

**Supplemental Figure 1** Diagram depicting the conserved YXXL motifs in Jak2 kinase and Hexim1.

**Supplemental Figure 2. Hexim1 and pY705Stat3 detection.**

Detection of Hexim1, and pY<sup>705</sup>Stat3 using confocal microscopy in the hypothalamus of a control fasted WT mouse not treated with leptin. A, Hexim1 (red), is present. B, pY<sup>705</sup>Stat3 (green) is absent. D, overlapping signals of Hexim1, pY<sup>705</sup>Stat3/nuclear staining with DAPI. C, mouse embryonic fibroblasts were isolated at stage 15 p.c., total protein extracts were used to evaluate Hexim1 protein expression in wild type, heterozygous and null fibroblasts by Western blot. D, we further confirmed the absence of Hexim1 in null fibroblasts using immunofluorescence with anti-Hexim1 antibodies and DAPI staining for nuclei identification.

**Supplemental Figure 3 Decrease expression of C/EBP beta in skeletal muscle.**

Western blotting of gastrocnemius muscle total protein extract showing decreased expression of C/EBP $\beta$  in the HT background of wild-type (WT), and heterozygous (HT) fed chow or high-fat diet (HFD) for 14 weeks. The graph shows quantification of C/EBP $\beta$  protein levels. Values are expressed as mean  $\pm$  SEM \*  $p < 0.05$  WT vs. HT obtained using one way Anova and Bonferroni's post test.

**Supplemental Figure 4 Hexim1 regulates leptin mediated induction of pY705Stat3 in HEK293 cells.**

A, quantitation of leptin mediated pY705Stat3 induction in presence of myc-Hexim1. Values are expressed as Means  $\pm$  s.e.m. \* $P < 0.05$  Ob-Rb vs. Ob-Rb+mycHexim1.

B, quantitation of leptin mediated pY705Stat3 induction in presence of myc-pY<sup>167</sup>T/pY<sup>291</sup>EYXXLHexim1. Values are expressed as Means  $\pm$  s.e.m. \* $P < 0.05$  Ob-Rb vs. Ob-Rb + myc-pY<sup>167</sup>T/pY<sup>291</sup>EYXXLHexim1.

Figure S1

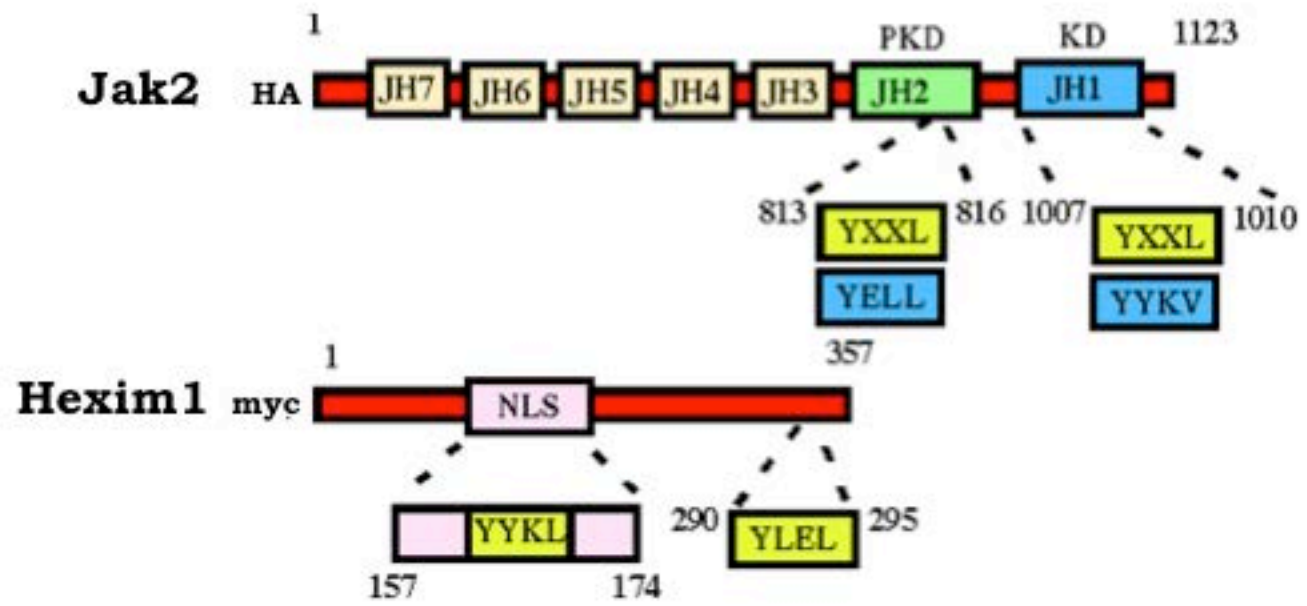


Figure S2

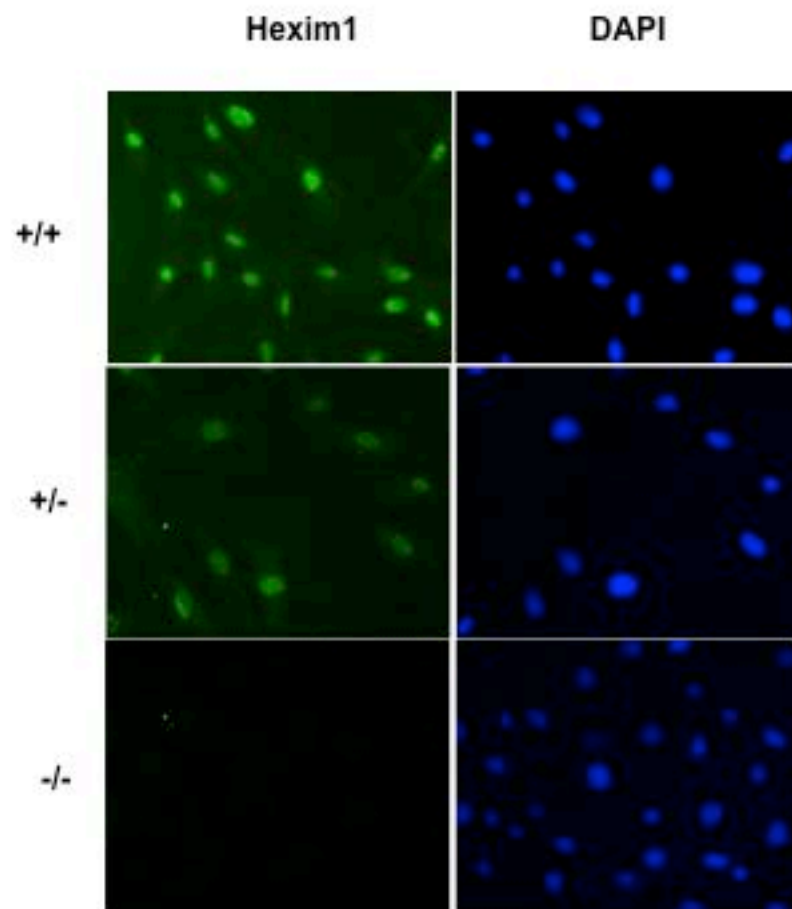
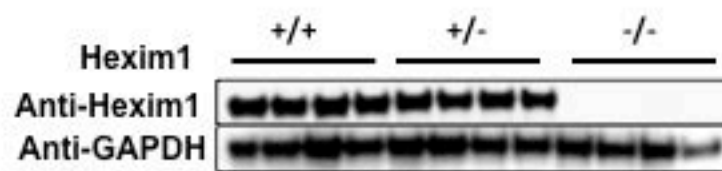
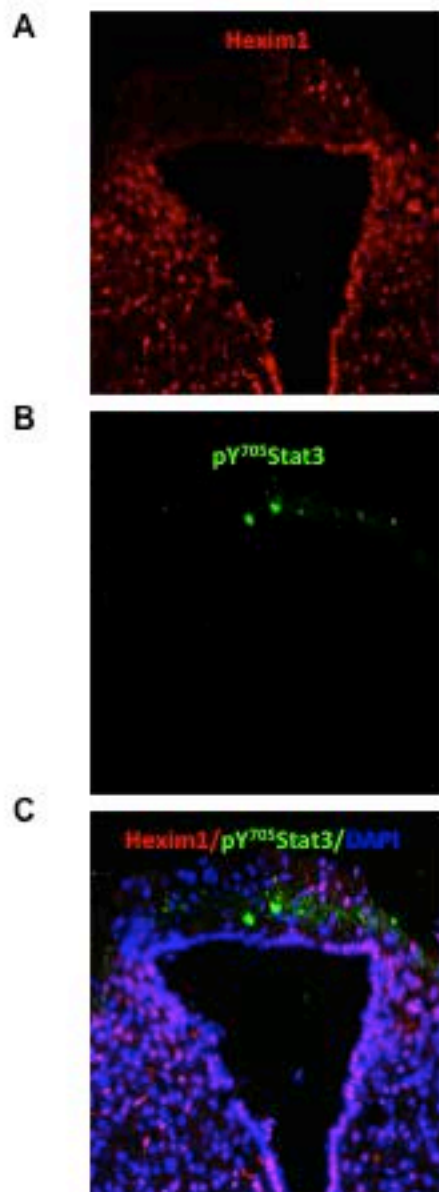


Figure S3

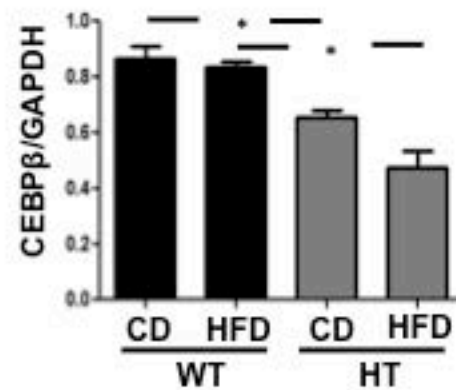
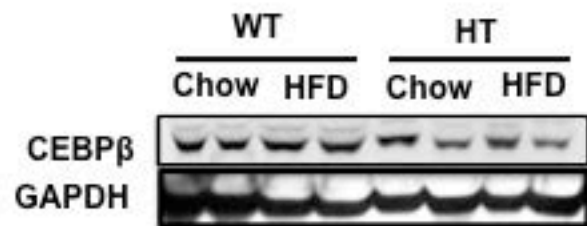


Figure S4

