**SUPPLEMENTARY TABLE SI**
**Nucleotide sequences of the Stau2 promoter mutants**

**WT (-198)**
CTGCAGCTGCTGGGGCCCGGCAGCCGCCAGGGGGCGGGAGCTGCGTCGCGAACAATGGCCGCGCTTGGT
CGCGGGCCGGCGGGAGGCGGAGTGGAGGTAGAGCCGGTGCCG**GGCGCGCGCGC**CGGCCGGGCGTGCTGG
GGCGCGGGAGCGGCTGCGCAGGCGGGGGCGCGCGGCGCGAGCGCGGGAGGGCGCGGCGGGA

**-198$^{E}$**
CTGCAGCTGCTGGGGCCCGGCAGCCGCCAGGGGGCGGGAGCTGCGTCGCGAACAATGGCCGCGCTTGGT
CGCGGGCCGGCGGGAGGCGGAGTGGAGGTAGAGCCGGTGCCG**GGaGaGaGaGC**CGGCCGGGCGTGCTGG
GGCGCGGGAGCGGCTGCGCAGGCGGGGGCGCGCGGCGCGAGCGCGGGAGGGCGCGGCGGGA

**-198$^{M}$**
CTGCAGCTGCTGGGGCCCGGCAGaaGCCAGGGGGaaaGAGCTGCGTCGCGAACAATGaaaGCGCTTGGT
CGCaaaCCGGCaaGAGGCaaAGTGGAGGTAGAGCCGGTGCCG**GGCGCGCGCGC**CGGCCGGGCGTGCTGG
GGCGCaaGAGCGaaTGCGCAGGCaaaGGCGCGCGGaaaGAGCGaaaGAGGGCGCGGCGGGA

**-149**
GAACAATGGCCGCGCTTGGTCGCGGGCCGGCGGGAGGCGGAGTGGAGGTAGAGCCGGTGCCG**GGCGCGC**
**GCGC**CGGCCGGGCGTGCTGGGGCGCGGGAGCGGCTGCGCAGGCGGGGGCGCGCGGCGCGAGCGCGGGAG
GGCGCGGCGGGA

**-99**
GAGCCGGTGCCG**GGCGCGCGCGC**CGGCCGGGCGTGCTGGGGCGCGGGAGCGGCTGCGCAGGCGGGGGCG
CGCGGCGCGAGCGCGGGAGGGCGCGGCGGGA

**-70**
GGCGTGCTGGGGCGCGGGAGCGGCTGCGCAGGCGGGGGCGCGCGGCGCGAGCGCGGGAGGGCGCGGCGG
GA

Mutations are indicated as lower case letters.

The putative E2F1 binding site is in bold.

**SUPPLEMENTARY TABLE SII**
**Inhibitor specificity**

| Name | Target | Other kinases | Specificity ($IC_{50}$)[1] |
|---|---|---|---|
| 118500 | ATM | | 13 nM |
| | | DNA-PK, mTOR, PI3K | 2.5, 9.3, 16.6 μM |
| | | ATR | > 100 μM |
| 118510 | ATR | | 12 nM |
| | | ATM, DNA-PK | > 8 μM |
| VE821 | ATR | | 13 nM |
| | | PIKKs, ATM, DNA-PK, mTOR and PI3K | Minimal activity |
| 681637 | CHEK1 | | 47 nM |
| | | Wee1 | 97 nM |
| | | PKC, Cdk4 and other CDKs | >3 μM |
| 220486 | CHEK2 | | 15 nM |
| | | Cdk1, CK1 | 12 μM |
| | | 31 other kinases including CHEK1 | Weak affects |
| NU7441 | DNA-PK | | 14 nM |
| | | PI3K | 5 μM |
| | | ATM, ATR | > 100 μM |

ATM inhibitor (118500), ATR inhibitor (118510), CHEK1 inhibitor (681637), and CHEK2 inhibitor (220486) were purchased from EDM Millipore. ATR inhibitor (VE821) and DNA-PK inhibitor (NU7441) were purchased from Selleckchem.

[1] : $IC_{50}$ as specified by the manufacturers

## SUPPLEMENTARY TABLE SIII
## Oligonuceotide sequences for RT-qPCR amplification

| Gene name | | Oligonucleotide sequence |
|---|---|---|
| Stau2 | Sense: | 5’-GCTCTGAAGCGAAATATGCCTGTC-3’ |
| | Antisense: | 5’-TTTAAGCTCCTGTAAGACGGTGGTCG-3’ |
| Stau2-FLAG | Sense: | 5’-GTACCGGACATATGCCCGGGAATT-3’ |
| | Antisense: | 5’-AGCTAAAGTCCTTGTGGTAGGCAG-3’ |
| Stau1 | Sense: | 5'-TTTGTGACCAAGGTTTCGGTTGGG-3' |
| | Antisense: | 5'-TGGGCTTGTCTGTGGCTTGACTAT-3' |
| GAPDH | Sense: | 5'-CATGTTCGTCATGGGTGTGAACCA-3' |
| | Antisense: | 5'-AGTGATGGCATGGACTGTGGTCAT-3' |
| β-actin | Sense: | 5’-GTTCACAATGTGGCCGAGGACTTT-3’ |
| | Antisense: | 5’-TTAGGATGGCAAGGGACTTCCTGT-3’ |
| APAF1 | Sense: | 5’-GCAGAATCTTTGCACACGGTTGGA-3’ |
| | Antisense: | 5’-TTTGCGAAGCATCAGAATGCGGAG-3’ |
| GRP78 | Sense: | 5’-TAGATGGGCAACTGGCTGAAAGGT-3’ |
| | Antisense: | 5’-TATTCTGCTCAGGGTCTGCCCAAA-3’ |
| Stau2 promoter | Sense: | 5’-AGCTGCGTCGCGAACAATGGCCG-3’ |
| | Antisense: | 5’-CCCCGCCTGCGCAGCCGCT-3’ |
| APAF1 promoter | Sense: | 5’-CATGAGCCGTGGCAGGAGTGCG-3’ |
| | Antisense: | 5’-GACAGCGGAGCAGTCAAATCCCG-3’ |
| HMBS | Sense: | 5’-CTCTTTACCCACCTGGCTGTGC-3’ |
| | Antisense: | 5’-CCAAGGCTGGTCCCTTTAACCT-3’ |

**SUPPLEMENTARY FIGURES**

**Supplementary Figure S1. Stau2 down-regulation in response to CPT occurs in transformed and untransformed cell lines.** HEK293T **(A,B,C)** and hTert-RPE1 **(D,E,F)** cells were treated for 24h with increasing concentrations of CPT as indicated (**A,D**). Both cell lines were also treated with CPT for different time periods and/or with different doses **(B,E)**. Protein expression was monitored by Western blotting using anti-Stau2, anti-PARP1 (as a marker of apoptosis) and anti-γH2AX (as a marker of DNA damage) antibodies. The Western blots are representative of 3 independently performed experiments. Quantification of Stau2 protein is shown. **(C,F)** Protein quantification and the RT-qPCR data represent the means and standard deviation of 3 independently performed experiments with 50 nM CPT for increasing time periods. For Stau2 protein and mRNA quantification, the ratios of Stau2 on β-actin or on GAPDH, respectively, were arbitrary fixed to 1. Statistical analyses (Student's *t*-test) are indicated when significant. ***, p value ≤ 0.001; **, p value ≤ 0.01; *, p value ≤ 0.05.

**Supplementary Figure S2. Quantification of Stau2 protein level from data shown in figure 2C and 2E.** HCT116 cells were irradiated with different doses of UVC **(A)** or IR **(B).** Cells were collected at different time points post-treatment and cell extracts were analyzed by Western blotting (see Figures 2 C,E). Stau2 protein expression was normalized to that of β-actin protein, the ratio in non-irradiated cells being fixed to 1. Data represent the means and standard deviation of 3 independently performed experiments. Statistical analyses (Student's *t*-test) are indicated when significant. *, p value ≤ 0.05; **, p value ≤ 0.01.

**Supplementary Figure S3. ATR regulation of Stau2 and E2F1 expression.** HCT116 cells were incubated in the presence of increasing concentrations of 2 different ATR inhibitors (118510, VE821)

for 8h. **(Left panels)** Cells were collected and Stau2 mRNA quantified by RT-qPCR. Stau2 mRNA expression was normalized to that of GAPDH mRNA, the ratio in untreated cells being fixed to 1. Data represent the means and standard deviation of 3 independently performed experiments. Statistical analyses (Student's *t*-test) are indicated when significant. *, p value ≤ 0.05; **, p value ≤ 0.01. **(Right panels)** Western blot analysis of Stau2 and E2F1 expression. Blots are representative of 3 independently performed experiments.

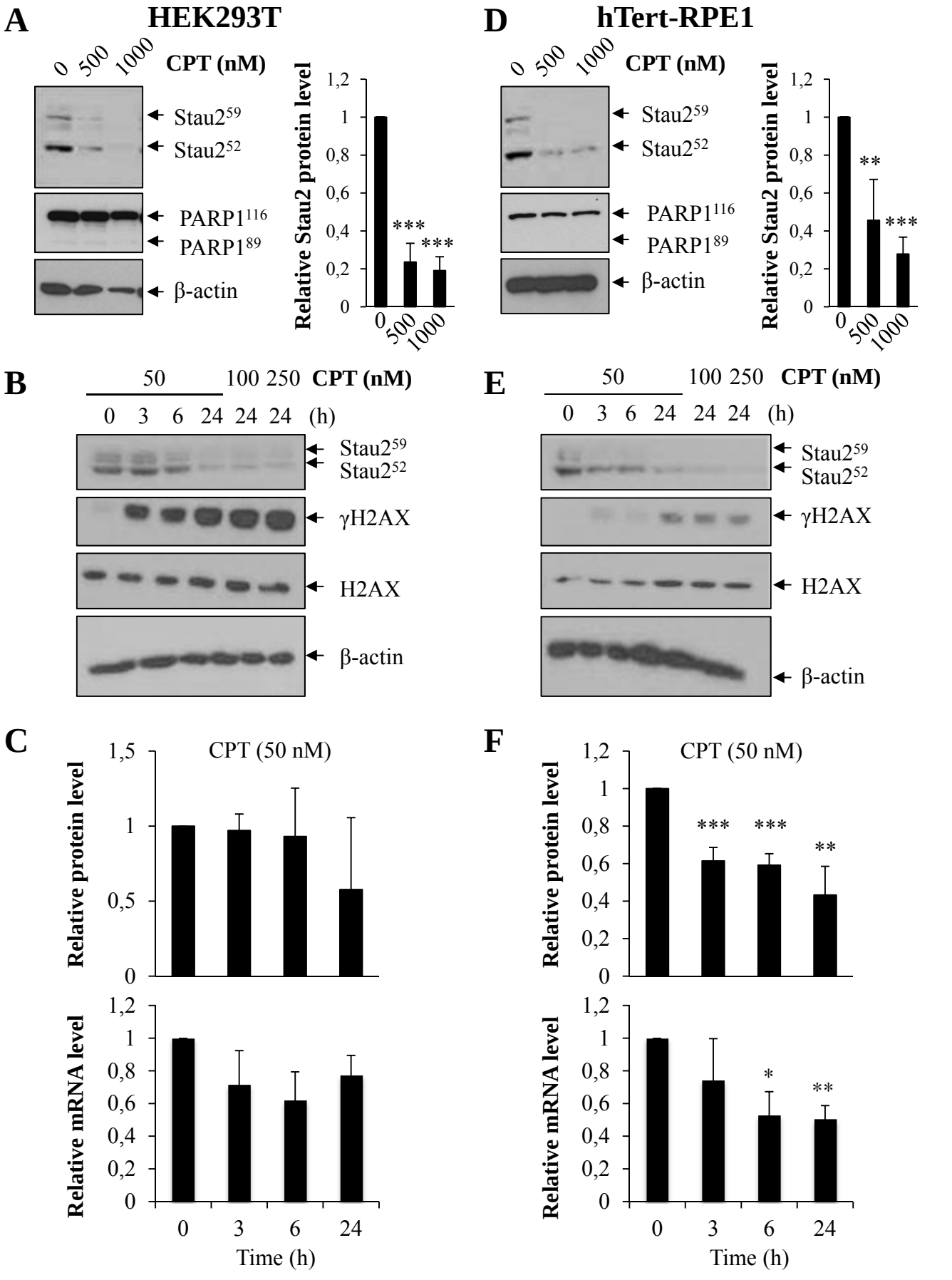
**Supplementary Figure S4. Inhibition of signaling pathways modulates p53 expression.** Cell extracts were analysed by Western blotting to monitor p53 activation by CPT **(A)**, UVC **(B)** or Doxo **(C)** in the presence or absence of kinase inhibitors. Western blots are representative of 3 independently performed experiments. Hsp90 or β-actin was used as loading controls. Quantification of p53 expression is shown below the blots. Data represent the means and standard deviation of 3 independently performed experiments. Statistical analyses (Student's *t*-test) are indicated when significant. *, p value ≤ 0.05. DMSO, dimethyl sulfoxide; DNA-PK (10 nM); ATM (20 nM); ATR (20 nM); CHEK1 (20 nM); CHEK2 (20 nM).

**Supplementary Figure S5. ATR and CHEK1 inhibition causes a decrease in E2F1 expression.** HCT116 were treated with kinase inhibitors in the presence (+) or absence (-) of CPT **(A),** UVC **(B)** or Doxo **(C)** as described in the legend of figure 3. **(Left panels)** Cells were collected and proteins analyzed by Western blotting. *, non-specific bands. **(Right panels)** E2F1 protein levels were normalized to that of β-actin protein, the ratio in DMSO-treated cells without inhibitors being fixed to 1. Data represent the means and standard deviation of 3 independently performed experiments. Statistical analyses (Student's *t*-test) are indicated when significant. ***, p value ≤ 0.001; **, p value ≤ 0.01; *, p value ≤ 0.05.

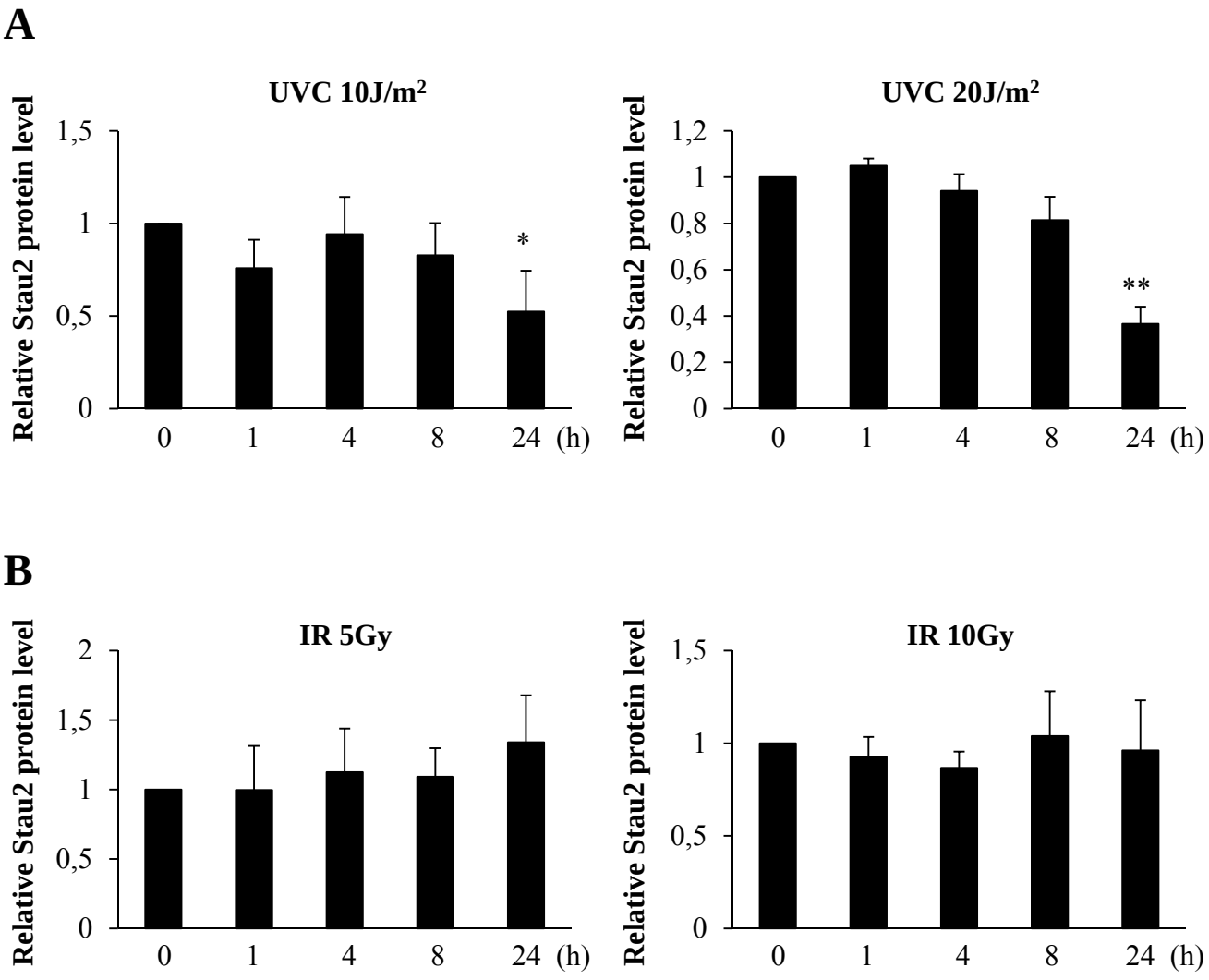
**Supplementary Figure S6. The transcription factor E2F1 up-regulates Stau2 expression.** HCT116 cells were transfected with plasmids coding for HA-ER or HA-ER-E2F1 as described in figure 6A. Cells were further incubated in the absence (-) or presence (+) of OHT (500 nM) and CPT (300 nM) for 24h. Expression of the proteins was analyzed by Western blotting.

**Supplementary Figure S7. Quantification of PARP1 cleavage in control and Stau2 shRNA-treated cells (from figure 9).** HCT116 cells were infected with a retrovirus expressing a non-targeting shRNA (Ctrl) or a shRNA against Stau2. Cells were selected on puromycin for 48h and then treated or not with increasing concentrations of CPT for 24h. Cell extracts were analyzed by Western blotting for Stau2 expression, PARP1 cleavage and loading (β-actin) (see figure 9B). Quantification of PARP1 cleavage ($PARP1^{89}/PARP1^{116}$) is shown in function of CPT concentration. The data represent the means and standard deviation of 3 independently performed experiments. *, p value $\leq 0.05$.

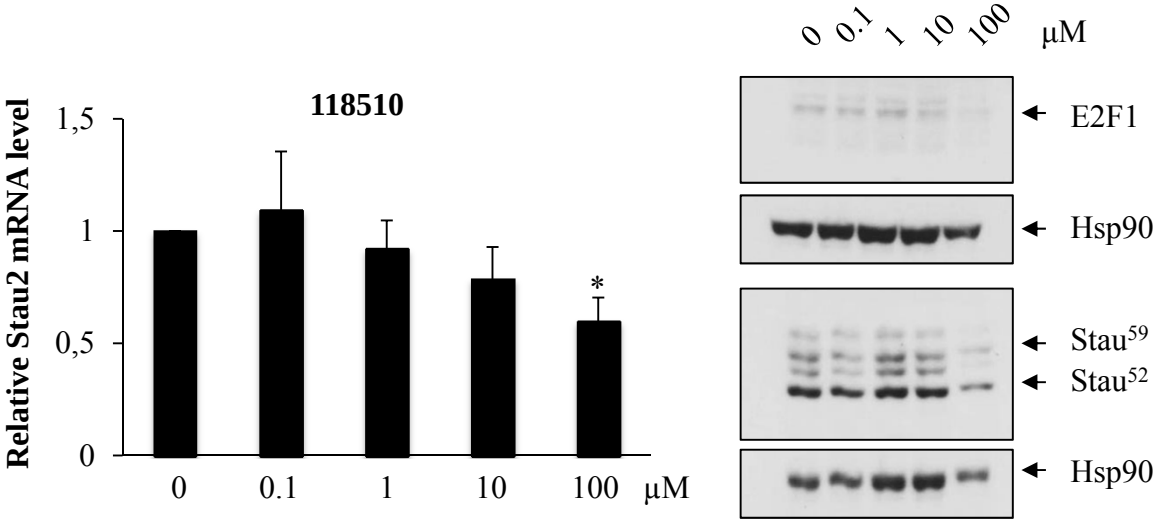
Supplementary Fig 1

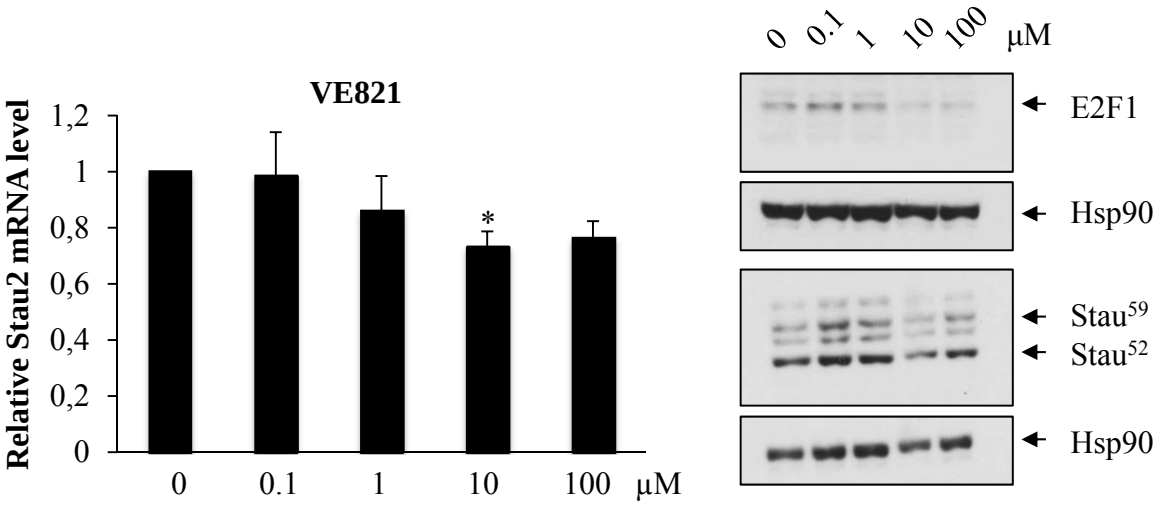


Supplementary Fig S2

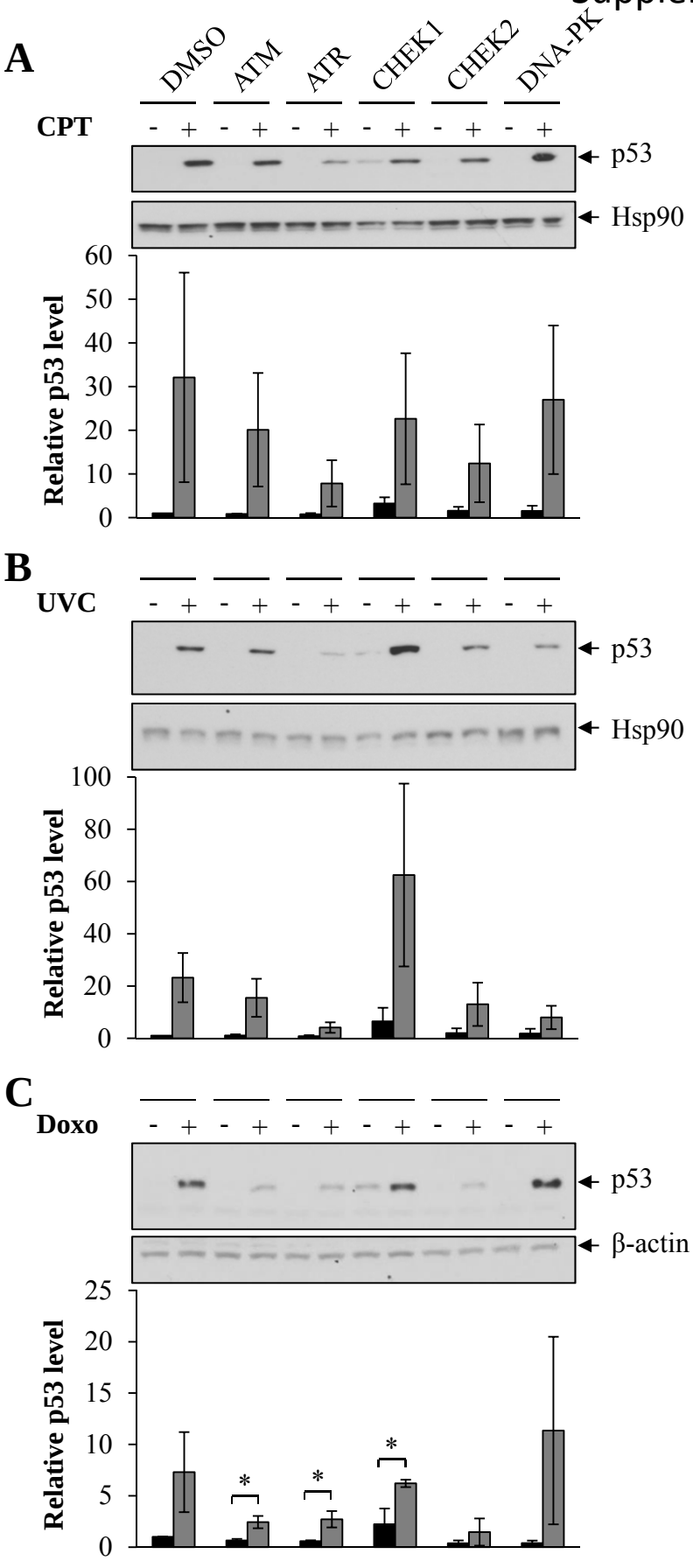


Supplementary Fig S3

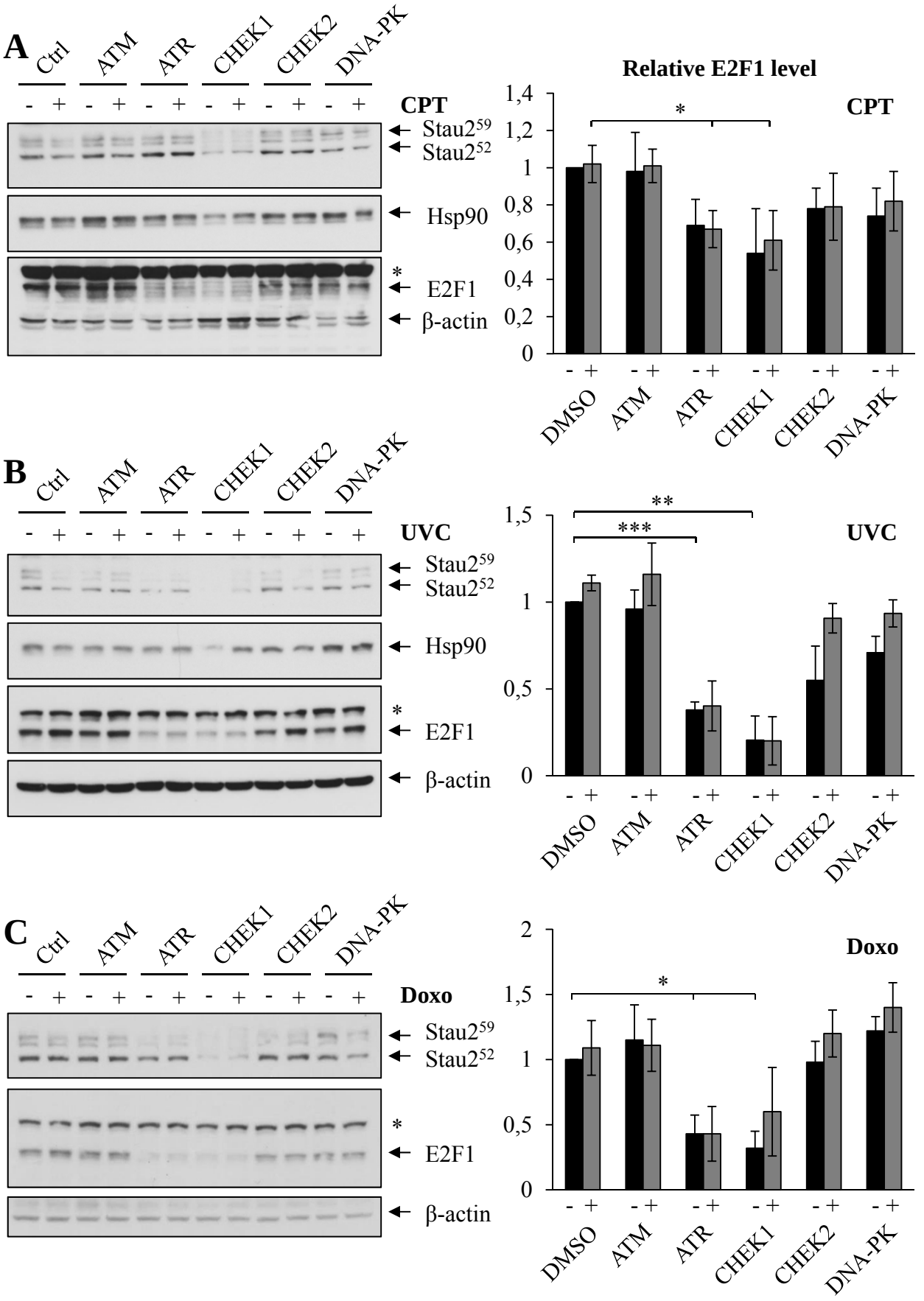


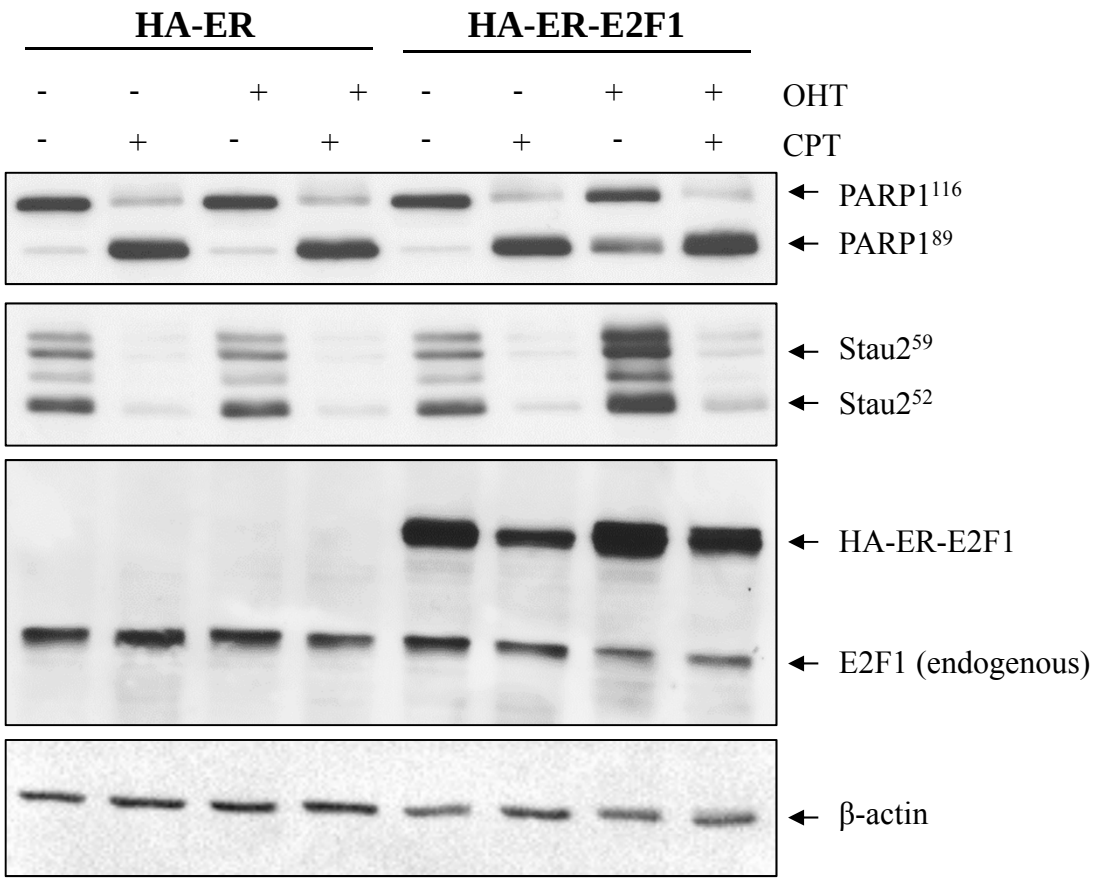
Supplementary Fig S4



Supplementary Fig S5



Supplementary Fig S6



Supplementary Fig S7