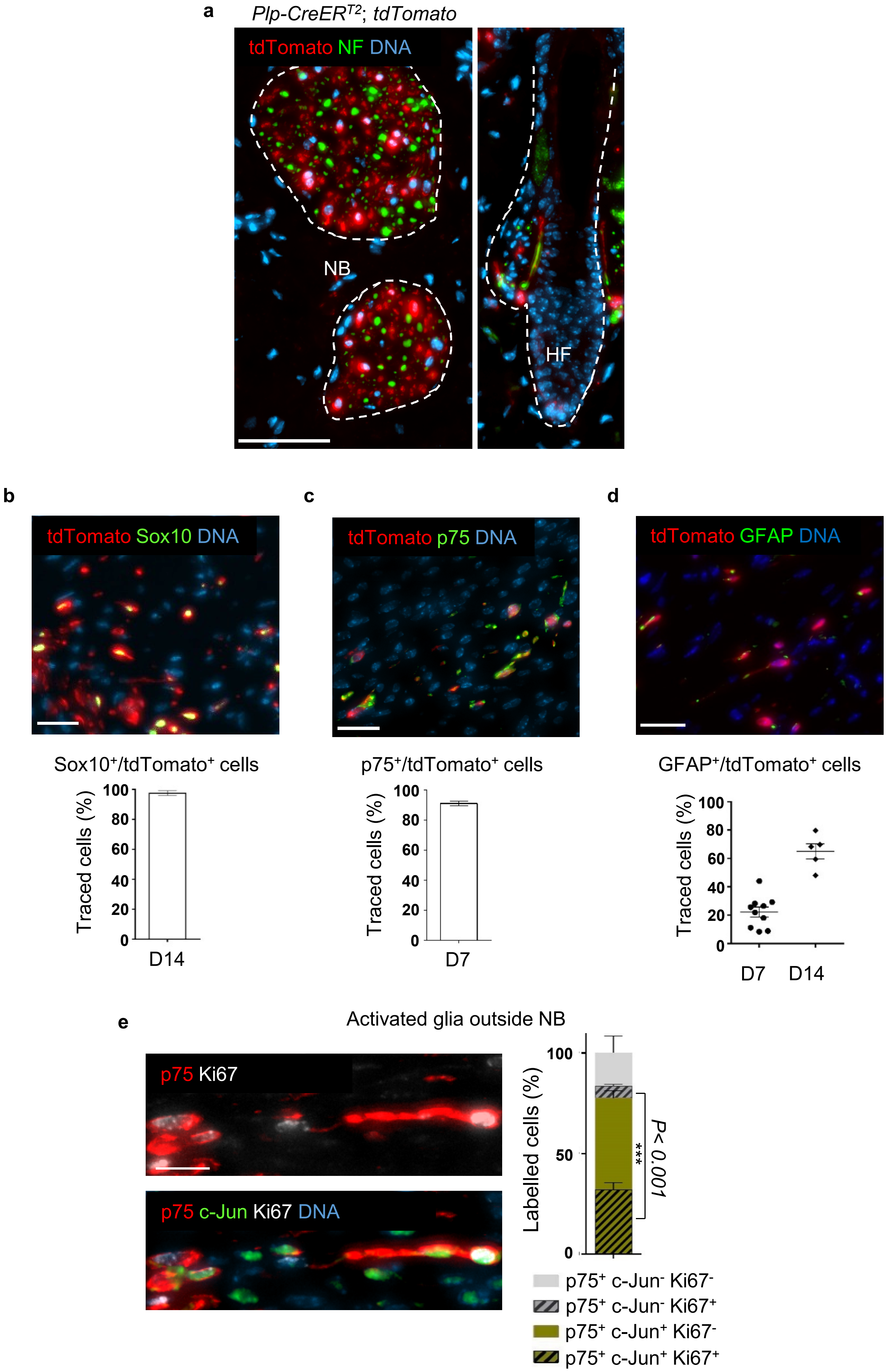
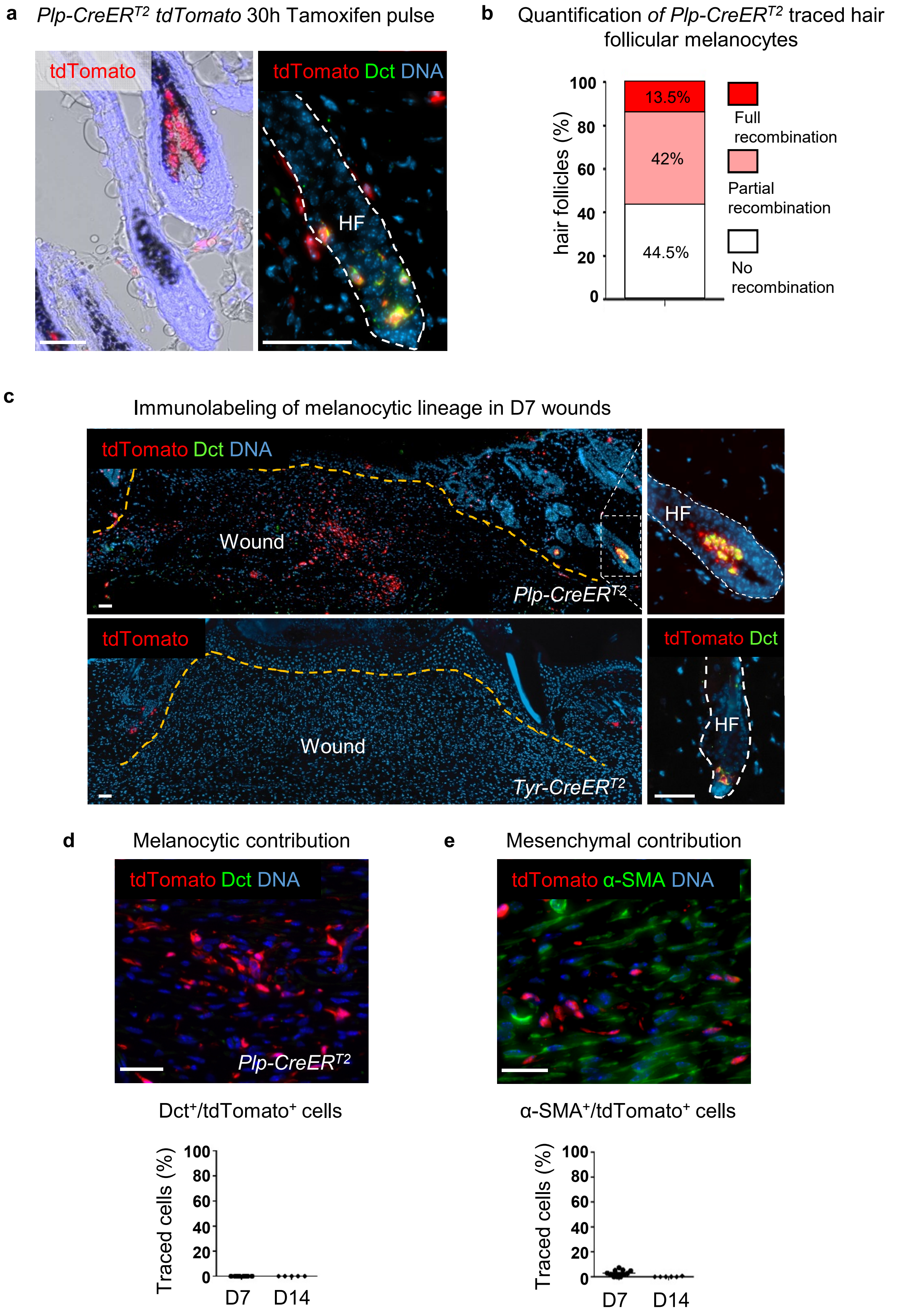


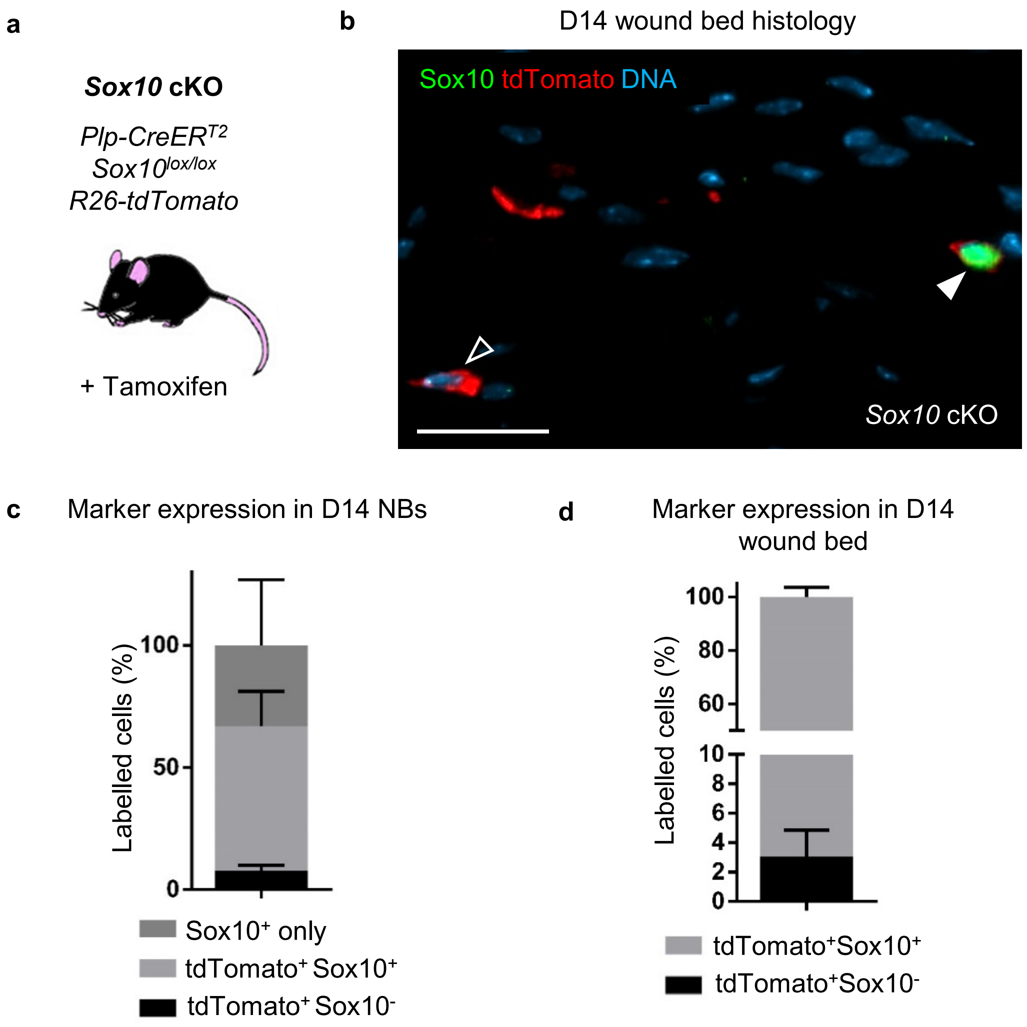
Supplementary Figure 1

Supplementary Figure 1 *Plp-CreER*^{T2} lineage tracing in intact and injured skin. **a** tdTomato reporter expression in nerve bundles (NB) and around hair follicles (HF). **b** Immunofluorescence staining of *Plp-CreER*^{T2} traced cells in granulation tissue for tdTomato (red) and Sox10$^+$ (green) and quantification of the percentage of Sox10$^+$ per tdTomato$^+$ cells in the granulation tissue of injured skin at D14 (N=2, n=6). **c** Immunofluorescence staining of tdTomato$^+$ *Plp-CreER*^{T2}-traced cells in granulation tissue (red) with p75$^+$ (green) and quantification of the percentage of p75$^+$ per tdTomato$^+$ cells in the granulation tissue of injured skin at D7 (N=4, n=10). **d** Immunofluorescence staining of D14 tdTomato$^+$ *Plp-CreER*^{T2} traced cells (red) with glial fibrillary acidic protein (GFAP) (green) and quantification of the percentage of GFAP$^+$ per tdTomato$^+$ cells in the granulation tissue of injured skin at D7 (N=3, n=10) and D14 (N=2, n=6). **e** Immunofluorescence and corresponding quantification of proliferative (Ki67$^+$), activated (c-Jun$^+$), de-differentiated (p75$^+$) glial cells outside NBs (N=6, n=9). Data are represented as mean±SEM. Scale bars, 50μm (**a**), 25μm (**b**,**c**,**d**).



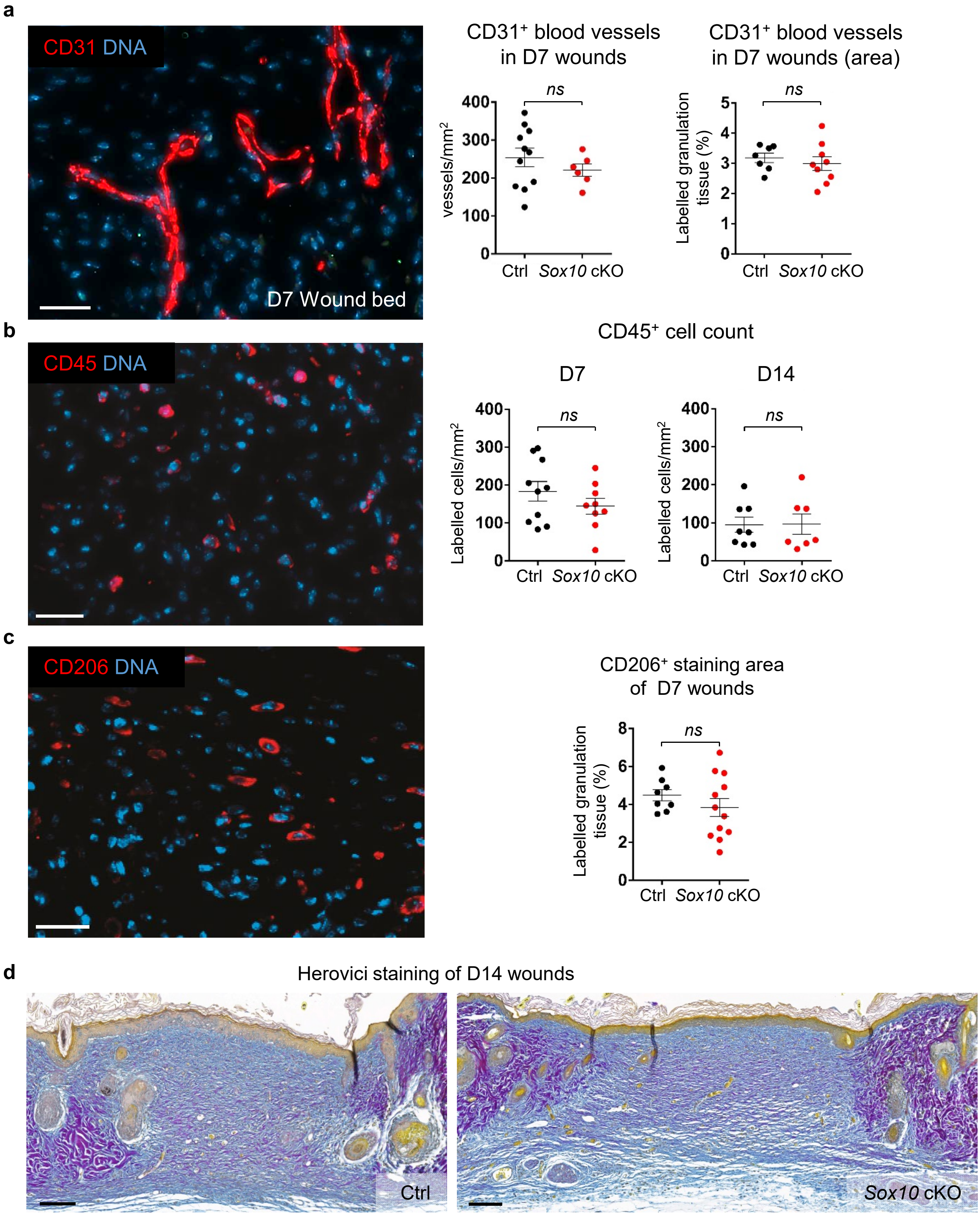
Supplementary Figure 2

Supplementary Figure 2 *Plp-CreER^{T2}*-mediated recombination of adult melanocytes in anagen hair follicles and absence of melanocytic lineage contribution to the wound bed of injured skin. **a** *Plp-CreER^{T2}* driven recombination of anagen murine skin shows only partial tdTomato reporter expression in hair follicles (HFs), 30h post TM injection. Co-labelling of tdTomato (red) and the melanocytic marker Dopachrome tautomerase Dct (green). **b** Quantification of percentage of HFs displaying no, partial or complete *Plp-CreER^{T2}* mediated recombination of their respective melanocytic population, 30h post-TM injection (n=220 HFs, N=1). **c** Immunolabelling for tdTomato reporter (red) and Dct (green) of *Plp-CreER^{T2}* and *Tyr-CreER^{T2}* traced melanocytic cells in D7 wound bed and in an adjacent HF fails to reveal traced melanocytes in the granulation tissue upon injury. Sections were counter stained with Hoechst 33258 (blue). **d** Immunofluorescence staining of tdTomato^{+} *Plp-CreER^{T2}* traced cells (red) in granulation tissue with melanocyte marker Dopachrome tautomerase (Dct) (green) and quantification of the percentage of Dct^{+} per tdTomato^{+} cells in the granulation tissue of injured skin at D7 (N=3, n=8) and D14 (N=2, n=5). **e** Immunofluorescence staining of tdTomato^{+} *Plp-CreER^{T2}* traced cells (red) with myofibroblast marker alpha smooth muscle actin (α-SMA) (green) and quantification of the percentage of α-SMA^{+} per tdTomato^{+} cells in the granulation tissue of injured skin at D7 (N=3 animals, n=11 wounds) and D14 (N=2, n=6). Scale bars, 50μm.



Supplementary Figure 3

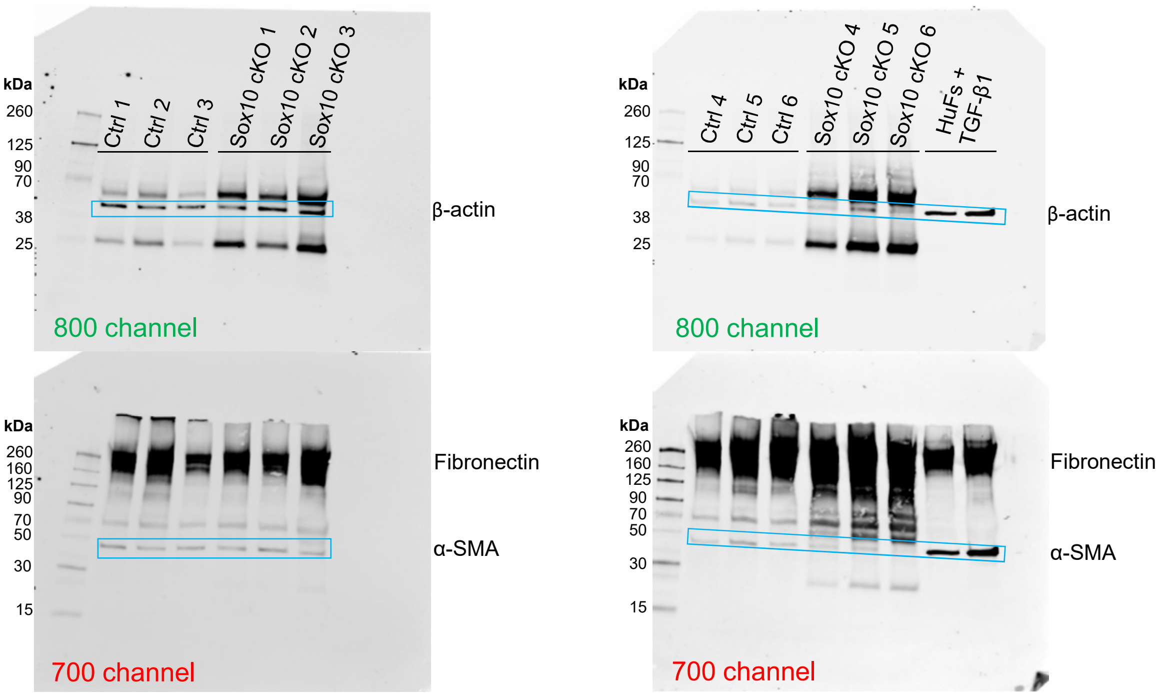
Supplementary Figure 3 Fate of *Plp-CreER*^{T2}-traced cells after *Sox10* cKO. **a** Schematic of the murine model used to trace glial cells in skin of *Sox10* cKO mice. **b** Immunolabelling of Sox10 (green) and tdTomato tracer (red) of D14 *Sox10* cKO wound bed. Black arrowhead, tdTomato^{+} Sox10^{-} cell; white arrowhead, tdTomato^{+} Sox10^{+} cell **c**,**d** Corresponding quantification of Sox10 expression among *Plp-CreER*^{T2}-traced tdTomato^{+} cells (**c**) within nerve bundles (NBs) and (**d**) in the wound bed (N=2 animals, n=4 wounds for each condition). Scale bar, 20µm.



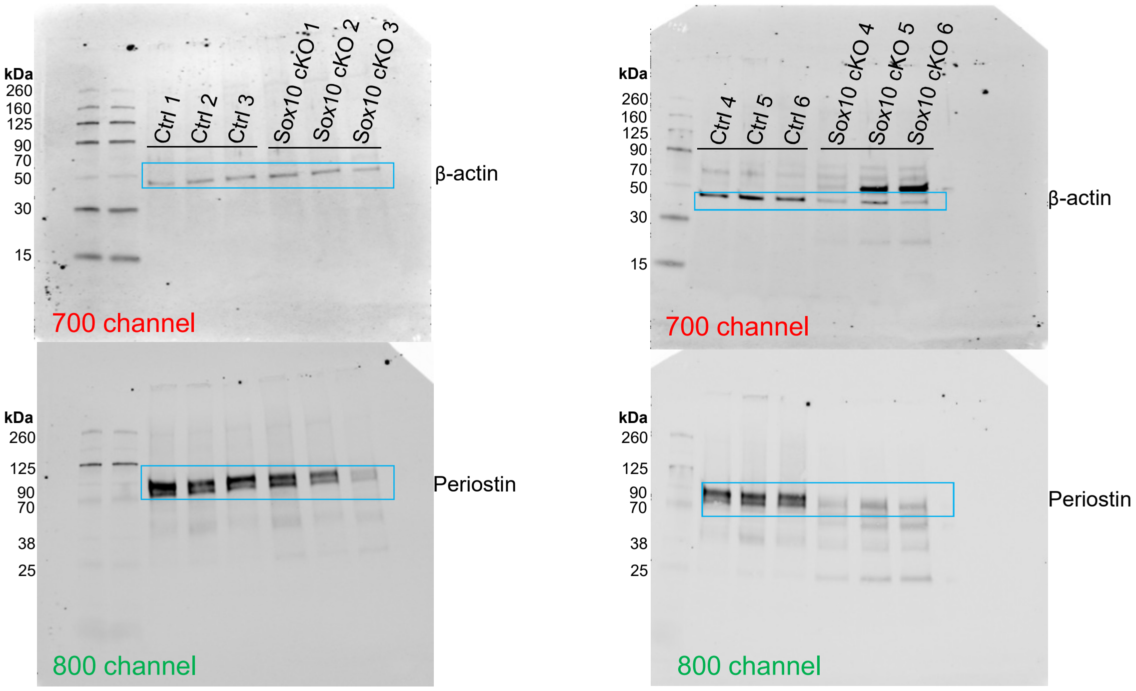
Supplementary Figure 4

Supplementary Figure 4 Neovascularization, immune cell infiltration and collagen maturation are not affected upon loss of glial contribution to tissue repair. **a** Immunolabelling of CD31 (red) in granulation tissue at D7 and related quantification of number of blood vessels mm^{-2} and percentage of $CD31^+$ area per total granulation tissue surface in skin wounds at D7 did not display noticeable differences upon loss of *Sox10*. **b** Immunolabelling of CD45 (red) in granulation tissue at D7 and quantification of $CD45^+$ cells in the skin wounds at D7 and D14 did not show any difference upon *Sox10* depletion. **c** Immunolabelling of CD206 (red) in granulation tissue at D7 and quantification of $CD206^+$ area in skin wounds at D7 showed no significant changes upon *Sox10* cKO. **d** Herovici staining for collagen maturation performed on D14 sections of Ctrl and *Sox10* cKO wounds. Data are represented as mean±SEM of N=3, n=11 (Ctrl), N=2, n=6 (*Sox10* cKO) (**a** – blood vessels mm^{-2}); N=3, n=7 (Ctrl), N=6, n=9 (*Sox10* cKO) (**a** – blood vessel area); N=3, n=10 (Ctrl D7), N=5, n=8 (Ctrl D14); N=5, n=9 (*Sox10* cKO D7), N=4, n=7 (*Sox10* cKO D14) (**b**); N=5, n=8 (Ctrl), N=8, n=12 (*Sox10* cKO) (**c**) Scale bars, 25µm (**a-c**), 100µm (**d**).

a Western blot analysis of α-SMA in total D7 wound protein



b Western blot analysis of Periostin in total D7 wound protein



Supplementary Figure 5

Supplementary Figure 5 Full scans of western blots performed on lysed wound samples. **a** Full scans of α-SMA western blots corresponding to quantification in Figure 5j (N=3, n=6) Human fibroblasts treated with TGF-β1 were used as control. **b** Full scans of Periostin western blots corresponding to quantification in Figure 5k (N=3, n=6) Samples were standardized to β-actin expression.

Supplementary Table 1 Top upregulated growth factor and cell signalling related genes with reported functional relevance.

Gene name	Log2 FC	Reported function
Tnn	3.007	Tenascin-W mediates neurite repulsion from hippocampal explants[1] and has anti-adhesion matrix modulating properties[2,3].
Areg	2.826	EGFR ligand amphiregulin is a growth factor for keratinocytes important in wound healing[4,5]. TGFβ regulates amphiregulin to promote lung fibrosis[6]. Important in inflammatory wound response[7].
Tnc	2.742	Tenascin-C loss leads to corneal wound healing delay and decreased myofibroblast generation[8] and regulates myofibroblast recruitment after cardiac injury[9]. It is strongly expressed by Schwann cells during Wallerian degeneration[10].
Wisp1	2.546	Role in wound healing suggested[11].
Inhba	2.477	Subunit of activin – a crucial factor in wound healing[12]. Expressed in the granulation tissue[13].
Aspn	2.476	Anti-fibrotic. Found after spinal cord injury[14] Inhibits TGF-β/SMAD signalling in osteoarthritis settings[15,16].
Tnfsf14	2.309	LIGHT plays role in the resolution of inflammation in wound healing[17], promotes collagen deposition and epidermal thickening and fibrosis in mouse skin[18]. It has been shown to be upregulated at the site of regeneration following nerve injury, but not reported in Schwann cells[19,20].
Btc	2.306	EGF family protein that regulates new hair follicle formation, hair cycle induction and angiogenesis after wounding[21]. Induces Schwann cell migration[22].
Fgf5	2.173	FGF5 expression is increased upon injury[23]. Promotes angiogenesis [24] and regulates hair growth cycle[25]. Found to be upregulated in the Schwann cells of the injured nerve[26].
Epha3	2.162	EphaA3 receptor is upregulated upon spinal cord injury [27].
Ltbp2	2.092	As an inhibitor of FGF-2 may modulate wound repair and contribute to fibrotic diseases[28]
Hilpda	1.965	Induced by hypoxia and HIF1[29], an important factor in wound healing[30].
Cd38	1.912	CD38 is found on several cell types in the brain including astrocytes and facilitates recovery from the brain injury[31].
Cpz	1.911	Carboxypeptidase Z (CPZ) – ECM protein that modulates Wnt signalling[32] Function in wound healing has not been reported so far.
Trf	1.897	Provided by PNS and necessary in amphibian limb regeneration blastemas[33]. Expressed in Schwann cells after injury[34].

Pdgfb	1.889	PDGF is important in wound healing[35] Topical application of PDGF BB enhances wound healing[36], however, conflicting data on the effects of PDGF BB exists[37].
Metrn	1.868	Neurotrophic factor Meteorin regulates glial cell differentiation and promotes axonal extension[38] and promotes gliogenesis after striatal injury[39].
Bgn	1.792	Biglycan is an ECM proteoglycan able to induce proto-myofibroblast phenotype and migration of fibroblasts[40].
Hgf	1.746	HGF promotes wound healing[41–43] and is implicated in PNS development and injury repair[44,45].
Lgmn	1.707	Legumain is essential for recovery after spinal cord injury in zebra fish[46] and determines bone marrow stem cell differentiation[47].
Gfra1	1.700	Found on Schwann cell membranes and can be secreted[48]. Important for injured motor neuron fate determination[49].
Igf1	1.646	IGF1 is important for keratinocyte migration and wound re-epithelialization[50]. Promotes wound healing in oestrogen-deprived mice[51]. Can be produced by Schwann cells upon injury[52] and facilitates nerve regeneration[53].

Supplementary Table 2 Top upregulated TGF-β signalling related genes with reported functional relevance.

Gene name	Log2 FC	Reported function
Postn	3.044	Activates TGF-β pathway[54]. Promotes wound healing[55,56] and myofibroblast differentiation in the wound[57]. Important for wound melanoma metastasis[58] and Schwann cell migration[59]. Astroglial periostin promotes axonal regeneration after spinal cord injury[60].
Adam12	2.628	Contributes to TGF-β signalling[61]. Secreted form promotes myogenesis[62], while anchored form interferes with re-epithelialization[63].
Fbn2	2.557	Found in wounds[64]. Needed for proper activation of latent TGF-β[61]. Sequesters BMP complexes in a latent state[65,66].
Wisp1	2.546	Role in wound healing suggested[11]. Inhibits SMAD2 mediated TGF-β1 signalling in osteoblasts[67].
Inhba	2.477	Subunit of activin – a crucial factor in wound healing[12] Expressed in the granulation tissue[13].
Aspn	2.476	Found after spinal cord injury[14] Inhibits TGF-β/SMAD signalling in osteoarthritis settings[15,16].
Ltbp2	2.092	May bind and modulate FGF-2 effects in wound repair and contribute to fibrotic diseases[28]. Does not bind to latent TGF-β, but might indirectly regulate the activation of TGF-β by releasing LTBP-1 from microfibrils[68,69].
Dab2	1.871	Dab2 attenuates brain injury by targeting TGF-β signalling pathway[70] and modulates TGF-β function in cancer[71].
Loxl2	1.716	Loxl2 promotes TGF-β signalling and is implicated in tissue fibrosis and fibroblast-to-myofibroblast conversion by inducing TGF-β2 secretion[72,73].
Plod1	1.697	Generates hydroxylysine residues from lysine residues in collagen peptides[74]. Mechanical state of the matrix can directly control the efficacy of TGF-β activation[75].
Cilp	1.638	Inhibition of TGF-β1 signalling[76]. TGF-β1 induces CILP suggesting functional feedback loop[77].
Lox	1.606	Profibrotic – increases ECM stiffness[78]. Binds to mature TGF-β1 and enzymatically regulates its signalling in the bone[79].
Tgfbi	1.455	Is induced by TGF-β and plays role in wound healing[80]. Inhibition of TGFBIp expression leads to reduced myofibroblast differentiation[81].
Bmp1	1.431	BMP1-like proteinases are essential to the wound healing of skin[82] BMP1 controls TGF-β1 activation[83].
Fstl1	1.369	Failure of wound closure in the absence of Follistatin1[84]. Binds BMP4[85].
Fbn1	1.271	Fbn1 regulates TGF-β1 bioavailability[86].

Plod2	1.258	Important enzyme in fibrosis[87]. Expression is regulated by an alternative downstream TGF-β1 activation mechanism[88]. Regulates ECM stiffness – myofibroblast differentiation[89].

Supplementary Table 3 Top upregulated chemotaxis and inflammation related genes with reported functional relevance.

Gene name	Log2 FC	Reported function
Cxcl5	3.653	A potent neutrophil chemoattractant during allergic airway inflammation[90].
Il1rl1	3.461	The resulting soluble and receptor proteins have emerged as key regulators of the inflammatory process implicated in a large variety of human pathologies[91].
Trem2	3.048	TREM1 and TREM2 activate myeloid cells by signalling through the adaptor protein DAP12[92].
Tnfsf14	2.309	LIGHT plays role in the resolution of inflammation in wound healing[17], promotes collagen deposition and epidermal thickening and fibrosis in mouse skin[18]. It has been shown to be upregulated at the site of regeneration following nerve injury, but not reported in Schwann cells[19,20].
Pla2g7	2.229	PAF acetylhydrolase has the substrate specificity and lipoprotein association of the native enzyme, and blocks inflammation in vivo[93].
Ccl8	1.700	Monocyte chemotactic protein-2 activates CCR5[94].
Cfp	1.648	Properdin plays a key role in allergen-induced airway inflammation and represents a potential therapeutic target for human asthma[95].
Cd36	1.450	A scavenger receptor involved in immunity, metabolism, angiogenesis, and behavior[96].
Cxcl2	1.417	It promotes the recruitment of myeloid-derived suppressor cells[97].

Supplementary Table 4 Top upregulated migration and adhesion related genes with reported functional relevance.

Gene name	Log2 FC	Reported function
Postn	3.044	Activates TGF-β pathway[54]. Promotes wound healing[55,56] and myofibroblast differentiation in the wound[57]. Important for wound melanoma metastasis[58] and Schwann cell migration[59]. Astroglial periostin promotes axonal regeneration after spinal cord injury [60].
Col8a1	2.817	Necessary for migration and proliferation of vascular smooth muscle cells and thus, has a potential role in the maintenance of vessel wall integrity and structure, in particular in atherogenesis[98].
Adam12	2.628	Anchored form interferes with re-epithelialization[62]. Marker that identifies a distinct pro-inflammatory subset of platelet-derived growth factor receptor-α-positive stromal cells that are activated upon acute injury in the muscle and dermis[99].
Emcn	2.561	Interferes with the assembly of focal adhesion complexes and inhibits interaction between cells and the extracellular matrix[100].
Thbs4	2.299	Role for the astrocyte-secreted protein Thbs4 in the migration of newly formed neurons within the RMS to the olfactory bulb[101].
Cdh11	2.225	Regulates collagen and elastin synthesis, both affecting the mechanical properties and contractile function of animal tissues[102].
Ccl6	2.224	Also known as MIP-1, it is abundant in acute wounds and serves as macrophage chemoattractant[103,104]. Leads to CCR1 mediated signalling[105].
Mfap4	2.125	May contribute to the elastic fibre assembly and/or maintenance[106].
Thbs2	1.922	Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Ligand for CD36 mediating antiangiogenic properties[107].
Ccdc80	1.764	Promotes cell adhesion and matrix assembly[108].
Fbln2	1.687	Acts as an adapter that mediates the interaction between FBN1 and ELN[109].
Mfap5	1.216	Protein associated with elastic fibre microfibrils[110].
Spp1	1.179	Binds tightly to hydroxyapatite. Appears to form an integral part of the mineralized matrix[111].

Supplementary Table 5 Top upregulated ECM related genes with reported functional relevance.

Gene name	Log2 FC	Reported function
Apln	3.778	Ectopic expression in keratinocytes induces enlarged but not leaky blood vessels in the dermis[112].
Col8a1	2.817	Necessary for migration and proliferation of vascular smooth muscle cells and thus, has a potential role in the maintenance of vessel wall integrity and structure, in particular in atherogenesis[98].
Adam12	2.628	Marker that identifies a distinct pro-inflammatory subset of platelet-derived growth factor receptor-α-positive stromal cells that are activated upon acute injury in the muscle and dermis[99].
Col1a1	2.616	Mutation in the gene cause Ehlers-Danlos syndrome, which is a connective tissue disorder characterized by hyperextensible skin, atrophic cutaneous scars due to tissue fragility and joint hyperlaxity[113]. Structural element of Type I Collagen, an ECM component important for wound matrix integrity at different stages of tissue repair[114].
Emcn	2.561	Interferes with the assembly of focal adhesion complexes and inhibits interaction between cells and the extracellular matrix[100]
Fbn2	2.557	Found in wounds[64]. Needed for proper activation of latent TGF-β[65]. Sequesters BMP complexes in a latent state[65,66].
Col3a1	2.543	Mutation in the gene cause Ehlers-Danlos syndrome 3 which is a connective tissue disorder characterized by hyperextensible skin, atrophic cutaneous scars due to tissue fragility and joint hyperlaxity. Is the major ligand of ADGRG1 in the developing brain and binding to ADGRG1 inhibits neuronal migration and activates the RhoA pathway by coupling ADGRG1 to GNA13 and possibly GNA12[115].
Eln	2.369	Essential determinant of arterial morphogenesis. Possess regulatory function during arterial development, controlling proliferation of smooth muscle and stabilizing arterial structure[116].
Col1a2	2.345	Structural element of Type I Collagen, an ECM component important for wound matrix integrity at different stages of tissue repair[114]. Loss of Col1a2 can cause Ehlers-Danlos syndrome[117].
Col5a2	2.343	Mutation in the gene cause Ehlers-Danlos syndrome classic type which is a connective tissue disorder characterized by hyperextensible skin, atrophic cutaneous scars due to tissue fragility and joint hyperlaxity[118].
Col6a5	2.090	Mutations in the gene reported to be associated with atopic dermatitis using a family-based association analysis[119].
Col5a1	2.020	Mutation in the gene cause Ehlers-Danlos syndrome classic type which is a connective tissue disorder characterized by hyperextensible skin, atrophic cutaneous scars due to tissue fragility and joint hyperlaxity[118].
Col6a1	1.964	COL6A1 may serve participate in the initiation and progression of cervical cancer. It correlates with poor prognosis in cervical cancer patients[120].

Serpine1	1.864	May function as a major control point in the regulation of fibrinolysis[121].

Supplementary Table 6 Top upregulated angiogenesis related genes with reported functional relevance.

Gene name	**Log2 FC**	**Reported function**
Esm1	4.015	May play role in new blood vessel formation, affects VEGF bioavailability[122].
Cxcl5	3.653	CXCL5 is required for increased intestinal angiogenesis during resection-induced adaptation[123].
Vash1	2.369	Vash1 inhibits neo-vascularization upon injury[124].
Sfrp2	2.302	Sfrp2 inhibits apoptosis in Hypertrophic scars[125].
Robo4	1.933	SLIT3/ROBO4 pathway is required for MSC-guided vascularization in engineered tissues[126].
Mdk	1.751	Mdk is associated with PGRN and promotes hepatocellular carcinoma angiogenesis[127]. Astrocyte secreted Mdk promotes CNS repair after injury[128].
Hgf	1.746	Enhances angiogenesis in skin wounds[41]. Scatter factor (hepatocyte growth factor) is a potent angiogenesis factor *in vivo*[129].
Fbln2	1.687	FBLN2 isoform has an important tumour-suppressive and anti-angiogenic role in nasopharyngeal carcinoma[130].
Vcan	1.678	Versican V2 isoform enhances angiogenesis by regulating endothelial cell activities[131].

Supplementary Table 7 Genotyping primers.

Allele	**Forward sequence**	**Reverse sequence**
Cre	CTATCCAGCAACATTTGGGCCAGC	CCAGGTTACGGATATAGTTCATGAC
Pten^{lox}	CAAGCACTCTGCGAACTGAG	AAGTTTTTGAAGGCAAGATGC
Rosa-LacZ	GGTCGGCTTACGGCGGTGATTT	AGCGGCGTCAGCAGTTGTTTTT
Sox10^{lox}WT	CAGGTGGGCGTTGGGCTCTT	TCCCAGGCTAGCCCTAGTG
Sox10^{lox}pos		GTGAGCCTGGATAGCAGCAG
TdTomato null	AAGGGAGCTGCAGTGGAGTA	CCGAAAATCTGTGGGAAGTC
TdTomato pos	CTGTTCCTGTACGGCATGG	GGCATTAAAGCAGCGTATCC

Supplementary Table 8 Primary antibodies.

Epitope	Reactivity	Producer	Catalog Nr.	Dilution
β-actin	human / mouse	Sigma	A5316	WB, 1:5000
CD271/p75	human / mouse	Alomone Labs	ANT-007	IF, 1:200
CD31	human / mouse	Abcam	ab28364	IF, 1:200
CD45	mouse	BD Pharmingen	550539	IF, 1:200
C-JUN	human / mouse	SC Biotechnology	SC-1694	IF, 1:200
DCT	human / mouse	SC Biotechnology	SC-10451	IF, 1:250
GFAP	human / mouse	Dako	Z0034	IF, 1:300
KI67	mouse	BioLegend	652402	IF, 1:100
LAMININ	human / mouse	Sigma	L9393	IF, 1:200
MBP	human / mouse	Abd Serotec	aa82-87	IF, 1:300
Neurofilament-M	human / mouse	EMD Millipore	AB1987	IF, 1:300
pAKT	human / mouse	Cell Signalling	4058	IF, 1:200
pERK1/2	human / mouse	Cell Signalling	9101	IF, 1:300
Periostin	human / mouse	SC Biotechnology	SC-49480	IF, 1:200 WB 1:1000
pSMAD2 (138D4)	human / mouse	Cell Signalling	3108	IF, 1:300
RFP	NA	EMD Millipore	AB3216	IF, 1:100
α-SMA	human / mouse	Sigma	A2547	IF, 1:100
α-SMA	mouse/rat	Abcam	ab5694	WB, 1:1000
SOX10	human / mouse	SC Biotechnology	SC-17342	IF, 1:100
TdTomato	NA	LS Bio	LS-C340696	IF, 1:200

Supplementary Table 9 Secondary antibodies.

Secondary antibody	**Producer**	**Catalog Nr.**
Cy3 Donkey anti-goat IgG (H+L)	Jackson	705-165-147
Alexa Fluor 488-conjugated AffiniPure Donkey anti-goat IgG (H+L)	Jackson	705-545-147
Cy3 Donkey anti-rabbit IgG (H+L)	Jackson	711-165-152
Alexa Fluor® 488-AffiniPure Donkey Anti-Rabbit IgG (H+L)	Jackson	711-545-152
Alexa Fluor 647-conjugated Affin Pure Donkey anti mouse IgG	Jackson	715-605-150
Alexa Fluor® 647-AffiniPure Donkey Anti-Rat IgG (H+L)	Jackson	712-605-153
Biotin-SP Donkey anti-rabbit IgG (H&L)	Jackson	711-065-152
HRP Streptavidin	Jackson	016-030-084
IRDye 800 CW Donkey anti-goat	Li-Cor	926-32214
IRDye 800 CW Donkey anti-mouse	Li-Cor	926-32212
RDye 680 LT Donkey anti-rabbit	Li-Cor	926-68022

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