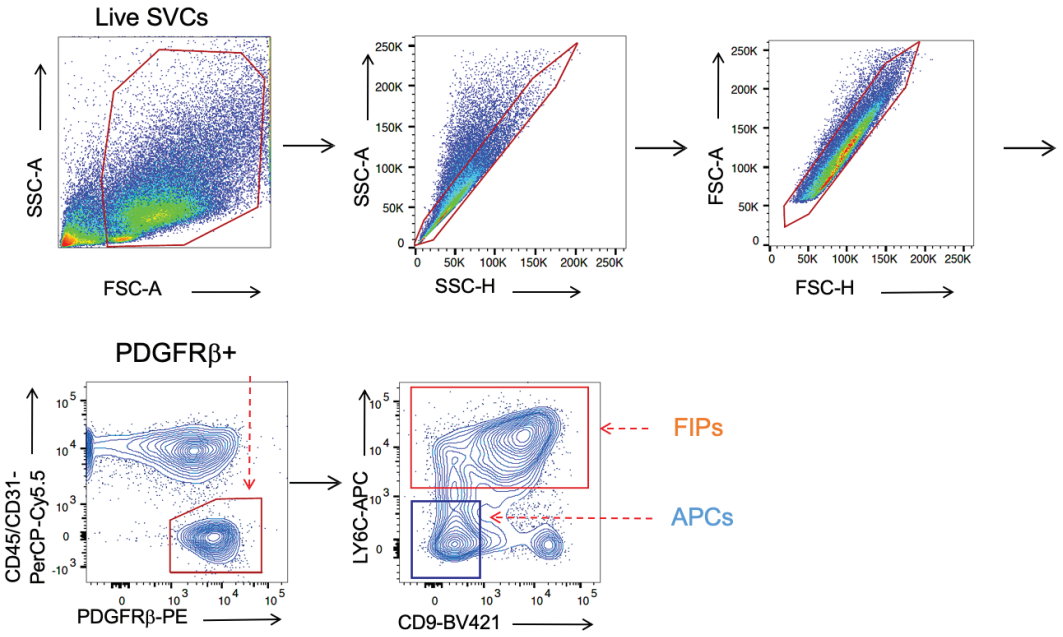
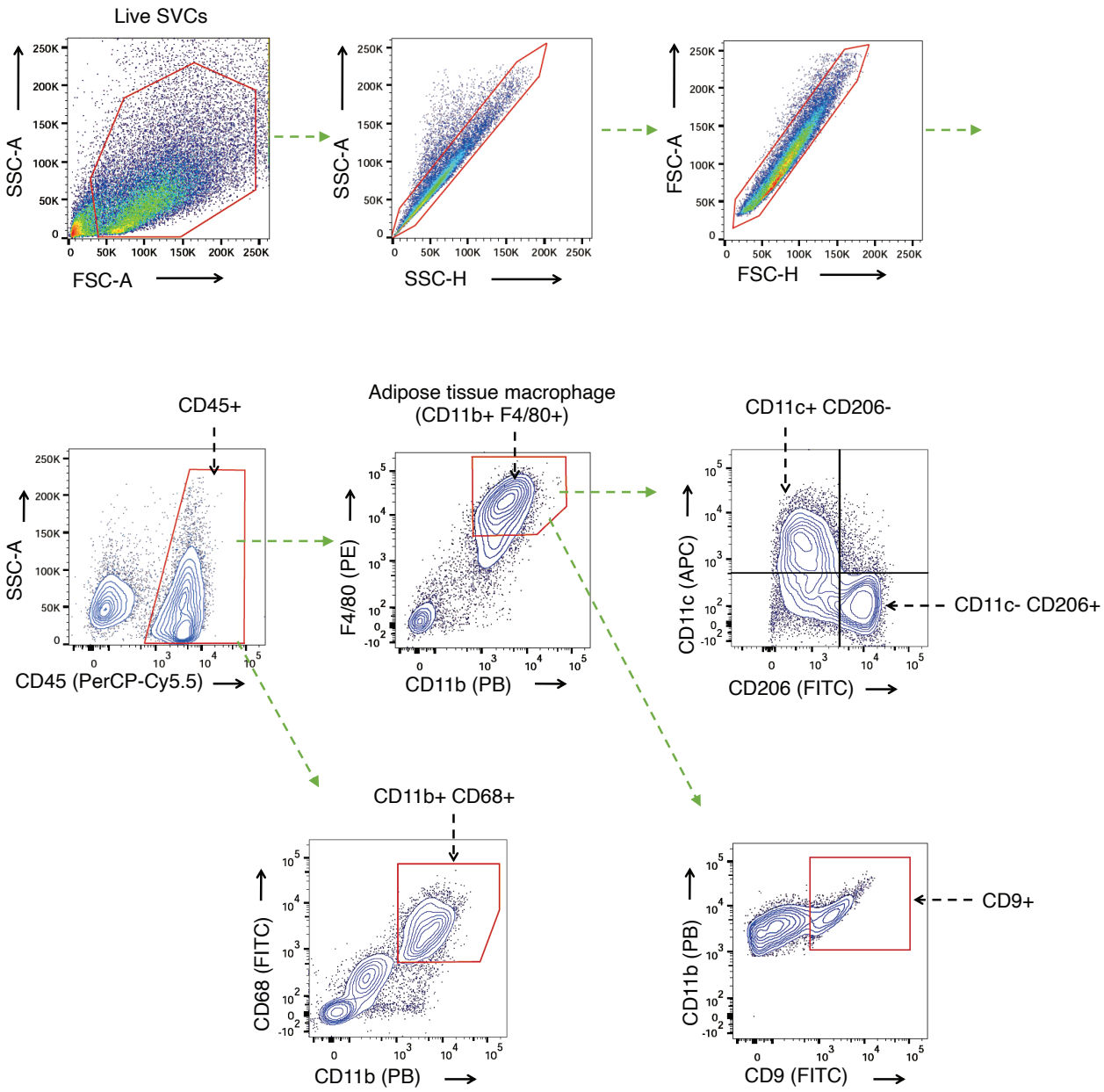


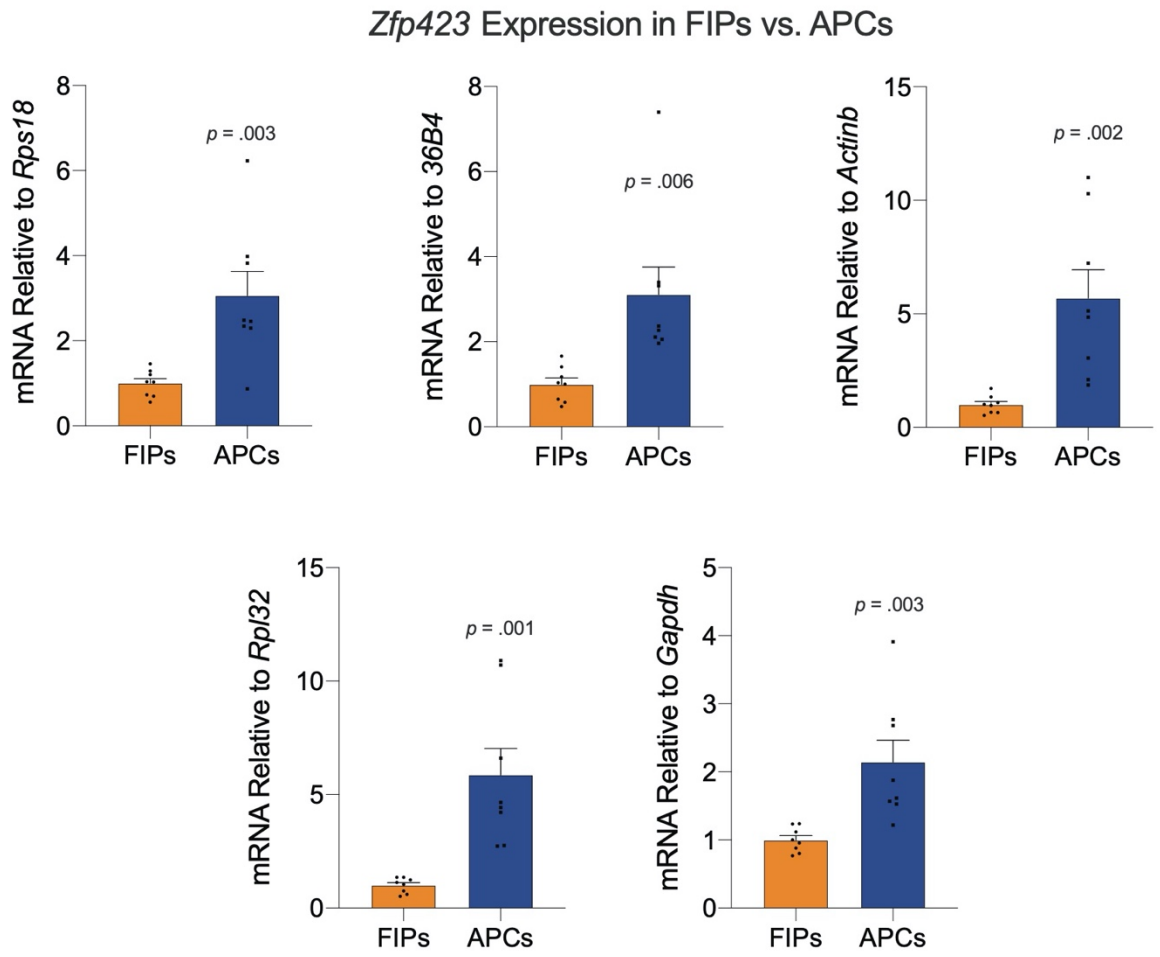
Supplementary Figure 1. FACS gating strategy for the isolation of FIPs and APCs from gonadal white adipose tissue of adult mice.

FIPs and APCs from the stromal vascular fraction of digested gonadal white adipose tissue were isolated through a multi-step FACS strategy. Upon selection of live cells/single cells from stromal vascular cells (Live SVCs), PDGFRβ+ cells are separated from CD45+ (hematopoietic) and CD31+ (endothelial) lineage cells and then further subdivided on the basis of LY6C and CD9 expression. LY6C+ PDGFRβ+ CD45- CD31- cells represent FIPs. LY6C- CD9- PDGFRβ+ CD45- CD31- cells represent APCs. In all figures, each sample (n) indicated in panels depicting flow cytometry data represent cells isolated from the SVF of two fat depots of one mouse through this strategy.



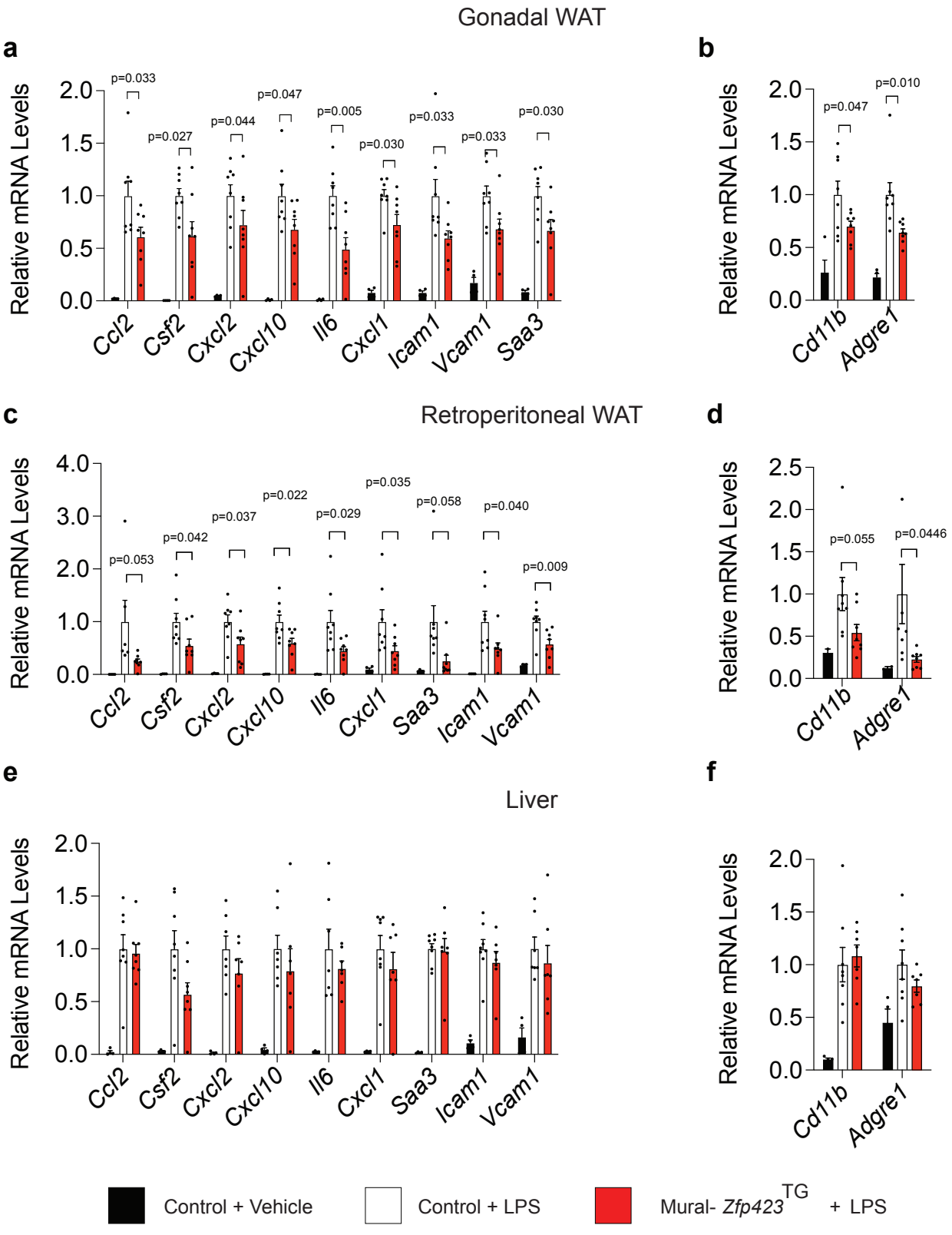
Supplementary Figure 2. Gating strategy for the detection and quantification of gonadal white adipose tissue macrophages by flow cytometry.

Upon selection of live cells/single cells from gonadal WAT stromal vascular fraction, CD45+ cells were segregated on the basis of CD11b and F4/80 expression or CD11b and CD68 expression for adipose tissue macrophages. Adipose tissue macrophages, defined as CD11b+ F4/80+ cells, were then separated on the basis of CD11c and CD206 expression, or CD9 expression. Pro-inflammatory macrophages were defined as CD11c+ CD206- or CD9+, and alternatively activated (anti-inflammatory) macrophages were defined as CD11c- CD206+.



Supplementary Figure 3. *Zfp423* expression in gonadal WAT FIPs and APCs.

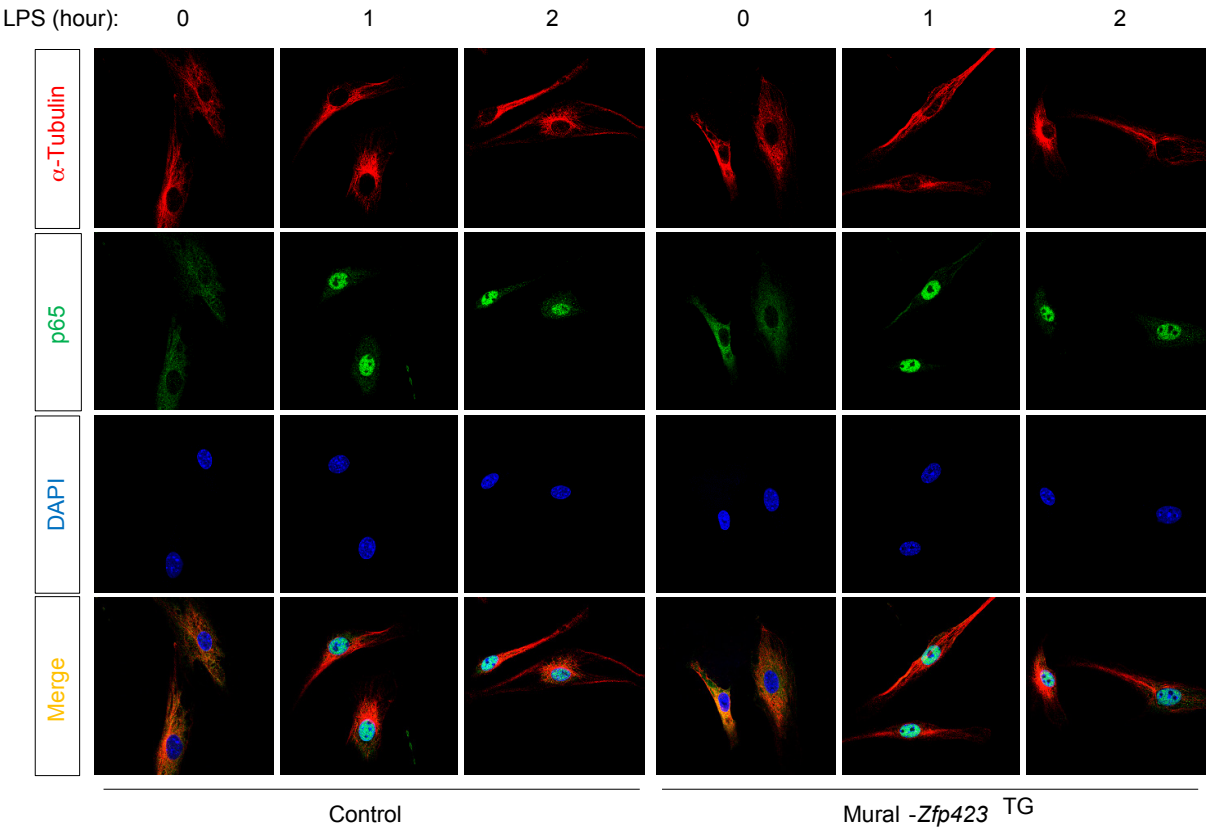
mRNA levels of *Zfp423* in freshly isolated FIPs and APCs from gWAT of wild-type mice (n=8) after 1 month of HFD feeding at thermoneutrality. *Zfp423* expression levels (determined by qPCR) are separately normalized to indicated housekeeping genes. Bars represent mean + s.e.m. Data is representative of two independent repetitions.


Gonadal WAT
a
b
Relative mRNA Levels
2.0
1.5
1.0
0.5
0.0
p=0.033
p=0.027
p=0.044
p=0.047
p=0.005
p=0.030
p=0.033
p=0.033
p=0.030
Ccl2
Csf2
Cxcl2
Cxcl10
Il6
Cxcl1
Icam1
Vcam1
Saa3
p=0.047
p=0.010
Cd11b
Adgre1
Retroperitoneal WAT
c
d
4.0
3.0
2.0
1.0
0.0
p=0.053
p=0.042
p=0.037
p=0.022
p=0.029
p=0.035
p=0.058
p=0.040
p=0.009
Ccl2
Csf2
Cxcl2
Cxcl10
Il6
Cxcl1
Saa3
Icam1
Vcam1
2.5
2.0
1.5
1.0
0.5
0.0
p=0.055
p=0.0446
Cd11b
Adgre1
Liver
e
f
2.0
1.5
1.0
0.5
0.0
Ccl2
Csf2
Cxcl2
Cxcl10
Il6
Cxcl1
Saa3
Icam1
Vcam1
Cd11b
Adgre1
Control + Vehicle
Control + LPS
Mural- Zfp423TG + LPS

Supplementary Figure 4. *Zfp423* overexpression in PDGFRβ+ cells limits LPS-induced whole WAT inflammatory gene expression *in vivo*.

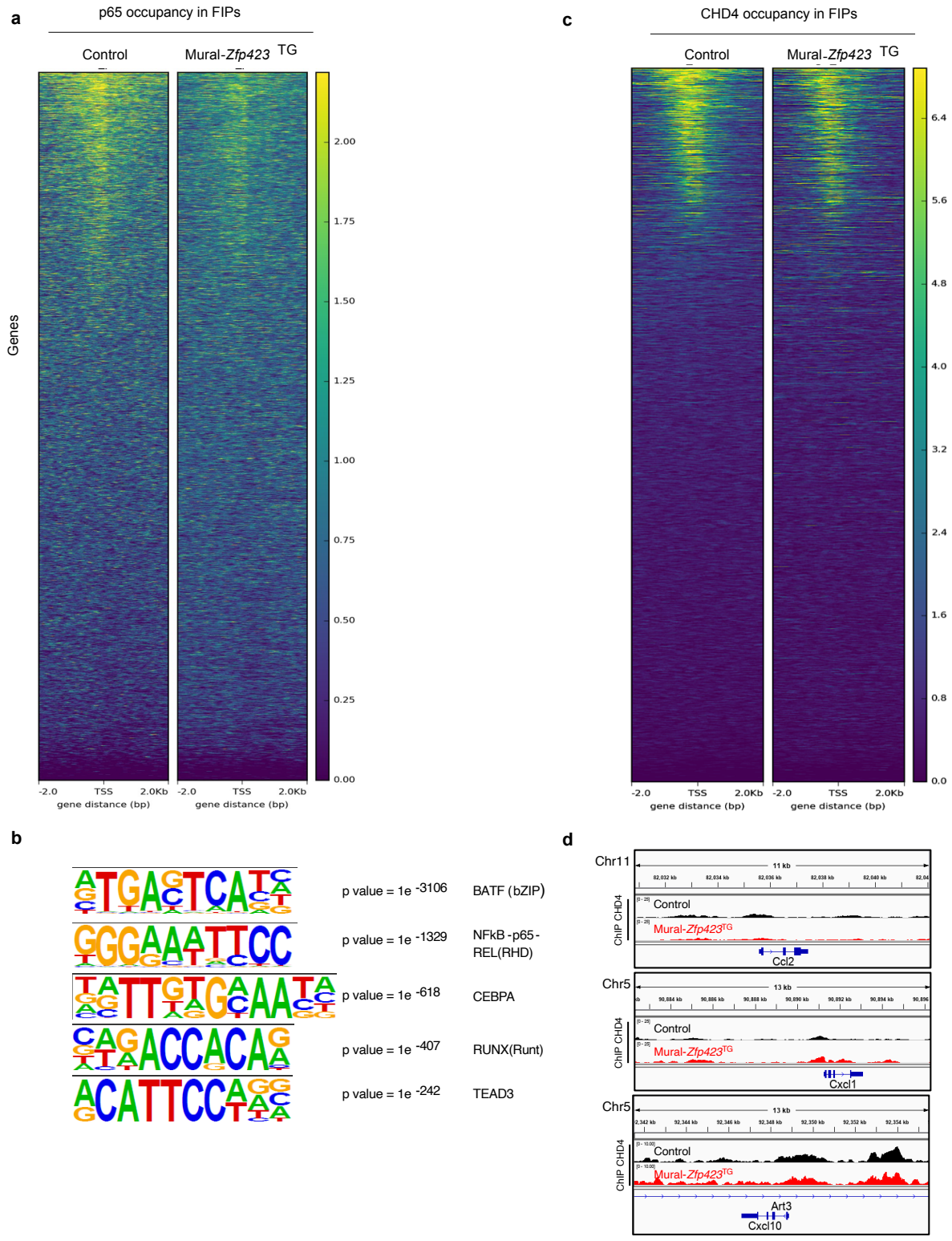
a, mRNA levels of selected pro-inflammatory genes within whole gonadal WAT depot 2 hours following vehicle or LPS injection.
b, mRNA levels of macrophage-selective genes within whole gonadal WAT depot 24 hours following vehicle or LPS injection.
c, mRNA levels of selected pro-inflammatory genes within whole retroperitoneal WAT depot 2 hours following vehicle or LPS injection.
d, mRNA levels of macrophage-selective genes within whole retroperitoneal WAT depot 24 hours following vehicle or LPS injection.
e, mRNA levels of selected pro-inflammatory genes within liver 2 hours following vehicle or LPS injection.
f, mRNA levels of macrophage-selective genes within liver 24 hours following vehicle or LPS injection.

For **a-f**, n=4 individual mice for Control + Vehicle group; n=8 for Control + LPS group; and n=8 for Mural-*Zfp423*^{TG} + LPS group. Data are shown as the mean ± s.e.m., *p* value are calculated by one-way ANOVA. Data were reproduced two times in independent experiments.



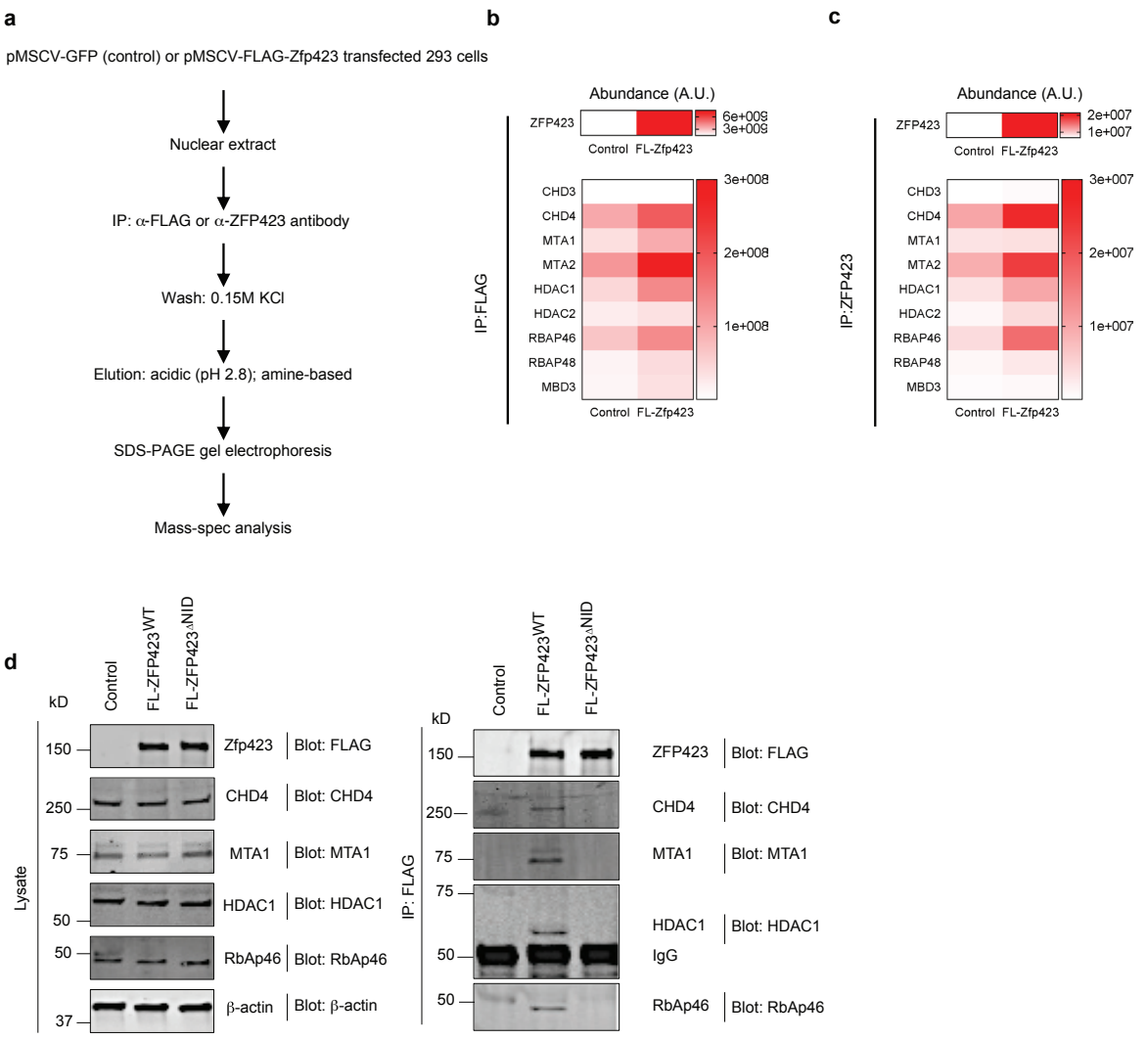
Supplementary Figure 5. *Zfp423* overexpression does not impact p65 cellular localization in FIPs.

Immunocytochemistry of p65 expression and localization in Control and Mural-*Zfp423*^{TG} FIPs (pooled of 2 mice for each genotype) at the indicated time points following LPS (100ng/ml) treatment of FIPs that were stained with antibodies recognizing tubulin (red) and p65 (green), and counterstained with DAPI (blue nuclei). Representative 63x magnification images are shown.


a
p65 occupancy in FIPs
Control
Mural-Zfp423 TG
Genes
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
-2.0
TSS
2.0Kb
gene distance (bp)
c
CHD4 occupancy in FIPs
Control
Mural-Zfp423 TG
6.4
5.6
4.8
4.0
3.2
2.4
1.6
0.8
0.0
b
p value = 1e -3106
BATF (bZIP)
p value = 1e -1329
NFkB-p65-REL(RHD)
p value = 1e -618
CEBPA
p value = 1e -407
RUNX(Runt)
p value = 1e -242
TEAD3
d
Chr11
11 kb
ChIP CHD4
Control
Mural-Zfp423TG
Ccl2
Chr5
13 kb
Cxcl1
Art3
Cxcl10

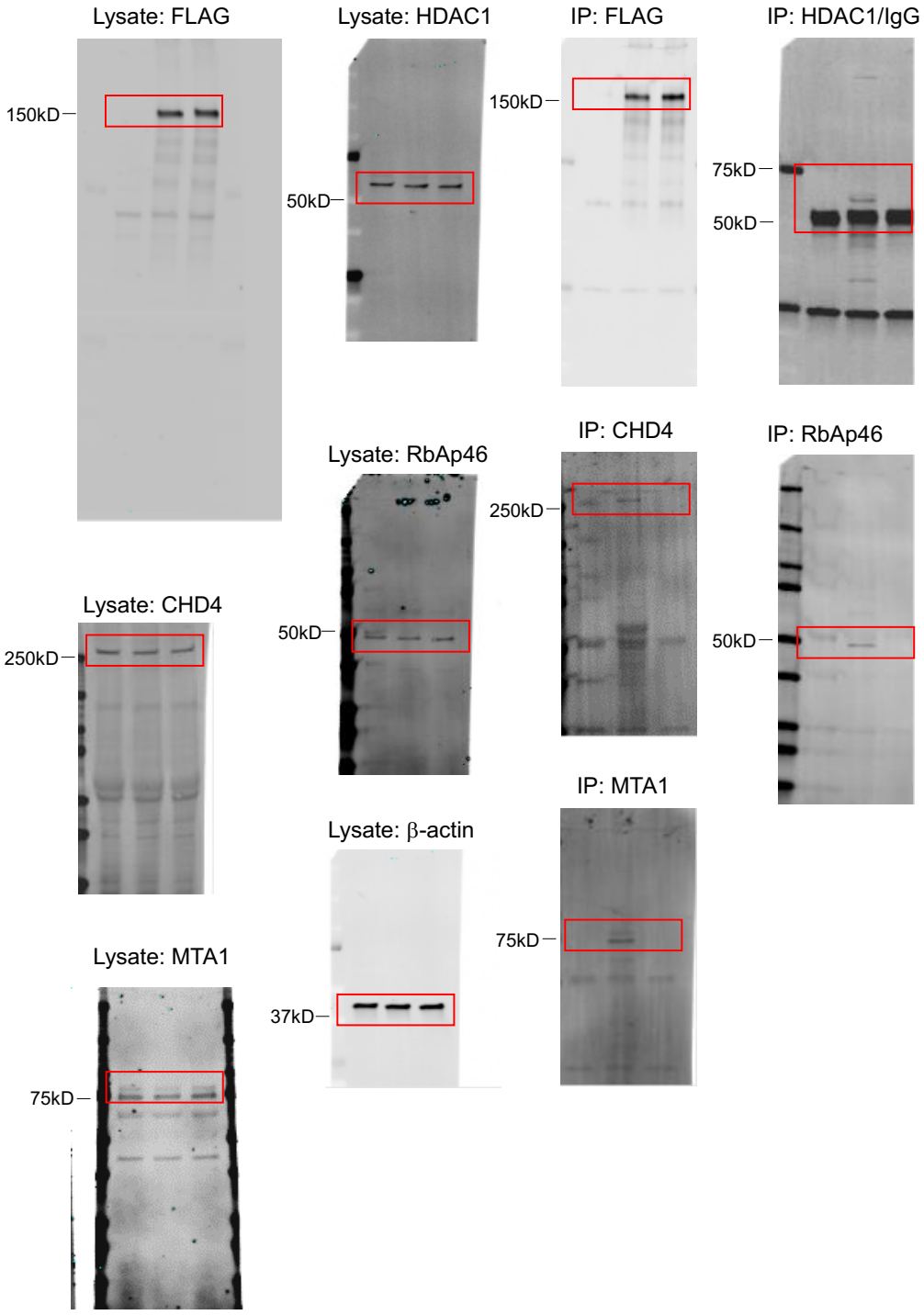
Supplementary Figure 6. Genome-wide p65 and CHD4 occupancy in gonadal WAT FIPs following LPS treatment.

a, Heatmap of p65 enrichment at genome-wide transcriptional start sites (TSS; regions - 2kb to + 2kb relative to TSS) in FIPs isolated from 10 weeks old Control (pooled from 10 mice) or Mural-*Zfp423*^{TG} (pooled from 10 mice) mice treated with 100 ng/ml LPS for 2 hours. One representative ChIP-seq experiment (of two independent repetitions) is shown.
b, Enriched transcription factor binding motifs within p65 occupied regions in FIPs of Control mice. Unadjusted p values represent enrichment of indicated binding motifs.
c, Heatmap of CHD4 enrichment at genome-wide transcriptional start sites (TSS; regions - 2kb to + 2kb relative to TSS) in FIPs isolated from 10 weeks old Control (pooled from 10 mice) or Mural-*Zfp423*^{TG} (pooled from 10 mice) mice treated with 100 ng/ml LPS for 2 hours. One representative ChIP-seq experiment (of two independent repetitions) is shown.
d, CHD4 enrichment at *Ccl2*, *Cxcl1* and *Cxcl10* loci in Control and Mural-*Zfp423*^{TG} FIPs treated with 100 ng/ml LPS for 2 hours.



Supplementary Figure 7. ZFP423 interacts with the NuRD co-repressor complex in FIPs

a, Experimental approach to identifying ZFP423-interacting proteins.
b, Heat map depicting enrichment of identified NuRD complex components in ZFP423 complexes immunoprecipitated using anti-FLAG antibody. A complete list of identified proteins from the mass spectrometry analysis is found in Supplementary Table 2.
c, Heat map depicting enrichment of identified NuRD complex components in ZFP423 complexes immunoprecipitated using anti-ZFP423 antibody. A complete list of identified proteins from the mass spectrometry analysis is found in Supplementary Table 2.
d, Western blot analysis of endogenous NuRD protein expression in FIPs whole cell lysates (left) and FLAG-ZFP423 immunoprecipitates (right) from primary FIPs transduced with either control retrovirus (empty vector), retrovirus expressing wild-type FLAG-tagged ZFP423 (FLAG-ZFP423^{WT}), or retrovirus expressing FLAG-ZFP423 lacking the 12 amino acid NuRD-interaction domain (NID) (FLAG-ZFP423$^{\Delta NID}$). ZFP423 associates with core components of the NuRD co-repressor complex via its NID. The experiment was performed twice with 6-8 mice pooled per experiment.



Supplementary Figure 8. Uncropped western blots from Supplementary Figure 7