Inhibition of histone deacetylase 2 reduces MDM2 expression and reduces tumor growth in dedifferentiated liposarcoma

SUPPLEMENTARY MATERIALS

Supplementary Table 1: Upstream regulator analysis results

| Gene  | Expression p-value | p-value of Overlap  |
|-------|-------------------|---------------------|
| IFNL1 | -                 | $2.19 \times 10^{-19}$ |
| TGFB1 | 0.54              | $4.43 \times 10^{-17}$ |
| TP53  | 0.001             | $4.75 \times 10^{-17}$ |
| PRL   | -                 | $5.00 \times 10^{-15}$ |
| ESR1  | 0.25              | $9.06 \times 10^{-15}$ |

Supplementary Figure 1: Co-expression of HDAC2 and MDM2. In both the TCGA (A) and MSKCC (B) datasets, expression of HDAC2 was most highly correlated HDAC gene co-expressed with MDM2. In both datasets, HDAC2 expression was positively correlated with MDM2 expression (TCGA: Spearman’s coefficient = 0.29, $p = 0.03$; MSKCC: Spearman’s coefficient = 0.57, $p < 0.001$).
**Supplementary Figure 2: HDAC2 mRNA expression in clinical DDLPS samples.** To assess the prediction of DFS OS by HDAC2 mRNA expression as a dichotomous variable, subjects were split into HDAC2 High (red points) and HDAC2 Low (black points) groups utilizing maximally selected rank statistics for each dataset. mRNA expression of HDAC2 as measured in the Cancer Genome Atlas (TCGA) by RNA-Seq (A). mRNA expression of HDAC2 as measured in the Memorial Sloan-Kettering Cancer Center Dataset (MSKCC) by microarray (B).

**Supplementary Figure 3: shRNA knockdown of HDAC2.** The LPS246 DDLPS cell line was incubated with lentiviral based scrambled shRNA (TTT) or shRNA MDM2-targeted vector (repeated five times, sh1-5). Cells underwent puromycin selection for 72 hours followed by 72 hours of incubation in normal media. Cells were then isolated for western blot analysis. Knockdown of HDAC2 was successful and resulted in a reduction of MDM2 and p21 expression.