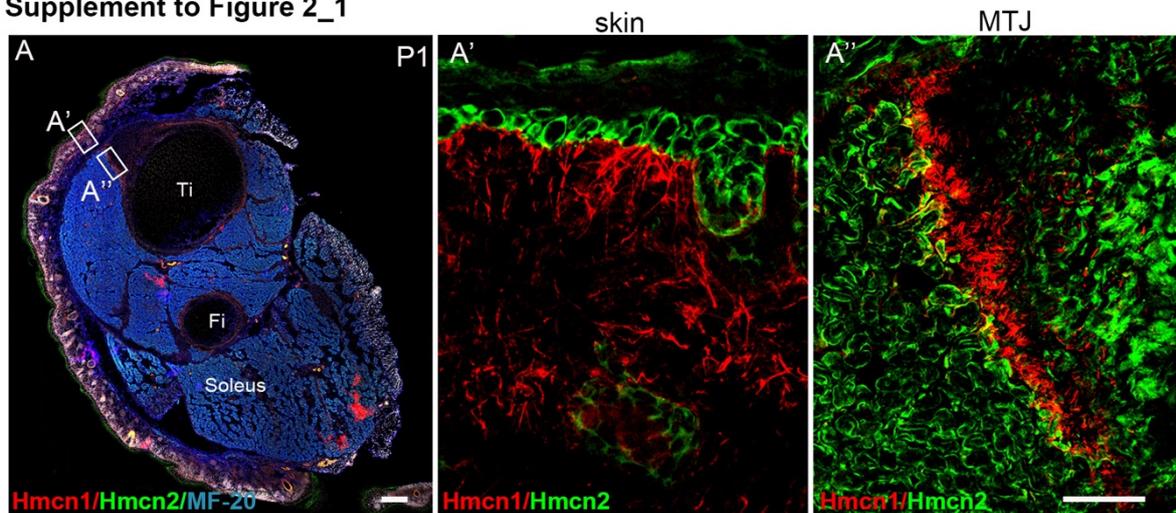


## Supplemental Information

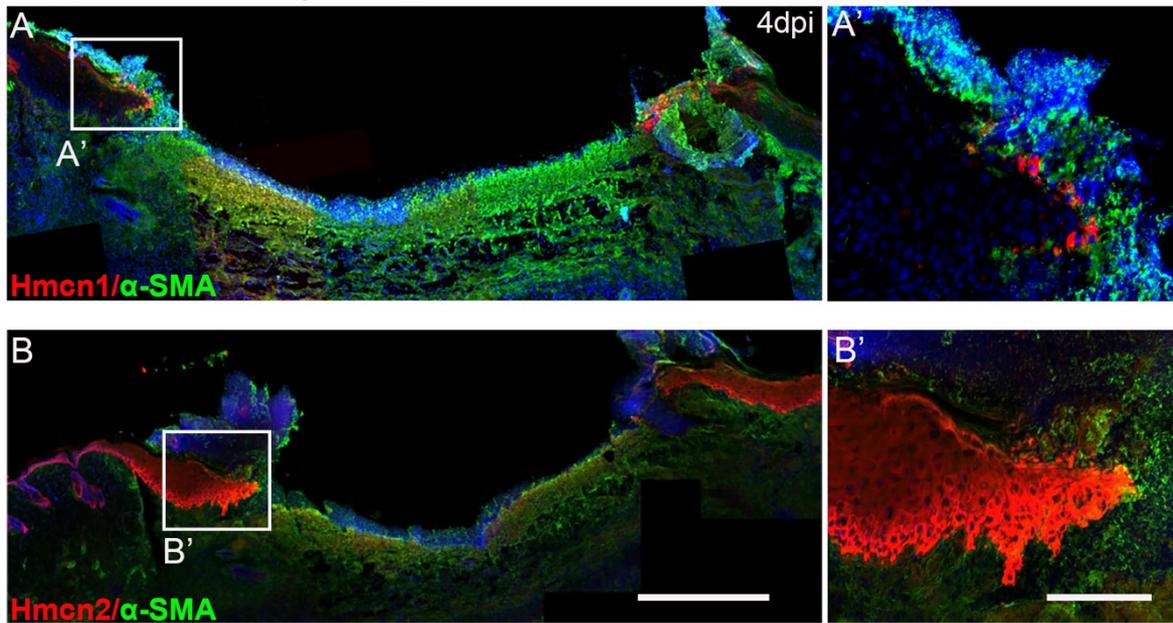
### Supplement to Figure 2\_1



**Supplementary Figure S2\_1. Differential localization of mouse Hmcn1 and Hmcn2 at the dermal-epidermal junction (DEJ) and muscle-tendon junction (MTJ).**

(A) Representative cross section through calf of neonate, immuno-stained with antibodies against Hmcn1 (red), Hmcn2 (green), MF-20 (blue). Higher magnification images of DEJ (A') and MTJ (A'') show clear differential expression of Hmcn2 in epithelial (epidermis, skeletal muscle) and Hmcn1 in mesenchymal (dermis, tendon) tissue. Scale bars A= 200  $\mu$ m; A', A''= 50  $\mu$ m.

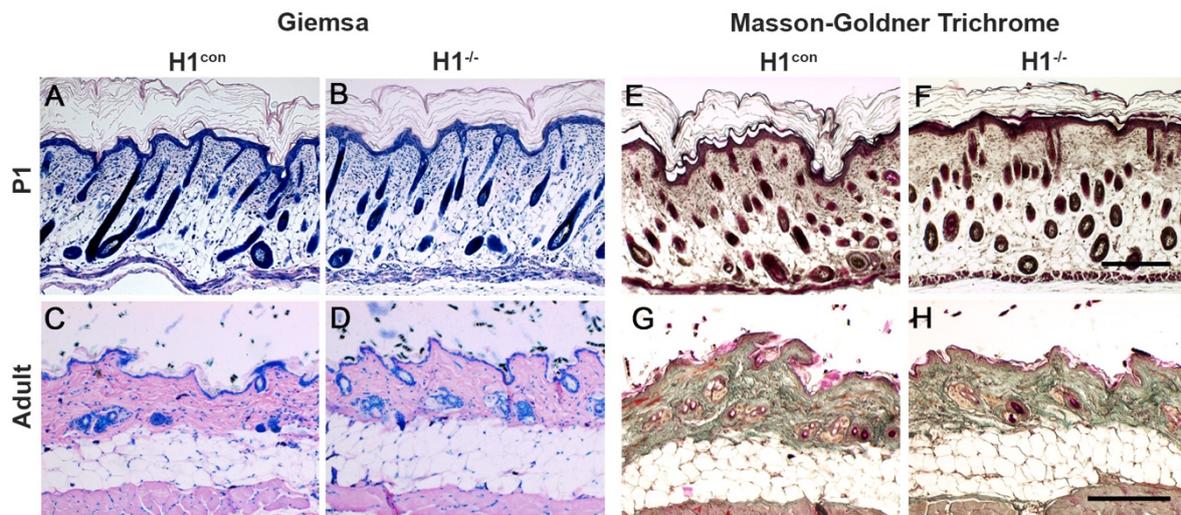
## Supplement to Figure 2\_2



**Supplementary Figure S2\_2. Hmcn1 and Hmcn2 protein localization during cutaneous wound healing.**

(A) Hmcn1 (red) is up-regulated in the dermis adjacent to the epidermal tongues of closing wounds. (B) Hmcn2 (red) is strongly up-regulated in the basal keratinocytes within the epidermal tongues of closing wound.  $\alpha$ -SMA (green), marker for myofibroblast differentiation and DAPI (blue) counterstains nuclei. Scale bars: A, B= 500  $\mu$ m; A', B'= 100  $\mu$ m.

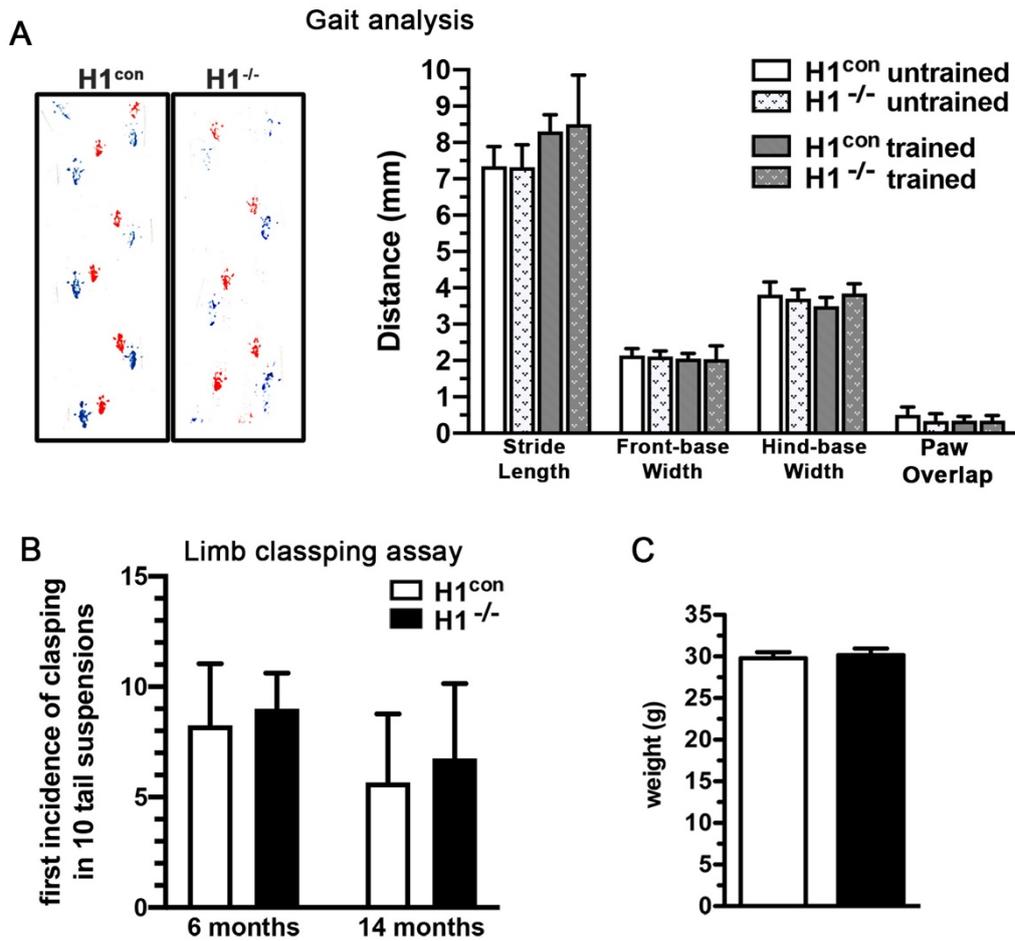
Supplement to Figure 5\_1



**Supplementary Figure S5\_1. Histological analysis of the back skin in newborn and adult mice.**

(A-D) Giemsa and (E-H) Masson-Goldner Trichrome staining show comparable dermal/ epidermal morphology, including skin appendages and collagen content between H1<sup>con</sup> and H1<sup>-/-</sup> mice. Scale bar represents 200  $\mu$ m. Abbreviations: H1<sup>-/-</sup>, *Hmcn1*<sup>-/-</sup> mutants; H1<sup>con</sup>, sibling controls of *Hmcn1*<sup>-/-</sup> mutants.

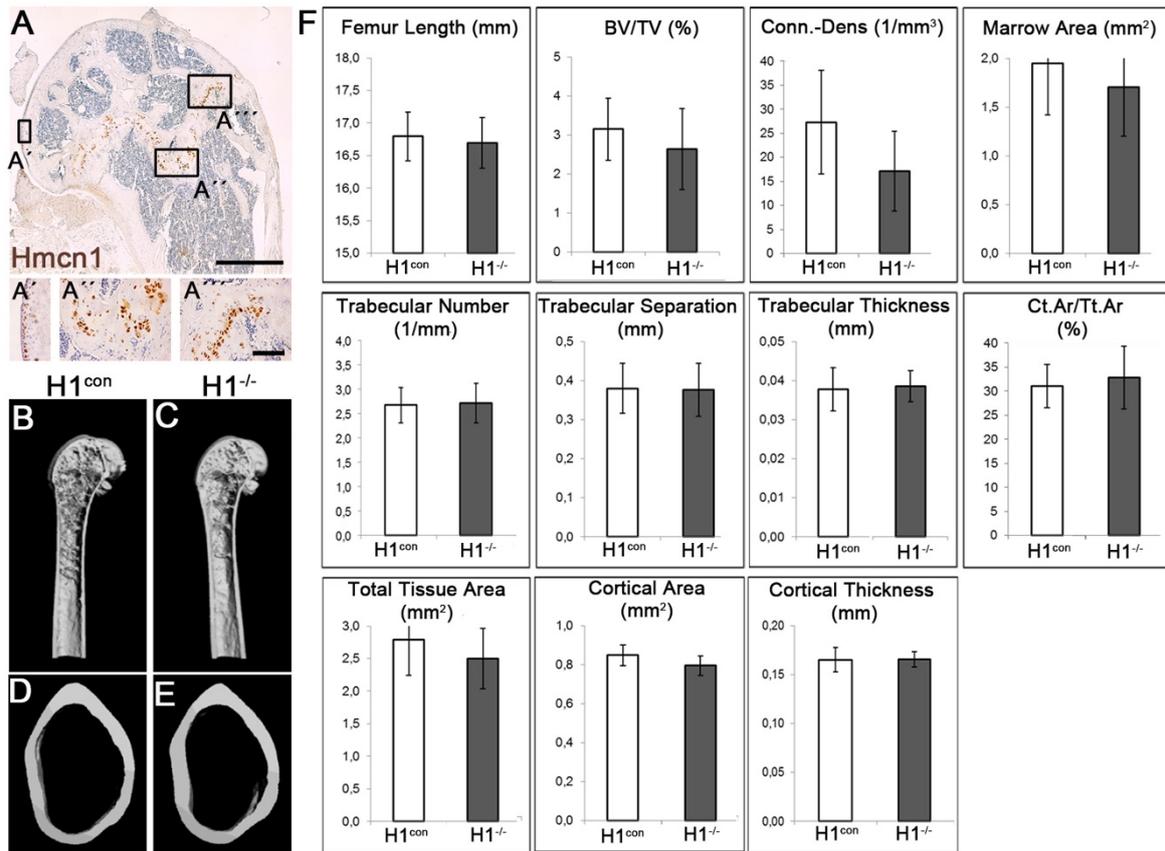
Supplement to Figure 5\_2.



**Supplementary Figure S5\_2. Locomotion tests**

(A) Footprint gait analysis of H1<sup>con</sup> and H1<sup>-/-</sup> mice that were trained or untrained. Non-toxic paint was applied to record the footprint placement pattern. Stride length, stride width, hind-base width and paw overlap were measured as specified in Materials and Methods, revealing no significant differences between 14-months old control and H1<sup>-/-</sup> mice. (B) Hindlimb clasping assay was tested in control (n=9) and H1<sup>-/-</sup> (n=9) mice of age of 6- and 14-months. Tail suspensions were performed up to ten times and stopped at first clear incidence of hindlimb clasping, revealing no significant differences between control and H1<sup>-/-</sup> mice. (C) No significant difference in body weights of tested 14-months old control and H1<sup>-/-</sup> mice. Abbreviations: H1<sup>-/-</sup>, *Hmcn1*<sup>-/-</sup> mutants; H1<sup>con</sup>, sibling controls of *Hmcn1*<sup>-/-</sup> mutants.

### Supplement to Figure 5\_3



### Supplementary Figure S5\_3. $\mu$ CT analysis of trabecular and cortical area of the femur

(A) Immunohistological staining against mouse *Hmcn1* (brown) shows the localization in the articular cartilage (A') and in the hypertrophic chondrocytes of the growth plate (A'', A'''). Nuclei were counterstained with hematoxylin. (B-E) Representative  $\mu$ CT 3D images of the femur of 15 months-old mice revealed no difference in bone structure between H1<sup>con</sup> controls and H1<sup>-/-</sup> mutants. Images show sagittal view of femur (B, C) or top view of the cortical bone of femur; 0.75mm around middiaphysis (D, E). (F) Quantification of the femur length, BV/TV (bone volume fraction), Conn.-Dens (connectivity density), marrow area, trabecular (Tt.Ar) and cortical area (Ct.Ar) of H1<sup>-/-</sup> mice (n=7) and H1<sup>con</sup> control siblings (n=9), as shown in (B-E). Scale bars A=500  $\mu$ m; A', A'', A'''=25  $\mu$ m. Abbreviations: H1<sup>-/-</sup>, *Hmcn1*<sup>-/-</sup> mutants; H1<sup>con</sup>, sibling controls of *Hmcn1*<sup>-/-</sup> mutants.