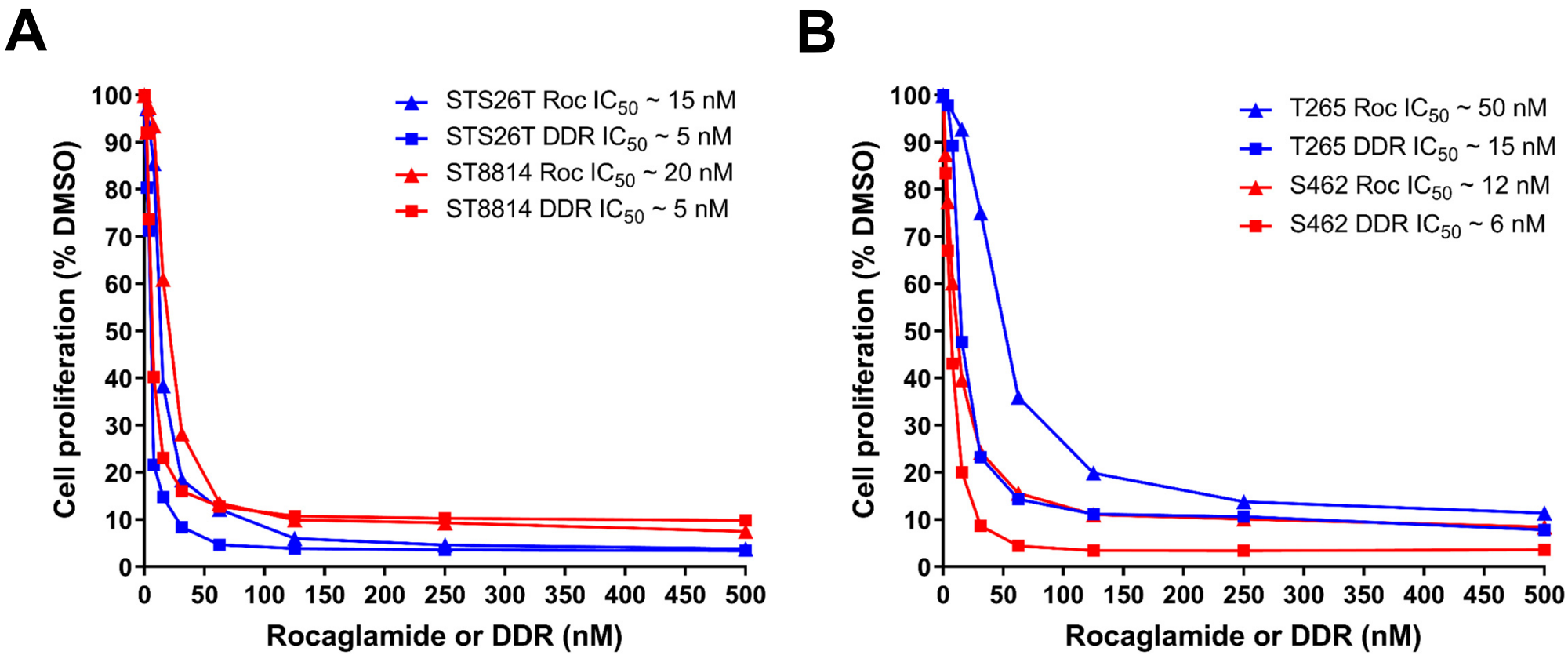
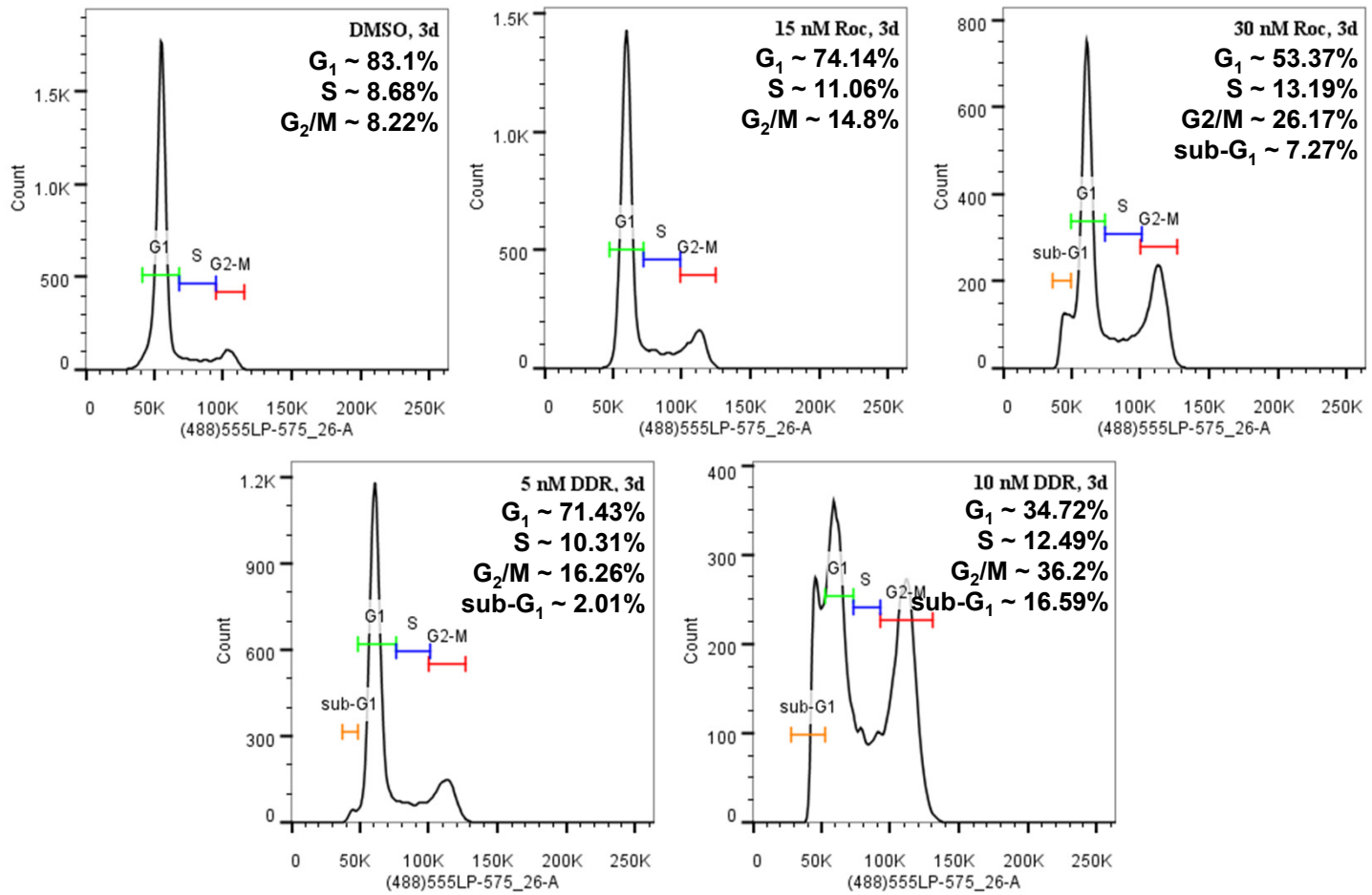
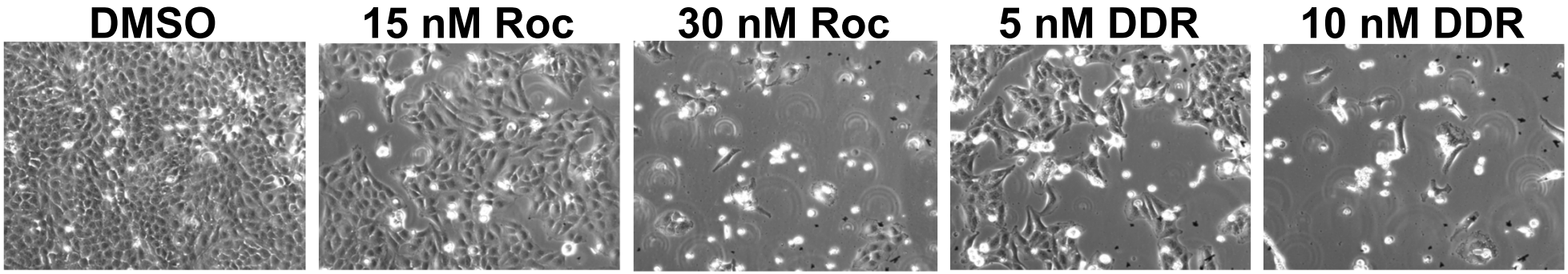


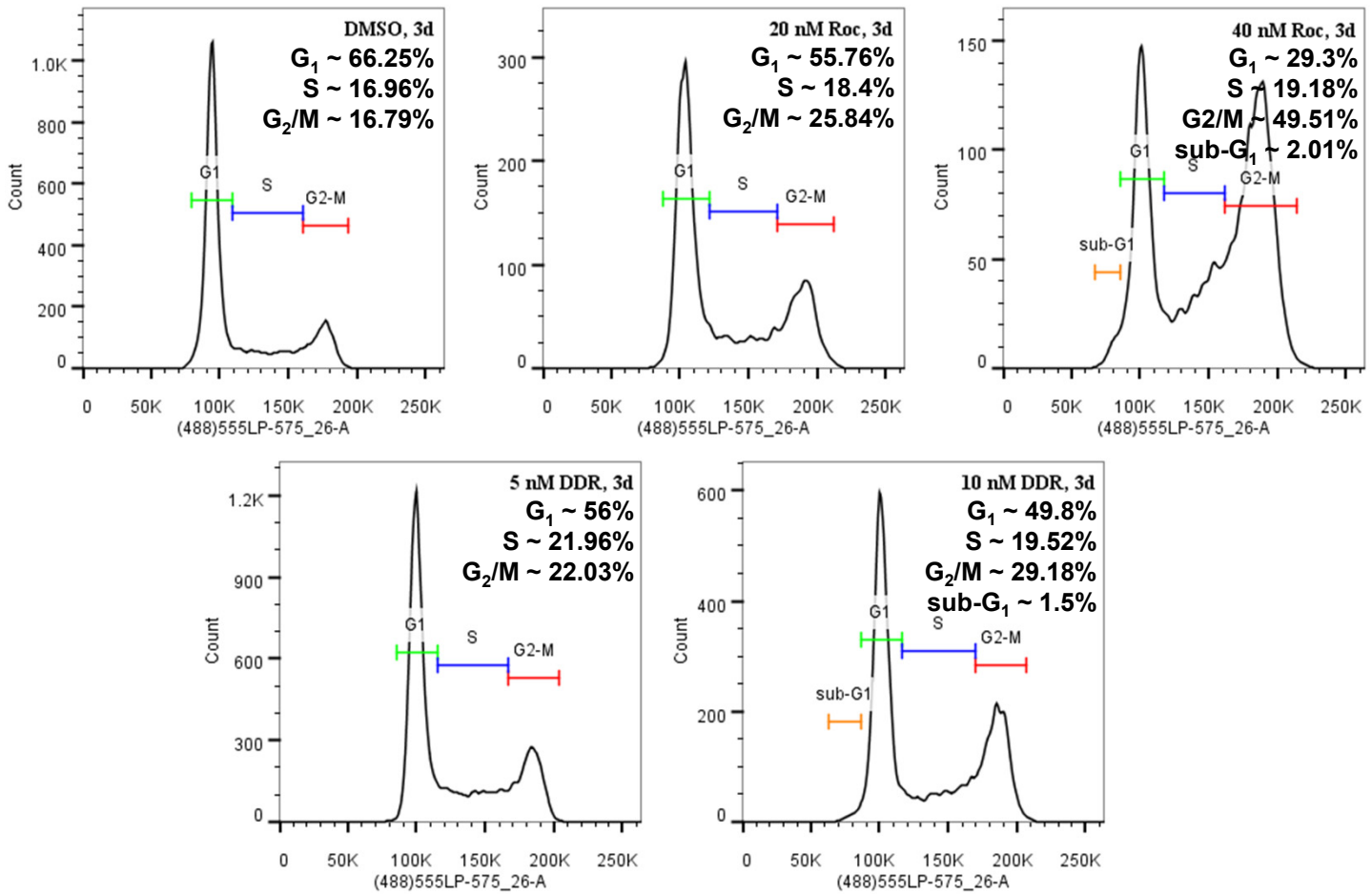
Supplementary Figure S1. Dose-response growth inhibition curves of DDR and Roc in MPNST cells. *NF1*-expressing STS26T (A) and T265 (B) (blue lines) and *NF1*-deficient ST8814 (A) and S462 (B) (red lines) MPNST cells were treated with various concentrations of DDR or Roc, followed by determination of cell proliferation as described in Methods. Experiments were performed in six replicates and were repeated three times. Data shown are the mean of replicates from one representative experiment for each cell line and compound. The graph inset shows the mean IC_{50} values derived from three independent experiments.

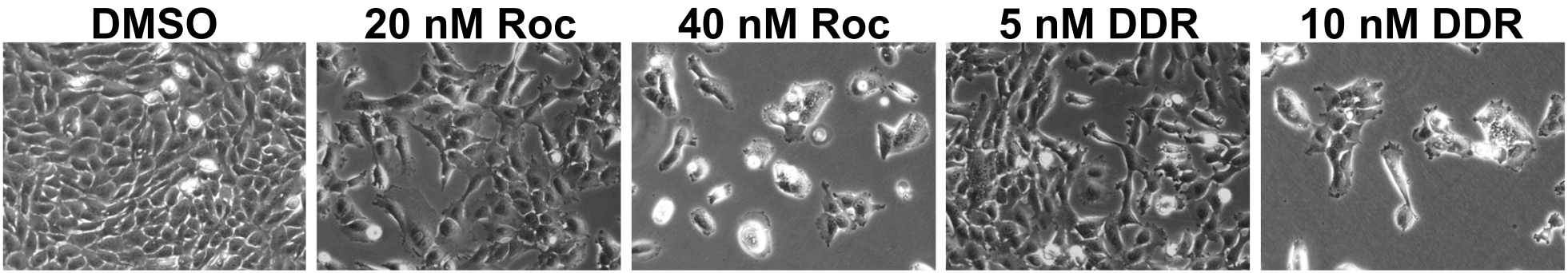
Supplementary Fig. S2A



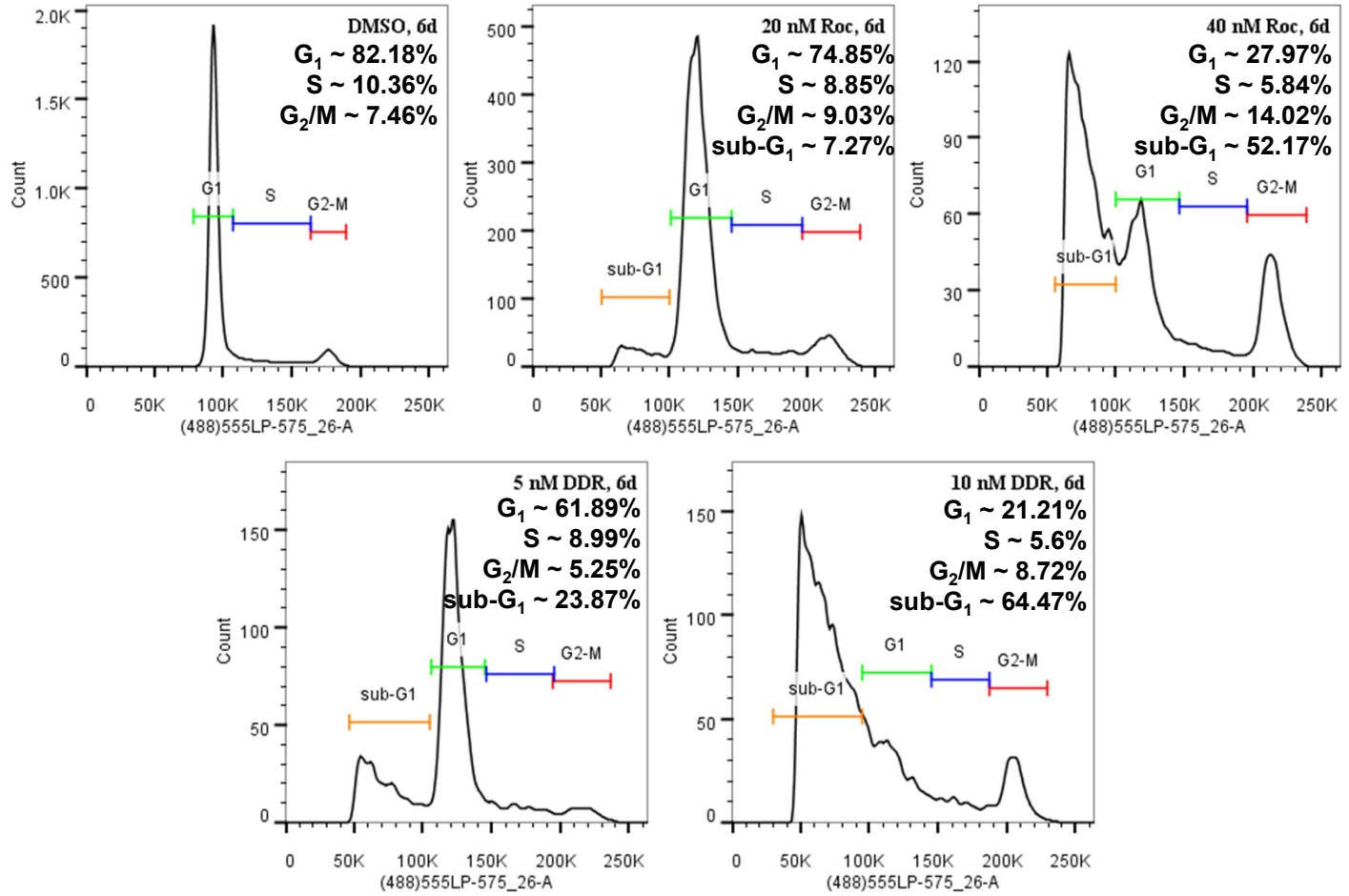


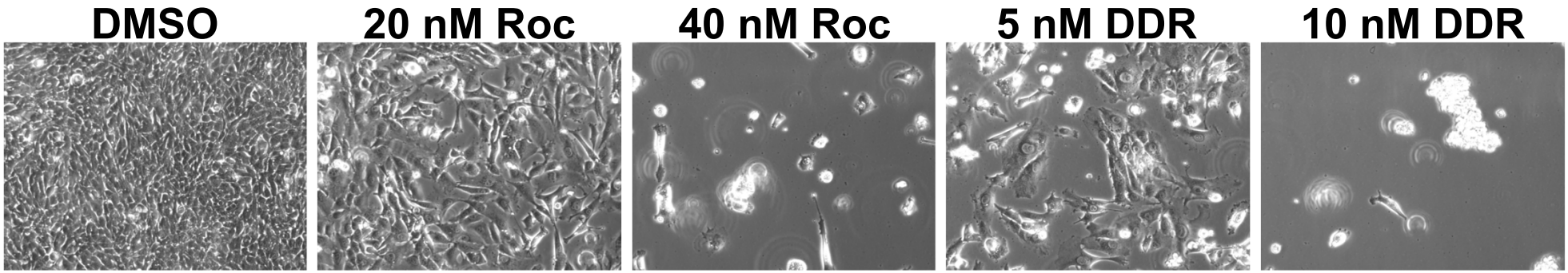
Supplementary Fig. S2B



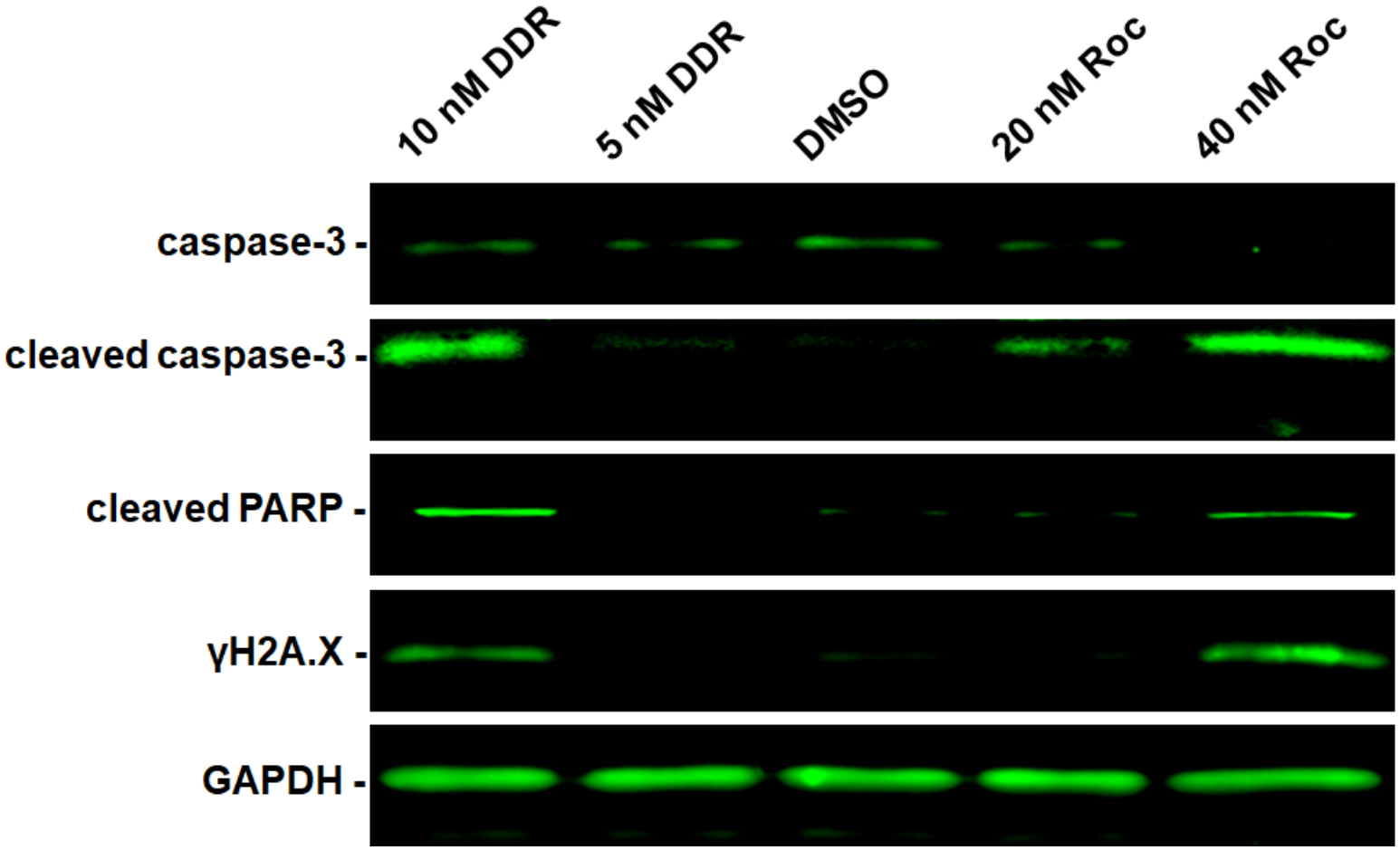


Supplementary Fig. S2C

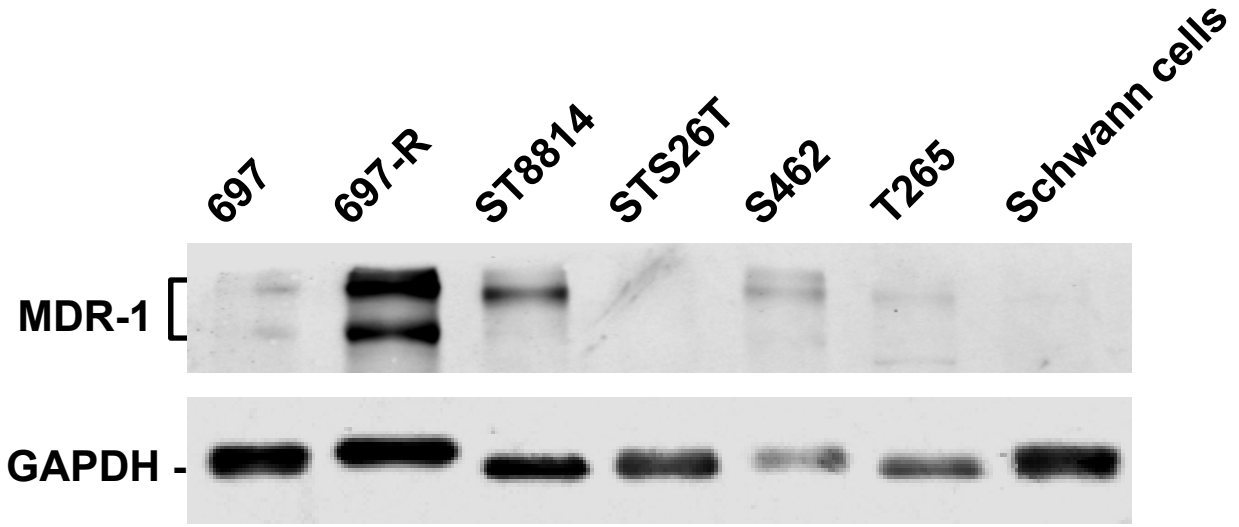




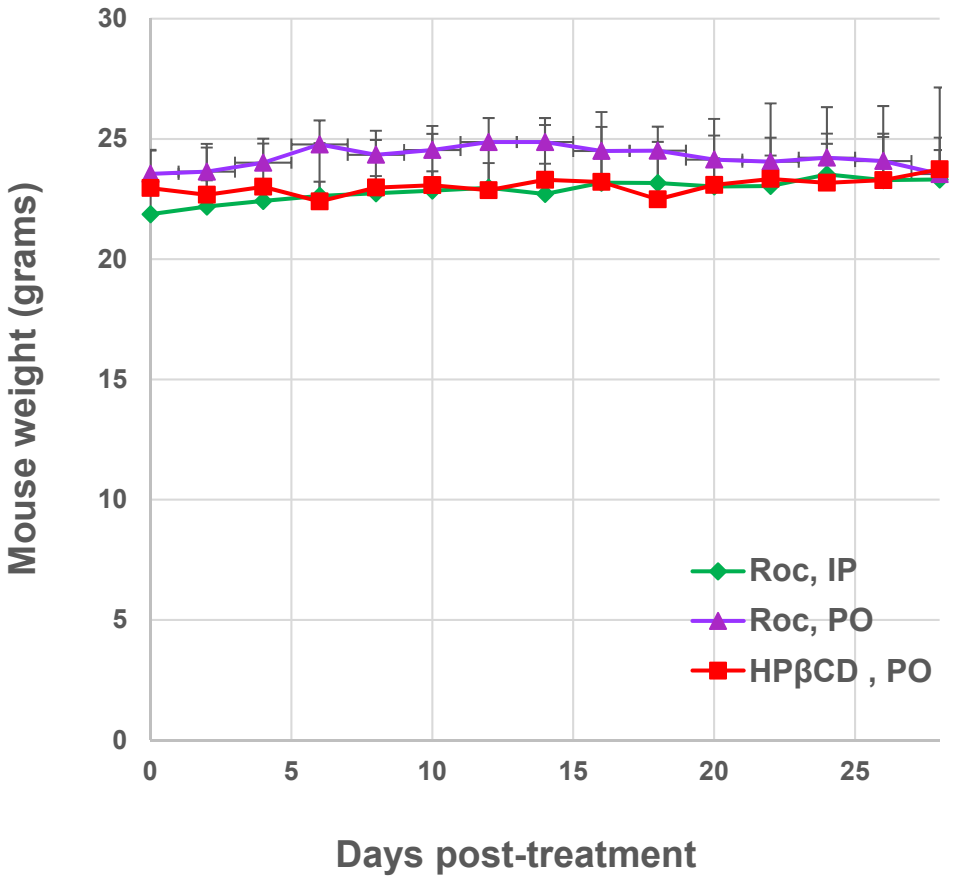
Supplementary Figure S2. DDR and Roc induce G_2/M arrest and increase sub-G_1 fraction in MPNST cells. (A) STS26T cells were treated with the indicated concentrations of DDR and Roc for three days, and phase-contrast images of treated cells were taken, followed by cell harvesting for flow cytometry analysis as described in Methods. Cell-cycle histograms of propidium iodide-labeled cells revealed a prominent increase in the G_2/M and sub-G_1 peaks after treatment. (B-C) Flow cytometry analysis and phase-contrast images of ST8814 cells treated with DDR or Roc for three (B) or six days (C) were conducted and showed an increased G_2/M fraction in treated cells. Also, a large increase in the sub-G_1 fraction was observed in cells treated for six days.



Supplementary Figure S3. DDR and Roc increase caspase-3 and PARP cleavage and elevate the levels of γH2A.X in *NF1*-deficient ST8814 cells. Protein lysates from ST8814 cells treated for 4 days with 1- or 2-IC_{50} of DDR or Roc were analyzed by Western blots for full-length and cleaved caspase-3, cleaved PARP, γH2A.X, and GAPDH as a loading control.

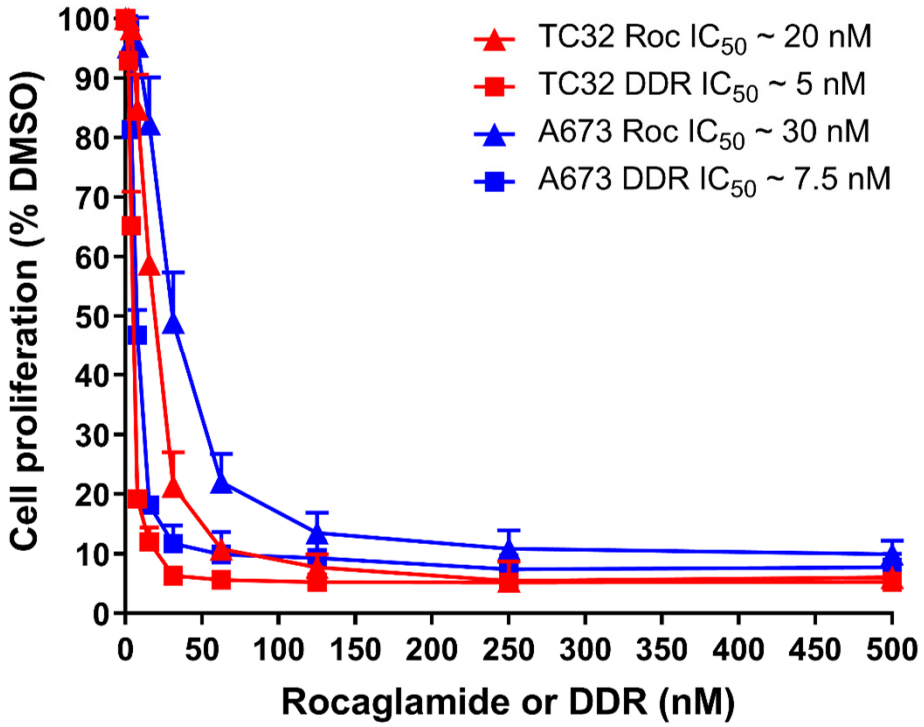


Supplementary Figure S4. Expression of the MDR1/Pgp protein in 697 and 697-R leukemic cells, various MPNST cell lines (ST8814, STS26T, S462, and T265), and primary human Schwann cells. Western blot analysis was conducted as described in Methods. GAPDH was used as a loading control.

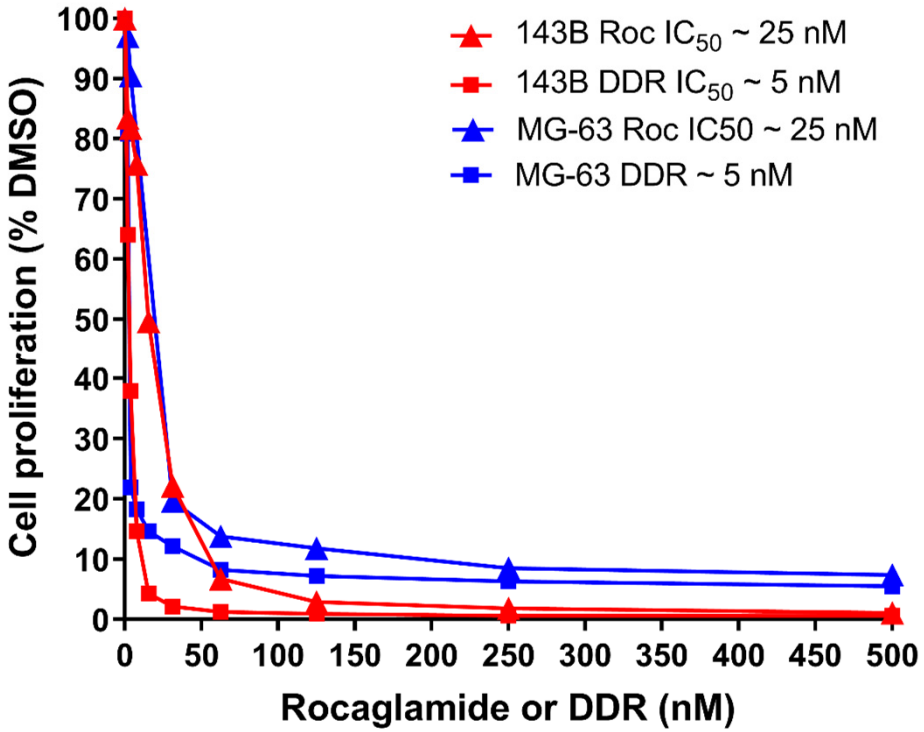


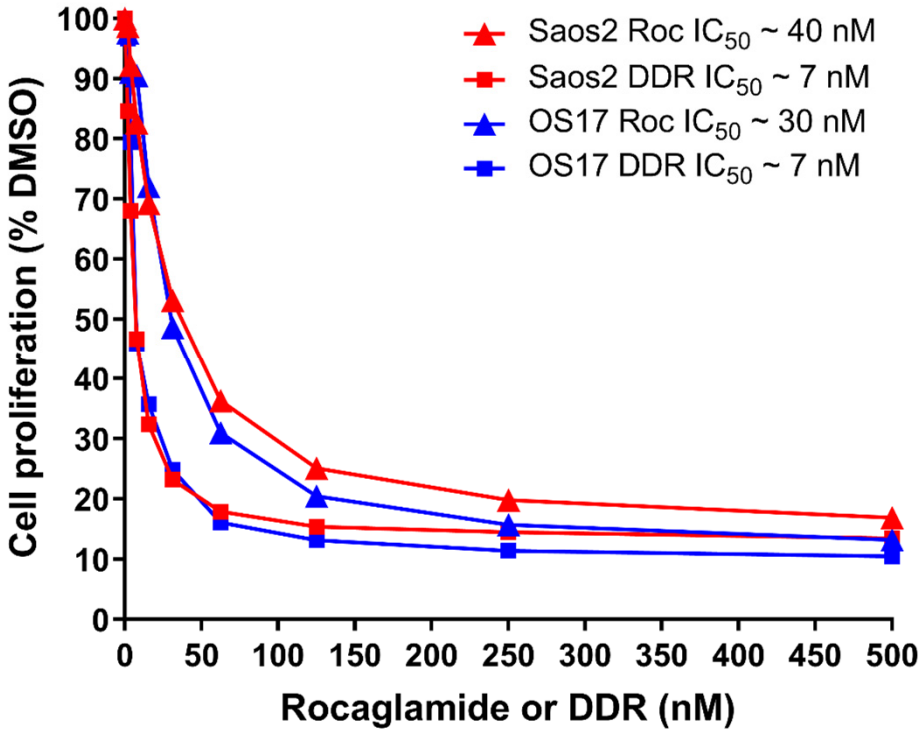
Supplementary Figure S5. Treatment with Roc did not significantly affect body weight, compared with vehicle-treated mice. ST8814-Luc MPNST-bearing NSG mice (n=10/group) were treated with Roc at 4mg/kg by IP, 1.2mg/kg by PO, or HPβCD vehicle every other day for four weeks. Mouse weights were measured every other day. Shown are the mean + standard deviation for each group of mice.

Supplementary Fig. S6A

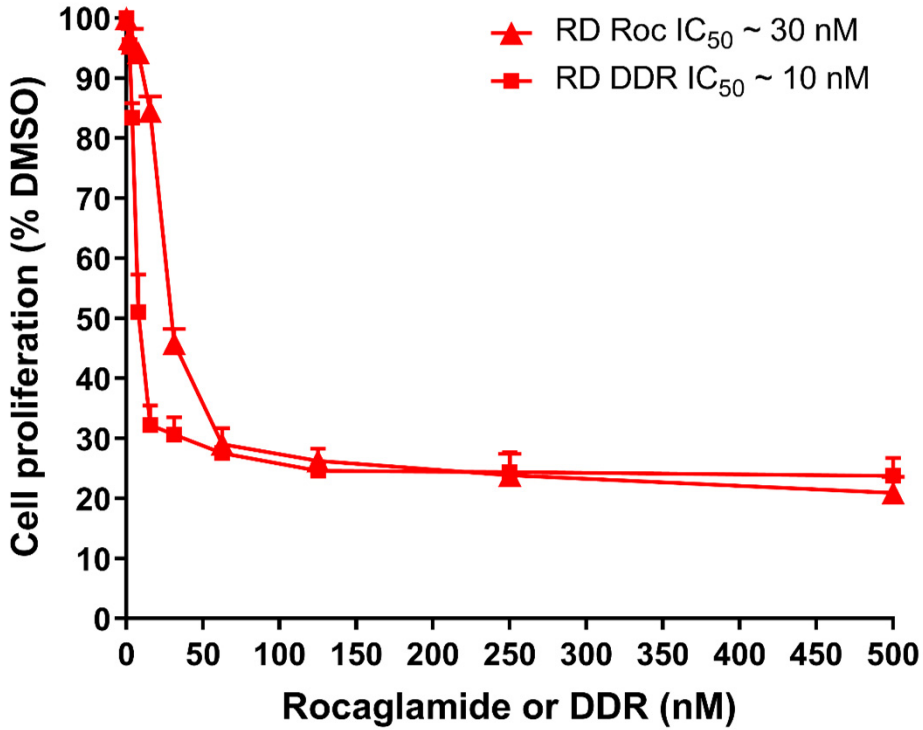


Supplementary Fig. S6B

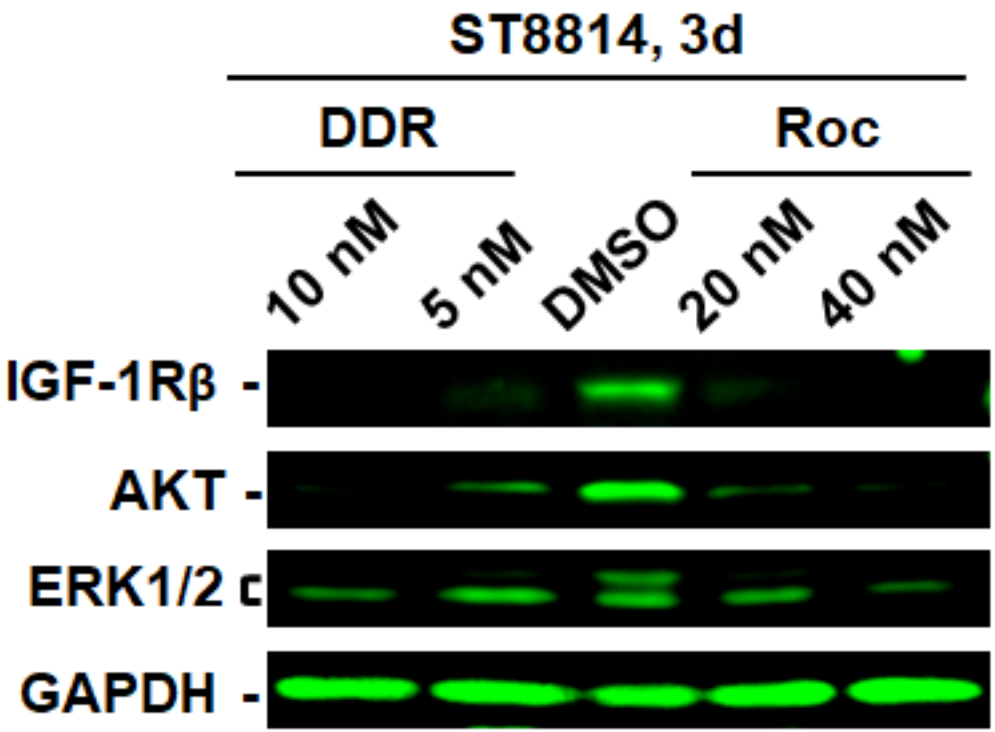




Supplementary Fig. S6C



Supplementary Figure S6. DDR and Roc possess potent growth inhibitory activities against various Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma cell lines. Cell proliferation assays were performed on the Ewing sarcoma cell lines A673 and TC32 (A), the osteosarcoma cell lines 143B, MG-63, Saos2, and OS17 (B), and the rhabdomyosarcoma cell line RD (C) treated with various concentrations of DDR (squares) or Roc (triangles) according to Methods. Each treatment was conducted in six replicates and the mean of replicates was calculated and used to generate the dose-response growth inhibition curve. Shown are representative curves for each cell line and treatment. The graph insets show the mean IC_{50} values derived from two independent experiments.



Supplementary Figure S7. DDR and Roc decrease the expression of IGF-1R, AKT and ERKs in MPNST cells. Protein lysates prepared from ST8814 cells treated for 3 days with 1- or 2-IC_{50} of DDR or Roc were analyzed by Western blots as described in Methods. GAPDH served as a loading control.