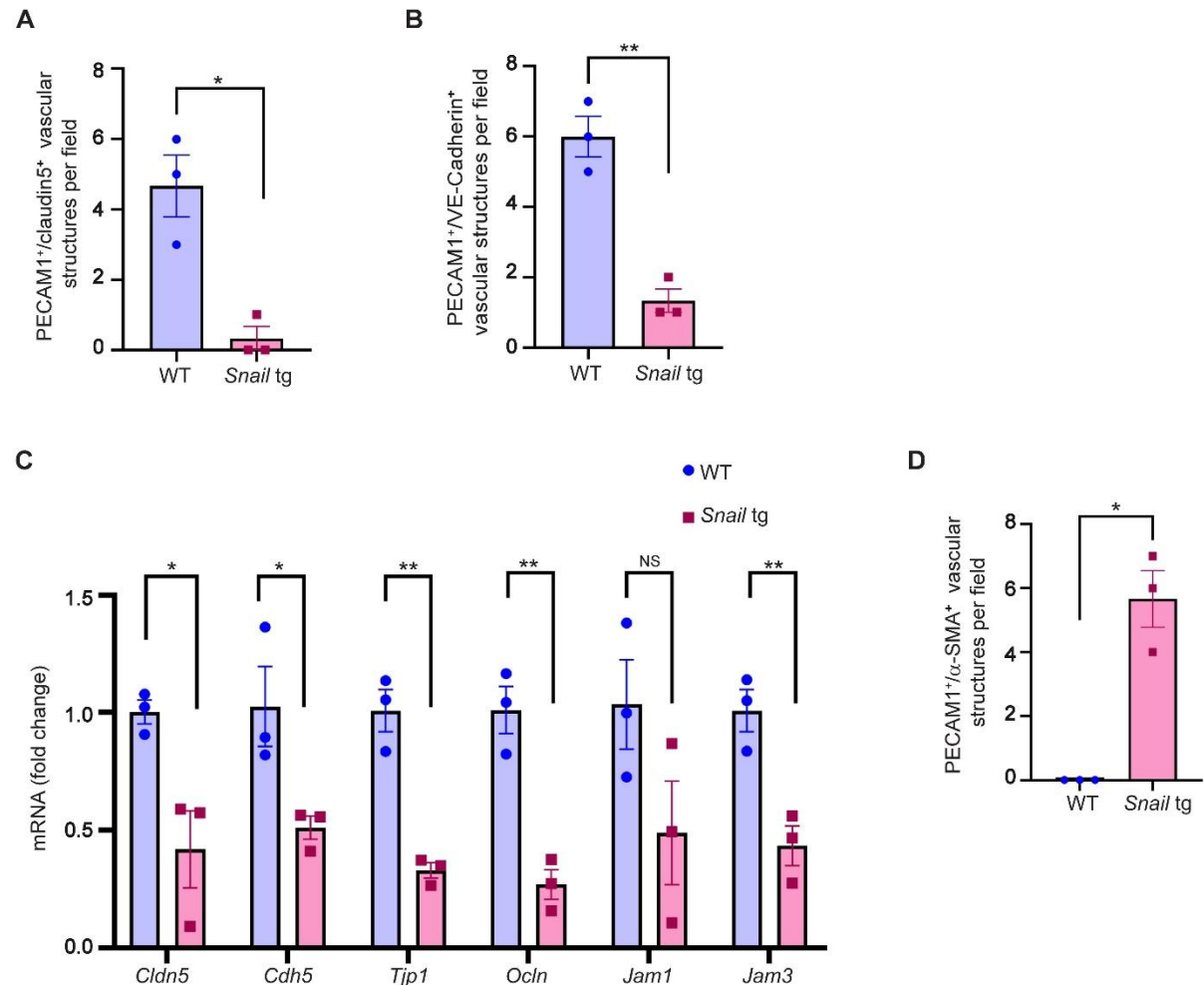


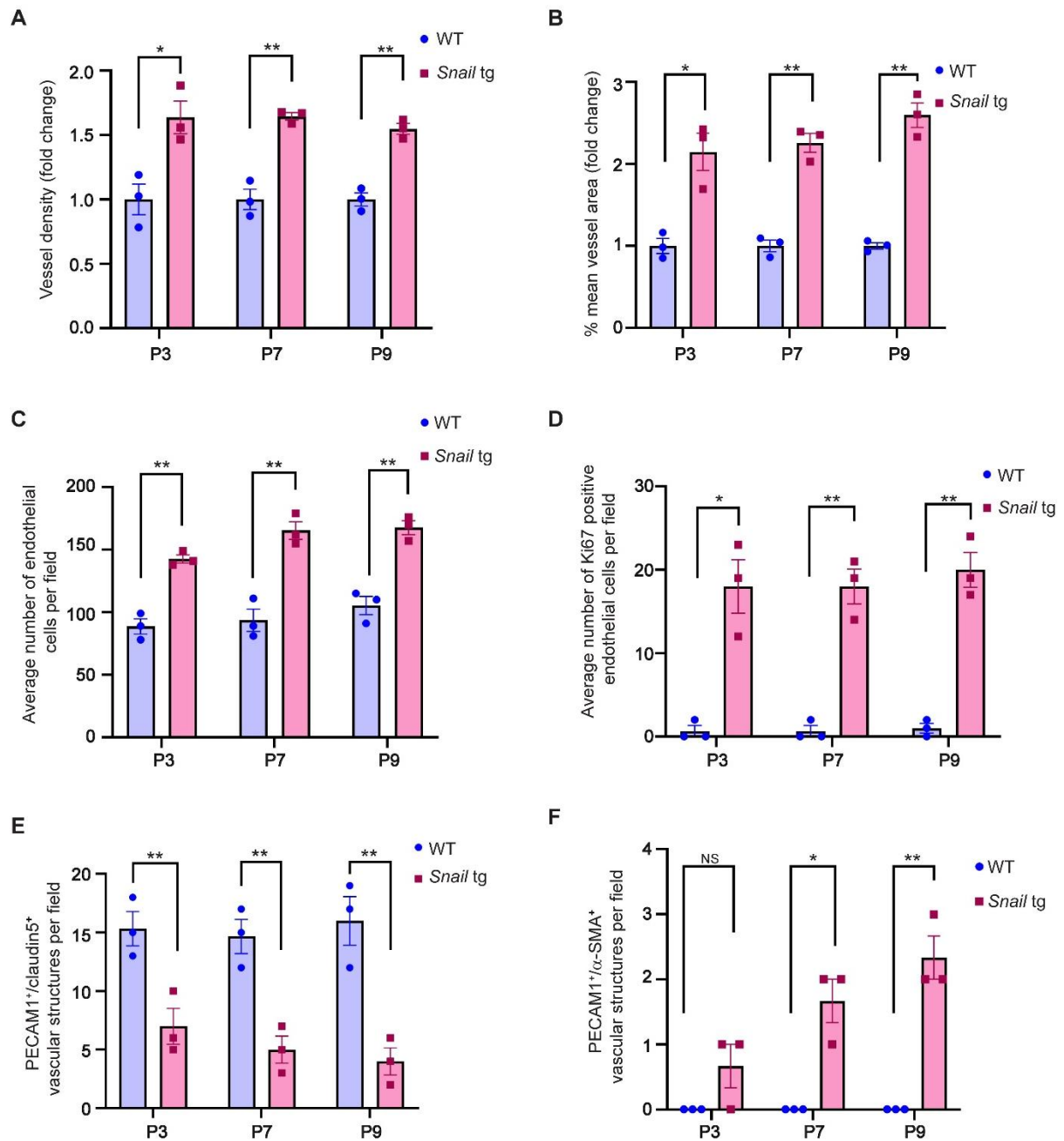
## Supplementary data

Supplementary Figure 1



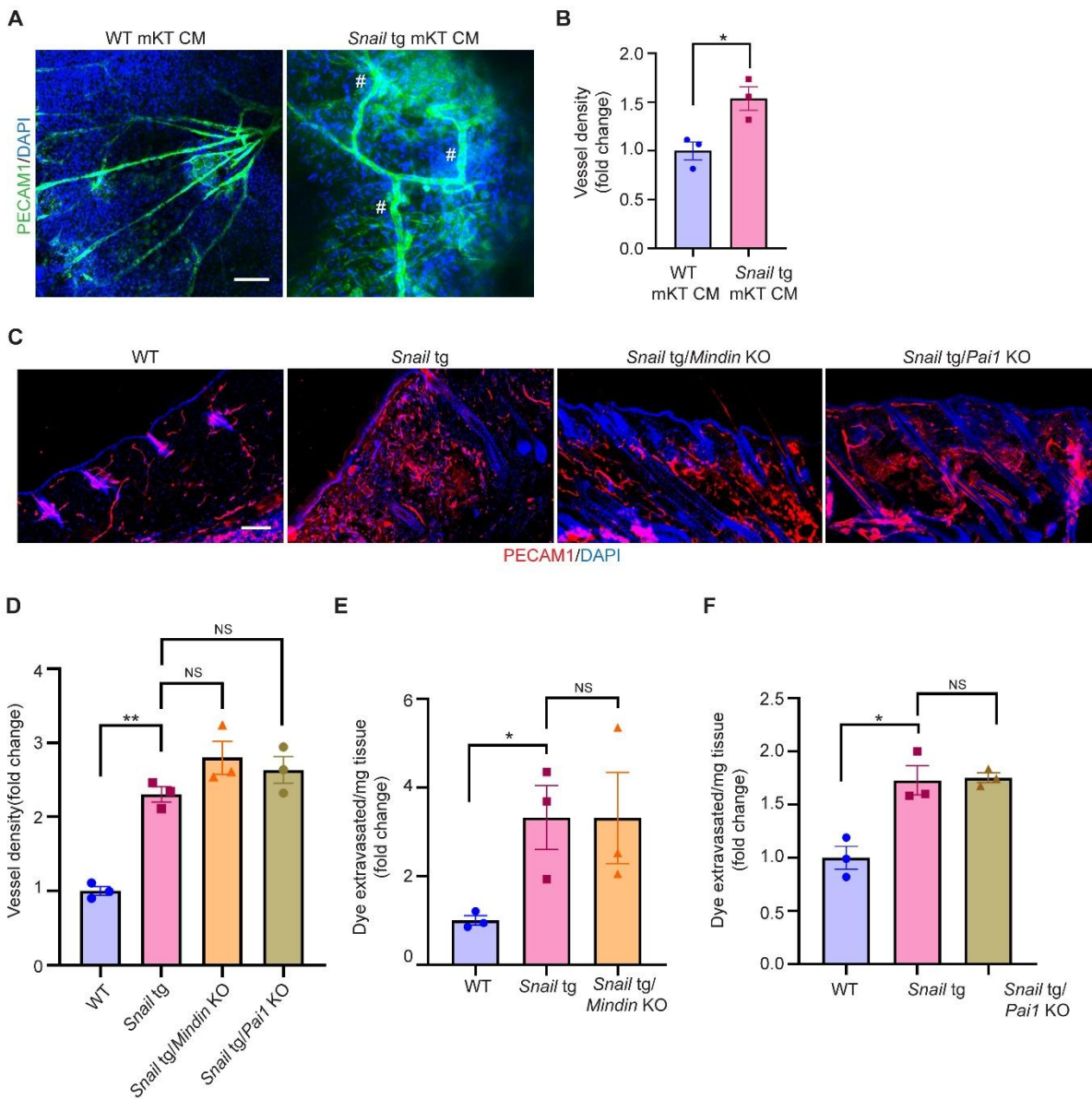
**Supplementary Figure 1: Adult *Snail* tg skin recapitulates the junctional perturbation and endoMT observed in SSC.** Quantification of (A) PECAM1<sup>+</sup>/claudin5<sup>+</sup> and (B) PECAM1<sup>+</sup>/VE-Cadherin<sup>+</sup> vascular structures in wild type (WT) and *Snail* tg mice skin. (C) qPCR analysis of gene expression of junction proteins (*Cldn5*, *Cdh5*, *Tjp1*, *Ocln*, *Jam1* and *Jam3*) in isolated endothelial cells from WT and *Snail* tg mice skin. (D) Quantification of PECAM1<sup>+</sup>/α-SMA<sup>+</sup> vascular structures in WT and *Snail* tg mice skin. Data are shown as mean ± SEM, p-values were calculated using unpaired Welch's t test. \* p < 0.05, \*\* p < 0.01, NS > 0.05. All experiments are n=3 biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

Supplementary Figure 2



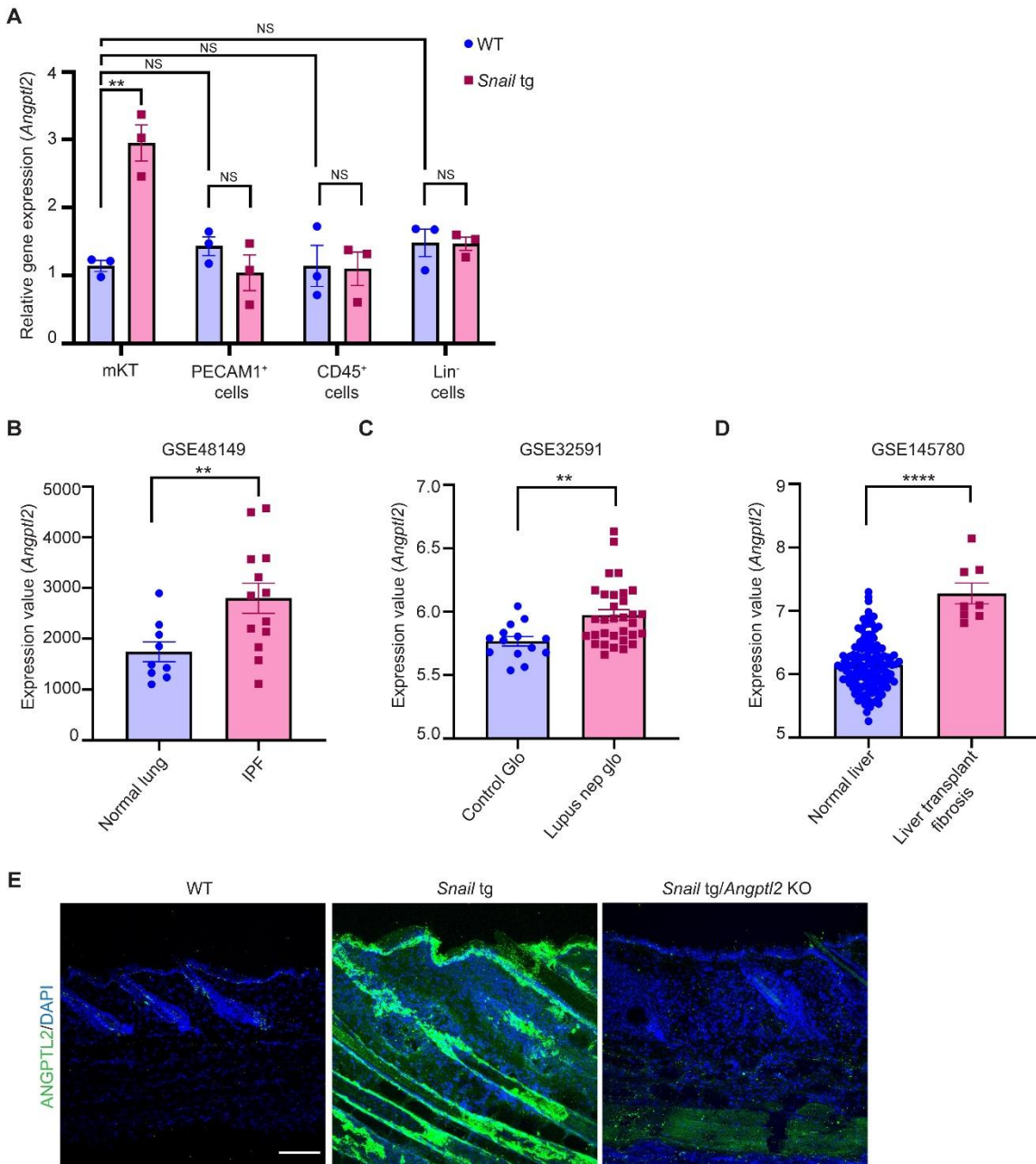
**Supplementary Figure 2: Developmental analysis of vascular morphometrics and junctional perturbation in *Snail* tg mouse skin.** Quantification of (A) vessel density, (B) mean vessel area, (C) number of endothelial cells, (D) PECAM-1<sup>+</sup>/Ki67<sup>+</sup> cells, (E) PECAM1<sup>+</sup>/claudin5<sup>+</sup> vascular structures and (F) PECAM1<sup>+</sup>/α-SMA<sup>+</sup> vascular structures in wild type (WT) and *Snail* tg mice skin at postnatal day 3, 7, and 9. Data are shown as mean ± SEM, p-values were calculated using unpaired Welch's t test. \* p < 0.05, \*\* p < 0.01, NS > 0.05. All experiments are n=3 biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

Supplementary Figure 3



**Supplementary Figure 3: Mindin and PAI1 do not mediate the vasculopathy in the *Snail* tg skin.** (A) PECAM1 (green) in skin explants treated with wildtype (WT) or *Snail* tg mouse keratinocyte (mKT) conditioned media. Dilated regions are marked by #. (B) Quantification of vessel density in skin explants treated with WT or *Snail* tg mKT conditioned media. (C) PECAM1 (red) in WT, *Snail* tg, *Snail* tg/*Mindin* KO and *Snail* tg/*Pai1* KO skin at P60. (D) Quantification of vessel density in WT, *Snail* tg, *Snail* tg/*Mindin* KO and *Snail* tg/*Pai1* KO skin at P60. (E), (F) Quantification of Evan's blue dye leakage assay. Nuclei are marked in blue. Scale bar: 50  $\mu$ m (A) and 100  $\mu$ m (C). Data are shown as mean  $\pm$  SEM, p-values were calculated using unpaired Welch's t test (B) and one-way ANOVA followed by Tukey's post hoc analysis (D-F). \*  $p < 0.05$ , \*\*  $p < 0.01$ , NS  $> 0.05$ . All experiments are  $n=3$  biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

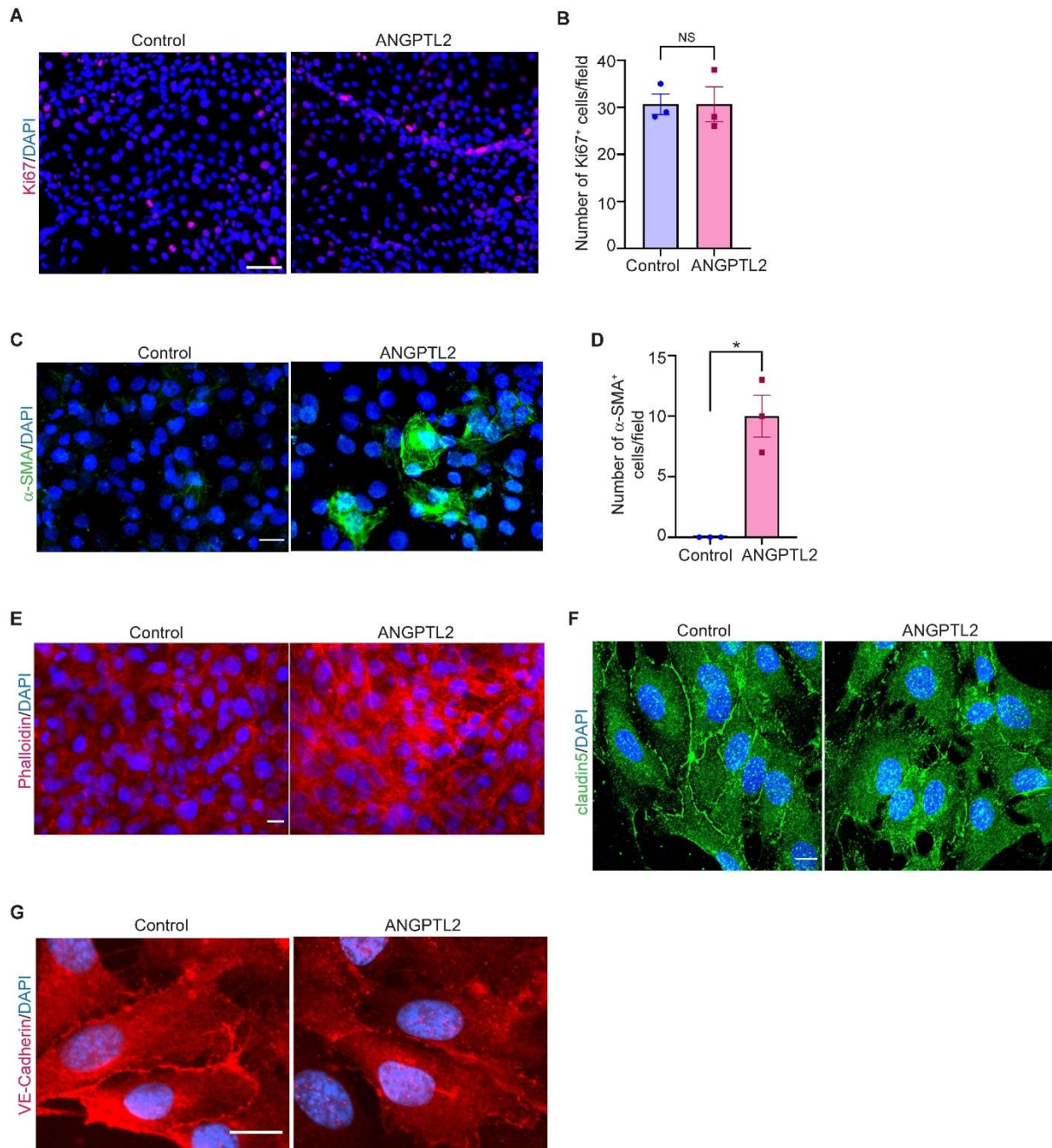
Supplementary Figure 4



**Supplementary Figure 4: ANGPTL2 is expressed by *Snail* tg keratinocytes and upregulated in human fibrotic diseases.** (A) qPCR analysis of relative gene expression of *Angptl2* (normalized to housekeeping gene) in isolated keratinocytes (mKT), PECAM1<sup>+</sup> cells (endothelial cells), CD45<sup>+</sup> cells (primarily immune cells) and lineage negative cells (lin<sup>-</sup>, primarily fibroblasts) from wild type (WT) and *Snail* tg mice skin. Expression of *Angptl2* in (B) lung with idiopathic pulmonary fibrosis (n=13 samples) compared to normal lung tissue (n=9 samples) (from GSE48149), (C) kidney glomeruli with lupus nephropathy (n=32 samples) compared to control glomeruli (n=14 samples) (from GSE32591), (D) Liver with fibrosis post-transplant (n=8 samples) compared to normal liver tissue (n=129 samples) (from GSE145780). The expression values are fetched from the GEO2R algorithm's output. (E) Immunofluorescence staining for ANGPTL2 (green) in WT, *Snail* tg and *Snail* tg/*Angptl2* KO skin. Nuclei are marked in blue. Scale bar: 100  $\mu$ m. n=3 biological replicates except (B-D).

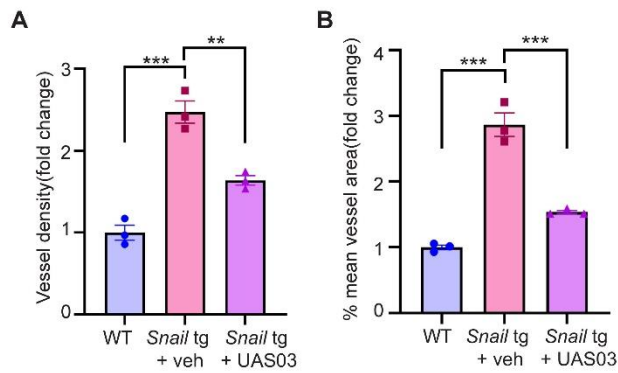
Data are shown as mean  $\pm$  SEM, p-values were calculated using unpaired Welch's t test. \*\* p < 0.001, \*\*\*\* p < 0.0001, NS > 0.05.

**Supplementary Figure 5**



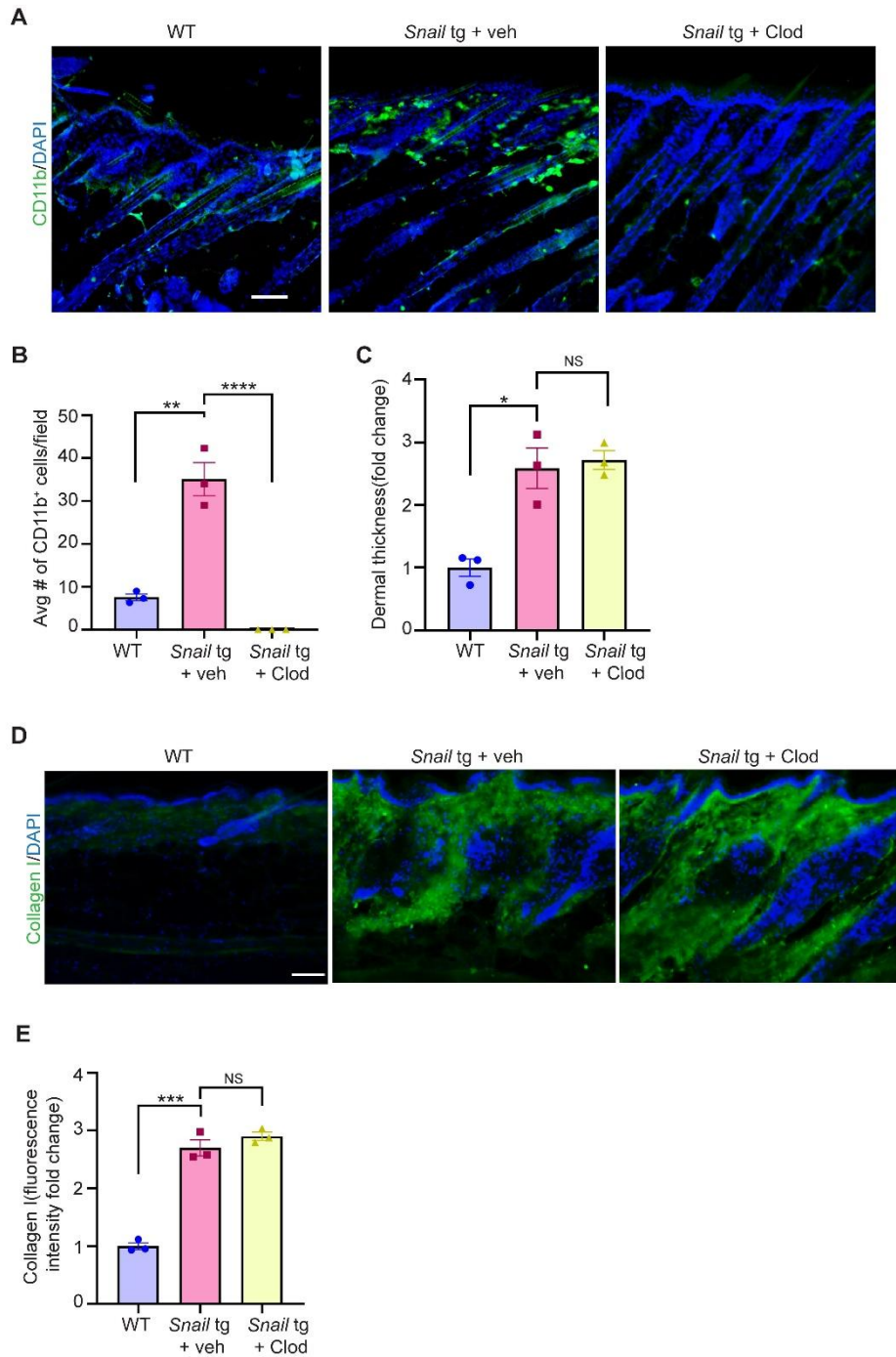
**Supplementary Figure 5: Effect of ANGPTL2 on endothelial cells.** Immunofluorescent staining and quantification for (A, B) Ki67 (red) and (C, D)  $\alpha$ -SMA (green) in control and ANGPTL2 treated SVEC4-10 cells. Immunofluorescent staining for (E) actin marked by Phalloidin (red), (F) claudin5 (green) and (G) VE-Cadherin (red) in control and ANGPTL2 treated SVEC4-10 cells. Nuclei are marked in blue. Scale bar: 50  $\mu$ m (A, C) and 10  $\mu$ m (E-G). Data are shown as mean  $\pm$  SEM, p-values were calculated using paired Student's *t* test. \*  $p < 0.05$ , NS  $> 0.05$ . All experiments are  $n=3$  biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

## Supplementary Figure 6



**Supplementary Figure 6: UAS03 reduces vasculopathy.** Quantification of (A) vessel density and (B) mean vessel area at P60 in wild type (WT), *Snail* tg + vehicle control (veh) and *Snail* tg + UAS03 injected mice. Data are shown as mean  $\pm$  SEM, p-values were calculated using one-way ANOVA followed by Tukey's post hoc analysis for multiple group comparisons. \*\*\* p < 0.001, \*\* p < 0.01. All experiments are n=3 biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

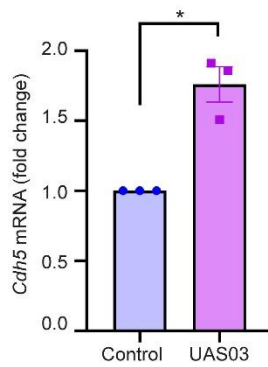
## Supplementary Figure 7



**Supplementary Figure 7: Depleting macrophages does not reduce fibrosis.** Staining (A) and (B) quantification of macrophages marked by CD11b (green) at P60 in wild type (WT), *Snail* tg + vehicle control (veh) and *Snail* tg + Clodronate (Clod) injected mice. Nuclei are marked in blue. (C) Quantification of dermal thickness at P60 in WT, *Snail* tg vehicle control and *Snail* tg Clodronate injected mice. Staining (D) and quantification (E) of Collagen I at P60 in WT, *Snail* tg + vehicle control and *Snail* tg + Clodronate injected mice. Scale bar: 50  $\mu$ m. Data are shown as mean  $\pm$  SEM, p-values were calculated using one-way ANOVA followed by Tukey's post hoc analysis for multiple group comparisons. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p <$

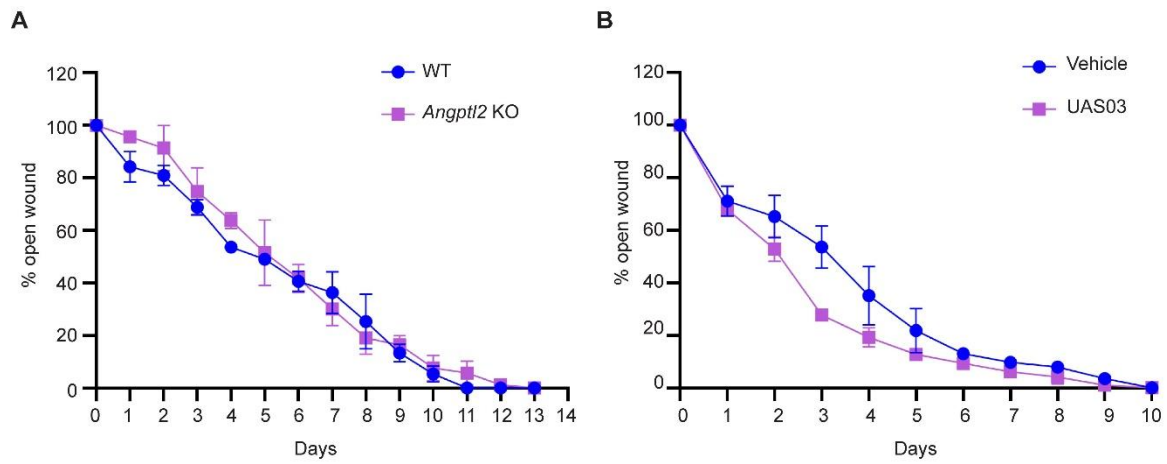
0.001, \*\*\*\*  $p < 0.0001$ , NS  $> 0.05$ . All experiments are  $n=3$  biological replicates. 3 FOI were analysed per biological replicate for quantification of images.

Supplementary Figure 8



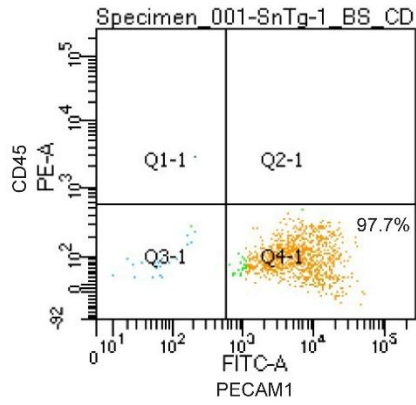
**Supplementary Figure 8: UAS03 upregulates endothelial adherens junction component VE-Cadherin.** qPCR analysis of mRNA levels of *Cdh5* in SVEC4-10 cells treated with Control or 50  $\mu$ M UAS03. Data are shown as mean  $\pm$  SEM, p-values were calculated using paired Student's *t* test. \*  $p < 0.05$ .  $n=3$  biological replicates.

### Supplementary Figure 9



**Supplementary Figure 9:** Wound closure kinetics in (A) *Angptl2* KO and (B) UAS03 treated mice compared to wildtype counterparts respectively. All experiments are n=3 biological replicates.

**Supplementary Figure 10**



**Supplementary Figure 10: Purity of isolated endothelial cells from mouse skin.** Plot showing purity of sorting with PECAM1<sup>+</sup> endothelial cell population previously sorted from *Snail* tg mouse skin using FACS. >95% cells isolated in a sample were pure PECAM1<sup>+</sup> population.

**Supplementary Table 1:** Differentially expressed genes in UAS03-treated SVEC4-10 cells compared to control-treated cells (available as a separate Excel file).

**Supplementary Table 2:** GO term enrichment analysis via gProfiler2 using upregulated and downregulated genes respectively from UAS03-treated SVEC4-10 cells compared to control-treated cells (available as a separate Excel file).