

Supplemental Table 1

qPCR primer sequences used in this study

Gene	Forward 5'-3'	Reverse 5'-3'
<i>Zfp423</i>	CAGGCCCAAGAAGAACAAG	GTATCCTCGCAGTAGTCGCACA
<i>Pparγ2</i>	GCATGGTGCCTTCGCTGA	TGGCATCTCTGTGTCAACCATG
<i>C/ebpα</i>	TGGCCTGGAGACGCAATGA	CGCAGAGATTGTGCGTCTTT
<i>Adiponectin</i>	AGATGGCACTCCTGGAGAGAA	TTCTCCAGGCTCCTTTTCT
<i>Fabp4</i>	GATGAAATCACCGCAGACGAC	ATTCCACCACCAGCTTGTCAC
<i>Lpl</i>	CATCGAGAGAGGATCCGAGTGAA	TGCTGAGTCCTTTCCCTTCTG
<i>Irs1</i>	CGATGGCTTCTCAGACGTG	CAGCCCGCTTGTTGATGTTG
<i>Ucp1</i>	TCTCAGCCGGCTTAATGACTG	GGCTTGCATTCTGACCTTAC
<i>Cidea</i>	TCCTATGCTGCACAGATGACG	TGCTCTTCTGTATCGCCCAGT
<i>Prdm16</i>	ACACGCCAGTTCTCCAACCTGT	TGCTTGTTGAGGGAGGAGGTA
<i>F4/80</i>	TGACTCACCTTGTGGTCCTAA	CTTCCAGAATCCAGTCTTTCC
<i>Cd115</i>	TGTCATCGAGCCTAGTGGC	CGGGAGATTCAGGGTCCAAG
<i>Cd11b</i>	GGCTCCGGTAGCATCAACAA	ATCTTGGGCTAGGGTTTCTCT
<i>Rps18</i>	CATGCAAACCCACGACAGTA	CCTCACGCAGCTTGTTGTCTA

Supplemental Figure Legends

Supplemental Figure 1: Inactivation of *Zfp423* in the *Pdgfra* lineage leads to growth defects including arrested adipose tissue development.

(A) Representative photograph of control and *Pdgfra*^{Lin}-Zfp423-KO mice at 3 weeks of age.

(B) Representative photographs and/or average depot mass of inguinal WAT (iWAT) gonadal WAT (gWAT), and interscapular brown adipose tissue (BAT) isolated from 3 weeks-old control and *Pdgfra*^{Lin}-Zfp423-KO mice.

(C) Relative mRNA levels of the indicated adipocyte-selective genes in iWAT isolated from 3 weeks-old control and *Pdgfra*^{Lin}-Zfp423-KO mice. * denotes $p < 0.05$ from student's t-test. $n=4-5$ mice

(D) Relative mRNA levels of the indicated adipocyte-selective genes in gWAT isolated from 3 weeks-old control and *Pdgfra*^{Lin}-Zfp423-KO mice. * denotes $p < 0.05$ from student's t-test. $n=4-5$ mice

Supplemental Figure 2: Cre activity in *Adiponectin*-Cre mice occurs in a subset of *Pdgfra*⁺ adipose precursor cells present in fetal inguinal WAT.

(A) *Pdgfra*⁺; *Lin*⁻ (CD31⁻; CD45⁻) cells were analyzed in the adipose stromal vascular fraction isolated from reporter mice carrying *Adiponectin*-Cre and *Rosa26R*^{loxP-stop-loxP-tdtomato} alleles.

(B) Representative FACS collection gate for the isolation of *Pdgfra*⁺; *Lin*⁻ cells is shown.

(C) Gating strategy to assess the frequency of tdTomato⁺; *Pdgfra*⁺; *Lin*⁻ cells. Cells from mice carrying only the *Rosa26R*^{loxP-stop-loxP-tdtomato} allele were used as negative controls.

(D) Representative dot plot highlighting the presence of tdTomato⁺; *Pdgfra*⁺; *Lin*⁻ cells in the stromal vascular fraction of iWAT from E18.5 *Adiponectin*-Cre; *Rosa26R*^{loxP-stop-loxP-tdtomato} embryos.

(E) Representative dot plot highlighting the number of tdTomato⁺ cells expressing the adipose precursor marker, *Pdgfra*, in the stromal vascular fraction of iWAT from E18.5 *Adiponectin*-Cre; *Rosa26R*^{loxP-stop-loxP-tdtomato} embryos.

(F,G) Representative dot plot highlighting the presence of tdTomato⁺; *Pdgfra*⁺; *Lin*⁻ cells in the stromal vascular fraction of iWAT (f) and gWAT (g) from 8 weeks-old *Adiponectin*-Cre; *Rosa26R*^{loxP-stop-loxP-tdtomato} mice.

(H) Representative dot plot highlighting the presence of tdTomato⁺; *Pdgfra*⁺; *Lin*⁻ cells in the stromal vascular fraction of gWAT from 6 day-old (P6) *Adiponectin*-Cre; *Rosa26R*^{loxP-stop-loxP-tdtomato} pups.

Supplemental Figure 3: Gross defects in the terminal differentiation of adipocytes in *Adiponectin-Cre; Zfp423^{loxP/loxP}* mice are restricted to the inguinal adipose depot.

(A) Relative mRNA levels of common adipocyte-selective genes and thermogenic genes in iWAT from 8 weeks-old control and Zfp423-AKO mice. * denotes $p < 0.05$ student's test. $n=6$ mice.

(B) Relative mRNA levels of thermogenic genes in fractionated iWAT adipocytes from 8 weeks-old control and Zfp423-AKO mice. $n=5$ mice.

(C) Relative mRNA levels of common adipocyte-selective genes and thermogenic genes in gWAT from 8 weeks-old control and Zfp423-AKO mice. * denotes $p < 0.05$ student's test. $n=6$ mice.

(D) Relative mRNA levels of common adipocyte-selective genes and thermogenic genes in the interscapular BAT depot from 8 weeks-old control and Zfp423-AKO mice. * denotes $p < 0.05$ student's test. $n=6$ mice.

(E-H) Representative H&E staining of gWAT **(E,F)** and BAT sections **(G,H)** obtained from 8 weeks-old control and Zfp423-AKO mice. Scale bar, 200 μm .

Supplemental Figure 4: Pathological remodeling of both inguinal and gonadal adipose tissue in *Adiponectin-Cre; Zfp423^{loxP/loxP}* mice upon high-fat diet feeding.

(A) Average adipocyte size in control and Zfp423-AKO iWAT after 8 weeks of HFD feeding. N.S. denotes not significant by student's test. $n=6-8$ mice.

(B,C) Representative immunofluorescence images of Perilipin (green) and F4/80 (red) expression in sections of gWAT from control and Zfp423-AKO mice after 8 weeks of HFD feeding. Scale bar, 200 μm .

(D,E) Relative mRNA levels of macrophage markers **(D)** and adipocyte-selective genes **(E)** in control and Zfp423-AKO gWAT after 8 weeks of HFD feeding. * denotes $p < 0.05$ student's test. $n=6$ mice.

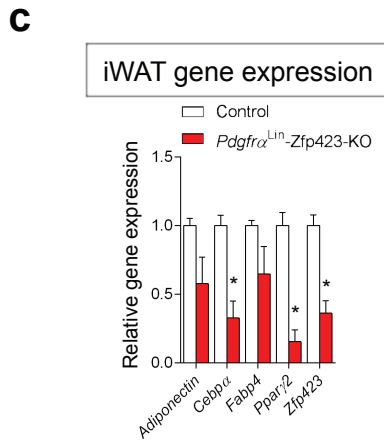
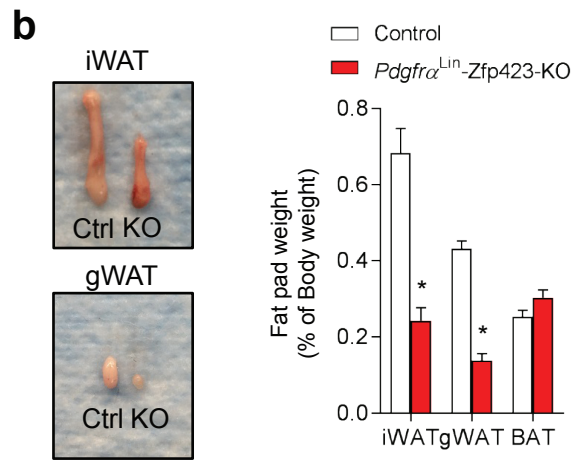
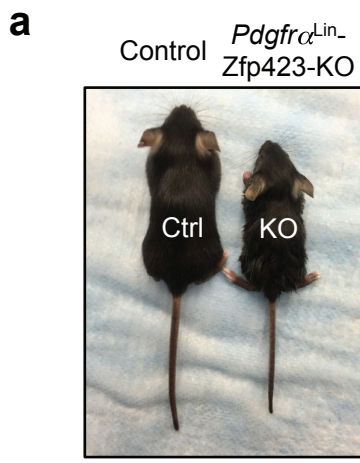
(F) Western blot analysis of phosphorylated-Akt (p-Akt) and total Akt protein levels in tissue extracts of gWAT and iWAT from 8-week HFD fed control and Zfp423-AKO mice administrated with insulin (2U/kg).

(G) Western blot analysis of serum adiponectin in control and Zfp423-AKO mice fed with chow, 8 or 16 weeks of HFD. For quantification, intensity of adiponectin band is normalized to that of the IgG band. * denotes $p < 0.05$ by two-way ANOVA. $n=4$ mice.

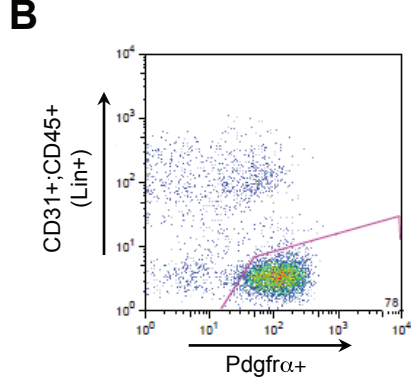
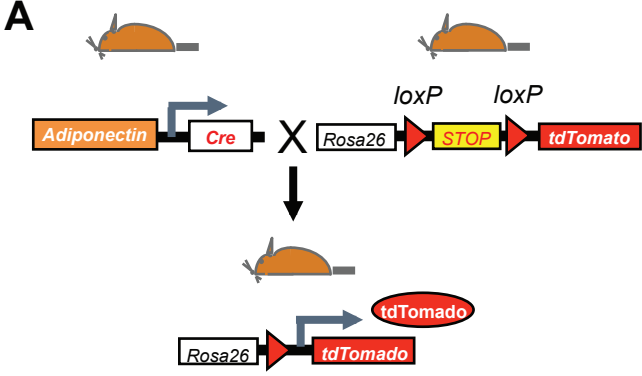
Supplemental Figure 5: Transient exposure of doxycycline to fetal *Adiponectin*-rtTA; TRE-Cre; *Zfp423*^{loxP/loxP} animals leads to inguinal white adipose depot-selective targeting of *Zfp423* (*Zfp423*-fetalAKO mice)

(A-C) Relative mRNA levels of *Zfp423* and other adipocyte genes in iWAT **(A)**, gWAT **(B)**, and BAT **(C)** of 5 weeks-old *Adiponectin*-rtTA; TRE-Cre; *Zfp423*^{loxP/loxP} mice exposed to doxycycline from E16 to P5. * denotes p < 0.05 student's test. n=6 mice.

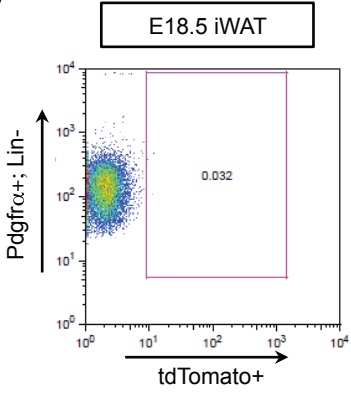
(D-I) Representative H&E staining of iWAT **(D,E)**, gWAT **(F,G)**, and BAT **(H,I)** sections obtained from 5 weeks-old control and *Zfp423*-fetalAKO mice. Scale bar, 200 μ m.



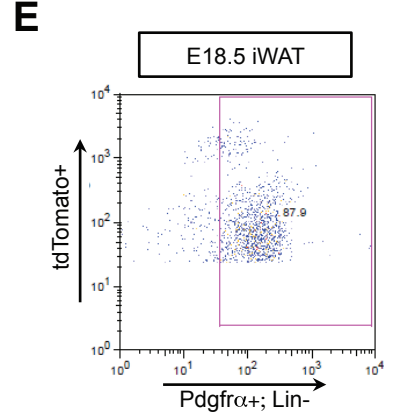
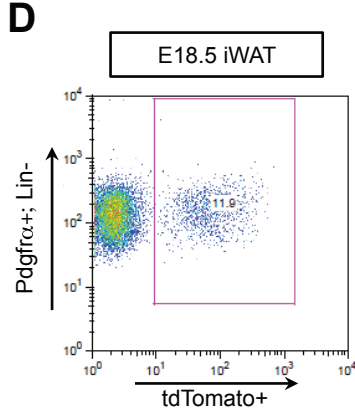
Supplementary Figure 1



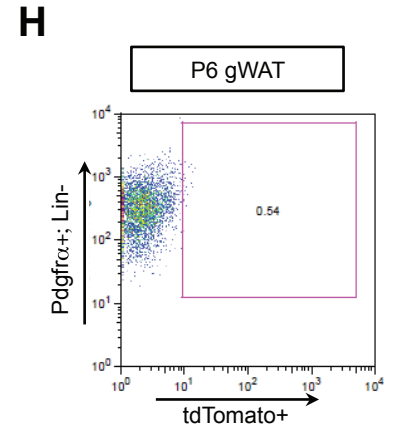
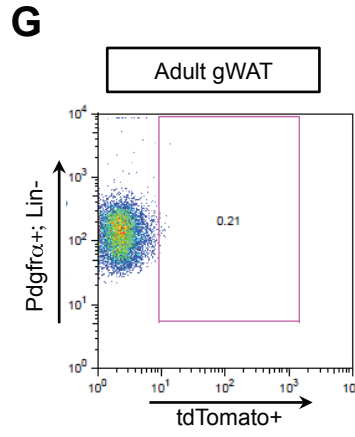
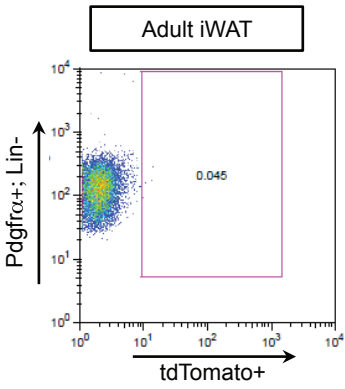
C *Rosa26R^{loxP-stop-loxP-tdTomato}*



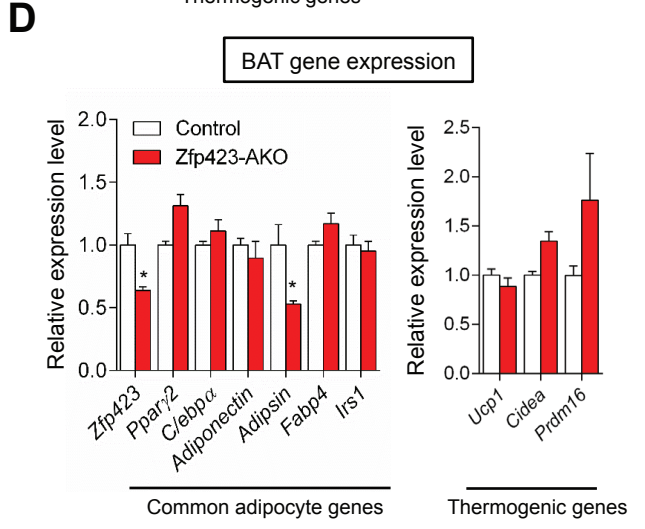
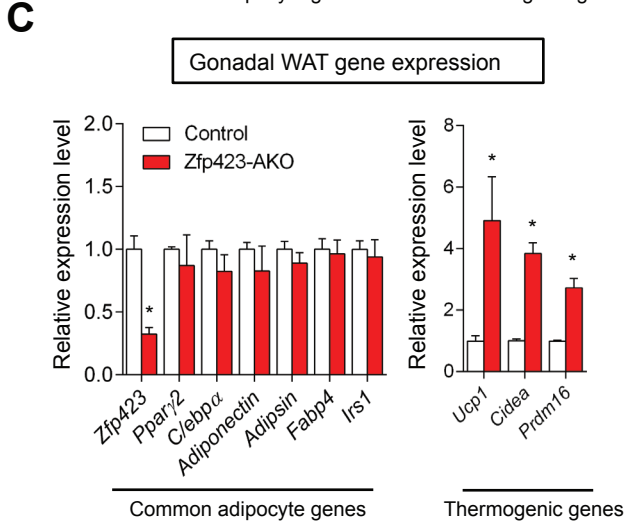
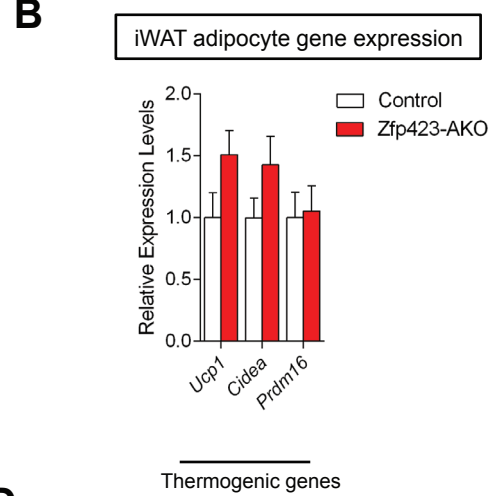
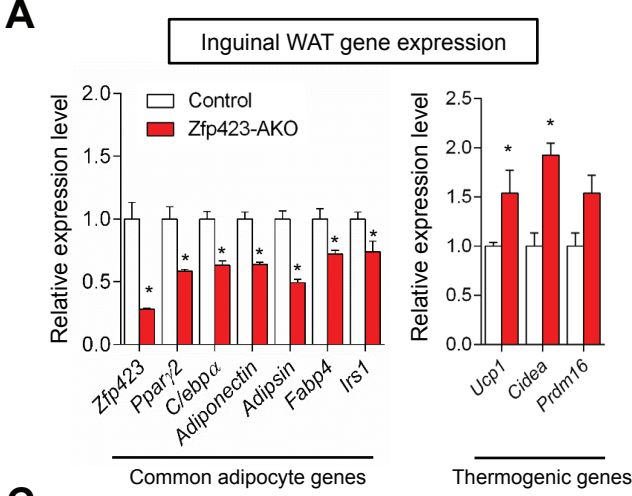
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F *Adiponectin-Cre; Rosa26R^{loxP-stop-loxP-tdTomato}*

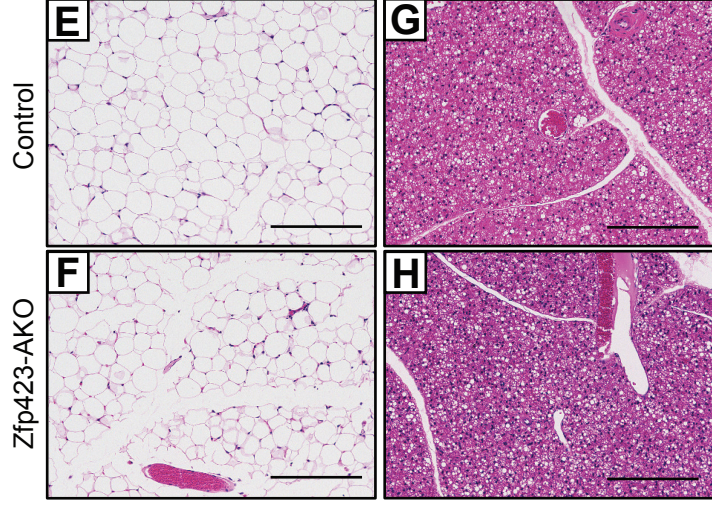


Supplementary Figure 2

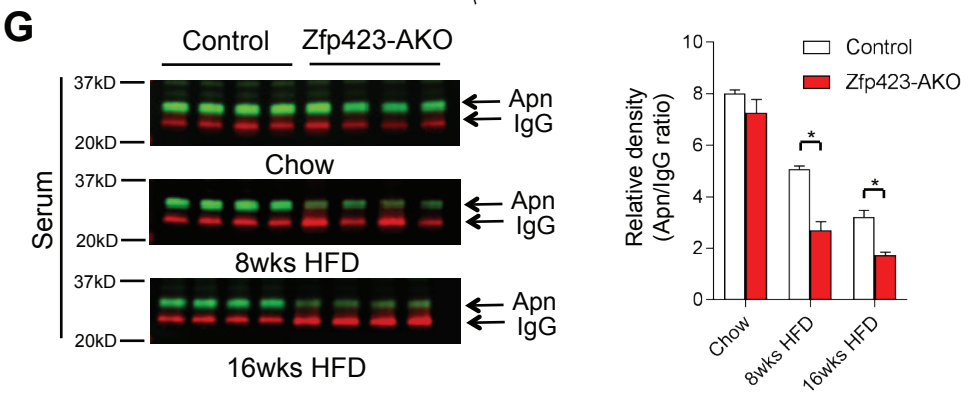
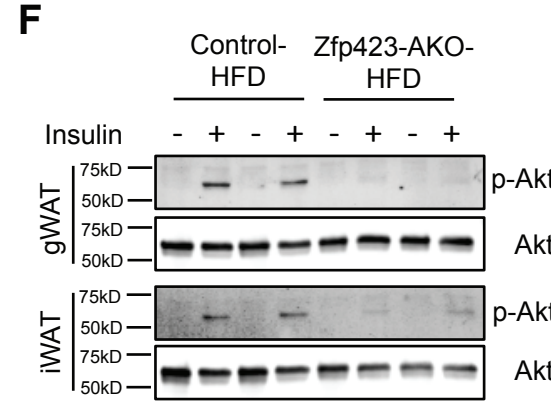
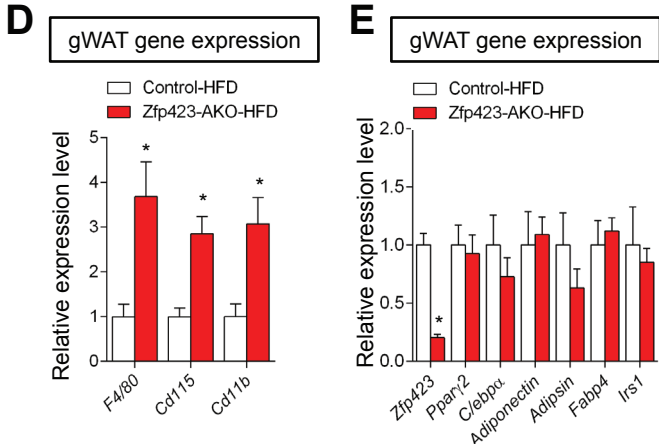
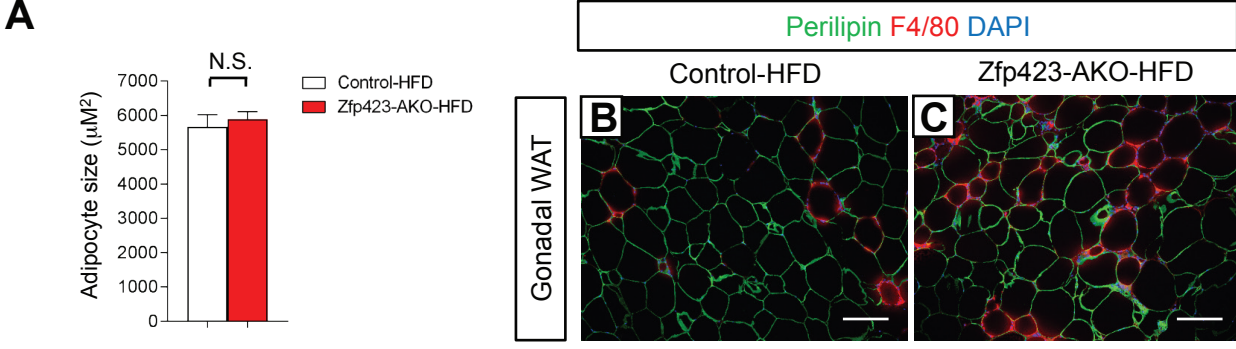


Gonadal WAT

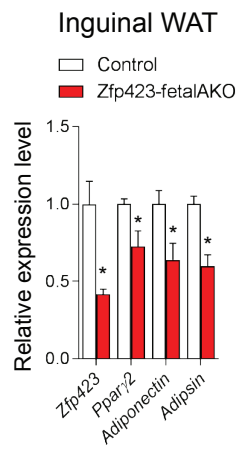
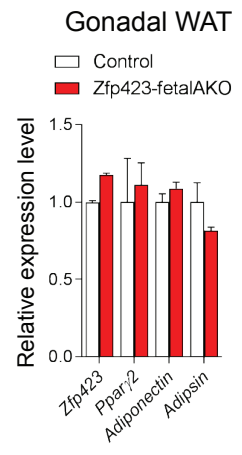
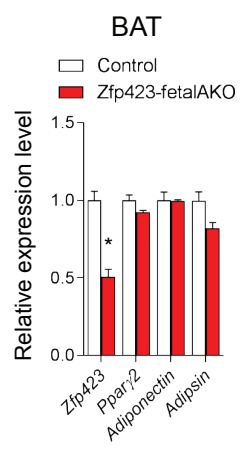
BAT



Supplementary Figure 3

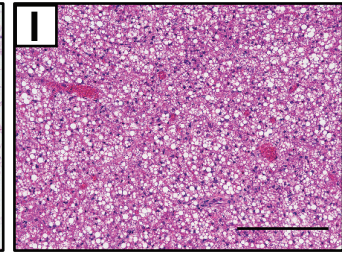
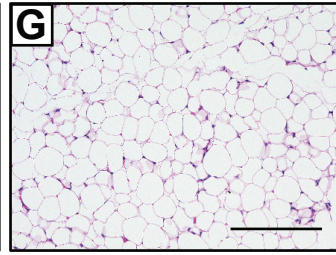
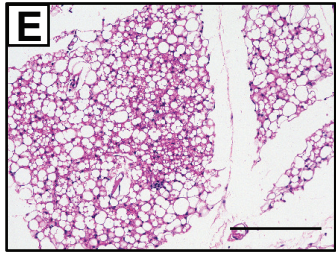
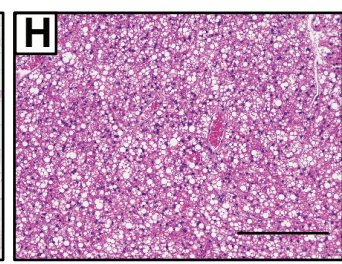
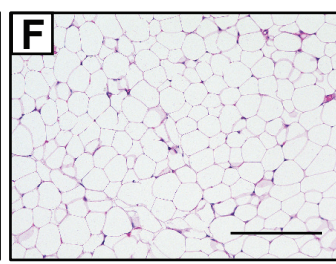
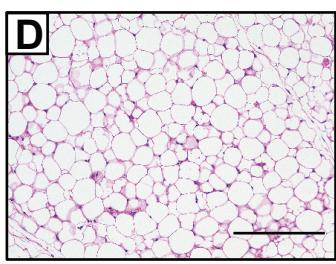


Supplementary Figure 4

A**B****C****Inguinal WAT****Gonadal WAT****BAT**

Control

Zfp423-fetalAKO



Supplementary Figure 5