Supplemental information – Kruppa et al.

Supplemental table legends

Supplemental Table S1. qPCR inflammation array, complete list of values for the analyzed genes.

Supplemental Table S2. Identified C-terminal cleavage sites.

Supplemental figure legends

Supplemental Fig. 1. Normal epidermal differentiation of healing meprin deficient epidermis. A, Epidermis of 14-day wounds stained for differentiation markers involucrin and loricrin. Nuclei were counterstained with DAPI (blue). Scale bar = 50 μm. **B**, Epidermal tongues of 3-day wounds and re-epithelialized epidermis of 7-day wounds stained for E-cadherin. Scale bar = 50 μm.

Supplemental Fig. 2. Similar speed of scratch wound closure by murine keratinocytes with combined meprin deficiency. Confluent monolayers of primary murine keratinocytes isolated from WT, *Mep1a*$^{-/-}$, *Mep1b*$^{-/-}$, and combined *Mep1a*$^{-/-}$/ *Mep1b*$^{-/-}$ adult tails were wounded with a pipet tip. Wound closure was followed over time. Shown is the remaining wound with time after wounding expressed as parts of the original wound area (0h). N = 3, per genotype, values represent mean ± S.D.

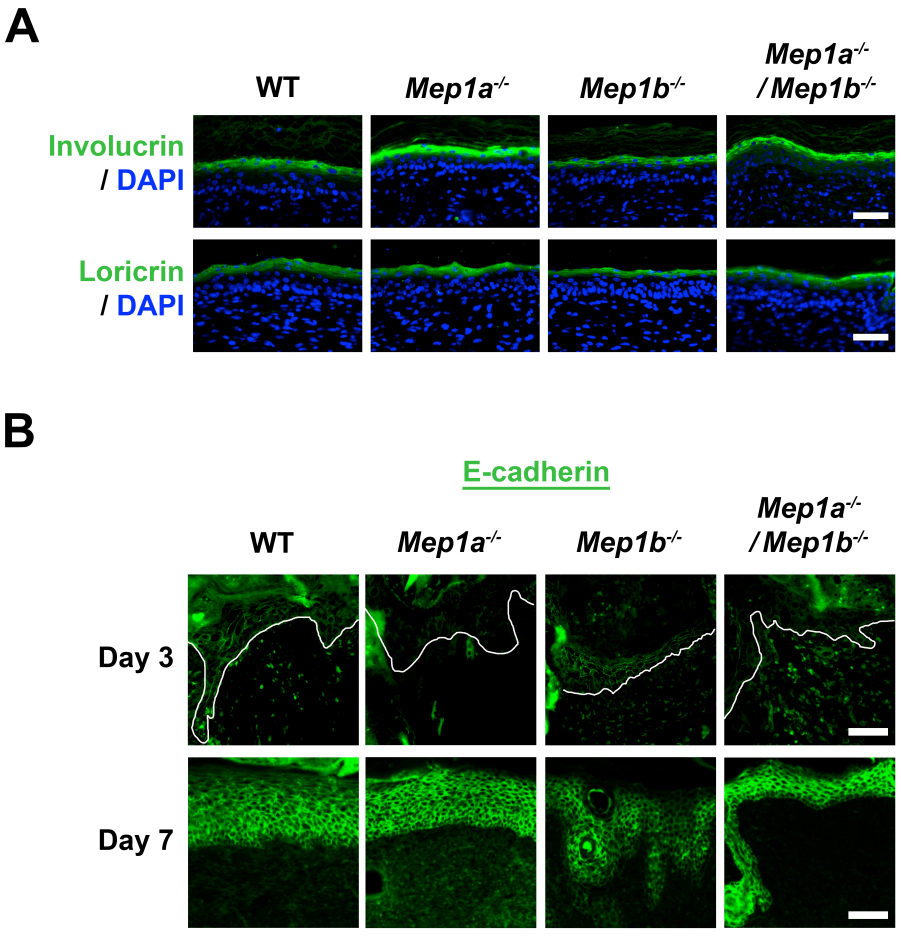
Supplemental Fig. 3. Meprin deficiency alters expression of IL-1 system-related genes. A, Genes that were identified so be significantly altered from a qPCR inflammation array. **B**, qPCR analysis of more wounds including wounds from mice with combined meprin deficiency to validate changes in expression of genes linked to the IL1 system observed in the array (A). The gene expression was normalized to *Gapdh* expression. For both A and B, 3-day-old wounds were analyzed. Values for individual wounds (n = 6), mean ± S.D. are shown, **P* < 0.05 as analyzed by one-way ANOVA with Tukey's correction.

Supplemental Fig. 4. Altered abundance in meprin deficient wounds of markers linked to dermal healing. A, Western blot of protein lysates from 7-day wounds probed for αSMA and β-tubulin as loading control. **B**, Bar graphs show quantification of fibronectin staining intensity as quantified by Image J for 7-day and 14-day wounds. Individual values (n = 6-13 for day 7 and n = 4-10 for day 14) mean ± S.D. are shown, **P* < 0.05; ***P* < 0.01; ****P* < 0.001as analyzed by one-way ANOVA with Tukey's correction.

Supplemental Fig. 5. *Bmp1/mTld* expression in WT and meprin deficient wounds. Real-time qPCR of cDNA from 3-day-old wounds. 3 to 6 wounds per genotype were analyzed. Gene expression of *Bmp1/mTld* was normalized to *Gapdh* expression and then further compared to the expression in WT. The data are plotted as percentage of WT with the mean value of WT set to 100%. Individual values, mean ± S.D. are shown.

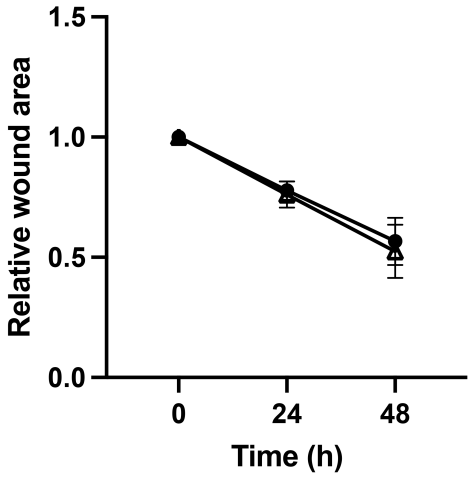
Supplemental Fig. 6. Meprin β activity in WT and RDEB mouse forepaw skin. Meprin β activity was measured in protein lysates prepared from forepaw skin from RDEB mice with heavy dermal fibrosis (8- and 12-week-old) and forepaw skin from age-matched WT littermates. Individual values, mean ± S.D. are shown. ***P* < 0.01; ****P* < 0.001 as analyzed by two-way ANOVA with Bonferroni correction.

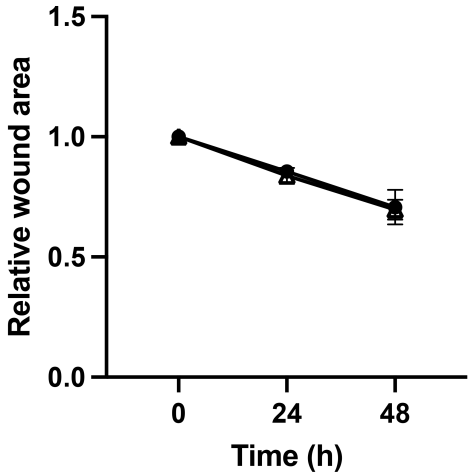
Supplemental Fig. 7. Meprin abundance is not reduced in cultured RDEB skin cells. Western blotting of protein lysates from subconfluent (80%) cultures of human keratinocytes and fibroblasts derived from WT donors or donors with complete collagen VII negative RDEB. The blots were probed for meprin α and meprin β. β-actin was used as loading control.

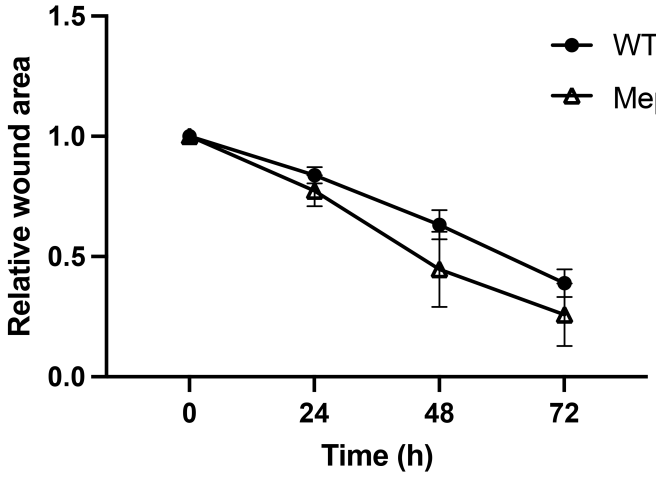


Supplemental Fig. 1

Keratinocyte scratch wound healing

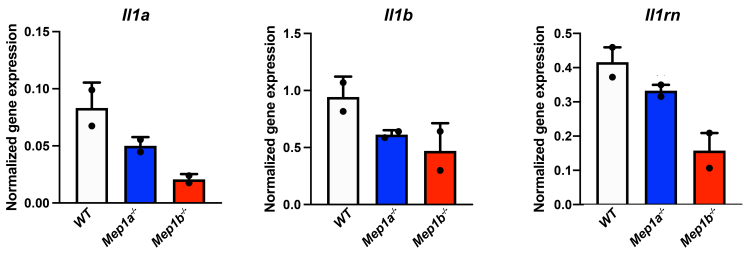




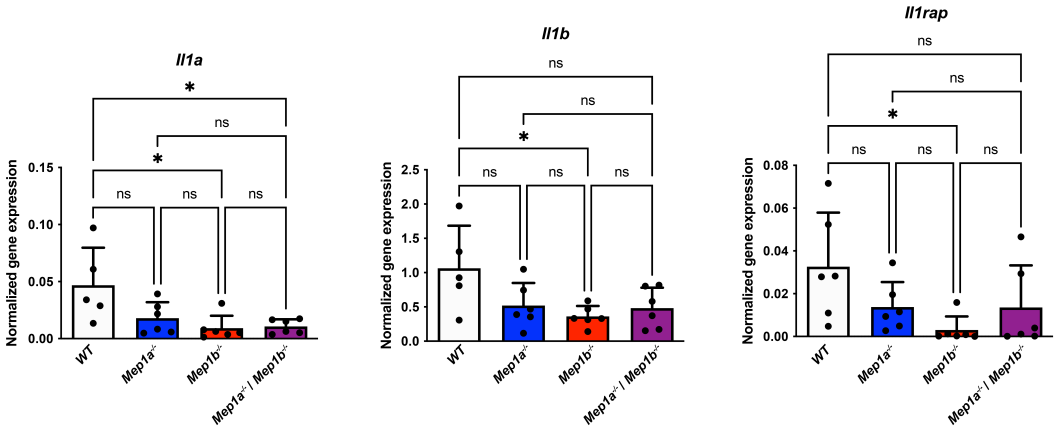


Supplemental Fig. 2

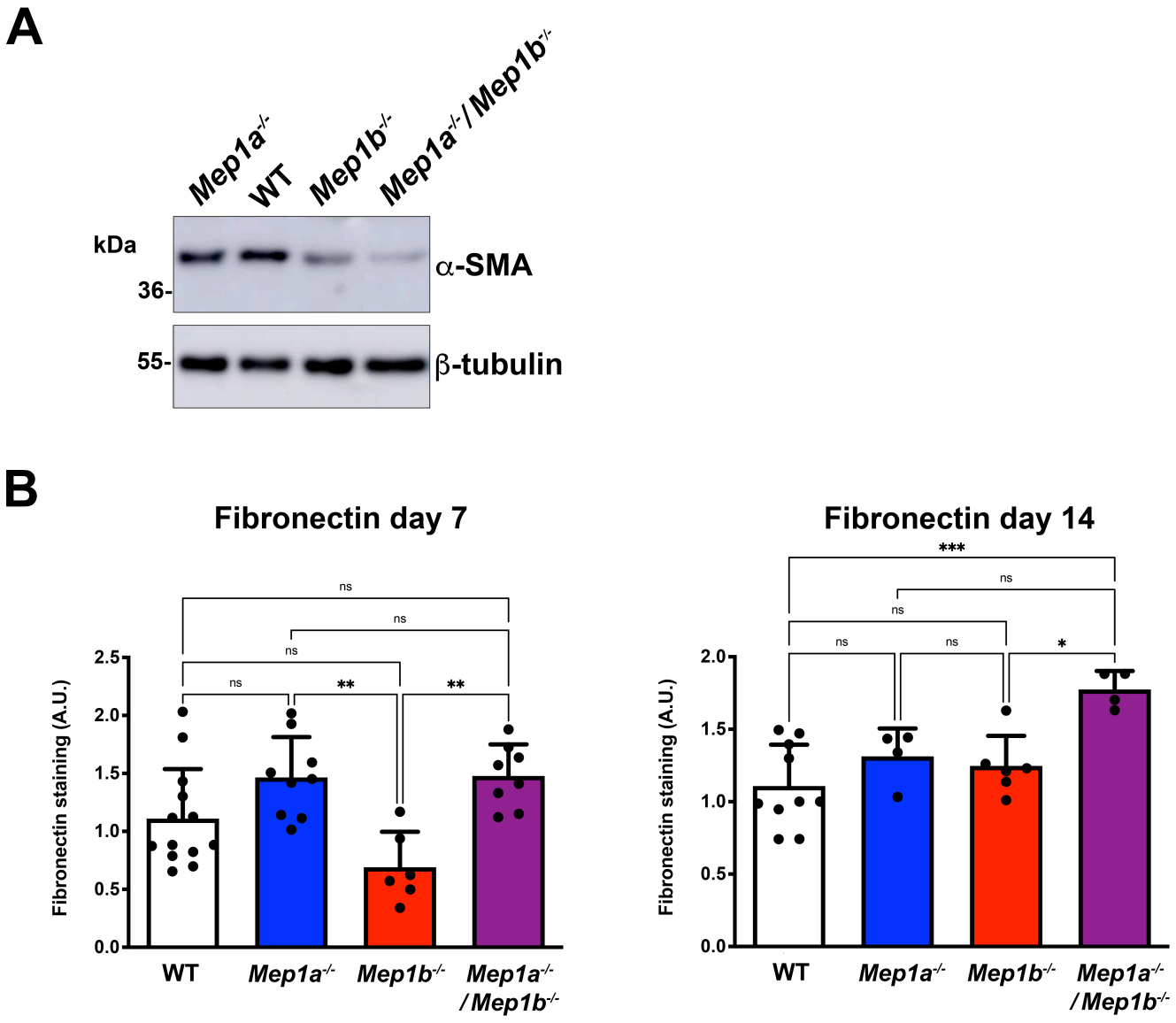
A



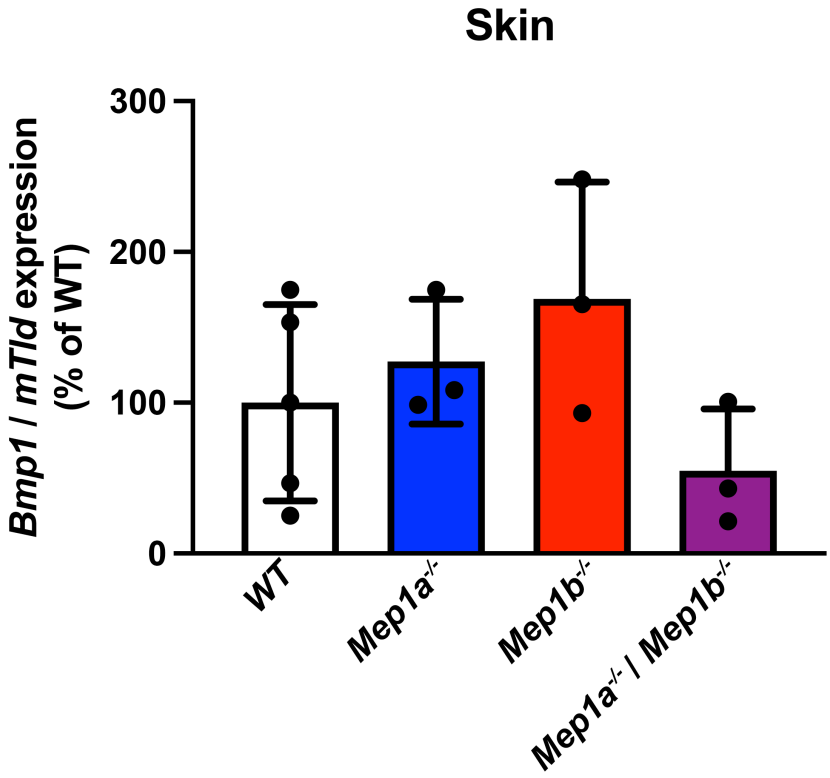
B



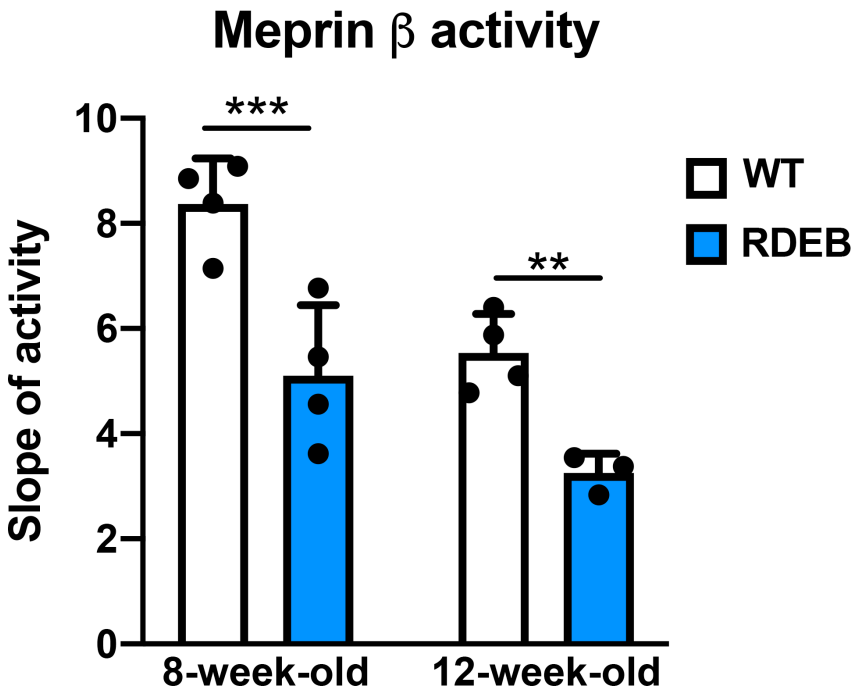
Supplemental Fig. 3



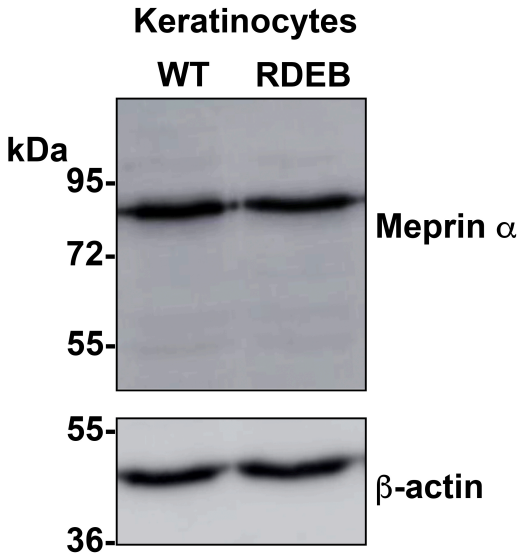
Supplemental Fig. 4

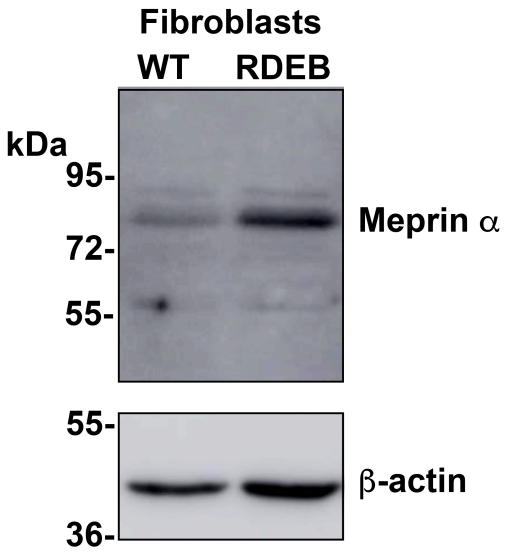


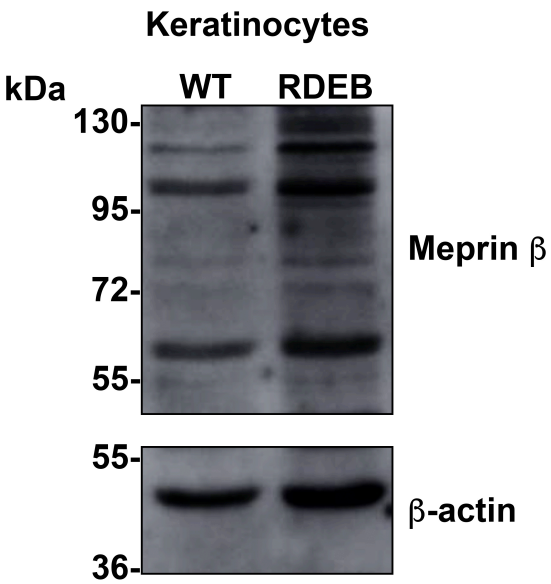
Supplemental Fig. 5

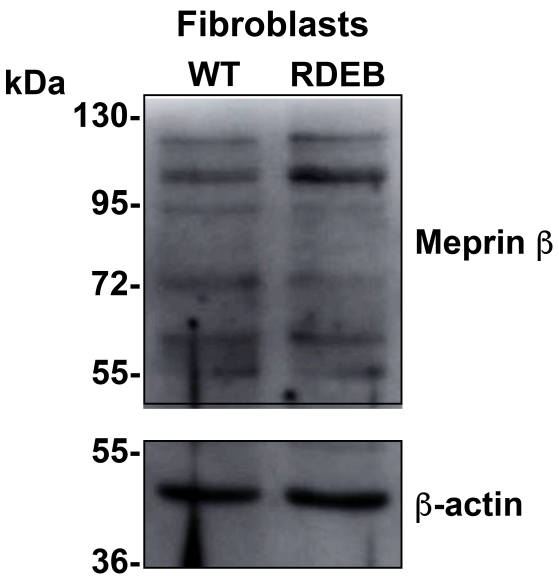


Supplemental Fig. 6









Supplemental Fig. 7