

Supplementary Figure 1.

Normal skin fibroblasts were incubated with TAK242 (as indicated) for indicated periods. **A.** After 24 h, cytotoxicity was determined (percent of LDH release). **B.** Fibroblasts from wt and TLR4 mutant mice skin transiently transfected with COL1A1-luc were incubated in medium with endotoxin-stripped Fn^{EDA} (1 ug/ml) in the presence or absence of TAK242 (3uM) for 24 h. Whole-cell lysates were assayed for their luciferase activities. Results are means \pm SD from three determinations. * $P = 0.004$, Fn^{EDA} alone versus treated with TAK242 in wt. $P = \text{ns}$, Fn^{EDA} alone versus treated with TAK242 in TLR4 mutant. Sidak's multiple comparison test. ns, not significant.

Supplementary Figure 2.

Fibroblasts from three healthy donors' skin were incubated in medium with TAK242 (3uM) for 24 h and mRNA levels were determined by real-time qPCR. Results, normalized with GAPDH, are means \pm s.d. compared to vehicle-treated controls. Control versus TAK242; Paired t-test. $P = \text{ns}$. not significant. Each dot and color represents an individual.

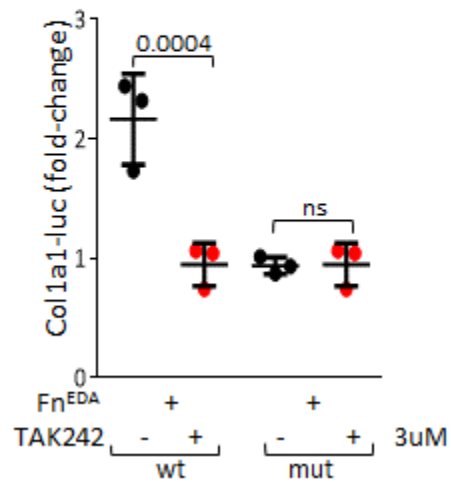
Supplementary Table 1

SSc fibroblasts derived from the subjects indicated below

Sample ID	Age	Sex	dc/lc	Disease stage	MRSS
SSc1107	48	M	dcSSc	Early	25
SSc1121	47	F	dcSSc	Late	26
SSc1068	49	F	dcSSc	Late	27
SSc1097	64	F	dcSSc	Early	9

dcSSc diffuse cutaneous SSc; F, female; M, male; mRSS, modified Rodnan skin score (1 to 51).

Supplementary Fig. 1



Supplementary Fig. 2

