

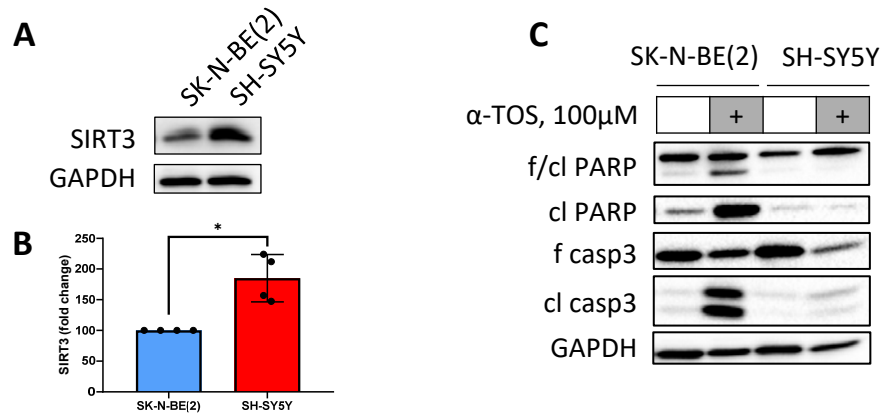


Figure S1. Higher SIRT3 level is associated with resistance to α -TOS in neuroblastoma cells. Representative immunoblot image of SIRT3 content in neuroblastoma cells (SK-N-BE(2), SH-SY5Y) (**A**); relative SIRT3 content (**B**); representative immunoblot image of apoptotic markers (PARP and caspase-3 cleavage) in neuroblastoma cells treated with 100 μ M α -TOS for 24 h (**C**). GAPDH was used as a loading control. Densitometric data were normalized to GAPDH and expressed as fold change relative to SK-N-BE(2) (set as 100%). Results are shown as the mean of four independent experiments $\pm$ SD. * $p < 0.05$.

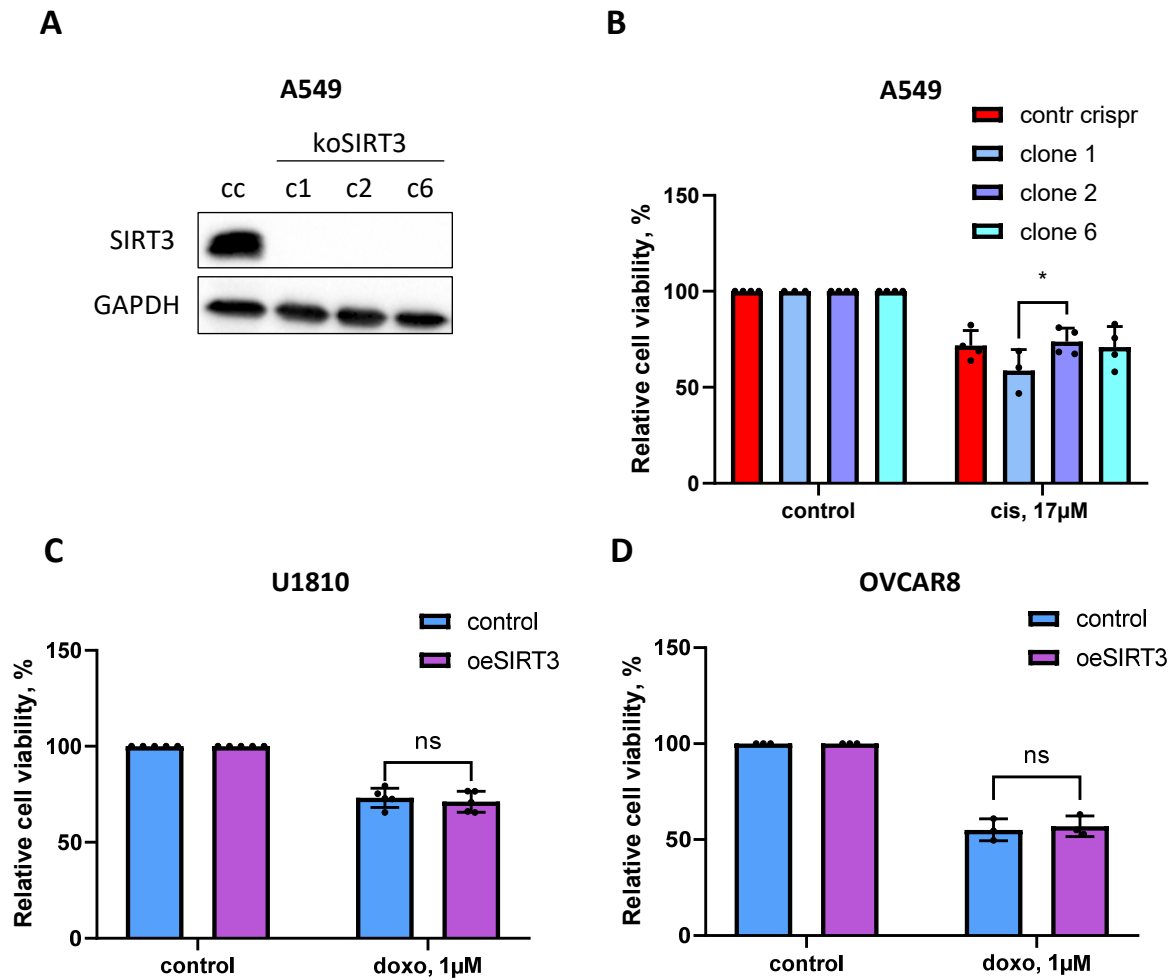


Figure S2. Modulating SIRT3 level does not change sensitivity to DNA-damaging agents. Representative immunoblot image of SIRT3 content in A549 SIRT3 knockout clones (cc – control CRISPR cell line, c1, c2, c6 – three independent knockout clones), GAPDH was used as a loading control (**A**); viability assay of A549 cells with SIRT3 knockout treated with 17 μ M cisplatin (cis) for 24 h (**B**); viability assay of SIRT3 overexpressing U1810 cells treated with 1 μ M doxorubicin (doxo) for 24 h (**C**); viability assay of SIRT3 overexpressing OVCAR8 cells treated with 1 μ M doxorubicin (doxo) for 24 h (**D**). Results are shown as the mean of at least three independent experiments $\pm$ SD. * $p < 0.05$, ns – not significant.

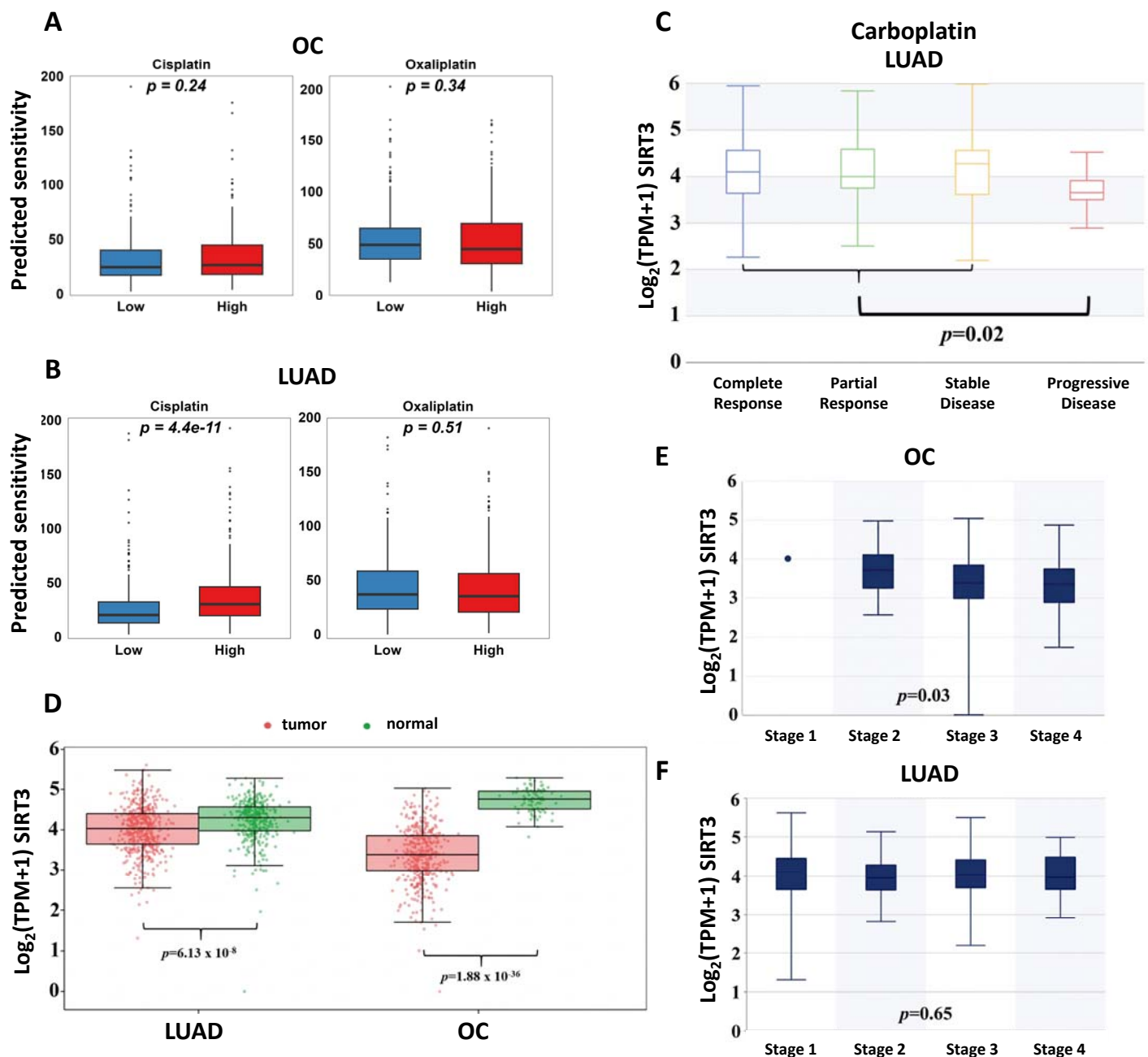


Figure S3. *In silico* analysis of *SIRT3* expression and its clinical relevance in LUAD and OC. OncoPredict drug response analysis for cisplatin and oxaliplatin according to *SIRT3* expression levels in (A) OC (n(low)=n(high)=214) and (B) LUAD (n(low)=n(high)=294) cohorts. Predicted drug sensitivity is presented as IC₅₀ values (μM). (C) *SIRT3* expression levels in LUAD patients categorized by clinical response to carboplatin treatment: clinical benefit group (CR+PR+SD, n=35) versus progressive disease group (PD, n=14). (D) The expression levels of *SIRT3* in LUAD and OC tumors compared to corresponding normal tissues (integrated TCGA and GTEx datasets). *SIRT3* expression levels across disease stages (I–IV) in (E) OC and (F) LUAD cohorts. TPM: Transcripts Per Million. CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; LUAD: lung adenocarcinoma; OC: ovarian serous cystadenocarcinoma; TCGA: The Cancer Genome Atlas; GTEx: Genotype-Tissue Expression. Statistical analysis and visualization were performed using R (v4.5.0) and the GEPIA3 platform.

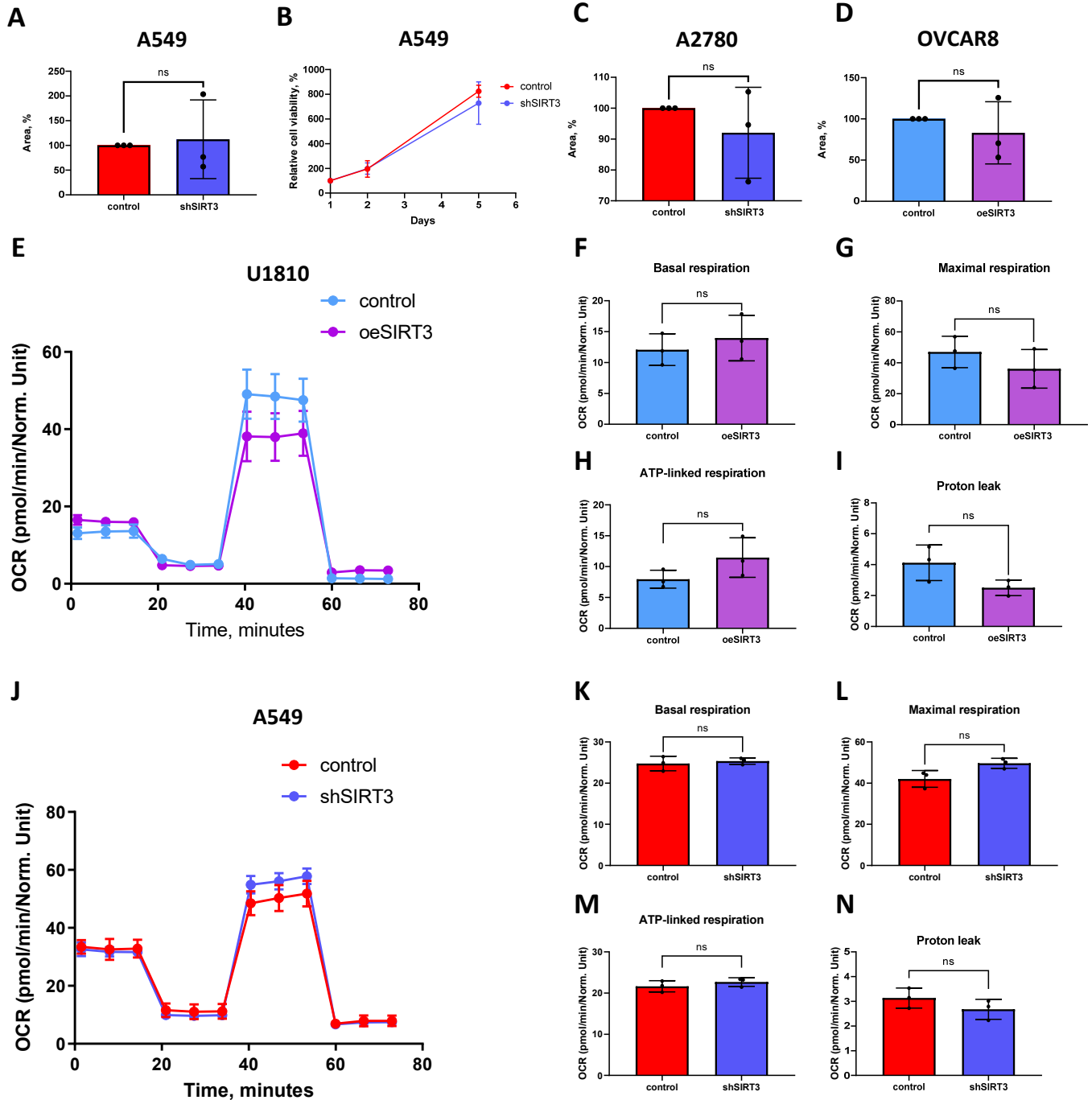


Figure S4. SIRT3 level modulation does not influence proliferation or mitochondrial respiration. Clonogenic assay of A549 cells with SIRT3 knockdown (shSIRT3) (A); proliferation assay of A549 cells with SIRT3 knockdown (B); clonogenic assay of A2780 cells with SIRT3 knockdown (C); clonogenic assay of SIRT3 overexpressing OVCAR8 cells (oeSIRT3) (D); OCR of SIRT3 overexpressing U1810 cells obtained using Seahorse MitoStressTest (E); parameters of mitochondrial respiration (basal, maximal, ATP-linked respiration, and proton leak, respectively) in SIRT3 overexpressing U1810 cells (F-I); OCR of A549 cells with SIRT3 knockdown obtained using Seahorse MitoStressTest (J); parameters of mitochondrial respiration (basal, maximal, ATP-linked respiration, and proton leak, respectively) in A549 cells with SIRT3 knockdown (K-N). Results are shown as the mean of at least three independent experiments $\pm$ SD, ns – not significant.

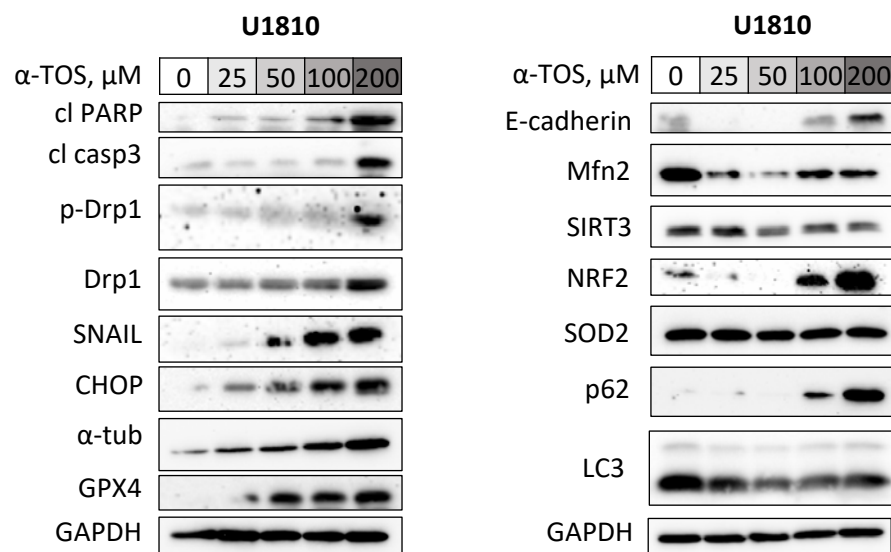


Figure S5. α -TOS treatment induces molecular remodeling in lung cancer cells. Representative immunoblot images of U1810 cells treated with 25-200 μ M α -TOS for 24 h. GAPDH was used as a loading control.

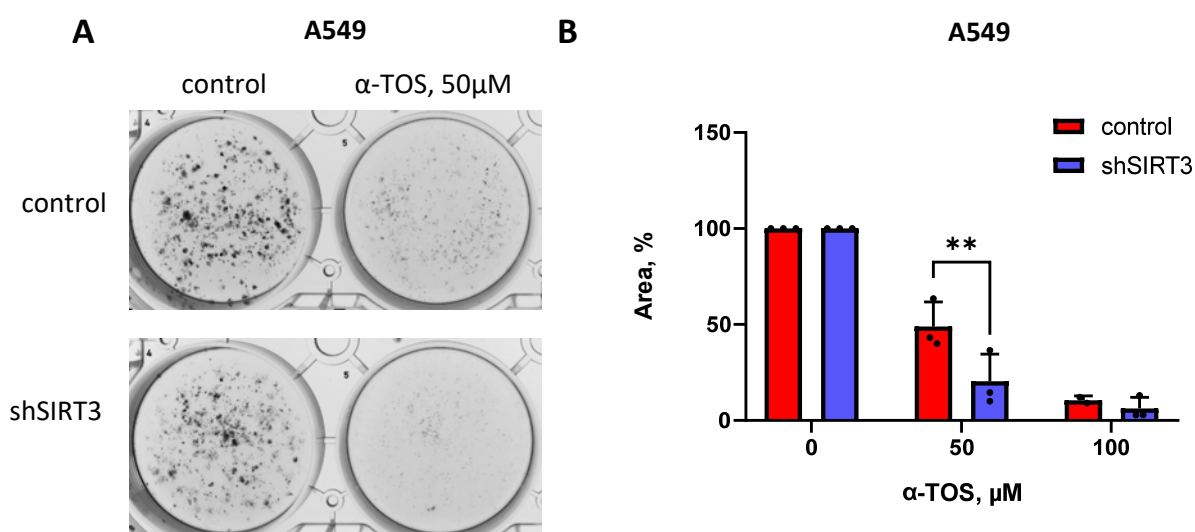


Figure S6. SIRT3-deficiency sensitizes tumor cells to α -TOS treatment. Representative clonogenic assay images of A549 cells with SIRT3 knockdown treated with 50-100 μ M α -TOS for 48 h (**A**); quantification of total colony area per well normalized to untreated control (**B**). Results are shown as the mean of at least three independent experiments $\pm$ SD. ** $p < 0.01$