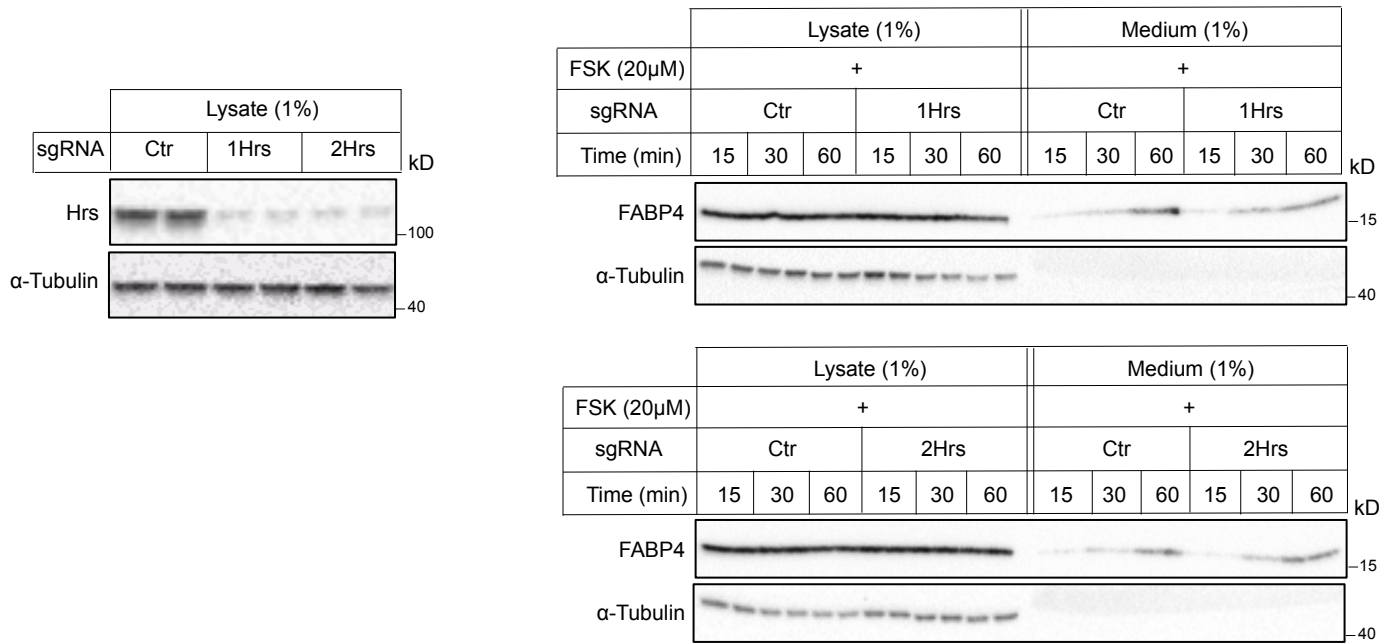
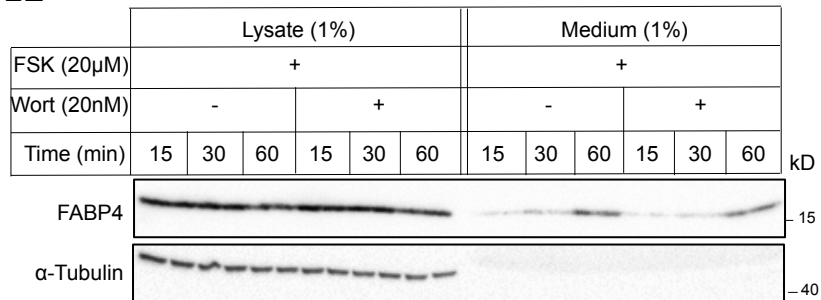


**Replicate Figure 1A: FABP4 secretion is induced by forskolin in adipocytes.** Adipocytes were incubated with increasing concentrations of forskolin (FSK) and at indicated time, medium fractions were collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium were analyzed by immunoblotting with anti-FABP4 and anti- $\alpha$ -tubulin antibodies.

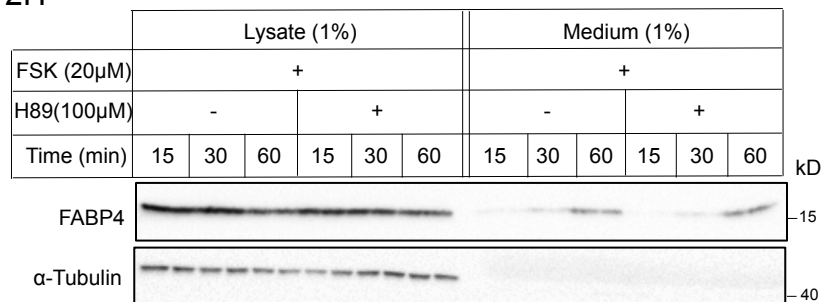


**Replicate Figure 2C: FABP4 secretion is independent of Hrs.** Wild type adipocytes and adipocytes depleted for Hrs using the CRISPR/cas9 system were incubated with 20 μM FSK and at indicated time, medium was collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium was analyzed by immunoblotting with anti-FABP4 and anti-α-tubulin antibodies. Knock out efficiencies were validated prior FSK stimulation for each sgRNA tested by immunoblotting with anti-Hrs antibody. In order to minimize the images included in the paper, the results presented in the figure are derived from the experiment performed as follows. One control sgRNA and two sgRNA targeting Hrs were tested in parallel, samples were loaded on the same gel, and immunoblotting with anti-Hrs antibody was performed for each condition tested from lysate and medium samples.

2E

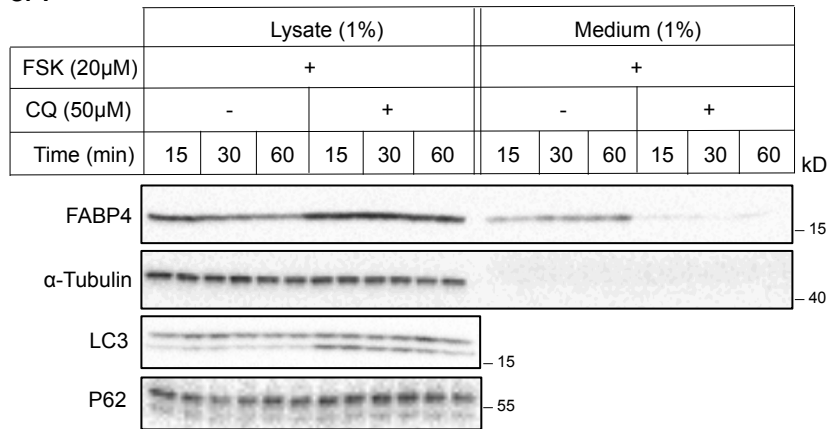


2H

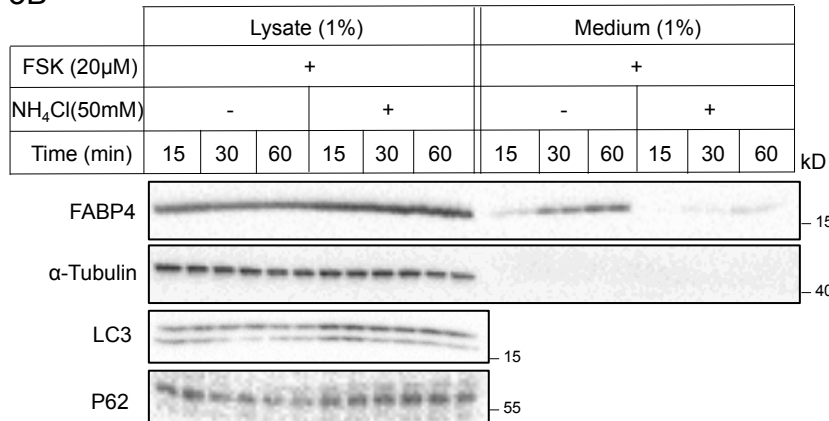


**Replicate Figure 2E & 2H: FABP4 secretion is independent of autophagy processes.** Adipocytes were incubated with 20  $\mu$ M FSK in the presence or absence of 20 nM wortmannin (Wort) (2E) or 100  $\mu$ M H89 (2H) and at indicated times, medium fractions were collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium fractions were analyzed by immunoblotting with anti-FABP4 and anti- $\alpha$ -tubulin antibodies.

3A

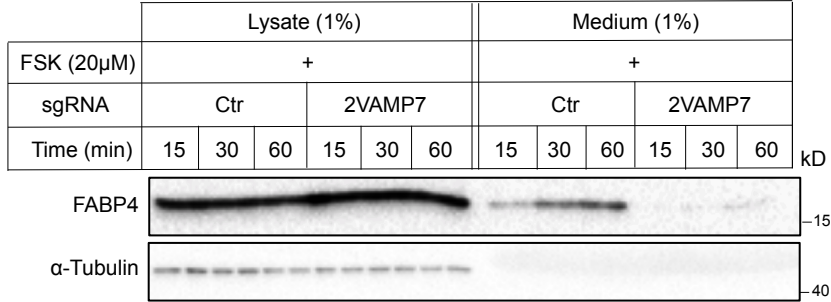
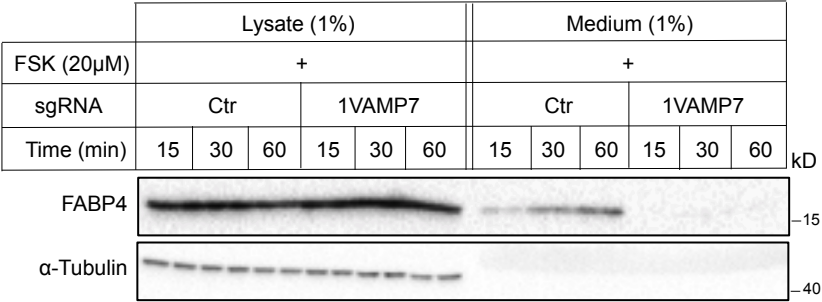
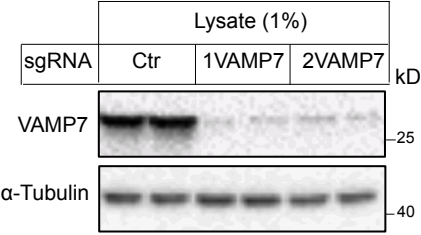


3B

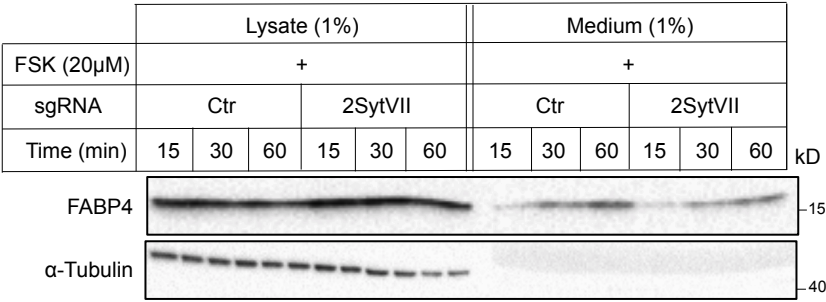
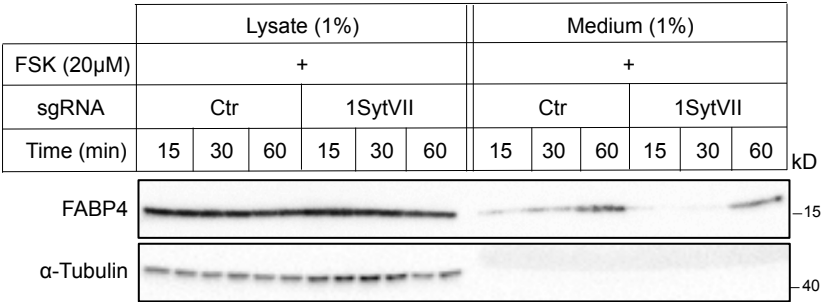
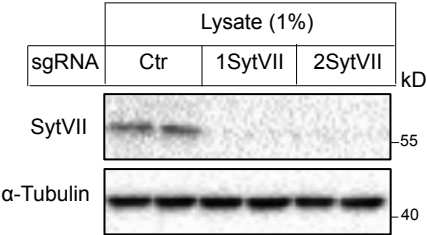


**Replicate Figure 3A & 3B: FABP4 secretion is inhibited by chloroquine and ammonium chloride.** Adipocytes were incubated with 20 μM FSK in the presence or absence of 50 μM chloroquine (CQ) (3A) or 50 mM ammonium chloride (NH<sub>4</sub>Cl) (3B) and at indicated times, medium fractions were collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium were analyzed by immunoblotting with anti-FABP4, anti-α-tubulin, anti-LC3 and anti-P62 antibodies. For these experiments the modest increase in expression of PE-LC3 and P62 inside the cells demonstrates the efficiency of drugs tested. LC3 and P62 proteins have approximately the same molecular weight as FABP4 and α-tubulin, respectively, therefore the lysates were probed separately with antibodies against LC3 and P62, respectively. However, in order to maintain the dimensions of the images presented in the paper, LC3 and P62 expression were tested in both lysate and medium.

3E

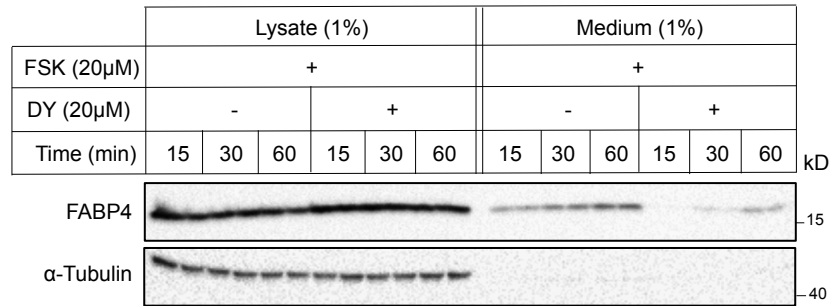


3F

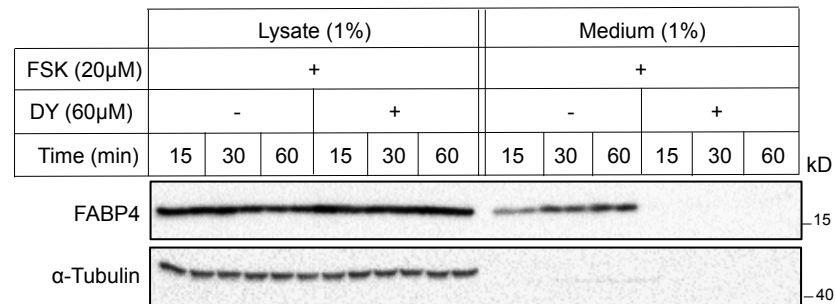


**Replicate Figure 3E & 3F: FABP4 secretion is mediated by secretory lysosomes.** Wild type adipocytes and adipocytes depleted for VAMP7 (3E) or synaptotagmin VII (3F) using the CRISPR/cas9 system were incubated with 20  $\mu$ M FSK and at indicated time, medium was collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium was analyzed by immunoblotting with anti-FABP4 and anti- $\alpha$ -tubulin antibodies. Knock out efficiencies were validated prior FSK stimulation for each sgRNA tested by immunoblotting with anti-VAMP7 and anti-synaptotagmin antibodies. In order to minimize the images included in the paper, the results presented in the figure are derived from the experiment performed as follows. One control sgRNA and two sgRNA targeting VAMP7 and synaptotagmin VII were tested in parallel, samples were loaded on the same gel, and immunoblotting with anti-VAMP7 and anti-synaptotagmin antibodies was performed for each condition tested from lysate and medium samples.

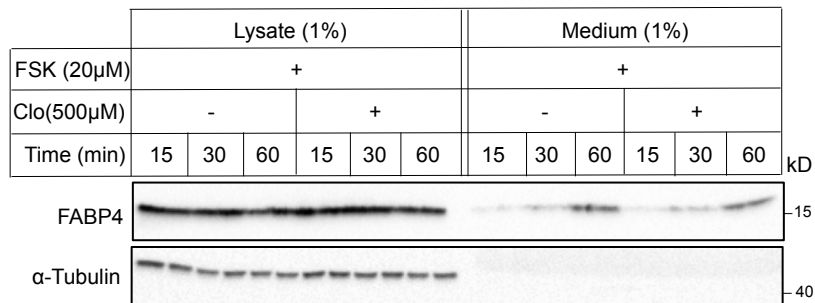
A



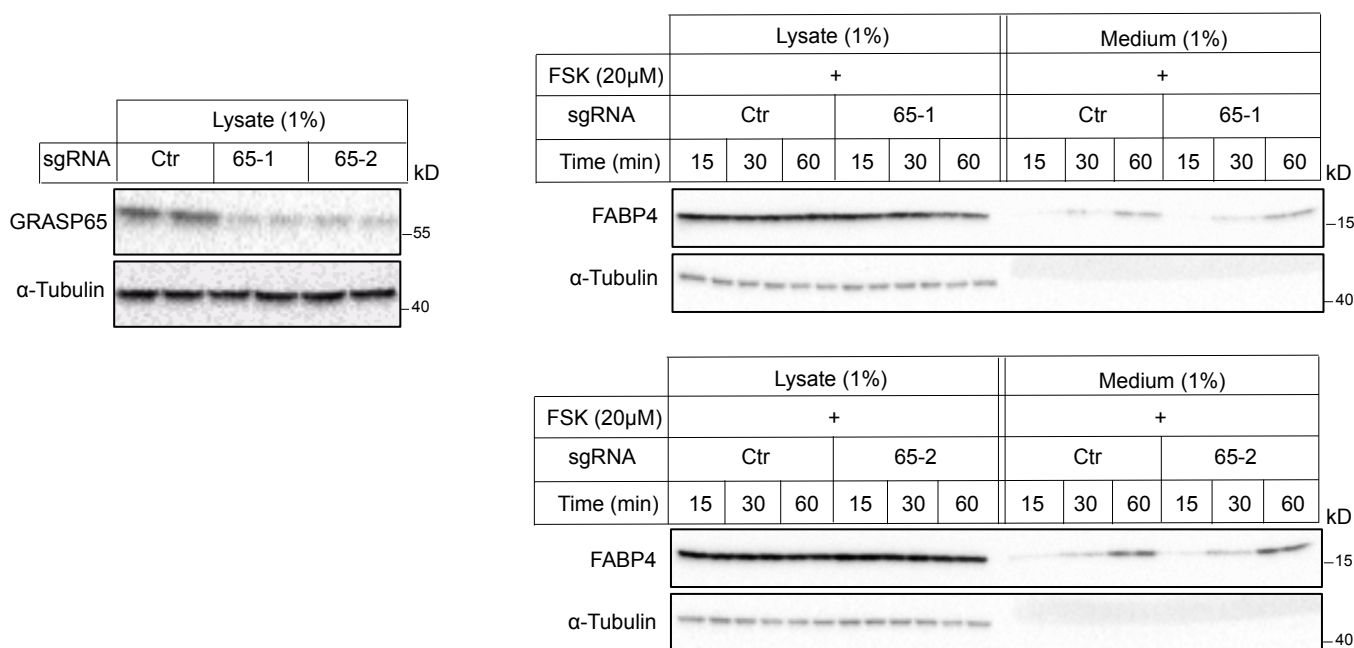
B



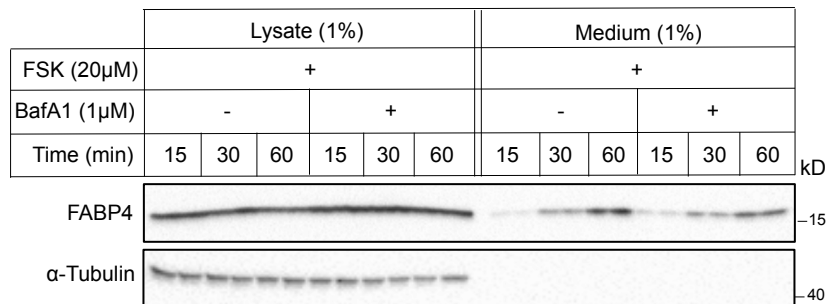
**Replicate Figure 6A & 6B: Forskolin-induced FABP4 secretion is inhibited by dynasore.** Adipocytes were incubated with 20  $\mu$ M FSK in the presence or absence of 20  $\mu$ M dynasore (A) or 60  $\mu$ M dynasore (B) and at indicated times, medium fractions were collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium was analyzed by immunoblotting with anti-FABP4 and anti- $\alpha$ -tubulin antibodies.



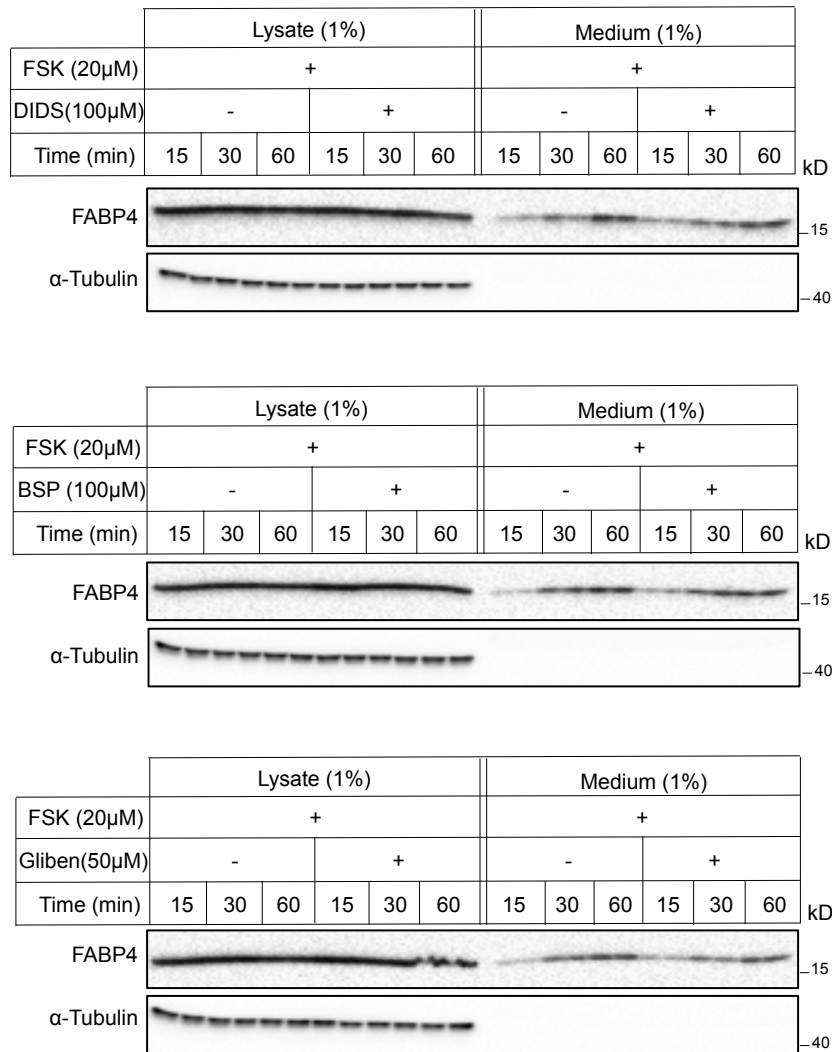
**Replicate Figure S2B: FABP4 secretion is independent of ERGIC dispersal.** Adipocytes were incubated with 20 μM FSK in the presence or absence of 500 μM clofibrate (Clo) and at indicated times, medium fractions were collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium fractions were analyzed by immunoblotting with anti-FABP4 and anti-α-tubulin antibodies.



**Replicate Figure S2D: FABP4 secretion is independent of GRASP65.** Wild type adipocytes and adipocytes depleted for GRASP65 using the CRISPR/cas9 system were incubated with 20 μM FSK and at indicated time, medium was collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium was analyzed by immunoblotting with anti-FABP4 and anti-α-tubulin antibodies. Knock out efficiencies were validated prior FSK stimulation for each sgRNA tested by immunoblotting with anti-GRASP65 antibody. In order to minimize the images included in the paper, the results presented in the figure are derived from the experiment performed as follows. One control sgRNA and two sgRNA targeting GRASP65 were tested in parallel, samples were loaded on the same gel, and immunoblotting with anti-GRASP65 antibody was performed for each condition tested from lysate and medium samples.



**Replicate Figure S3C: FABP4 secretion is inhibited by bafilomycin A1 in adipocytes.** 3T3-L1 cells differentiated into adipocytes were incubated with 20 μM FSK in the presence or absence of 1 μM bafilomycin A1 and at indicated time, medium was collected and cells lysed. For each condition performed in duplicate, 1% of total cell lysate and medium was analyzed by western blotting with anti-FABP4 and anti- $\alpha$ -tubulin antibodies.



**Replicate Figure S4B: FABP4 secretion is not impaired by ABC transport inhibitors.** Adipocytes were incubated with 20 μM FSK in the presence or absence of 100μM DIDS (upper paned), 100μM BSP(mid panel) or 50μM glibenclamide (bottom panel) and at indicated time, medium was collected and cells lysed. For each condition, performed in duplicate, 1% of total cell lysate and medium was analyzed by western blotting with anti-FABP4 and anti-α-tubulin antibodies. In order to minimize the images included in the paper, the results presented in the figure are derived from the experiment performed as follows. DIDS, BSP and glibenclamide were tested in parallel and samples were loaded on the same gel.