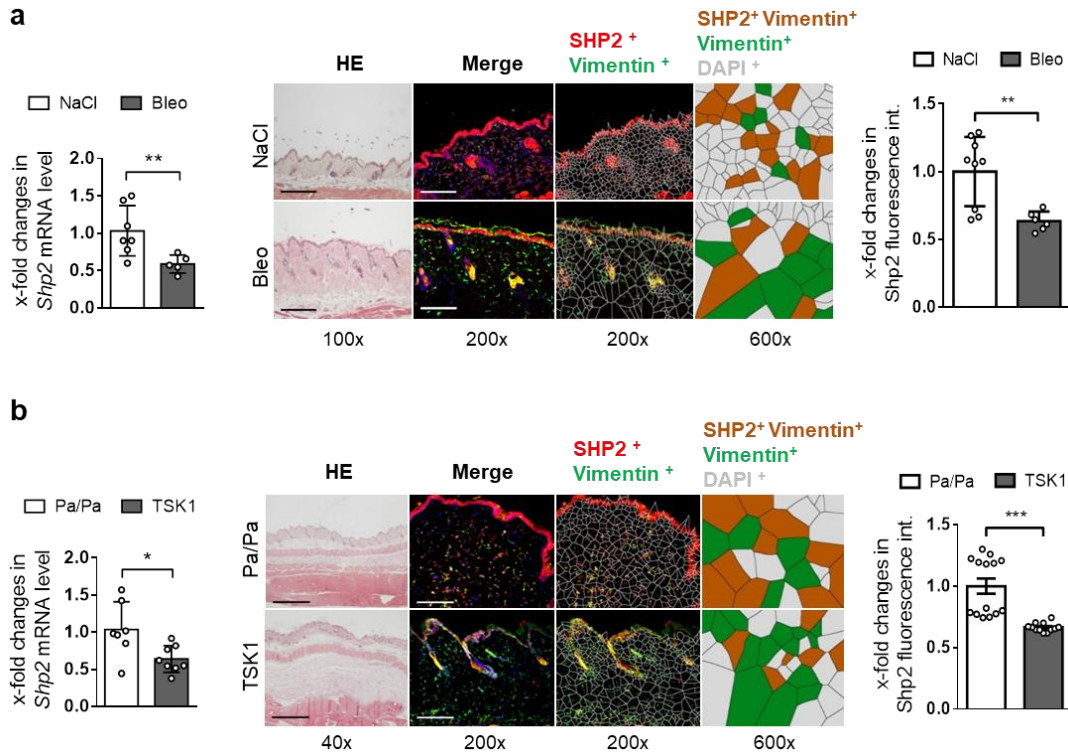


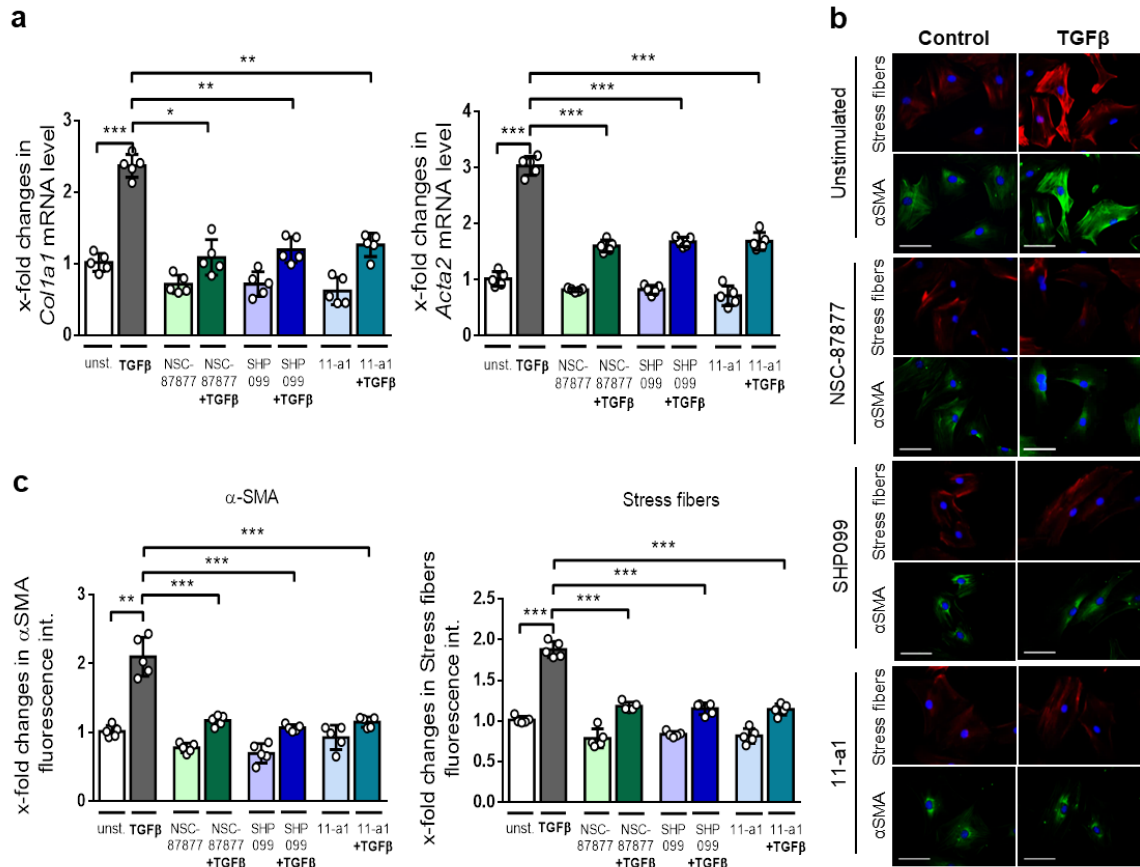
**Supplementary Information:**

**The tyrosine phosphatase SHP2 controls TGF $\beta$ -induced  
STAT3 signaling to regulate fibroblast activation and fibrosis**

***Zehender et al.***

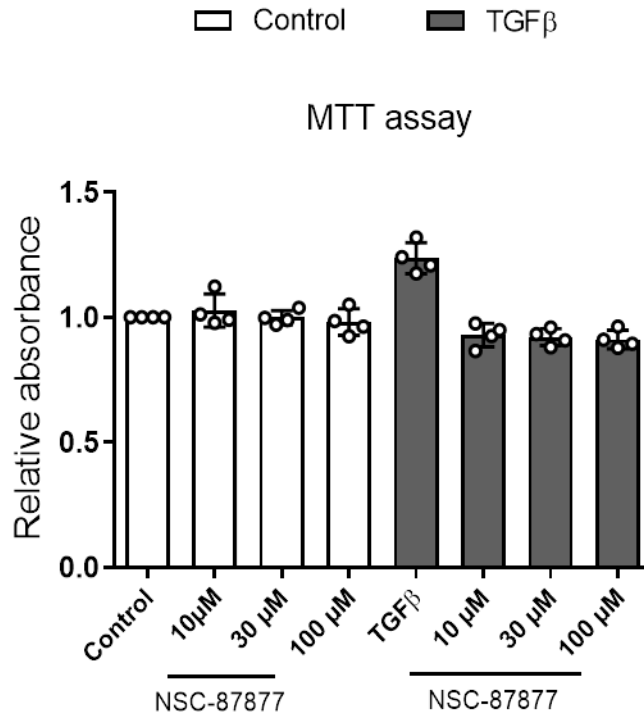


**Supplementary Figure 1: Decreased expression of SHP2 in experimental skin fibrosis. a:** Decreased expression of Shp2 and reduced mRNA levels of *Shp2* in the skin of mice challenged with bleomycin ( $n \geq 5$ ). Representative HE images and immunofluorescence staining of SHP2, vimentin and DAPI shown at 200- and 600-fold magnification. Horizontal scale bar, 500  $\mu\text{m}$ . Voronoi tessellated pictures and histograms of respective Immunofluorescence signals are included. **b:** Reduced mRNA levels of *Shp2* in TSK1 mice (2 mg tamoxifen over 5 days) ( $n \geq 7$ ). Representative images stained for SHP2, vimentin and DAPI shown at 200- and 600-fold magnification. Results shown are representative of a minimum of two independent experiments per model. All data are presented as median  $\pm$  s.e.m. The p-values are expressed as follows:  $0.05 > p > 0.01$  as \*;  $0.01 > p > 0.001$  as \*\*;  $p < 0.001$  as \*\*\*; ns= not significant. Significance was determined by Mann–Whitney test. NSC-87877= SHP1/SHP2 inhibitor; TSK1= Tight skin; Pa/Pa= Tight skin control; Bleo= Bleomycin.

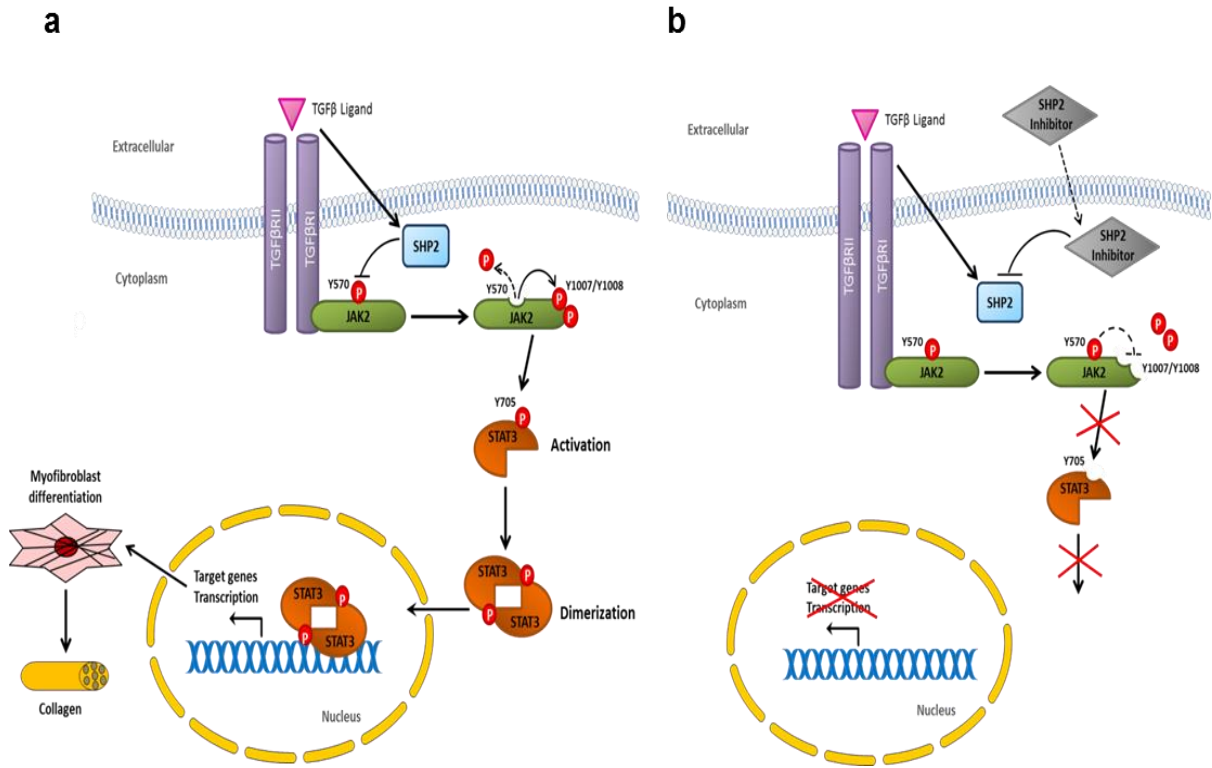


**Supplementary Figure 2: Inhibition of Shp2 by NSC-87877 (100 μM), SHP099 (1.4 μM) and 11-a1 (0.2 μM) inhibitors in cultured dermal fibroblasts. a:** mRNA levels of *Colla1* and *Acta2* (n = 5). **b-c:** Representative immunofluorescence staining of αSMA, Stress fibers and DAPI shown at 400-fold magnification (**b**) with quantification (**c**). Horizontal scale bar, 500 μm. Results shown are representative of three independent experiments. All data are presented as median ± s.e.m. The p-values are expressed as follows: 0.05 > p > 0.01 as \*; 0.01 > p > 0.001 as \*\*; p < 0.001 as \*\*\*; ns= not significant. Significance was determined by Mann–Whitney test. NSC-87877, SHP099 and 11-a1 are SHP1/SHP2 inhibitor; unst.= unstimulated.

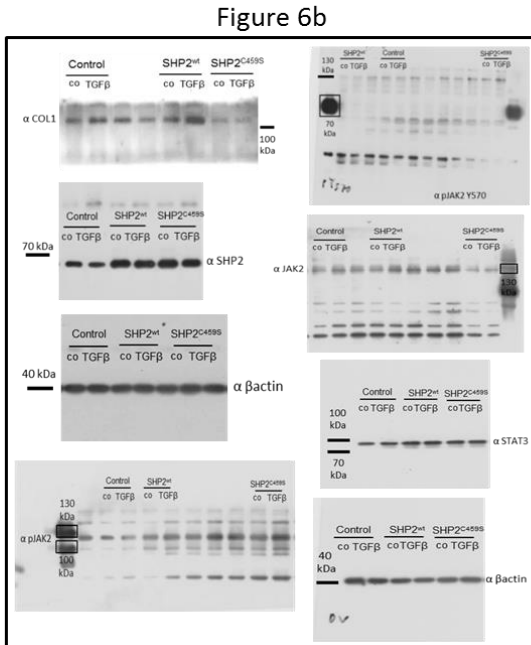
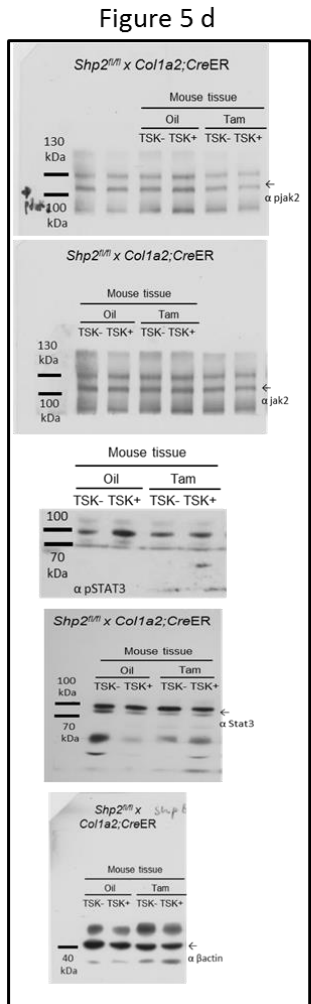
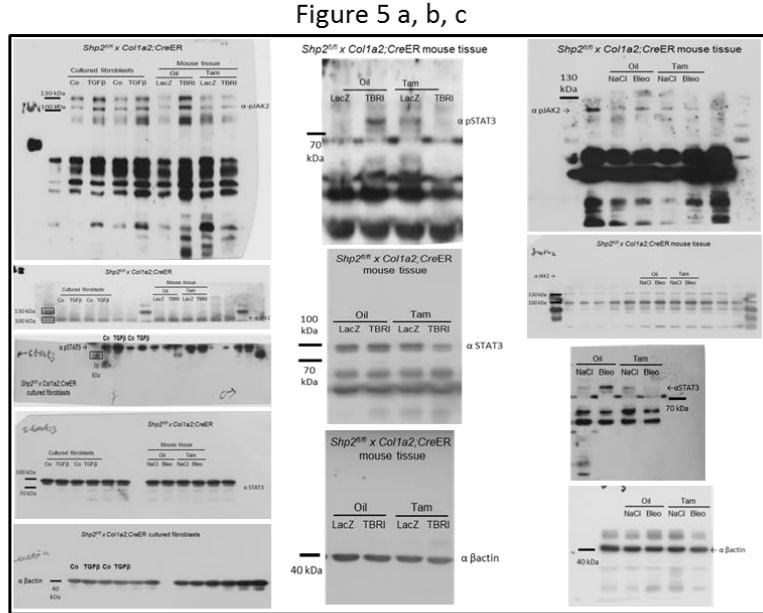
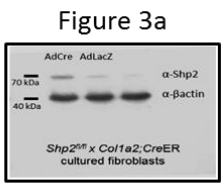
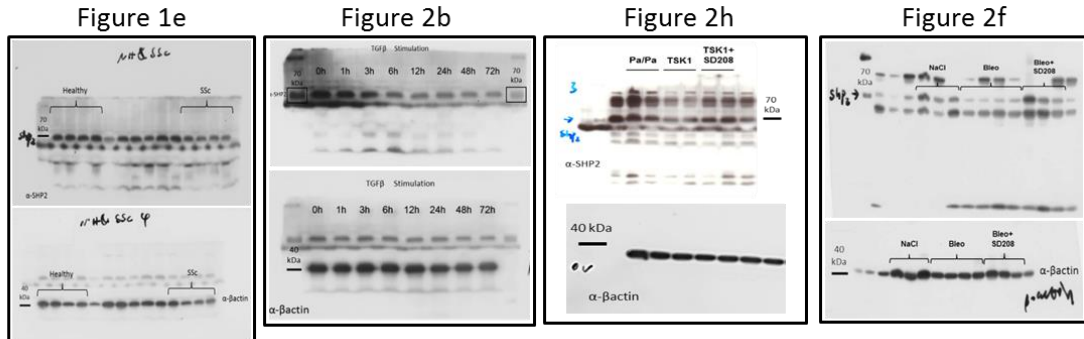
**a**



**Supplementary Figure 3: a:** Treatment with NSC-87877 does not modify the metabolic activity in resting fibroblasts, but prevents the increase induced by TGFβ. Results shown are representative of two independent experiments (n = 4). All data are presented as median ± s.e.m. The p-values are expressed as follows: 0.05 > p > 0.01 as \*; 0.01 > p > 0.001 as \*\*; p < 0.001 as \*\*\*; ns= not significant. Significance was determined by Mann–Whitney test. NSC-87877= SHP1/SHP2 inhibitor; MTT= tetrazolium dye.



**Supplementary Figure 4:** Schematic summary of the proposed role of SHP2 in TGFβ-dependent fibroblast activation **(a)** and of the effects of SHP2-inhibitors **(b)**. The Figure was created by the authors using in part images from Servier Medical Art, licensed under a Creative Common Attribution 3.0 Generic License. <http://smart.servier.com/>. P= Phosphorylation



Supplementary Figure 5: Uncropped scan of Original Western blots.

Figure 7e

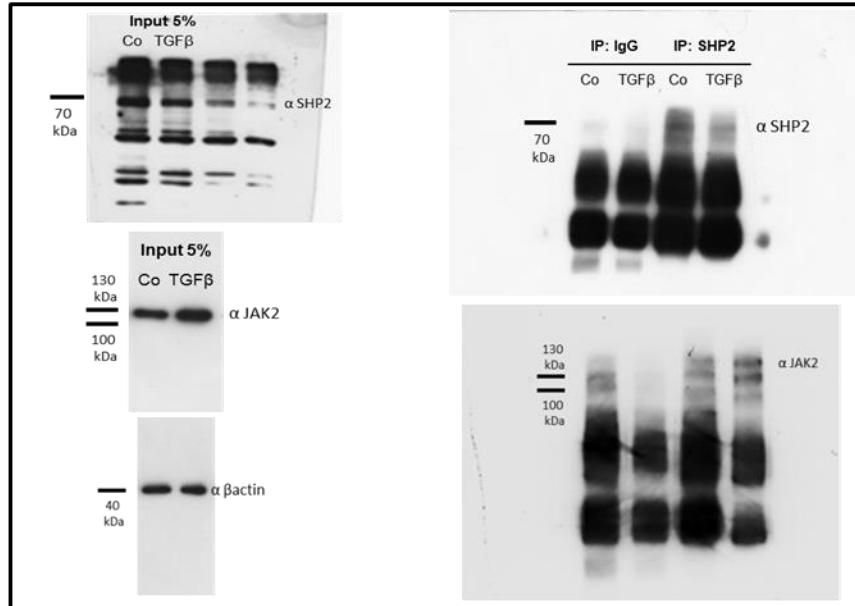
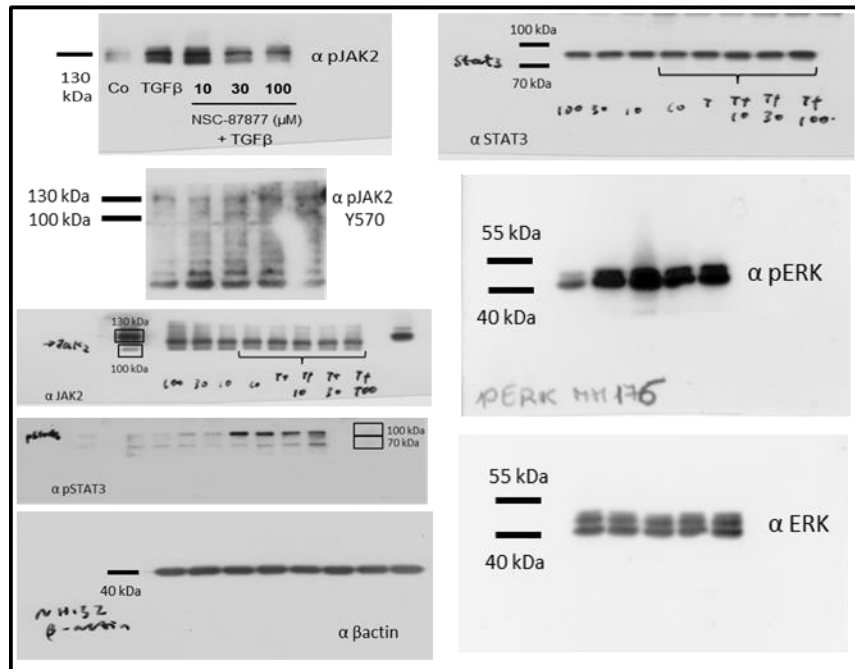


Figure 8d



Supplementary Figure 6: Uncropped scan of Original Western blots.

**Supplementary Table 1: primers**

human $\beta$ -ACTIN forward	5'-AGA AAA TCT GGC ACC ACA CC-3'
human $\beta$ -ACTIN reverse	5'-TAG CAC AGC CTG GAT AGC AA-3'
human SHP2 forward	5'-TAT CCT CTG AAC TGT GCA GAT CC-3'
human SHP2 reverse	5'-TCT GGC TCT CTC GTA CAA GAA AA-3'
human COL1A1 forward	5'-ACG AAG ACA TCC CAC CAA TC-3'
human COL1A1 reverse	5'- ATG GTA CCT GAG GCC GTT C-3'
human ACTA2 forward	5'-TGG GCT GAA GCG CAC TGA CC-3'
human ACTA2 reverse	5'- CCG CGG CTC TTG CCC ACA T-3'
murine $\beta$ -actin forward	5'-TCT TTG ATG TCA CGC ACG AT-3'
murine $\beta$ -actin reverse	5'-TAC AGC TTC ACC ACC ACA-3'
murine shp2 forward	5'-GGA GAG CAT CGT GGA TGC-3'
murine shp2 reverse	5'-TCC CAG CGC TGC AGT GAA-3'
murine Acta2 forward	5'-ATG CCT CTG GAC GTA CAA CTG-3'
murine Acta2 reverse	5'-CAC ACC ATC TCC AGA GTC CA-3'