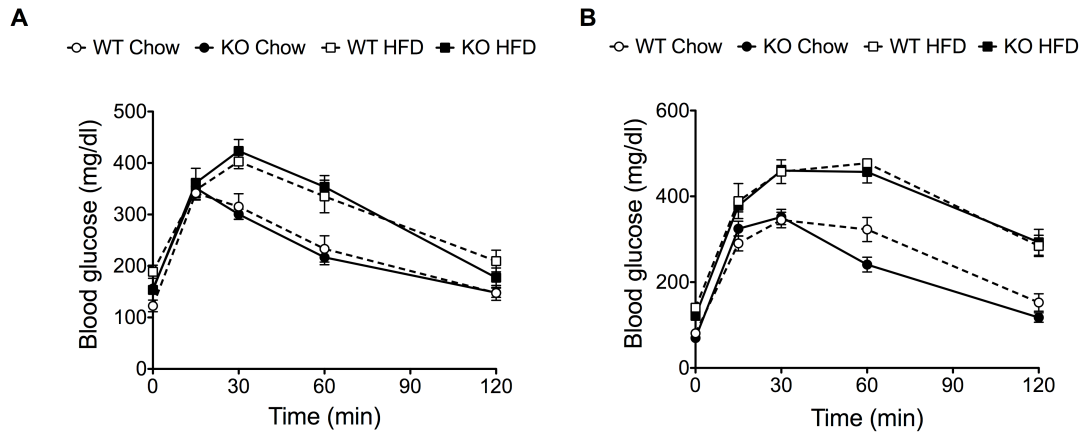
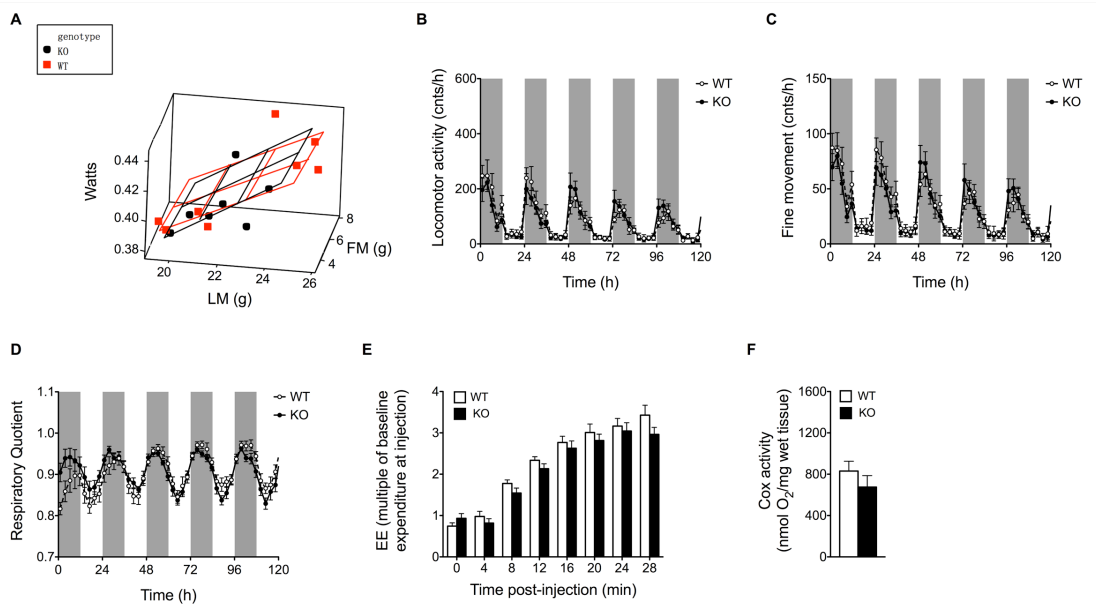


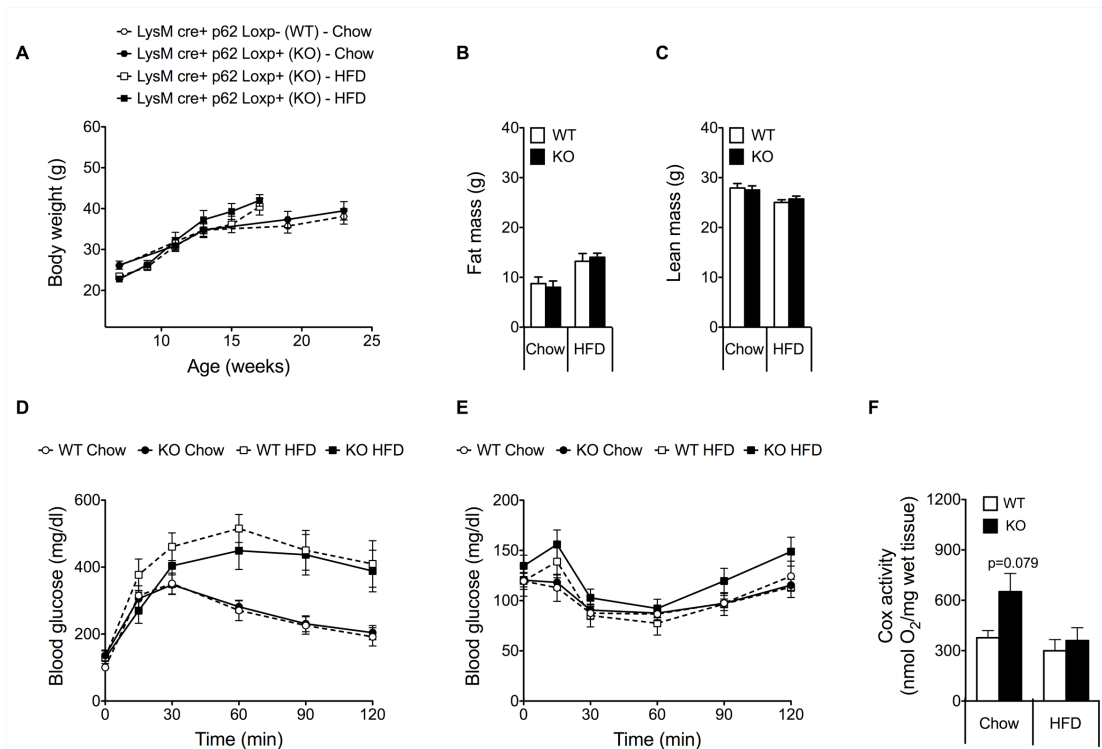
Supplementary Figure 1. Schematic representation of *p62* locus organization and *p62* targeting strategy resulting in deletion of exon 1 after Flp- and Cre-mediated recombination. Exons are indicated by black boxes (A). Southern blot analysis of targeted allele (B). Genotype of *p62*^{fl/fl} mice by PCR with primers F1 and R1 (C). Western blot analysis of tissue-specific deletion of *p62* in different tissues (D,E).



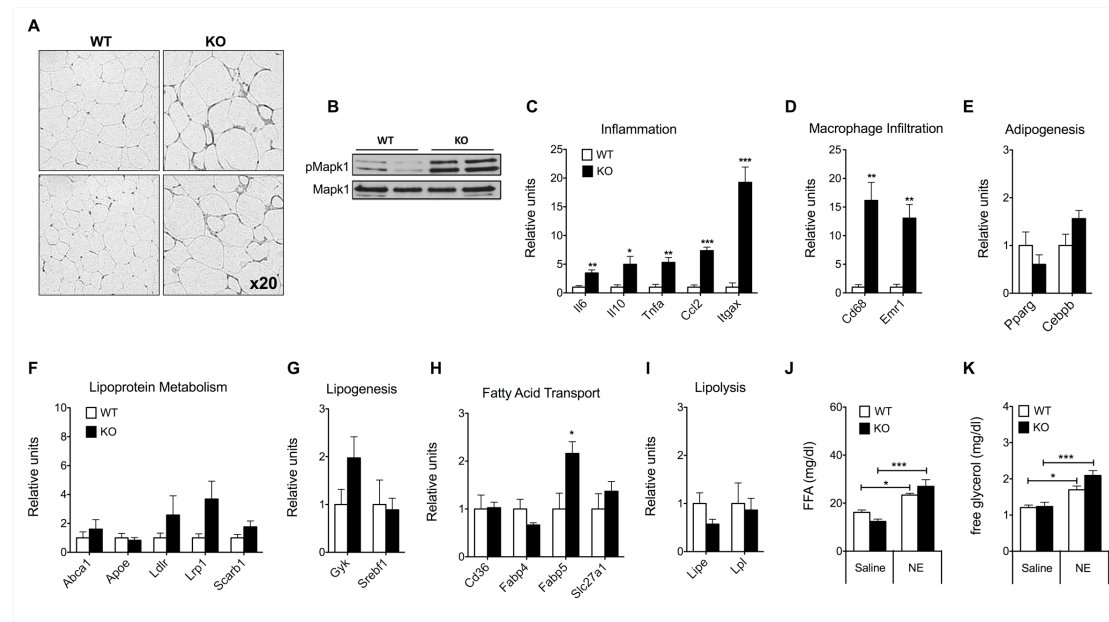
Supplementary Figure 2. Measurement of glucose tolerance in tissue-specific p62^{-/-} mice. Glucose tolerance (ip GTT, 2.5g glucose/kg BW) of mice with tissue specific p62 deletion in the liver (A) or skeletal muscles (B). Data represent means \pm SEM. N=7-9 mice each group.



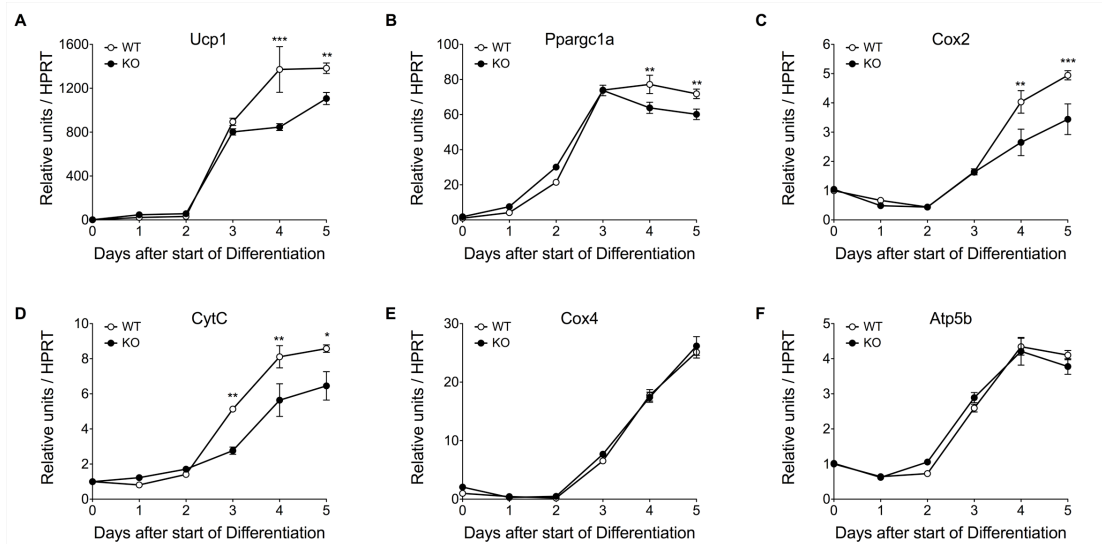
Supplementary Figure 3. Measurement of energy metabolism in muscle-specific p62^{-/-} mice. Energy expenditure of 17 week old chow-fed muscle-specific p62^{-/-} and wt control mice analyzed by ANCOVA using body fat and lean tissue mass as covariates (**A**). Locomotor activity (**B**), fine movement (**C**) and respiratory exchange ratio (**D**) of muscle-specific p62^{-/-} and wt control mice. Measurement of energy expenditure (expressed as multiples of expenditure at injection) following s.c. challenge with norepinephrine (1 mg/kg) (**E**) and Cox activity in BAT of muscle-specific p62^{-/-} and wt control mice. Panels **A-D** comprises N=7-8 mice each group, panel **E** comprises N=11-13 animals each group and panel **F** comprises N=6 mice each group. Data represent means ± SEM.



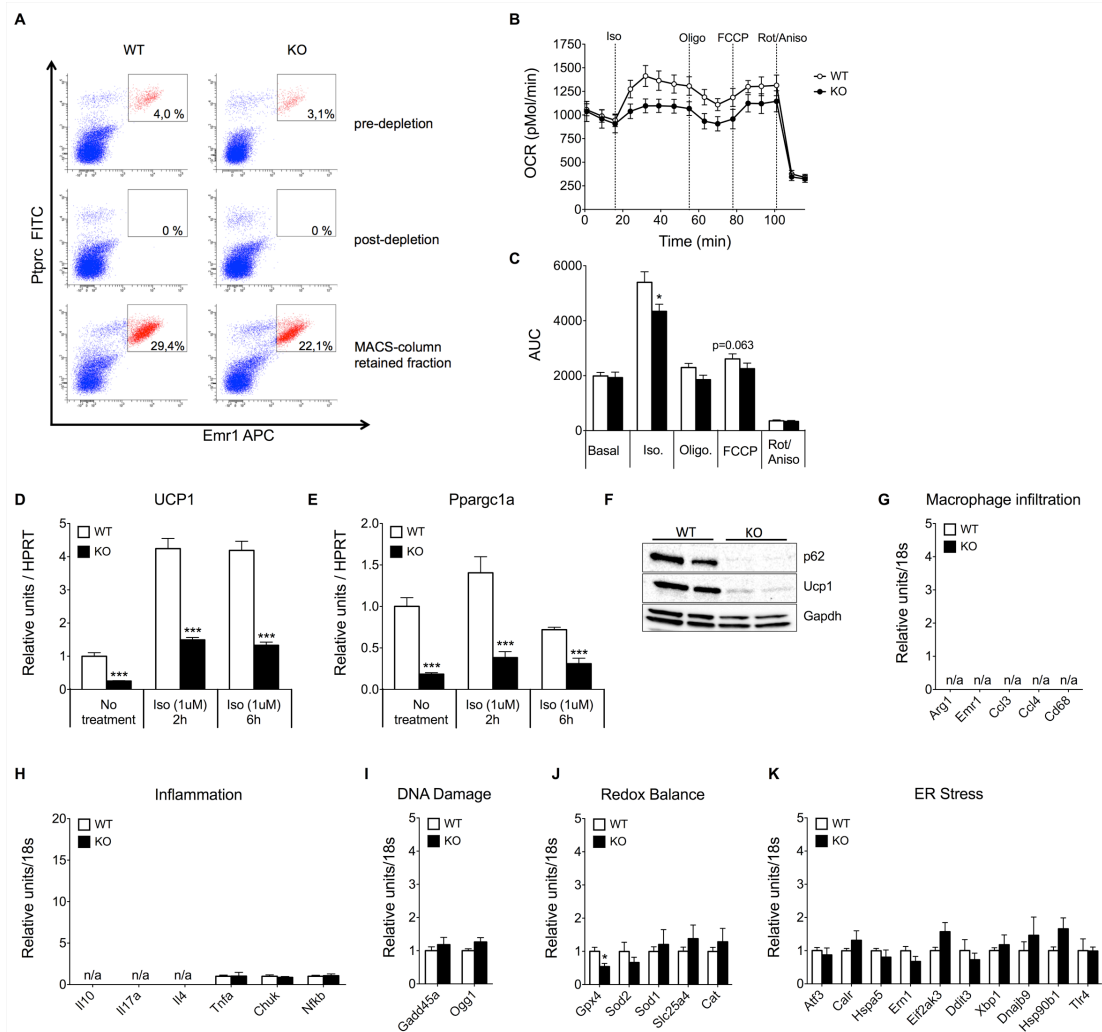
Supplementary Figure 4. Lack of p62 in myeloid lineage does not reveal a metabolically relevant phenotype. Body weight (A), body composition (B,C) as well as glucose and insulin sensitivity (D,E) of mice that lack p62 selectively in the myeloid lineage and controls. N=5-7 mice each group. Measurement of cox activity in BAT of myeloid-lineage-specific p62^{-/-} and wt control mice (N=3 mice each group) (F). Data represent means ± SEM.



Supplementary Figure 5. Histological analysis and gene expression profiling in the white adipose tissues of chow-fed adipocyte-specific p62^{-/-} mice. Hematoxylin-Eosin staining of epididymal white adipose tissue (eWAT) (A). Western blot analysis of total and phosphorylated Mapk1 in eWAT (B). mRNA levels genes related to inflammation, macrophage infiltration, adipogenesis, lipoprotein metabolism, lipogenesis, fatty acid transport and lipolysis (C-I). Plasma free fatty acids (J) and free glycerol (K) measured 30 min after the i.p. injection of either saline or norepinephrine (1 mg/kg). N=7-8 mice each genotype. Data represent means \pm SEM. Asterisks indicate: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.



Supplementary Figure 6. Time-course of thermogenic and adipogenic genes during adipocyte differentiation. mRNA levels of *Ucp1*, *Ppargc1a*, *Cox2*, *CytC*, *Cox4* and *Atp5b* in BAT primary cells obtained from global p62^{-/-} and wt control mice (N=6 mice each genotype) during adipocyte differentiation. Data represent means \pm SEM. Asterisks indicate: * , p<0.05; ** , p<0.01; *** , p<0.001.



Supplementary Figure 7. Cell autonomous effect of p62 on mitochondrial function in macrophage-depleted BAT primary cells. Flow cytometric detection of macrophages in BAT primary cells before and after MACS depletion of Cd11b positive cells. Macrophages were identified as Ptprc+ Emr1+ cells. Displayed results are representative for 2 independent experiments (N=5 per genotype) (A). Measurement of oxygen consumption rate (OCR) of 7 day differentiated BAT primary cells following treatment with isoproterenol (0.5 μ M), Oligomycin (2 μ g/ml), FCCP (1 μ M) and Rotenon/Antimycin A (2.5 μ M each) (N=10 wells/genotype) (B,C). mRNA levels of *Ucp1* (D) and *Ppargc1a* (E) following stimulation with isoproterenol (0.5 μ M) for 6 h (N=8 each genotype). Protein levels of Ucp1 (F) and mRNA levels of marker indicative of macrophage infiltration, inflammation, DNA damage, redox balance and ER stress (N=4 each genotype).