Supplementary Material

Supplementary Figures

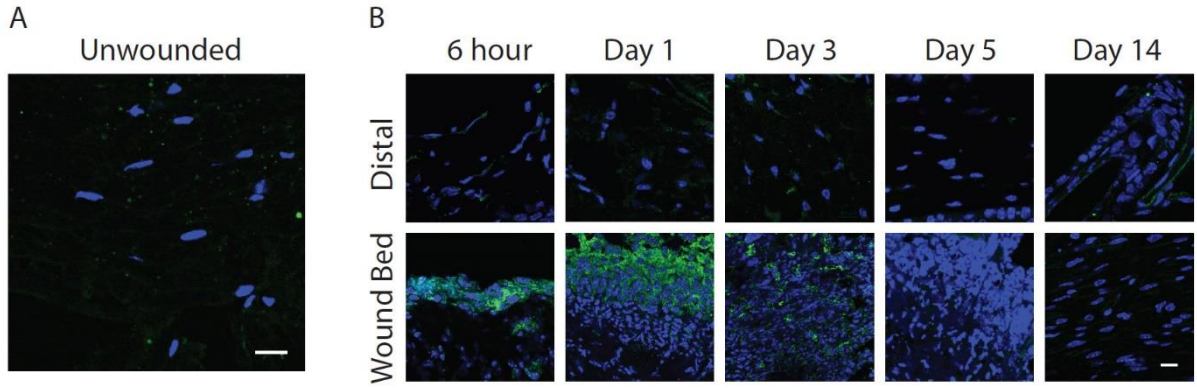

Figure S1. Lrg1 expression in mouse skin. Immunofluorescence staining detecting LRG1 (green) or DAPI (4′,6-diamidino-2-phenylindole; blue) in **A)** unwounded normal skin and **B)** distal intact skin and wound bed at different time points following wound creation. Scale bar: 20μm.

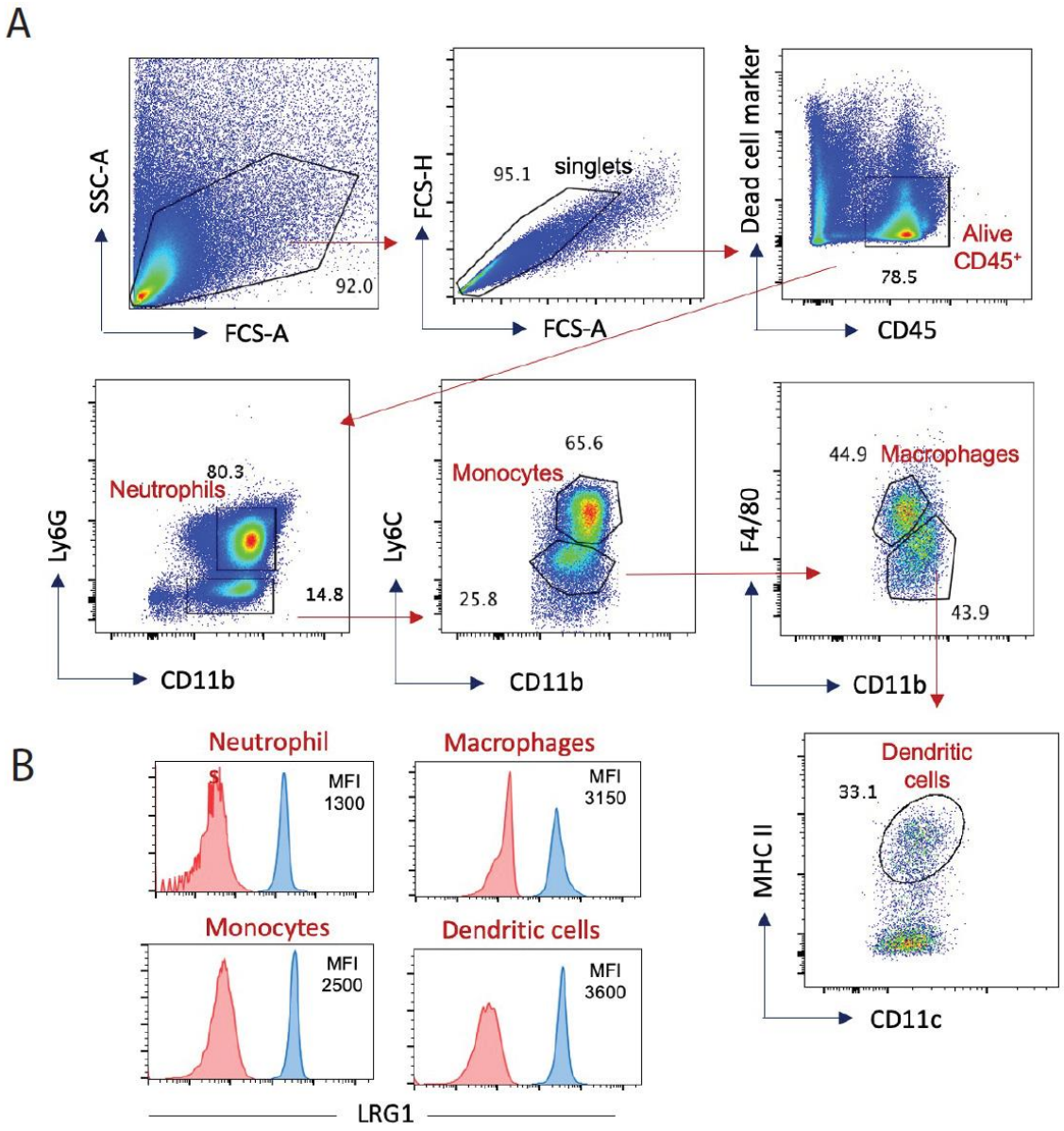

Figure S2. Flow cytometry analysis of LRG1 expressing myeloid cells present in wounds. (A) Isolated cells were stained with anti CD45 (pan leukocyte), anti-Ly6G (neutrophils), anti Ly6C (monocytes), anti F4/80 (macrophages) and anti CD11c together with MHC class II (dendritic cells). (B) Histogram show the expression of Lrg1 in the correspondent myeloid population: blue histogram: anti-Lrg-1 Ab; red histogram: negative control. The mean of fluorescence intensity (MFI) indicates the expression level of Lrg1.

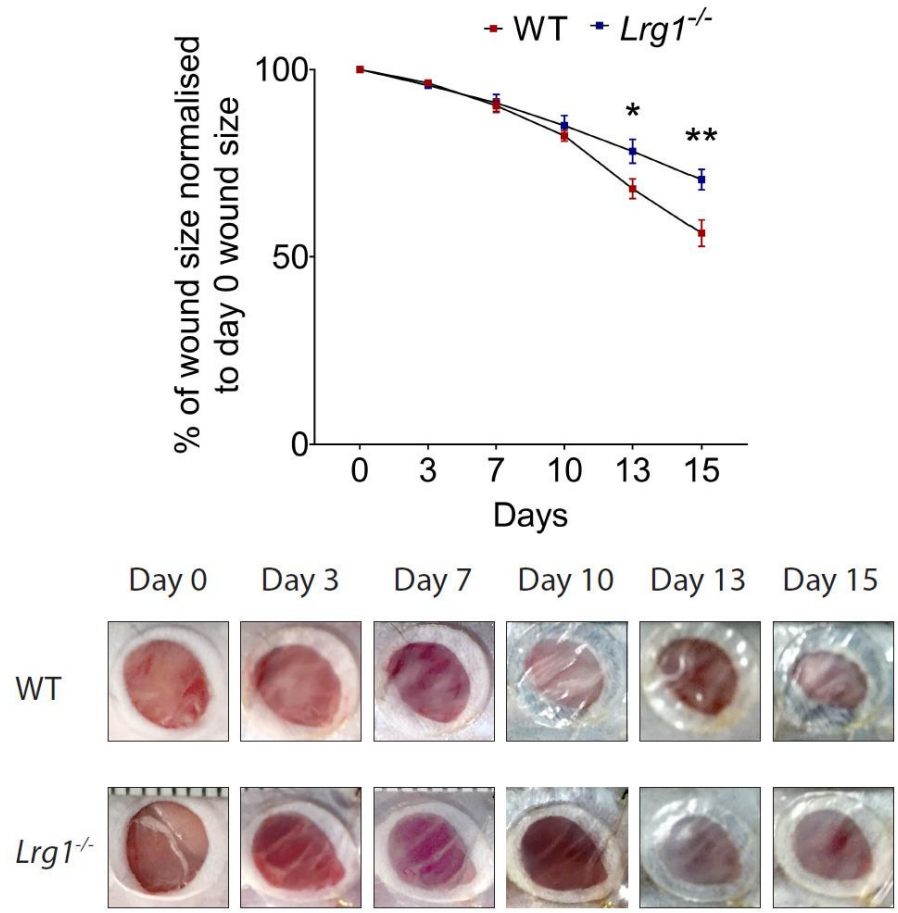

Figure S3. Splinted excisional wound closure over time. Representative pictures splinted wounds and quantification of wound closure immediately following injury, and 3, 7, 10, 13 and 15 days after wounding. Data represent mean ± SEM of n = 7 animals. Significance was determined by student's t-test. *p<0.05, **p < 0.01.

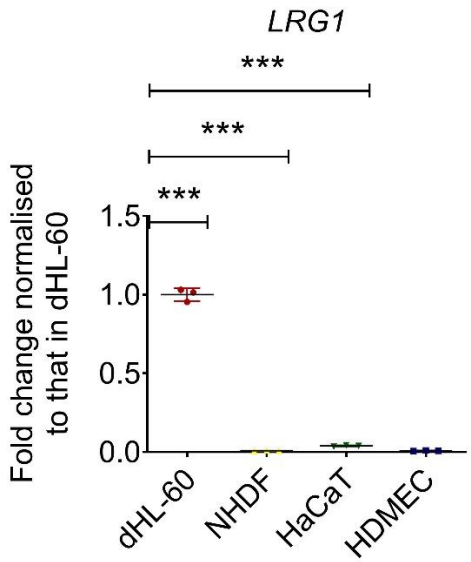

Figure S4. LRG1 is expressed at a high level in dHL-60 cells. qRT-PCR analysis demonstrated that LRG1 is highly expressed in dHL-60 cells. NHDF indicates normal human dermal fibroblasts, HaCaT is an immortalized human keratinocyte cell line, and HDEMC indicates human dermal microvascular endothelial cells. Data are represented as mean ± SD of n = 3 independent experiments. Significance was determined by one - way ANOVA followed by Tukey multiple comparisons test, ***P<0.001.

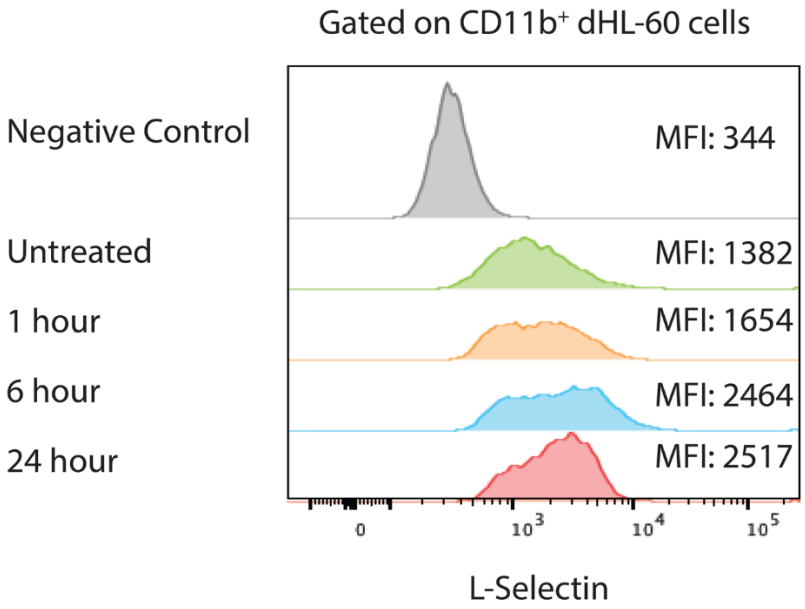

Figure S5. Representative flow cytometry results of rhLRG1-treated dHL-60 cells at different time points.

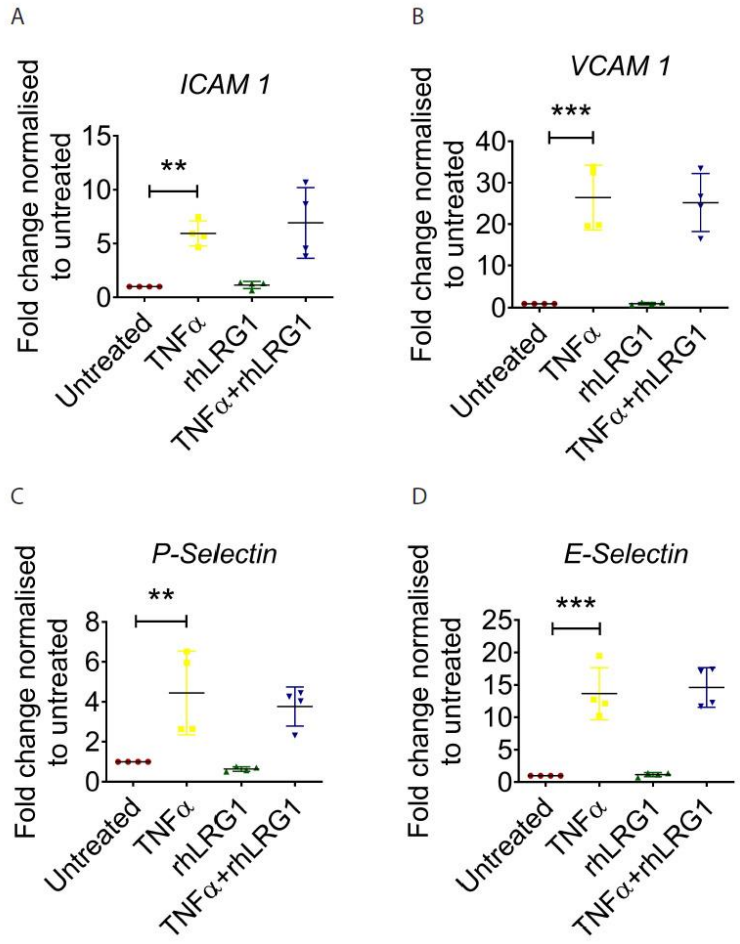

Figure S6. rhLRG1 doesn't affect the TNFα-induced expression of endothelial adhesion molecules. qRT-PCR analysis of the expression of endothelial adhesion molecules in the presence of TNFα and/or rhLRG1. Data are represented as mean ± SD of n = 4 independent experiments. Significance was determined by one - way ANOVA followed by Tukey multiple comparisons test, **P<0.01, ***P<0.001.

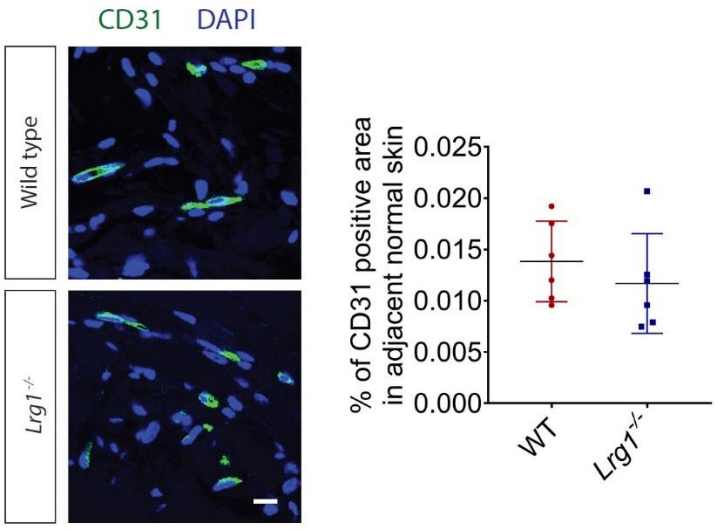

Figure S7. Characterization of vascular density in the distal part of skin from wild-type and *Lrg1-/-* mice. Representative immunofluorescence staining of CD31 (Green) and DAPI (blue) (left) and quantification of vessel density (right). Scale bar: 15μm. Data are represented as mean ± SD of n=6 mice. Significance was determined by student's t-test.

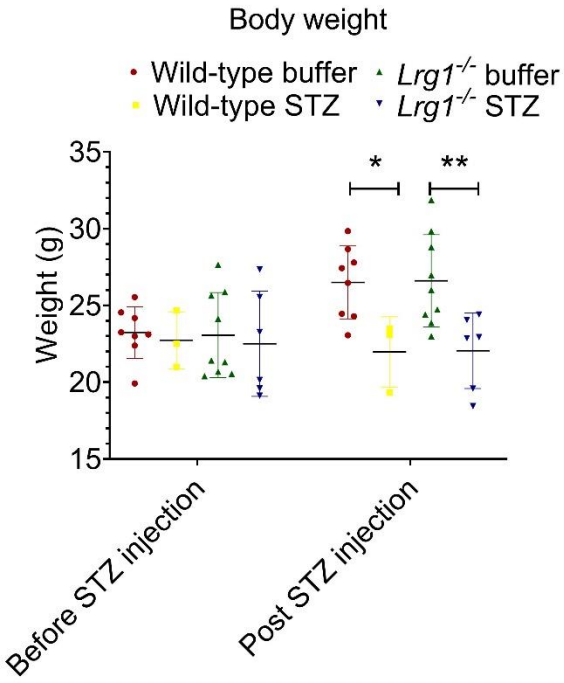

Figure S8. The body weight in streptozotocin-induced diabetic wild-type and *Lrg1*$^{-/-}$ mice. Data are represented as mean ± SD of n > 6 animals. Significance was determined by two - way ANOVA followed by Tukey multiple comparisons test student's t-test. *P<0.05, **P<0.01.