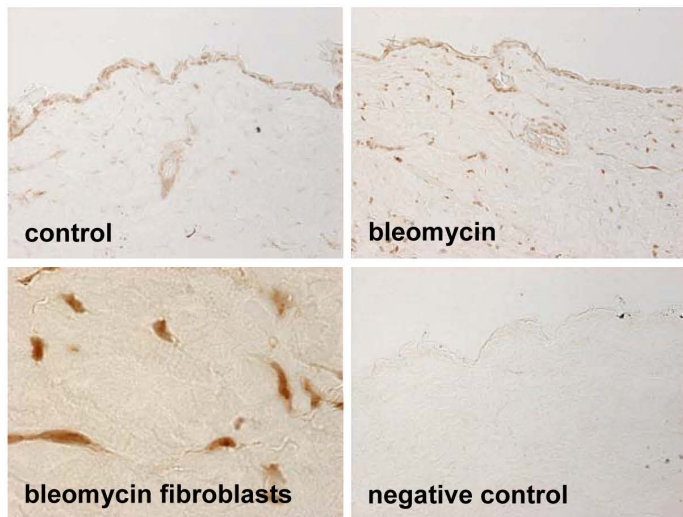
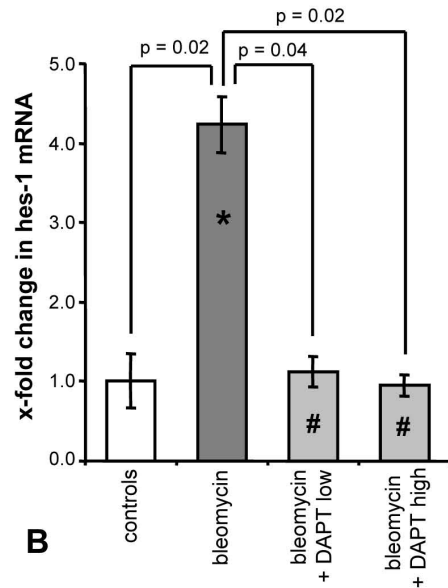


**Supplementary Figure 1:** Notch signaling is activated during impaired wound healing. Staining for the NICD in hypertrophic scars and keloids showed an increased activation of Notch signaling in fibroblasts, endothelial cells and keratinocytes. Representative pictures are shown at 200 fold magnification, fibroblasts are shown at 1000 fold magnification.

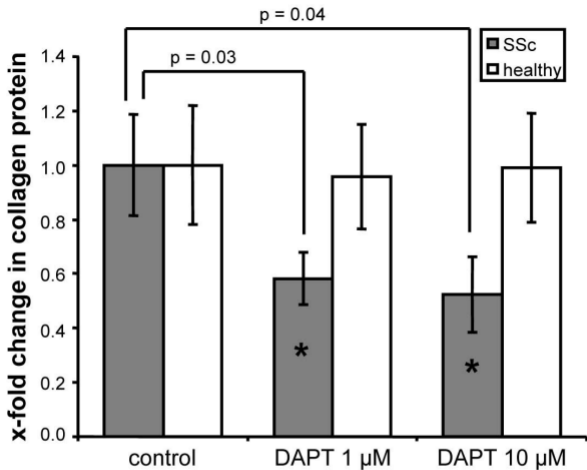


**A**

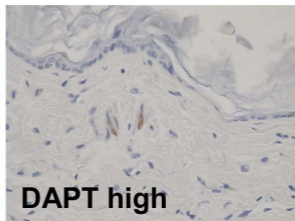
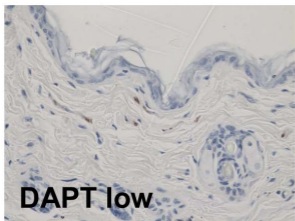
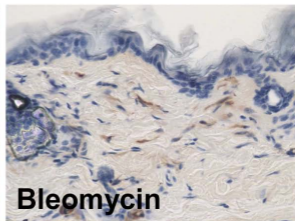
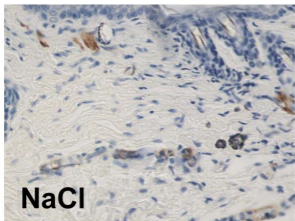


**B**

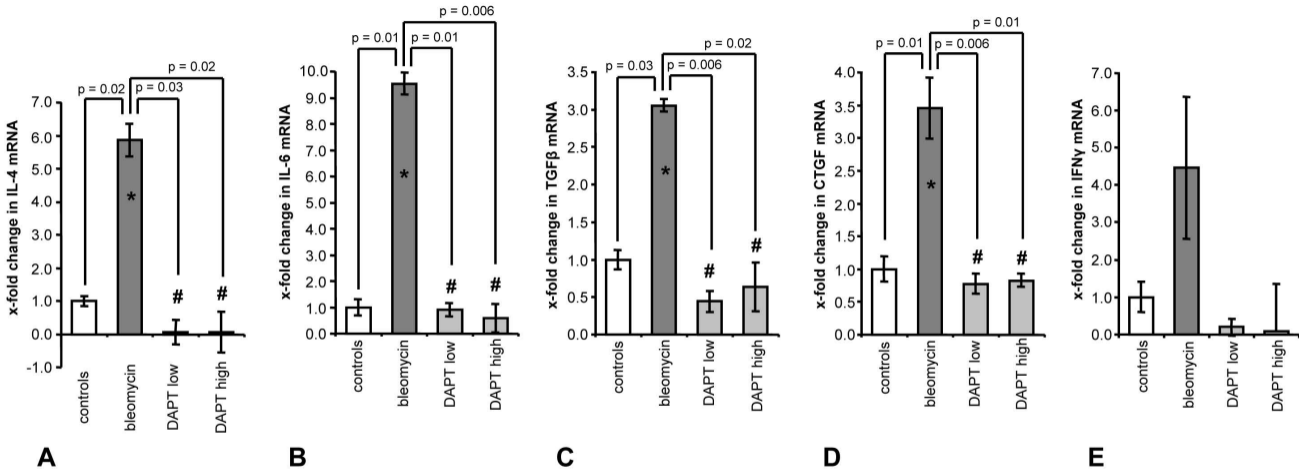
**Supplementary Figure 2:** Notch signaling is activated in experimental fibrosis. **A**, Immunohistochemistry for the NICD in skin sections of bleomycin injected mice and control mice showed a prominent activation of Notch signaling in fibroblasts upon bleomycin challenge. Representative tissue sections are shown at 200 fold magnification. **B**, Consistent with the increased release of the NICD, elevated mRNA levels of the Notch target gene hes-1 were detected in the skin of bleomycin treated mice which was completely abrogated upon treatment with DAPT. \* indicates statistical significant differences compared to control mice injected with NaCl. # indicates statistical significant differences compared to bleomycin-challenged mice without anti-fibrotic treatment.



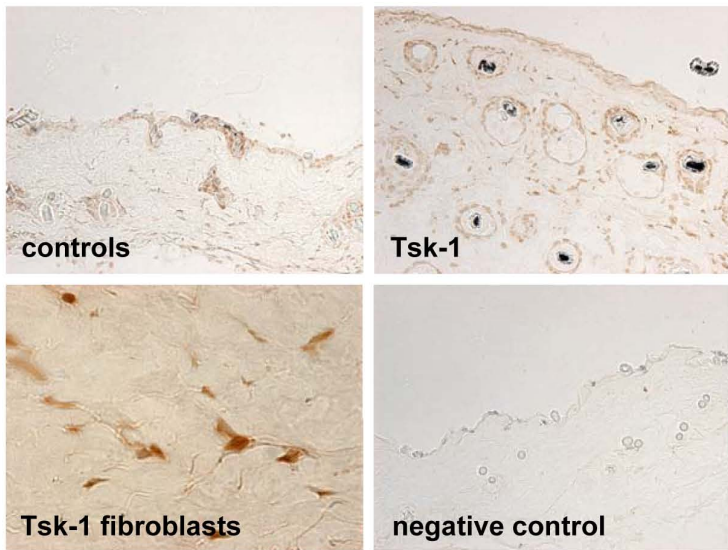
**Supplementary Figure 3:** DAPT reduces collagen production in dermal fibroblasts. Incubation of dermal fibroblasts reduced collagen release selectively in SSc but not in healthy dermal fibroblasts. \* indicates statistical significant differences compared to untreated fibroblasts.



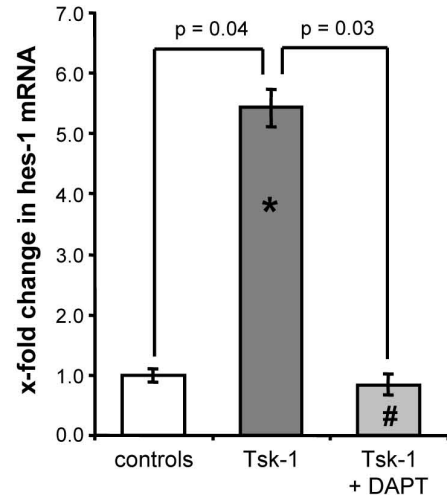
**Supplementary Figure 4:** Reduced number of myofibroblasts upon treatment with DAPT. The differentiation of resting fibroblasts into metabolically active myofibroblasts can be prevented by inhibition of  $\gamma$ -secretase with DAPT.



**Supplementary Figure 5:** Notch signaling regulates cytokine expression in bleomycin-induced fibrosis. Inhibition of the Notch pathway by DAPT decreased the mRNA levels of IL-4 (A), IL-6 (B), TGFβ (C), CTGF (D) and IFNγ (E). Similar results were obtained in Tsk-1 mice. \* indicates statistical significant differences compared to control mice injected with NaCl. # indicates statistical significant differences compared to bleomycin challenged mice without anti-fibrotic treatment.



**A**



**B**

**Supplementary Figure 6:** Notch signaling is activated in Tsk-1 mice. **A**, Increased staining for the NICD in fibroblasts of Tsk-1 mice compared to control mice as analyzed by immunohistochemistry. Representative tissue sections at the same magnification (200 fold) are shown. **B**, The expression of hes-1 mRNA is strongly elevated in Tsk-1 mice compared to controls and is reduced upon treatment with DAPT. \* indicates statistical significant differences compared to control mice. # indicates statistical significant differences compared to Tsk-1 mice without anti-fibrotic treatment.