Supplemental Figures S1-8 and Tables S1 and S2:

FIGURE S-1. High magnification of collagen organization visualized after Masson trichrome histology in unwounded and wounded skin of WT, TS5$^{-/-}$, CD44$^{-/-}$/TS5$^{-/-}$ and CD44$^{-/-}$ mice.

Tissue was processed for histology and stained with Masson trichrome as described in the Methods. Size bars (=25 um) are shown. White arrows on images from day 8 and 15 wounds of TS5$^{-/-}$ mice the presence of cell aggregates in the regenerating dermis.

FIGURE S-2. Confocal imaging of section stained with anti-DLS, non-immune (NI) rabbit IgG and Sytox Green (SG).

Sections from post-wounded skin at days 4 and 15 from WT (left panels) and TS5-/- (right panels) mice were stained for confocal microscopy as described in Methods. Images shown were taken under 10X magnification. Green fluorescence=nuclei; red fluorescence=aggrecan or rabbit IgG. Note a minor background red fluorescence at the epithelial layer.

FIGURE S-3. Localization of versican and hyaluronan, in un-wounded skin and 4, 8 and 15 days post-wounding from WT and TS5$^{-/-}$ mice

Sections were stained for confocal microscopy as described in Methods. Images shown were taken under 10X magnification. Green fluorescence=nuclei; red fluorescence=aggrecan yellow=intracellular or pericellular aggrecan. Aggrecan-+ve cell aggregates in TS5-/- wounds are shown by white circles. Also see Fig.S-2 for non-immune controls. Size bar is 100um.

Fig.S-4 Western analysis of aggrecan in dermal wounds

Two additional sets of WT and TS5-/- wounds were assayed for aggrecan at days 4 (panel A) and at days 8 and 15 (panels A and B). The (-) and (+) signs refer to without and with Chase ABC digestion.

FIGURE.S-5 Quantitative PCR for adamts5, adamts4 and cd44 expression in un-wounded and wounded skin from WT and TS5$^{-/-}$ mice.

RNA preparation and PCR reactions were done performed as described in Materials and Methods. Data for wounded tissue (at day 4=granulation tissue; day8= contraction and day 15=dermal regeneration) are expressed as fold-change relative to unwounded tissue. Each data point represents the mean +/- SD of triplicate assays from three individual mice.

FIGURE S-6 Western blot of ADAMTS-generated versican-G1 product in uninjured and regenerating skin in WT and ADAMTS5-/- mice

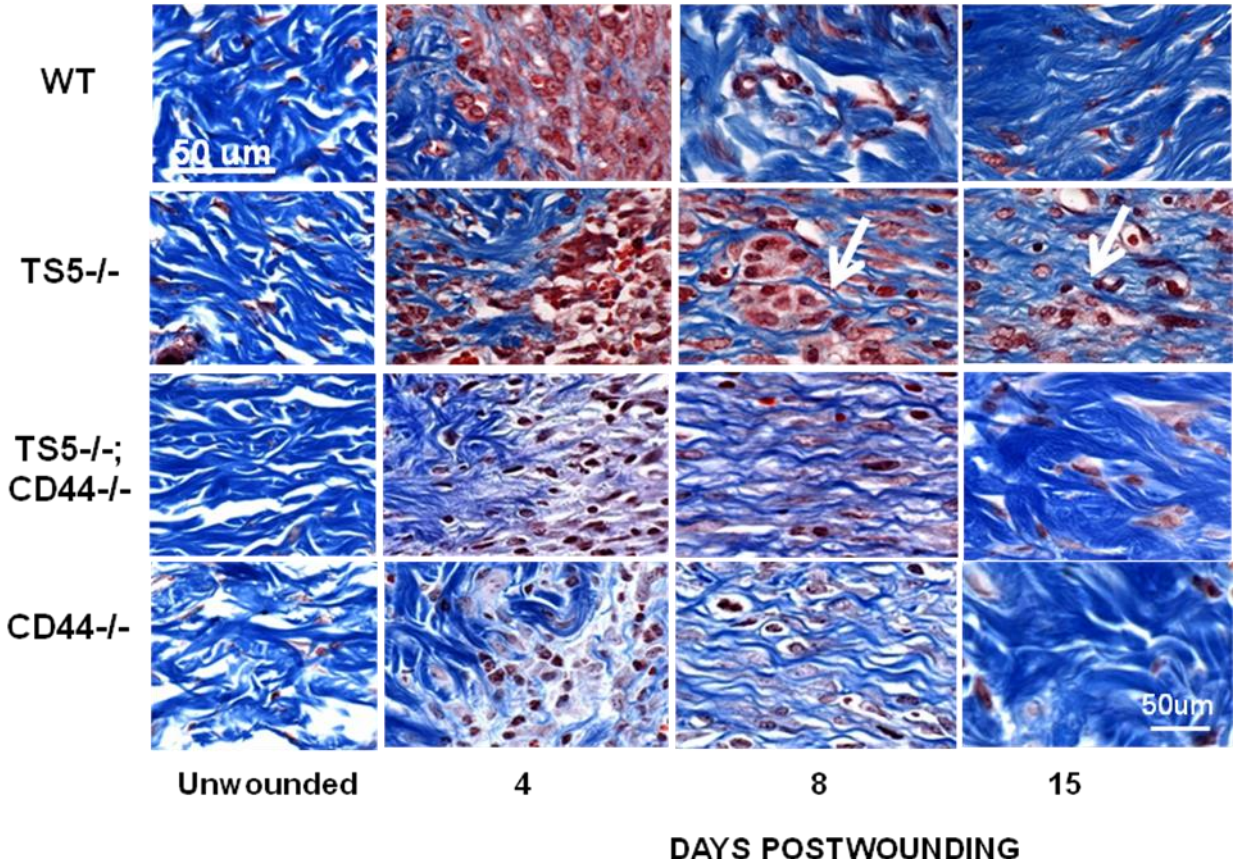
Proteoglycans were prepared for Western analysis with α–DPE. Each lane was loaded with 20% of the proteoglycan-rich fraction isolated from the four wound sites combined from one mouse. Samples loaded without and with chondroitinase ABC digestion are marked (-) and (+) respectively.

FIGURE S-7. Typical Western analysis of total and phosphorylated Smad2, Smad3C and Smad 1/5/8 in WT, TS5$^{-/-}$, CD44;TS5$^{-/-}$ and CD44$^{-/-}$ newborn skin fibroblasts.

Cell cultures, extractions and Western analyses were done as described in the Methods section. Abundance of phosphorylated Smad proteins was determined by integrated pixel density measurements and the data are shown in Fig. 9. Images separated by dividing lines were from different gels.

FIGURE S-8. Western analysis of aggrecan in cell layers of fibroblast cultures from WT and TS5$^{-/-}$ mice

(**A**) Proteoglycans were purified by DE52 chromatography for Western analysis with α-DLS and α–G1. (**B**) Cell layers were incubated with S. Hyase as described in the Methods, released digests and cell associated extracts were then prepared for Western analysis with anti-aggrecan (αDLS) and α–NITEGE. Each lane was loaded with 50% of the proteoglycan-rich fraction isolated from one 100 mm confluent culture. All samples were pretreated with chondroitinase ABC before electrophoresis. Images separated by dividing lines were from different lanes of the same gel.


WT
TS5-/-
TS5-/-;
CD44-/-
CD44-/-
50 um
50um
Unwounded
4
8
15
DAYS POSTWOUNDING

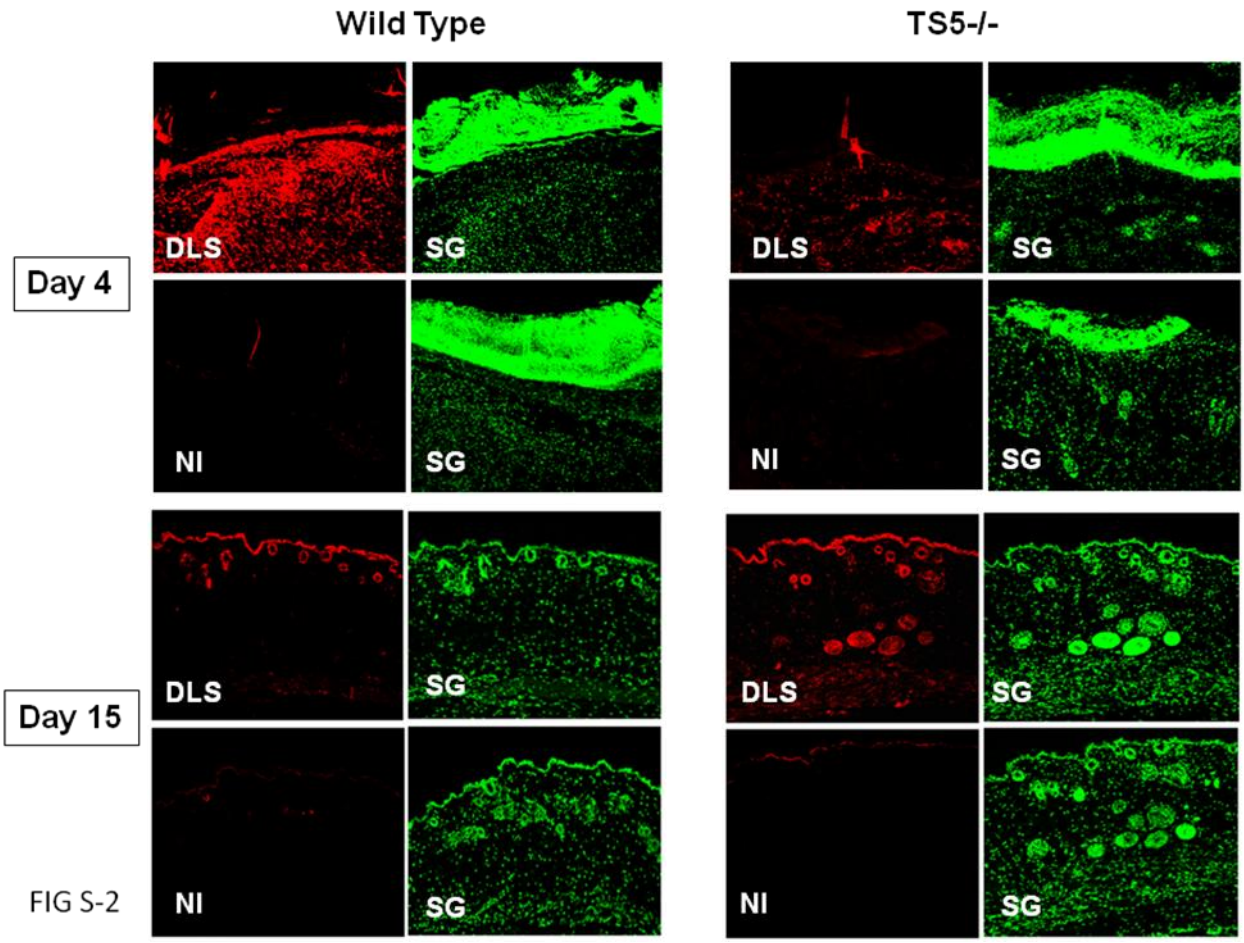

Wild Type
TS5-/-
Day 4
Day 15
DLS
SG
NI
SG
DLS
SG
NI
SG
DLS
SG
NI
SG
DLS
SG
NI
SG

FIG S-2

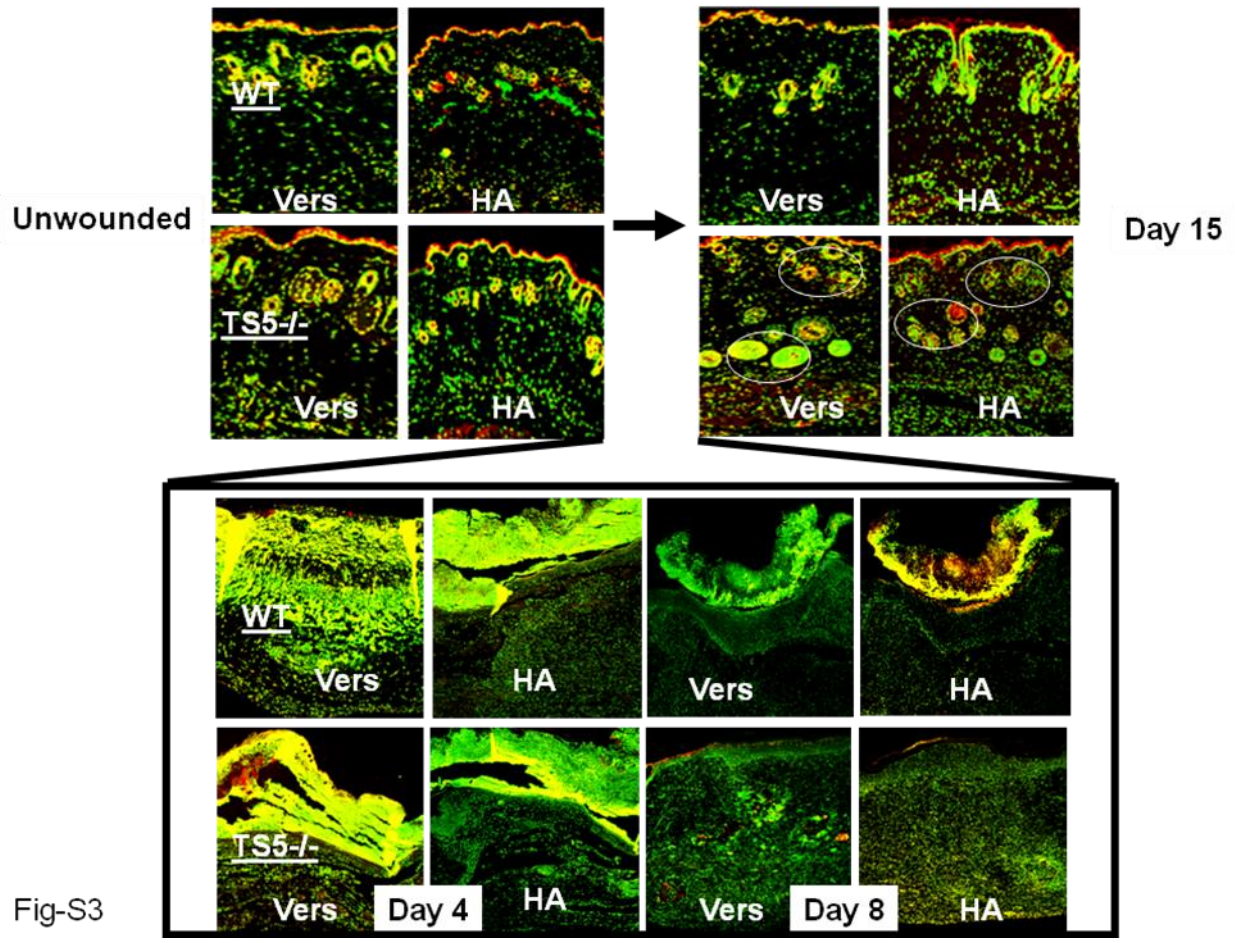
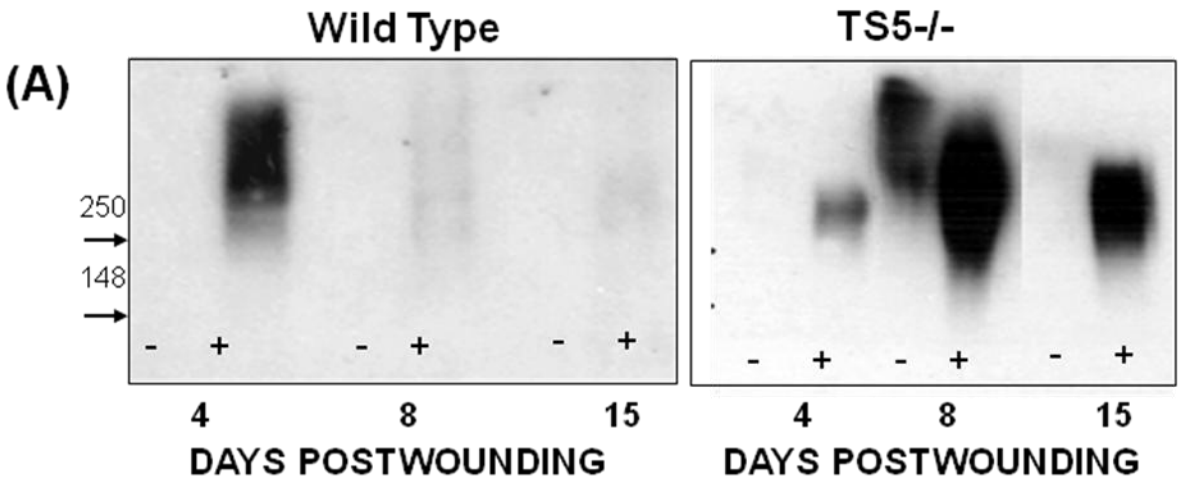

Unwounded
WT
Vers
HA
TS5-/-
Vers
HA
Vers
HA
Vers
HA
Day 15
WT
Vers
HA
Vers
HA
TS5-/-
Vers
Day 4
HA
Vers
Day 8
HA

Fig-S3


(A)
Wild Type
TS5-/-
250
148
- + - + - +
- + - + - +
4 8 15
4 8 15
DAYS POSTWOUNDING
DAYS POSTWOUNDING

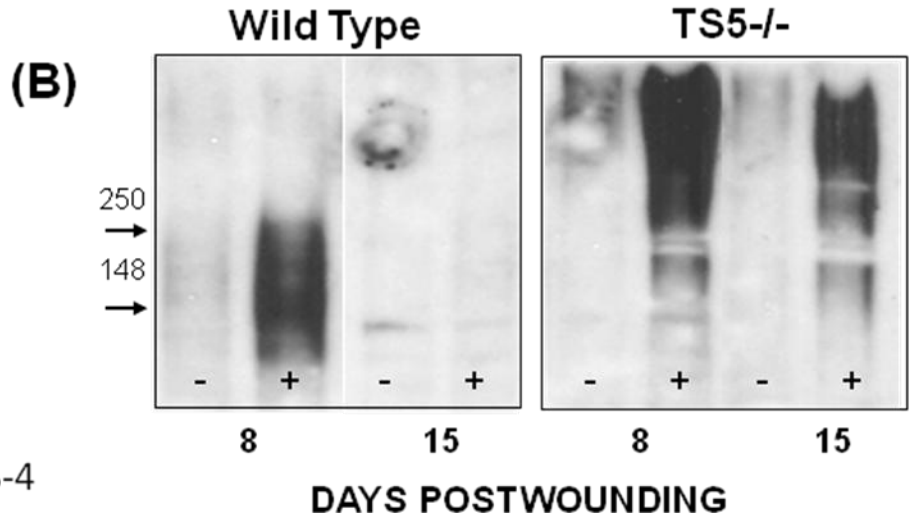

(B)
Wild Type
TS5-/-
250
148
- + - +
- + - +
8 15
8 15
DAYS POSTWOUNDING

Fig S-4

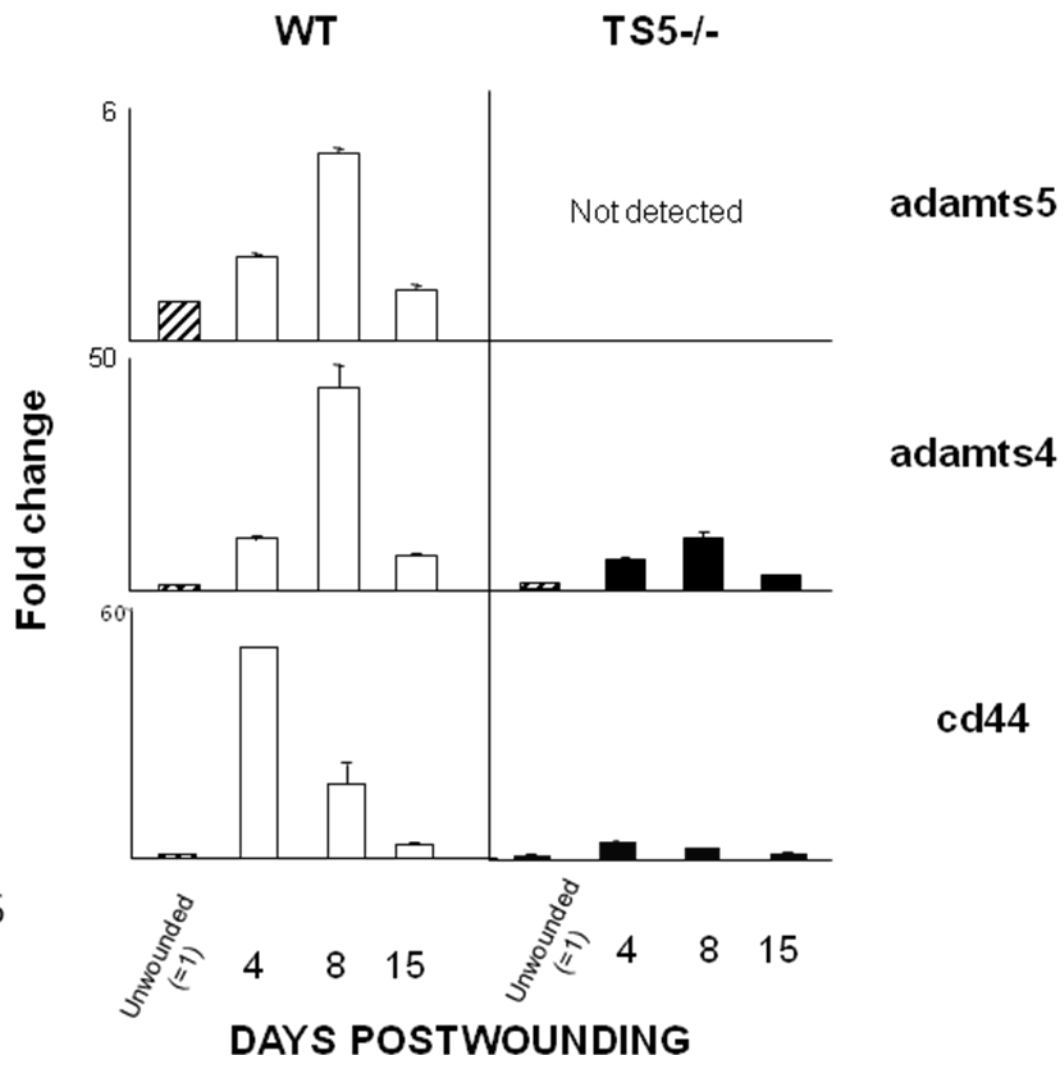

WT
TS5-/-
6
Not detected
adamts5
50
adamts4
60
cd44
Fold change
Unwounded (=1)
4
8
15
Unwounded (=1)
4
8
15
DAYS POSTWOUNDING

Fig S-5

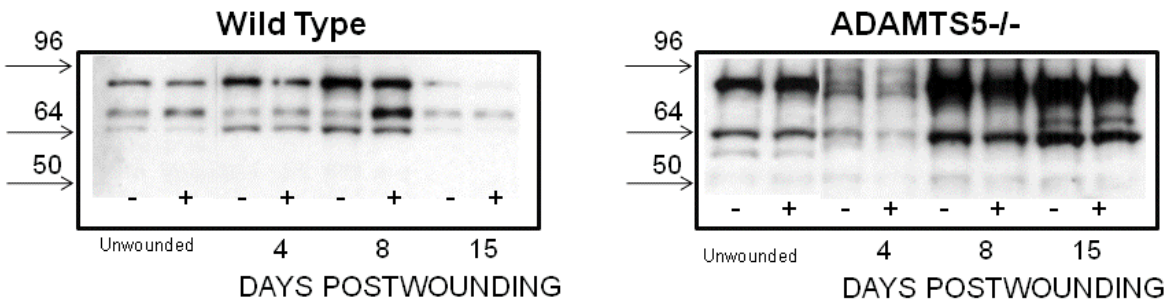

Wild Type
96
64
50
- + - + - + - +
Unwounded
4
8
15
DAYS POSTWOUNDING
ADAMTS5-/-
96
64
50
- + - + - + - +
Unwounded
4
8
15
DAYS POSTWOUNDING

Fig.S-6

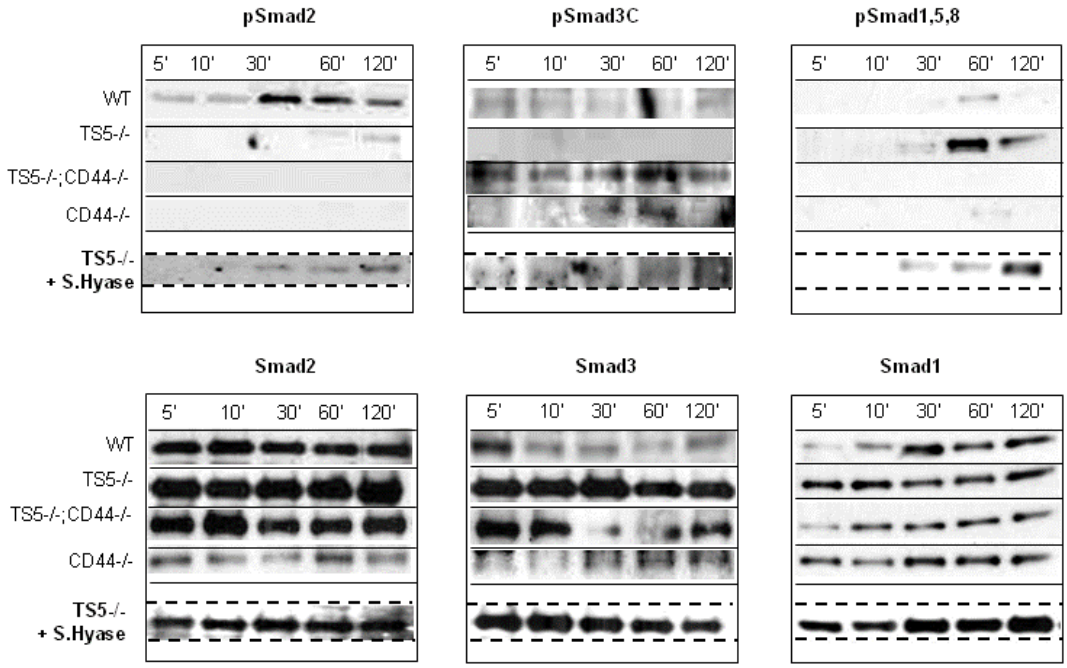

pSmad2
pSmad3C
pSmad1,5,8
5' 10' 30' 60' 120'
WT
TS5-/-
TS5-/-;CD44-/-
CD44-/-
TS5-/-
+ S.Hyase
Smad2
Smad3
Smad1

Fig.S-7

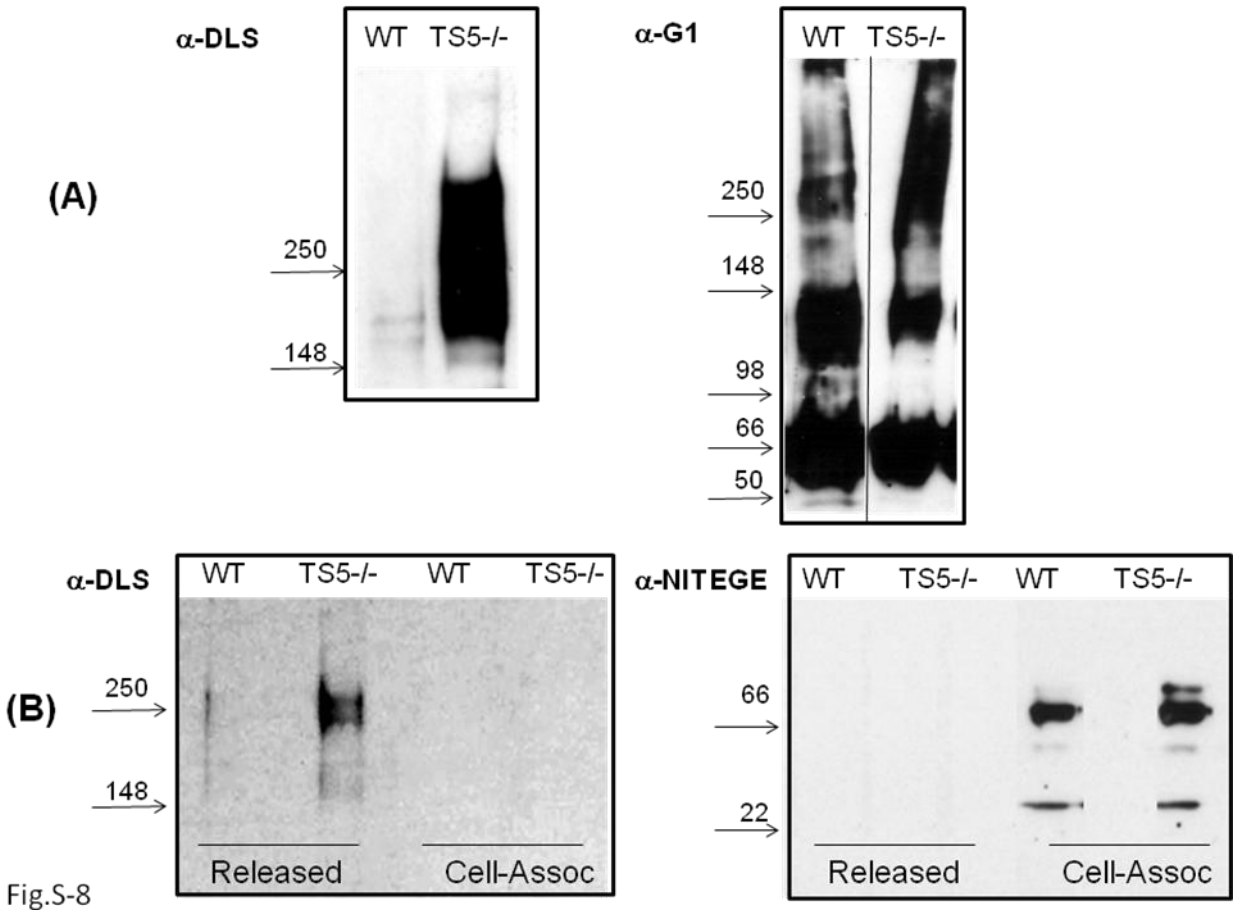

(A)
α-DLS
WT
TS5-/-
250
148
α-G1
WT
TS5-/-
250
148
98
66
50
(B)
α-DLS
WT
TS5-/-
WT
TS5-/-
250
148
Released
Cell-Assoc
α-NITEGE
WT
TS5-/-
WT
TS5-/-
66
22
Released
Cell-Assoc

Fig.S-8

Table S-1: Basal Levels of Gene Expression in Unwounded Skin from WT and KO mice

	WT (ΔCT)[1]	TS5-/-(ΔCT)[1]		TS5-/-//CD44-/- (ΔCT)[1]		CD44-/- (ΔCT)[1]	
Gene	Mean(SD)	Mean(SD)	*p*	Mean(SD)	*p*	Mean(SD)	*p*
agg	17.64(1.11)	***14.82(0.85)**	***0.025***	***13.31(0.55)**	***0.018***	Not detected	
vers	15.79(0.30)	***14.00(0.52)**	***0.010***	***14.33(0.21)**	***0.04***	***17.23(0.34)**	***0.047***
col1	12.69(2.63)	10.56(2.03)	*0.33*	***8.64(1.10)**	***0.002***	13.06(0.43)	*0.12*
col3	5.88(1.04)	4.24(0.98)	*0.12*	5.97(0.23)	*0.99*	6.26(0.22)	*0.4*
tgfb1	8.05(0.37)	***6.80(0.45)**	***0.031***	***6.16(0.53)**	***0.015***	8.31(0.78)	*0.98*
tgfbRII	9.59(0.28)	***8.17(0.69)**	***0.035***	***7.85(0.25)**	***0.004***	9.97(1.12)	*0.98*
alk5	7.33(0.11)	***6.62(0.23)**	***0.010***	7.16(0.23)	*0.87*	7.63(0.47)	*0.87*
alk1	7.55(0.48)	7.54(0.45)	*0.99*	7.82(0.35)	*0.99*	7.96(0.46)	*0.78*

[1]ΔCT= relative to GAPDH. Data represent triplicate analyses of RNA preparations from 3 separate mice of each genotype.
*= significantly ($p<0.05$) increased or decreased relative to WT expression.

Table S-2: Basal Levels of Gene Expression in NBF from WT and TS5-/- mice

Gene	WT (ΔCT)[1] Mean(SD)	TS5-/-(ΔCT)[1] Mean(SD)
agg	10.49(0.13)	10.72(0.07)
vers	5.18(0.18)	5.72(0.71)
col1	7.82(0.27)	7.95(0.69)
col2	Not Detected	Not Detected
col3	1.17(0.12)	4.35(0.76)
sox9	4.11(0.25)	4.82(0.45)

[1]ΔCT= relative to GAPDH. Data represent triplicate analyses of RNA preparations from 3 separate cell preparations from each genotype.