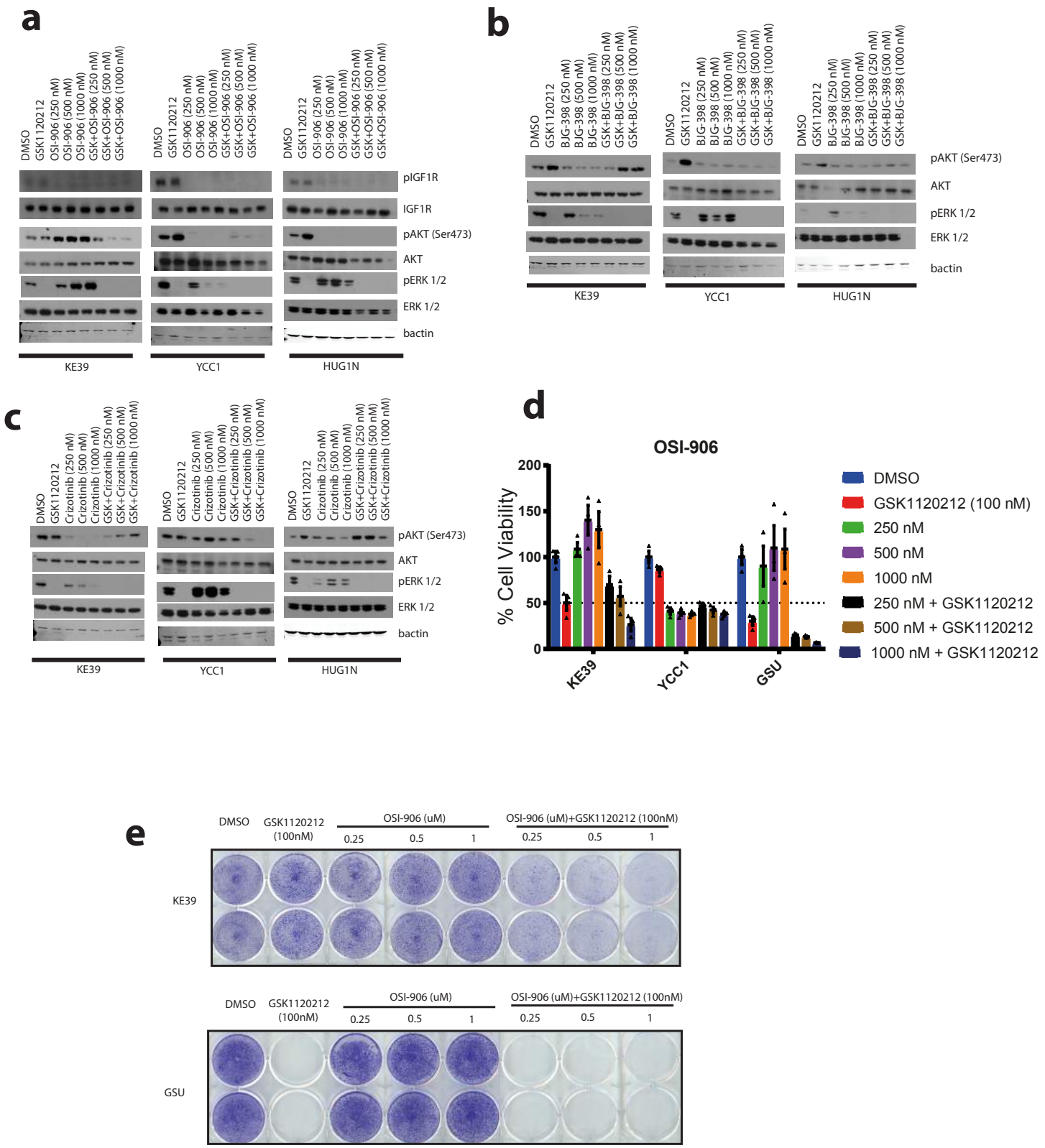
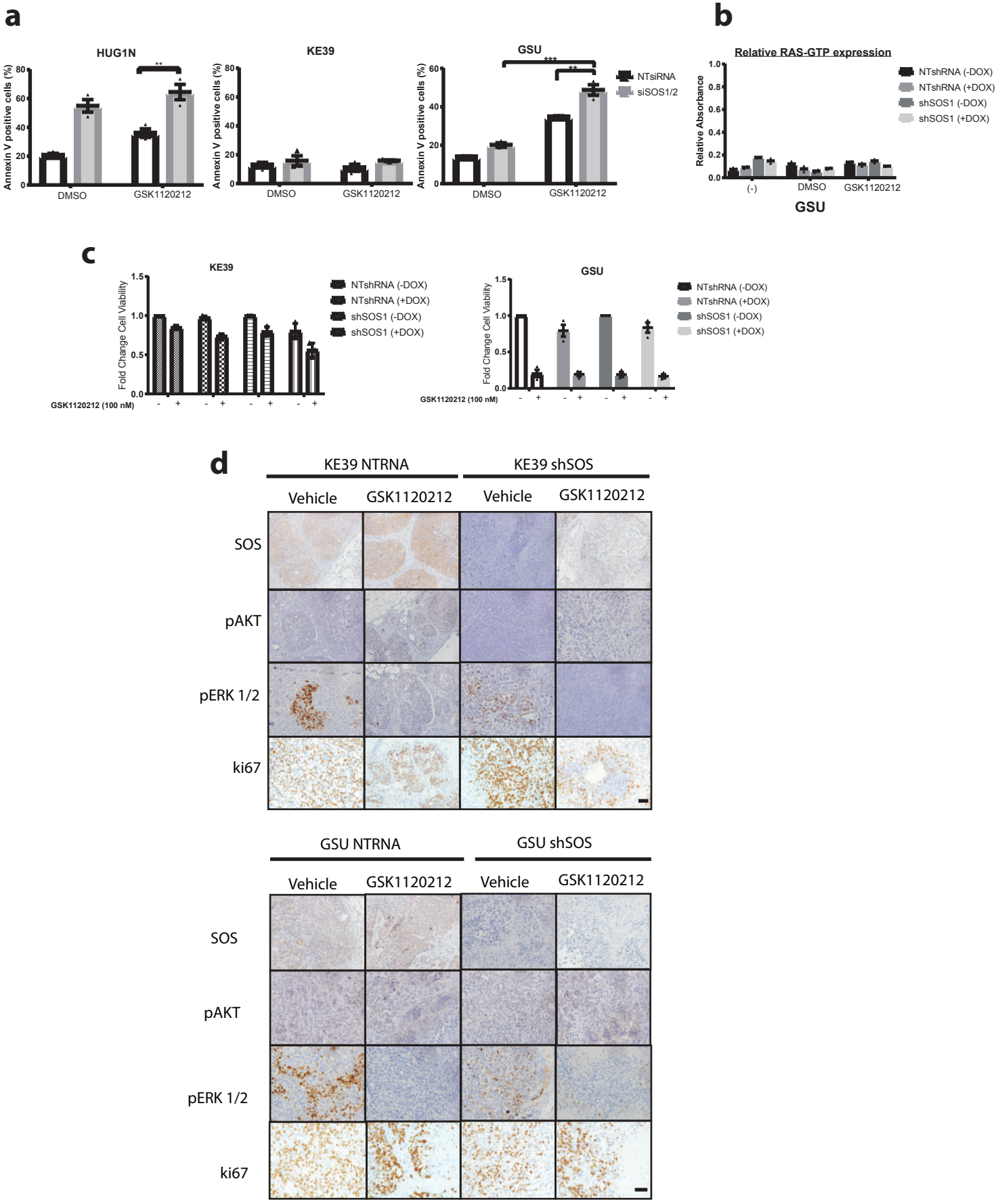


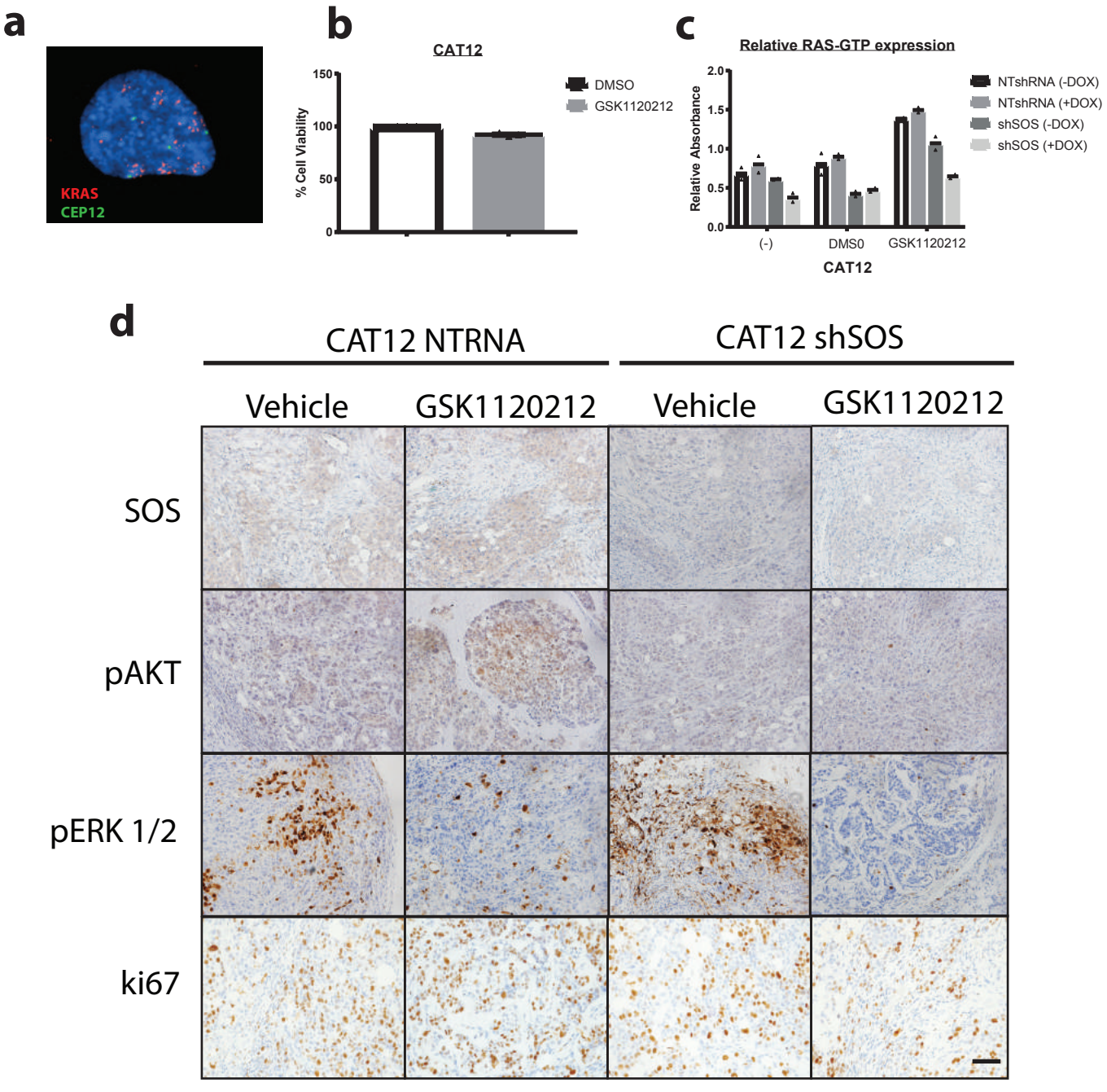
Supplementary Figure 7



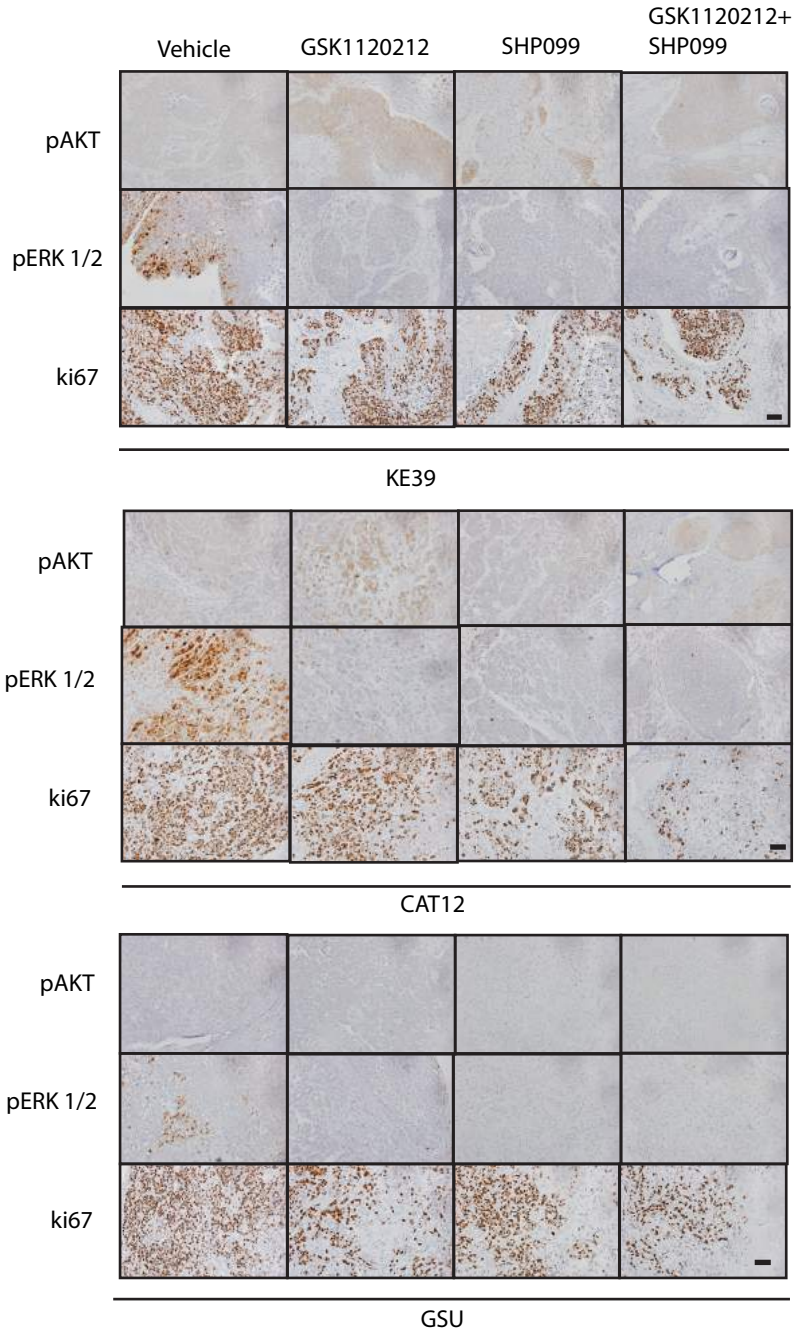
Supplementary Figure 8



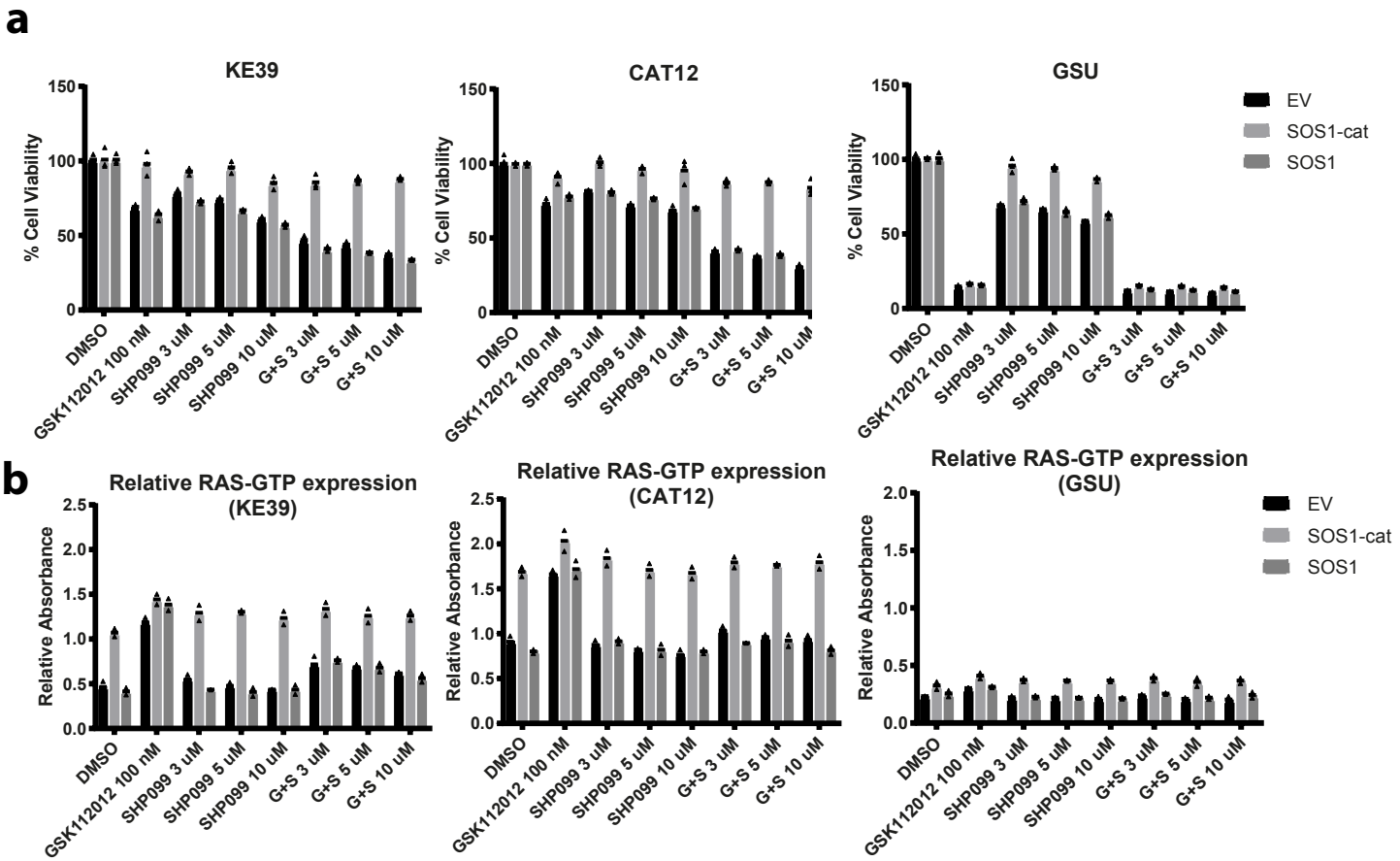
Supplementary Figure 9



SUPPLEMENTARY FIGURE 10



SUPPLEMENTARY FIGURE 11



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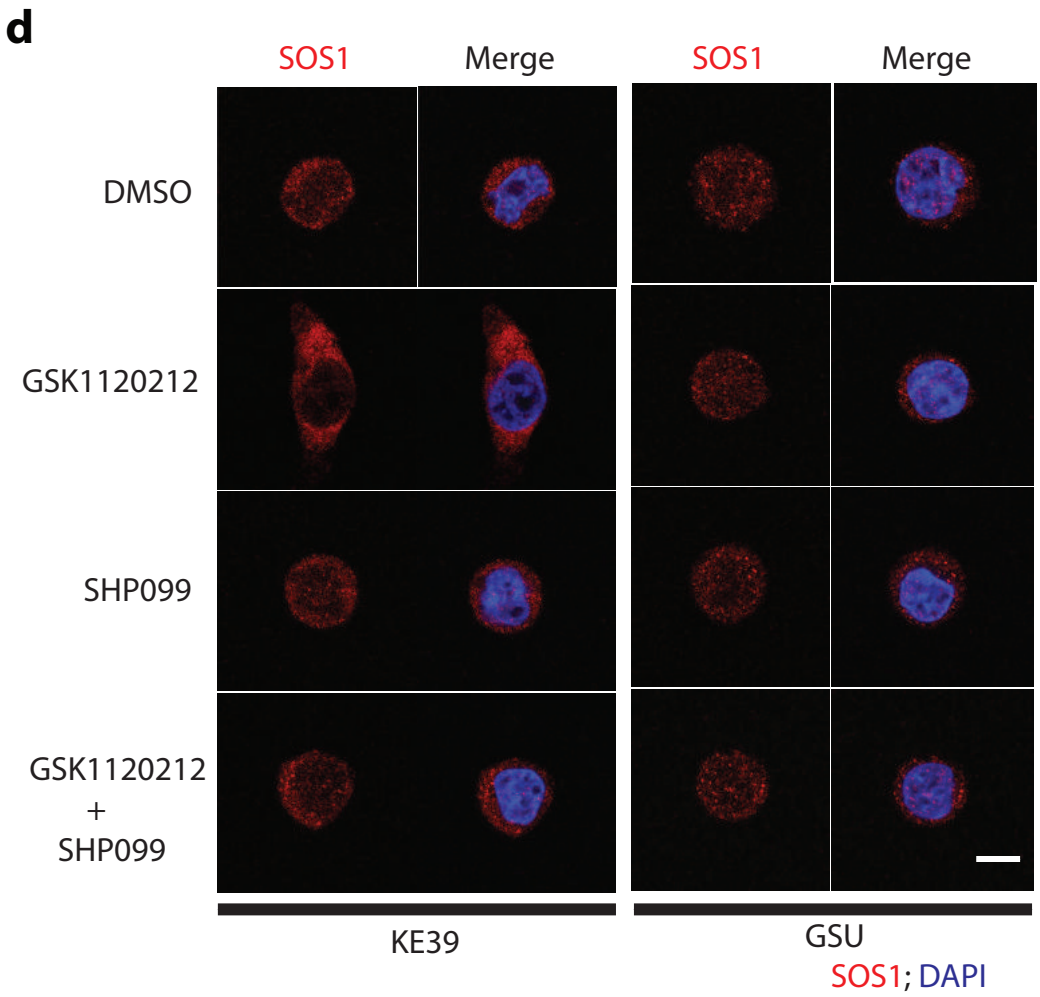
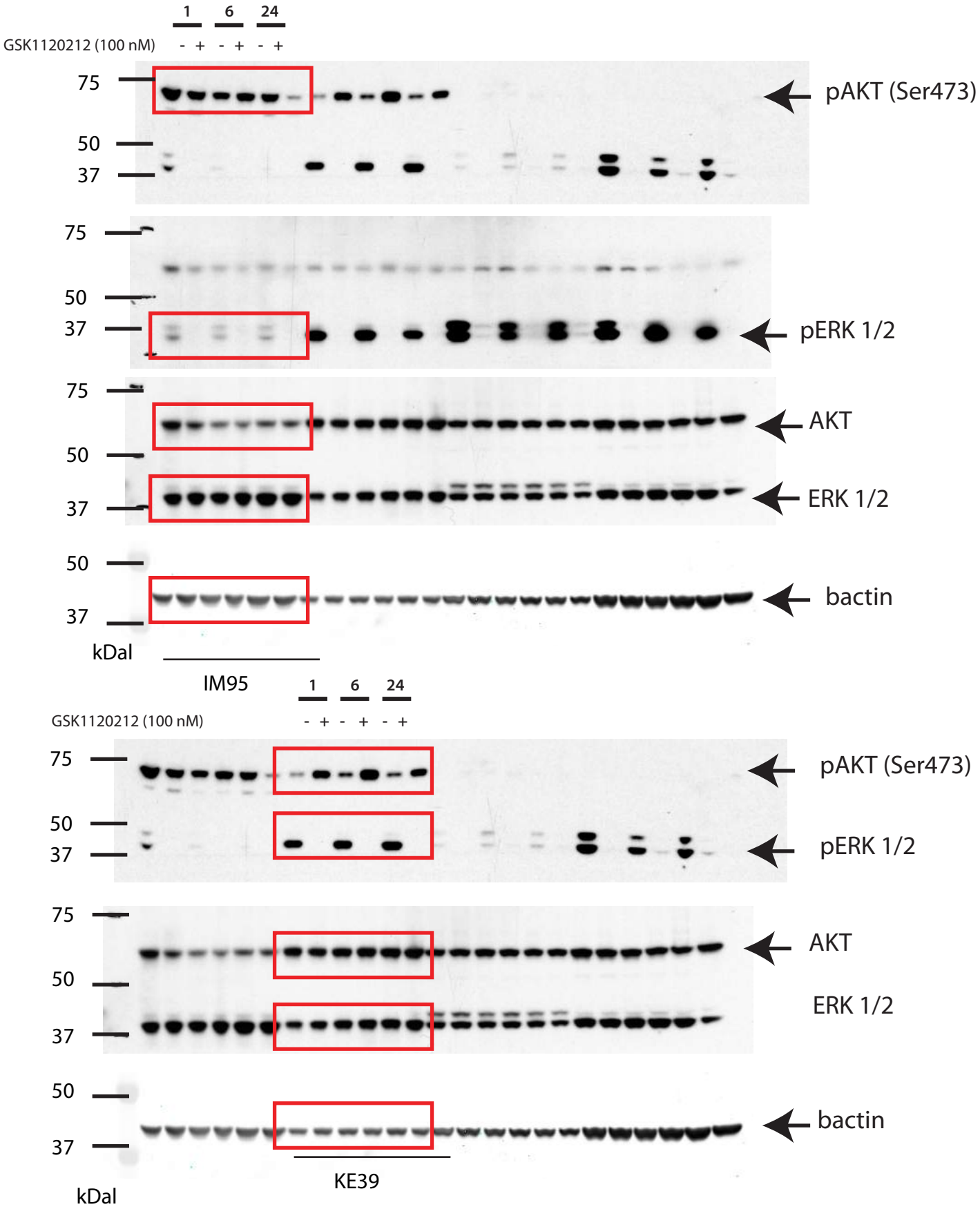


SUPPLEMENTARY FIGURE 12

From Figure 2c



SUPPLEMENTARY FIGURE 12

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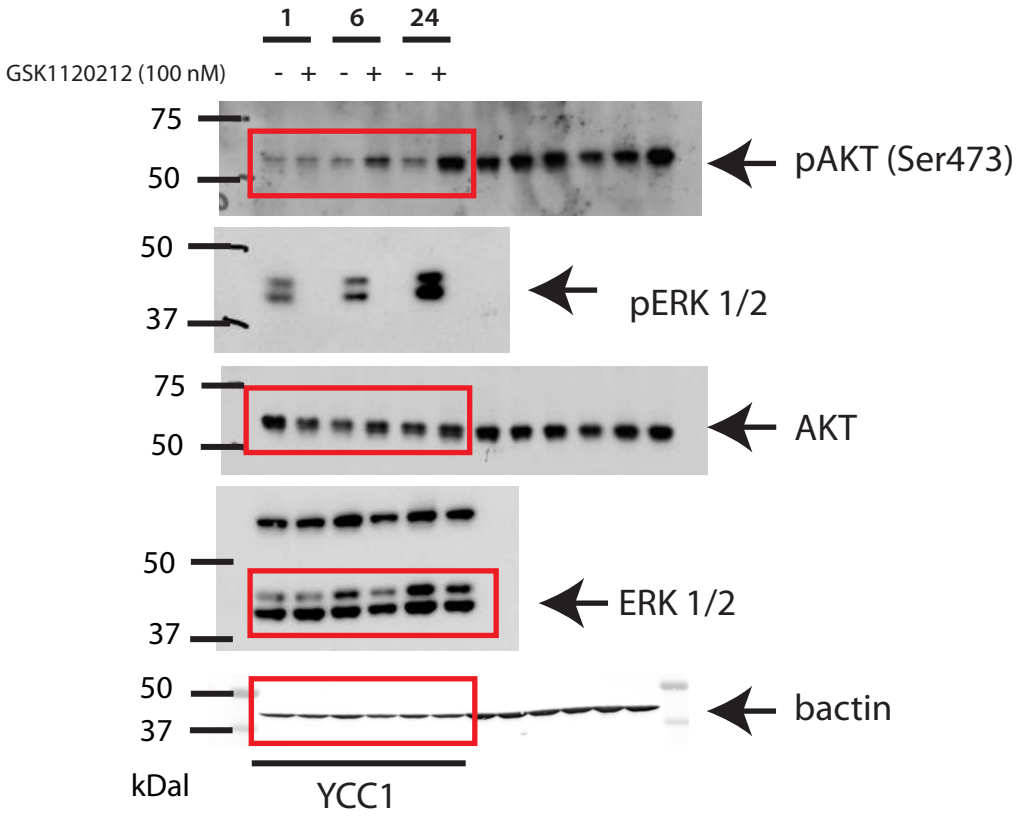
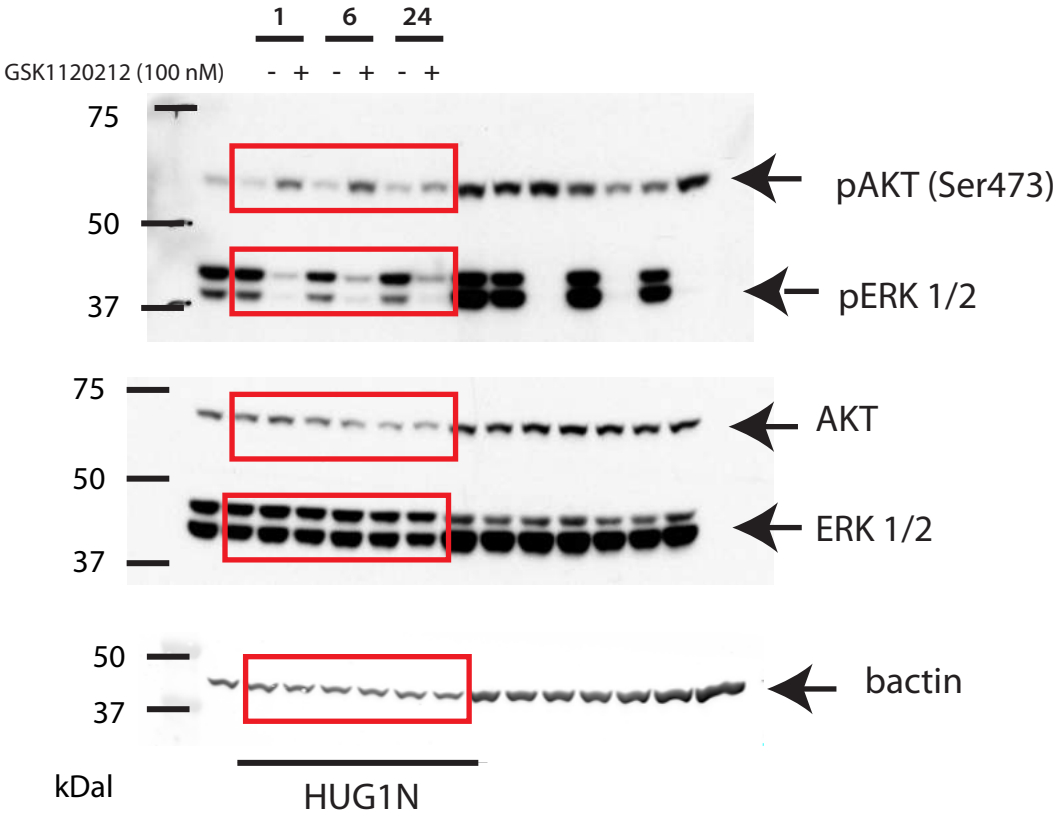
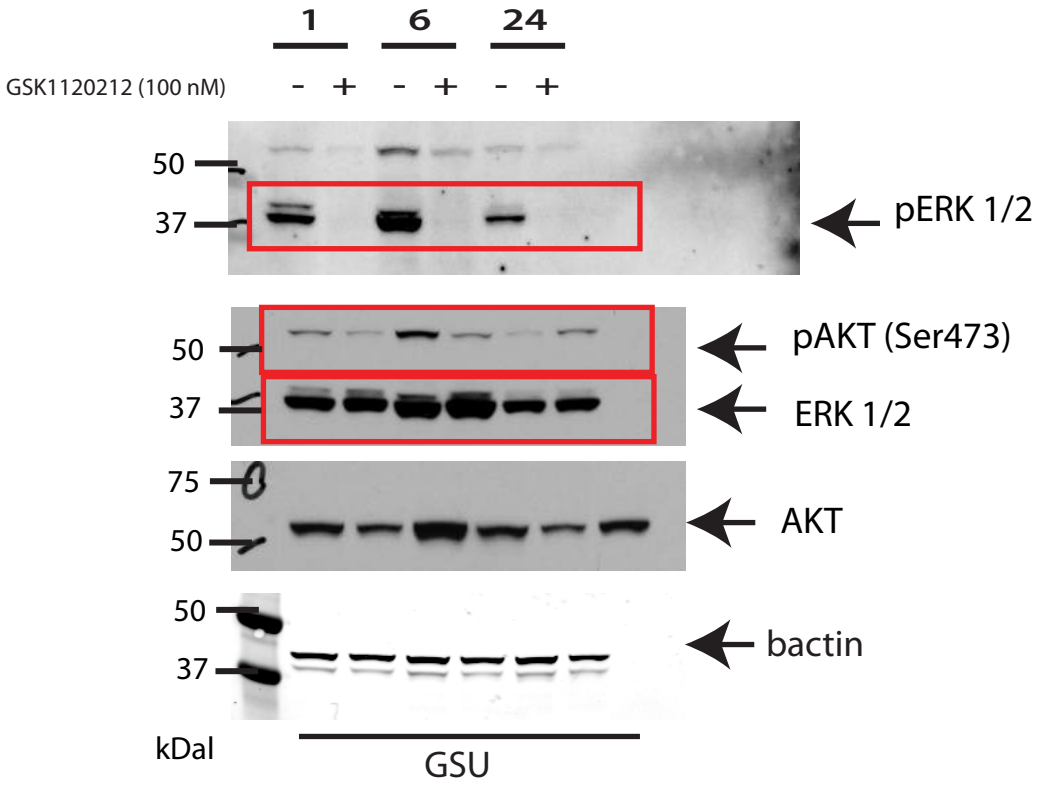
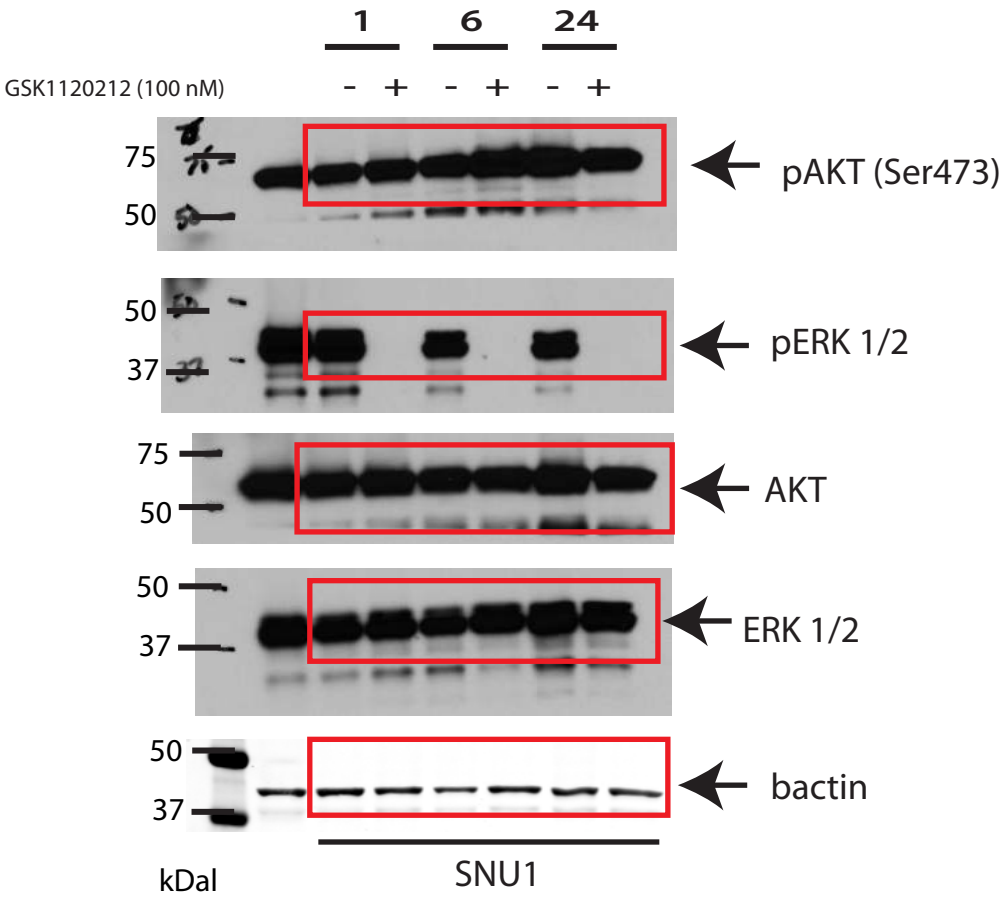




SUPPLEMENTARY FIGURE 12

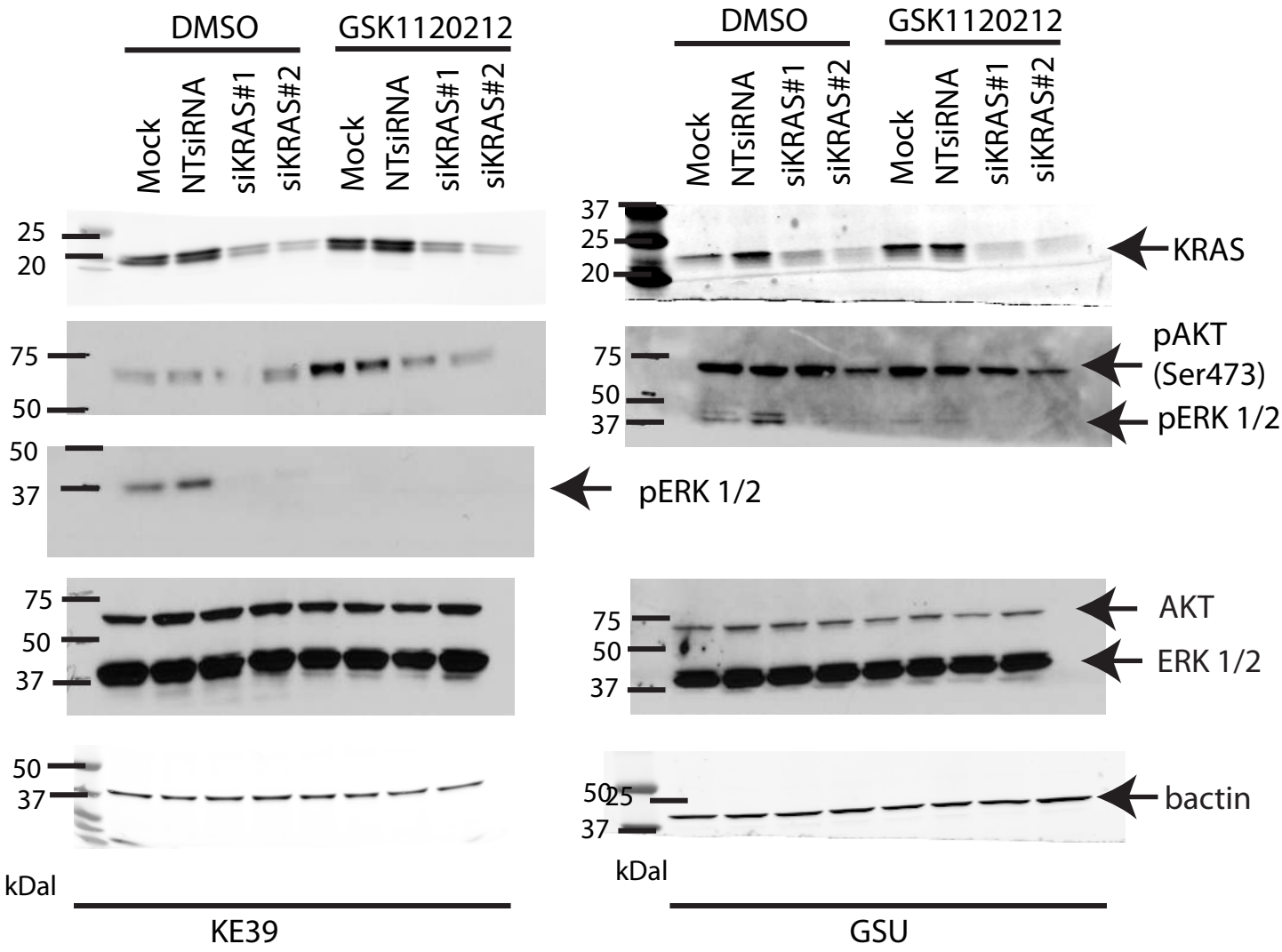
From Figure 2c (continued)



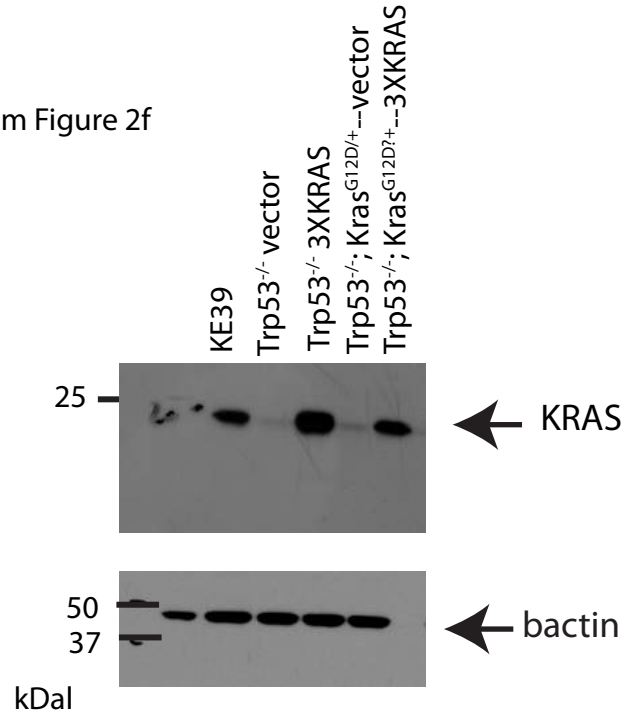


SUPPLEMENTARY FIGURE 12

From Figure 2e

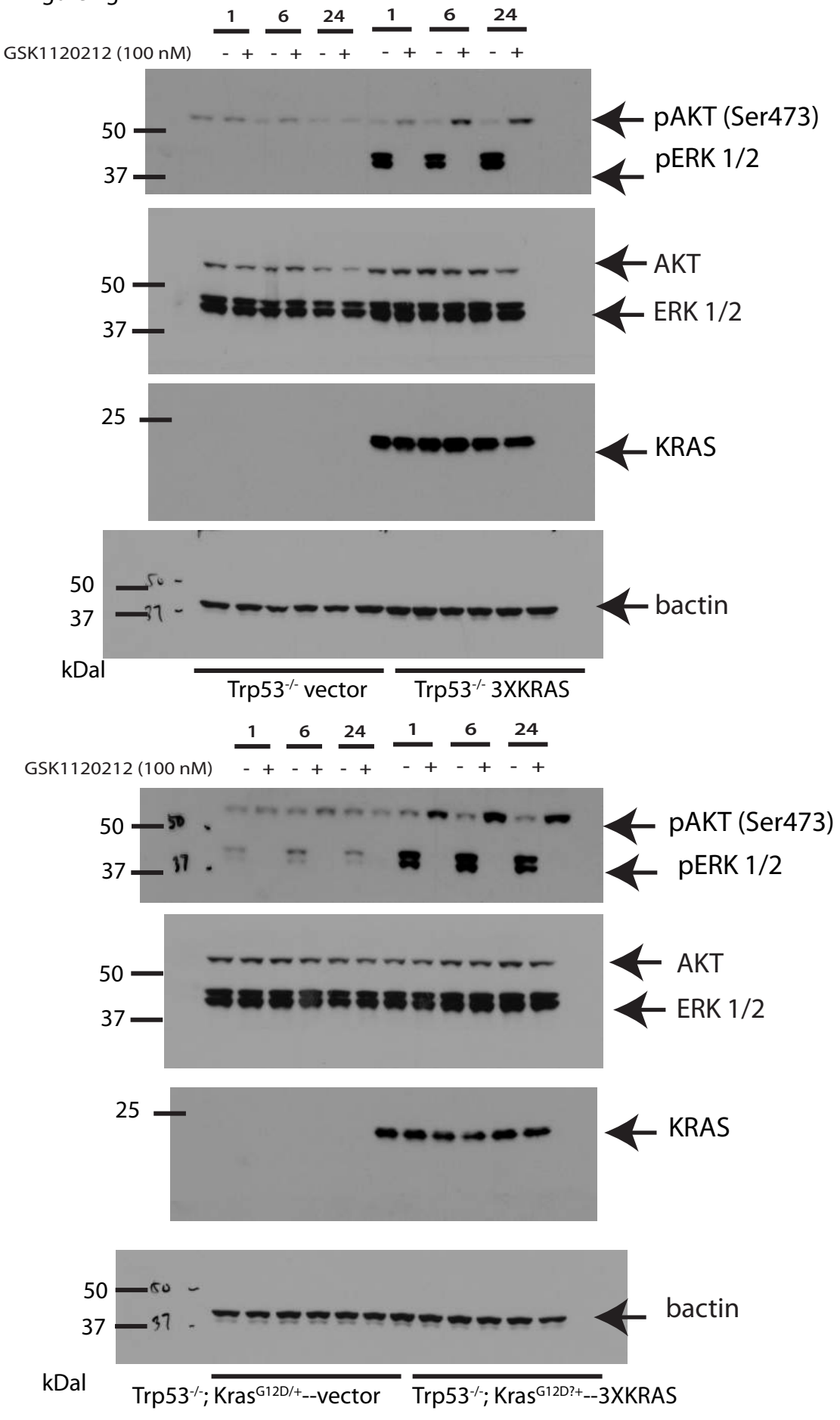


From Figure 2f



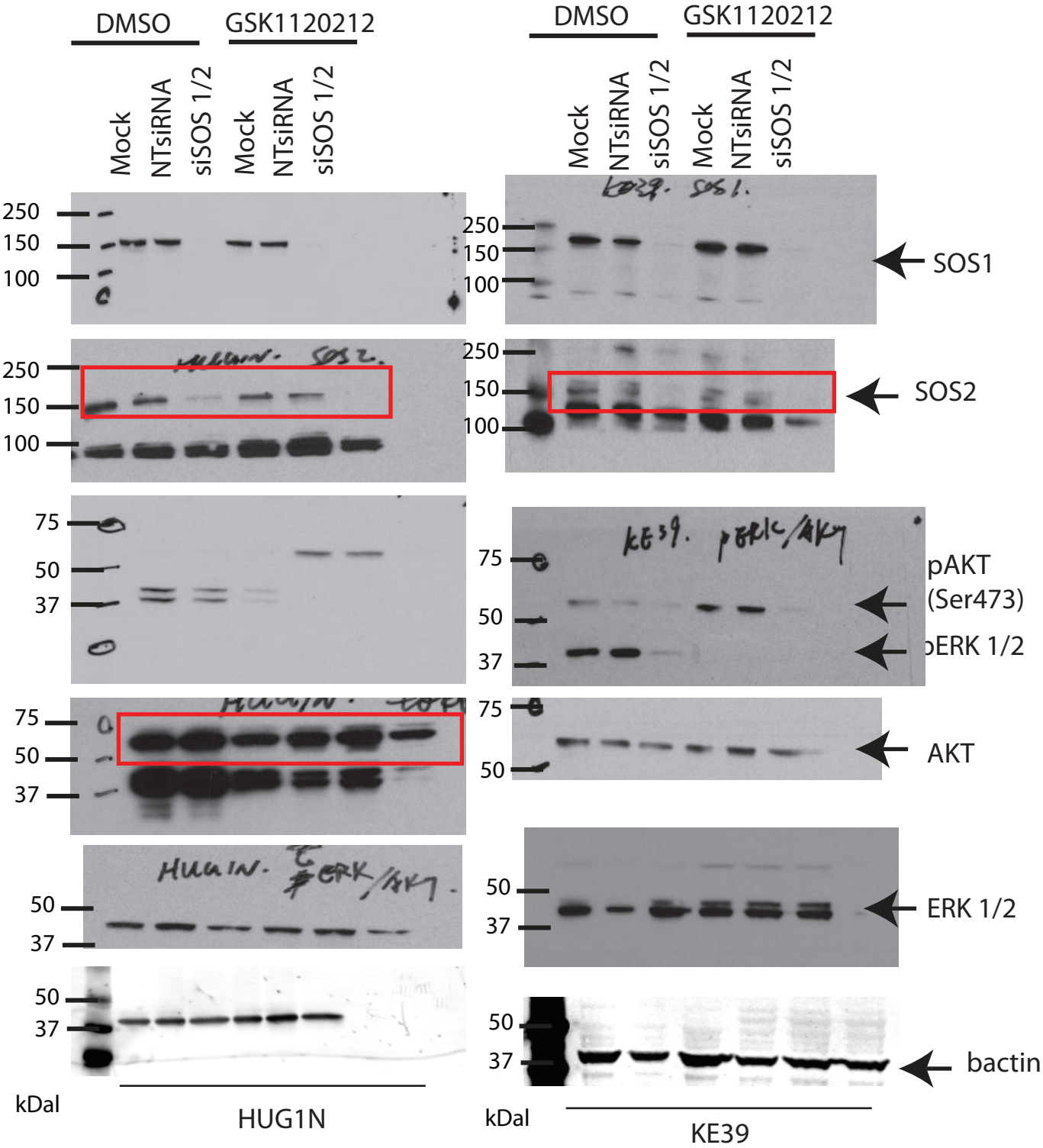
SUPPLEMENTARY FIGURE 12

Figure 2g



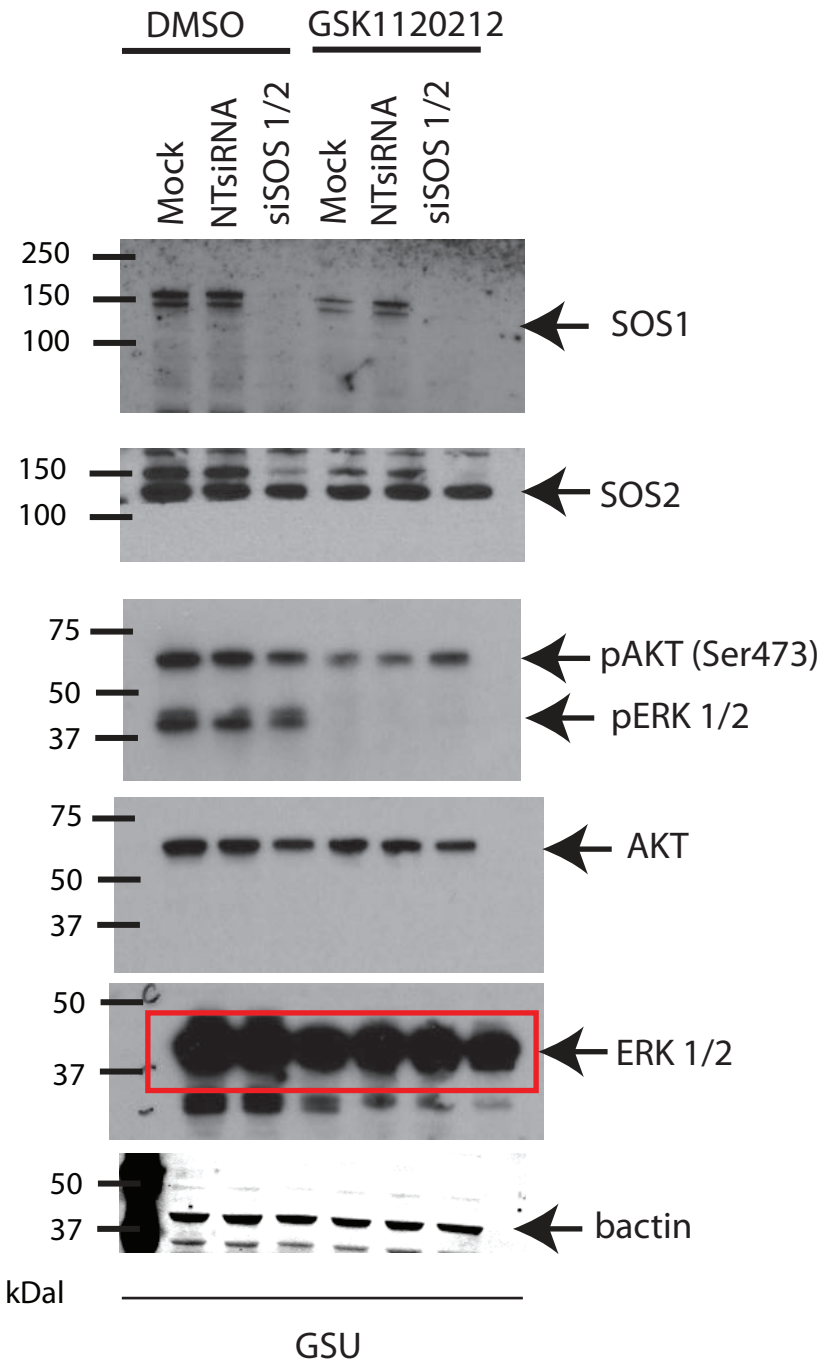
SUPPLEMENTARY FIGURE 12

From Figure 3a



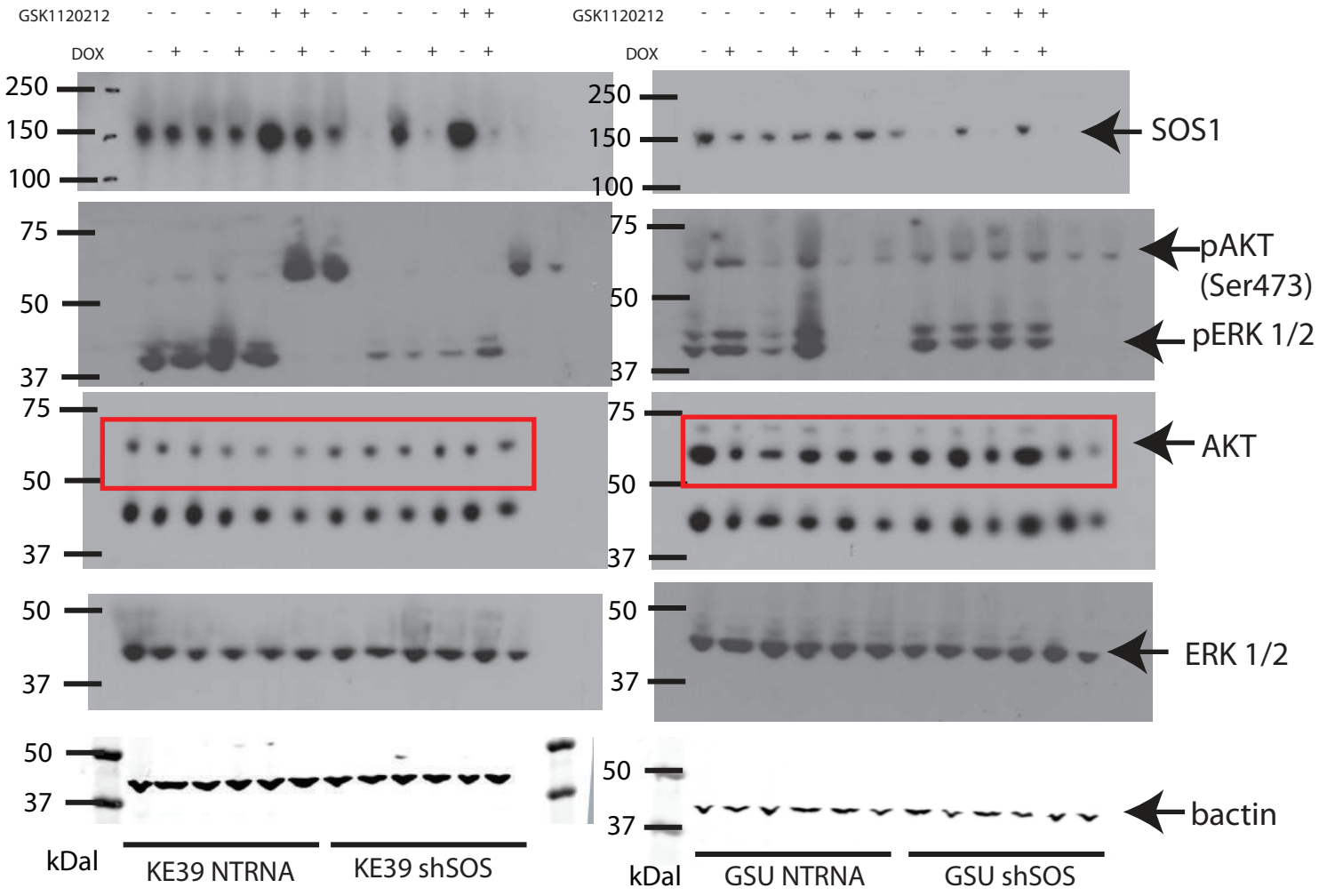
SUPPLEMENTARY FIGURE 12

From Figure 3a



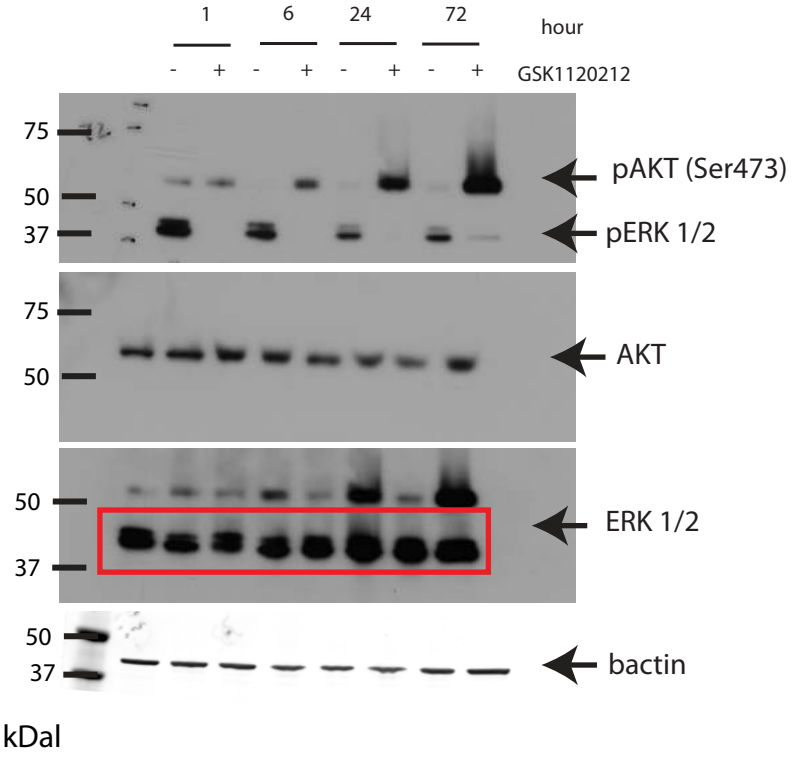
SUPPLEMENTARY FIGURE 12

From Figure 3c

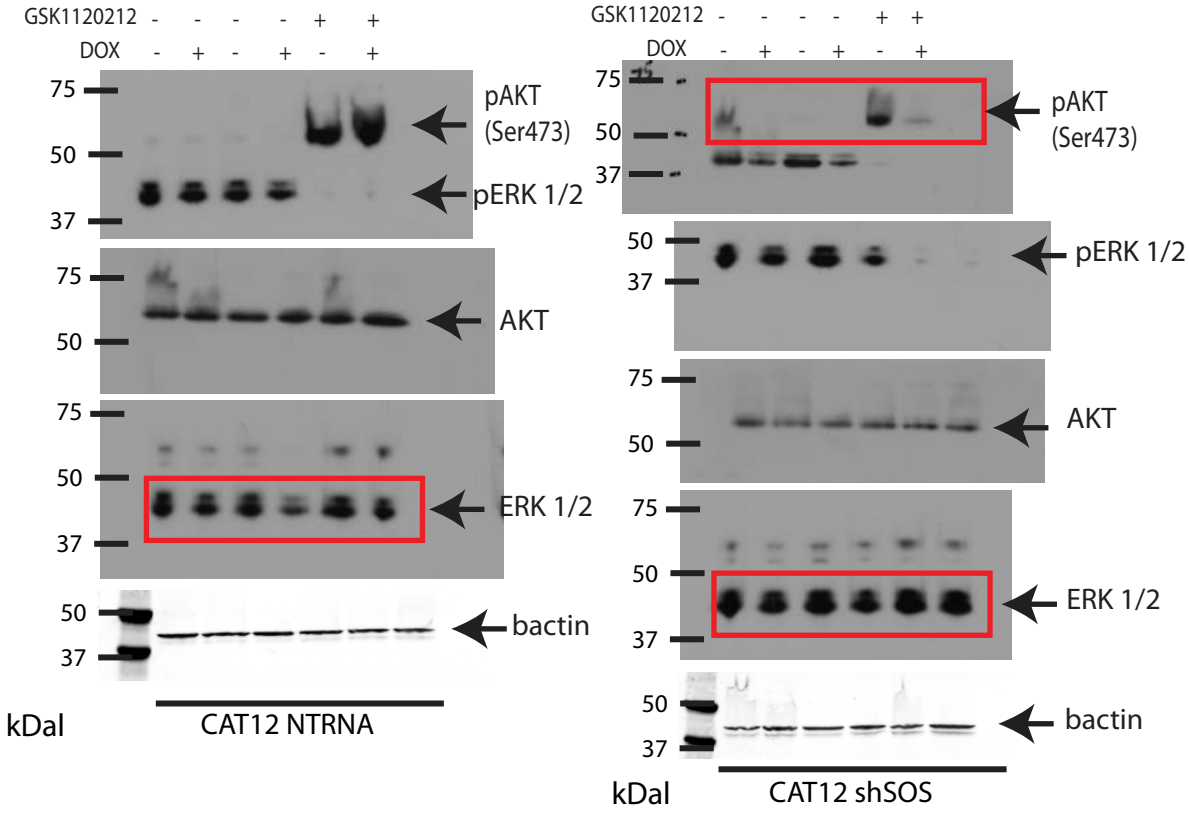


SUPPLEMENTARY FIGURE 12

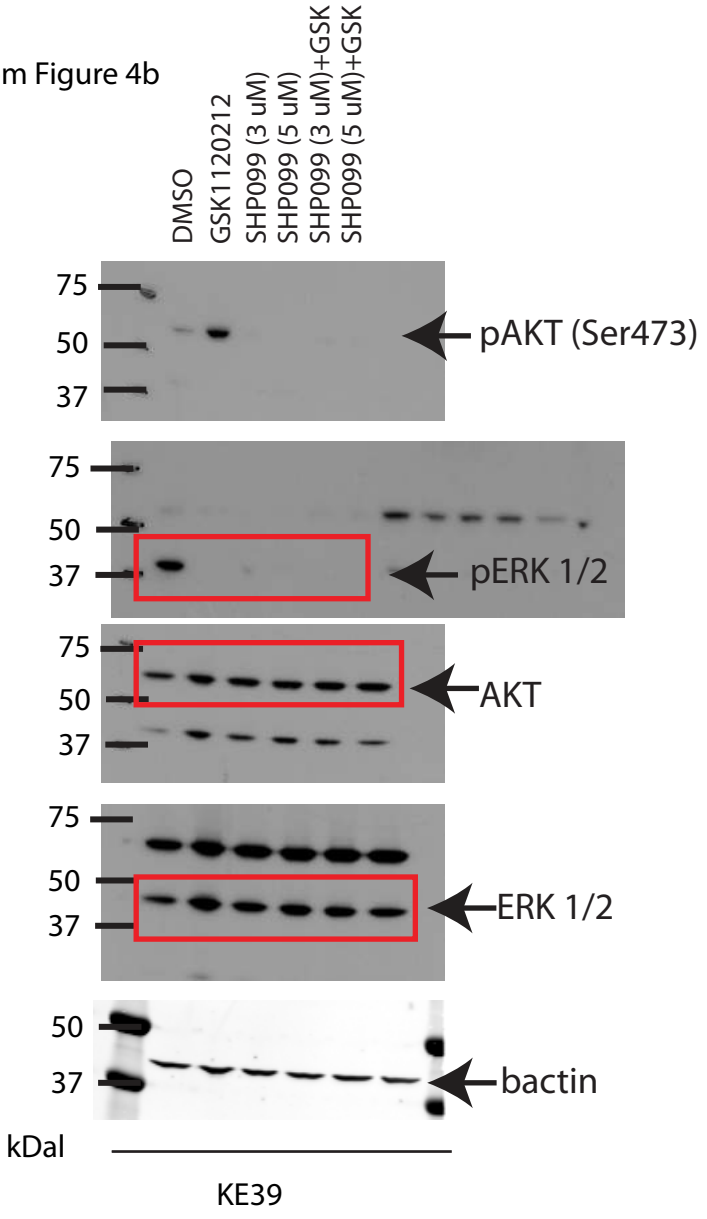
From Figure 3f

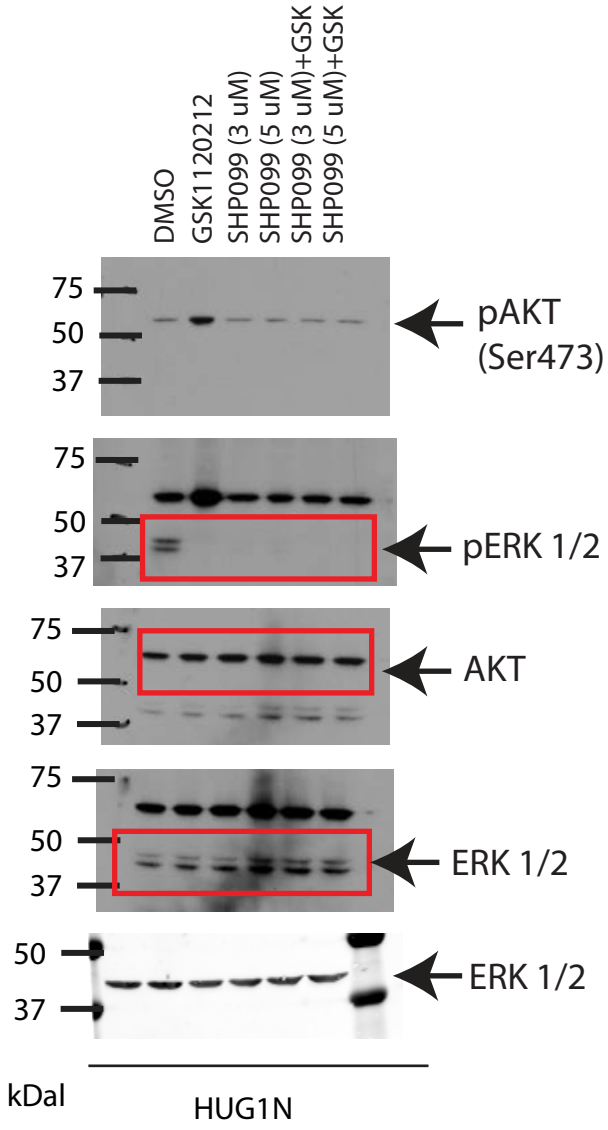


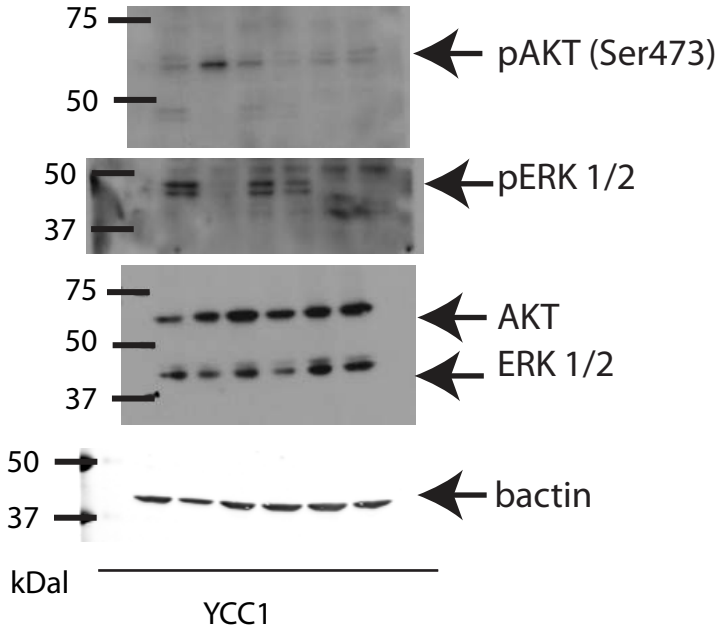
From Figure 3g



From Figure 4b







Supplementary Table 1: Frequencies of KRAS amplification in select cancer types

Type	Dataset	Altered	Total	Altered ratio (%)	AMP_ Mut	AMP_only	Mut_only	Wild	AMP frequency (%)	Note
Esophageal Carcinoma	Broad_ Nature Genetics_2013	30	146	20.5	1	24	5	116	16.4	
Stomach Adenocarcinoma_CIN	TCGA Nature 2014	26	147	17.7	2	19	5	121	12.9	
Ovarian Serous Cysadenocarcinoma	TCGA Nature 2011	36	316	11.4	0	34	2	280	10.8	
Uterine Carcinosarcoma	TCGA Provisional	10	56	17.9	1	3	6	46	5.4	
Lung Adenocarcinoma	TCGA Nature 2014	82	230	35.7	7	6	67	148	2.6	1 deletion, 1 truncating mutation
Lung Squamous Cell Carcinoma	TCGA Provisional	5	178	2.8	0	4	1	173	2.2	
Pancreatic Adenocarcinoma	TCGA Provisional	67	90	74.4	6	2	59	23	2.2	
Bladder Urothelial Carcinoma	TCGA Nature 2014	3	127	2.4	3	2	0	124	1.6	1 deletion
Breast Invasive Carcinoma	TCGA Nature 2012	11	482	2.3	0	7	4	471	1.5	
Skin Cutaneous Melanoma	TCGA Provisional	8	278	2.9	1	4	3	270	1.4	
Head and Neck Squamous Carcinoma	TCGA Provisional	5	300	1.7	0	4	1	295	1.3	
Uterine Corpus Endometriod Carcinoma	TCGA Nature 2013	53	240	22.1	3	3	47	187	1.3	
Adrenocortical Carcinoma	TCGA Provisional	1	88	1.1	0	1	0	87	1.1	
Glioblastoma	TCGA Cell 2013	5	281	1.8	1	3	1	276	1.1	
Liver Hepatocellular Carcinoma	TCGA Provisional	6	193	3.1	0	2	4	187	1.0	
Stomach Adenocarcinoma_NON-CIN	TCGA Nature 2014	22	148	14.9	1	1	20	126	0.7	

Supplementary Figure Legends:

Supplementary Figure 1: Wild-type *KRAS* amplification is correlated with elevated KRAS expression in gastric cancer patients and gastric cancer cell lines.

a) Whisker box plot of *KRAS* mRNA expression in wildtype *KRAS* amplified tumors (n=5) compared to tumors with *KRAS* mutations (n=14). *KRAS* mRNA expression quantified from RNA-sequencing is plotted along the y-axis on a $\log_2$ scale. Source: TCGA Stomach Adenocarcinoma (STAD) dataset. In the box plots, the central rectangle spans the first quartile to the third quartile the central line inside the box plot refer to the mean and the whiskers above and below the box refer to the maximum and minimum of the interquartile range. Statistical analysis performed using Mann-Whitney test. (2-sided significance) P=0.003.
b) Kaplan-Meier survival analyses from a TCGA STAD cohort of mixed Eastern and Western cases (n=478) comparing [left panel] percentage disease-free survival. Log Rank (Mantel-Cox) test. P= 0.0138 and [Right panel] overall survival of gastric cancer patients, Log Rank (Mantel-Cox) test, 2-side significant P value= 0.492 with *KRAS* amplification (red line) to patients without *KRAS* amplification (blue line).
c) Kaplan-Meier survival analysis comparing percentage overall survival of gastric cancer patients in a Western cohort with high KRAS expression (red line; n=27) to patients with low KRAS expression (blue line, n=366). Log Rank (Mantel-Cox) test. 2 sided significant P value= 0.0203
d) Immunoblotting analysis for baseline KRAS expression in panel of gastric cancer cell lines with *KRAS* amplification (KE39/YCC1/HUG1N), *KRAS* mutation (GSU/SNU1) and with non-amplified *KRAS*, non-*KRAS* mutant (IM95). Baseline KRAS expression was measured using densitometry and fold change values was normalized to IM95. Data is representative of 3 independent experiments.

Supplementary Figure 2: Amplified *KRAS* gastric cancer cells are dependent on *KRAS* for proliferation and display increased and sustained KRAS activation compared to mutant *KRAS* gastric cancer cells

[Top panels] Representative Immunoblots (of n=2 independent experiments) showing KRAS siRNA-mediated knockdown of KRAS in gastric cancer (GC) cell lines with *KRAS* amplification (KE39, YCC1, HUG1N) and with *KRAS* mutations (GSU, SNU1) as well as a GC cell line without *KRAS* amplification or mutation (IM95) using two independent siRNAs specific to KRAS and a non-targeting siRNA as a control. [Bottom panels] Impact of siKRAS knockdown in *KRAS* amplified and *KRAS* mutant GC lines on cell proliferation with cell viability quantified using Cell-Titer Glo. Values represent fold change (of n=3 independent experiments) in proliferation relative to the 72-hour time point (means ± SD).

Supplementary Figure 3: *KRAS* mutant and amplified gastric cancer cells show modest and equivalent sensitivity to single agent PI3K/AKT inhibition.

KRAS amplified (YCC1/HUG1N) and *KRAS* mutant (GSU) gastric cancer cells were seeded in triplicate at equal density and treated with increasing concentrations of PI3K inhibitor

(GDC0941) or AKT inhibitor (MK2206) for 72 hours. Percentage cell viability (of n= 3 independent experiments) was determined using Cell Titer Glo cell viability assay. Bar graph represents percentage cell viability (means ± SD).

Supplementary Figure 4: *KRAS* amplified gastric cancer cells display adaptive response after ERK inhibition and stably represses ERK phosphorylation after 72 hours of MEK inhibition

a) *KRAS* amplified (KE39/HUG1N) and *KRAS* mutant (SNU1) gastric cancer cells were treated with 100 nM SCH772984 and lysates were harvested at 1, 6 and 24 hours after treatment and subjected to immunoblot analysis. Lysates were probed with indicated antibodies. Bactin was used as a loading control. Data is representative of 3 independent experiments.
b) *KRAS* amplified (KE39) and *KRAS* mutant (GSU) gastric cancer cells were treated with 100 nM of MEK inhibitor GSK1120212. Total RNA was harvested at 1, 6, 24 and 72-hour timepoints and relative mRNA expression for downstream ERK substrates (FOS, DUSP4, DUSP6 and SPRY4) was measured using SYBR Green primers. GAPDH was used as a housekeeping gene. Bar graphs represent
c) *KRAS* amplified (KE39/YCC1) gastric cancer cells were treated with 100 nM of MEK inhibitor GSK1120212 at 1, 6, 24 and 72 hours. Protein lysates were harvested and immunoblotting analysis was carried out using antibodies probing for pAKT(Ser473), AKT, pERK1/2 and ERK 1/2. Bactin was used as a loading control. Data is representative of 3 independent experiments

Supplementary Figure 5: Adaptive resistance of *KRAS* amplified gastric cells to MEK inhibition is dependent upon KRAS and PI3-K activity but independent of ERBB3 RTK signaling, NRAS or HRAS.

a) *KRAS* amplified (HUG1N/YCC1), *KRAS* mutant (GSU) and non-amplified, non-mutant (IM95) gastric cancer cells were treated with DMSO, 100 nM GSK1120212, 100 nM GDC0941, 100 nM GSK112012 in combination with 20, 100 or 500 nM GDC0941 were treated for 24 hours. Protein lysates were harvested and subjected to immunoblot analysis. Lysates were probed with indicated antibodies. Bactin was used as a loading control. Data is representative of 2 independent experiments
b) Bar graphs measuring percentage cell viability (from n=3 independent experiments) of *KRAS* amplified (KE39/YCC1) and *KRAS* mutant (GSU) gastric cancer cells. Cells were treated with DMSO, 100 nM GSK1120212, 100 nM GSK1120212, 250, 500 or 1000 nM GDC0941 and in combination with 100 nM GSK1120212 for 5 days. Cell viability was determined using Cell Titer Glo cell viability assay. Bar graph represents percentage cell viability (means ± SD).
c) [Upper panel] Panel of gastric cancer lines was treated with either DMSO or 100 nM GSK1120212 for 6 hours. Protein lysates were harvested and phosphorylation status of receptor tyrosine kinases and other signaling molecules was screened using PathScan RTK antibody array. Bar graphs represent relative fluorescent intensities (means, n=2 technical replicates) of 3 signaling pathways (pERK1/2 (Thr202/204), pAKT (Ser473) and pan-ERBB3) with significant differences between DMSO and treated *KRAS* amplified gastric cancer cells. [Lower panel] Pathscan RTK antibody array of HUG1N

cells treated with GSK1120212 or DMSO. Each RTK antibody is spotted in duplicate. pERBB3, pAKT (Ser473) and pERK ½ were marked in circles. Data is representative of 2 independent experiments.

d) Validation of PathScan RTK antibody array using immunoblot analysis. Protein lysates were probed with indicated antibodies. Data is representative of 2 independent experiments.

e) Bar graph measuring percentage cell viability (from n=3 independent experiments) of *KRAS* amplified (HUG1N) and *KRAS* mutant (GSU) gastric cancer cells after treatment with DMSO, 100 nM GSK1120212, or 100 nM GSK1120212 with 100 or 500 nM Afatinib for 72 hours. Percentage cell viability was determined using Cell Titer Glo cell viability assay and values represent means±SD.

f) *KRAS* amplified (HUG1N), *KRAS* mutant (SNU1) and non-amplified, non-mutant *KRAS* (IM95) gastric cancer cells were treated with either DMSO, 100 nM GSK1120212, 100 nM Afatnib or 100 nM GSK1120212 in combination with 20, 100 or 500 nM Afatinib for 24 hours. Protein lysates were harvested and subjected to immunoblot analysis for indicated antibodies. Bactin was used as a loading control. Data is representative of 2 independent experiments

g) *KRAS* amplified (HUG1N) gastric cancer cells were transfected with 20 nM of pooled siHER3 or control non-targeting siRNA for 48 hours. Transfected cells with only Lipofectamine RNAiMax are used as Mock group. Transfected cells were treated with 100 nM GSK1120212 for 6 hours and protein lysates were harvested and subjected to immunoblot analysis. Lysates were probed with indicated antibodies. Bactin was used as a loading control. Data is representative of 2 independent experiments

h) Panel of gastric cancer cell lines with *KRAS* amplification (KE39/YCC1/HUG1N), *KRAS* mutation (GSU/SNU1) and with non-amplified *KRAS*, non-*KRAS* mutant (IM95). Levels of active RAS-GTP were measured using a RAS-GTP precipitation assay and lysates were subject to immunoblotting analysis. Immunoblotting analysis for baseline KRAS expression was also performed on whole cell lysate input (3%) with B-actin levels shown as a loading control. Data is representative of 3 independent experiments.

i) Immunoblot analysis of active RAS-GTP levels in gastric cancer cell line with *KRAS* amplification (KE39) and gastric cancer cell line with *KRAS* mutation (GSU) after treatment with 100 nM GSK1120212 at 1, 6 and 24-hour time points. Whole cell lysates were harvested and RAS-GTP levels were determined using a RAF-RBD immunoprecipitation assay and probed for NRAS, HRAS and KRAS. Immunoblotting analysis for NRAS, HRAS and KRAS expression was also performed on whole cell lysate input (3%) with B-actin shown as a loading control. Data is representative of 2 independent experiments

j) *KRAS* amplified (KE39) gastric cancer cells were transfected with 10 nM of pooled siNRAS or control non-targeting siRNA for 48 hours. Transfected cells with only Lipofectamine RNAiMax are used as Mock group. Transfected cells were treated with 100 nM GSK1120212 for 6 hours and protein lysates were harvested and subjected to immunoblot analysis. Lysates were probed with indicated antibodies. Bactin was used as a loading control. Data is representative of 2 independent experiments.

k) Bar graph of RAS-GTP levels (from n=2 independent experiments) of *KRAS* amplified (KE39) gastric cancer cells after transfection with 10 nM siNRAS or control non-targeting siRNA for 48 hours and treatment with 100 nM GSK1120212 for 24 hours.

DMSO was used as a vehicle group. GTP bound RAS is quantified by measuring absorbance in 96-wells with the RAS-G-LISA assay. Values in fold change in RAS-GTP levels is relative to DMSO control group at each time-point.

l) Immunoblot analysis of GC *KRAS* amplified cell line (YCC1). Cells were transfected with 2 independent siRNAs to KRAS and non-targeting control siRNA at 10 nM for 48 hours and treated with 100 nM GSK1120212 for 24 hours. Protein lysates were harvested and probed with pAKT (Ser473), total AKT, pERK1/2 and total ERK1/2 with B-actin as a loading control. Data is representative of 2 independent experiments.

m) Bar graph of RAS-GTP levels (from n=2 independent experiments) of *KRAS* amplified (KE39) and *KRAS* mutant (SNU1) gastric cancer cells after transfection with 10 nM of 2 independent siRNAs towards KRAS or control non-targeting siRNA for 48 hours and treatment with 100 nM GSK1120212 for 24 hours. DMSO was used as a vehicle group. GTP bound RAS is quantified by measuring absorbance in 96-wells with the RAS-G-LISA assay. Values in fold change in RAS-GTP levels is relative to DMSO control group at each time-point.

Supplementary Figure 6: *KRAS* amplified gastric cell lines and isogenic organoids display dynamic RAS activation

a) Cells from GC cell lines with *KRAS* amplification (KE39/HUG1N) or *KRAS* mutation (GSU/SNU1) were serum starved overnight and KRAS activation was measured at 0,15, 30 and 60 minutes after 50 ng/mL recombinant EGF stimulation. Whole cell lysates were harvested and active GTP-bound KRAS was determined using a RAS-GTP pulldown assay and probed for KRAS expression. Immunoblotting for KRAS expression was also performed on whole cell lysate input (3%) with B-actin shown as a loading control. Data is representative of 3 independent experiments.

b) Bar graph comparing RAS-GTP levels (from n= 2 independent experiments) of primary gastric organoids; (1) (*Trp53*$^{-/-}$*-3X KRAS*; (2) control *Trp53*$^{-/-}$*-vector*; (3) *Trp53*$^{-/-}$*; Kras*$^{G12D/+}$*-3X KRAS* and (4) control *Trp53*$^{-/-}$*; Kras*$^{G12D/+}$*-vector*) treated with 50 nM of GSK1120212 at 1, 6 and 24 hours after 5 days of treatment with 50 nM GSK1120212. DMSO was used as vehicle control. GTP bound RAS is quantified by measuring absorbance in 96-wells with the RAS-G-LISA assay. Values in percentage RAS-GTP levels is relative to DMSO control group at 1 hr. Comparisons were performed using 2-tailed , unpaired Student's t-test; (*) $P < 0.05$; (**) $P < 0.01$

Supplementary Figure 7: Basal Receptor Tyrosine Kinase signaling promotes cellular adaptation of *KRAS* amplified cell lines to MEK inhibitor therapy

a) Immunoblot analysis of *KRAS* amplified (KE39/YCC1/HUG1N) gastric cancer cells after treatment with DMSO, 100 nM GSK1120212, 250 nM, 500 nM and 1000 nM OSI-906 and in combination with 100 nM GSK1120212 for 24 hours. Whole cell lysates were harvested and probed with indicated antibodies. Data is representative of 2 independent experiments.

b) Immunoblot analysis of *KRAS* amplified (KE39/YCC1/HUG1N) gastric cancer cells after treatment with DMSO, 100 nM GSK1120212, 250 nM, 500 nM and 1000 nM BGJ-398

and in combination with 100 nM GSK1120212 for 24 hours. Data is representative of 2 independent experiments.

c) Immunoblot analysis of *KRAS* amplified (KE39/YCC1/HUG1N) gastric cancer cells after treatment with DMSO, 100 nM GSK1120212, 250 nM, 500 nM and 1000 nM Crizotinib and in combination with 100 nM GSK1120212 for 24 hours. Data is representative of 2 independent experiments.

d) Bar graphs measuring percentage cell viability (from n= 3 independent experiments) of *KRAS* amplified (KE39/YCC1) and *KRAS* mutant (GSU) gastric cancer cells. Cells were treated with DMSO, 100 nM GSK1120212, 100 nM GSK1120212, 250, 500 or 1000 nM OSI-906 and in combination with 100 nM GSK1120212 for 5 days. Cell viability was determined using Cell Titer Glo cell viability assay. Bar graph represents percentage cell viability (means ± SD).

e) Clonogenic assay of *KRAS* amplified (KE39) and *KRAS* mutant (GSU) gastric cancer cells treated with DMSO, 100 nM GSK1120212, 250 nM, 500 nM and 1000 nM OSI-906 and both drugs in combination with 100 nM GSK1120212 for 14 days. Data is representative of 3 independent experiments.

Supplementary Figure 8: Genetic knockdown of SOS increases apoptosis and decreases cell viability of *KRAS* amplified cells

a) Bar graph measuring percentage apoptosis in *KRAS* amplified (KE39/HUG1N) and *KRAS* mutant (GSU) GC cells after SOS1/2 silencing with pooled siRNAs followed by treatment with 100 nM GSK1120212 for 72 hours. Cells are stained with Annexin V-FITC and PI and analyzed by flow cytometry to quantify percentage of cells undergoing apoptosis. DMSO was used as a vehicle control. Bar graphs represent relative percentage apoptosis (means ± SD, n=3). Statistical analysis was performed using 2-tailed, unpaired Student's t-test; (*) $P<0.05$; (**) $P<0.001$.

b) Bar graph measuring relative RAS-GTP levels (from n= 2 independent experiments) of GSU expressing indicated constructs with or without 48-hour induction with doxycycline and 6 hours of treatment with 100 nM GSK1120212. DMSO is used as a treatment control. Relative RAS-GTP levels means were quantified using the G-LISA RAS activation assay.

c) Bar graph measuring percentage cell viability (from n=3 independent experiments) in *KRAS* amplified (KE39) and *KRAS* mutant (GSU) GC lines expressing indicated shRNA constructs with or without 48 hours induction with 1 uM doxycycline followed by treatment with 100 nM GSK1120212 for 72 hours. Cell viability was determined using Cell Titer Glo cell viability assay. Bar graphs represent percentage cell viability means ± SD. Statistical comparisons were performed using 2-tailed, unpaired Student's t-test; (*) $P < 0.05$; (**) $P < 0.01$

d) Immunohistochemical analysis of SOS, pAKT (Ser473), pERK ½ and Ki67 (marker of proliferation) expression in tumor tissue from KRAS amplified (KE39) and KRAS mutant (GSU) gastric cancer xenografts expressing doxycycline-induced pTRIPz shSOS or control shRNA constructs and treated with GSK1120212 (2 mg/kg/day) or vehicle for 5 weeks or 3 weeks respectively. Scale bar: 50 uM. Data is representative of 2 independent experiments.

Supplementary Figure 9: Silencing of SOS increases MEK inhibitor sensitivity in patient-derived *KRAS* amplified gastric tumors

a) Fluorescent *in situ* hybridization/CEP12 (FISH/CEP12) assay for *KRAS* amplification in CAT12 cells, a *KRAS* amplified patient-derived xenograft cell line. High KRAS amplification (red; 45 copies of KRAS) signal compared to CEP12 (green) signal observed. Data is representative of 2 independent experiments.
b) Bar graph measuring cell viability (from n=3 independent experiments) in CAT12 cells after 72 hours of MEK inhibition with GSK1120212 (100 nM). DMSO was used as a vehicle control. Cell viabilities (means ± SD) were normalized to DMSO control group.
c) Bar graph measuring relative RAS-GTP levels (from n= 2 independent experiments) of CAT12 cells expressing inducible pTRIPz shSOS or control constructs with or without 48-hour induction with 1 uM doxycycline followed by 6 hours of treatment with 100 nM GSK1120212. DMSO is used as a treatment control. Relative RAS-GTP levels means were quantified using the G-LISA RAS activation assay.
d) Immunohistochemical analysis of SOS, pAKT (Ser473), pERK ½ and Ki67 (marker of proliferation) expression in tumor tissue from patient-derived *KRAS* amplified (CAT12) xenografts expressing doxycycline-induced pTRIPz shSOS or NTRNA constructs and treated with GSK1120212 (2 mg/kg/day) or vehicle for 5 weeks. Scale bar: 50 uM.

Supplementary Figure 10: Combination of SHP099 and GSK1120212 decrease adaptive response in *KRAS* amplified gastric xenografts

Immunohistochemical analysis of pAKT (Ser473), pERK ½ and Ki67 (marker of proliferation) expression in tumor tissue from *KRAS* amplified (KE39), patient-derived *KRAS* amplified (CAT12) and *KRAS* mutant (GSU) xenografts treated with vehicle, GSK1120212 (1 mg/kg), SHP099 (50 mg/kg) or both drugs in combination for five or three weeks respectively. Scale bar: 50 uM. Data is representative of 2 independent experiments

Supplementary Figure 11: Constitutive activation of SOS leads to rescue from SHP099 and GSK1120212 inhibition in *KRAS* amplified GC cells.

a) Bar graph measuring percentage cell viability (from n= 3 independent experiments) of *KRAS* GC amplified (KE39/CAT12) and *KRAS* mutant (GSU) lines engineered to stably express pGLX-empty vector (EV), pGLX-HA-SOS-cat (SOS1-cat) and pGLX-SOS1 (SOS1) following 5 days of treatment with GSK1120212 (100 nM), SHP099 (3, 5 or 10 uM), SHP099 (3, 5 or 10 uM) in combination with GSK1120212 (100 nM). DMSO was used as vehicle control. Cell viabilities (means ± SD) were normalized to DMSO control/empty vector group.
b) Bar graph measuring relative RAS-GTP levels (from n=2 technical replicates) of GC *KRAS* amplified (KE39/CAT12) and *KRAS* mutant (GSU) lines engineered to stably express pGLX-empty vector (EV), pGLX-HA-SOS-cat (SOS1-cat) and pGLX-SOS1 (SOS1) following 6 hours of treatment with GSK1120212 (100 nM), SHP099 (3, 5 or 10 uM), SHP099 (3, 5 or 10 uM) in combination with GSK1120212 (100 nM). DMSO was used as vehicle control. Relative active RAS-GTP levels means were quantified using the G-LISA RAS activation assay. Data is representative of 2 independent experiments.

c) Immunoblotting analysis of *KRAS* amplified (KE39/CAT12) and *KRAS* mutant (GSU) cell lines engineered to stably express pGLX-empty vector (EV), pGLX-HA SOS1-cat (SOS-cat) and pGLX-SOS1 (SOS1) after 24 hour treatment with GSK1120212 (100 nM), SHP099 (3, 5 or 10 uM), SHP099 (3, 5 or 10 uM) in combination with GSK1120212 (100 nM). DMSO was used as vehicle control. Protein lysates were harvested and probed for antibodies to SOS1, HA tagged SOS, pAKT(Ser473), AKT, pERK1/2 and ERK1/2. B-actin was used as a loading control. Data is representative of 2 independent experiments
d) Representative fluorescent confocal images (from n=2 independent experiments) illustrating SOS localization in GC *KRAS* amplified (KE39) and *KRAS* mutant (GSU) cells after 6 hour treatment with GSK1120212 (100 nM), SHP099 (10 uM) and in combination. [left panels] SOS1(red); [middle panel] DAPI (blue) and [right panels] Merged image of SOS1 and DAPI. Scale bar: 10 μM. Data is representative of 2 independent experiments

Supplementary Figure 12: Uncropped immunoblots

Supplementary Table 1: Frequencies of *KRAS* amplification in select cancer types