

SUPPLEMENTARY FIGURES

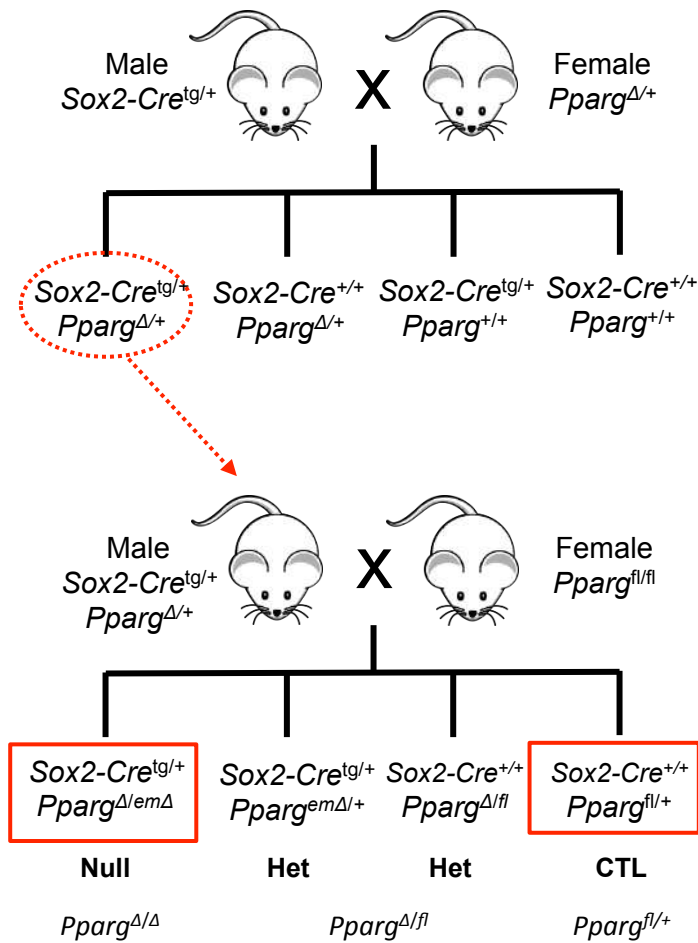


Figure S1. Mating strategy and genotypes of $Pparg^{\Delta/\Delta}$ mice and their littermates

The $Sox2-Cre$ transgene must be transmitted by a male mouse. $Sox2-Cre^{tg/+}$: carrier of one $Sox2-Cre$ expressing allele. $Sox2-Cre^{+/+}$: no transmission of the $Sox2-Cre$ transgene; $Pparg^+$: wild-type allele; $Pparg^{fl}$: functional $Pparg$ allele carrying 2 flox sites flanking exon 1 and 2 of $Pparg$; $Pparg^{\Delta}$: $Pparg$ allele deleted of the genomic region encompassing exon 1 and exon 2, resulting in a non functional allele; $Pparg^{em\Delta}$: $Pparg$ allele deleted during development in all the cells forming the embryo (epiblast deletion) but still present in the trophoblastic cells allowing a normal placental development. The last line gives the corresponding simplified names.

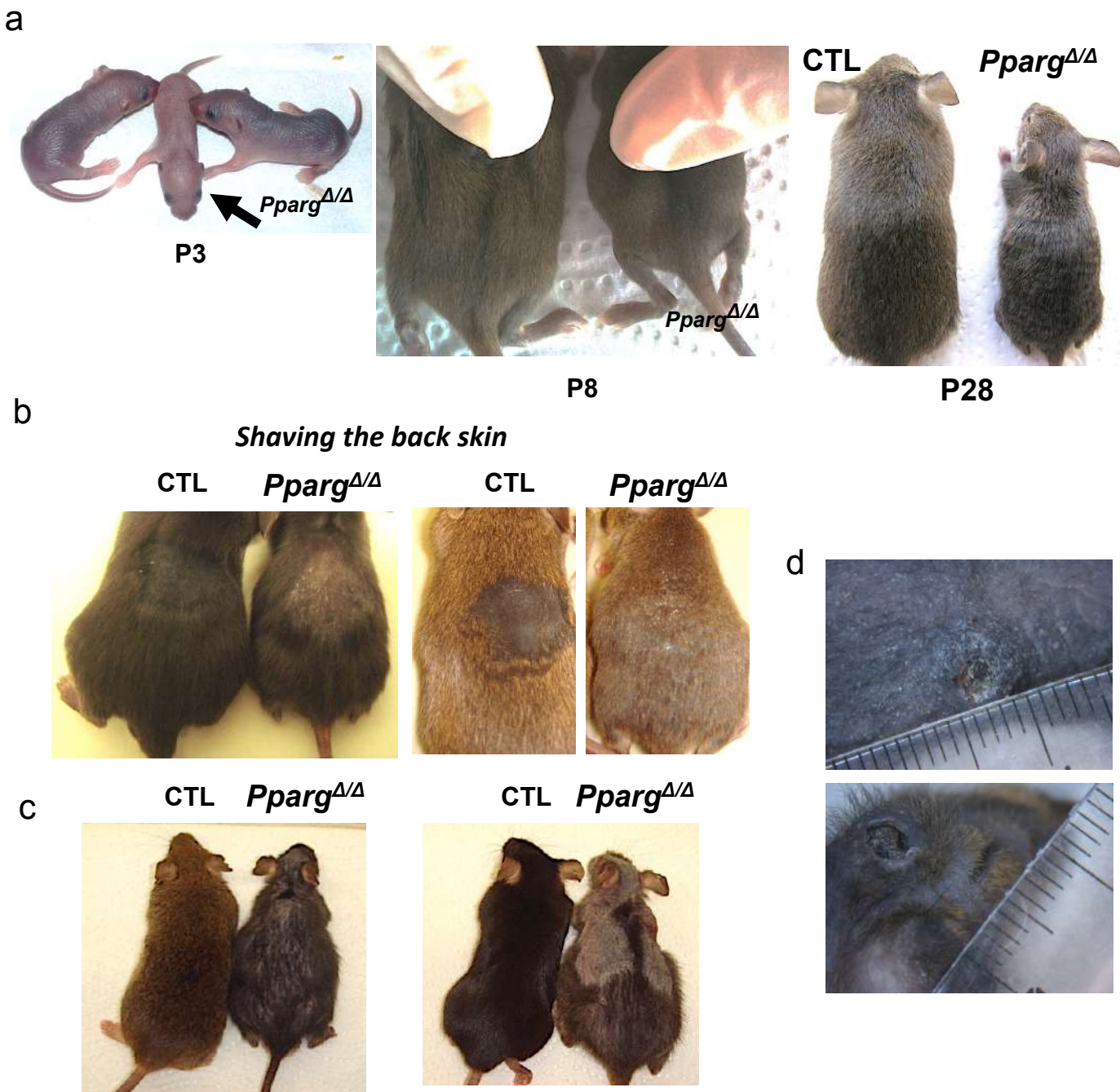


Figure S2: Skin and hair phenotype in $Pparg^{\Delta/\Delta}$ mice

(a) Representative pictures of $Sox2-Cre^{tg/+};Pparg^{\Delta/em\Delta}$ ($Pparg^{\Delta/\Delta}$) and littermates taken at P3, P8 and P28. (b) Representative pictures of 4-5 weeks old $Pparg^{\Delta/\Delta}$ and littermate control mice just shaved on the back. The shaved area is less recognizable in $Pparg^{\Delta/\Delta}$, due to their shorter hair, but shows flaking skin. (c) Representative pictures of patchy hair loss in 6 months old $Pparg^{\Delta/\Delta}$ and control mice (CTL). (d) Representative pictures of skin lesions in $Pparg^{\Delta/\Delta}$ mice.

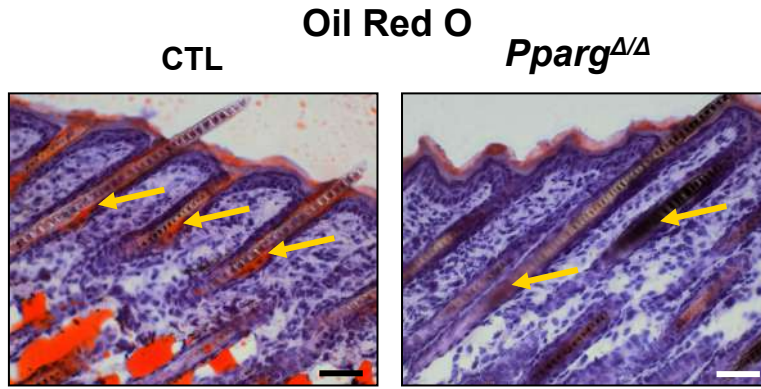


Figure S3: Lack of sebaceous glands in *Pparg*^{Δ/Δ} skin

Oil Red O staining of back skin cryosections from *Sox2-Cre*^{tg/+};*Pparg*^{Δ/emΔ} (*Pparg*^{Δ/Δ}) and control (CTL) mice at P28. Yellow arrows indicate the sebaceous glands in control mice and the place where sebaceous glands should be in *Pparg*^{Δ/Δ} mice. Scale bar= 50μm.

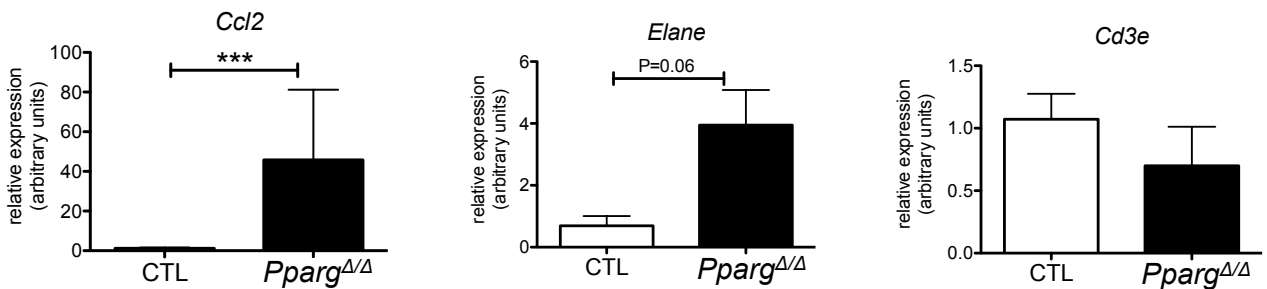


Figure S4: Gene expression analysis of inflammatory markers in *Pparg*^{Δ/Δ} skin at P28

Gene expression analysis of markers of immune cells, chemokine (C-C motif) ligand 2 (*Ccl2*) for macrophages, neutrophil elastase (*Elane*) for neutrophils, CD3 (*Cd3e*) for T lymphocytes. RNA was isolated from total skin of *Sox2-Cre*^{tg/+};*Pparg*^{Δ/emΔ} (*Pparg*^{Δ/Δ}) and control mice at P28 (n=4). Data are normalized to *Eef1a1* and expressed as mean ± SEM. *** represents p value <0.001.

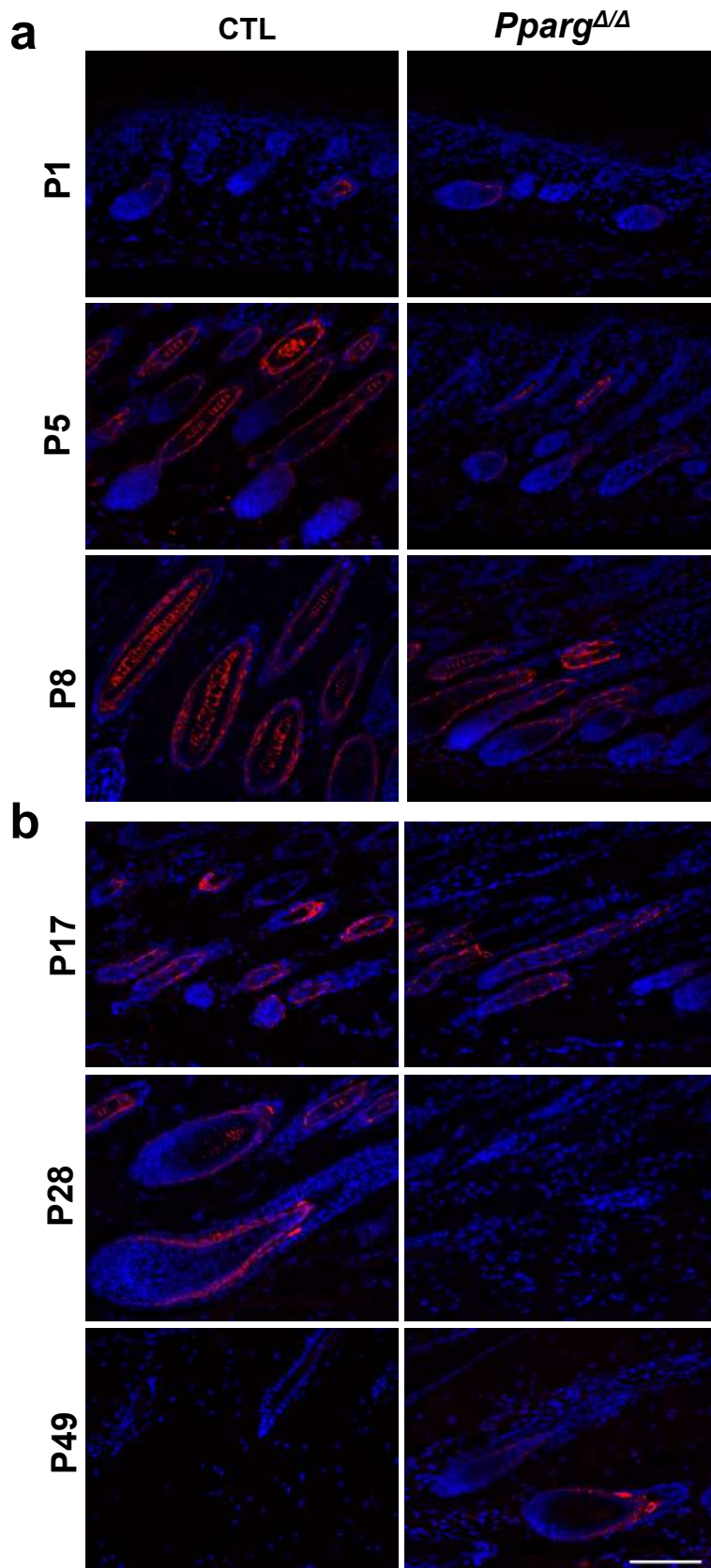


Figure S5: Trichohyalin protein expression is desynchronized in *Pparg*^{Δ/Δ} skin
 Representative images of IF staining of trichohyalin (red) in skin from *Sox2-Cre*^{tg/+}; *Pparg*^{Δ/emΔ} (*Pparg*^{Δ/Δ}) and littermate controls (CTL) at different stages of HF morphogenesis (a) and of HF cycle (b) Nuclei are stained in blue. Scale bar=100μm.

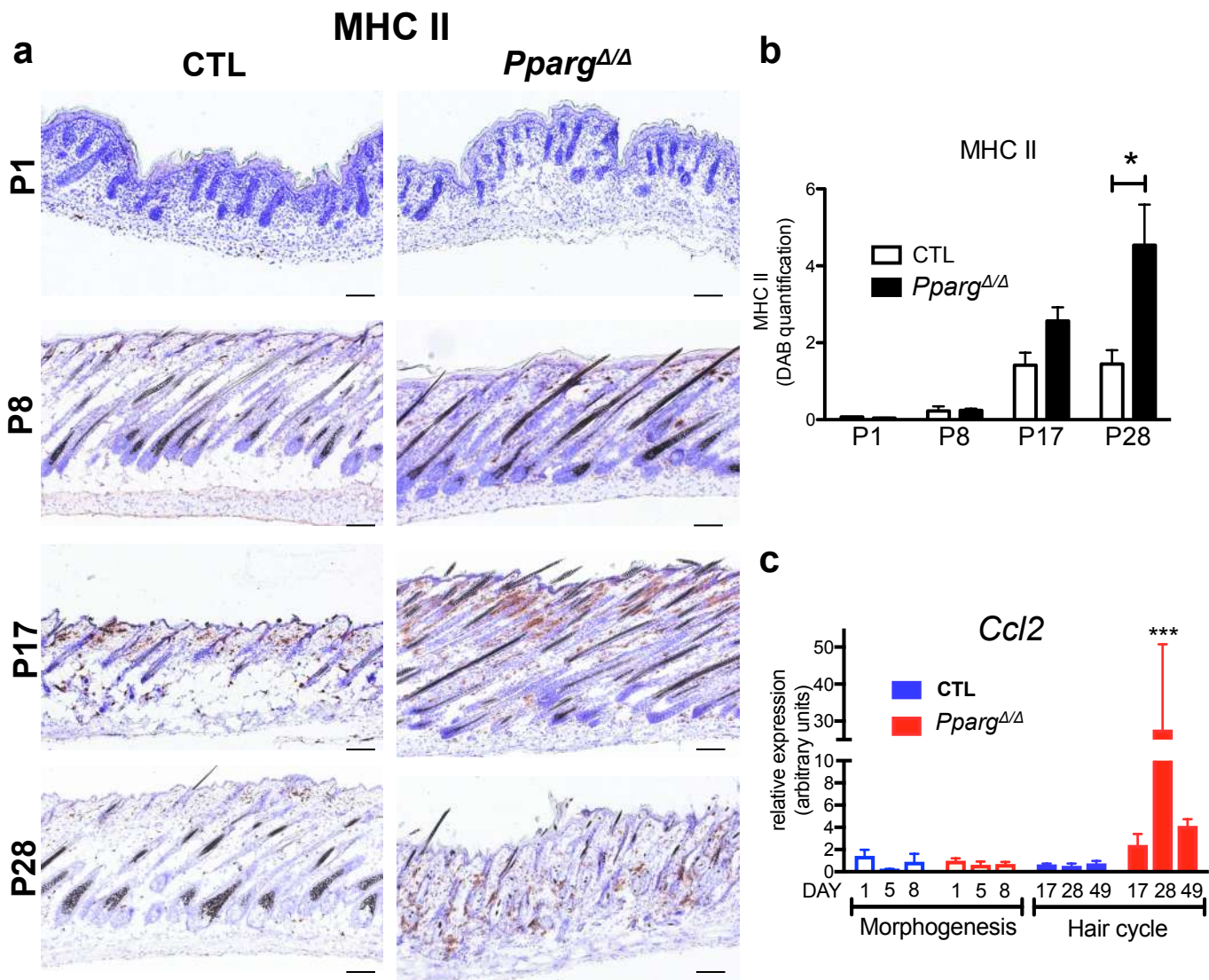


Figure S6: Inflammatory infiltrate appears in *Pparg*^{Δ/Δ} skin starting from P17 onwards

(a) Staining with antibody against major histocompatibility complex class II (MHC II) of skin sections from *Sox2-Cre*^{tg/+};*Pparg*^{Δ/emΔ} (*Pparg*^{Δ/Δ}) and control (CTL) mice. Scale bar=100μm (b) DAB staining quantification, normalized to the skin area of each section. Data are expressed as mean ± SEM. * represents p<0.05 (c) Gene expression analysis of skin from *Pparg*^{Δ/Δ} (*y*^{Δ/Δ}; red bars) and control (CTL; blue bars) mice at different stages of hair morphogenesis: P1 (n=5), P5 (n=6) and P8 (n=5); and hair cycle: P17, P28 and P49 (n=4). mRNA levels of Chemokine (C-C motif) ligand 2 (*Ccl2*), as macrophage marker, are shown. Data were normalized to *Eef1a1* and expressed as mean ± SEM. *** represents p<0.001.

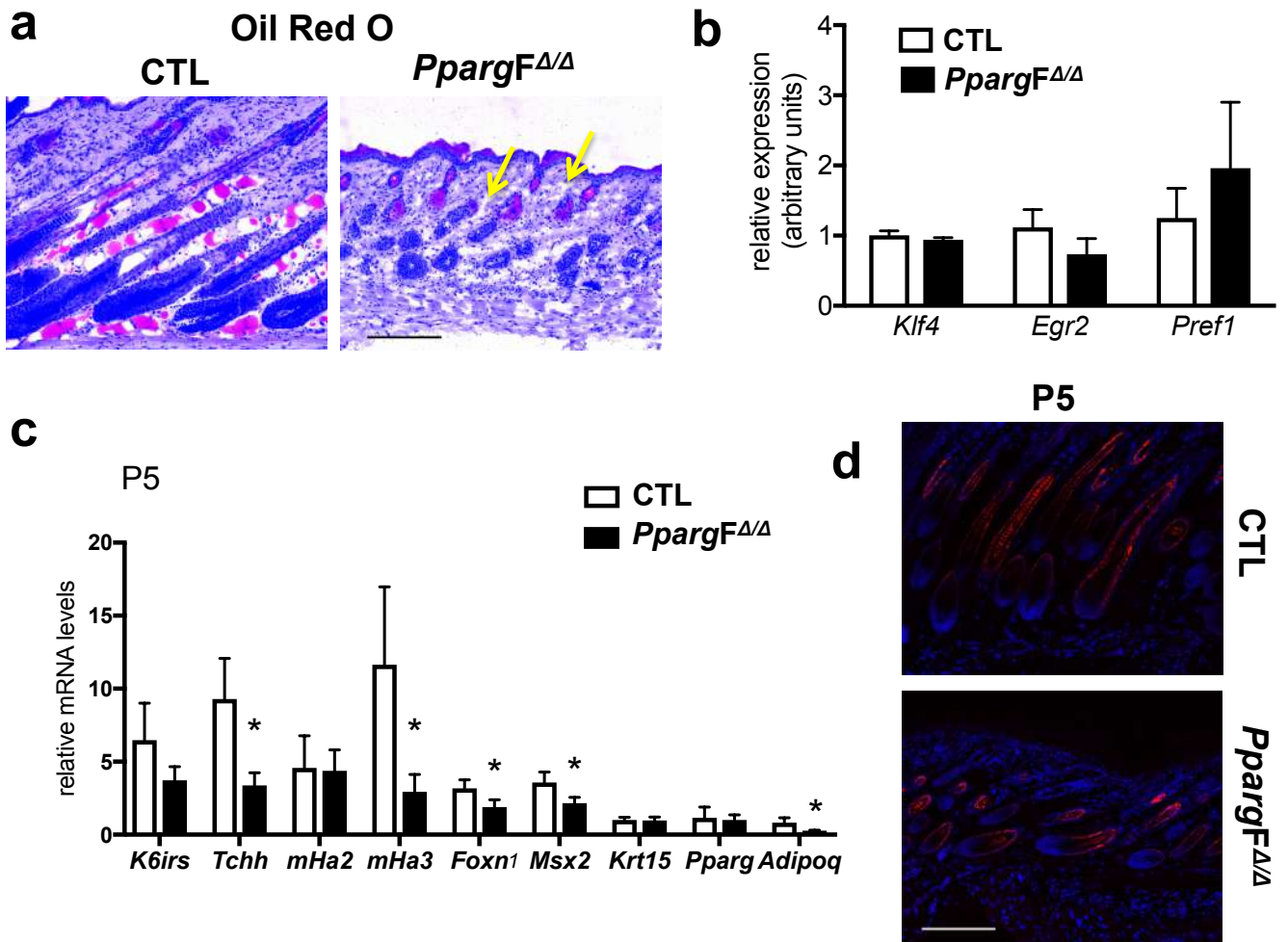


Figure S7: HF morphogenesis phenotype of fat-specific *Pparg* knock-out mice

(a) Oil Red O staining of back skin cryosections from *Adipoq-Cre^{tg/+};Pparg^{fl/fl}* (*Pparg*^{F Δ/Δ}) and control (CTL) mice at P28. Yellow arrows indicate the sebaceous glands in *Pparg*^{F Δ/Δ} mice. (b) Gene expression analysis in full thickness skin of preadipocyte-markers, kruppel like factor 4 (*Klf4*), early growth response 2 (*Egr2*) and preadipocyte factor 1 (*Pref1*) in *Pparg*^{F Δ/Δ} and control (CTL) mice at P1 (n=4 for CTL, n=3 for *Pparg*^{F Δ/Δ}). Data are normalized to *Eef1 α 1* and expressed as mean \pm SEM. (c) Gene expression analysis in full thickness skin of keratin 72 (*K6irs*), trichohyalin (*Tchh*); murine type I hair keratins *mHa2* and *mHa3*; forkhead box N1 (*Foxn1*), homeobox msh-like 2 (*Msx2*), Keratin 15 (*Krt15*), *Pparg* (*Pparg*) and adiponectin (*Adipoq*) in *Pparg*^{F Δ/Δ} and control (CTL) mice at P5 (n=4 for CTL, n=3 for *Pparg*^{F Δ/Δ}). Data are normalized to *Eef1 α 1* and expressed as mean \pm SEM. * represents p<0.05. (d) Representative images of IF staining of trichohyalin (red) in skin from *Pparg*^{F Δ/Δ} and control (CTL) mice at P5. Nuclei are stained in blue. Scale bar=200 μ m.

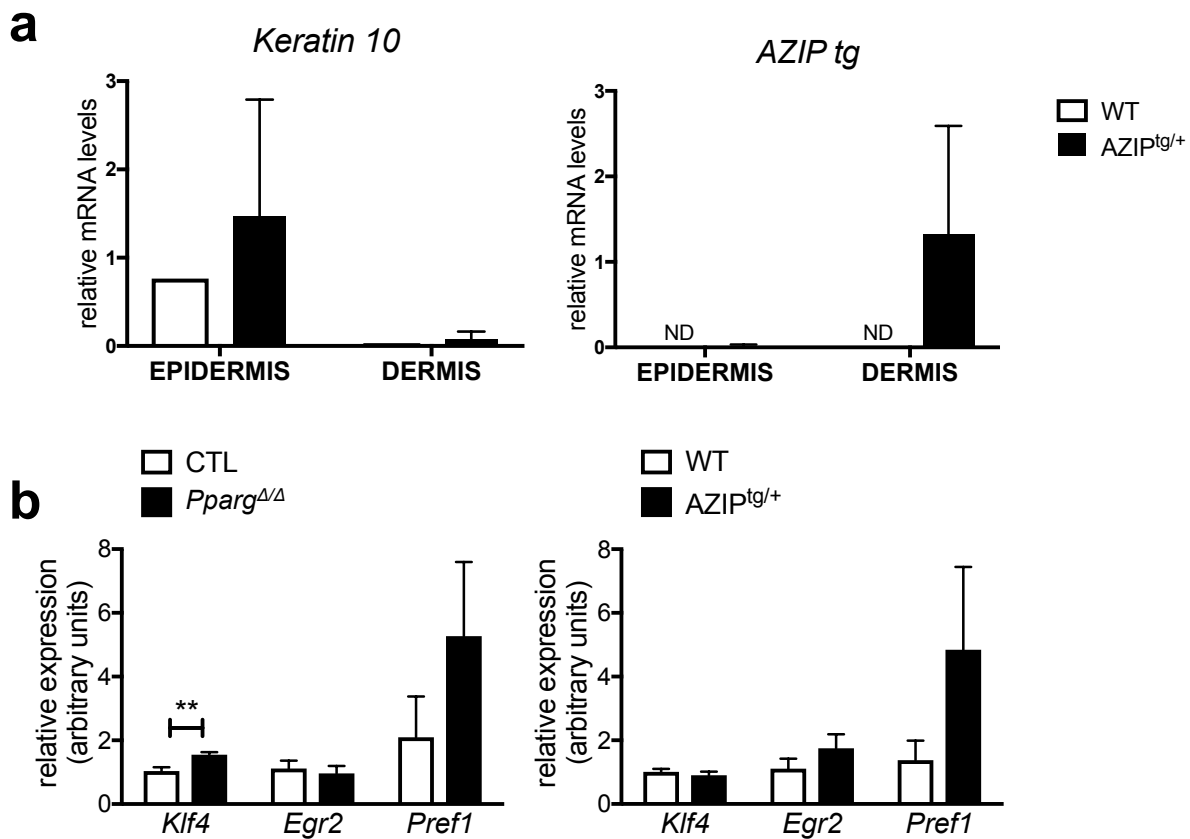


Figure S8: Skin expression of the AZIP transgene and of preadipocyte markers in AZIP^{tg/+} mice

(a) Epidermis and dermis fractions were separated from the skin of AZIP^{tg/+} and littermate wild type control mice. Gene expression analysis of Keratin 10, as a marker of epidermis, and of the AZIP transgene (AZIP tg) were evaluated. (b) Gene expression analysis of preadipocyte-markers, kruppel like factor 4 (*Klf4*), early growth response 2 (*Egr2*) and preadipocyte factor 1 (*Pref1*). RNA was isolated from total skin of *Pparg*^{Δ/Δ} AZIP^{tg/+} and the respective control mice at P1 (n=7 for CTL, n=5 for *Pparg*^{Δ/Δ}, n=4 for AZIP^{tg/+} and WT). Data are normalized to *Eef1a1* and expressed as mean ± SEM. ** represents p value <0.01.

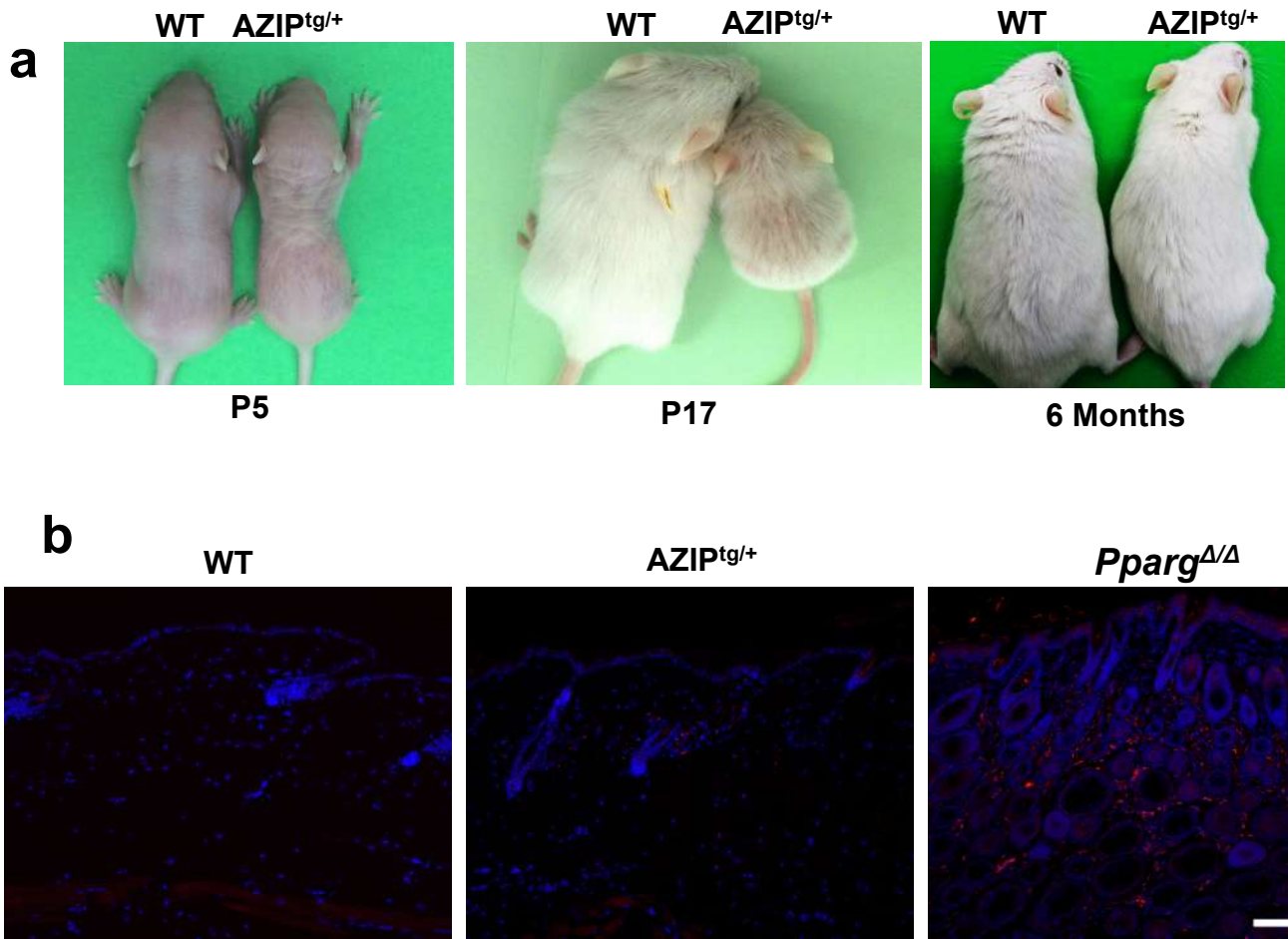


Figure S9: AZIP^{tg/+} mice show delayed hair growth, but no skin inflammation at adult stage

(a) Representative pictures of AZIP^{tg/+} and littermate controls taken at P5, P17 and 6 months. **(b)** IF staining of Iba1⁺ macrophages (red) in the skin of 6 months old AZIP^{tg/+} and littermate controls (nuclei are stained in blue). Skin from *Pparg*^{Δ/Δ} (right panel) was used as positive control. Scale bar=200μm.

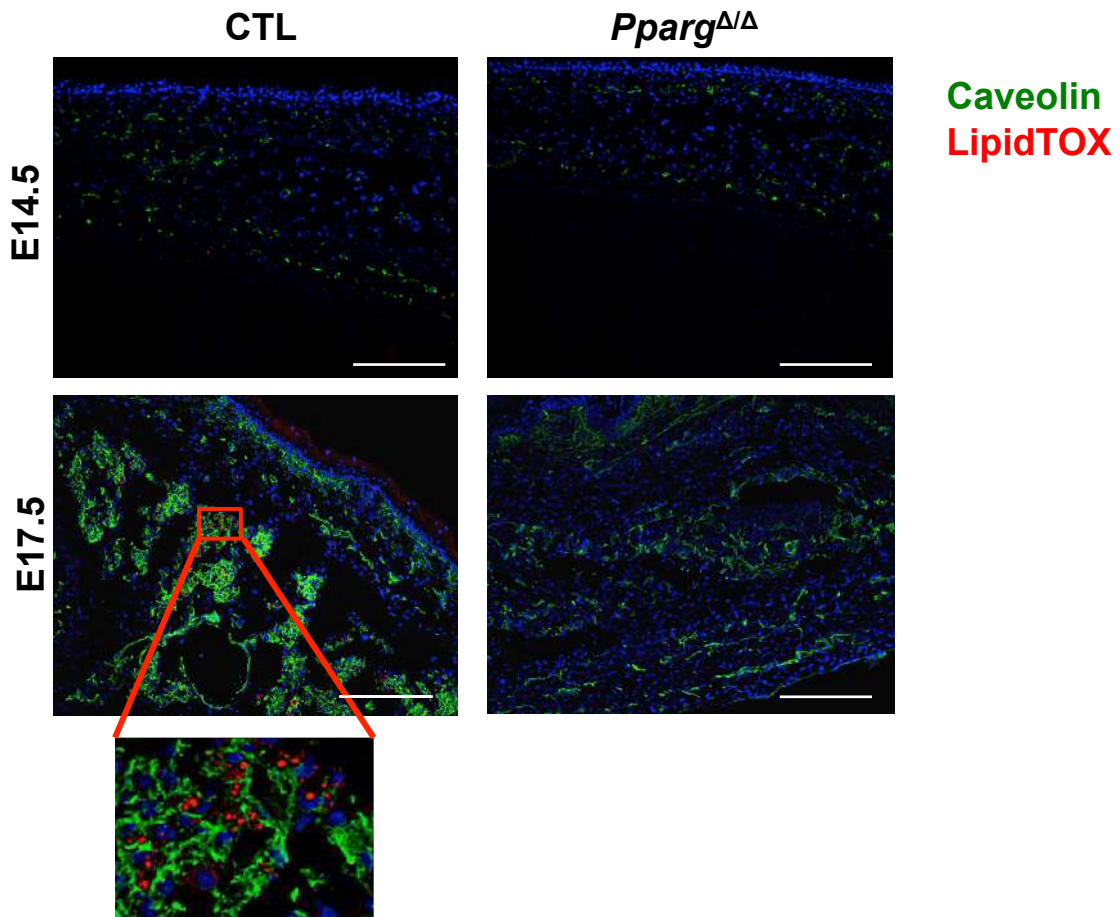


Figure S10: Mature adipocytes appear at E17.5 during embryogenesis

Frozen sections of embryos at E14.5 and E17.5 from *Sox2-Cre*^{tg/+};*Pparg*^{Δ/emΔ} (*Pparg*^{Δ/Δ}) and control (CTL) mice were stained in double immunofluorescence with rabbit anti-caveolin 1 (green) and HCS LipidTOX (red) to mark mature adipocytes, as described in Le Lay et al. 2010. Scale bar=200μm.

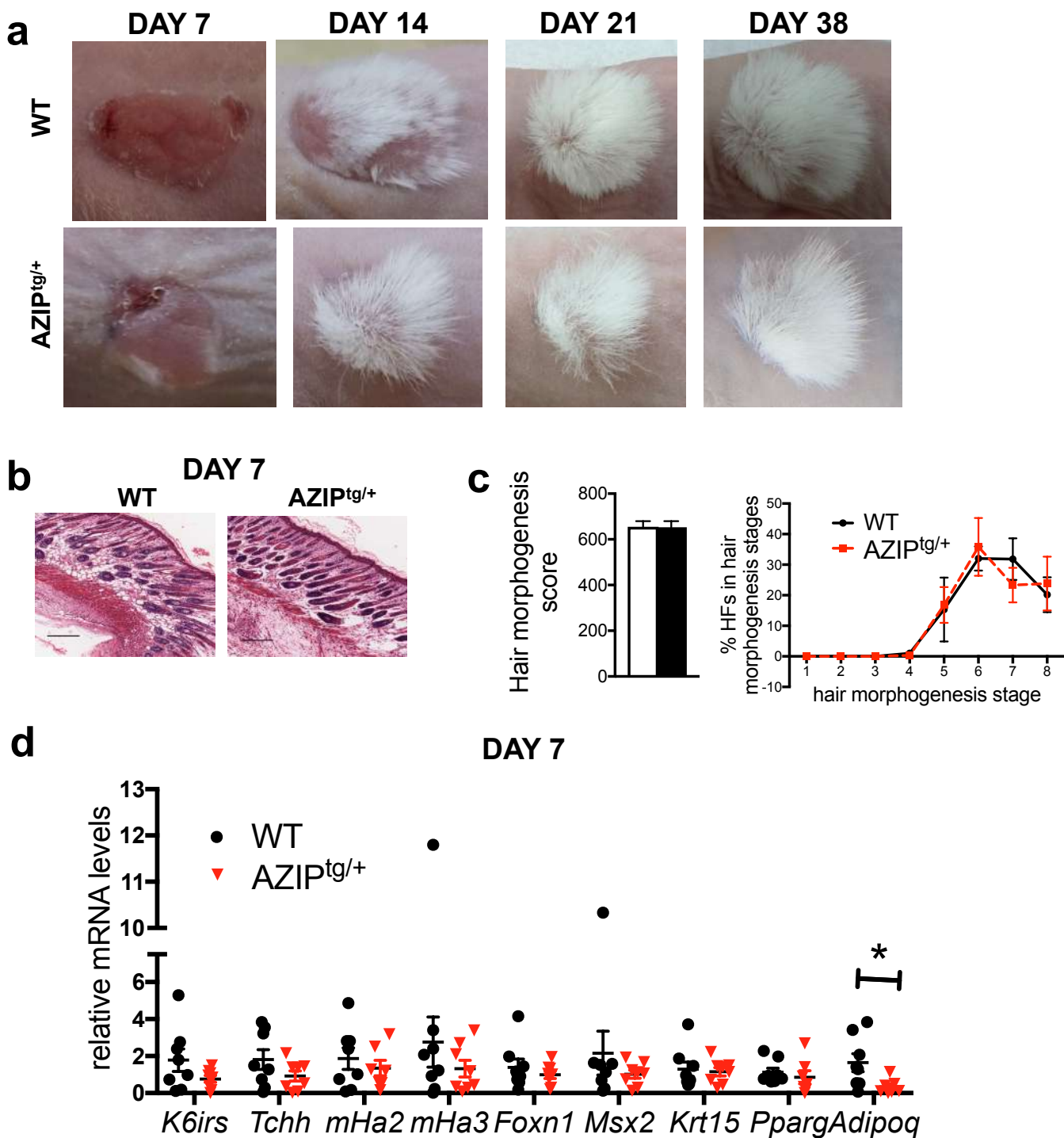


Figure S11: Role of adipose tissue for hair follicle postnatal differentiation

(a) Representative images of skin grafts from AZIP^{tg/+} and wild-type (WT) embryos on *Foxn1^{nu/nu}* mice, 7, 14, 21 and 38 days after engraftment. Scale bar=200 μ m (b) Representative picture 7 days after engraftment and (c) Quantitative histomorphometry analysis of hair morphogenesis. Hair morphogenesis score (left panel); % of HFs found in the different hair morphogenesis stages (right panel; n=6). (d) Gene expression of keratin 72 (*K6irs*), trichohyalin (*Tchh*); murine type I hair keratins *mHa2* and *mHa3*; forkhead box N1 (*Foxn1*), homeobox msh-like 2 (*Msx2*); Keratin 15 (*Krt15*), *Pparg* and adiponectin (*Adipoq*). Data are normalized to *Eef1a1* and expressed as mean \pm SEM (n=8). * represents p<0.05.

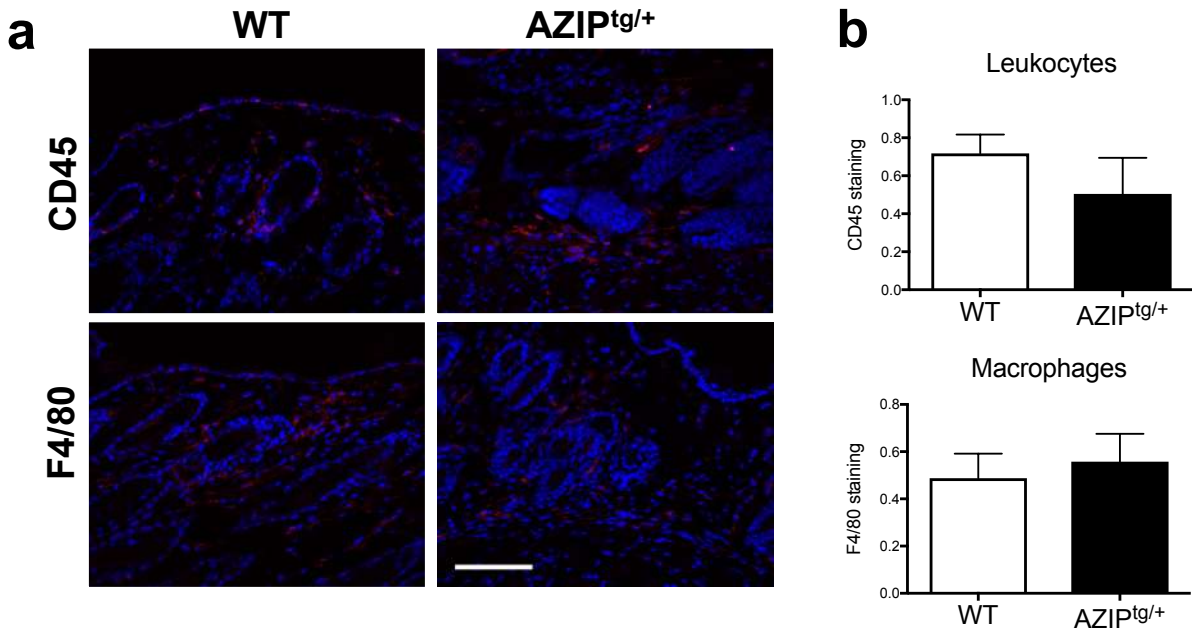


Figure S12: No inflammation in AZIP^{tg/+} grafts

38 days after engraftment: **(a)** CD45 (leucocytes) and F4/80 (macrophages) immunostaining (red) and **(b)** their quantification. Scale bar=100 μ m.