A

No Cre   + Cre

B

	Brightfield	Tomato	EGFP
BAT			
WAT			

C

	Brightfield	Tomato	EGFP	
Kidney				
Lung				

DAPI Tomato EGFP

D

Testis   a   b
Ovary   c   d

DAPI Tomato EGFP

% Offspring with global reporter expression

aP2-Cre male   *aP2-Cre* female

E

Tumor-free survival

Days

— *Adipoq-Cre;SmoM2*
— *aP2-Cre;SmoM2*

F

Relative expression

Cre⁻ Cre⁺   Cre⁻ Cre⁺
  WAT   BAT

***   ***

G

Tumor-free survival

Days

— *Ucp1-Cre;SmoM2*
— *aP2-Cre;SmoM2*

H

Relative expression

Cre⁻ Cre⁺   Cre⁻ Cre⁺
  WAT   BAT

***

Figure S1. Related to Figure 1. Localization of aP2-Cre expressing cells in *aP2-Cre;R26-mT/mG* animals.

(A) Schematic of the *R26-mT/mG* allele and *aP2-Cre* mediated recombination.

(B) Representative whole mount images of BAT (intrascapular brown adipose) and WAT (inguinal white adipose) from *R26-mT/mG* mice (n = 3). Scale bars, 3mm.

(C) Representative whole mount and fixed tissue sections of lung and kidney from *aP2-Cre;mT/mG* mice (n = 3). Scale bars, 3mm (whole mount), 50 µm (tissue sections). Arrowheads denotes perineal adipose.

(D) Representative fixed tissue sections of testis (a and b) and ovaries (c and d) from *aP2-Cre;mT/mG* mice and percent of global Cre recombination observed in *aP2-Cre* mice (male n = 36; female n = 698). Scale bars, 500 µm (a and c), 100 µm (b and d). Arrowhead denotes adipose adjacent to ovary.

(E) Kaplan-Meier Survival curves showing tumor free survival of *Adipoq-Cre;Smo*$^{M2/+}$ mice (n = 6) in comparison to AS mice (n = 49) (Hatley et al., 2012).

(F) Real-time PCR of SmoM2-YFP expression in BAT and WAT from *Adipoq-Cre;Smo*$^{M2/+}$ and *Smo*$^{M2/+}$ mice. Data shown are normalized to *Actb* expression and expressed relative to Cre negative controls (n = 3, mean ± SEM).

(G) Kaplan-Meier Survival curves showing tumor free survival of *Ucp1-Cre;Smo*$^{M2/+}$ (n = 23) mice in comparison to AS mice (n = 49) (Hatley et al., 2012).

(H) Real-time PCR of SmoM2-YFP expression in BAT and WAT from *Ucp1-Cre;Smo*$^{M2/+}$ and *Smo*$^{M2/+}$ mice. Data shown are normalized to *Actb* expression and expressed relative to Cre negative controls (n = 3, mean ± SEM).
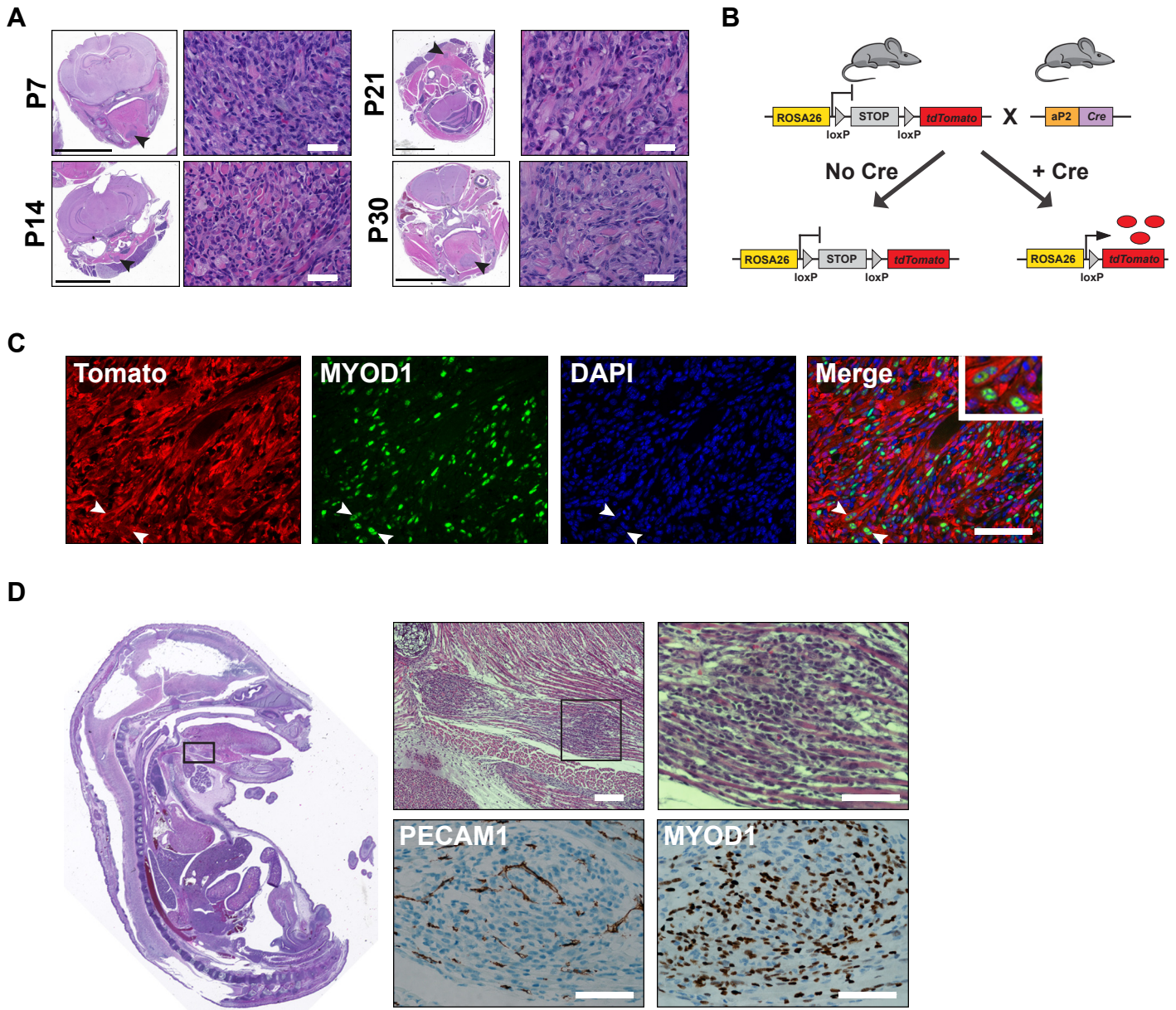
*** p < 0.001

Figure S2. Related to Figure 2. Characterization of tumors from a*P2-Cre; Smo*[M2/+]*;R26-tdTom* animals.

(A) Gross cross sections and histology (H & E) of head and neck tumors from P7, P14, P21 and P30 AST mice. Arrows denote tumor localization. Scale bars, 5 mm (left), 25 μm (right).

(B) Schematic of AT breeding.

(C) Representative immunofluorescence of AST tumors showing MYOD1 (green), Tomato (red) and DAPI (blue)(n = 3). Arrows denotes region of high magnification inset shown on upper right. Scale bars, 50 μm.

(D) Representative sagittal sections of E16.5 *Fabp4-Cre;Smo*[M2/+] embryos (n = 3). Insets of boxed regions are shown at low magnification (scale bar, 100 μm) and high magnification (scale bar, 50 μm).

A
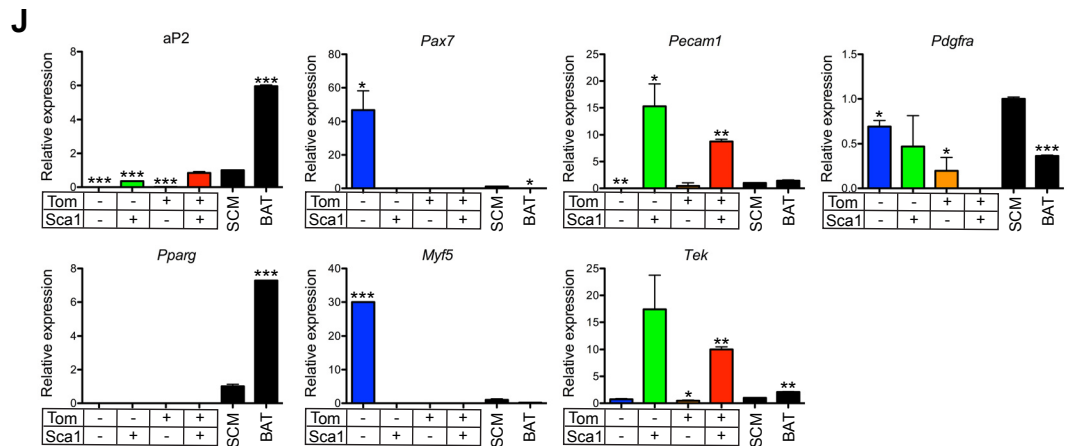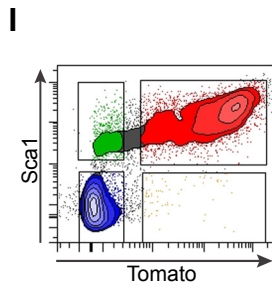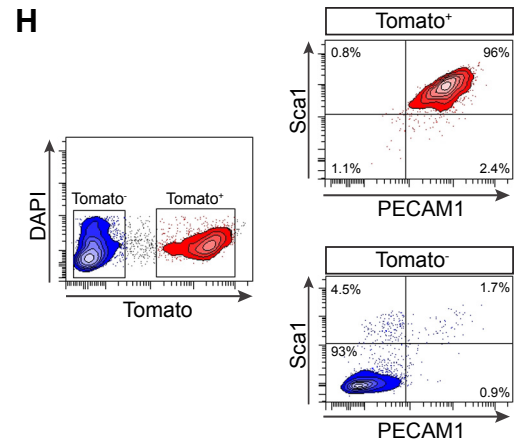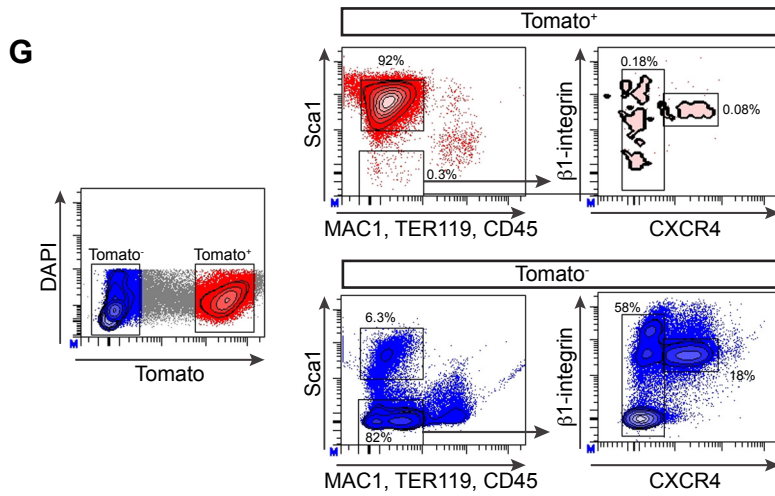
Tomato Pax7 DAPI

B

% of DAPI⁺ cells — PAX7⁺, Tom⁺, colocalized

C

−Log₁₀ p value vs Log Ratio Tom⁺ versus Tom⁻

Pdgfra, Peg3, Myf5, Peg3 (blue); Sox18, Tek, Gata2, Cdh5, Kdr, Pecam1 (red)

D

Log₂ ratio Tom⁺/Tom⁻ — Genes up in Twist2⁺ cells

E

Tomato PECAM1 DAPI

F

Tomato, PECAM1, DAPI, Merge

G

DAPI vs Tomato — Tomato⁻, Tomato⁺

Tomato⁺: Sca1 vs MAC1, TER119, CD45 (92%, 0.3%); β1-integrin vs CXCR4 (0.18%, 0.08%)

Tomato⁻: Sca1 vs MAC1, TER119, CD45 (6.3%, 82%); β1-integrin vs CXCR4 (58%, 18%)

H

DAPI vs Tomato — Tomato⁻, Tomato⁺

Tomato⁺: Sca1 vs PECAM1 (0.8%, 96%, 1.1%, 2.4%)

Tomato⁻: Sca1 vs PECAM1 (4.5%, 1.7%, 93%, 0.9%)

I

Sca1 vs Tomato

J

aP2, Pax7, Pecam1, Pdgfra, Pparg, Myf5, Tek
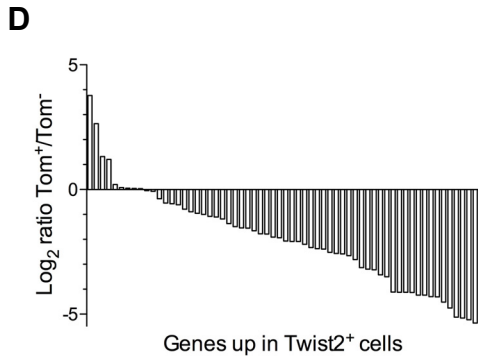
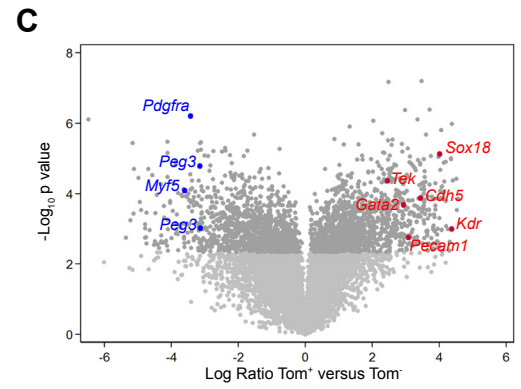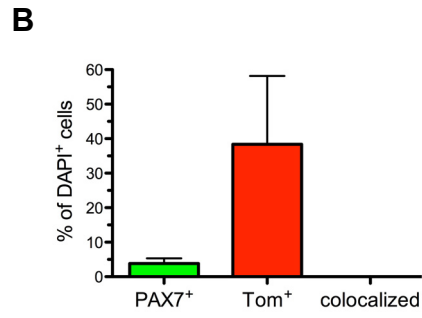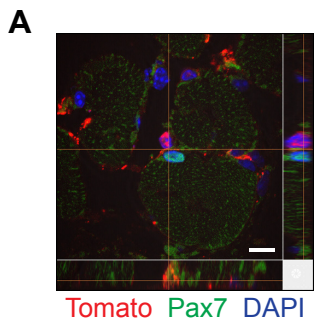Relative expression; Tom / Sca1 / SCM / BAT

Figure S3. Related to Figure 3. aP2-Cre labels endothelial cells within the muscle interstitium.

(A) Confocal microscopy illustrating 3D cross sections from SCM of AT mice. PAX7 (green), TOMATO (red) and DAPI (blue) shown. Scale bar, 10 µm.

(B) Quantitation of Tomato and PAX7 co-localization from sections in Figure 3A. 909 cells were counted from 22 fields from SCM sections of 5 AT mice. 34 (3.8%) of the cell nuclei were PAX7$^+$. There was no co-localization with any of the 335 tomato positive cells and PAX7. Bars are mean $\pm$ SEM.

(C) Volcano plot of the Log of the p value versus the log fold change in expression between the tomato positive (Tom$^+$) and negative (Tom$^-$) cells isolated from AT SCM by FACS. Solid grey dots indicate FDR > 0.05.

(D) Log$_2$ ratio of expression in Tom$^+$ versus Tom$^-$ cells isolated from SCM of AT mice for genes enriched in Twist2 expressing muscle interstitial cells (Liu et al., 2017) illustrating only 4 of 63 genes similarly enriched in Tom$^+$ cells from AT SCM.

(E) Gross histology and immunofluorescence of E18.5 AT sagittal section showing PECAM1 (green), TOMATO (red) and DAPI (blue). Scale bars, 100 µm.

(F) High magnification split channel images of boxed inset from (D). Scale bars, 50 µm.

(G-H) Flow cytometric analysis of Tom$^+$ and Tom$^-$ cells from AT SCM for MAC1, Ter119, CD45, Sca1, β1integrin and CXCR4 (G) and Sca1 and PECAM1 (H).

(I) FACS plot showing isolation of Tom$^-$;Sca1$^-$, Tom$^-$;Sca1$^+$, Tom$^+$;Sca1$^-$, and Tom$^+$;Sca1$^+$ cells from AT SCM.

(J) Real-time PCR of isolated populations from (I) compared to mature SCM and BAT from *Smo*$^{M2/M2}$ mice. Data shown are normalized to *Actb* expression and expressed relative to mature SCM. Bars are mean $\pm$ SEM.

*p < 0.05, ** p < 0.01, *** p < 0.001

A

| H&E | DESMIN | MYOD1 | PECAM1 |
| CD34 | KDR | ERG | MECA32 |

B

| H&E | DESMIN | MYOD1 |
| Myogenin | S100 | PECAM1 |

C

| H&E | DESMIN | MYOGENIN | MYOD1 |
| CK-Oscar | CK-HMW | VIMENTIN | S100 |
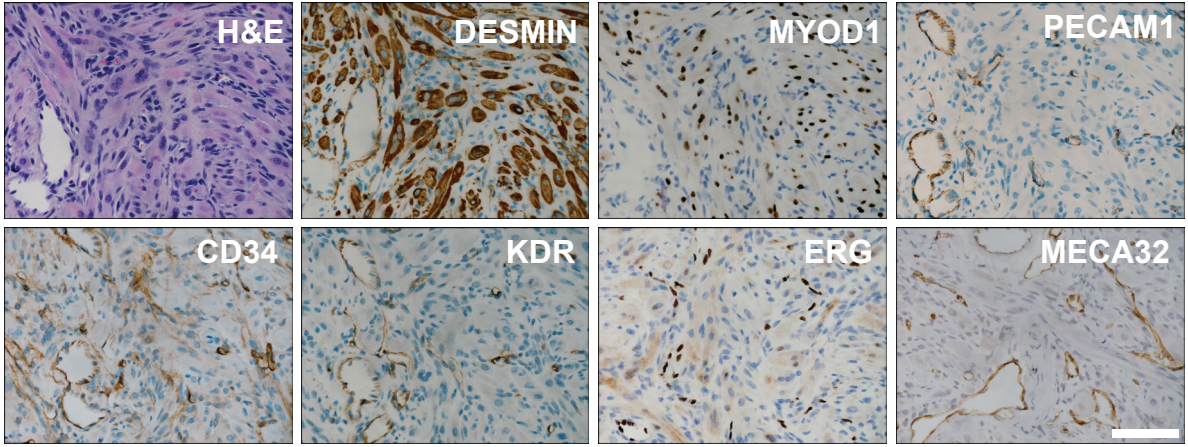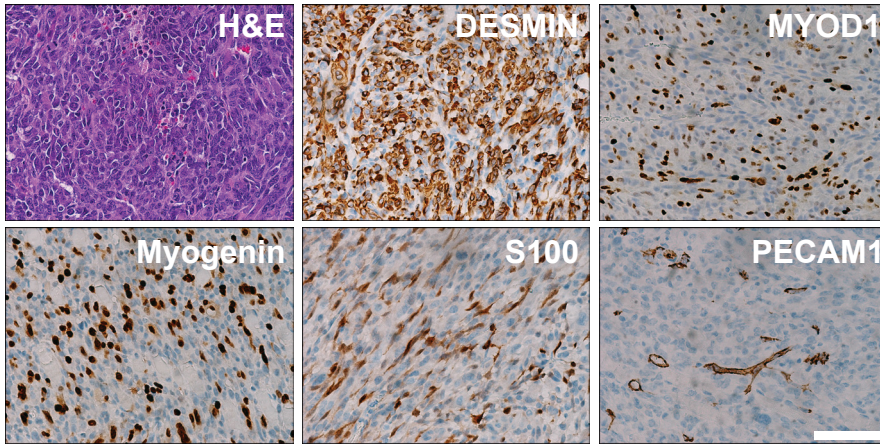
Figure S4: Related to Figure 4. Oncogenic KRAS does not drive FN-RMS in *aP2-Cre* expressing cells

(A) Representative H&E staining and IHC for RMS markers (DESMIN and MYOD1) and angiosarcoma markers (PECAM1, CD34, KDR, ERG, and MECA32) in *aP2-Cre;Smo$^{M2/+}$;R26-tdTom* FN-RMS tumors (n = 3). Scale bars, 50 μm.

(B) *aP2-Cre;LSL-Kras^{G12D};Cdkn2a$^{Flox/Flox}$* malignant triton tumor showing H&E staining and IHC (DESMIN, MYOD1, MYOGENIN, S100 and CD31)(n = 1). Scale bars, 50 μm.

(C) *aP2-Cre;LSL-Kras^{G12D};Cdkn2a$^{Flox/Flox}$* pleomorphic spindle cell carcinoma showing H&E, and IHC (DESMIN, MYOGENIN, MYOD1, CK-OSCAR, CK-HMV, VIMENTIN and S100)(n = 1). Scale bars, 50 μm.
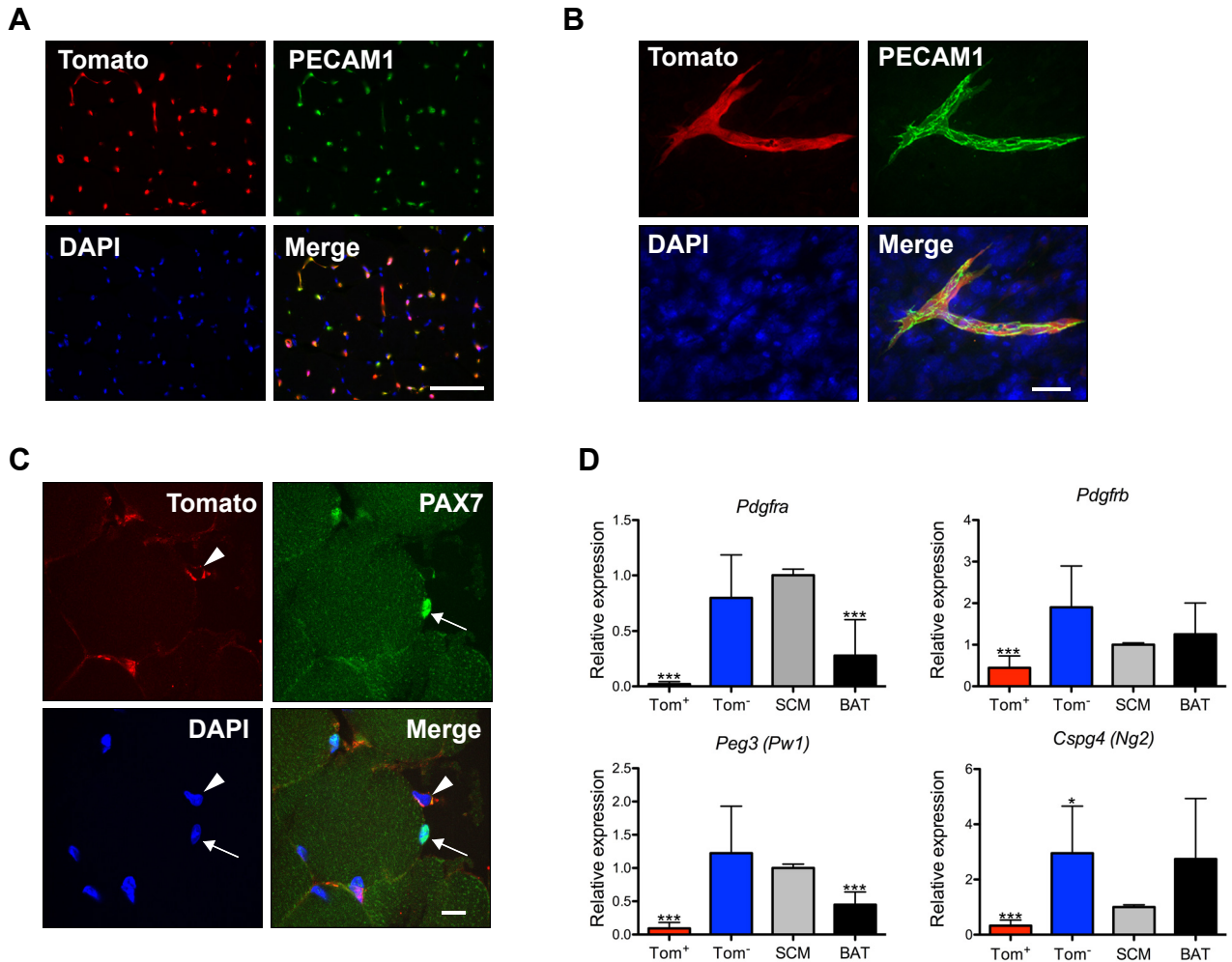
Figure S5. Related to Figure 5. Further characterization of aP2-Cre expressing cells from aP2-Cre;Smo^{M2/+};R26-tdTom SCM.

(A) Immunofluorescence of AST SCM cross sections for PECAM1 (green), TOMATO (red) and DAPI (blue). Scale bars, 50 μm.

(B) Immunocytochemistry of *aP2-Cre* expressing cells. Mononuclear cells were isolated from AST SCM, grown until confluence and stained for PECAM1 (green) TOMATO (red) and DAPI (blue). Scale bars, 50 μm.

(C) Immunofluorescence of AST SCM cross sections for PAX7 (green), TOMATO (red) and DAPI (blue). Scale bars, 10 μm. Arrowheads denote Tom$^+$ cells and arrows denote PAX7$^+$ cells.

(D) Real-time PCR of isolated Tom$^+$ and Tom$^-$ cells from AST SCM in comparison to SmoM2 SCM and BAT. Data shown are normalized to *Actb* expression and expressed relative to mature SCM (n = 3, mean ± SEM)

*p < 0.05, ** p < 0.01, *** p < 0.001

A

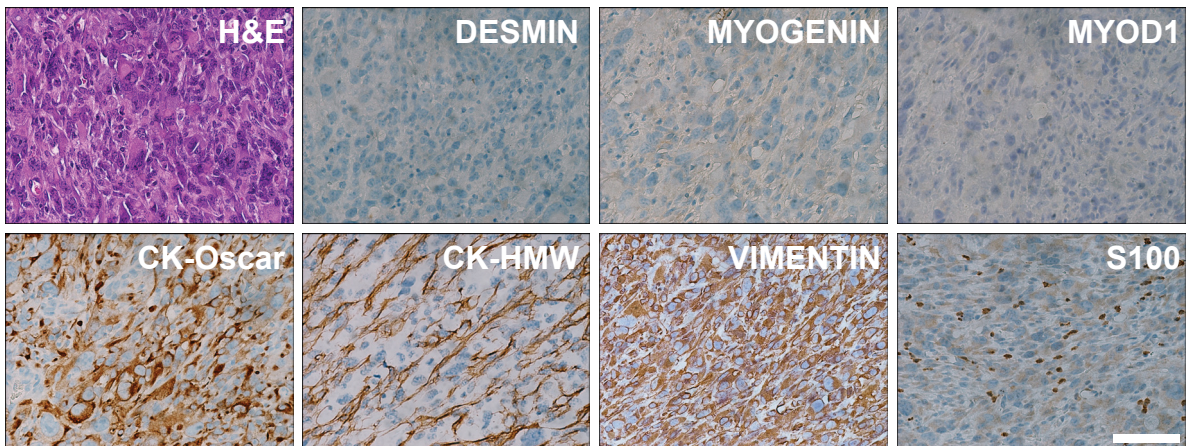GO term

- response to interferon-gamma — 7
- cellular response to cytokine stimulus — 11
- cellular response to interferon-gamma — 6
- extracellular structure organization — 9
- extracellular matrix organization — 9
- cell chemotaxis — 6
- chemotaxis — 7
- taxis — 7
- negative regulation of response to external stimulus — 6
- interferon-gamma-mediated signaling pathway — 4
- type I interferon signaling pathway — 4
- response to type I interferon — 4
- cellular response to type I interferon — 4
- cytokine-mediated signaling pathway — 7
- regulation of angiogenesis — 5
- positive regulation of angiogenesis — 4
- regulation of vasculature development — 5
- regulation of type I interferon-mediated signaling pathway — 3

$-\log_{10}$ p value

B

PC2 17%

PC3 13.3%   PC1 29.9%

- ● Tomato-positive/PECAM1-negative
- ● Tomato-positive/PECAM1-positive
- ● Tomato-negative/PECAM1-negative

C

Log ratio
Tomato-pos:Pecam1-neg cells/SCM

Log ratio aP2-Cre;SmoM2 tumor/SCM

D

- RD_SOFT_TISSUE
- RH41_SOFT_TISSUE
- SJRH30_SOFT_TISSUE
- RH30_SOFT_TISSUE
- KYSE140_OESOPHAGUS
- G402_SOFT_TISSUE

$-\log_{10}$ p value

E

$-\log_{10}$ p value

Log ratio Tom$^+$/PECAM1$^+$ from tumor
vs Tom$^+$ from SCM

F

GO term

- angiogenesis — 60
- regulation of epithelial cell migration — 38
- regulation of endothelial cell migration — 30
- regulation of angiogenesis — 37
- regulation of vasculature development — 38
- positive regulation of cell migration — 44
- positive regulation of cell motility — 44
- positive regulation of cellular component movement — 44
- positive regulation of epithelial cell migration — 23
- positive regulation of locomotion — 44

$-\log_{10}$ p value

G

Aldh1a3, *Bmp4*, *Foxd1*, *Foxf1*, *Hey1*, *Heyl*, *Lef1*, *Lgr4*, *Msc*, *Prox1*, *Sox9*, *Tbx3*

Relative expression

| Tomato | − | + | + |
| Pecam1 | − | − | + |

H

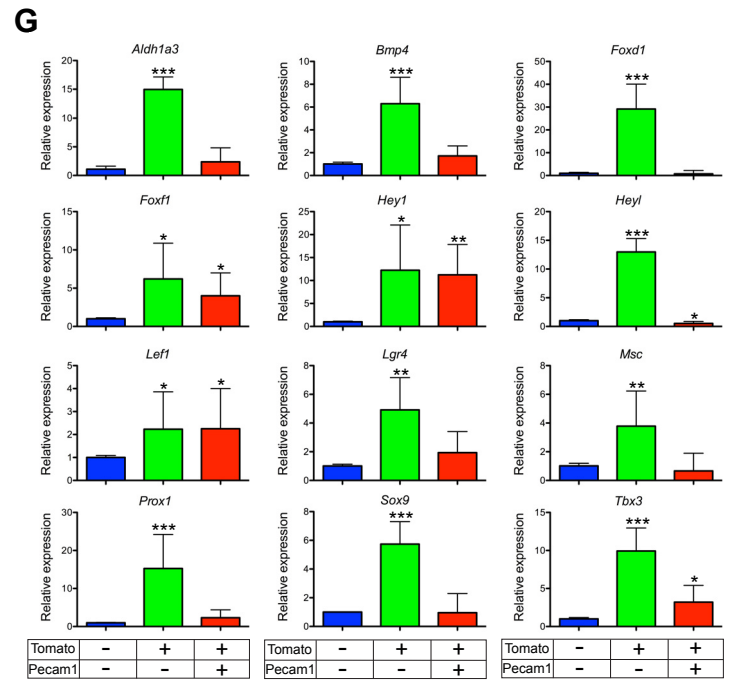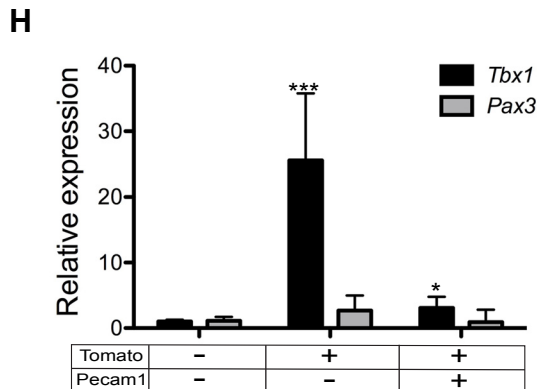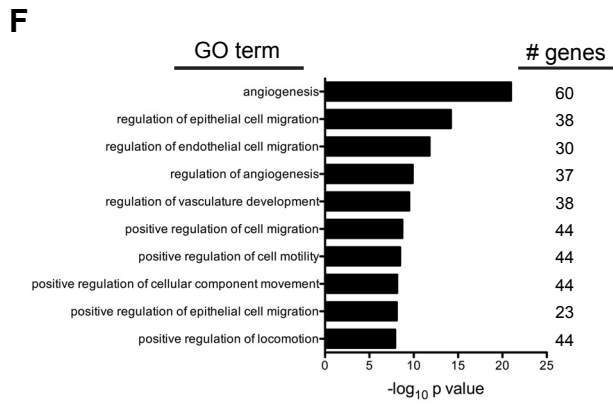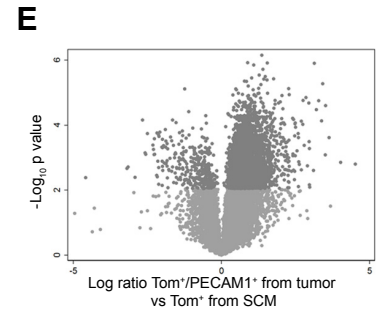Relative expression

- ■ *Tbx1*
- □ *Pax3*

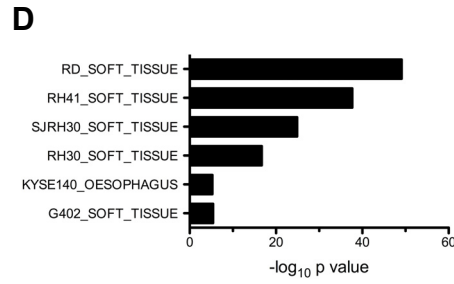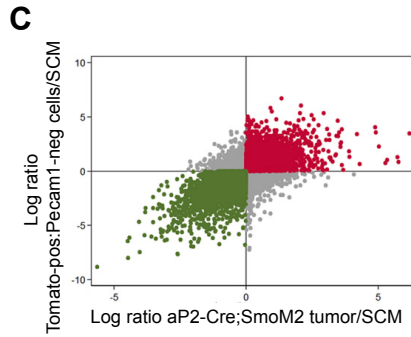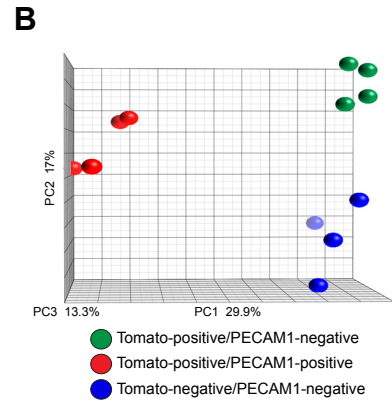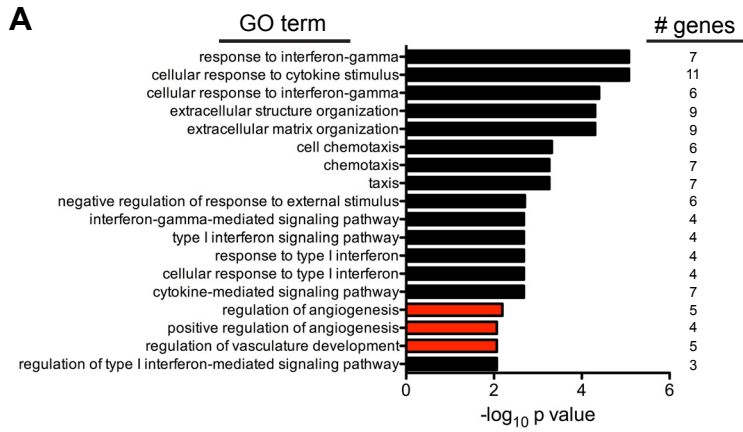| Tomato | − | + | + |
| Pecam1 | − | − | + |

Figure S6. Related to Figure 6. Characterization of cell populations isolated from *aP2-Cre;Smo$^{M2/+}$;R26-tdTom* tumors by FACS

(A) GO term analysis of genes upregulated in *aP2-Cre;Smo$^{M2/+}$* tumors in comparison to *Myog-Cre;Smo$^{M2/+}$* tumors (GSE 40359) (Hatley et al., 2012).

(B) Principal component analysis of isolated tumor cell populations from AST animals. Coordinates describe 60.2% of the data (PC1 = 29.9%, PC2 = 17% and PC3 = 17%).

(C) Comparison of isolated Tom$^+$PECAM1$^-$ tumor cells to whole tumors from *aP2-Cre;Smo$^{M2/+}$* animals. 55% of 16,957 gene pairs showed agreement in genes upregulated or downregulated in comparison to normal SCM. Pearson correlation = 0.56 (GSE 40359 and 85834).

(D) Comparison of genes enriched in isolated Tom$^+$PECAM1$^-$ with respect to Tom$^-$PECAM1$^-$ to genes enriched in cancer cell lines from cancer cell line encyclopedia.

(E) Volcano plot of the Log of the p value versus the log fold change in expression between the Tom$^+$ cells isolated from AT SCM and Tom$^+$PECAM1$^+$ cells isolated from AST tumors by FACS. Solid grey dots indicate 4663 genes with FDR > 0.05. Of total 4663 genes 4518 (97%) were similarly expressed.

(F) GO term analysis of genes upregulated in Tom$^+$PECAM1$^+$ cells with respect to Tom$^-$PECAM1$^-$ cells.

(G) Real-time PCR of populations isolated from AST tumors by FACS. Data shown are normalized to *Actb* expression and expressed relative to Tom$^-$PECAM1$^-$ cells (n = 3, mean ± SEM).

(H) Real-time PCR analysis of *Tbx1* and *Pax3* expression in populations isolated from AST tumors. Data shown are normalized to *Actb* expression and expressed relative to Tom$^-$PECAM1$^-$ cells (n = 3, mean ± SEM).

*p < 0.05, ** p < 0.01, *** p < 0.001

Table S1. Related to Figure 6. Genes upregulated in *aP2-Cre;Smo*$^{M2/+}$ tumors when compared to *Myogenin-Cre;Smo*$^{M2/+}$ tumors (GSE 40359) ($\geq$ 2 fold; p value < 0.05).

Gene	aP2-Cre;Smo$^{M2/+}$/ Myogenin-Cre;Smo$^{M2/+}$		Gene	aP2-Cre;Smo$^{M2/+}$/ Myogenin-Cre;Smo$^{M2/+}$	
	Fold change	p value		Fold change	p value
Mmp10	9.1	0.048	C1qb	2.5	0.006
Ii	8.6	0.013	H2-DMa	2.5	0.007
Ii	8.6	0.008	H2-Dmb1	2.5	0.010
H2-Ab1	6.9	0.010	D11Ertd759e	2.5	0.017
H2-Ab1	6.8	0.020	Fbln1	2.4	0.020
H2-Eb1	6.6	0.004	Rgs5	2.4	0.036
H2-Ab1	5.9	0.009	1500015O10Rik	2.4	0.001
H2-Ab1	5.8	0.005	Fcgr3	2.4	0.002
Comp	4.6	0.023	Xlr4a	2.4	0.014
Ppfibp1	4.4	1.99E-06	Cfd	2.4	0.002
2310061N23Rik	4.1	0.006	C1qg	2.3	0.021
Cxcl14	3.9	0.037	Ibsp	2.3	0.010
H2Aa	3.7	0.005	Psmb8	2.3	1E-04
Spp1	3.4	0.024	Laptm5	2.2	0.021
Ii	3.3	0.002	Aif1	2.2	0.002
Fcrl3	3.3	0.003	H2-Q2	2.2	0.008
Dbp	3.2	0.002	Ms4a6d	2.2	0.015
Lama1	3.2	0.008	Col181a	2.2	0.043
H2-DMa	3.2	0.006	Psmb9	2.2	0.003
Gbp2	3.1	0.048	Mpeg1	2.2	0.006
Ccl8	3.0	0.017	Ly86	2.2	0.012
H2-L	2.9	0.001	Parp14	2.1	0.032
Oasl2	2.9	0.003	Hsp105	2.1	0.014
Wnt5a	2.9	0.042	LOC381292	2.1	0.004
H2-Dmb2	2.9	0.002	Ctsh	2.1	0.023
B2m	2.8	0.003	Scd1	2.1	9.36E-05
Gbp4	2.8	0.026	Wisp2	2.1	0.023
Col8a1	2.8	0.038	Tmepai	2.1	0.021
C1qtnf3	2.8	0.049	Wnt5a	2.1	0.011
Gvin1	2.7	0.037	Cx3cr1	2.1	0.016
Usp18	2.7	0.005	Cxcl16	2.1	0.02
H2-D1	2.7	0.006	Apoe	2.1	0.025
Cd52	2.7	0.032	Bcl2a1d	2.1	0.048
Cd72	2.6	0.002	Ptgis	2.1	0.017
Vcam1	2.6	0.035	Stat1	2.1	0.008
Slamf9	2.6	0.014	Sla	2.0	0.018
B2M	2.6	0.013	Chad	2.0	0.04
LOC56628	2.6	0.005	Oas1g	2.0	0.001
H2-L	2.6	0.003	Col81a	2.0	0.033
Ms4a7	2.5	0.005			

Table S2. Related to Figure 6. Gene ontology functional analysis of 382 genes upregulated in sorted Tom⁺PECAM1⁺ cells with respect to Tom⁻PECAM1⁻ cells isolated from AST tumors($\geq$ 2 fold; p value < 0.05).

GO Biological Process	Genes	Overlap	Adjusted p value
Actin-myosin filament sliding	*Mybpc1; Actn3; Actn2; Tnnc1; Tnnc2; Neb; Myl6b; Ttn; Acta1; Actc1; Des; Myh3; Myl1; Tnnt1; Tnnt2; Tnnt3; Myh8; Tnni1*	18/38	9.29E-16
Muscle filament sliding	*Mybpc1; Actn3; Actn2; Tnnc1; Tnnc2; Neb; Myl6b; Ttn; Acta1; Actc1; Des; Myh3; Myl1; Tnnt1; Tnnt2; Tnnt3; Myh8; Tnni1*	18/38	9.29E-16
Muscle contraction	*Ryr1; Chrna1; Smpx; Tshz3; Myl6b; Ttn; Csrp3; Sgca; Mb; Cacng1; Chrnb1; Mybpc1; Dtna; Actn2; Tnnc1; Tnnc2; Pgam2; Klhl41; Trdn; Acta1; Myh1; Des; Actc1; Myh3; Myl1; Tnnt1; Myot; Tnnt3; Myh8; Sntb1*	30/195	9.29E-16
Muscle system process	*Ryr1; Chrna1; Tshz3; Smpx; Atp2a1; Myl6b; Ttn; Csrp3; Sgca; Mb; Cacng1; Myog; Chrnb1; Mybpc1; Dtna; Actn2; Tnnc1; Tnnc2; Pgam2; Klhl41; Trdn; Acta1; Myh1; Actc1; Des; Myh3; Myl1; Tnnt1; Myot; Tnnt3; Myh8; Sntb1*	32/237	1.46E-15
Actin-mediated cell contraction	*Mybpc1; Actn3; Actn2; Tnnc1; Tnnc2; Neb; Myl6b; Ttn; Acta1; Actc1; Myh3; Des; Myl1; Tnnt1; Tnnt2; Tnnt3; Myh8; Tnni1*	18/46	5.76E-15
Tissue morphogenesis	**Lama5; Hhip; Lef1; Tcf21; Ttn; Sall1; Hey1; Sox18; Tnni1; Gpc3; Sostdc1; Sox9; Pitx2; Tbx1; Foxd1; Foxf1; Tnnc1; Ptch1; Wnt5a; Prox1; Bmp7; Pgf; Tbx3; Bmp4; Aldh1a3; Heyl; Actc1; Pax7; Tnnt2; Myf6; Met; Lgr4; Fgfr2; Frem2; Myf5**	**35/358**	**2.27E-13**
Actin filament-based movement	*Mybpc1; Actn3; Actn2; Tnnc1; Tnnc2; Neb; Myl6b; Ttn; Acta1; Actc1; Myh3; Des; Myl1; Tnnt1; Tnnt2; Tnnt3; Myh8; Tnni1*	18/61	2.51E-13
Regulation of muscle cell differentiation	*Tbx1; Myog; Cav3; Megf10; Tshz3; Mamstr; Foxf1; Prox1; Tbx3; Klhl41; Bmp4; Myod1; Myf6; Smyd1; Sox9; Cdh15; Rbm24; Fgfr2; Cdon; Myf5*	20/122	8.82E-11
Striated muscle contraction	*Chrna1; Dtna; Smpx; Tnnc1; Pgam2; Tnnc2; Klhl41; Ttn; Csrp3; Myh3; Actc1; Myl1; Tnnt1; Mb; Tnnt3; Myh8*	16/71	2.90E-10
Tube development	*Robo2; Tgfb2; Foxf2; Tshz3; Foxf1; Wnt5a; Tcf21; Cobl; Prox1; Gata2; Bmp7; Bmp4; Heyl; Calb1; Sall1; Sox18; Plxna2; Sox9; Fgfr2; Stra6*	20/164	9.35E-09

Table S3. Related to Figure 7. Genes upregulated in both Tom$^+$PECAM1$^+$ and Tom$^+$PECAM1$^-$ cells with respect to Tom$^-$PECAM1$^-$ cells isolated from AST tumors by FACS. Data shown as fold change from expression arrays.

Gene	Tom$^-$;PECAM1$^-$ /Tom$^+$; PECAM1$^-$		Tom$^-$; PECAM1$^-$ /Tom$^+$; PECAM1$^+$		Tom$^+$; PECAM1$^-$ /Tom$^+$; PECAM1$^+$	
	Fold change	p value	Fold change	p value	Fold change	p value
9530026P05Rik	2.0	0.005	2.1	0.004	-1.1	0.741
9630013A20Rik	2.1	0.023	4.0	0.001	-1.9	0.013
Ablim3	2.3	0.020	16	1.1E-04	-7.0	8.2E-04
Adamts9	2.0	0.003	4.7	3.6E-05	-2.3	7.0E-05
Cdh13	2.3	0.001	4.8	2.1E-05	-2.1	0.001
Cdh5	2.1	0.005	36	1.8E-05	-17	3.8E-05
Chp2	2.4	0.008	5.1	2.3-04	-2.1	0.015
D930048N14Rik	2.1	0.002	2.6	4.4E-04	-1.2	0.186
Dach1	2.1	0.018	11	1.3E-04	-5.4	1.6E-05
Dock6	2.0	0.007	3.8	1.8E-04	-1.9	0.003
Enpp3	2.5	0.008	8.8	1.5E-04	-3.6	8E-04
Enpp6	4.4	0.002	4.7	0.003	-1.1	0.720
Gata2	2.0	0.006	4.7	5E-04	-2.3	0.010
Gt(ROSA)26Sor	2.4	1.1E-04	3.3	4.3E-05	-1.4	0.004
Itga3	2.0	0.003	4.4	5.1E-05	-2.2	0.002
Lama5	2.1	0.002	3.4	1.4E-04	-1.7	0.010
Lepr	3.7	1.5E-04	3.2	3.6 E-04	1.2	0.348
Lmo7	2.6	0.002	4.3	3.7E-04	-1.7	0.010
Mamstr	2.4	0.002	4.1	7.2E-04	-1.7	0.042
Mpzl1	2.1	0.004	2.0	0.004	1.0	0.870
Nqo1	2.5	0.002	2.6	0.005	-1.0	0.860
Pcdh17	2.9	0.017	4.8	0.004	-1.6	0.060
Plxna2	2.3	0.011	3.6	0.001	-1.6	0.050
Ptprk	2.3	0.015	4.3	8.1E-04	-1.9	0.014
Samd5	2.1	7.7E-04	5.4	1.5E-06	-2.6	1.9E-04
Sncaip	2.1	4.8E-04	7.9	1.5E-05	-3.8	4.7E-05
Sox18	3.1	8.7E-05	19	7.7E-06	-6.1	6.8E-05
Tanc1	2.1	8.1E-04	2.5	0.003	-1.2	0.393
Thsd7a	2.0	0.007	3.1	6.8E-04	-1.5	0.009
Tspan12	2.1	0.007	3.7	3.8E-04	-1.8	0.004
Tspan7	2.2	0.017	11	1.2E-04	-5.1	5.1E-05
Wipf3	2.5	0.034	2.3	0.032	1.1	0.736

Table S4. Related to STAR Methods. Antibodies used for Immunostaining.

Antigen	Sections	Catalog/ Vendor	Concentration	Antigen Retrieval	Secondary	Detection
CD34	FFPE	553731 BD bioscience	1:50	CC1 950-500 Roche	Omap Rat, 760-4457, Roche	DAB
Desmin	FFPE	RB-9014, ThermoFisher	1:500	CC1 950-500 Roche	OmniMap Rabbit, 760-4311, Roche	DAB
ERG	FFPE	ab133264, Abcam	1:1700	ER2 AR9640 Leica	Bond Polymer DS9800, Leica	DAB
CK-Oscar	FFPE	465-01 Covance	1:250	CC1, 950-500 Roche	Rabbit Anti-Mouse OmniMap Rabbit, 760-4311, Roche	DAB
CK-HMV	FFPE	M063029 DAKO	1:750	Proteinase K S302030 DAKO	Rabbit Anti-Mouse OmniMap Rabbit, 760-4311, Roche	DAB
KDR	FFPE -IF	AF644, R&D systems	1:50	pH6 Citrate Buffer C9999, Sigma	Anti-Goat HRP A16005, ThermoFisher	TSA – Fluorescein
	FFPE-IHC	AF644, R&D systems	1:20	Target Retrieval pH6 S1699 DAKO	Anti-Goat HRP SC-2042, Santa Cruz	Strep-HRP, DAB
Laminin	Frozen	L9393, Sigma	1:500	N/A	Anti-Rabbit Cy5 A10523, ThermoFisher	N/A
Meca32	FFPE	553849, BD Bioscience	1:50	Target Retrieval pH6 S1699 DAKO	Rat Polymer RT517L, Biocare Medical	DAB
MHC	Frozen	MF20, DSHB	1:25	N/A	Anti-Mouse AlexaFluor488 A11029, ThermoFisher	N/A
	FFPE	MF20, DSHB	1:25	pH6 Citrate Buffer C9999, Sigma	Anti-Mouse AlexaFluor488 A11029, ThermoFisher	N/A
MyoD1	FFPE-IF	M3512, DAKO	1:50	Target Retrieval pH9 S2367 DAKO	Goat Anti Mouse IgG1HRP S2969 SantaCruz	TSA – Fluorescein
	FFPE-IHC	386R-18, Cell Marque	undiluted	ER2 AR9640, Leica	Bond Polymer DS9800, Leica	DAB
Myogenin	FFPE-IHC	M3559, DAKO	1:200	Target Retrieval pH9 S2367 DAKO	Mouse on Mouse polymer HRP MM510L, Biocare Medical	DAB
Pax7	Frozen	DSHB	1:10	pH6 Citrate Buffer C9999, Sigma	Anti mouseIgG1 AlexaFluor488 A21121, ThermoFisher	N/A
Pecam1	Cultures/ Frozen	550274 BD bioscience	1:50	N/A	Anti Rat AlexaFluor488 A11006, ThermoFisher	N/A
	FFPE - IF	Dianova Dia 310	1:20	pH6 Citrate Buffer C9999, Sigma	Anti rat HRP AP136P, Millipore	TSA – Fluorescein
	FFPE-IHC	Dianova Dia 310	1:100	CC1 950-500 Roche	OmniMap Rat 760-4457 Roche	DAB
S100	FFPE-IHC	Z031129 Dako	1:2,000	CC1 950-500 Roche	OmniMap Rabbit, 760-4311, Roche	DAB
Tomato	Frozen (Pax7 only)	600-401-379 Rockland	1:100		Anti Rabbit AlexaFluor568, A11056, A10042 ThermoFisher	N/A
	FFPE-IHC	600-401-379 Rockland	1:100		Anti Rabbit AlexaFluor568, A11056, ThermoFisher	N/A
	RNAscope/ IHC	LS-C340696 LS Bio	1:20,000	CC1,950-500 Roche	OmniMap Rabbit, 760-4311, Roche	DAB
Vimentin	FFPE-IHC	NBP1-40730, Novus	1:1000	ER1, AR9961 Leica	Bond Polymer DS9800, Leica	DAB

Table S5. Related to STAR Methods. Antibodies used for Flow Cytometry.

	Clone	Catalog # /Company	Concentration
β-1 integrin-FITC	Ha2/5	561796 BD Biosciences	1:50
CD11b-APC	M1/70	553312 BD Biosciences	1:50
CD45-APC	30-F11	561018 BD Biosciences	1:50
CXCR4-Biotin	2B11/CXCR4	551968 BD Biosciences	1:50
Streptavidin PE-Cy7		25-431782 eBioscience	1:50
Pecam1-APC	Mec13.3	551262 BD Biosciences	1:50
Pecam1-FITC	Mec13.3	561813 BD Biosciences	1:50
Sca1-PerCP-Cy5.5	D7	25-5981-82 eBioscience	1:50
Ter119-APC		557909 BD Biosciences	1:50

Table S6. Related to STAR Methods. SYBR primers used for quantitative real-time PCR.

	Right Primer	Left Primer
Actb	ATGGAGGGGAATACAGCCC	TTCTTTGCAGCTCCTTCGTT
Aldh1A3	GACGAAAAAGGCATGAAGGA	TCAGCTGGCTGACCTTGTAG
aP2	CACTTTCCTTGTGGCAAAGC	AATGTGTGATGCCTTTGTGG
Bmp4	AGCCCGCTTCTGCAGGA	AAAGGCTCAGAGAAGCTGCG
Cdh5	CGTTGGACTTGATCTTTCCC	CGCCAAAAGAGAGACTGGAT
Cspg4	ACTCTGGTCAGAGCTGAGGG	TCTTACCTTGGCCTTGTTGG
Foxd1	GTCTGGTCCAAGAATCCGAA	GGGAGAGCGAAGGTAGGACT
Foxf1	TGGGCGACTGTGAGTGATAC	ACTCCCTGGAGCAGCCATAC
Gata2	GCCATAAGGTGGTGGTTGTC	CACTACCTGTGCAATGCCTG
Gli1	ATTGGATTGAACATGGCGTC	GGATGAAGAAGCAGTTGGGA
Hey1	TCCGATAGTCCATAGCCAGG	TTGCAGATGACTGTGGATCA
Heyl	TCTCTGCGCCGTTTCTCTAT	CCATCGATGTGGGTCAAGAG
Kdr	TCCAGAATCCTCTTCCATGC	CCAGAGACCCTCGTTTTCAG
Lef1	AAATGGGTCCCTTTCTCCAC	TCGTCGCTGTAGGTGATGAG
Myf5	GACAGGGCTGTTACATTCAGG	TGAGGGAACAGGTGGAGAAC
Myod1	GTCGTAGCCATTCTGCCG	AGCACTACAGTGGCGACTCA
Pax7	GTCGGGTTCTGATTCCACAT	GCGAGAAGAAAGCCAAACAC
Pdgfra	AGAAAATCCGATACCCGGAG	AGAGGAGGAGCTTGAGGGAG
Pdgfrb	TGGTATCACTCCTGGAAGCC	AACAGAAGACAGCGAGGTGG
Pecam1	AGTTGCTGCCCATTCATCAC	CTGGTGCTCTATGCAAGCCT
Peg3	TCAACTGATCTCCCCTTGCT	TTTGGAGACAACTGGCAAGA
Pparg	TCTTCCATCACGGAGAGGTC	GATGCACTGCCTATGAGCAC
Prox1	GGCATTGAAAAACTCCCGTA	TTGTGAGCTATACCGAGCCC
Ptch1	AATTCTCGACTCACTCGTCCA	CTCCTCATATTTGGGGCCTT
Sox9	TCCACGAAGGGTCTCTTCTC	AGGAAGCTGGCAGACCAGTA
Sox18	AAGTGCTGCACACGCAAC	CACAACGCAGTACTGAGCAAG
SmoM2-YFP	GGGATCCATTCATTCCCGCA	AAACGGCCACAAGTTCAGC
Tbx3	CATTGCCAGTGTCTCGAAAA	TCCCGGAAACAGAATTCATC
Tcf7l2	GGGATCATGATGAAGGGGTA	TAAATCCCGGGAAAGTTTGG
Tcf21	GGCTGGCGTCCAGCTACATCG	TGCCGGCCACCATAAAGGGC
Tomato	AGTTCATGTACGGCTCCAAGG	AGCGCGTGATGAACTTCGA
Tomato2	GGCATTAAAGCAGCGTATCC	CTGTTCCTGTACGGCATGG
Tek	TTTCGGCATCAGACACAAGA	CCGGCTTAGTTCTCTGTGGA
Vwf	CCGTCTTCAGTAGCTGGCAT	GTGTAAACGGGCATCTCCTC
Ucp1	AGAAGCCACAAACCCTTTGA	TCTCTGCCAGGACAGTACC