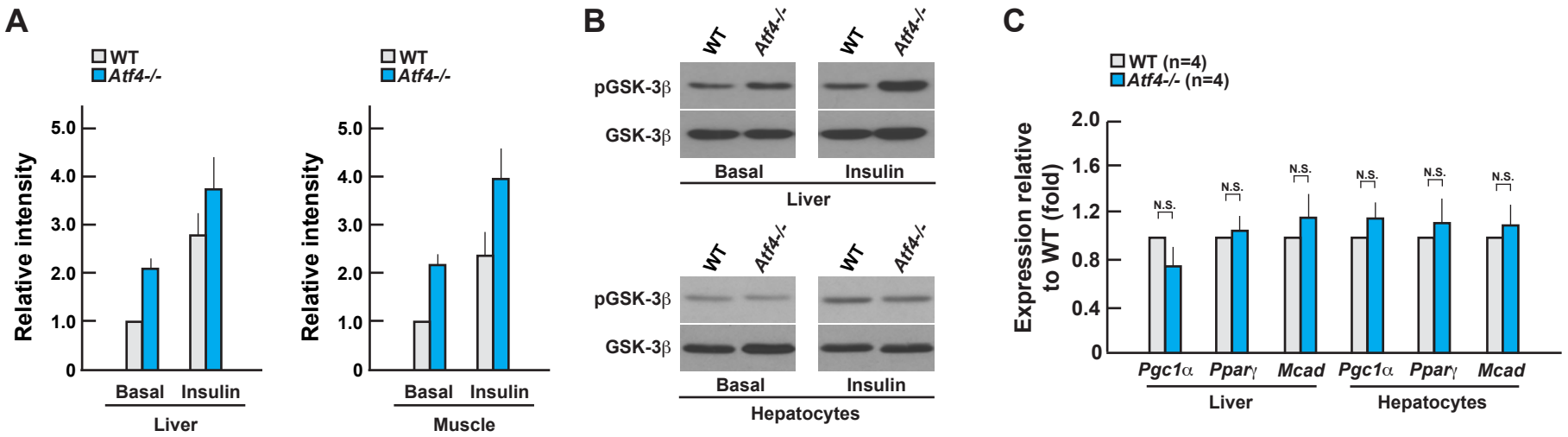
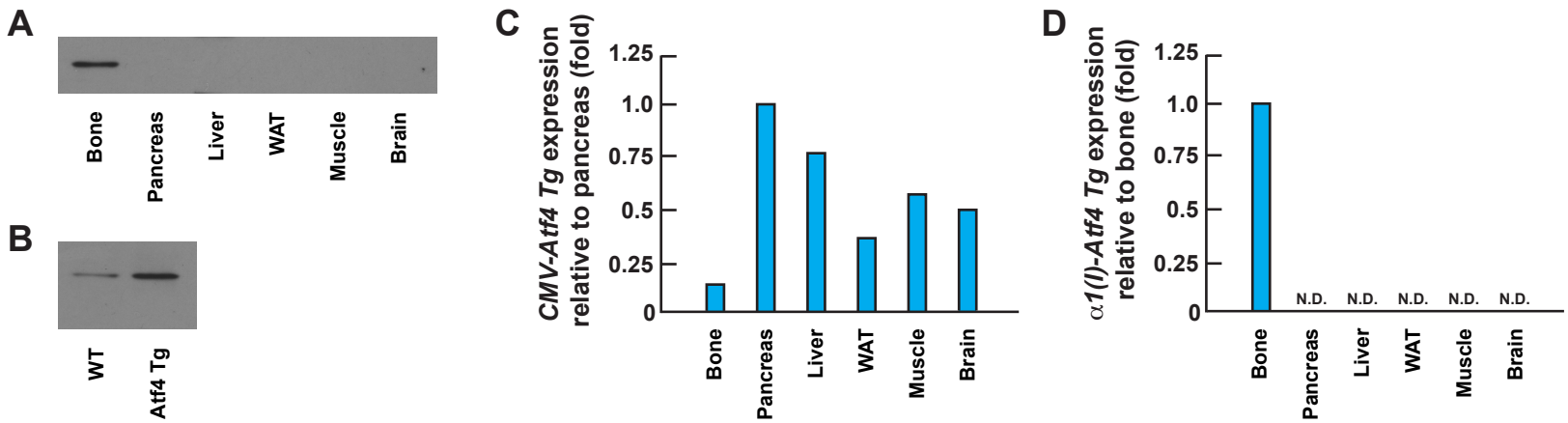
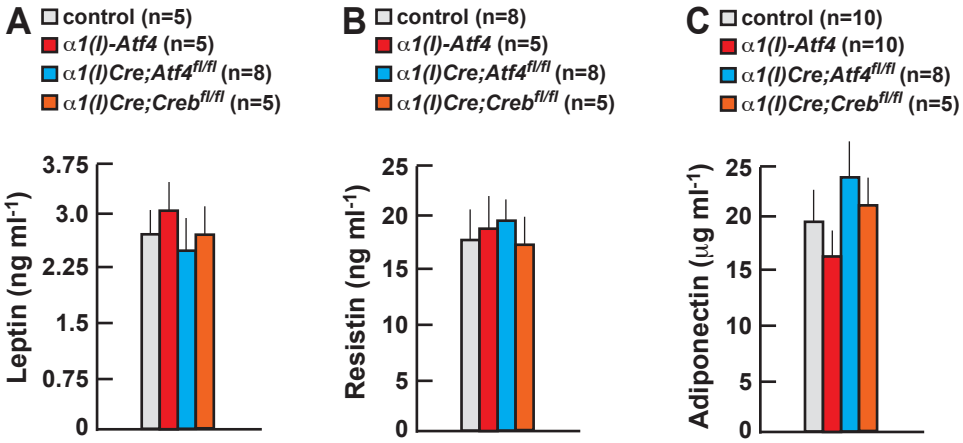


Supplemental figure 1

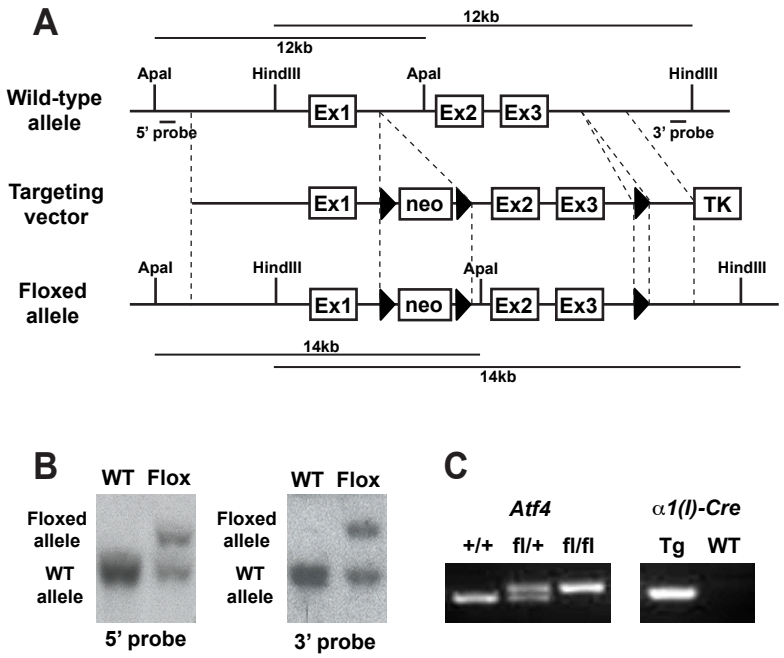
Comparison of insulin signaling pathway and gene expression in *Atf4-/-* liver and hepatocytes. (**A**) Quantification of Akt phosphorylation in *Atf4-/-* liver and muscle at basal and insulin stimulated condition. (**B**) Phosphorylation of GSK-3β in *Atf4-/-* liver (upper panel) or cultured hepatocytes at basal and insulin stimulated condition. (**C**) Expression of *Pgc1α*, *Pparγ* and *Mcad* in *Atf4-/-* liver or cultured hepatocytes. N.S.: not significant.



Supplemental figure 2
Quantification of *Atf4* transgene. (**A**) Atf4 protein expression in several tissues of α*1(I)Collagen-Atf4* tranegenic mice. (**B**) Atf4 protein expression in bone of WT and α*1(I)Collagen-Atf4* tranegenic mice. (**C**) Expression of *CMV-Atf4* transgene in various tissues relative to pancreas in *CMV-Atf4* tranegenic mice. (**D**) Expression of α*1(I)Collagen-Atf4* transgene in various tissues relative to bone in α*1(I)Collagen-Atf4* tranegenic mice.
N.D.: not detected.

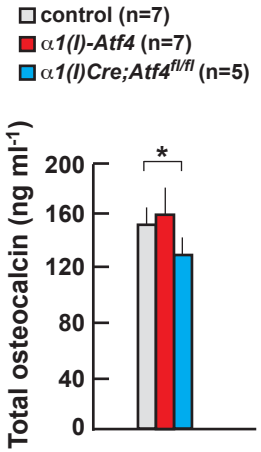


Supplemental figure 3
Levels of Adipokines in mutant mice. Serum (**A**) leptin, (**B**) resistin and (**C**) adiponectin levels in α*1(I)Collagen-Atf4*, α*1(I)Collagen-Cre*;*Atf4fl/fl* and α*1(I)Collagen-Cre*;*Crebfl/fl* mice.

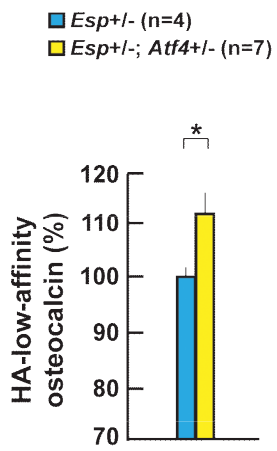


Supplemental figure 4

Generation of *Atf4osb-/-* mice. (**A**) Targeting construct for conditional inactivation of *Atf4*. White box, exon; black triangles, LoxP sites. (**B**) Southern blot analysis of *Atf4-flox* clone. The 5' probe detected a 12 kb WT and 14 kb targeted band while 3' probe detected 12 kb WT and 14 kb targeted band. (**C**) PCR genotyping of *Atf4osb-/-* mice. WT and floxed allele yield 600 bp and 640 bp products, respectively. α*1(I)collagen-Cre* transgenic mice harbor a transgene-specific band.



Supplemental figure 5
Level of osteocalcin in mutant mice. Serum total osteocalcin level in *α1(I)Collagen-Atf4* and *α1(I)Collagen-Cre*;*Atf4fl/fl* mice.



Supplemental figure 6
Serum uncarboxylated osteocalcin levels in *Esp*+/- and *Esp*+/-; *Atf4*+/- mice. Error bars, mean + SEM. *: P<0.05

Table S1 **Insulin sensitivity analysis of eight week-old *Atf4$_{osb}$* -/- mice analyzed by hyperinsulinemic-euglycemic clamps.**

Genotype	**Control (n=3)**	***Atf4$_{osb}$* -/- (n=3)**
Body weight (g)	25.0 ± 1.1	20.0 ± 0.3*
Basal glucose (mg/dl)	120.0 ± 12.7	94.7 ± 9.0
Clamp glucose (mg/dl)	101.7 ± 8.7	118.0 ±14.0
Glucose infusion rate (mg/kg/min)	47.2 ± 4.2	69.3 ± 2.5*
Basal hepatic glucose production (mg/kg/min)	10.4 ± 0.8	13.2 ± 0.9
Clamp hepatic glucose production (mg/kg/min)	2.4 ± 1.1	0.6 ± 1.6
Liver action (%)	77.5 ± 11.2	90.5 ± 9.0
Glucose turnover (mg/kg/min)	49.6 ± 4.2	69.9 ± 3.0*
Whole body glycolysis (mg/kg/min)	32.9 ± 7.6	28.2 ± 1.6
Glycogen synthesis (mg/kg/min)	16.7 ± 7.2	41.7 ± 4.3*

*: $P < 0.05$