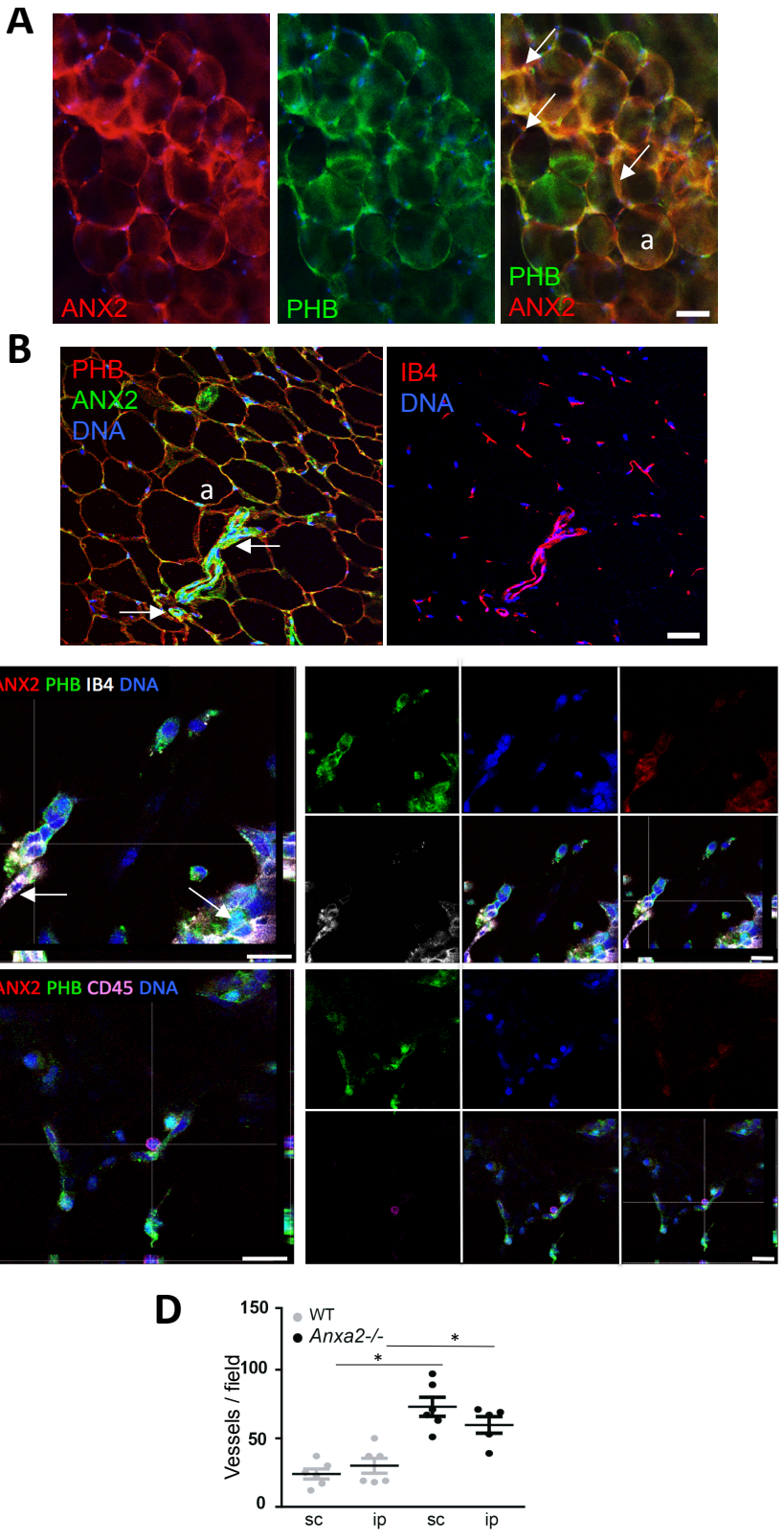
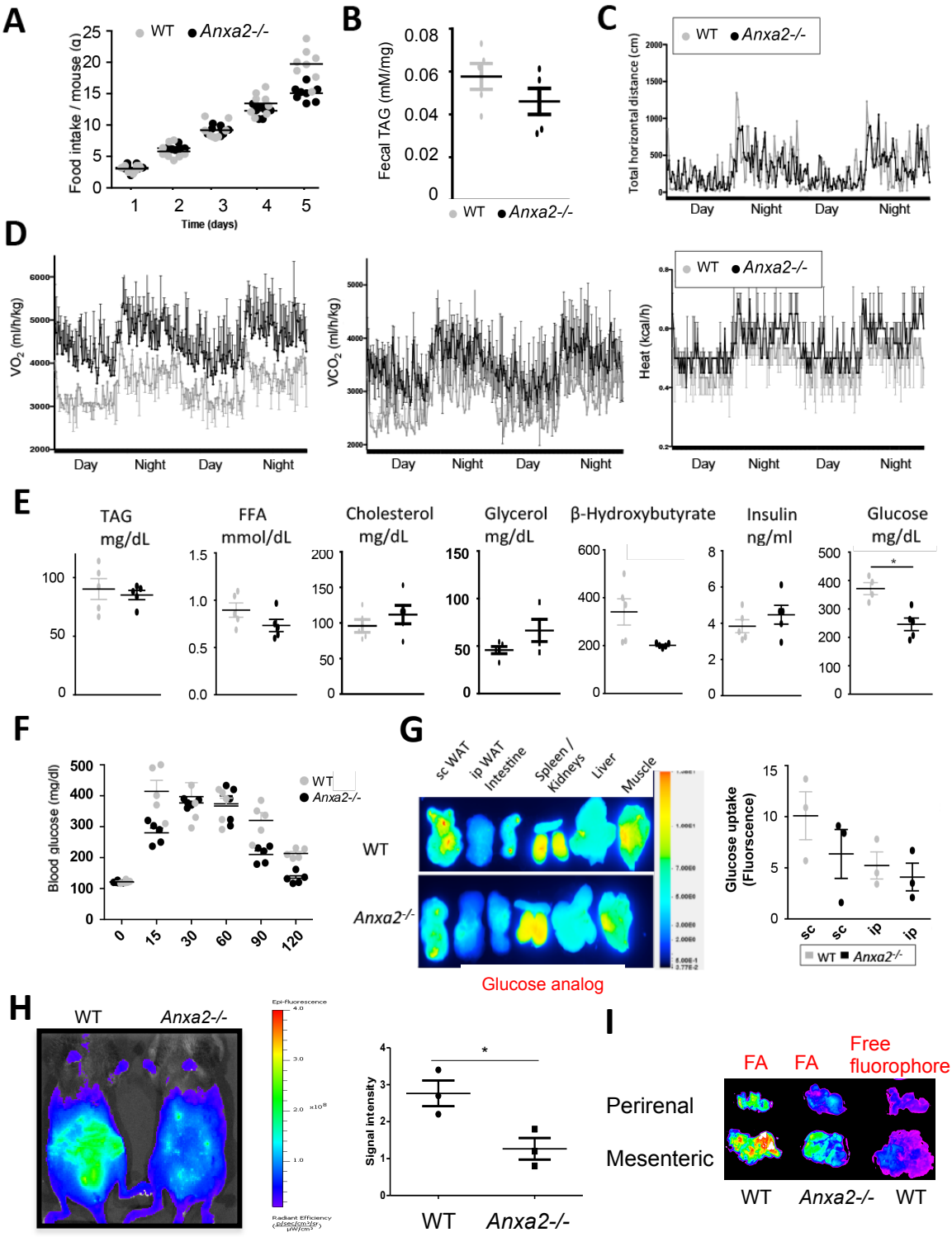
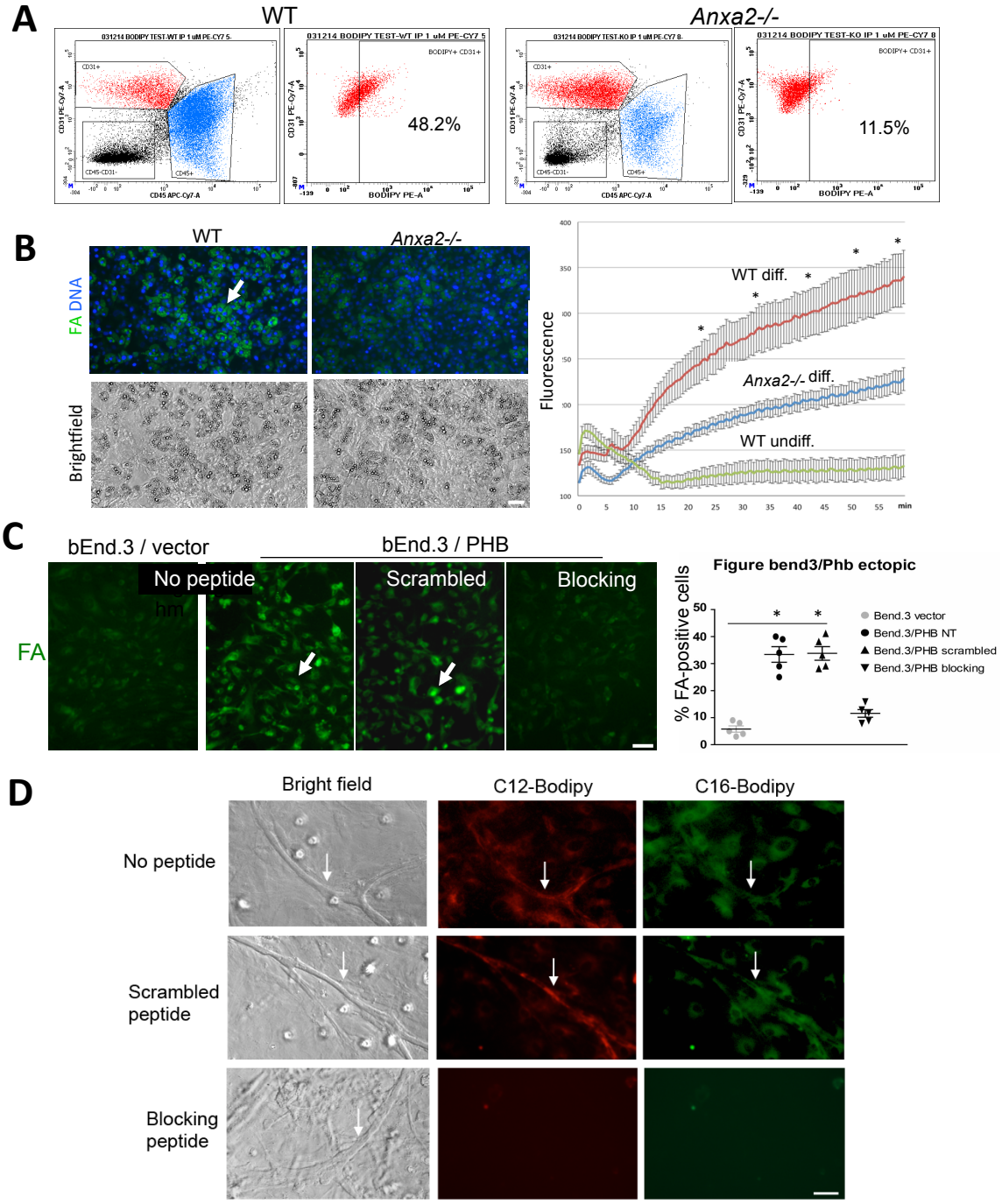


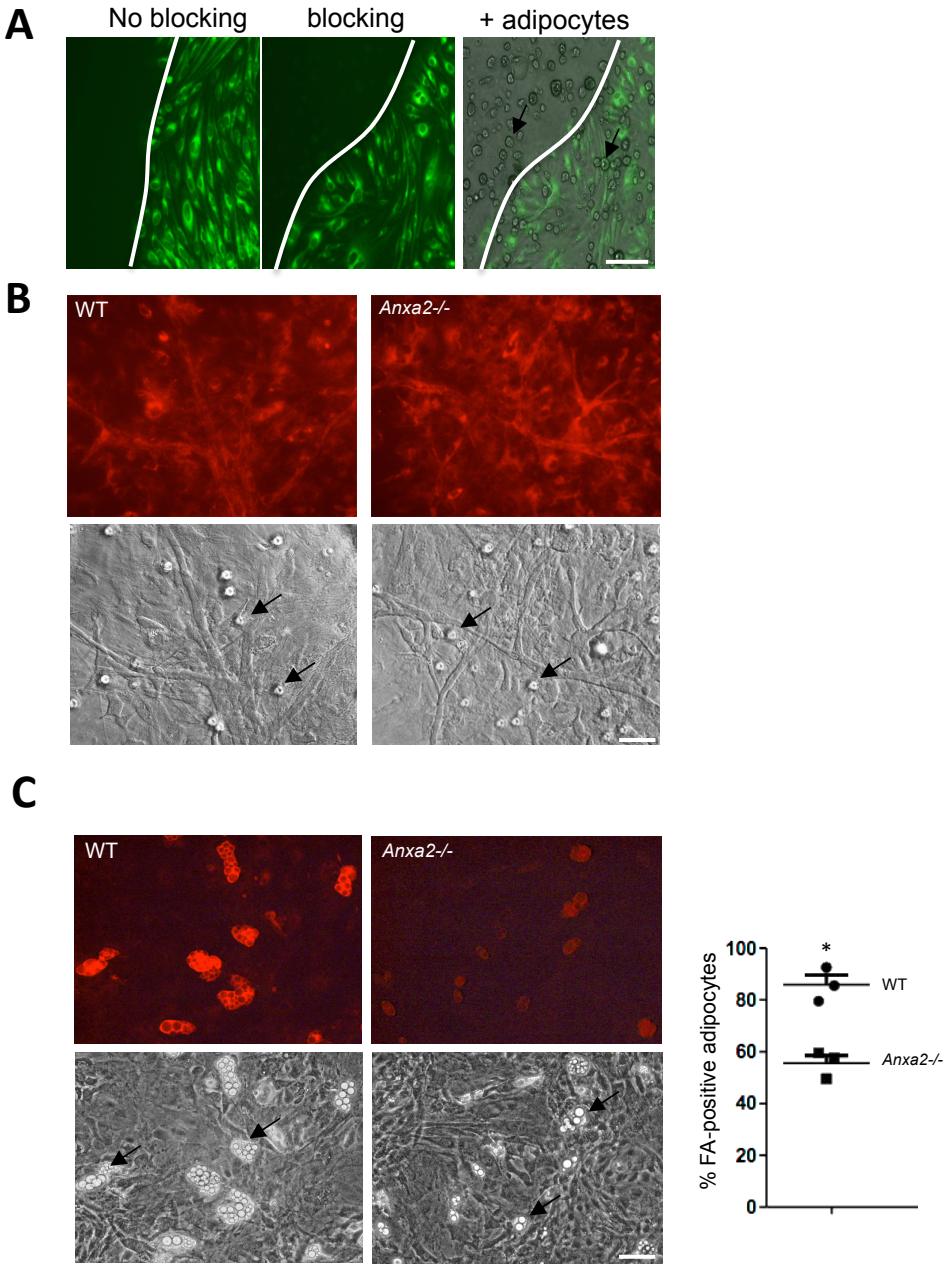
Supplemental Figure 1. PHB and ANX2 co-localize in WAT endothelium and adipocytes. (**A**) Immunofluorescence (IF) analysis of WT mouse WAT whole mounts with ANX2 (red) and PHB (green) antibodies. (**B**) IF analysis of WT mouse WAT paraffin sections with PHB(red) and ANX2 (green) antibodies. A serial section is stained with isolectin B4 (IB4) identifying the endothelium. Co-localization of PHB and ANX2 in the vasculature (arrows) and adipocytes (a) is indicated. (**C**) Stromal/vascular cells from WT WAT adherent to plastic in tissue culture for 12 hrs were subjected to IF without permeabilization. Confocal projections of median series demonstrate colocalization of IB4, PHB and ANX2 in endothelial colonies (arrows). CD45 IF below demonstrates that CD45+ leukocytes do not express ANX2 or PHB on the surface. (**D**) Quantification of WAT vascular density for Fig 2C in n=6 view fields. Error bars: SEM. *, $P<0.05$ (Student's t-Test, WT vs *Anxa2*$^{-/-}$).



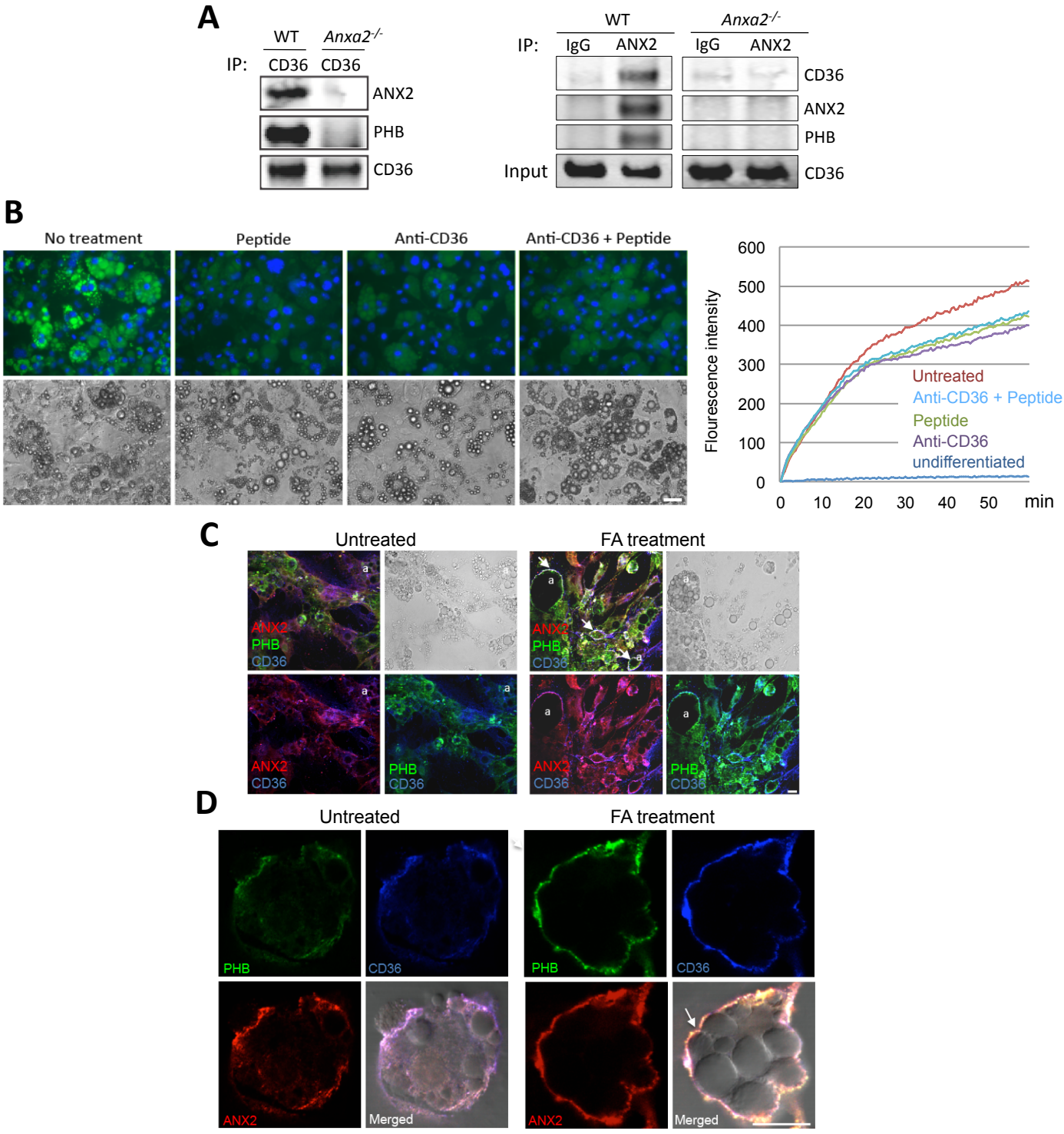
Supplemental Figure 2. Analysis of *Anxa2*$^{+/+}$ and *Anxa2*$^{-/-}$ DIO mice. (**A**) Cumulative high-fat diet consumption analyzed over a 5-day period is comparable for WT and *Anxa2*$^{-/-}$ mice (n=8). (**B**) Triacylglycerol (TAG) concentration in feces is comparable for WT and *Anxa2*$^{-/-}$ mice. (**C-D**) Metabolic chamber data for WT and *Anxa2*$^{-/-}$ males (n=5) raised on high-fat diet for 3 months: spontaneous locomotor activity (**C**) and heat generation (**D**) calculated as a function of oxygen consumption (VO_2) and carbon dioxide production (VCO_2). (**E**) Plasma levels of free FAs, insulin, glycerol, triglycerides, cholesterol, β-hydroxybutyrate and glucose for *Anxa2*$^{-/-}$ and WT mice (n=5). (**F**) Blood glucose clearance upon ip glucose infusion into pre-starved *Anxa2*$^{-/-}$ and WT mice. (**G**) Biodistribution of fluorescently labeled glucosamine-IRDye800CW conjugate measured by LI-COR Pearl Impulse system 1 hr after ip infusion quantified in the graph. (**H**) Biodistribution of C_{16} FA labeled with IRDye-680CW. As quantified for n=4 abdominal locations (graph), a significantly lower signal is observed for *Anxa2*$^{-/-}$ mice compared to WT mice. (**I**) Analysis of individual organs recovered from WT and ANX2-null mice 15 min after injection boron-dipyrromethene (BODIPY) C_{12} FA conjugate (558/568 nm) or uncoupled fluorophore (right). In all panels *, P<0.05 (Student's t-Test, WT vs *Anxa2*$^{-/-}$).



Supplemental Figure 3. PHB / ANX2 complex regulates FA intercellular transport. (**A**) Flow cytometric analysis of SVF from WT and ANX2-null mice 5 minutes after injection with boron-dipyrromethene (BODIPY) C_{12} FA. Gating on BODIPY+ viable (DAPI-negative) CD31+ endothelial cells (red), separated from CD45+ leukocytes and CD31-CD45-stromal cells, was set based on BODIPY channel background in cells from uninjected mice. (**B**) Left: BODIPY-FL-C_{16} (green) uptake by WT and ANX2-null adipocytes. Right: Real-time measurement of FA uptake in WT and ANX2-null SVF undifferentiated (undiff) or subjected to adipogenesis induction (diff). Intracellular BODIPY-C_{12} accumulation was monitored by measuring fluorescence using the QBT™ Assay. Error bars: SEM, n=3. *, P<0.05 (Student's t-Test, WT vs *Anxa2*$^{-/-}$ diff). (**C**) Endothelial bEnd.3 cells transduced with lentivirus control (vector) or expressing full-length PHB were incubated with 1 µM BODIPY-FL-C_{16} (green) in the presence of 0.1 mM blocking peptide (AKGRRAEDGSVIDYELI) or scrambled peptide (RDAGRSDALVIYEIGKE). Graph quantifies FA+ endothelial cells in n=5 view fields. Error bars: SEM. *, P<0.05 (Student's t-Test). (**D**) SVF cells from WT mice plated to semi-confluence and grown for 6 days in 10% FBS supplemented with VEGF and b-FGF until endothelial structures formed. After washing and starving the cultures in FA-free medium containing 1% BSA overnight, cells were subjected to 30 min pre-treatment with the blocking AKGRRAEDGSVIDYELI or scrambled RDAGRSDALVIYEIGKE peptide followed by induction with a mixture of 1 µM red fluorescent BODIPY-FL-C_{12} and green fluorescent BODIPY-FL-C_{16} for 10 min and subsequent washing with 1% BSA. Arrows indicate FA uptake. Scale bar=50 µm.



Supplemental Figure 4. FA transfer from endothelium to adipocytes. (**A**) Representative images of cells from step 2 in the assay described in Fig. 5B after loading of endothelial cells (EC) with boron-dipyrromethene (BODIPY) C_{16} FA. The image on the right shows the sedimentation of adipocytes (arrows) before FA trafficking from EC is complete (green fluorescence / brightfield overlay). The white line is the boundary of the EC monolayer scrape-off. (**B**) WT and *Anxa2*$^{-/-}$ SVF monolayers, which had been incubated with 4 µM of BODIPY-FL-C_{12} and washed, were exposed to suspended 3T3-L1 adipocytes (arrows), which were forced to interact with EC using the magnetic field. Pictures were taken just after adipocytes sedimentation. (**C**) Subsequent transfer of FA into adherent adipocytes, which is more efficient from WT than from *Anxa2*$^{-/-}$ EC. Graph quantifies FA+ adipocytes from n=3 view fields based on an arbitrary fluorescence signal cut off normalized for all images. Arrows: adipocytes. *, $P<0.05$ (Student's t-Test, WT vs *Anxa2*$^{-/-}$).



Supplemental Figure 5. ANX2 / PHB interaction in CD36-mediated FA transport. (**A**) Membrane proteins immunoprecipitated (IP) with CD36 antibodies (left) or with non-immune IgG or ANX2 antibodies (right) from WT or ANX2-null SVF were subjected to immunoblotting with antibodies against CD36, ANX2, or PHB. Input: extract prior to IP. (**B**) 3T3-L1 adipocytes were treated as indicated by 0.25 mM peptide blocking the PHB / ANX2 binding (AKGRRAEDGSVIDYELI), 10 mg/ml CD36-inhibitory antibody MF3 (Abcam ab80080), or their combination. Left: BODIPY-FL-C_{16} (green) uptake; nuclei are blue. Right: real-time measurement of FA uptake by undifferentiated cells (undiff) or cells subjected to adipogenesis induction (diff). Intracellular BODIPY-C_{12} accumulation was monitored by measuring fluorescence using the QBT™ Assay. (**C-D**) 3T3-L1 adipocytes either untreated or treated with 1 µM palmitic acid (**C**) 1 % Intralipid (**D**) for 10 minutes were fixed and without permeabilization subjected to IF with ANX2 (red), PHB (green) and CD36 (blue) antibodies. Low magnification upright fluorescence micrographs (**C**) and high magnification confocal sections (**D**) demonstrate cell membrane co-localization of the three proteins (white) in adipocytes (a) upon FA treatment (arrows). Channels are merged as indicated. Scale bar=50 µm.