SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1: a, western blot analyses of p53 acetylation in U2OS cells transfected with control (siLUC) or different siRNAs against TSPYL2. Transfected cells were treated with MG132 to stabilize p53 protein levels and then with etoposide to induce p53 acetylation. The fold induction of acetylated p53 relative to total p53 is indicated. **b**, U2OS cells were transfected with control (siCTRL), TSPYL2 and CCAR2 siRNAs as indicated. 48hrs later cells were treated or not with etoposide and p53 acetylation was analyzed by western blot. The fold induction of acetylated p53 relative to total p53 is shown.

Supplementary Fig. 2: **a**, example of western blot analysis of SIRT1 deacetylation assay performed in control and TSPYL2 depleted cells. **b**, western blot analyses of p53 acetylation in TSPYL2 depleted cells treated with MG132 and then with or without the SIRT1 inhibitor nicotinamide (NAM) and etoposide. The fold induction of acetylated p53 relative to total p53 is reported. **c**, example of western blot analysis of p300 acetyl-transferase assay performed in control and TSPYL2 depleted cells. **d**, Example of p300 acetyl-transferase assay performed in U2OS SIRT1-WT and –KO cells. **e**, Example of p300 acetyl-transferase assay performed in U2OS cells transfected with control or SIRT1 siRNAs.

Supplementary Fig.3: a, SIRT1 was immunoprecipitated from control (siLUC) and SIRT1 silenced cells before and after etoposide treatment. Co-immunoprecipitated p300 was determined by western blot. IP, immunoprecipitates; PC, negative control; Input, total lysate. **b**, p300 was immunoprecipitated from siLUC and sip300 cells before and after etoposide. Co-immunoprecipitated SIRT1 was analyzed by western blot. IP, immunoprecipitates; PC, negative control; Input, total lysate.

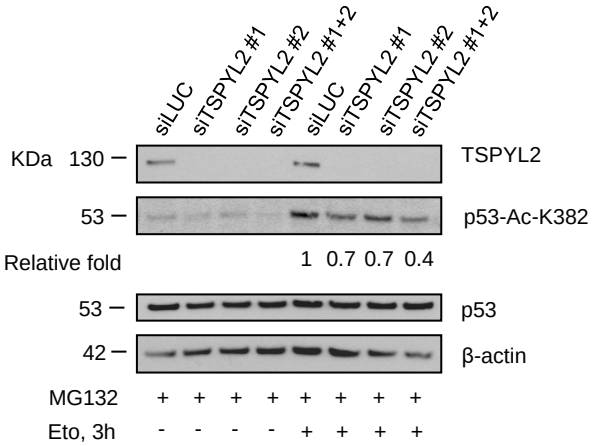
Supplementary Fig. 4: TSPYL2 was immunoprecipitated from untreated and etoposide treated cells and analyzed by western blot with general anti-acetyl-lysine antibody. p300 was immunoprecipitated from etoposide treated cells and used as positive control. IP, immunoprecipitates; PC, negative control; Input, total lysate.

Supplementary Fig. 5: Western blot analysis of TSPYL2 depletion in siRNAs transfected U2OS cells used for RT-qPCR analyses (**a**) and luciferase assays (**b**).

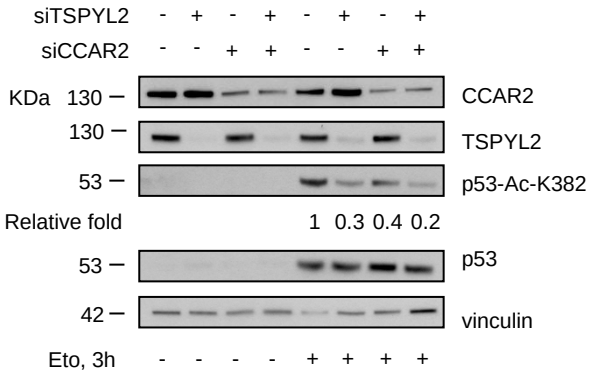
Supplementary Fig.6: a, U2OS cells were transfected with control or different siRNAs against TSPYL2. 48hrs later cells were treated with etoposide and the percentage of dead cells was determined by trypan blue exclusion test 30 hrs after treatment. **b**, U2OS cells were transfected with control, TSPYL2 and CCAR2 specific siRNAs. The induction of PARP cleavage was evaluated 30 h after etoposide treatment (20μM) by western blot. **c**, control and TSPYL2 silenced U2OS cells were treated with UV (20J/m^2) or gemcitabine (10μM). 30 hrs later, the percentage of dead cells was determined by trypan blue staining.

Supplementary Fig. 1

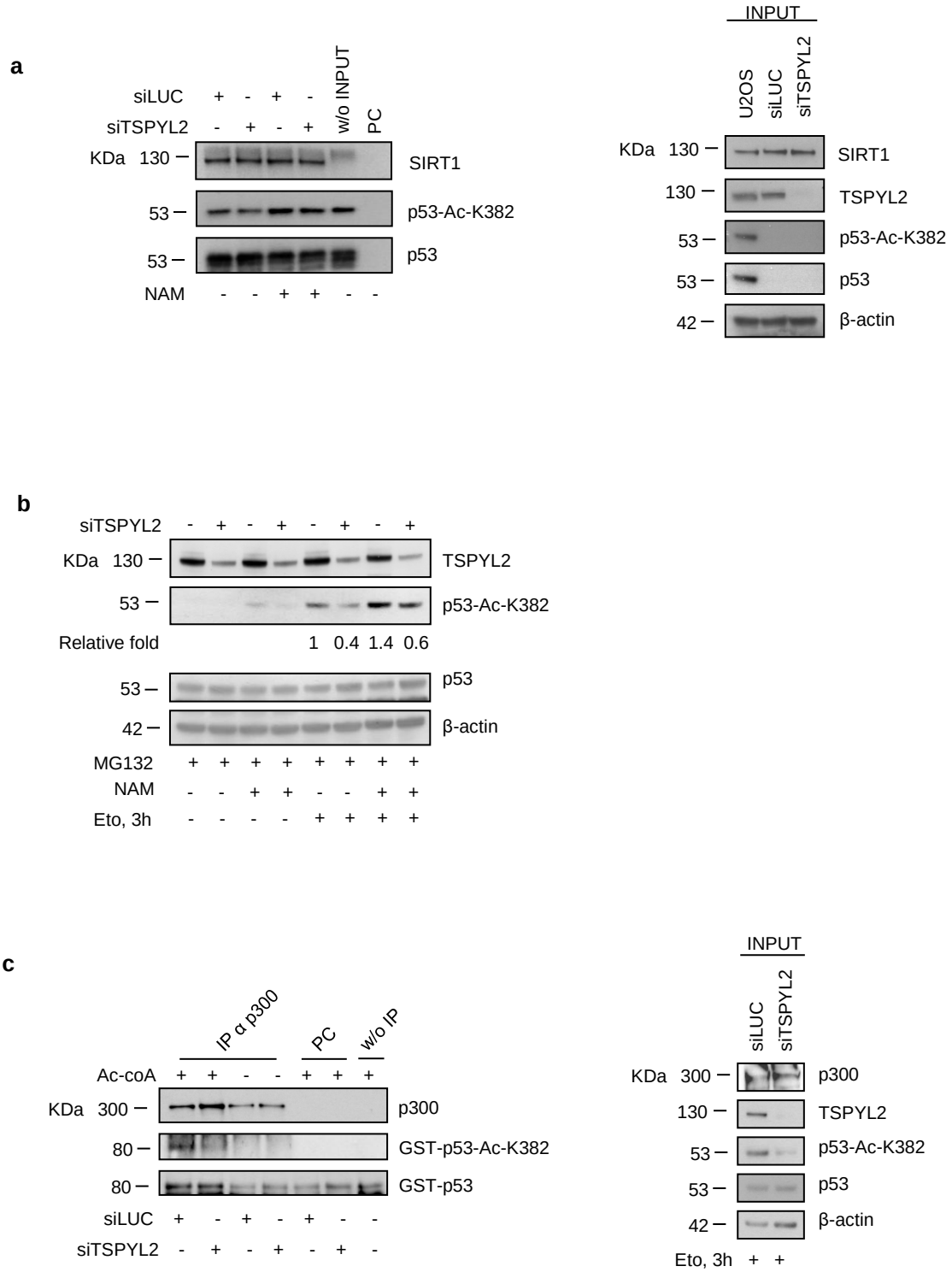
a



b



Supplementary Fig. 2



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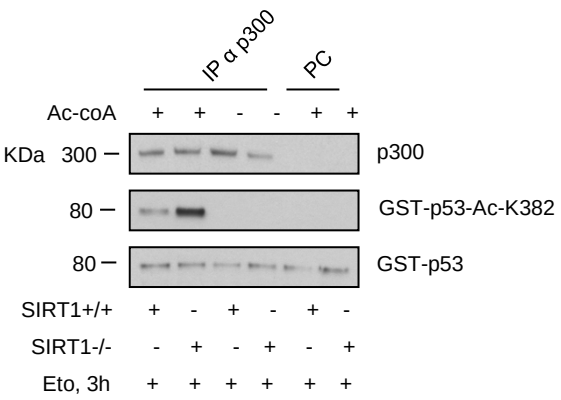
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PC
Ac-coA + + - - + +
KDa 300
p300
80
GST-p53-Ac-K382
80
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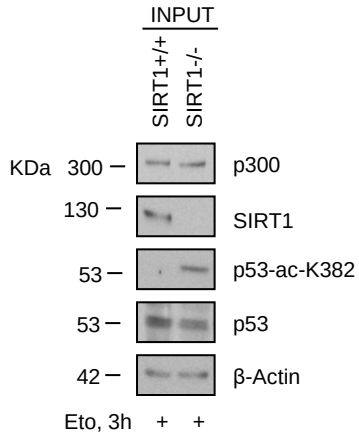
SIRT1+/+ + - + - + -
SIRT1-/- - + - + - +
Eto, 3h + + + + + +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SIRT1-/-
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p300
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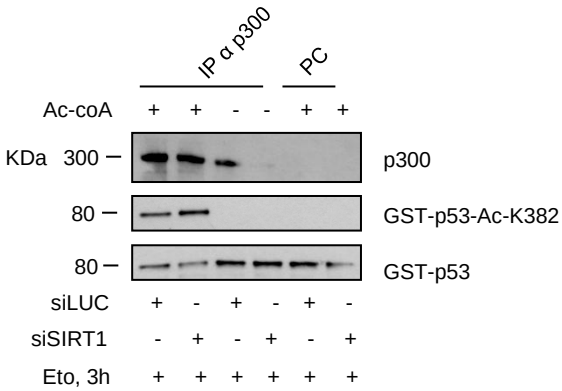
SIRT1
53
p53-ac-K382
53
p53
42
β-Actin
Eto, 3h + +

e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PC
Ac-coA + + - - + +
KDa 300
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80
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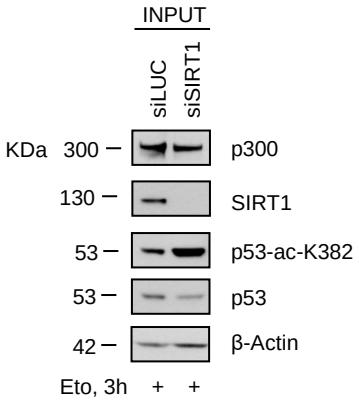
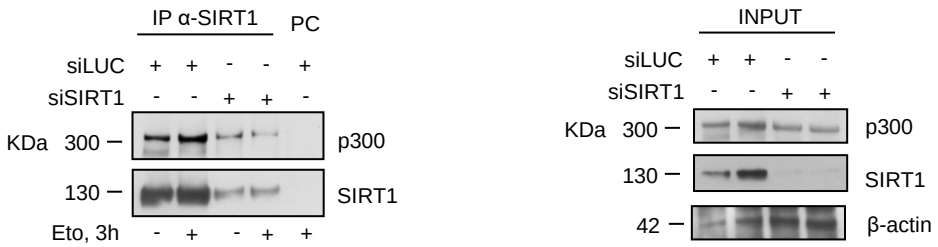
siLUC + - + - + -
siSIRT1 - + - + - +
Eto, 3h + + + + + +


INPUT
siLUC
siSIRT1
KDa 300
p300
130
SIRT1
53
p53-ac-K382
53
p53
42
β-Actin
Eto, 3h + +

Supplementary Fig. 3

a



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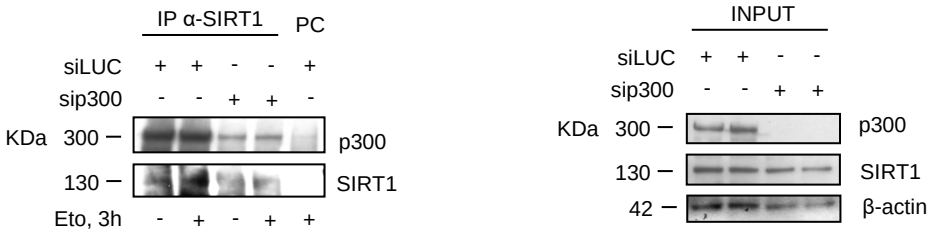
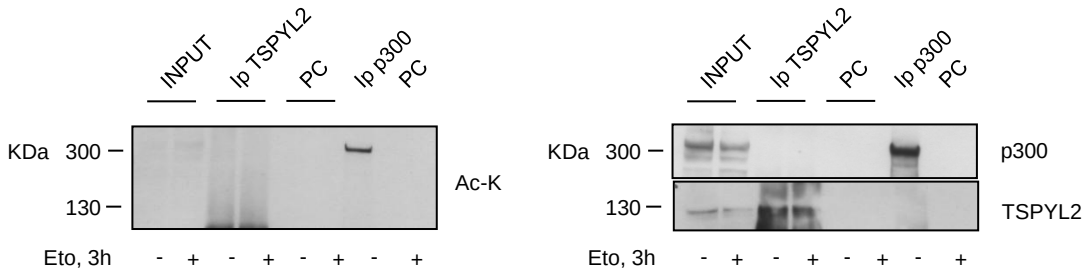
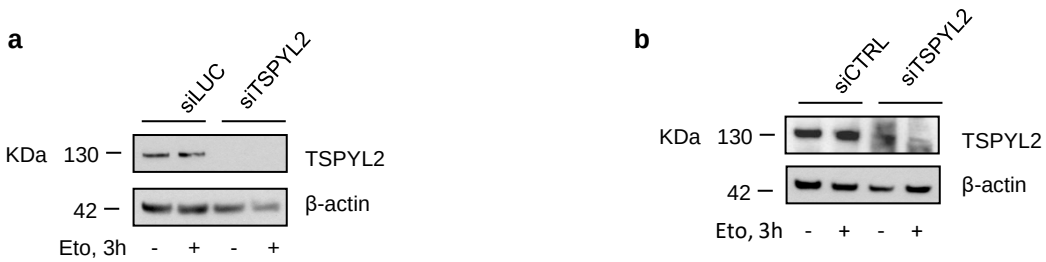


Supplementary Fig. 4



Supplementary Fig. 5



Supplementary Fig. 6