Supplemental Figure legends

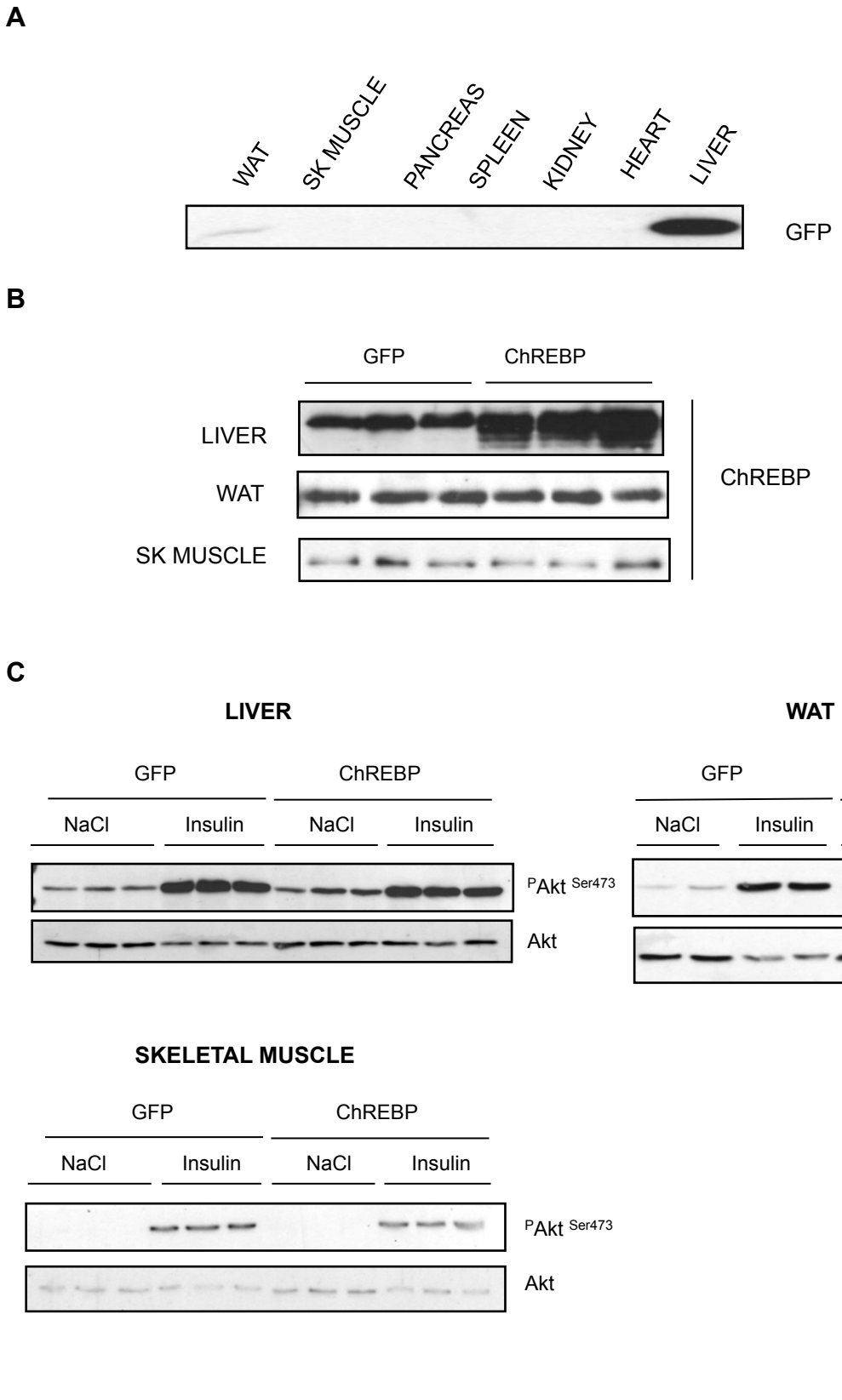
Supplemental Figure 1. ChREBP adenoviral delivery increases ChREBP protein content in liver but not in white adipose tissue or in skeletal muscle. All analyses were carried out in fed GFP and ChREBP mice 4 weeks after adenoviral delivery. Representative Western blots are shown. n = 6-10/group. (**A**). GFP protein content in various tissues from ChREBP mice as indicated (**B**). ChREBP protein content in liver, white adipose and skeletal muscles from GFP and ChREBP mice. (**C**). Western blot analysis of phospho Akt (Ser473) and total Akt content in liver, white adipose tissue and skeletal muscles from GFP and ChREBP mice under basal (PBS) and insulin stimulation conditions (1U/kg, 3 min) as indicated in the *Methods* section.

Supplemental Figure 2. Expression of glycolytic and lipogenic genes and insulin signaling in liver of fasted mice overexpression ChREBP. C57BL/6J mice were injected intravenously with a single dose of 5.10^9 pfu of GFP or ChREBP adenovirus (Day1). Four weeks later, mice are sacrificed after an overnight fast. (**A**). qRT-PCR analysis of L-PK, ACC, FAS and SCD1 in livers of fasted GFP *vs*. fasted ChREBP mice. Results are the mean ± S.E.M, n = 10-12/group. *, P<0.05, **, P<0.01 ChREBP vs. GFP mice. (**B**). Insulin signaling in liver of ChREBP mice. Following an overnight fast, mice treated with either GFP and ChREBP were injected with 1 unit of regular human insulin *via* the portal vein (n=6/10 group). Three minutes after the insulin injection, livers were snap frozen in liquid nitrogen. Western blot shows insulin-stimulated liver lysates blotted with phosphorylated Akt (Ser473) and phosphorylated GSK3β (Ser9) antibodies. Antibodies for total Akt, GSK3β and ChREBP were used.

Supplemental Figure 3. Effect of palmitate on Akt phosphorylation in primary hepatocytes. Twenty four hour after plating, mouse hepatocytes were infected with 3 pfu of GFP before being incubated for 24h with 0.48 mM of albumin-bound palmitate (PALM), with or without 10nM of SCD1 inhibitor ($SCD1^{inhib}$), as indicated. An insulin (1 nM) time-course was performed for 2 and 5 min**. (A).** Western blot analysis of total Akt and of the insulin-mediated Akt phosphorylation on Ser473. Representative western blots are shown. (n=4 independent cultures). (**B**). Quantification of the ratio of Ser473 Akt phosphophorylation compared to total Akt protein content is shown. *, P<0.05 *vs*. GFP BSA (**C**). The Δ9-desaturation index was measured as described in the *Material and Methods* section.

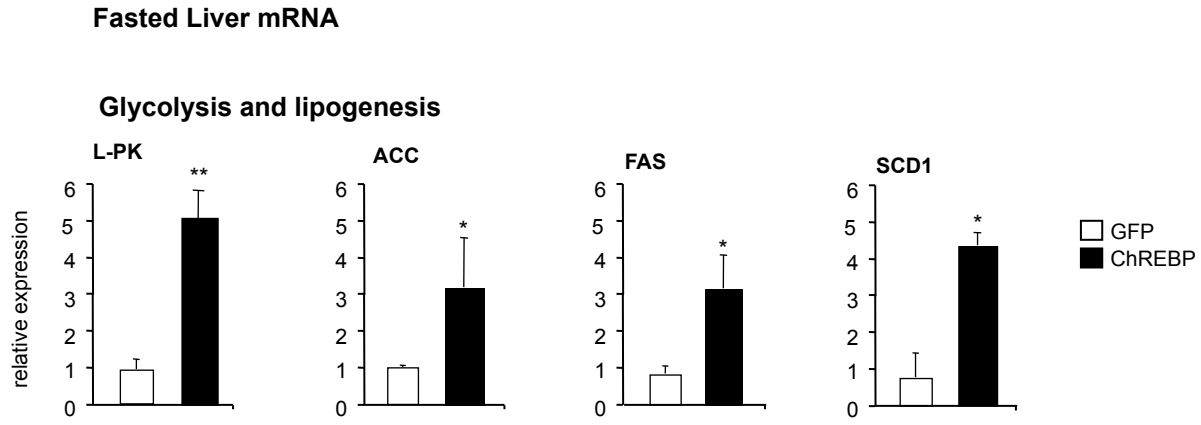
Supplemental Figure 4. Measurement of glucose production in vitro. Twenty-four hour after plating, mouse hepatocytes were infected with 3 pfu of GFP or ChREBP adenovirus before being incubated for 24h with 0.48 mM of albumin-bound palmitate (PALM) with or without 10nM of SCD1 inhibitor ($SCD1^{inhib}$). Rates of glucose production were then measured under basal and insulin (100nM) conditions as indicated in the *Material and Methods section*. n=6 independent cultures. *, P<0.05, **, P<.0.01 insulin vs. basal conditions. $^{\#}$, P<0.05, GFP PALM vs. GFP BSA (Basal conditions).

Supplemental Figure 5. Overexpression of SCD1 in vitro recapitulates the beneficial effect of ChREBP on Akt phosphorylation. Twenty-four hour after plating, mouse hepatocytes were infected with a combination of adenovirus as indicated (GFP, SCD1, ChREBP, shCTRL and/or ShSCD1) and described in the *Methods* section. Cells were then incubated for 24h with BSA or 0.48 mM of albumin-bound palmitate (PALM). An insulin (1nM) time-course was performed for 2 and 5 min. n=6 independent cultures. Quantification of the ratio of Ser473 compared to total Akt protein content is shown. *, P<0.05 SCD1 PALM compared to GFP PALM; $^{\#}$, P<0.05 ChREBP shSCD1 vs. ChREBP shCTRL.



Supplemental Figure 1

A



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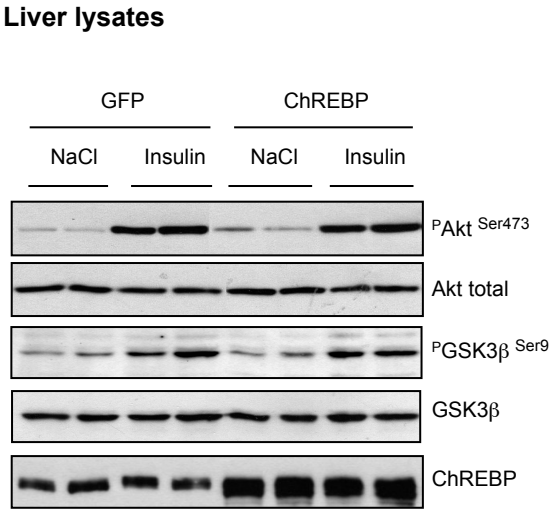
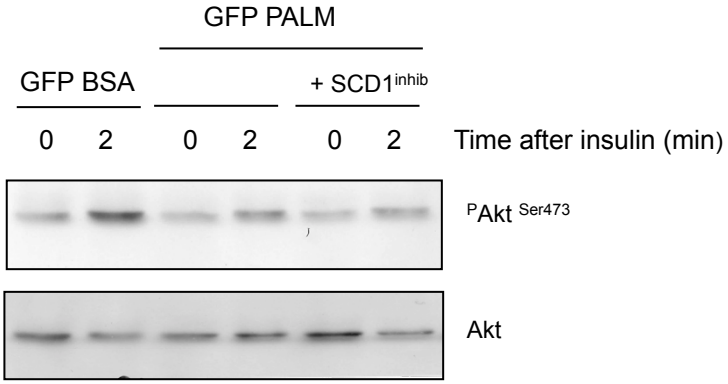


Supplemental Figure 2

A



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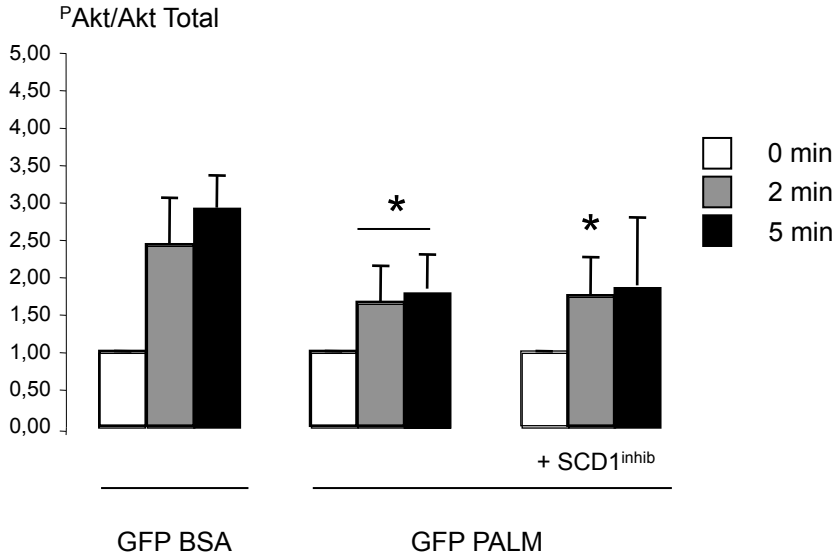

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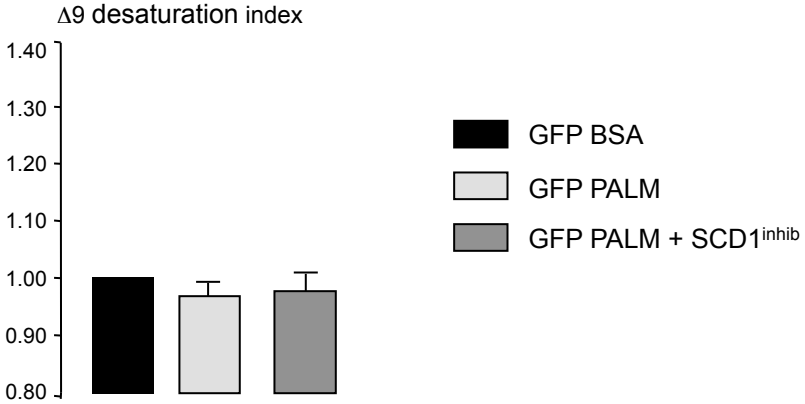
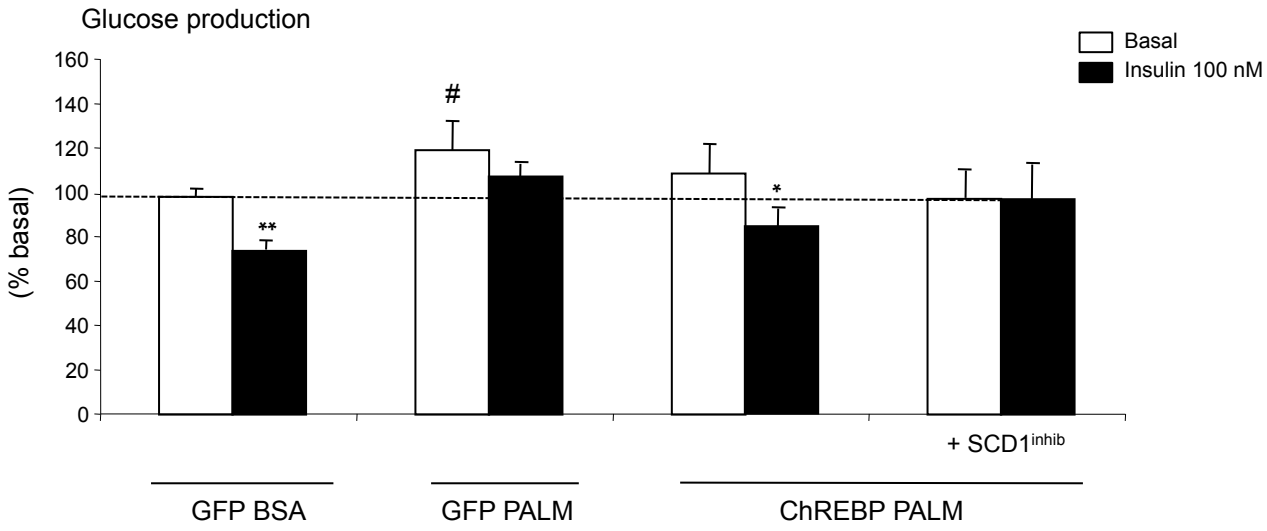
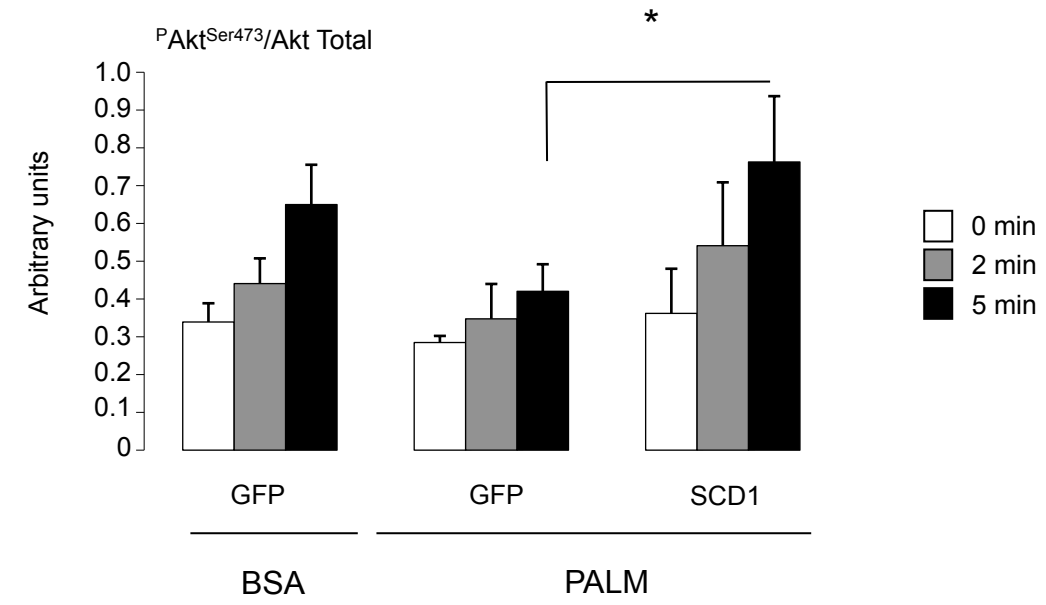
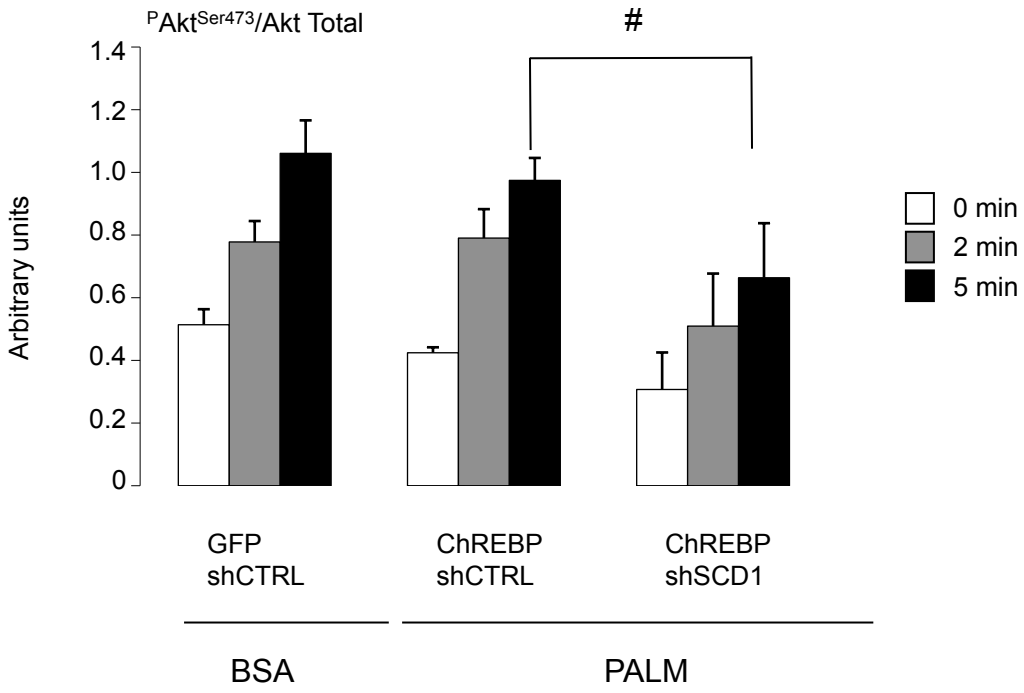


Supplemental Figure 3



Supplemental Figure 4





Supplemental Figure 5