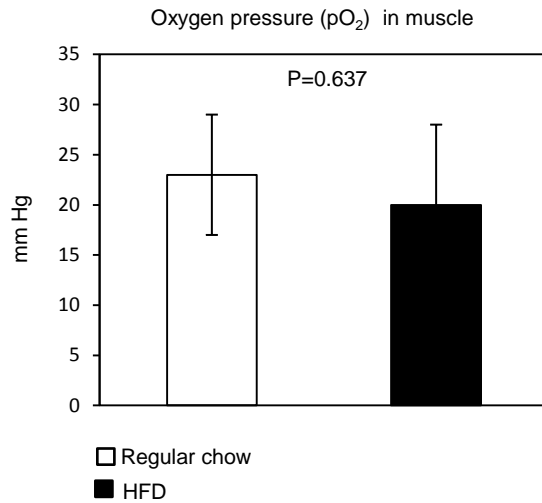
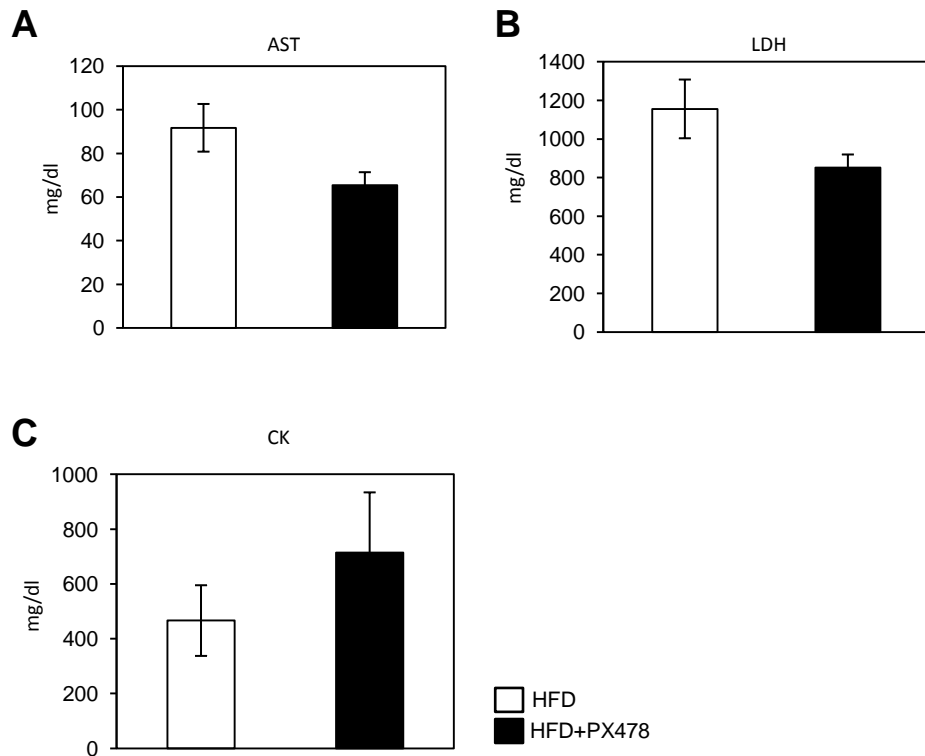


Supplementary Figure 1



Suppl. Fig. 1: Oxygen Pressure in Gastrocnemius Muscle Does not Change During HFD Feeding. pO₂ measurements for the mice before and after HFD feeding by EPR spectrometry in the gastrocnemius muscle (n=4 for each group). The peak-to-peak line width was used to calculate the pO₂ using the standard calibration curve.

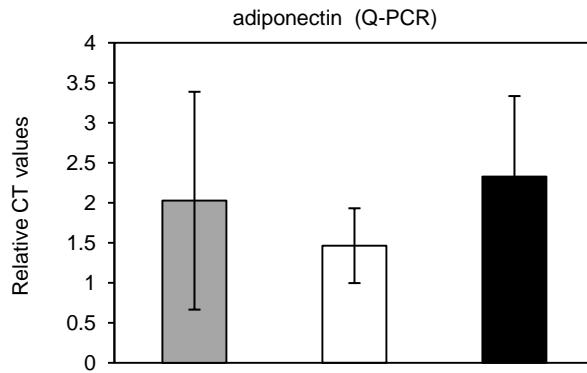
Supplementary Figure 2



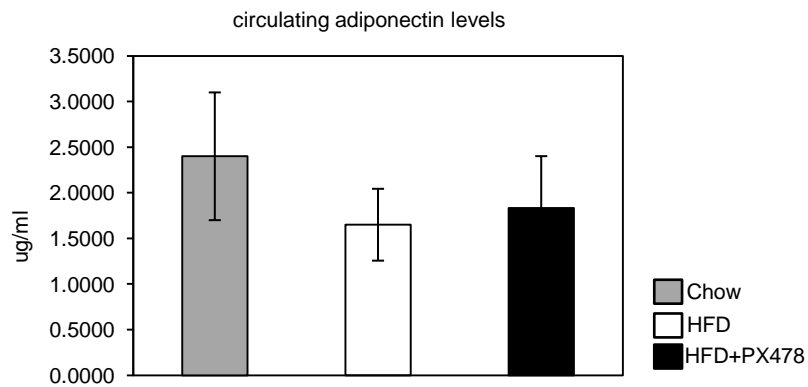
Suppl. Fig. 2: PX-478 Treatment Does Not Have Toxic Effects in The Mice. AST, LDH and CK measurement in the serums of the PX-478 treated mice and their littermate control groups (n=5 for each group).

Supplementary Figure 3

A

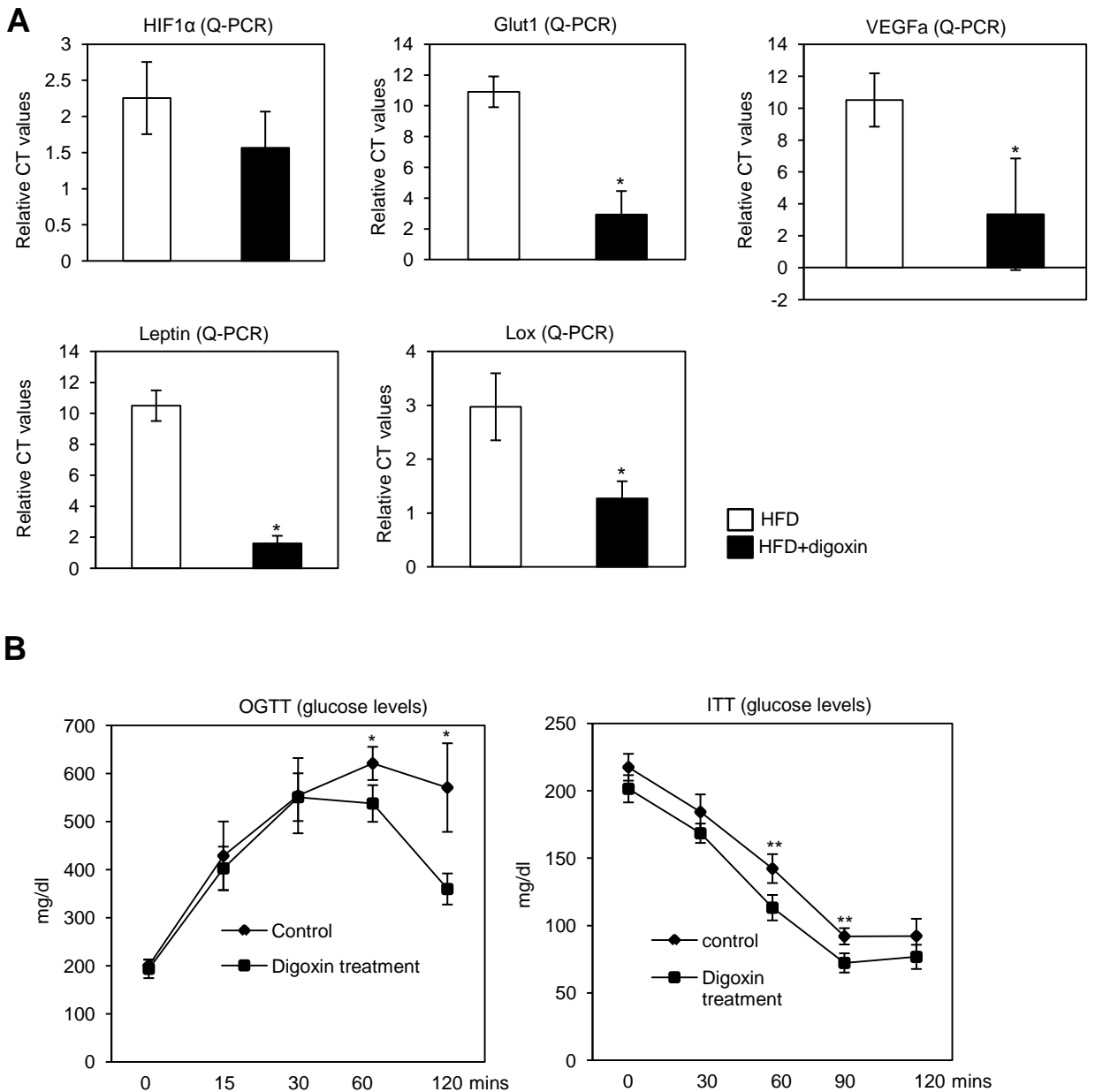


B



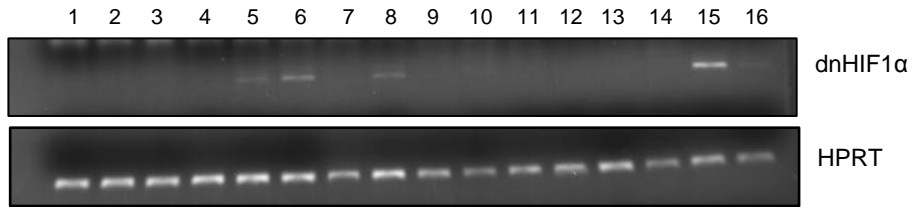
Suppl. Fig. 3: PX-478 Treated Mice Have Slightly Increased Adiponectin Expression and Slightly Increased Circulating Adiponectin Levels. (A) Q-PCR analysis for adiponectin WATs in mice fed with regular chow, HFD and HFD plus PX-478 for 50 days. **(B)** Circulating adiponectin levels in mice fed with regular chow, HFD and HFD plus PX-478 for 50 days.

Supplementary Figure 4



Suppl. Fig. 4: Digoxin Down-regulates HIF1 α Target Genes And Improves Glucose Tolerance and Insulin Sensitivity in Treated Mice. (A) Q-PCR analysis for HIF1 α and its target genes Glut1, VEGFa, leptin and LOX after digoxin treatment (n=4 for each group). * p<0.05. **(B)** Circulating glucose levels for an OGTT and an ITT in digoxin treated mice and their littermate controls (n=4 for each group).

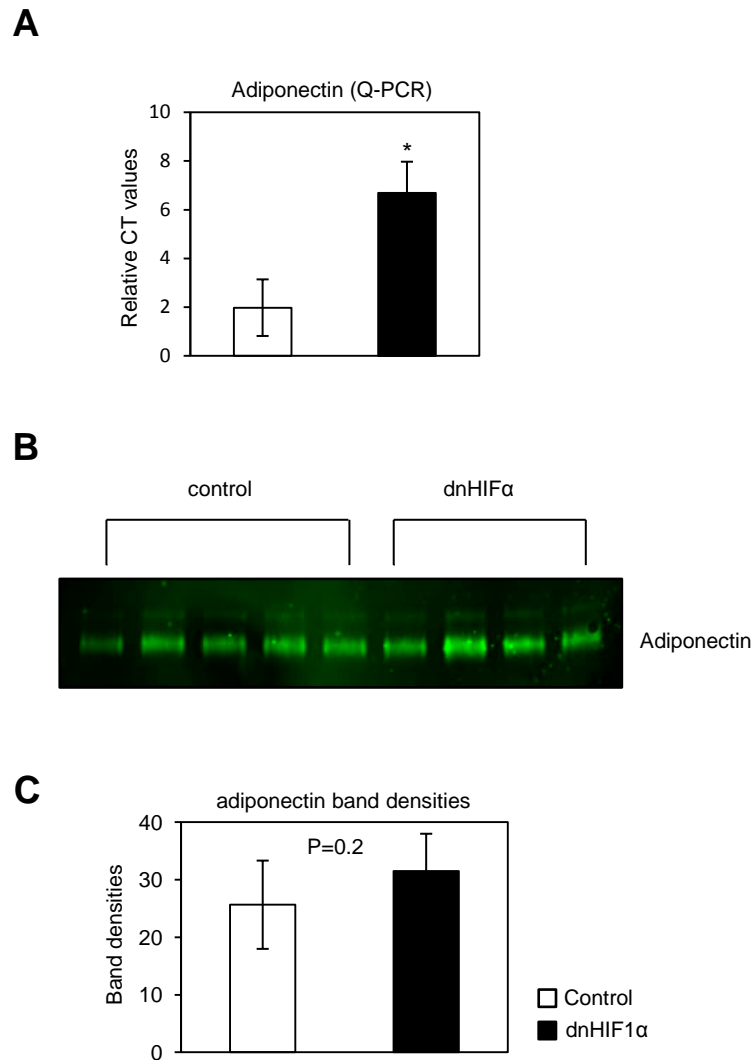
Supplementary Figure 5



1. liver; 2. kidney; 3. spleen; 4. skeletal muscle; 5. MWAT; 6. EWAT; 7. gonad 8. BAT; 9. colon;
10. heart; 11. lung; 12. brain; 13. pancreas; 14. intestine; 15. SWAT; 16. macrophage

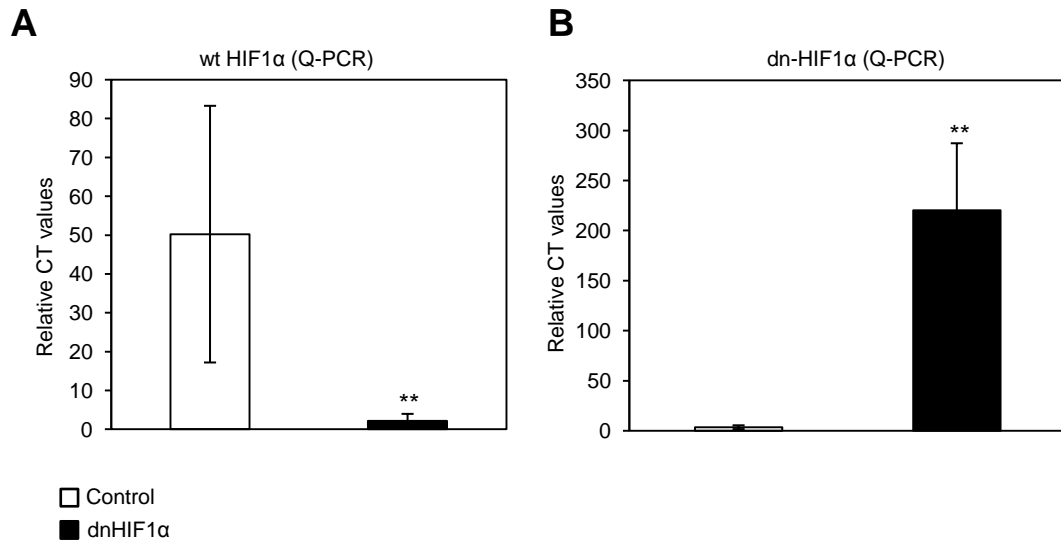
Suppl. Fig. 5: Dn-HIF1 α Is Exclusively Overexpressed in Fat Tissues After Adipose Tissue-specific Dox Induction. PCR products of dn-HIF1 α using 500 ng of cDNAs from different tissues in the dn-HIF1 α transgenic and their littermate control mice after Dox induction.

Supplementary Figure 6



Suppl. Fig. 6: Overexpression of Dn-HIF1 α Up-regulates Adiponectin Expression Significantly But Only Slightly Increases Circulating Adiponectin Levels in HFD Feeding Mice. (A) Q-PCR analysis of adiponectin in EWATs of dn-HIF1 α transgenic and their littermate wild type control mice (n=4 for each group). **(B)** Circulating adiponectin levels in dn-HIF1 α transgenic and their littermate wild type control mice (n=5 for controls; n=4 for dn-HIF1 α transgenic mice). **(C)** Quantitative measurements of the band densities in **(B)** by ImageJ.

Supplementary Figure 7



Suppl. Fig. 7: Overexpression of Dn-HIF1 α Down-regulates Endogenous HIF1 α Expression Levels in HFD Feeding Mice. (A) Q-PCR analysis of endogenous HIF1 α in SWATs of dn-HIF1 α transgenic or their littermate controls (n=4 for each group). **(B)** Q-PCR analysis of dn-HIF1 α in SWATs of dn-HIF1 α transgenic or their littermate control mice (n=4 for each group).