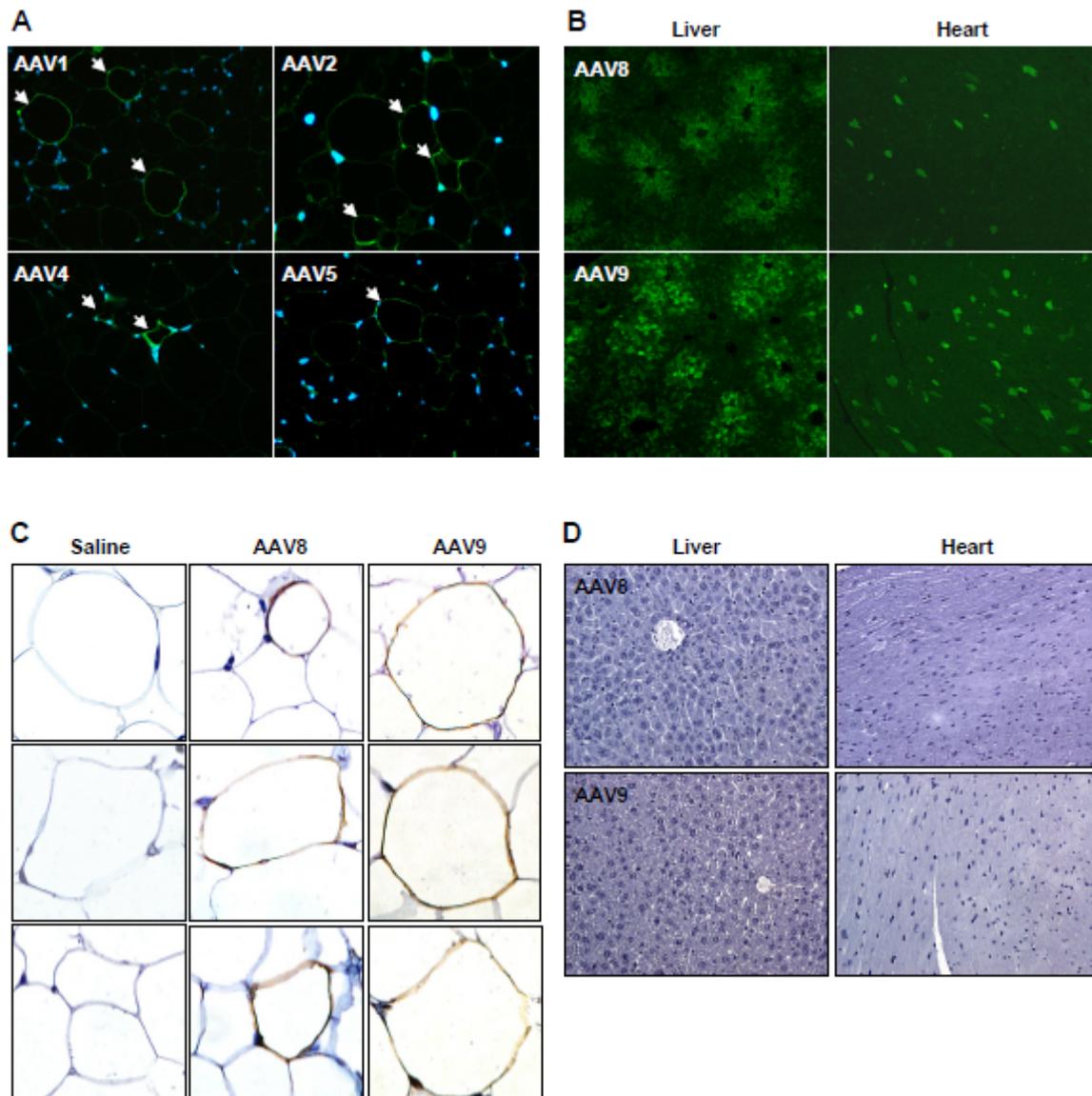


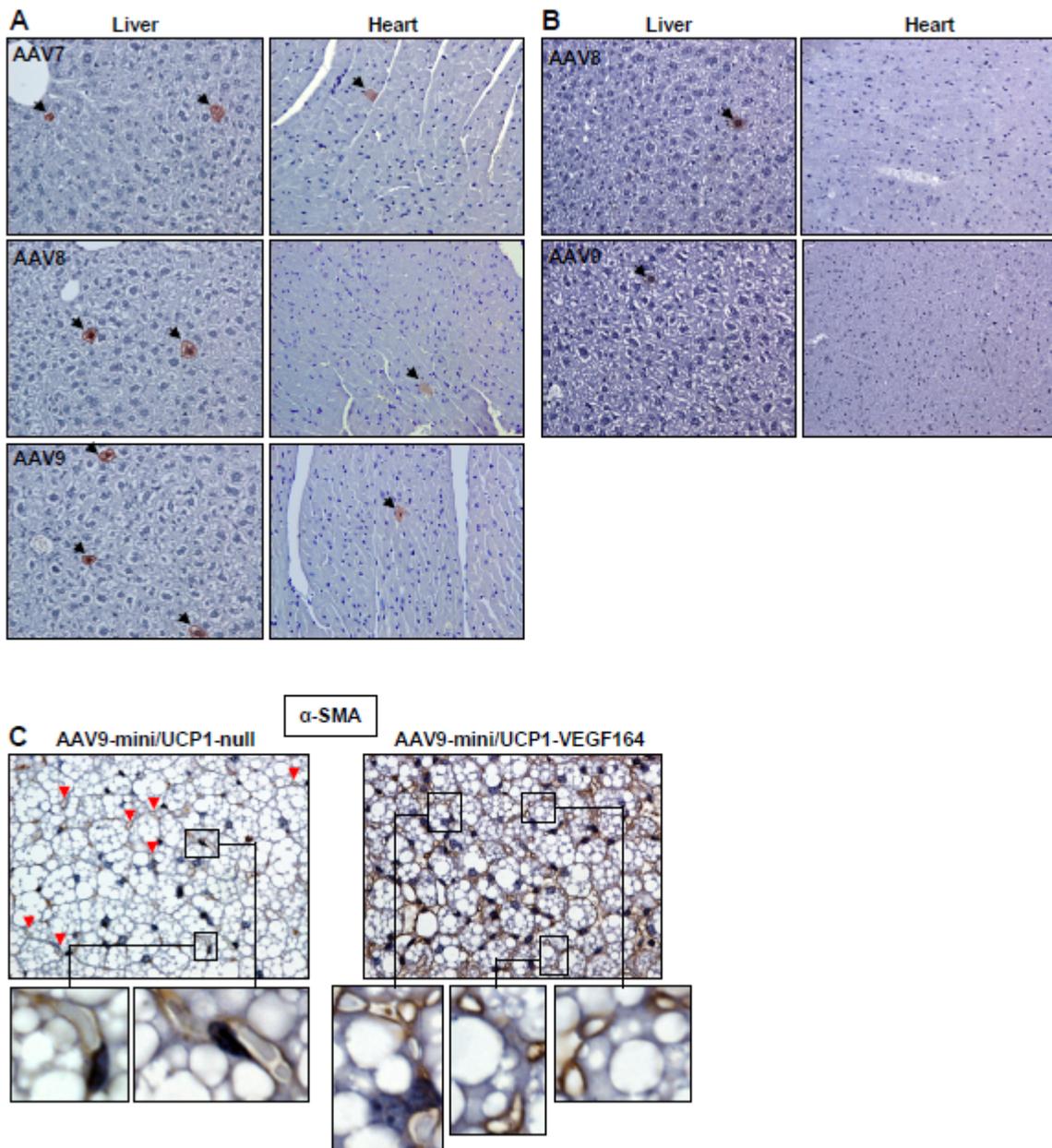
SUPPLEMENTARY DATA

Supplementary Figure 1. Transduction of adipocytes after intra-eWAT administration of AAV vectors. *A*: Immunostaining against GFP (green) in sections of eWAT two weeks after the intra-eWAT administration of 2×10^{11} vg of AAV-CAG-GFP vectors of serotypes 1, 2, 4 or 5. Blue, nuclei. Arrows indicate transduced white adipocytes. Original magnification $\times 200$. *B*: Transduction of non-adipose organs was evaluated by immunostaining against GFP (green). Two weeks post injection, GFP expression was ~~only~~ detected in the liver and heart of animals injected intra-eWAT with 2×10^{11} vg of AAV8 or AAV9-CAG-GFP vectors. Original magnification $\times 100$. *C*: Representative images of immunostaining against GFP (brown) in eWAT two weeks after intra-eWAT administration of saline or 10^{12} vg of AAV8 or AAV9-mini/aP2-GFP vectors. Original magnification $\times 400$. *D*: GFP immunostaining (brown) was not observed in the liver or heart of the same cohort of animals. Original magnification $\times 200$.



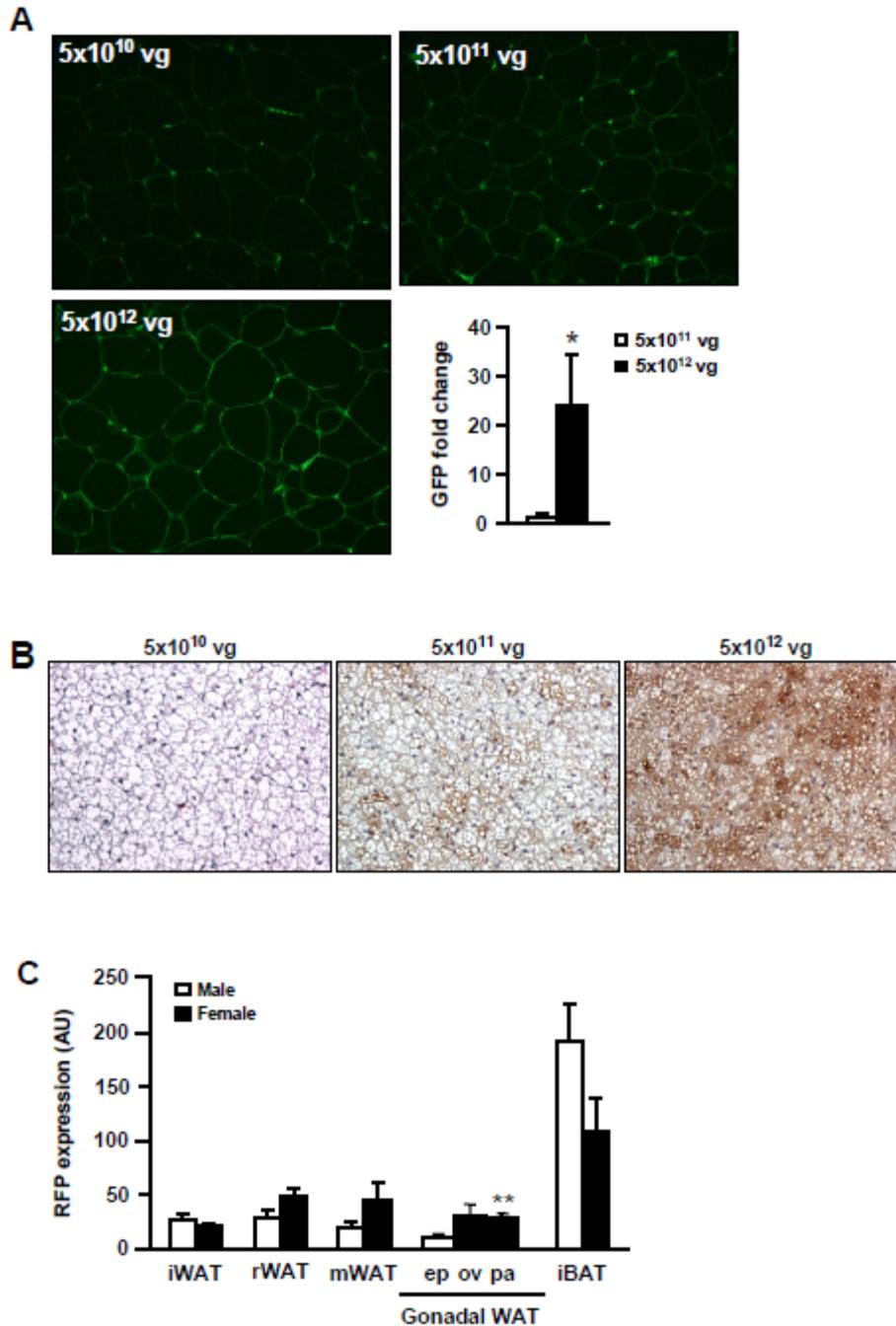
SUPPLEMENTARY DATA

Supplementary Figure 2. Intra-iBAT administration of AAV vectors. **A:** Transduction of non-adipose organs was evaluated by immunostaining against RFP (brown) two weeks after the intra-iBAT administration of 10^{10} vg of AAV-CMV-RFP. RFP production was detected in the liver and heart of animals treated with vectors of serotypes 7, 8 and 9. Arrows indicate transduced cells. Original magnification x200. **B:** Transduction of non-adipose organs was evaluated by immunostaining against GFP (brown) two weeks after intra-iBAT administration of 2×10^{11} vg of AAV8 or AAV9-mini/UCP1-GFP vectors. GFP production was undetectable in the heart, and only a few scattered positive cells were observed in the liver. Arrows indicate transduced hepatocytes. Original magnification x200. **C:** Immunostaining against α -SMA (brown) in iBAT administered with 2×10^{11} vg of AAV9-mini/UCP1-VEGF164 or AAV9-mini/UCP1-null vectors two weeks post-injection. Red arrowheads indicate vessels. Original magnification x400 and x1000 (insets).



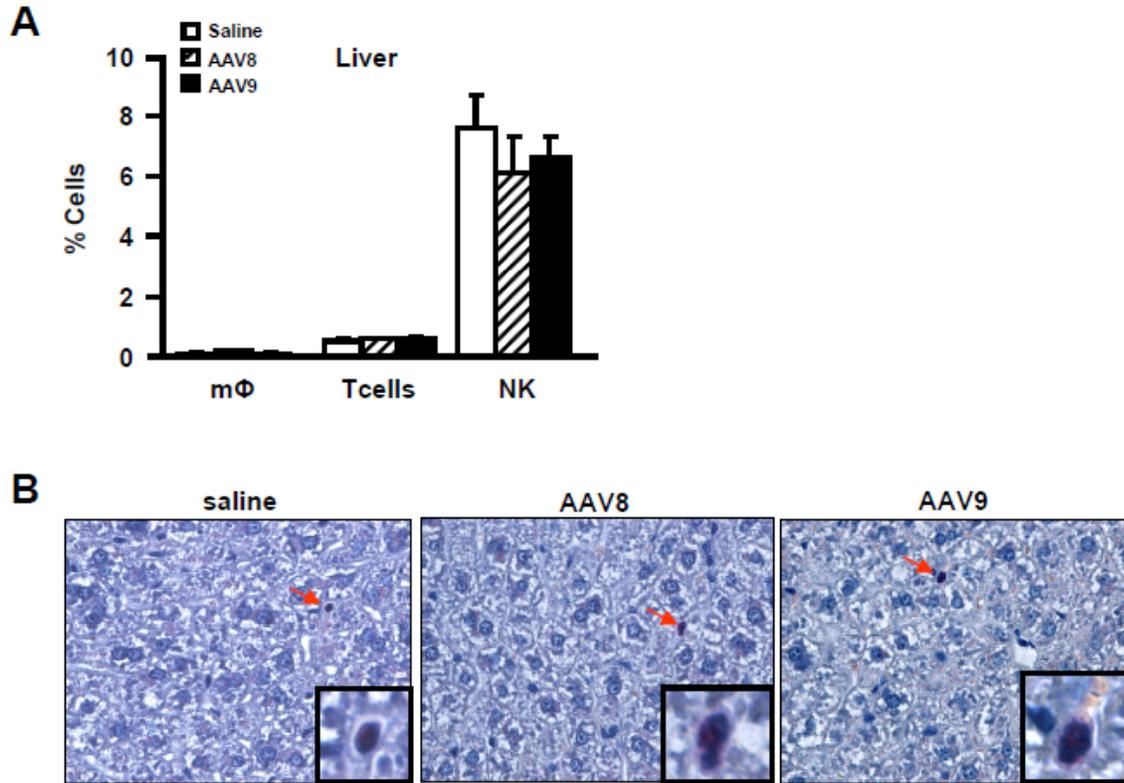
SUPPLEMENTARY DATA

Supplementary Figure 3. Transduction of white and brown adipose tissue after systemic administration of AAV vectors. *A-B*: Immunostaining against GFP (A, green; B, brown) in eWAT (A) and iBAT (B) sections two weeks after iv administration of 5×10^{10} vg, 5×10^{11} vg or 5×10^{12} vg of AAV8 or AAV9-CAG-GFP vectors. Blue, nuclei. Original magnification x200. *C*: RFP expression levels in iWAT, rWAT, mWAT, eWAT and iBAT depots two weeks after iv administration of 5×10^{12} vg of AAV8 or AAV9-CMV-RFP vectors in male and female C57Bl6 mice ($n=5$). Values shown are means \pm SEM. ** $p < 0.01$ vs. male.



SUPPLEMENTARY DATA

Supplementary Figure 4. Assessment of liver inflammation after systemic administration of AAV vectors. *A*: Flow cytometric quantification of the number of macrophages (mΦ), T lymphocytes (T cells) and natural killer cells (NK) in the liver of C57Bl6 mice ($n=3-4$) one month after iv administration of saline or 3×10^{12} vg of AAV8 or AAV9-CAG-GFP vectors. *B*: Detection of neutrophils (purple) in the liver by Leder staining after iv administration of saline, 2×10^{12} vg of AAV8 or AAV9-CAG-null vectors in C57Bl6 mice. Red arrows indicate neutrophils. Original magnification x400 and x1000 (insets). Values shown are means \pm SEM.



SUPPLEMENTARY DATA

Supplementary Figure 5. Specific transduction of adipocytes after systemic administration of AAV-mini/aP2-GFP or AAV-mini/UCP1-GFP vectors. **A:** Immunostaining against GFP (brown) in the liver and heart two weeks after systemic delivery of 2×10^{12} vg of AAV9 -mini/aP2-GFP or AAV9-mini/UCP1-GFP vectors. GFP production was undetectable in the heart and very marginal in the liver. Arrows indicate transduced hepatocytes. Original magnification $\times 100$. **B:** GFP expression levels in eWAT, iWAT and iBAT two weeks after iv administration of 2×10^{12} vg of AAV9-CAG-GFP, AAV9-mini/aP2-GFP or AAV9-mini/UCP1-GFP vectors ($n=4$). Values shown are means \pm SEM. * $p < 0.05$.

