SUPPLEMENTAL DATA.

Supplemental figure 1: *Adamts5*$^{-/-}$ dermal fibroblasts have an altered cell shape but normal proliferation. A. Images of calcein-labeled cells are shown (representative of analysis of 50 cells from each genotype, using 4 pairs of *Adamts5*$^{-/-}$ and WT mice). **B.** Morphometric analysis showed *Adamts5*$^{-/-}$ fibroblasts had an expanded surface area (*$p<0.01$) and a significantly reduced minor/major aspect ratio (*$p<0.01$) indicative of altered cell shape (analysis of 50 cells from each genotype, using 4 pairs of *Adamts5*$^{-/-}$ and WT mice). **C**. Cell proliferation (quantified by BrdU intake) did not show a difference between *Adamts5*$^{-/-}$ and WT fibroblasts (triplicate analysis of cells obtained from 3 pairs of *Adamts5*$^{-/-}$ and WT mice). Error bars indicate standard deviation (S.D.).

Supplemental figure 2: Adding exogenous ADAMTS5 to *Adamts5*$^{-/-}$ dermal fibroblasts ameliorates altered cell shape, versican cleavage and SMAD phosphorylation. A. Images of calcein-labeled cells are shown (representative of analysis of more than 50 *Adamts5*$^{-/-}$ dermal fibroblasts and 25 WT dermal fibroblasts, obtained from 2 pairs of *Adamts5*$^{-/-}$ and WT mice). **B.** Morphometric analysis showed that addition of exogenous ADAMTS5 to *Adamts5*$^{-/-}$ fibroblasts restored normal cell surface area (*$p<0.01$, **$p<0.05$) and aspect ratio (*$p<0.01$, **$p<0.05$) indicative of altered cell shape (representative of analysis of more than 50 cells in *Adamts5*$^{-/-}$ dermal fibroblasts phenotype and 25 cells WT dermal fibroblasts, from 2 pairs of *Adamts5*$^{-/-}$ and WT mice). **C**. Western blot analysis using anti-pSMAD2 and anti-DPEAAE shows that adding exogenous ADAMTS5 reduced Smad2 phosphorylation, concomitantly with increased versican proteolysis. Error bars indicate standard deviation (S.D.).

Supplemental figure 3: Immunfluorescence of *Adamts5*$^{-/-}$ dermal fibroblasts shows strong expression of SMA that is abrogated by *Vcan* haploinsuffiency. Immunofluorescence for SMA (green) was coupled with phalloidin-FITC labeling for cellular actin (red). The left-hand column shows monochrome images of SMA staining, whereas the right-hand column shows dual color images of Actin and SMA staining. Note the strong expression of SMA in *Adamts5*$^{-/-}$ dermal fibroblasts, compared to WT fibroblasts(representative of n=3 biological replicates). Note also the lack of significant SMA signal in *Adamts5*$^{-/-}$/ *Vcan*$^{hdf/+}$ dermal fibroblasts compared to *Adamts5*$^{-/-}$ dermal fibroblasts.

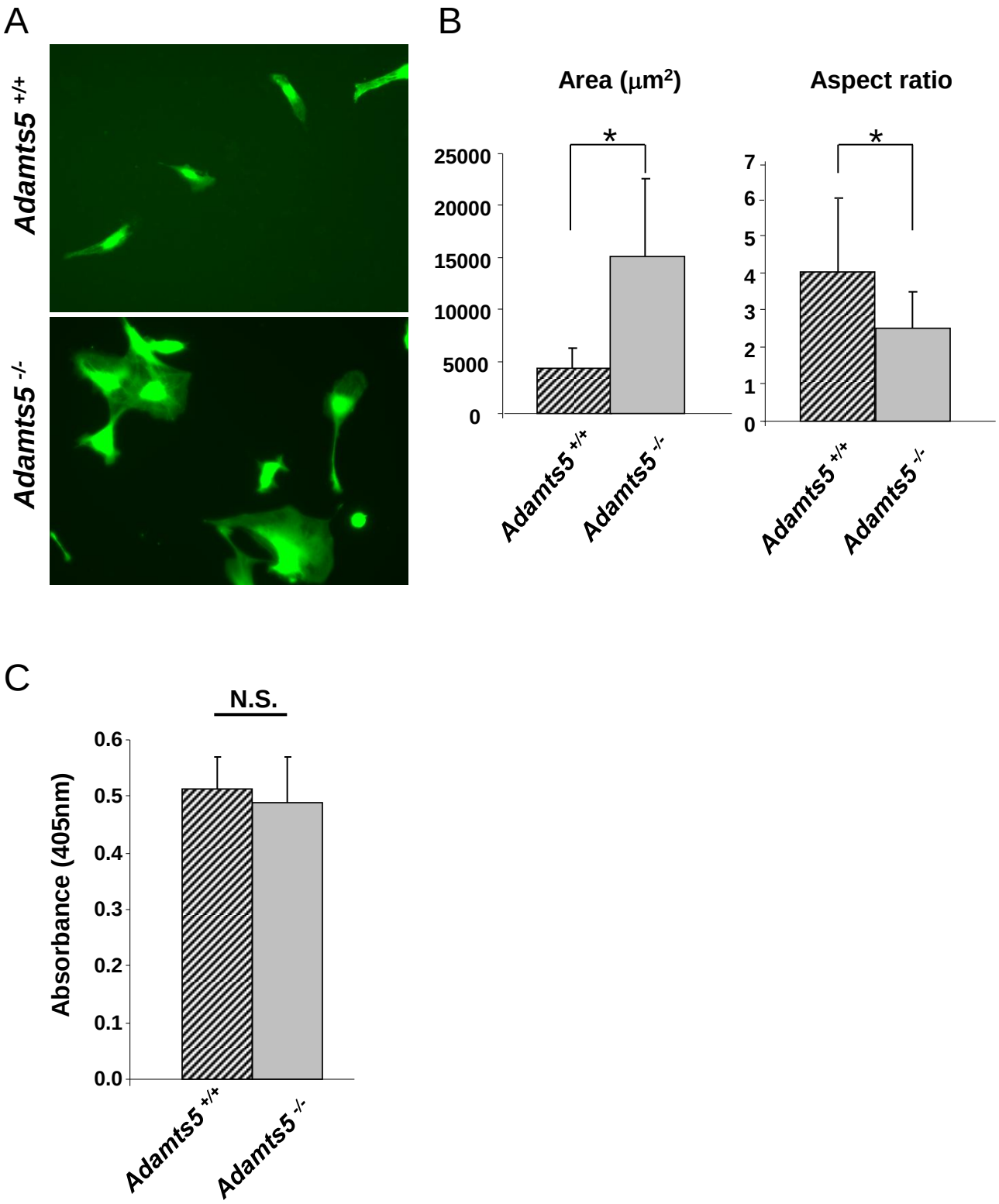
Supplemental figure 4: SMA immunofluorescence of mouse skin. No difference in the distribution, density or type of labeled cells (e.g., arrow) was seen in comparison of skin from *Adamts5*$^{-/-}$ and WT littermates (representative of n=2 pairs of mice).

Supplemental figure 5: Hyaluronan levels and hyaluronan synthase mRNA levels are not significantly affected in *Adamts5*$^{-/-}$ fibroblasts.
A. The amount of hyaluronan measured by FACE did not differ between *Adamts5*$^{-/-}$ fibroblasts and WT dermal fibroblast monolayers (n=3). N.S.= not significant. Error bars indicate standard deviation (S.D.).

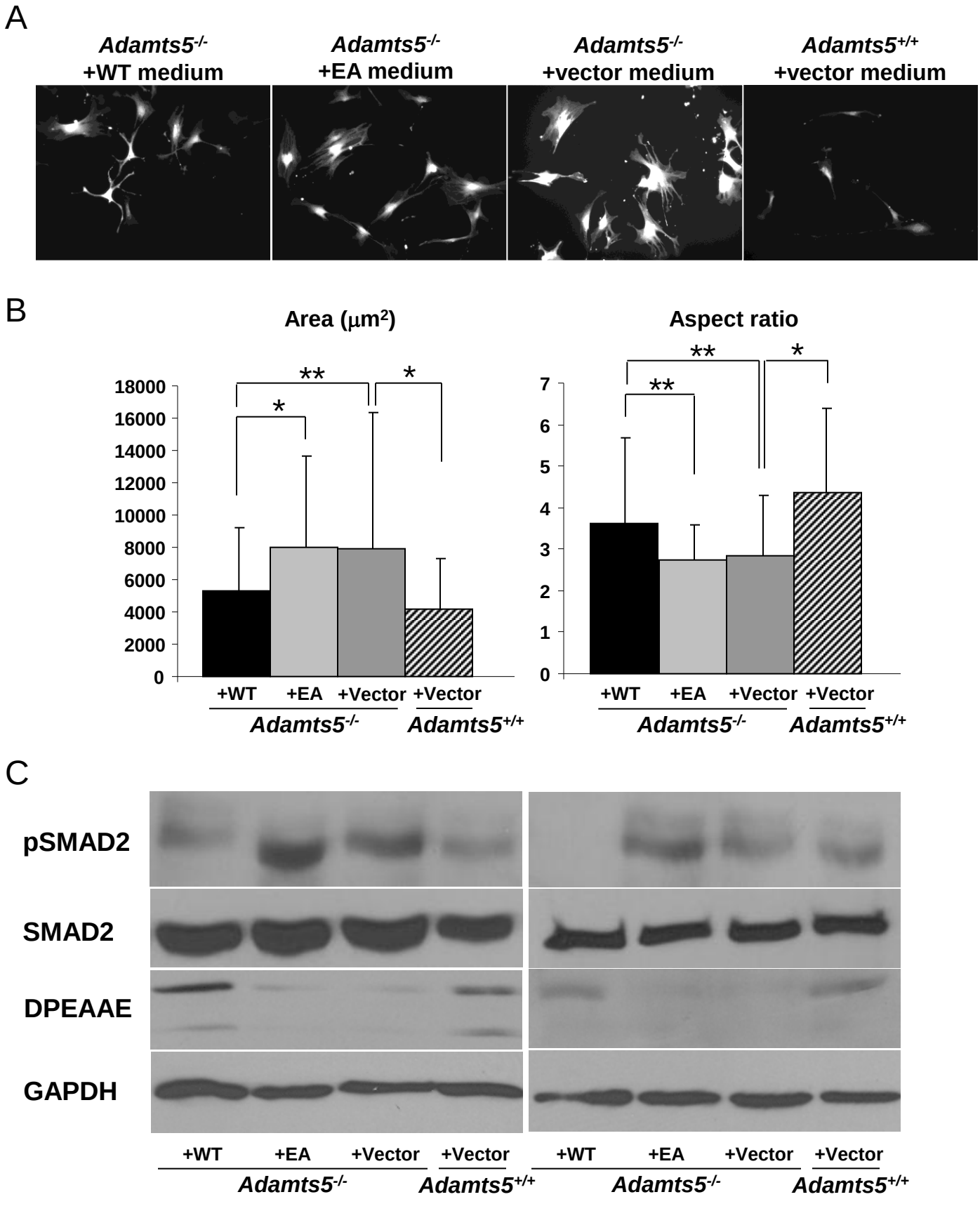
B. RT-PCR of mouse dermal fibroblasts for *hyaluronan synthase 1* (*Has1*) and *Has2*. No expression of *Has3* was seen (data not shown). There was no difference between *Adamts5*$^{-/-}$ and WT fibroblasts.

Supplemental figure 6: A. Western blotting of fibroblast monolayer extracts with an antibody to versican (anti-GAGβ) after chondroitinase ABC treatment shows the differences in versican content in the four indicated genotypes. The expected position of V0 and V1 versican is indicated. The smaller molecular weight species likely represent proteolytic products. Note increased versican levels in *Adamts5*$^{-/-}$ monolayers, and low levels in *Vcan*$^{hdf/+}$ cells compared to WT (*Adamts5*$^{+/+}$) cells. *Adamts5*$^{-/-}$*;Vcan*$^{hdf/+}$ dermal fibroblasts have reduced versican relative to *Adamts5*$^{-/-}$ cells (representative of two independent analyses). **B.** Collagen gel contraction by *Adamts5*$^{-/-}$ fibroblasts is unaltered by addition of the G1-DPEAAE^{441} fragment of versican V1 when compared to the effect of control medium from empty-vector-transfected cells. N=3. N.S.= not significant. Error bars indicate standard deviation (S.D.).

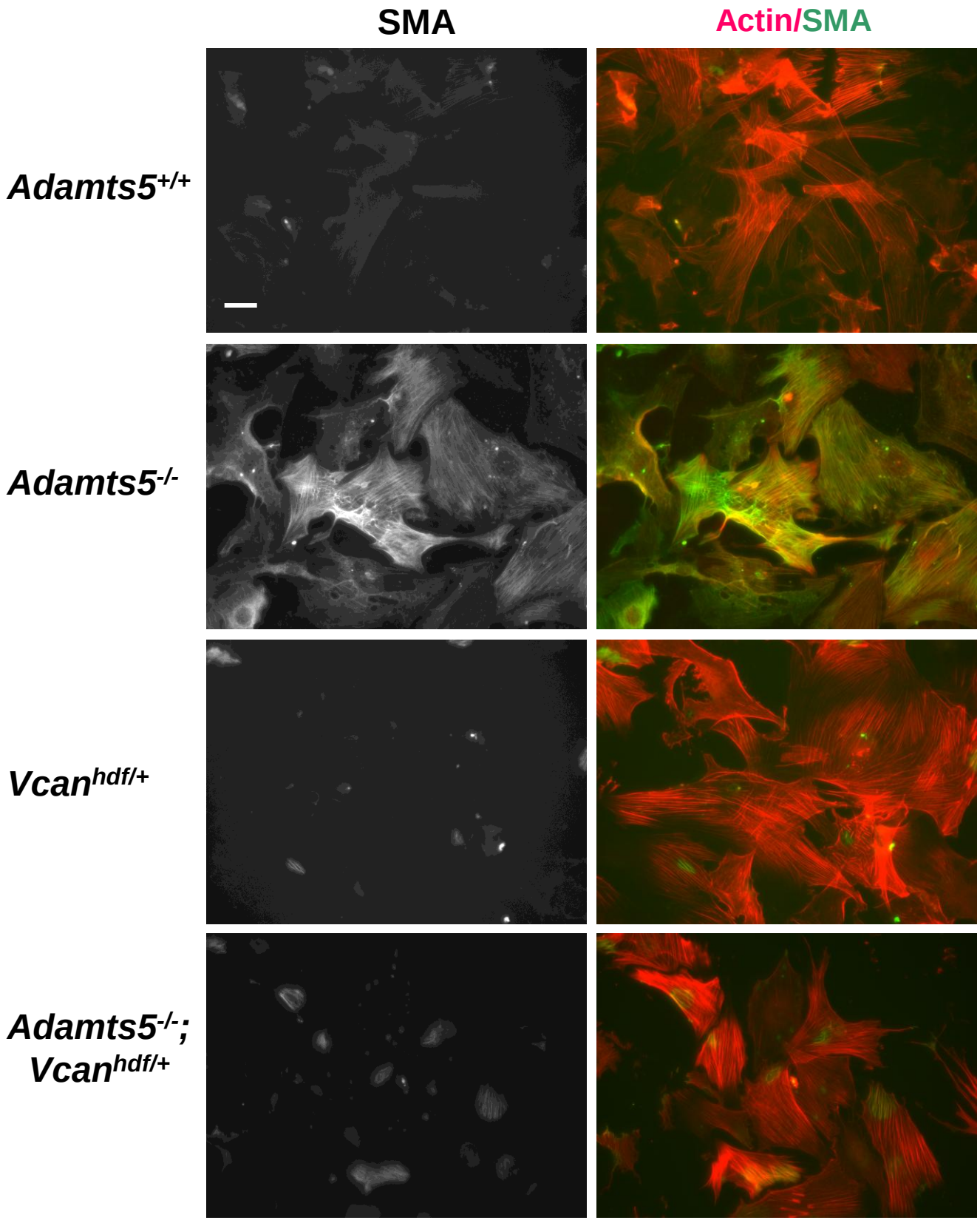
Supplemental figure 7: Versican over-expression induces accumulation of PCM around cultured human dermal fibroblasts and alters cell shape. A. Exclusion of RBCs around calcein-labeled fibroblasts shows accumulation of PCM around *Vcan* over-expressing cells (representative of n=20). The exclusion zone is indicated by arrows. **B.** Images of calcein-labeled cells are shown. **C.** Morphometric analysis showed *Vcan* over-expressing cells had expanded surface area (*$p<0.01$) and a significantly minor/major aspect ratio (*$p<0.01$) indicative of altered cell shape (the analysis used 50 cells for each genotype). Error bars indicate standard deviation (S.D.).



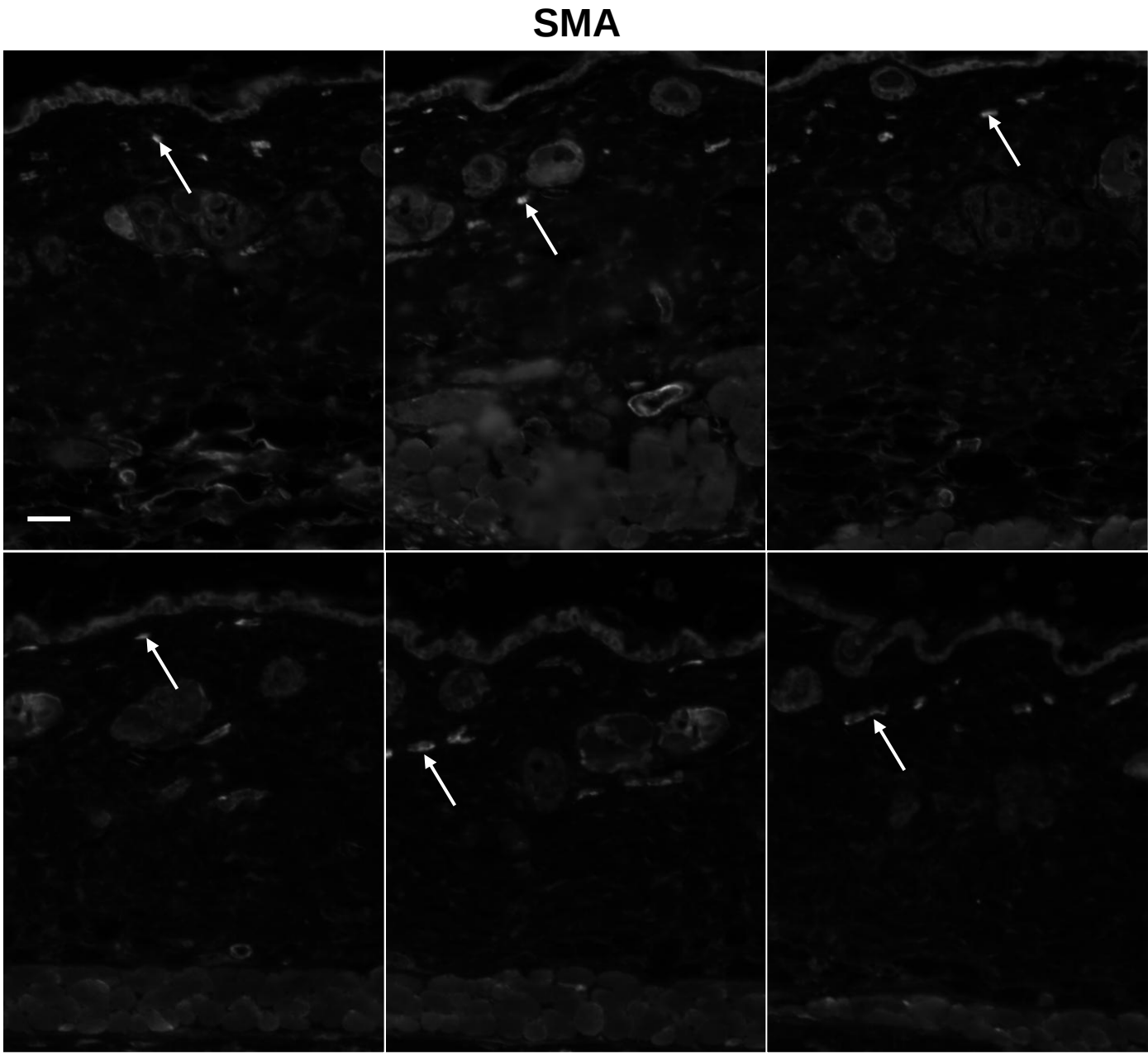
Supplemental Fig 1. Hattori et al.



Supplemental Fig 2. Hattori et al.



Supplemental Fig 3. Hattori et al.



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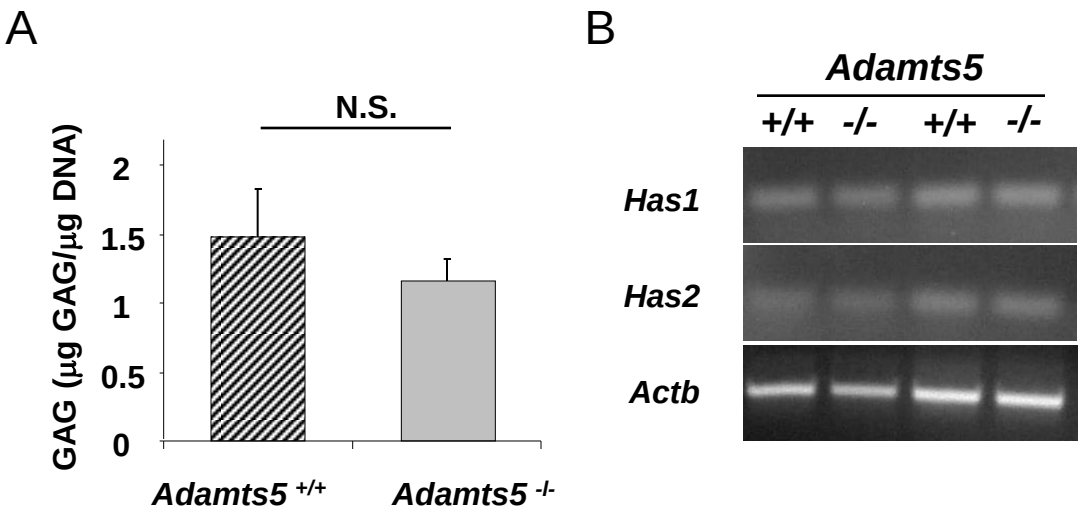
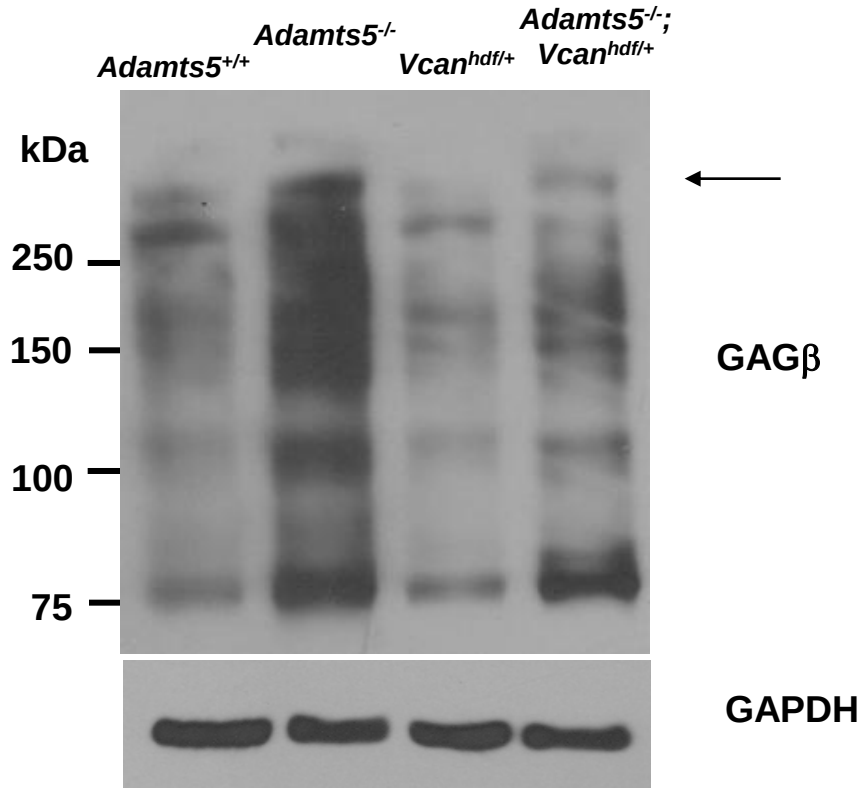


Supplemental Fig 5. Hattori et al.

A



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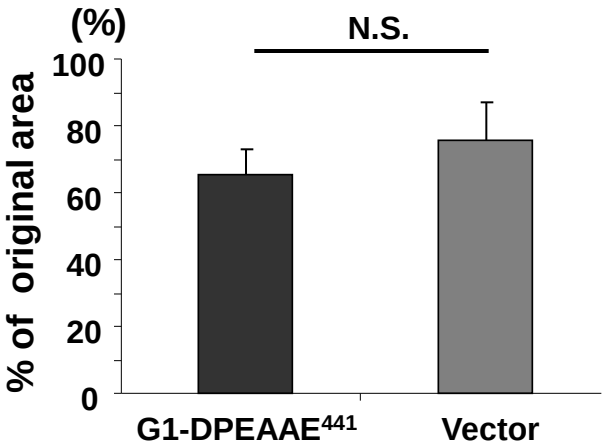
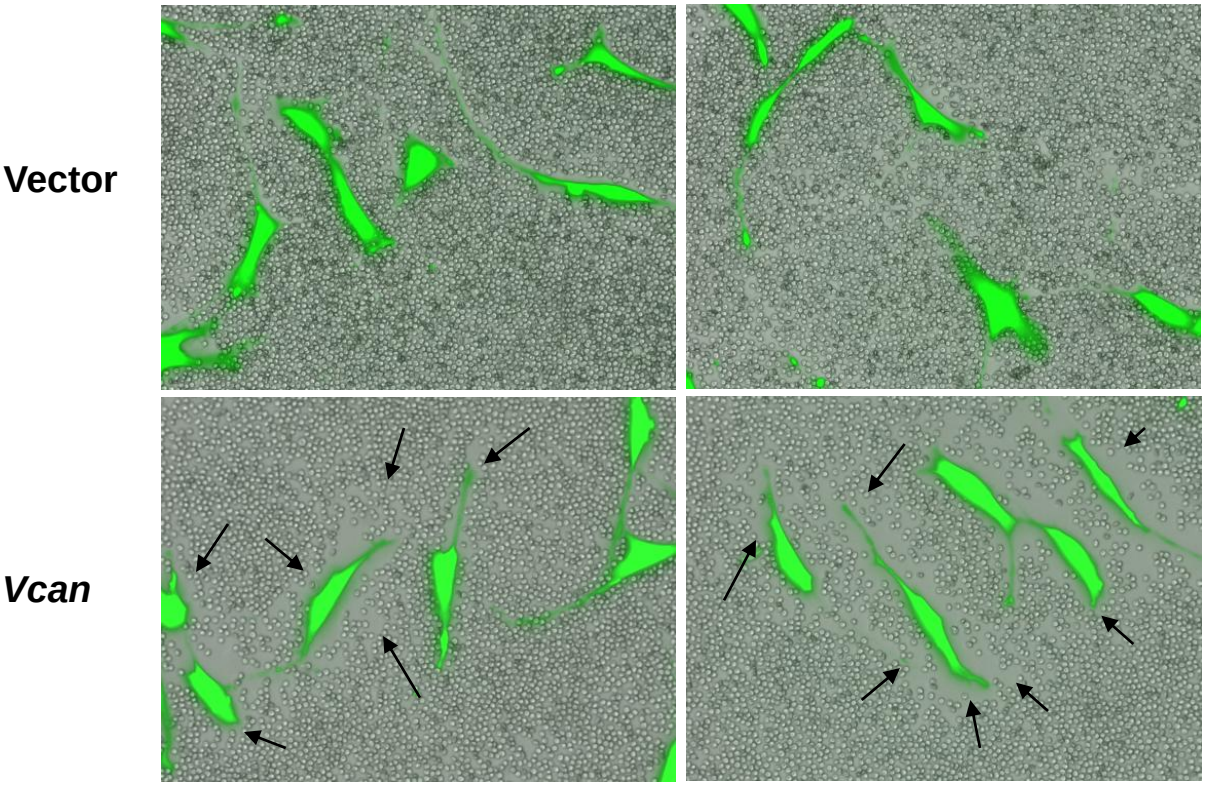


Supplemental Fig 6. Hattori et al.

A



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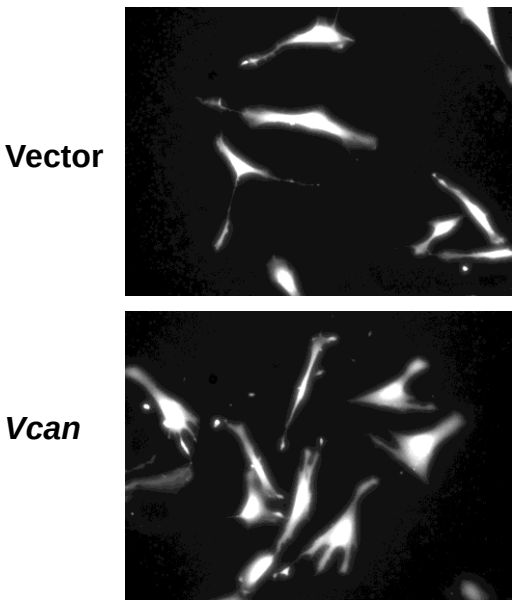

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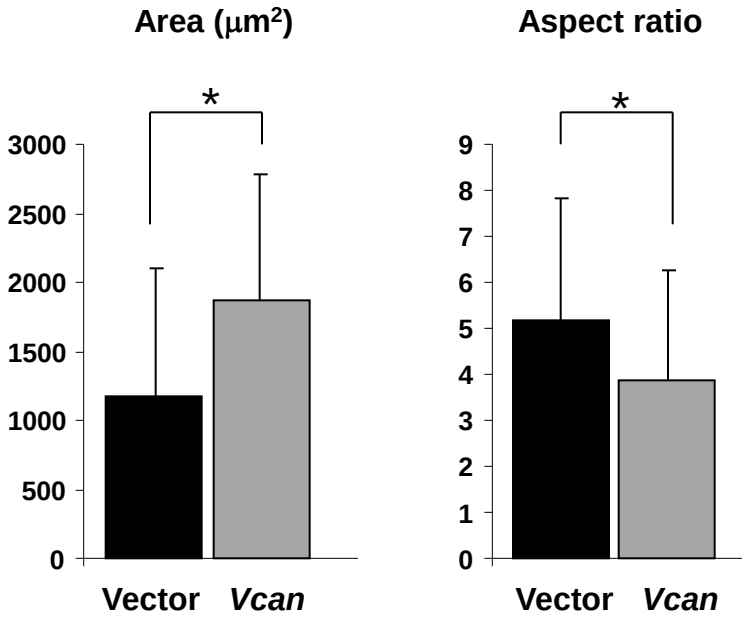

Supplemental Fig 7. Hattori et al.