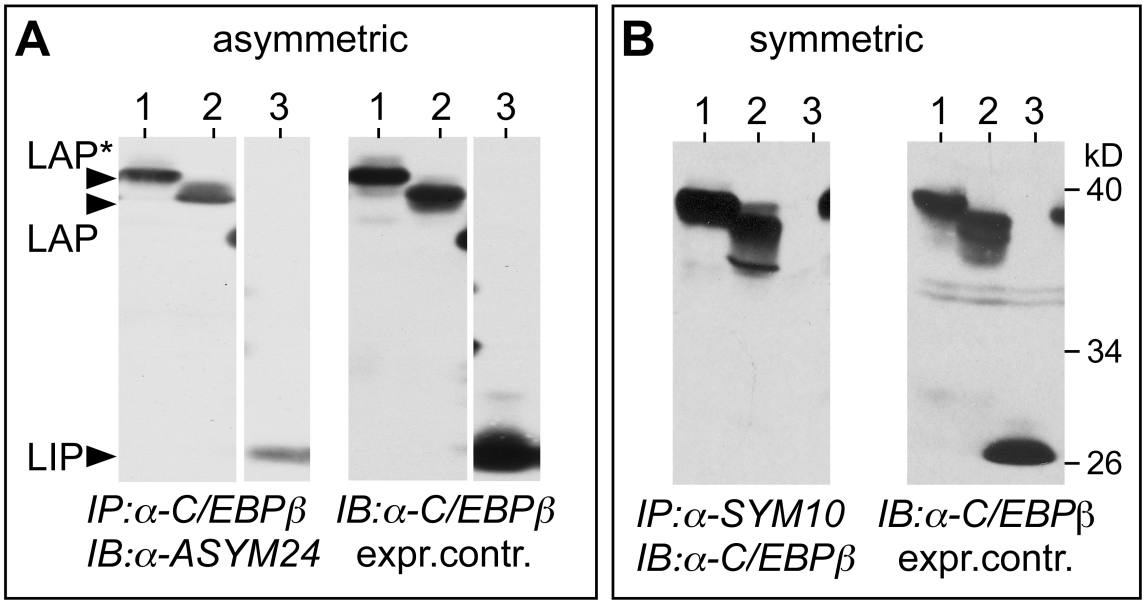
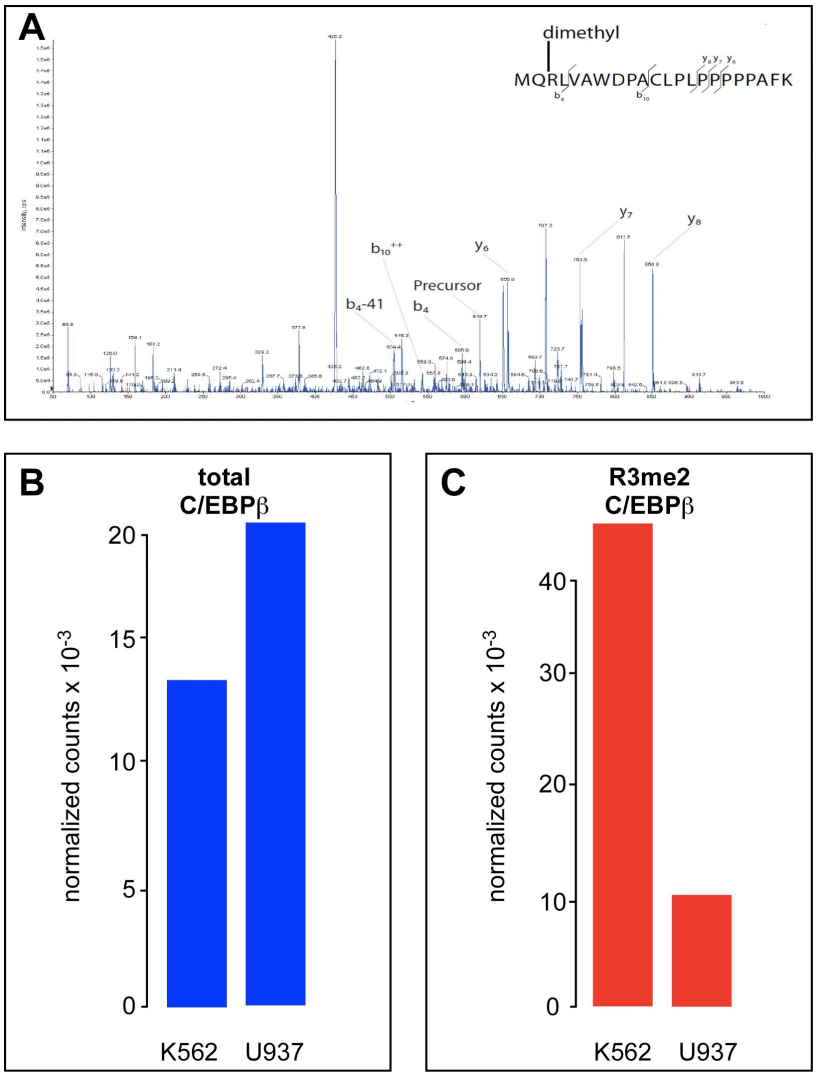
Supplementary Figure 1: Differential interaction of C/EBPβ isoforms with isomer specific Rme2-antibodies.



(A) QT6 fibroblasts were transfected with LAP*/C/EBPβ1, LAP/C/EBPβ2 or LIP/C/EBPβ3 and immunoprecipitated with the anti-C/EBPβ antibody. Immunoblots were revealed with the anti-ASYM24 antibody.

(B) QT6 fibroblasts were transfected as in (A) and immunoprecipitated with the anti-SYM10 antibody. Immunoblots were revealed with the anti-C/EBPβ antibody.

Supplementary Figure 2: Multiple reaction monitoring (MRM) of cellular C/EBPβ.

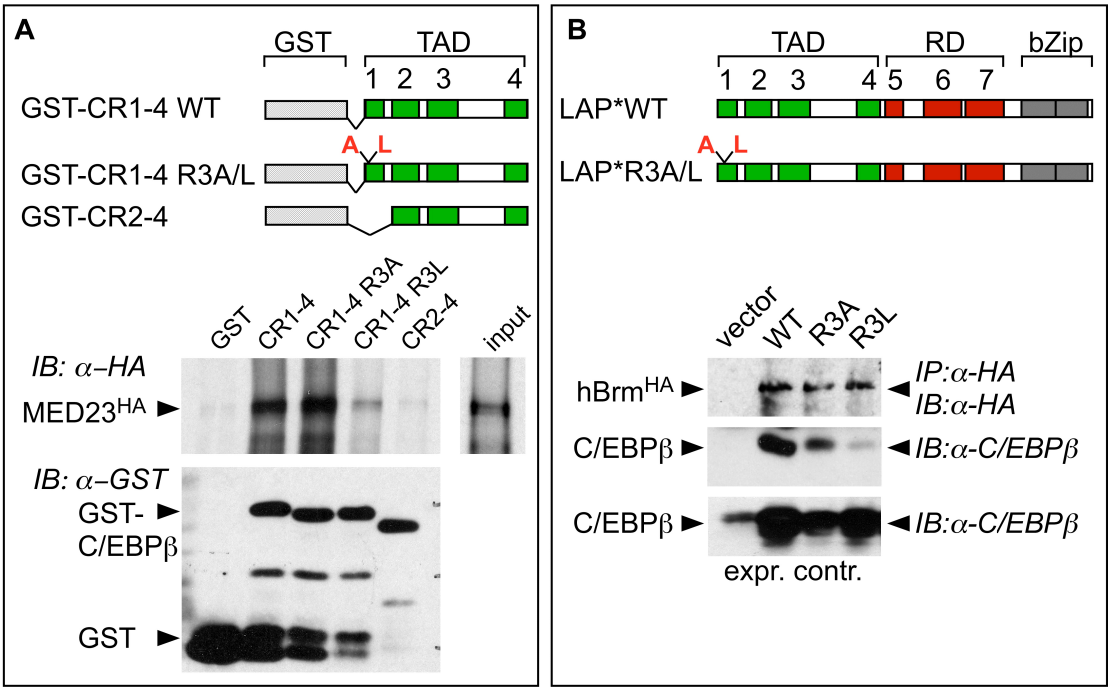


(A) Fragment spectrum of a model peptide derived of the N-terminal sequence of human C/EBPβ. The peptide carries a di-methylated arginine at position 3. Fragment ions selected for the MRM-measurement are indicated.

(B) Relative quantification of C/EBPβ in total cell lysates from K562 and U937 cells.

(C) MRM-based quantification of the arginine modified N-terminal C/EBPβ peptide in total cell lysates from K562 and U937 cells.

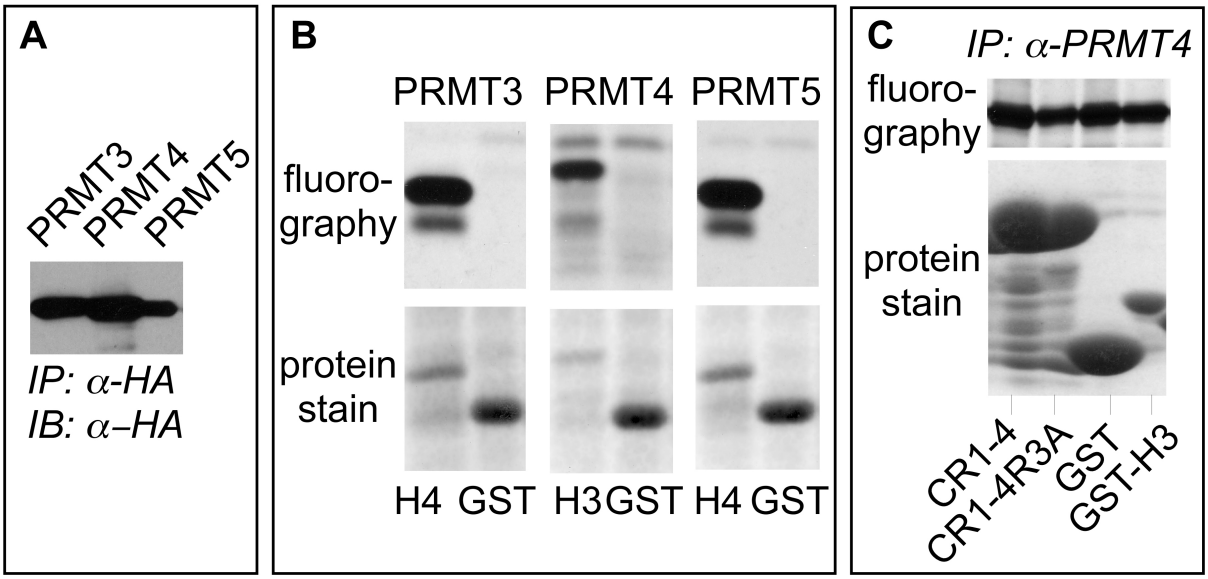
Supplementary Figure 3: LAP*/C/EBPβ1 R3 mutations alter interactions with SWI/SNF and Mediator complexes.



(A) Interaction of recombinant C/EBPβ N-terminal GST-proteins with MED23. Top: Scheme of recombinant GST-C/EBPβ TAD fusion proteins comprising GST, GST-CR1-4 (WT), GST-CR1-4 R3A or GST-CR1-4 R3L, or a CR1 deletion. Bottom: MED23-HA was expressed in HEK-293 cells, cell lysates were incubated with 2 µg of recombinant proteins. Immunoblots (IB) were developed with anti-HA and anti-GST as indicated.

(B) hBrm interaction with LAP*/C/EBPβ1 WT, LAP*/C/EBPβ1 R3A or LAP*/C/EBPβ1 R3L. Top: Scheme of LAP*/C/EBPβ1 WT, R3A and R3L mutant proteins. Bottom: C33A cells were transfected with LAP*/C/EBPβ1 WT, LAP*/C/EBPβ1 R3A or LAP*/C/EBPβ1 R3L mutants in the presence of hBrm-HA as indicated. Cell lysates were immunoprecipitated with anti-HA and immunoblots were incubated with anti-HA or anti-C/EBPβ, respectively. IP: immunoprecipitation. IB: immunoblot.

Supplementary Figure 4: Expression and functional controls of PRMTs.

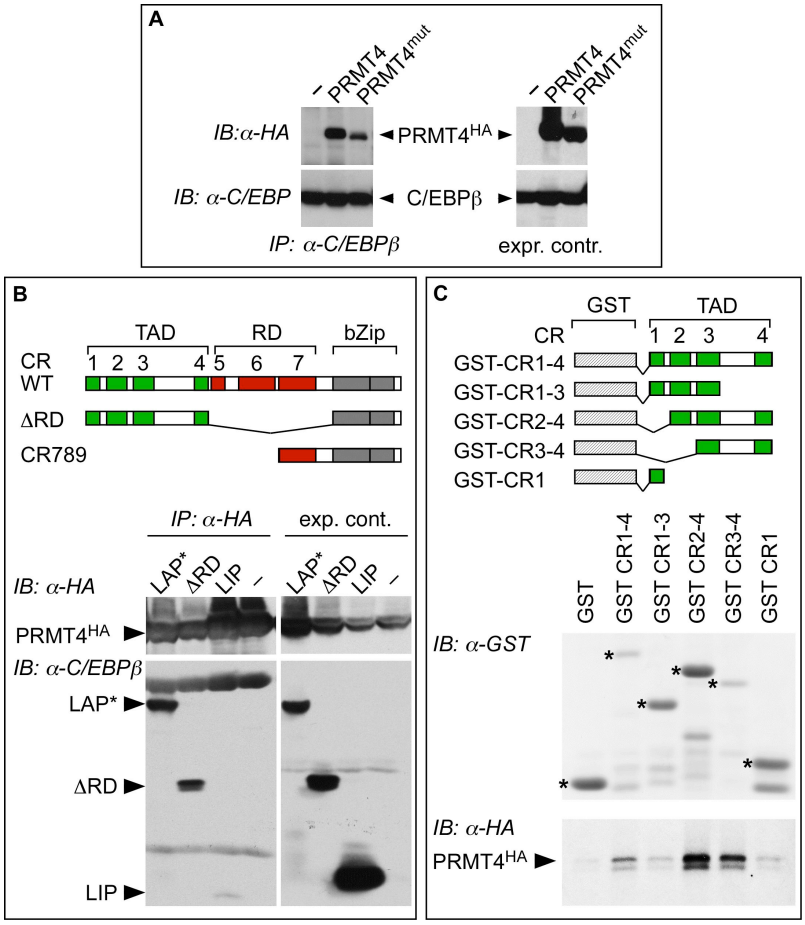


(A) Immunoprecipitation control of PRMT 3,4, and 5. HA-tagged PRMTs were expressed in HEK-293 cells and purified from cell lysates by immunoprecipitation with anti-HA. Western blots were incubated with anti-HA. IP: immunoprecipitation. IB: immunoblot.

(B) Top: fluorography of incorporated [methyl-^{3}H] label from S-adenosyl-L-[methyl-^{3}H] methionine into recombinant GST-H3 and GST-H4 proteins by PRMT3, 4, or 5, as indicated. Bottom: Coomassie staining of recombinant GST-H3 and GST-H4 input proteins after fluorography.

(C) Immunoprecipitated PRMT4/CARM1 is automethylated. Top: PRMT4/CARM1 was expressed in HEK-293 cells, purified from cell lysates by immunoprecipitation with anti-HA, separated on SDS-PAGE and incorporated S-adenosyl-L-[methyl-^{3}H]methionine revealed by fluorography. Bottom: Coomassie staining of SDS-PAGE separated recombinant C/EBPβ GST-CR1-4 TAD WT, C/EBPβ GST-CR1-4 TAD R3A mutant, GST or GST-H3 input proteins of *in vitro* methylation reactions.

Supplementary Figure 5: Interaction of PRMT4/CARM1 with C/EBPβ.

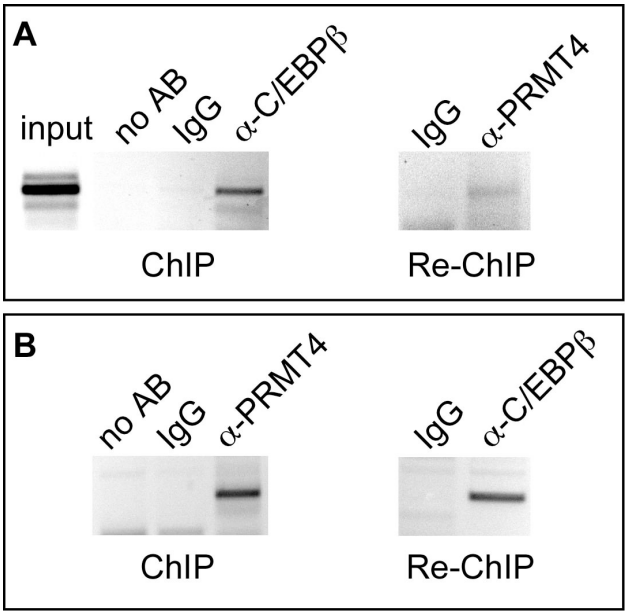


(A) LAP*/C/EBPβ1 WT was co-expressed with HA-tagged PRMT4/CARM1 WT or the PRMT4/CARM1$^{VLD/AAA}$ mutant protein in QT6 fibroblasts, cells lysates were immunoprecipitated with anti-C/EBPβ and western blots were incubated with anti-HA or anti-C/EBPβ as indicated. IP: immunoprecipitation. IB: immunoblot.

(B) Top: Scheme of LAP*/C/EBPβ1, LAP*/C/EBPβ RD deletion mutant (ΔRD) and LIP/C/EBPβ3. Bottom: LAP*/C/EBPβ, ΔRD, or LIP/C/EBPβ3 were expressed in the presence of HA-tagged PRMT4/CARM1 in HEK-293 cells, proteins were immunoprecipitated with anti-HA and immunoblotted with anti-HA or anti-C/EBPβ, as indicated.

(C) PRMT4/CARM1 binds to CR3-4 in the C/EBPβ TAD. Top: Scheme of recombinant GST-C/EBPβ TAD fusion proteins. Bottom: In vitro translated HA-tagged PRMT4 was incubated with 2 µg of each recombinant GST, GST-CR1-4, GST-CR1-3, GST-CR2-4, GST-CR3-4, and GST-CR1 proteins. Immunoblots were incubated with anti-GST and anti-HA, as indicated. IB: immunoblot.

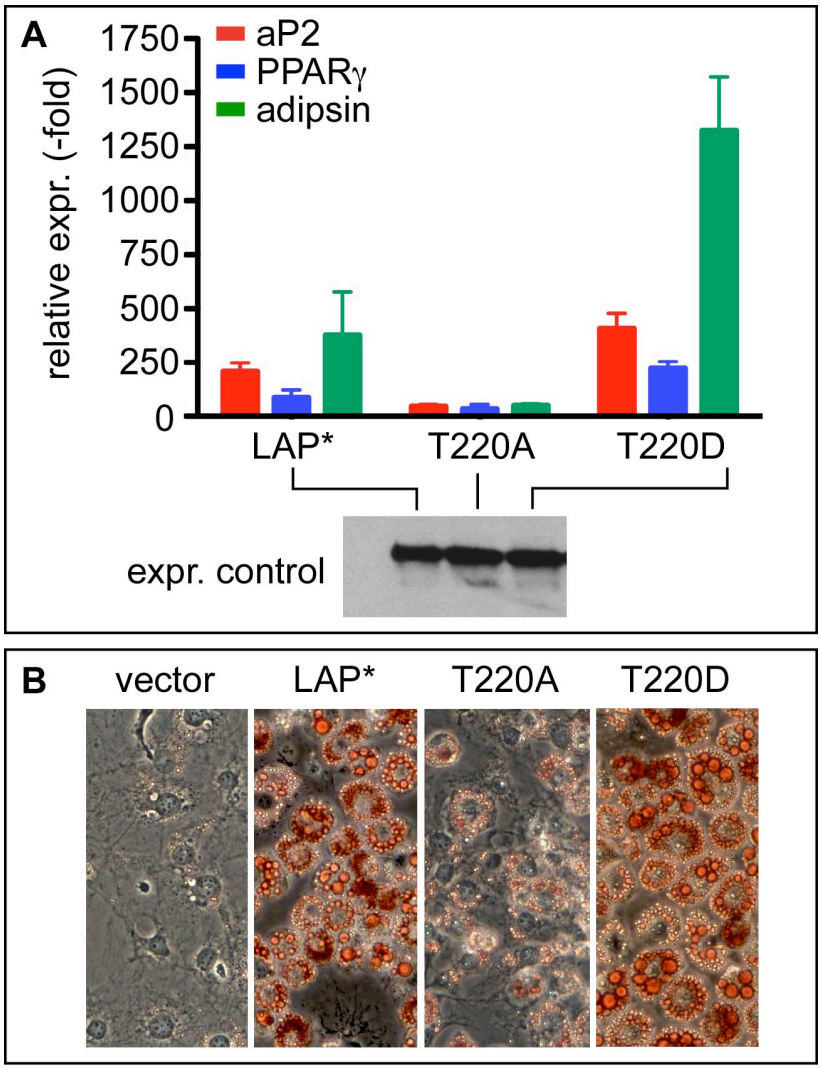
Supplementary Figure 6: C/EBPβ and PRMT4/CARM1 co-occupy the *hELA2* gene promoter in U937 cells.



(A) ChIP assay from U937 cells with antibodies directed against C/EBPβ. Re-ChIP with PRMT4/CARM1 antibodies. Immunoglobulin fraction served as negative control (IgG). PCR amplified *hELA2* promoter products were separated by agarose gel electrophoresis and stained with ethidium bromide.

(B) ChIP assay as in (A) with primary antibodies directed against PRMT4/CARM1 and Re-ChIP with anti-C/EBPβ.

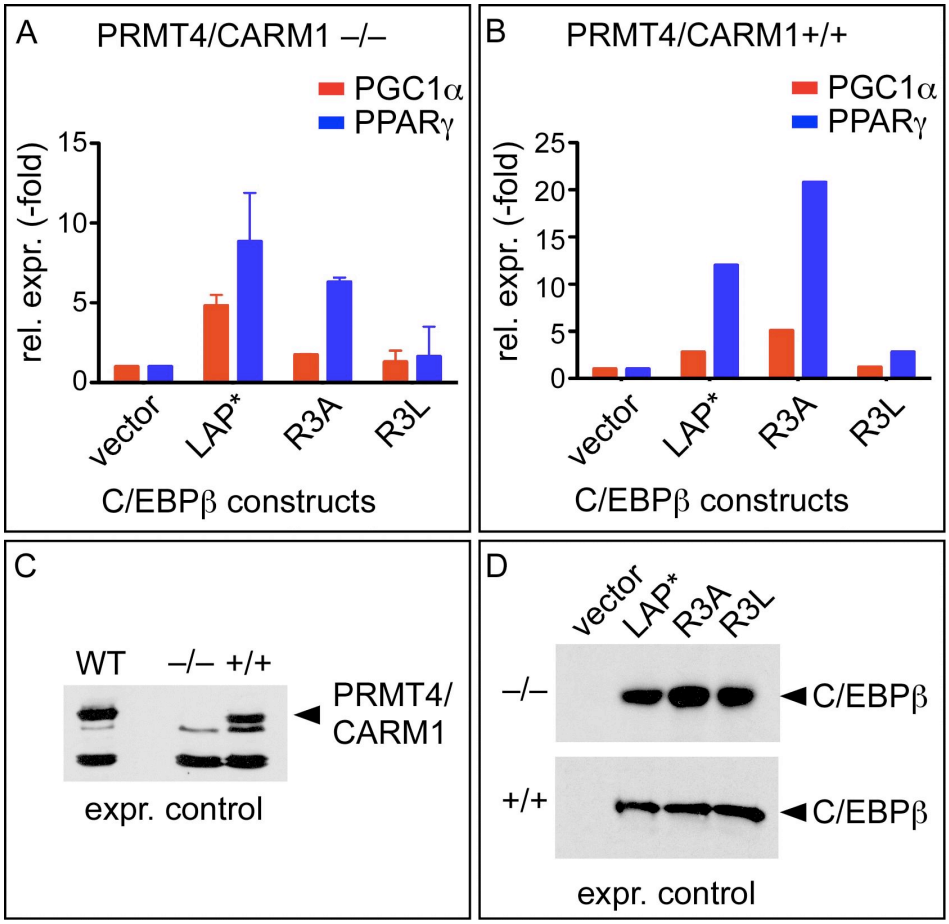
Supplementary Figure 7: Adipogenic gene regulation by LAP*/C/EBPβ1 WT and MAPkinase target site mutants.



(A) Top: Activation of PPARγ, aP2, and adipsin expression by LAP*/C/EBPβ1 WT or the T220A, D mutants in NIH 3T3 L1 cells, in the absence of adipogenic differentiation hormone cocktail. NIH 3T3 L1 cells were transfected with vector, LAP*/C/EBPβ1 WT, LAP*/C/EBPβ1 T220A, and LAP*/C/EBPβ1 T220D and stable transfectants selected by puromycin. Cells were grown to confluency, maintained for 10 days and examined by RT-PCR. Results were normalized to GAPDH expression. Bottom: Protein expression control of stably transfected C/EBPβ1 constructs.

(B) Oil-red-O staining of stably transfected NIH 3T3 L1 cells, 10 days post confluency, as shown in (A).

Supplementary Figure 8: Activation of early adipogenic regulators in the absence of PRMT4/CARM1 by C/EBPβ.



(A) LAP*/C/EBPβ1 WT R3A, and R3L mutant constructs were expressed in PRMT4/CARM1 KO MEFs, as indicated. PPARγ and PGC1α gene expression was analyzed by RT-PCR and normalized to GAPDH expression.

(B) LAP*/C/EBPβ1 WT and R3A, R3L mutant constructs were expressed in PRMT4/CARM1 rescued MEFs (see: Yadav et. al., 2003), as indicated. PPARγ and PGC1α gene expression was analysed by RT-PCR and normalized to GAPDH expression.

(C) Expression control of PRMT4/CARM1 in MEF WT, KO and PRMT4/CARM1 rescued cells.

(D) Expression control of LAP*/C/EBPβ1 WT, R3A, and R3L mutant constructs detected by immunoblotting.