Figure S1. Effect of Notch inhibitor CB103 on human well-differentiated liposarcoma (WDLPS) cell lines. Representative dose-response curves of WDLPS-80.2 (A) and WDLPS-135 (B) cell lines in varying concentrations of CB103, and the corresponding IC_{50} values (n = 6). Data are presented as mean ± SD, *P < 0.05, **P < 0.001.

Figure S2. Effect of Notch inhibitors on apoptosis of liposarcoma cell lines. A. TUNEL (terminal deoxynucleotidyl transferase dUTP nick end labeling) staining to assess cell apoptosis in mouse liposarcoma cell line mLPS1 and human DDLPS cell line LPS246 after treat with Notch signaling inhibitors CB103 for 20 μM. The mLPS1 cells treat IMR1 for 20 μM and LPS246 cells treat IMR1 for 4 μM. **B.** TUNEL staining to assess cell apoptosis in mLPS1 and mLPS1-ΔNICD cell lines. TUNEL signal is shown in red and cell nuclei is stained in blue by DAPI. Scale bars, 50 μm.

Figure S3. Effect of Notch inhibitor CB103 on liposarcoma growth *in vivo*. A. Experimental design for subcutaneous transplantation of mLPS1 cells into the flanks of NRG mice. CB103 (40mg/kg/day) was intra-peritoneally injected 15 days later when palpable tumors were detectable, daily injections of vehicle or CB103 were administrated from day 15 to day 27 (n = 5 mice/group, one mouse in the CB-103 group died from unknown cause during treatment). **B.** Photographic images of NSG mice carrying subcutaneously xenografts of mLPS1 tumors. Note that skin necros (reflected by the dark purple color) is more apparent in the vehicle group. **C.** Tumor growth curve of vehicle and CB103 groups, based caliper measurement of tumor width and length. **D.** Tumor morphology after dissected from mice at the d28 end point. **E.** average weight of the tumors shown in D.

Figure S4. Notch activation suppresses mLPS1 cell differentiation into adipocytes. A. RT-qPCR analysis showing expression of mature adipocyte marker genes in mLPS1 and $mLPS1^{\Delta NICD}$ cells. **B.** Fluorescent staining images of lipid droplets (labeled with BODIPY in green as indicator of adipogenic differentiation) in mLPS1 and $mLPS1^{\Delta NICD}$ cells after treated with adipocyte differentiation medium, visualized by immunofluorescence microscopy. Scale bars, 50 μm. Nuclei were counterstained with DAPI (blue). **C.** RT-qPCR analysis showing relative levels of mature adipocyte markers in mLPS1 cells at 24 h after expose to adipocyte differentiation medium. **D.** RT-qPCR analysis of mature adipocyte marker expression levels in $mLPS1^{\Delta NICD}$ cells at 24 h after

expose to adipocyte differentiation medium. Data are represented as mean ± SD. *P < 0.05, **P < 0.001. n.s., not significant.

Figure S5. Gene expression in response to abrogation of NICD^{OE} in mLPS1 cells. **A** and **B.** RT-qPCR analysis *Notch1* and *Ppargc1a* expression in mLPS1 and mLPS1$^{\Delta NICD}$ cells. **C.** Heatmap visualization of the top 20 co-upregulated and 20 co-downregulated genes in mLPS1$^{\Delta NICD}$ relative to mLPS1 cells. **D.** RT-qPCR analysis of *PPARGC1α* mRNA expression level in human liposarcoma cell line LPS246 treat with Notch inhibitor IMR1 and CB103. Data are represented as mean ± SD. *P < 0.05, **P < 0.001. n.s., not significant.

Figure S6. Effects of PGC1α expression and activation on migration and differentiation of mLPS1 liposarcoma cells. A. Wound healing assay to analyze cell migration of mLPS1 and PGC1α overexpressing mLPS1 cells. Areas between red lines were scraped and cell migration into the scraped area were subsequently analyzed at 6 h and 20 h. Scale bars, 100 μm. **B.** Relative wound area (area without cells) of mLPS1 cell migration (n = 3). **C.** Immunofluorescent staining of lipid droplets (Bodipy labeling) in mLPS1 cells treat with adipocyte differentiation medium with or without PGC1α agonist Forskolin. Cell nuclei were counterstained with DAPI. Data are presented as mean ± SD, *P < 0.05, **P < 0.001.