# *Supplementary Materials*

## Supplementary Data

### Table S1. Clinical and pathological information of WDLPS and DDLPS cases analyzed in this study

| | Code No. | Age (years) | Sex* | Tumor site | MDM2/CDK4 Amplification§ | Amplification of other genes§ | Mutation§ |
|---|---|---|---|---|---|---|---|
| DDLPS | D11 | 55 | M | Extremity | Yes | | |
| | D16 | 62 | M | Extremity | Yes | *DDR2* | |
| | D25 | 55 | M | Extremity | Yes | *IGF1R* | |
| | D01 | 52 | F | Retroperitoneal | Yes | *ROS1* | |
| | D06 | 74 | M | Retroperitoneal | Yes | *RAC1, MYC, CRKL* | |
| | D18 | 74 | M | Retroperitoneal | Yes | | |
| | D19 | 63 | M | Retroperitoneal | Yes | | |
| | D20 | 64 | M | Retroperitoneal | Yes | | *ARID1A* |
| | D40 | 76 | F | Retroperitoneal | Yes | *ROS1, CD274, EP300* | *FGFR1* |
| WDLPS | W07 | 30 | M | Extremity | Yes | *MDM4* | |
| | W09 | 44 | M | Extremity | Yes | *ERBB3* | |
| | W11 | 47 | M | Extremity | Yes | | |
| | W18 | 81 | M | Extremity | Yes | *DDR2* | |
| | W14 | 60 | F | Retroperitoneal | Yes | *NTRK1* | |
| | W16 | 59 | F | Retroperitoneal | Yes | *IDH1* | |
| Normal adipose tissue | F03 | 40 | F | Extremity | | | |
| | F05 | 44 | M | Extremity | | | |
| | F04 | 71 | F | Extremity | | | |
| | F06 | 66 | F | Extremity | | | |
| | F07 | 43 | F | Extremity | | | |
| | F08 | 74 | M | Extremity | | | |

*M: Male, F: Female

§Reference: Asano N. et al. Oncotarget. 2017;8(8):12941-52

**Table S2. Primers for RT-qPCR**

| Gene symbol | Sequence (forward) | Sequence (reverse) | Annealing temp. (˚C) |
|---|---|---|---|
| *GAPDH* | AGGTGAAGGTCGGAGTCAACG | AGGGGTCATTGATGGCAACA | 58 |
| *PPARG1* | AGAAGCCAACACTAAACCACAAA | CAGAATGGCATCTCTGTGTCAAC | 58 |
| *PPARG2* | CTGTCTGCAAACATATCACAAG | GGAGTGGTCTTCCATTACGG | 57 |
| *STAT5* | CCTTCTTGTTGCGCTTTAGTG | ATGGTTTCAGGTTCCACAGG | 58 |
| *FABP4* | TGCAGAAATGGGATGGAAAATCA | CATAAACTCTCGTGGAAGTGACG | 58 |

## Supplementary Figures

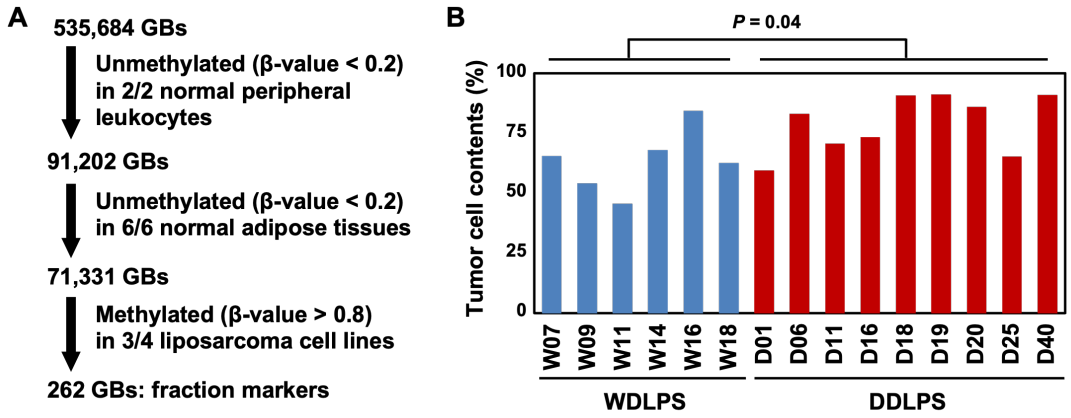


**Figure S1**

Tumor cell contents in liposarcomas. (A) Isolation of the fraction markers. Tumor cell contents were estimated using DNA methylation statuses of 262 genomic blocks (GBs) unmethylated (β-value < 0.2) in normal peripheral leukocytes and normal adipose tissues but methylated (β-value > 0.8) in three or more of four liposarcoma cell lines. (B) Tumor cell contents of WDLPSs and DDLPSs. DDLPSs exhibited higher tumor cell contents than WDLPSs. Statistical significance was tested using an unpaired Student's *t*-test.

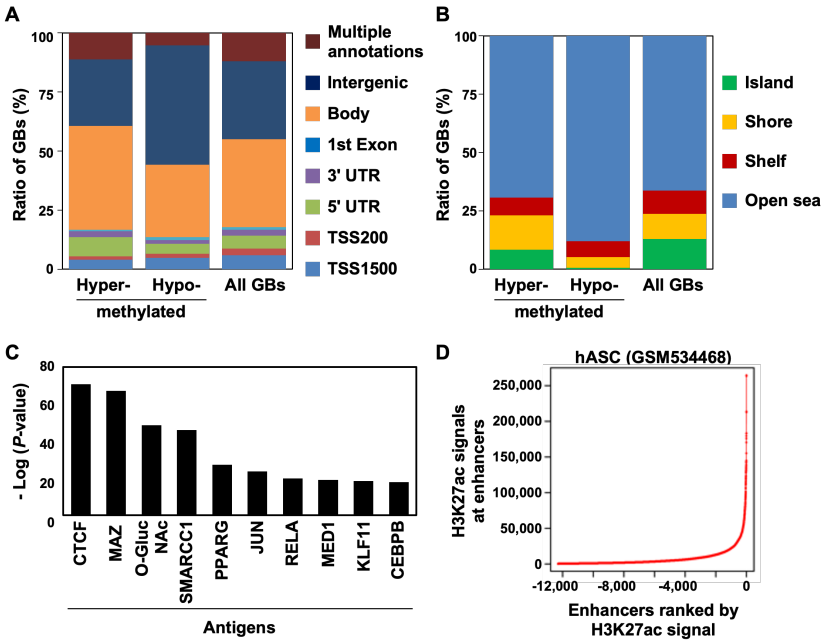


**Figure S2**

Genomic features of differentially methylated GBs. (A) Positions of differentially methylated GBs against a gene. GBs hypermethylated in DDLPSs were enriched at 5' UTR and the gene body, whereas GBs hypomethylated in DDLPSs were in the intergenic regions. (B) Positions of differentially methylated GBs against a CpG island. GBs hypermethylated and hypomethylated in DDLPSs were enriched at the shore of CGIs and the open sea, respectively. (C) Enrichment analysis using ChIP-Atlas. GBs hypermethylated in DDLPSs significantly overlapped the binding regions of transcription regulators, including *PPARG*. (D) Isolation of super-enhancers in adipocyte. Typical and super-enhancers in adipocytes were identified based on the aggregated intensity of histone H3K27 acetylation.

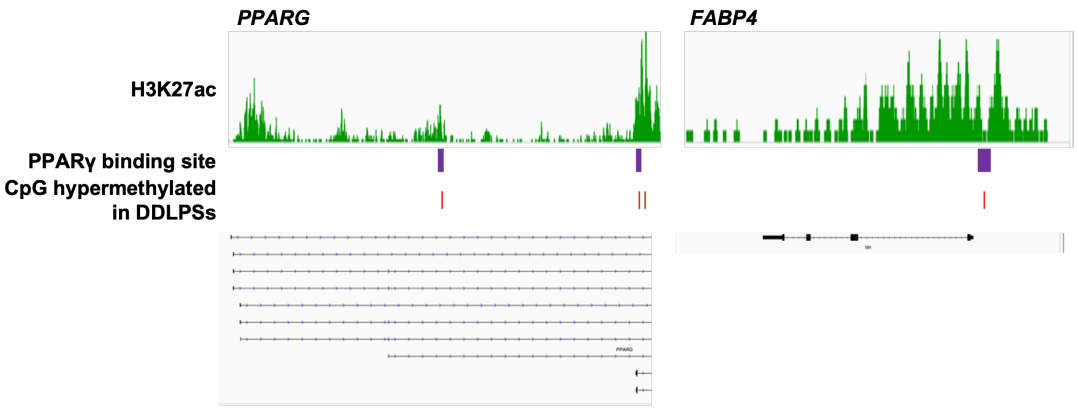


**Figure S3**

Relationship among H3K27 acetylation peaks and PPARγ binding sites in adipocytes, and CpG sites hypermethylated in DDLPSs. At the loci of *PPARG2* and *FABP4*, the PPARγ binding sites with H3K27ac in adipocytes were hypermethylated in DDLPSs.

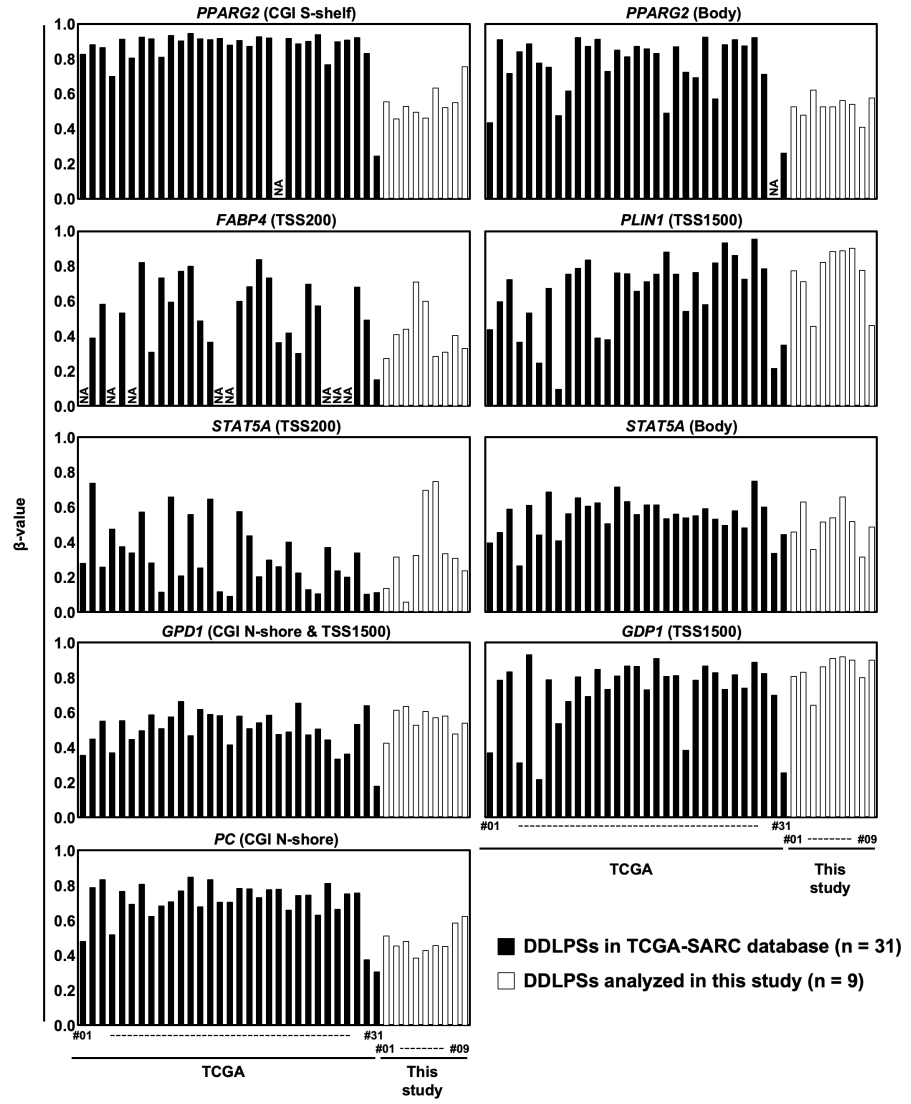


**Figure S4**

Validation of aberrant DNA methylation of PPARγ downstream genes in DDLPSs. DNA methylation profiles of 31 DDLPSs were obtained from the TCGA-SARC database. Focusing on probes common to both Infinium EPIC and 450K arrays, consistent DNA methylation of *PPARG2*, *FABP4*, *PLIN1*, *GPD1*, and PC was observed in an independent cohort from the TCGS-SARC database.

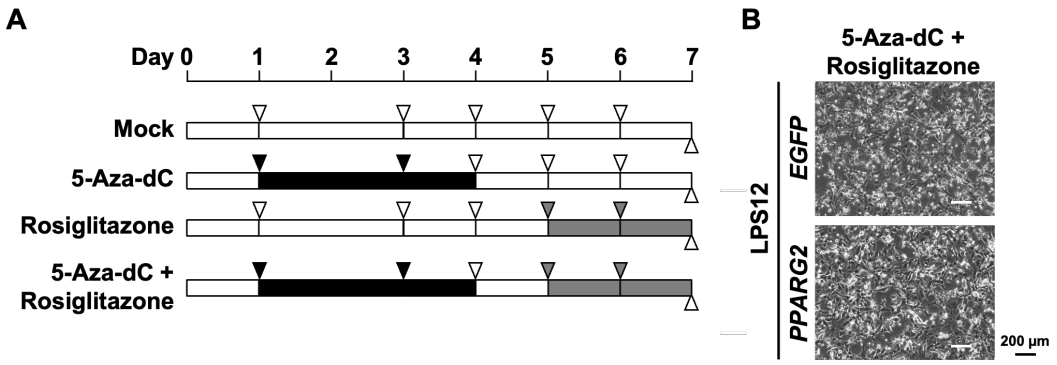


**Figure S5**

Treatment of DDLPS cell lines with 5-aza-dC and a PPARγ agonist. (A) Schedule of the combined treatment of 5-aza-dC (0.3 μM) and rosiglitazone (50 μM). (B) Representative cell morphology. No clear difference in cell morphology was observed between *EGFP*- and *PPARG2*-expressing LPS12 cells after treatment with 5-aza-dC and rosiglitazone. Scale bar = 200 μm.

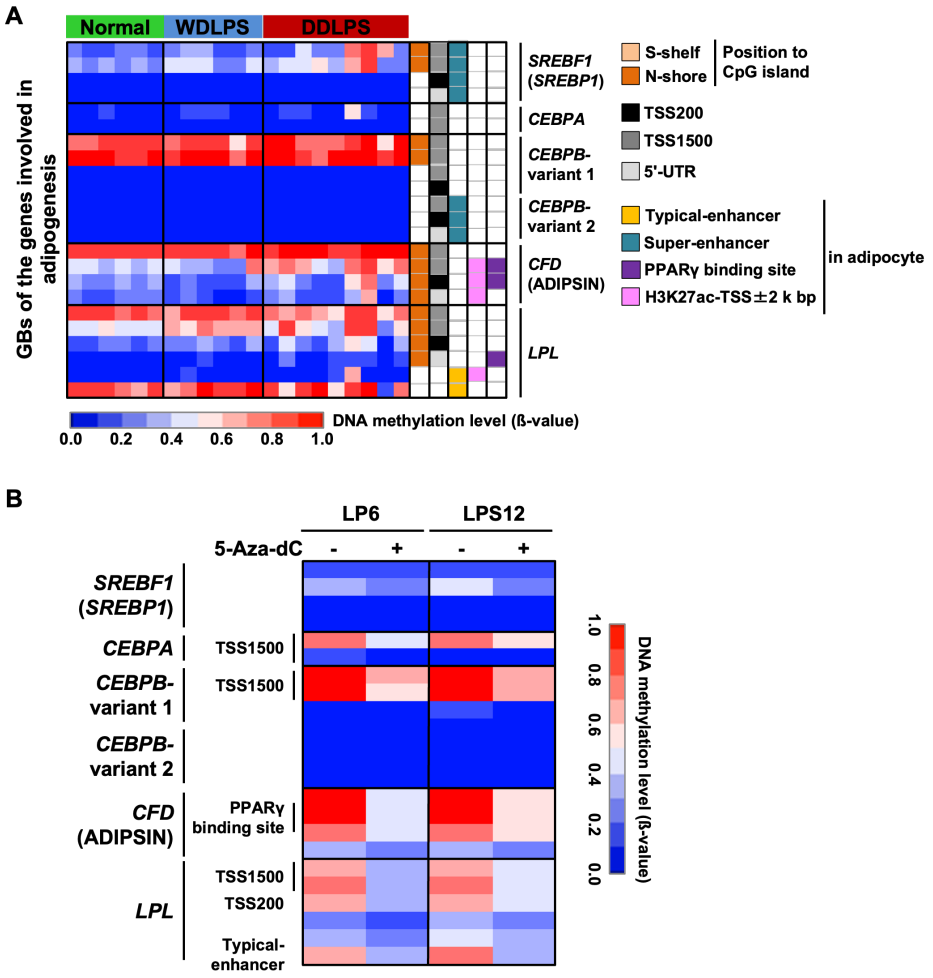


**Figure S6**

DNA methylation statuses of the genes involved in adipogenesis. (A) DNA methylation levels of the genes involved in adipogenesis in normal adipose tissues, WDLPSs, and DDLPSs. The regulatory regions of *SREBF1* and *CFD* were more methylated in DDLPSs. (B) DNA methylation levels of the genes involved in adipogenesis in LP6 and LPS12 cells. The regulatory regions of *CEBPA*, *CEBPB*, *CFD*, and *LPL* were demethylated by 5-aza-dC treatment.