**Supplemental Figure 1.** HepG2 cells were transfected with GLI luciferase reporter construct (pGL38XGLI), EWS-FLI1 luciferase reporter construct (NROB1-Luc) with or without GLI1, EWS-FLI1 and cDNAs respectively. Renilla-TK construct was used as transfection control for signal normalization. Twenty-four hrs after transfection, cells were treated with 3μM Arsenic Trioxide for 24hrs. Bars represent the means of the relative luciferase activity, which is calculated by dividing the luciferase activity by the renilla activity used as a transfection control. Error bars are the standard deviations (***P<0.001, ns = not significant using a two-tailed Student's t-test). Transfection assays were performed in triplicate.

**Supplemental Figure 2.** Localization of the EGFP-GLI1WT and EGFP-GLI1AHA, and EGFP-GLI1WT with HA-Dyrk1 was detected by green florescence. Shown are more cells per 20 X field than in Figure 2. Arrows mark the nuclei.

**Supplemental Figure 3**. (A) GLI1 was immobilized on a CM5 Biacore chip and an SPR analysis was performed by injecting DNA oligos that contained a single GLI consensus binding site (Wild type oligo) with or without 10 μM ATO in running buffer. A DNA oligo that contained a mutated consensus site (Mutant oligo) was used as a negative control. Each colored line represents a single concentration oligo injection, which was repeated 3 times in every experiment. Oligos were injected at 100 nM, 50 nM, 25 nM, 12.5 nM, 6.25 nM, 3.13 nM, and 1.56 nM. Black lines represent curve fit for a 1:1 binding model using Biacore T-100 evaluation software.

**Supplemental Figure 4.** $IC_{50}$ graphs for ESFT cell lines. Cells were plated in a 96 well plate and then treated with 1 nM to 10 μM ATO for 4 days.

**Supplemental Figure 5.** $IC_{50}$ graphs for non-ESFT cell lines. Cells were plated in a 96 well plate and then treated with 1 nM to 10 μM ATO for 4 days.

**Supplemental Figure 6.** Overexpression or Knockdown of GLI1 changes sensitivity to ATO. **(**A) COS7 cells were transfected with EGFP alone or EGFP- GLI1. 24hrs after transfection, cells were treated with 1 μM ATO for 24 hrs. Bars represent the means of the total number of viable cells. Error bars are the standard deviations. (**P<0.01, ns = not significant using a two-tailed Student's t-test). Transfection assays were performed in triplicate. (B) COS7 cells were transfected with Control or GLI1 siRNA. 48hrs after transfection, cells were treated with 10 μM ATO for 24 hrs. Bars represent the means of the total number of viable cells. Error bars are the standard deviations. (**P<0.01, ns = not significant using a two-tailed Student's t-test). Transfection assays were performed in triplicate.

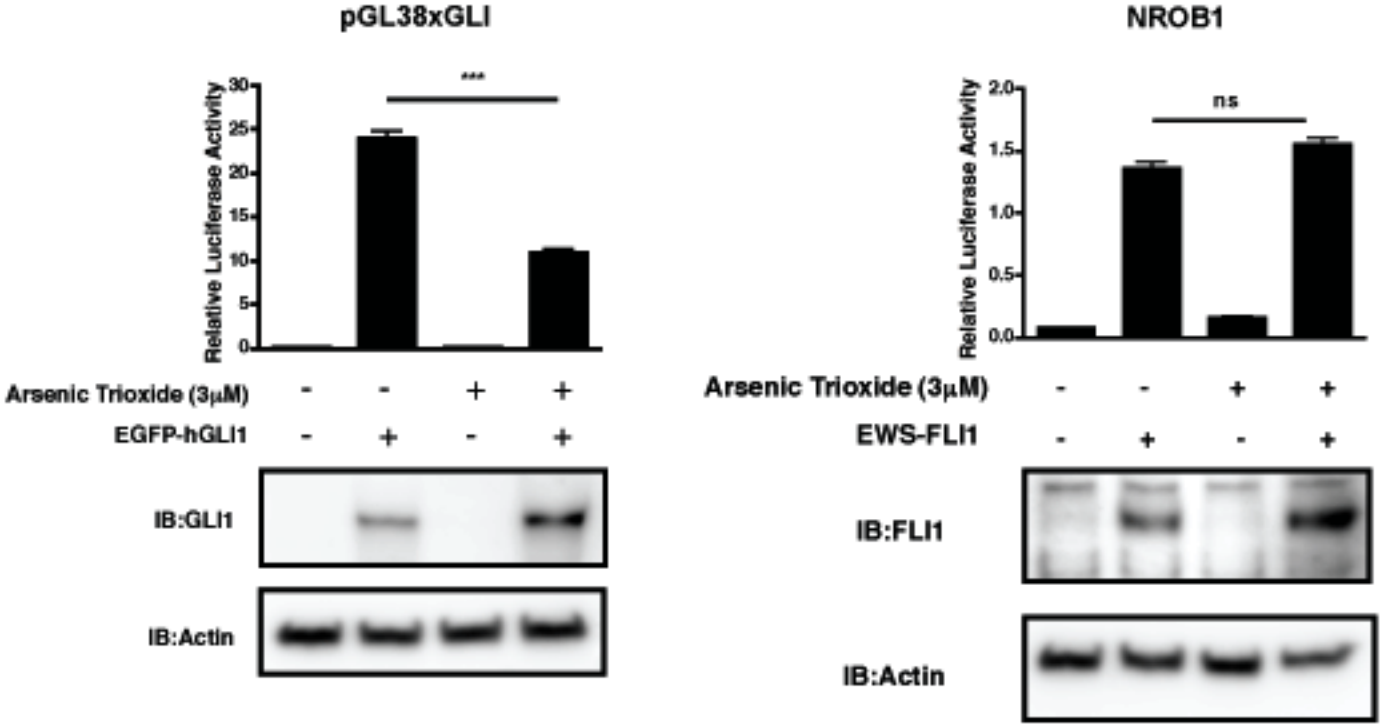
GLI1 protein levels following EGFP-GLI1 transfection or siRNA treatment are evaluated by western blot analysis and provided next to each bar graph.

**Supplemental Figure 7.** (A) TC71 cells were treated with DMSO, 3 μM ATO alone, 10 μM JNK inhibitor SP600125 alone or the two drugs combined for 24 hrs. Proliferation was measured continuously every ten minutes using an Electric Cell-substrate Impedance Sensing (ECIS) assay. JNK activation was measured by immunoblotting for phospho-JNK. Total JNK levels are shown as a loading control. (B) COS7 cells were transfected with GLI luciferase reporter construct (pGL38XGLI), and GLI1 construct. The Renilla-TK construct was used as a control for normalization. Twenty-four hrs later, cells were treated for 24hrs with DMSO, 3 μM ATO alone, 10 μM JNK inhibitor SP600125 alone or the two drugs combined. Bars represent the means of the relative luciferase activity, which is calculated by dividing the luciferase activity by the renilla activity, is plotted. *Error bars* are the standard deviations. Transfection assays were performed in triplicate. Expression of GLI2 was detected by immunoblotting.

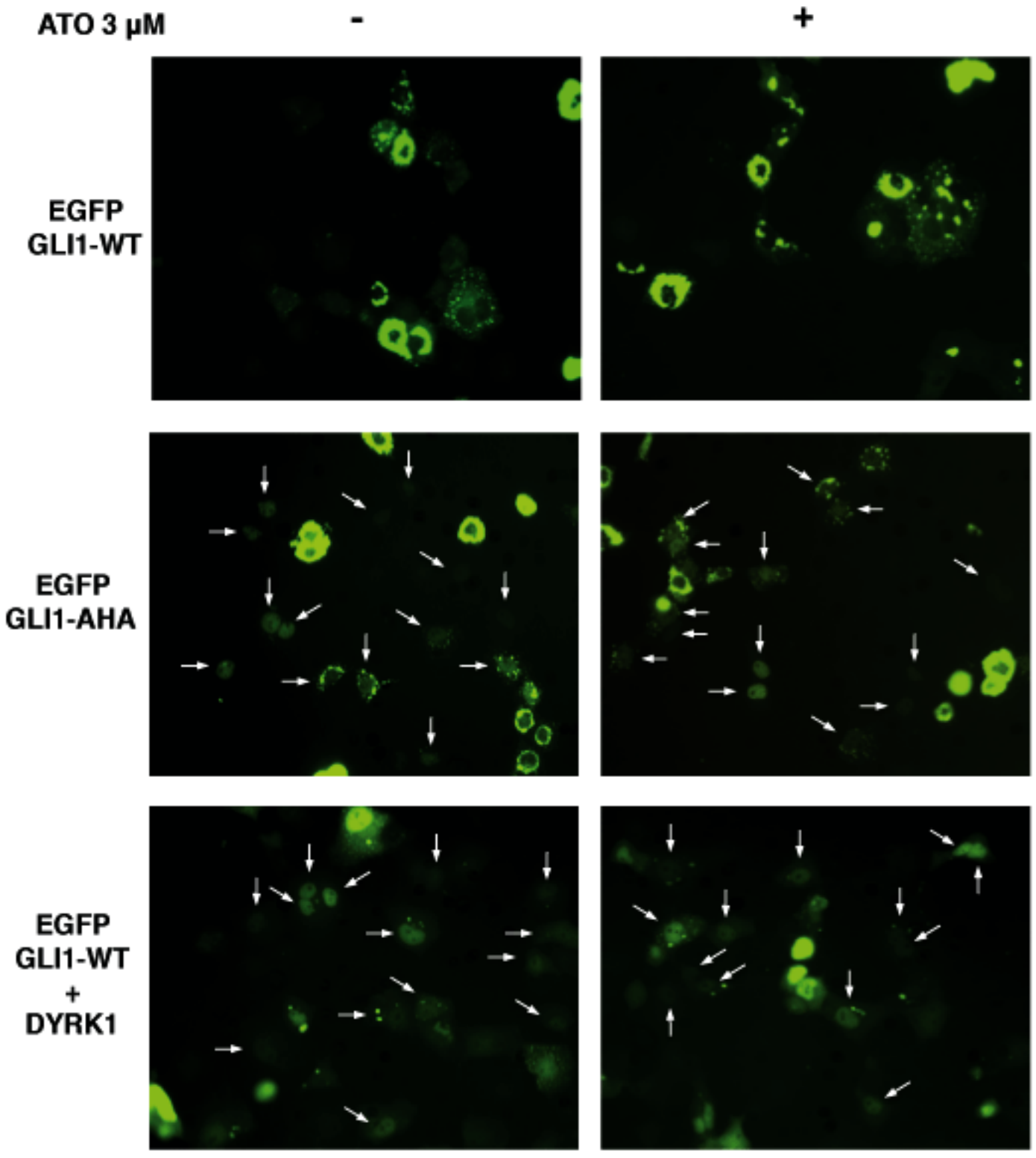
**Supplemental Figure 8.** TC71 cells were treated with DMSO, 3 μM ATO alone, 10 μg/ml LPS alone or the two drugs combined for 24 hrs. Proliferation was measured continuously every ten minutes using an ECIS. NFkB activation was measured by immunoblotting for phospho-NFkB p65. Total NFkB p65 levels are shown as a loading control.

**Supplemental Figure 9.** COS7 cells were treated with 10 and 30 μM of either ATO from Cephalon or ATO from Sigma. Proliferation was measured continuously every hour using ECIS.

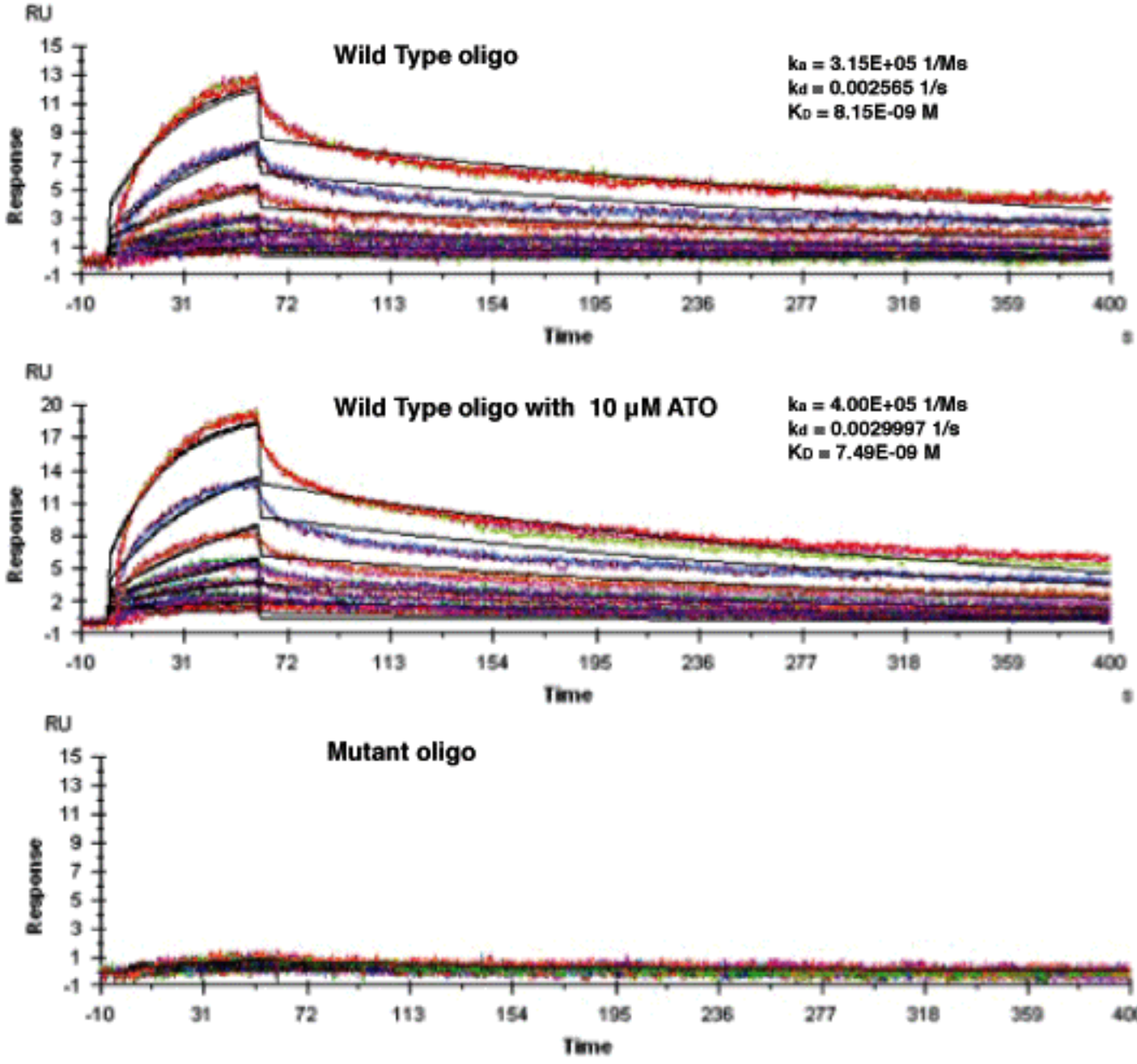
# Supplemental Figure 1



# Supplemental Figure 2

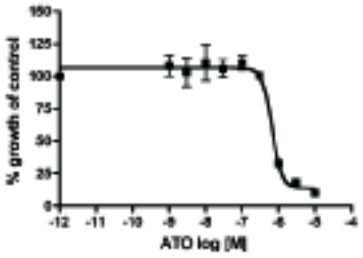


# Supplemental Figure 3



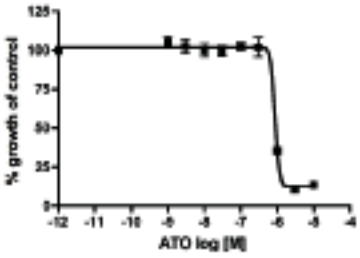
# Supplemental Figure 4- ESFT cells

TC71



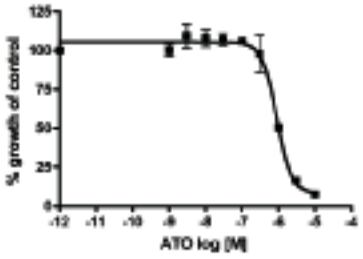

IC50 = 0.6 μM

RDES



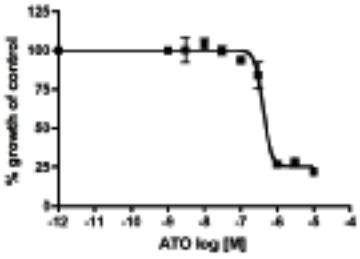

IC50 = 0.9μM

ES925



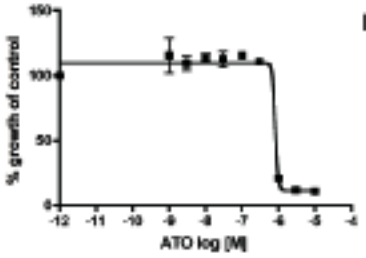

IC50 = 0.9μM

A4573



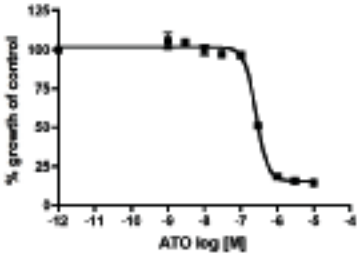

IC50 = 0.5μM

CHP100



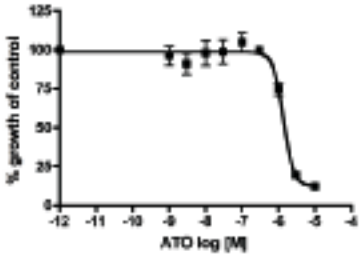

IC50 = 0.9μM

SKES



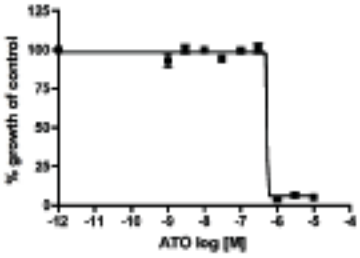

IC50 = 0.3μM

TC32



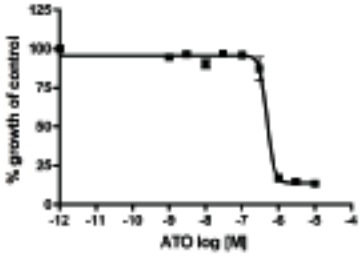

IC50 =1.4 μM

A673



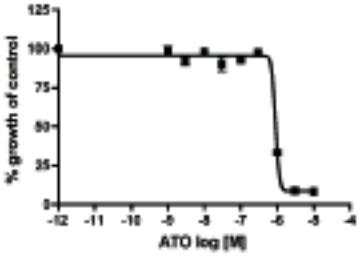

IC50 = 0.5μM

MMHES-1




IC50 = 0.5 μM

STAET72

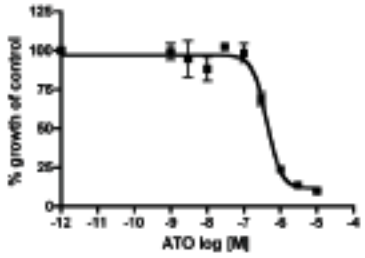



IC50 = 0.9 μM

# Supplemental Figure 5- Non-ESFT cells

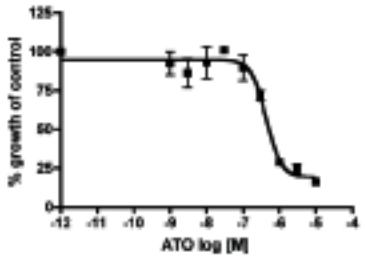
## Medulloblastoma

DAOY




IC50 = 0.4 μM

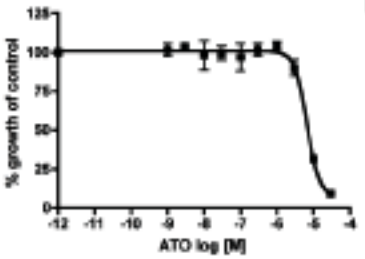
D556




IC50 = 0.4 μM

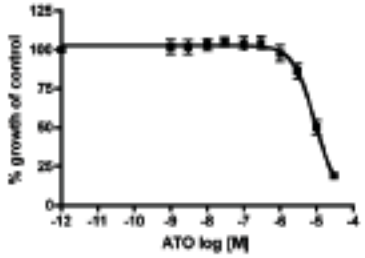
## Controls

HepG2



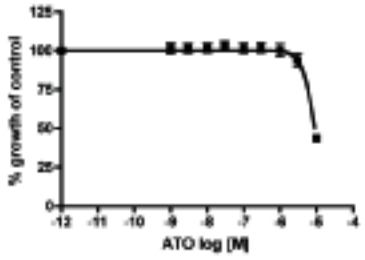

IC50 = 6.6 μM

Panc1



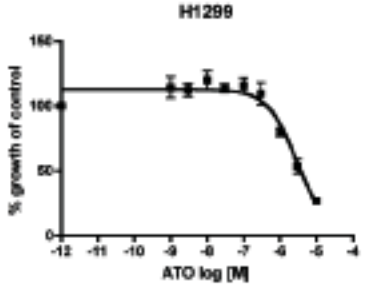

IC50 = 9.1 μM

CAPAN1



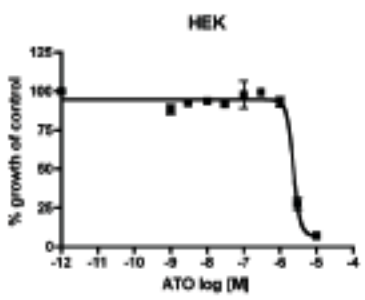

IC50 = 9.0 μM

H1299



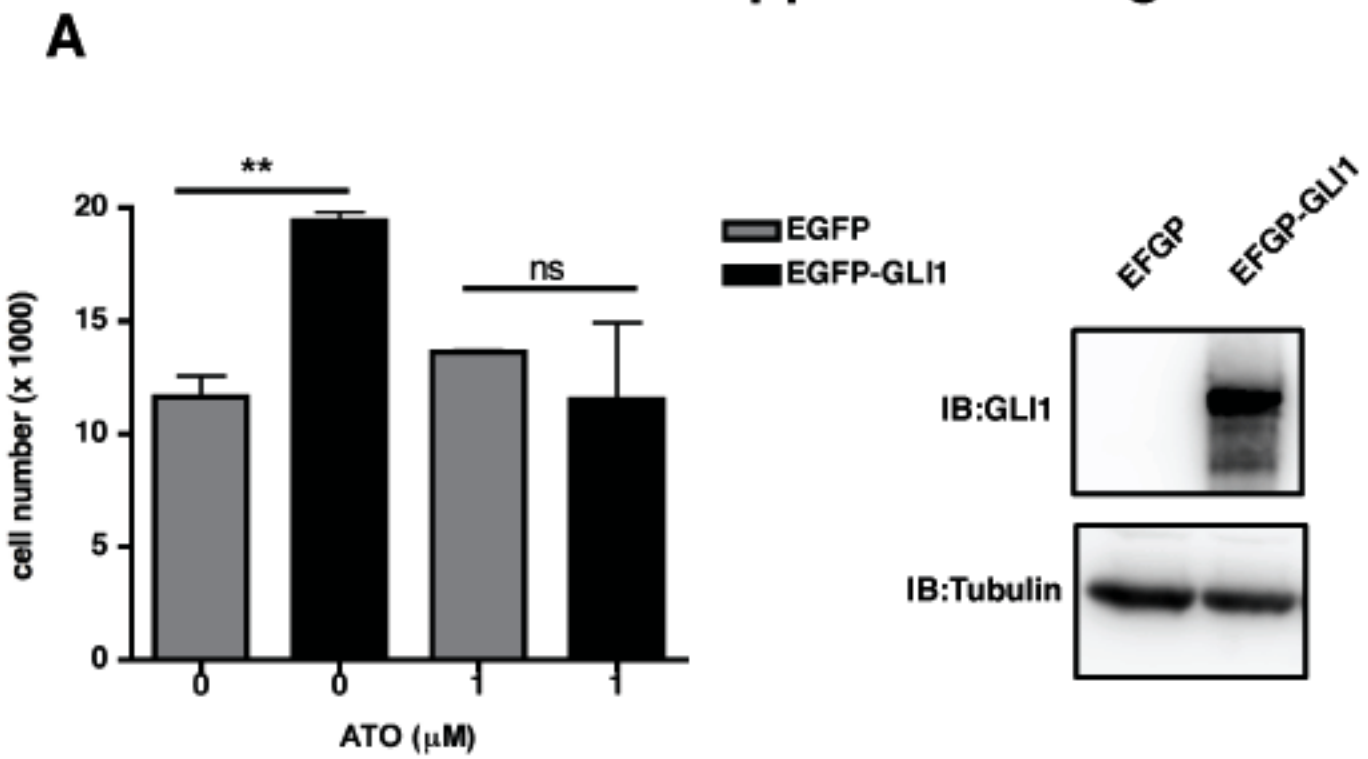

IC50 =2.9 μM

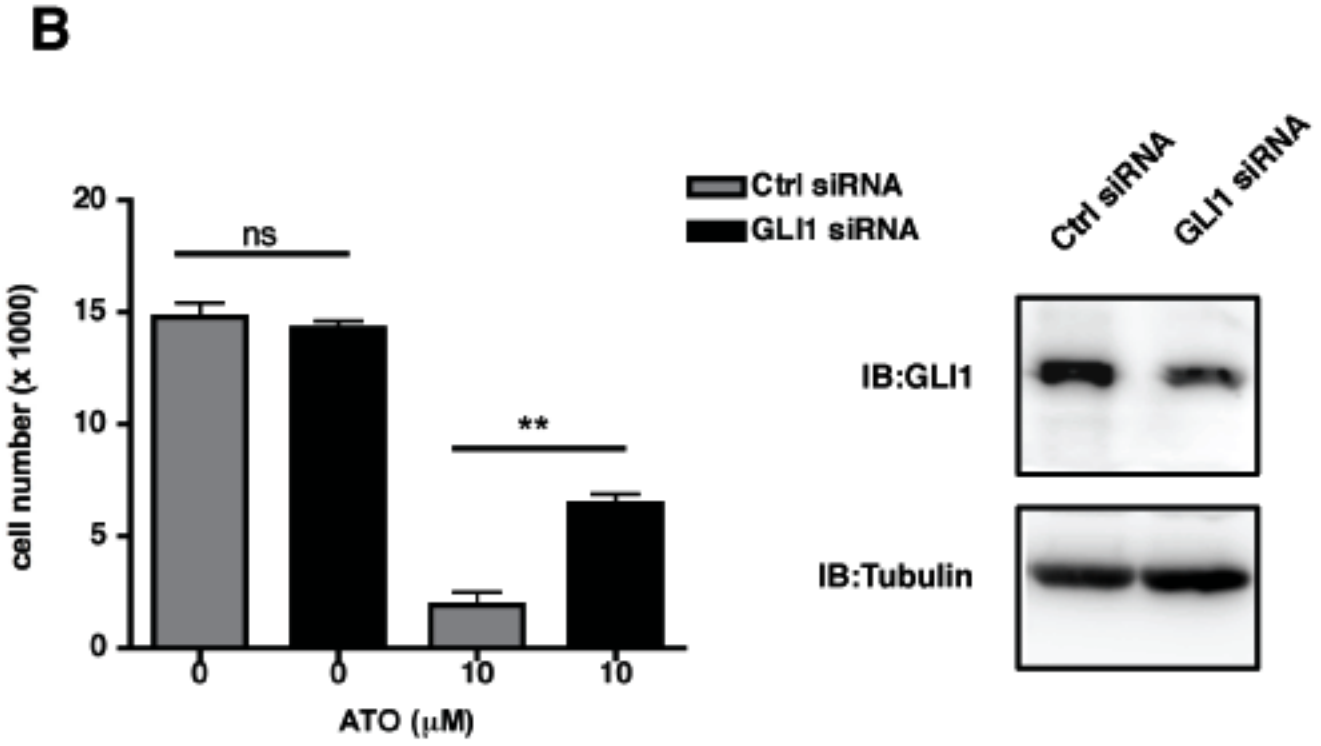
HEK



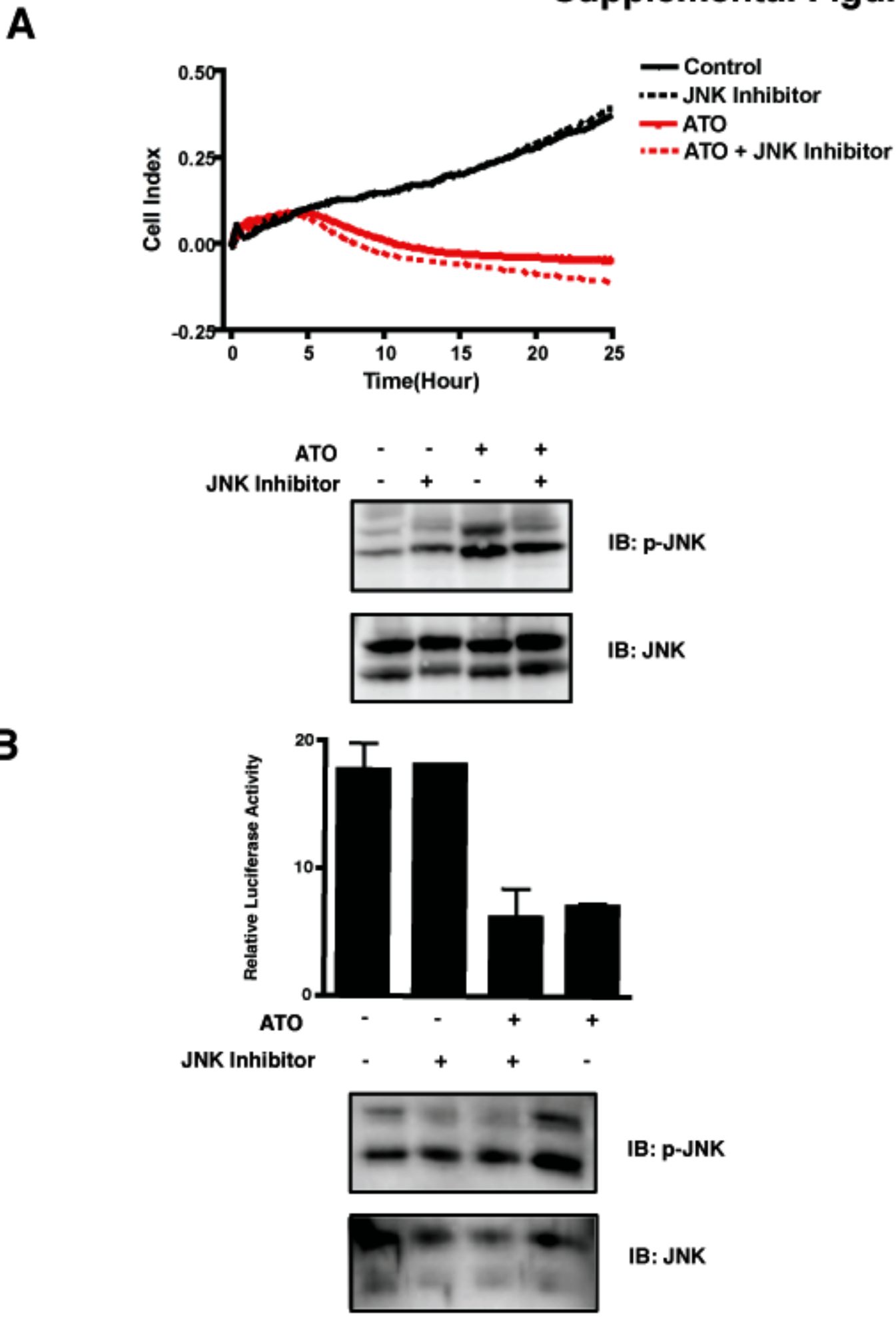

IC50 =2.3 μM

# Supplemental Figure 6

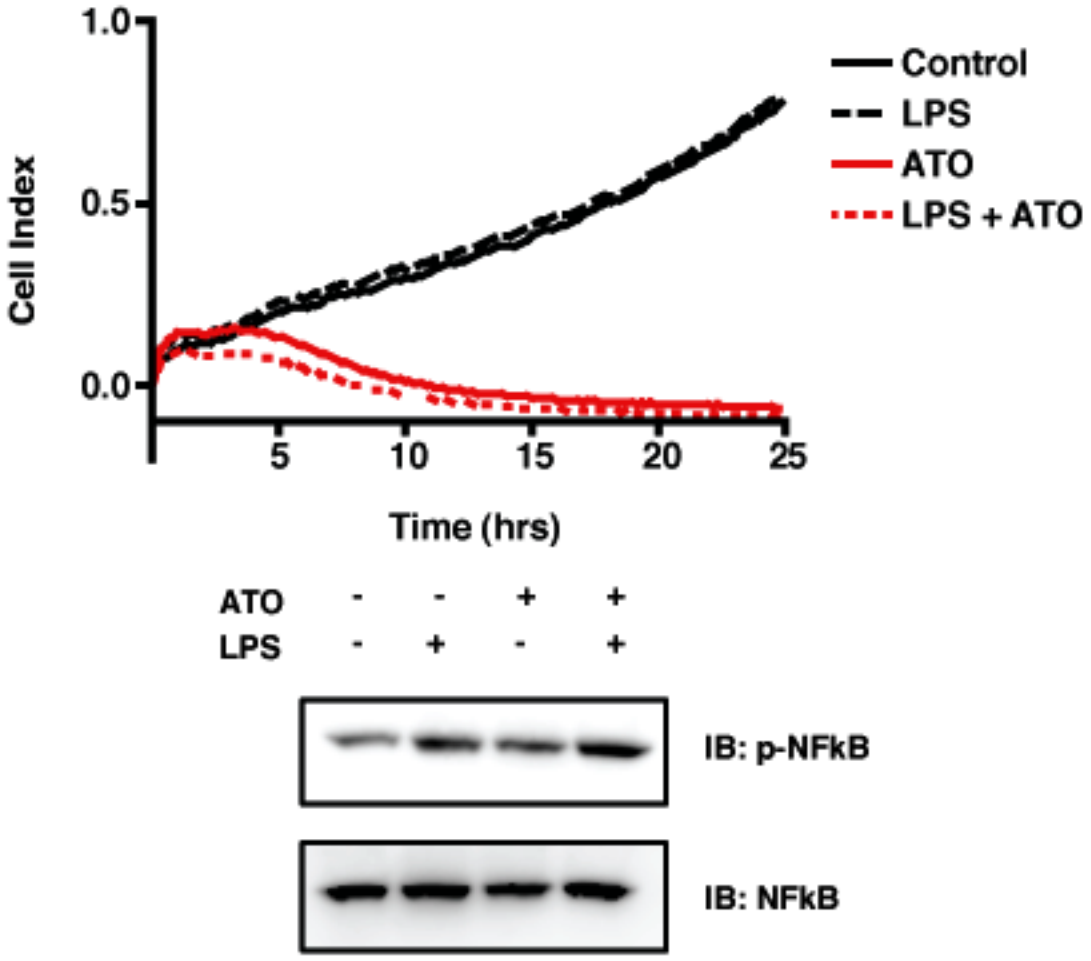


# Supplemental Figure 7

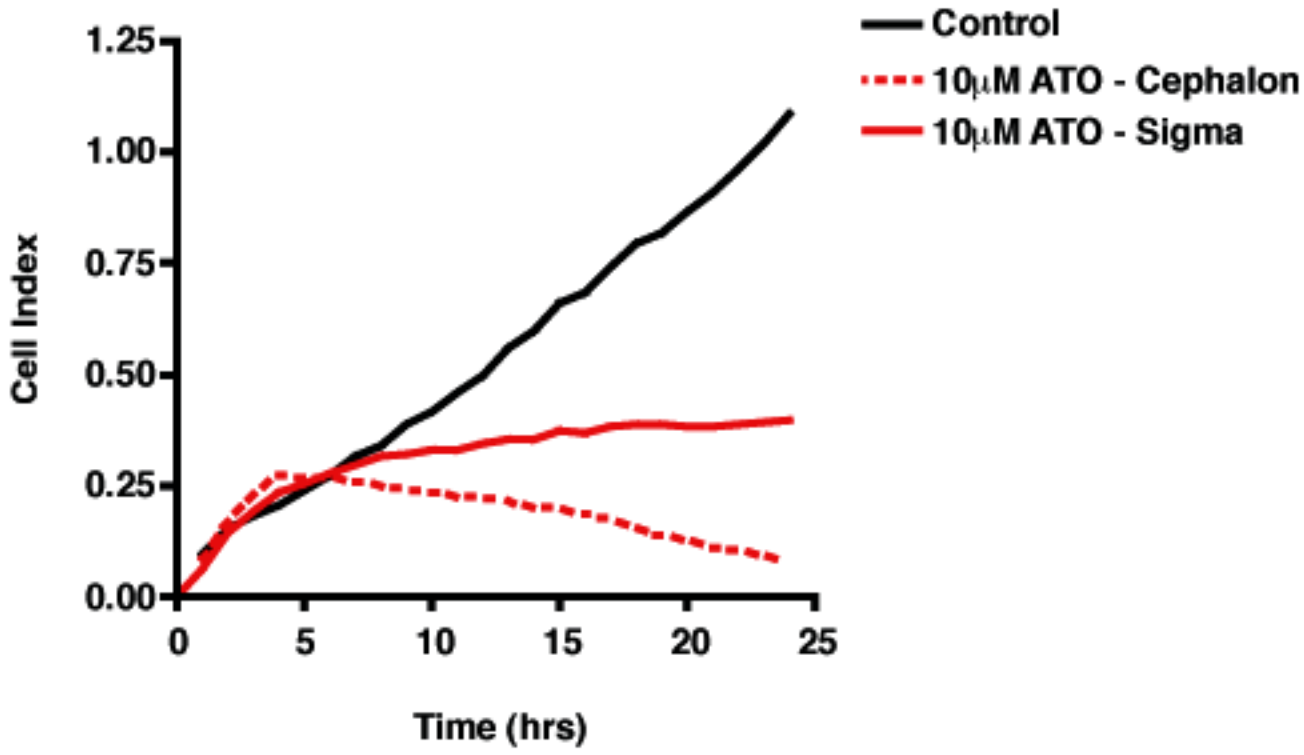


# Supplemental Figure 8



# Supplemental Figure 9

**A**




**B**