**Supplementary Figure legends**

**Supplementary Figure 1.** Kaplan-Meier survival plot. Survival probability of dysregulation of the *NFATC4* pathway in ovarian cancer TCGA data set. *p<0.05.

**Supplementary Figure 2.** Evaluation of *NFATC4* constructs. **A** *NFATC4* and *RCAN1* mRNA expression of 3 HGSOC cells lines transduced with IcNFATC4 or ILuc control (n=3). **B** Representative images of NFAT3 protein localization in IcNFATC4 SKOV3 and IcNFATC4 HEY1 cells treated with or without doxycycline (100ng/mL, n=2). Image scale bars are 50 μm.

**Supplementary Figure 3.** The transient cNFATC4 construct loses more YFP expression than the Control-YFP construct (n=3). Flow cytometry analysis of A2780 cells expressing Control-YFP or cNFATC4 constructs.

**Supplementary Figure 4.** No difference in apoptosis or SABG staining between *NFATC4* and control constructs. SABG staining of A2780 cNFATC4 or Control-YFP (n=12). Quantification of SABG staining; the cyclin D1/CDK4 and CDK6 inhibitor Ribociclib was used as a positive control for senescence.

**Supplementary Figure 5.** lcNFATC4 expressing cells have a reduction in cell size. **A** IncuCyte growth curves of IcNFATC4 or ILuc HEY1 and SKOV3 cells treated with or without doxycycline (n=3). Red box indicates the confluency used to validate changes in cell morphology. Forward scatter flow cytometry of; **B** A2780 cNFATC4 vs Control-YFP cells, **C** HEY1 ILuc and lcNFATC4 cells treated with or without doxycycline. **D** Quantitation HEY1 cell size (n=3). **p<0.01. ****p<0.0001.

**Supplementary Figure 6.** ***NFATC4*** promotes chemoresistance. Cell viability ILuc and IcNFATC4 SKOV3 cells treated with or without doxycycline and co-treated with varying concentrations of cisplatin (n=6).**p<0.01.

**Supplementary Figure 7.** Representative images of NFAT3 protein localization in cisplatin sensitive and cisplatin resistant paired ovarian cancer cell lines. Cisplatin sensitive (PEO1, A2780) and cisplatin resistant (PEO4, A2780CisR) paired ovarian cancer cell lines were treated with or without 1ug/mL cisplatin for 72h before NFAT3 immunofluorescence was performed (n=2). Image scale bars are 50 μm.

**Supplementary Figure 8.** Taxol partially activates *NFATC4* signaling in ovarian cancer cell lines. OVSAHO, COV362 and HEY1 cells were treated with or without 3 uM and 9 uM of Taxol for 72 h before *RCAN1* and *NFATC4* expression was validated using qPCR. Results were expressed as fold change to untreated control, n=2.

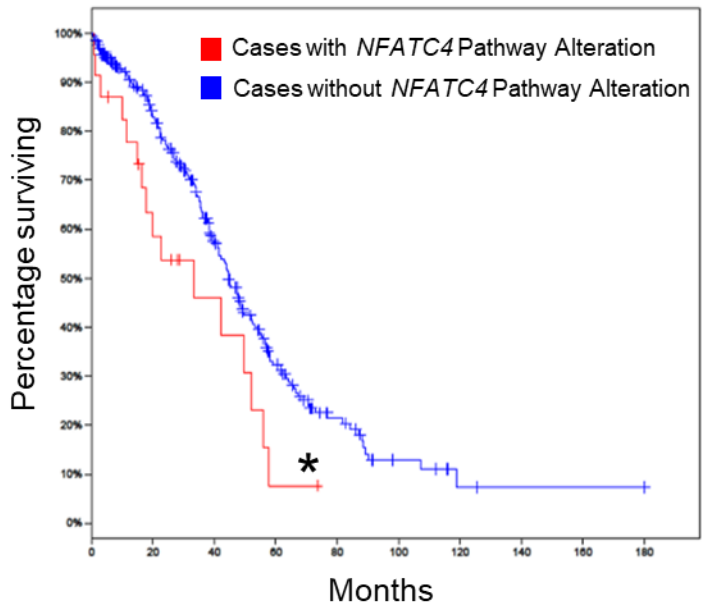
**Supplementary Figure 9.** *NFATC4* constructs expression is lost in vivo. Flow cytometry analysis of control-YFP and cNFATC4 expression in tumors (n=2).

**Supplementary Figure 10.** Doxycycline recovery cell counts of *NFATC4* expressing SKOV3 and HEY1 cells lines. **A** HEY1 and SKOV3 cells expressing the IcNFATC4 and ILuc constructs were treated for 72h with 100 ng/mL doxycycline. After 72h doxycycline was removed and cells were grown in doxycycline free media for 120-144 h. Cell counts were performed daily. **B** after recovering from quiescence, cells were treated with dox for 96 h, then re-plated at 30 K cells and grown in the presence of dox for an additional 72-96h. Cell counts were recorded daily. n=2.

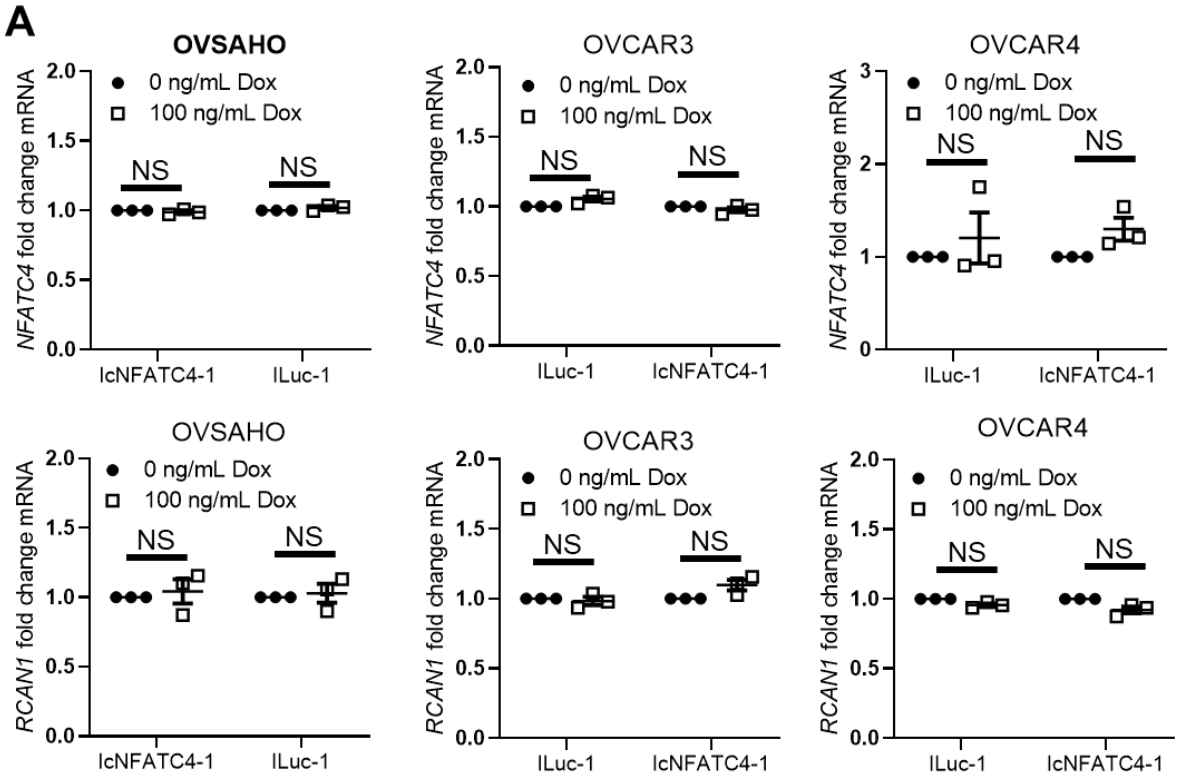
**Supplementary Figure 11.** Doxycycline recovery qPCR of *NFATC4* target genes in *NFATC4* expressing SKOV3 and HEY1 cells lines. HEY1 and SKOV3 cells expressing the IcNFATC4 and ILuc constructs were treated for 72h with 100 ng/mL doxycycline. After 72h doxycycline was removed and cells were grown in doxycycline free media for 120 h. After recovering from quiescence, cells were treated with dox for another 144h. RNA was extract and qPCR performed for *NFATC4*, FST, *RCAN1* and *MYC* at each of the listed time points. n=2.

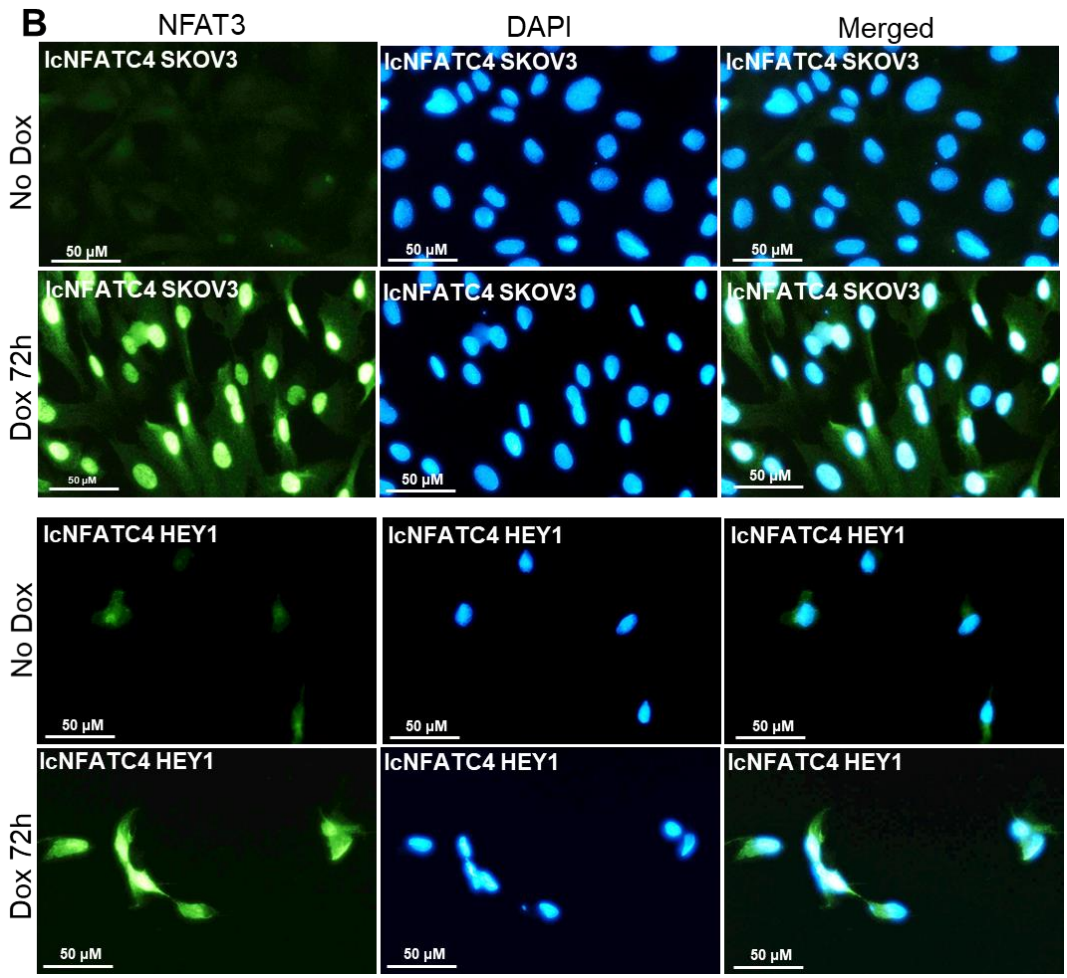
**Supplementary Table 1.** Cisplatin and Taxol IC50 values for ovarian cancer cell lines used in this study.

**Supplementary Table 2.** qPCR primer sequences.

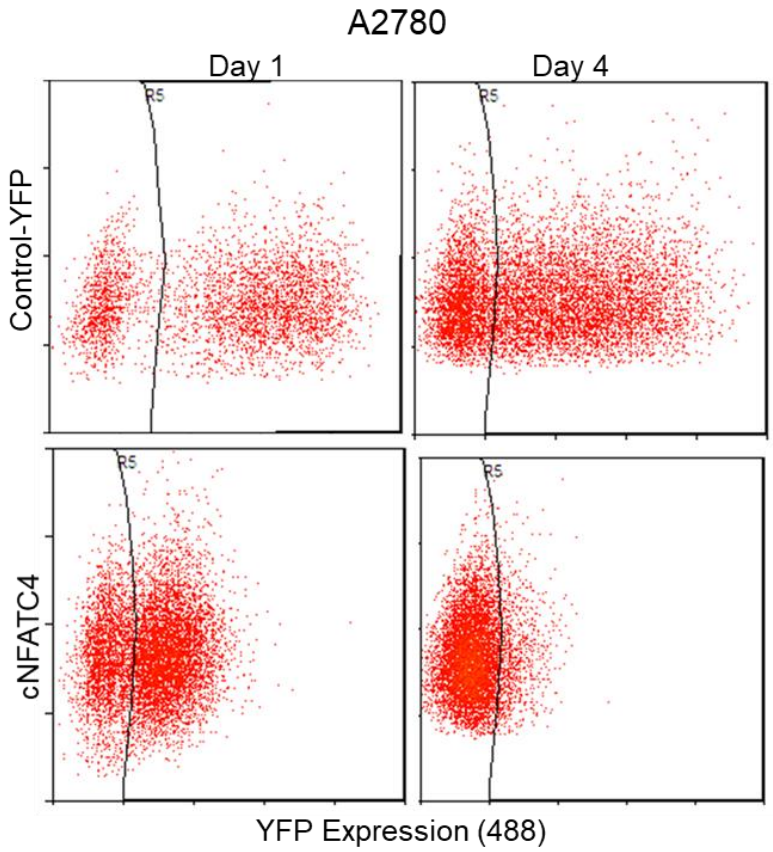



**Supplementary Figure 1**

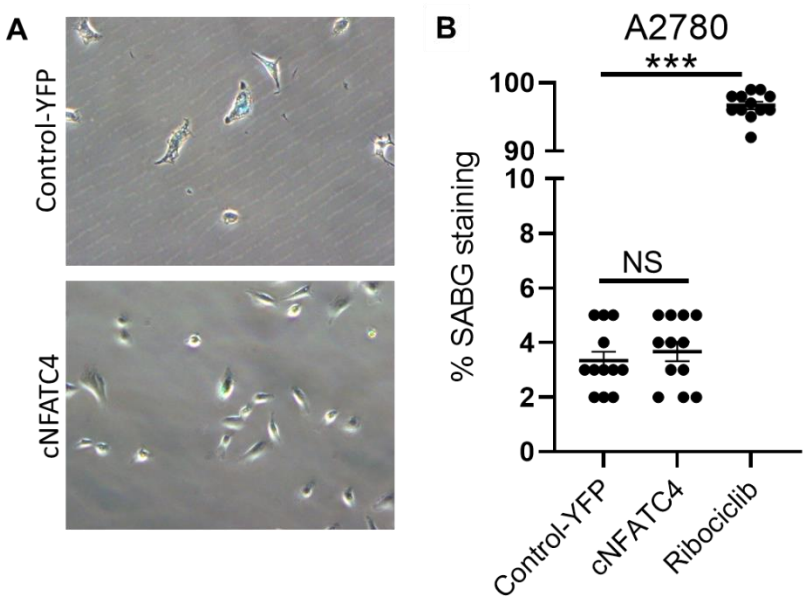

A
OVSAHO
OVCAR3
OVCAR4
0 ng/mL Dox
100 ng/mL Dox
NS
NFATC4 fold change mRNA
RCAN1 fold change mRNA
lcNFATC4-1
lLuc-1


B
NFAT3
DAPI
Merged
No Dox
Dox 72h
lcNFATC4 SKOV3
lcNFATC4 HEY1
50 µM

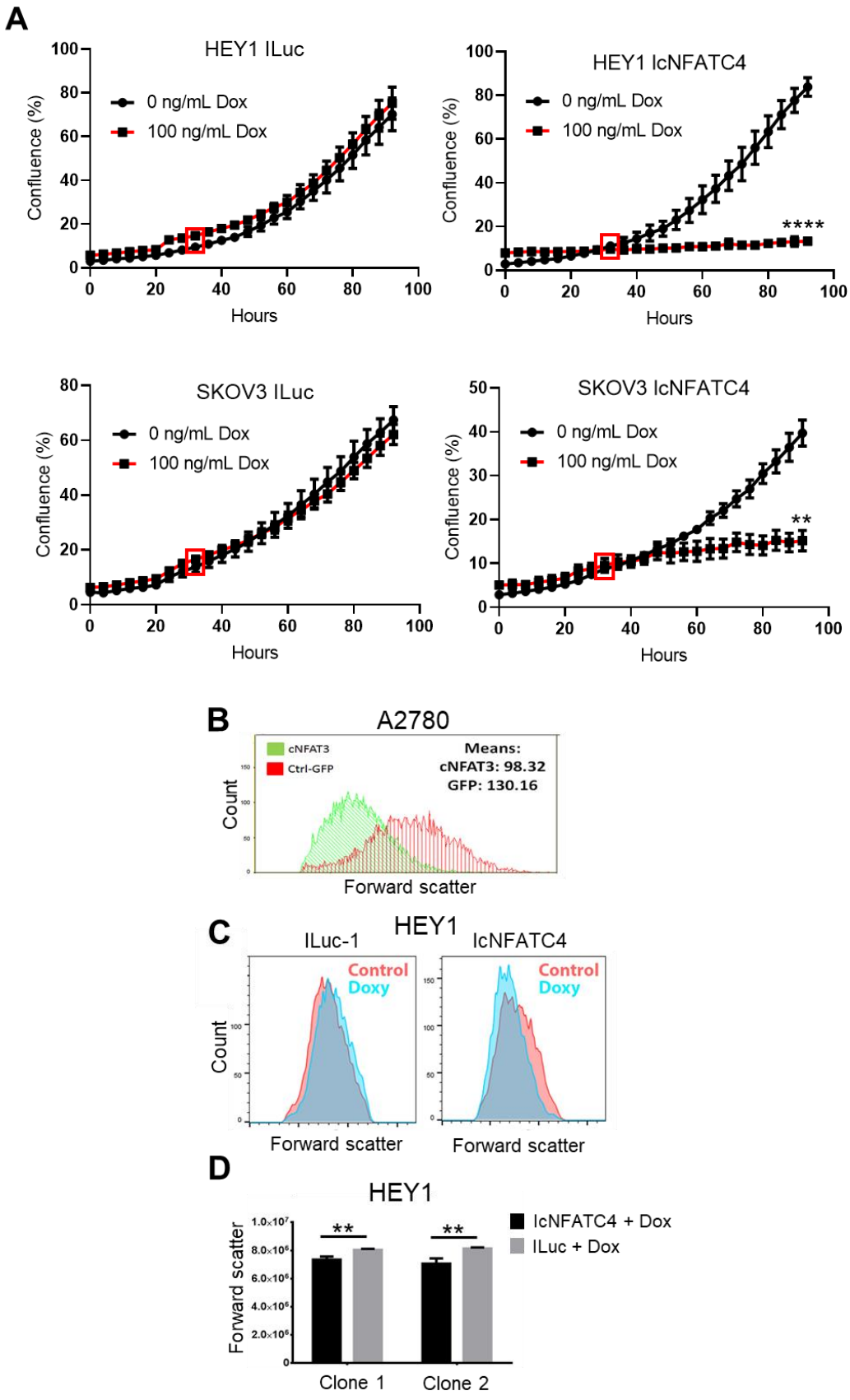
**Supplementary Figure 2**



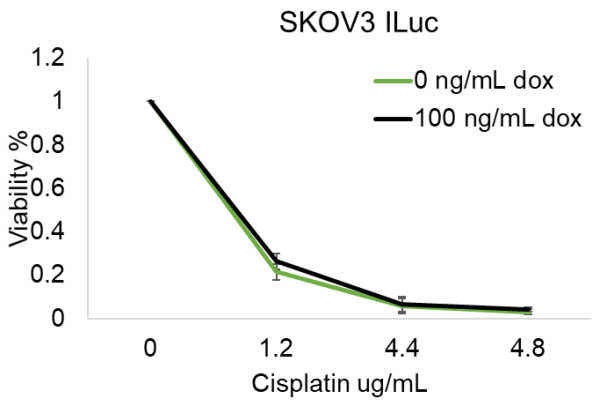

**Supplementary Figure 3**

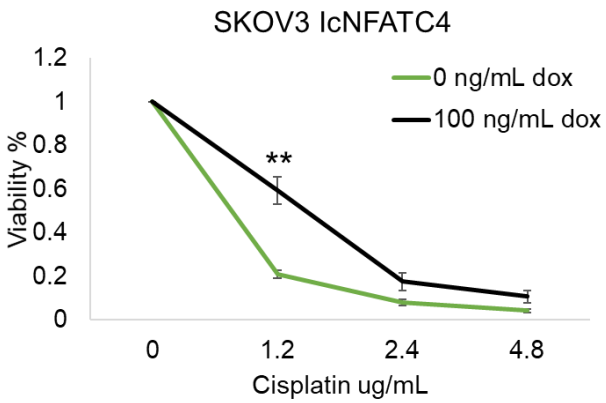



**Supplementary Figure 4**

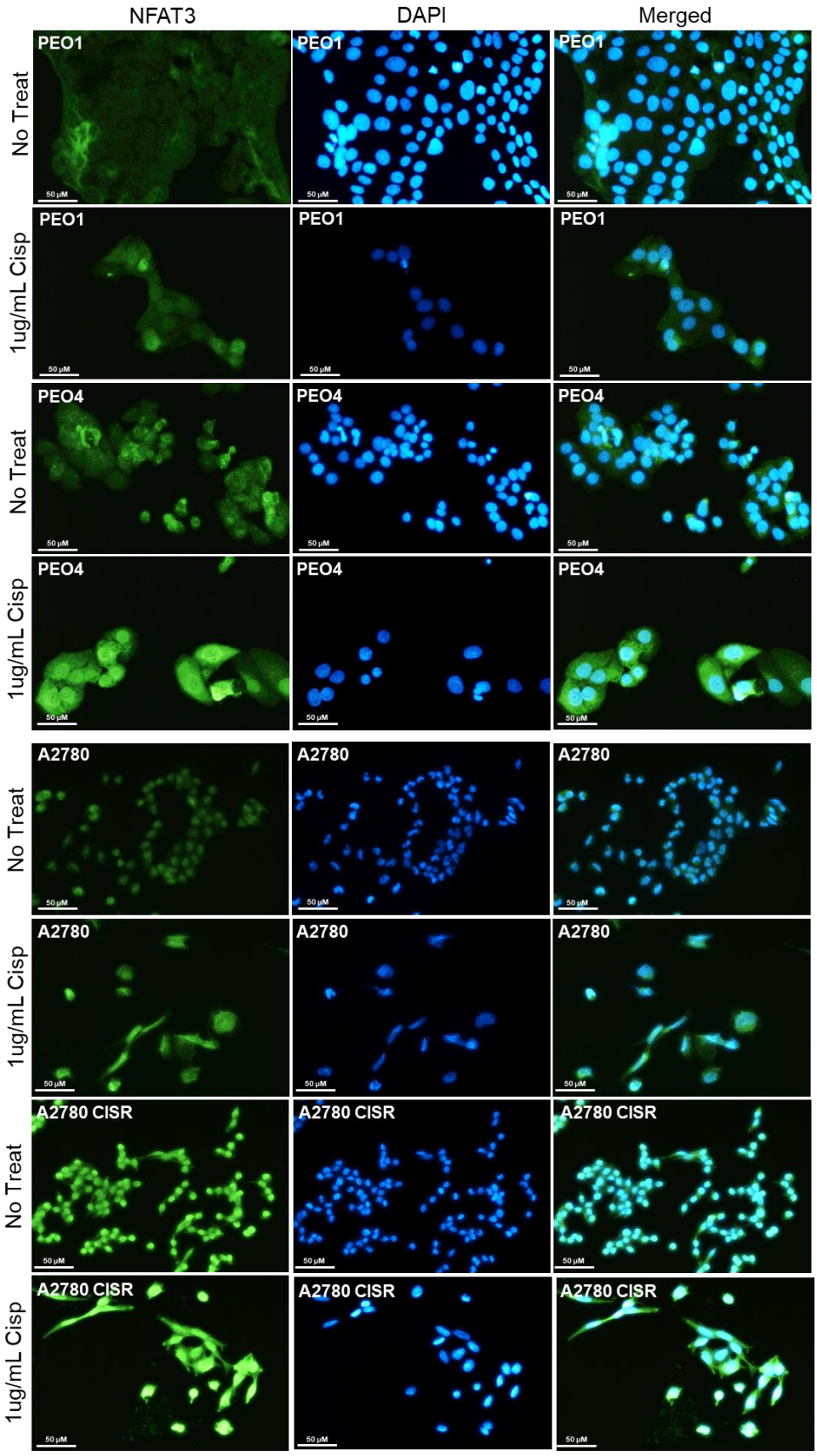



**Supplementary Figure 5**

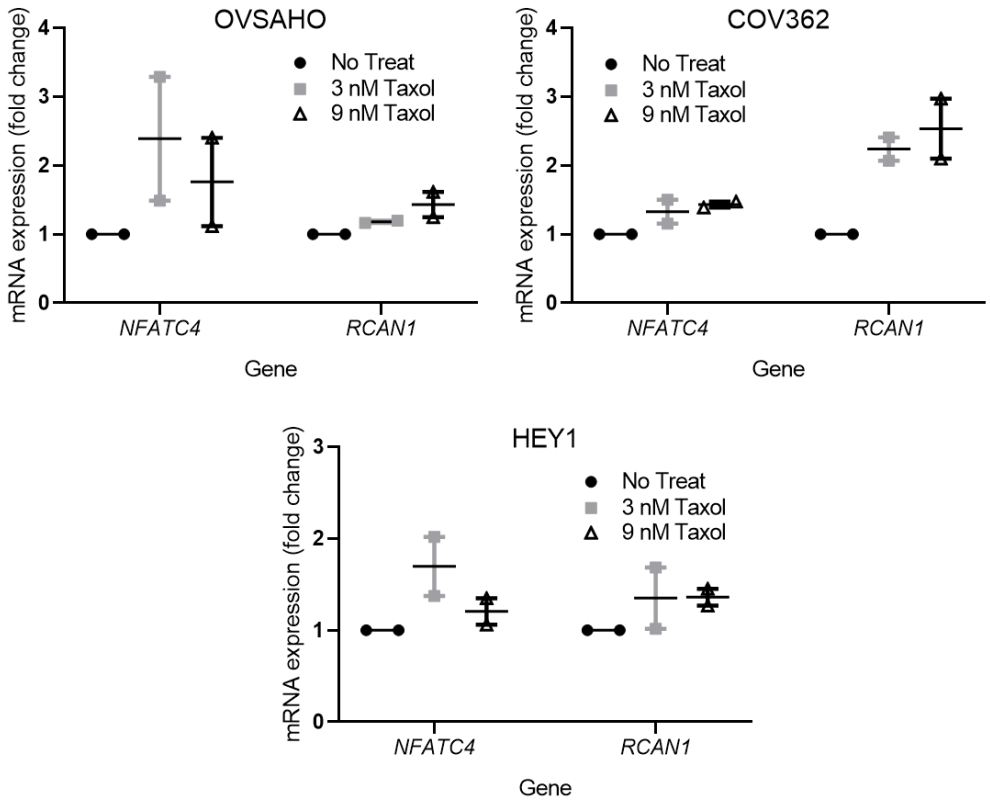


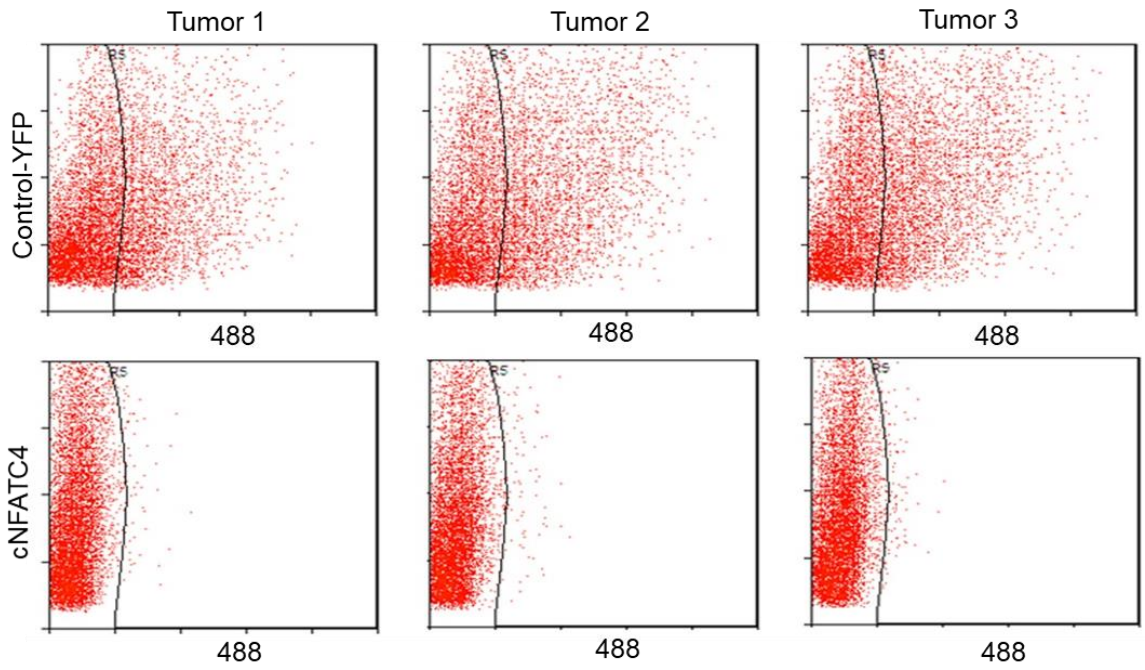

**Supplementary Figure 6**



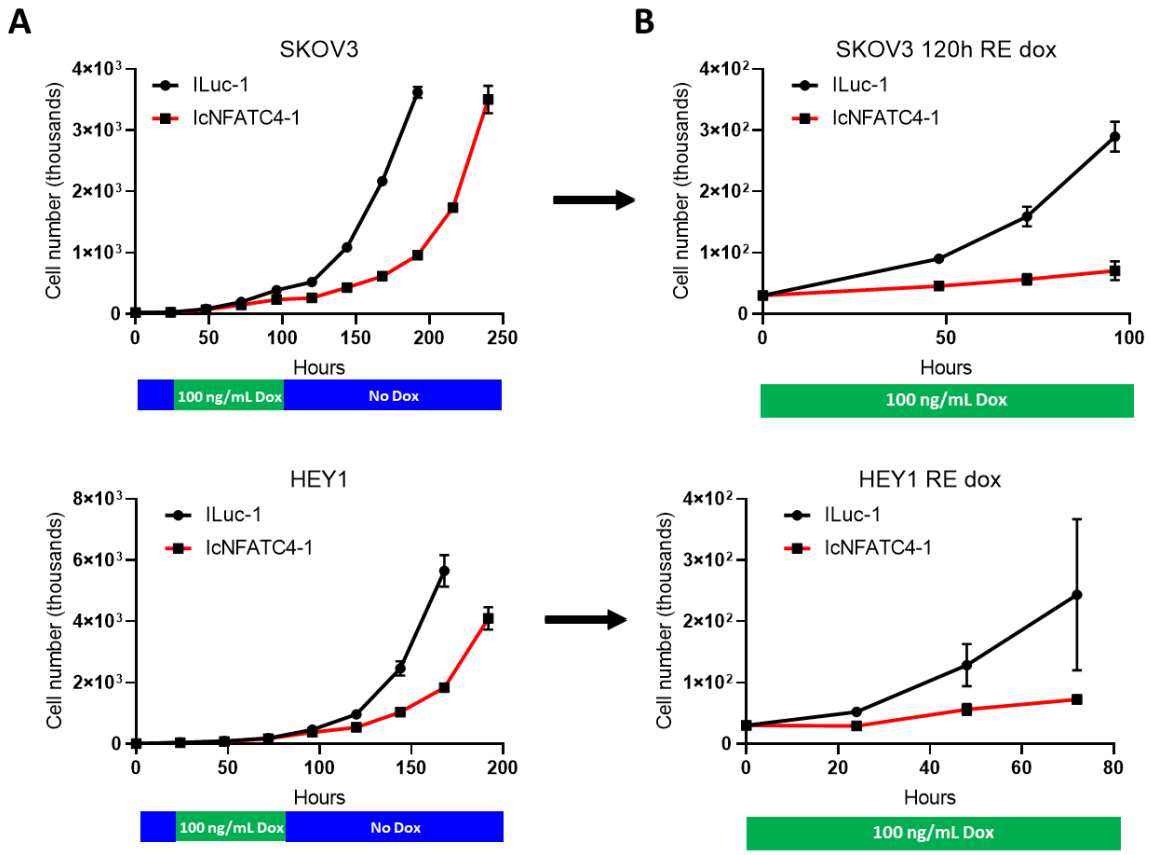

**Supplementary Figure 7**



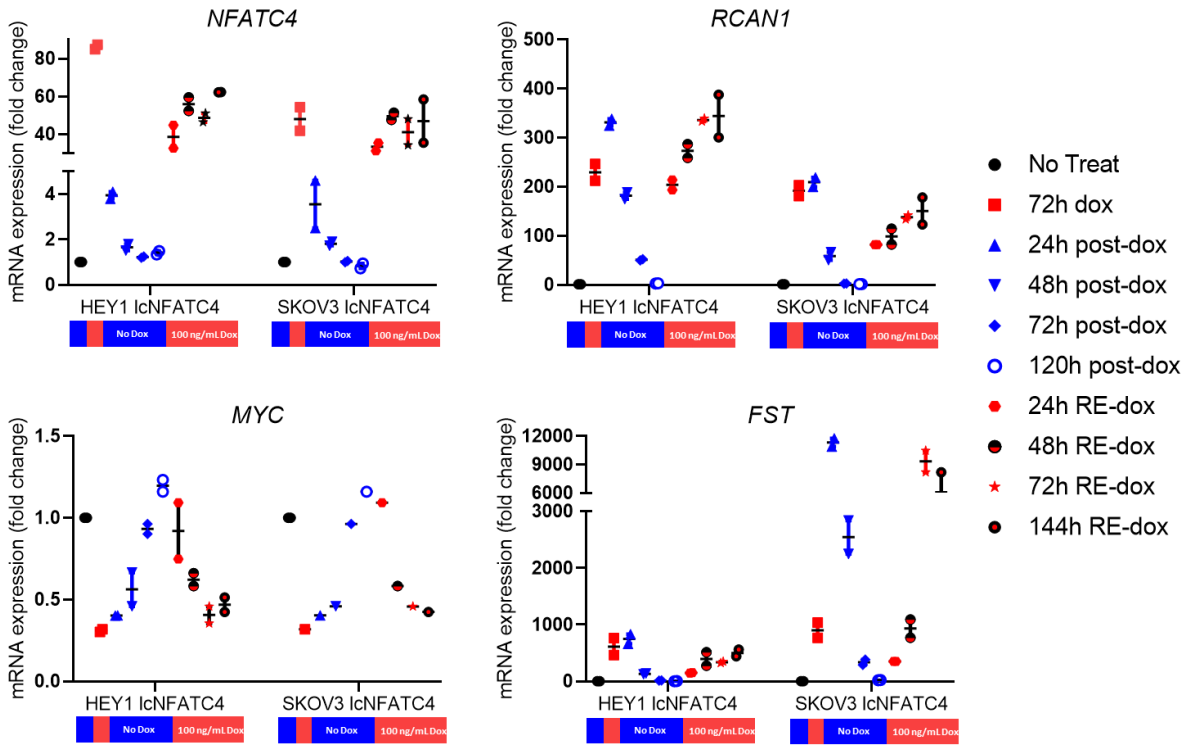

**Supplementary Figure 8**




**Supplementary Figure 9**




**Supplementary Figure 10**




**Supplementary Figure 11**

| Cell Line | IC50 Cisplatin (ug/ml) | IC50 Taxol (nM) |
|---|---|---|
| SKOV3 | 0.69 | 7 |
| OVSAHO | 0.48 | 5.73 |
| A2780 | 0.23 | N/A |
| COV362 | 1.29 | 10.8 |
| CaOV3 | 2.54 | 3.88 |
| HEY1 | 0.59 | 2.18 |

**Supplementary Table 1**

| ***Gene*** | **Direction** | **Sequence** |
|---|---|---|
| *NFATC4* | Forward | AGAACTGGACTCAGAGGATG |
| | Reverse | ATGGAGGTGATGCGGATG |
| *RCAN1* | Forward | GCTCCGCCAAATCCAGACAA |
| | Reverse | GCTGCGTGCAATTCATACTTTTC |
| *GAPDH* | Forward | CTGGGCTACACTGAGCACC |
| | Reverse | AAGTGGTCGTTGAGGGCAATG |
| *FST* | Forward | ACGTGTGAGAACGTGGACTG |
| | Reverse | CACATTCATTGCGGTAGGTTTTC |
| *cNFATC4* | Forward | ATTGAGAGGGGTCCTGATGGA |
| | Reverse | CGGGGATGGTGAGAGTCAAT |
| *MYC* | Forward | GGCTCCTGGCAAAAGGTCA |
| | Reverse | CTGCGTAGTTGTGCTGATGT |

**Supplementary Table 2**