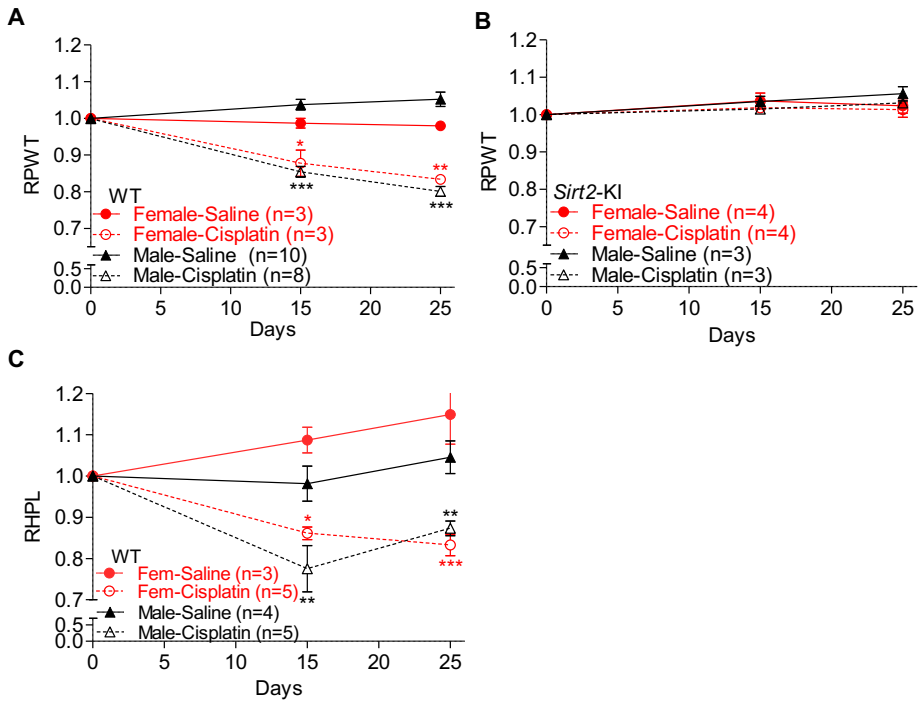
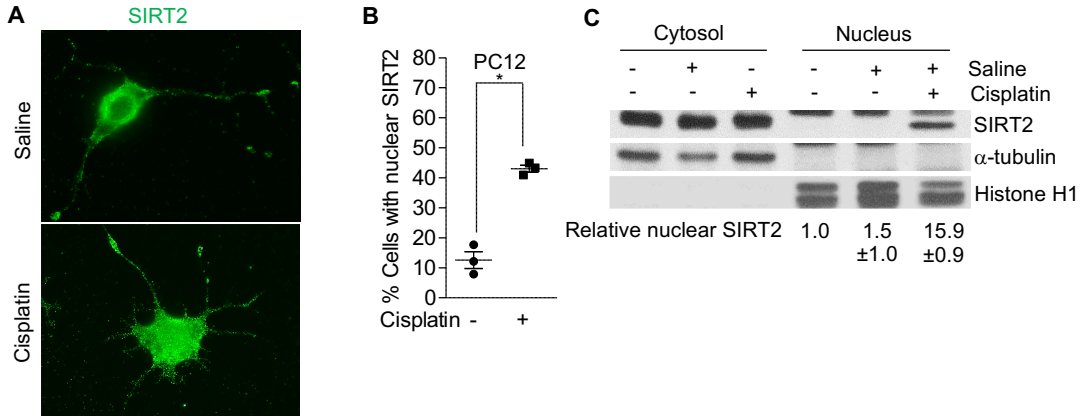
Supplemental Figures

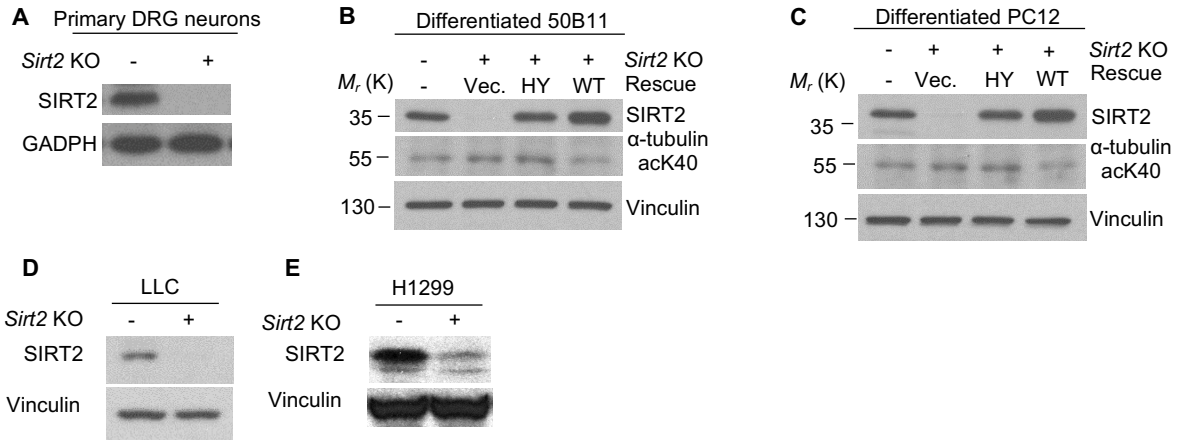


Supplemental Figure 1. Differential response of cisplatin-induced peripheral neuropathy in female and male mice.
Responses of female and male mice to mechanical and thermal pain stimulation after 2.3 mg/kg cisplatin treatment. (**A**) Mechanical thresholds of female and male WT mice receiving saline or cisplatin. (**B**) Mechanical pain response in male and female *Sirt2*-KI mice after saline or cisplatin treatment. (**C**) Responses of female and male WT mice to thermal stimulation as measured by hot plate tests. For (**A**) and (**C**), two-way ANOVA showed a main effect for treatment at days 15 and 25 and treatment-by-gender interaction at day 25. **P* <0.05, ***P* <0.01, and ****P* <0.001 denote significance levels among various gender/treatment groups and at different time points detected by Bonferroni posttest.

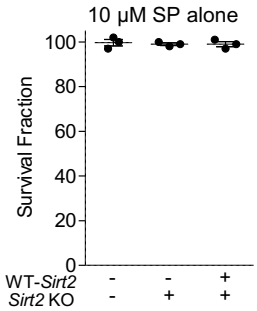


Supplemental Figure 2. SIRT2 accumulates in the nucleus of neuronally differentiated cells following cisplatin treatment.

(**A**) Images (400x) of immunofluorescence-stained neuronally differentiated PC12 cells 48h after treatment with saline and cisplatin. An anti-SIRT2 antibody was used to visualize SIRT2. (**B**) Quantitative analysis of PC12 cells that were treated with saline and cisplatin. Cells with nuclear SIRT2 were counted in 3 different fields. Data points are mean values ± SEM, n=3. **P* <0.05 denotes the significance level detected by two-tailed Student's t-test. (**C**) PC12 cells were treated with saline or cisplatin (2 μg/mL). Lysates were harvested after 24 h and separated into nuclear and cytoplasmic fractions, which were resolved by SDS-PAGE and subsequently probed with a SIRT2 antibody. Histone H1 served as the nuclear protein loading control while α-tubulin was the cytoplasmic protein loading control. Relative nuclear SIRT2 represents band intensity of nuclear SIRT2 normalized to the corresponding Histone H1 relative to nuclear SIRT2 intensity without treatment. All images and western blots represent one of three replicates.



Supplemental Figure 3. Manipulation of SIRT2 expression in neuronal and tumor cells.
(A) Western blot of primary DRG neurons showing the effect of *Sirt2* knockout. **(B & C)** Western blots showing the effects of *Sirt2* knockout and WT or HY-SIRT2 rescue expression in neuronally differentiated 50B11 and PC12 cells, respectively. Acetylated tubulin was used as a *Sirt2* activation marker, and vinculin as an equal loading control. **(D & E)** Western blots show the efficiencies of *Sirt2* KO in LLC and H1299 cells, respectively. Vinculin was used as an equal loading control. Data represent one of three replicates.



Supplemental Figure 4. Cell viability following spironolactone administration.
WT, *Sirt2*-KO, and rescued cells showed no difference in viability after receiving SP in the absence of cisplatin. Data points are mean values ± SEM (n=3) and were analyzed with one-way ANOVA with post-hoc Tukey test.