

# **Expanded View Figures**

#### Figure EV1. Attenuation of wound contraction and increased scar area in $miR-223^{Y/-}$ mice.

- A Representative images using H&E staining of wound sites at day 7 in WT (n = 8) and miR- $223^{Y/-}$  (n = 6) mice. Scale bars: 500  $\mu$ m.
- B Representative images of Masson's Trichrome staining of collagen fibers (blue) in skin wound tissues of WT (n = 7) and  $miR-223^{Y/-}$  (n = 8) mice at day 14 after injury. Scar sites were visualized at the mid-point of the wound (indicated by dotted line). Nuclei are stained black, and cytosol is stained red. Scar formation is clearly recognizable by day 14 after injury. Scale bars: 500 µm.
- C Measurement of granulation tissue area at wound sites from WT (day 7; n = 8, day 14; n = 7) and  $miR-223^{\gamma/-}$  (day 7; n = 6, day 14; n = 8) mice.
- D Representative images of  $\alpha$ SMA-positive woundinfiltrated myofibroblasts at day 7 in wound sites from WT and  $miR-223^{Y/-}$  mice (n = 7). Scale bars: 50 um.
- E Quantification of expression of  $\alpha$ SMA at day 7 in wound sites from WT and  $miR-223^{Y/-}$  mice (n = 7).

Data information: All values represent the mean  $\pm$  SD. Unpaired *t*-tests were used to generate *P*-values indicated in the Figure. \*P < 0.05, \*\*P < 0.01.





### Figure EV2. Macrophage infiltration of wound sites in miR-223<sup>Y/-</sup> and WT mice.

- A Representative images of F4/80-positive macrophages at wound sites from WT (day 3; n = 6, day 7; n = 5) and  $miR-223^{\gamma/-}$  (day 3; n = 6, day 7; n = 4) mice. Scale bars: 50  $\mu$ m.
- B Quantification of F4/80-positive macrophages at wound sites from WT (day 3; n = 6, day 7; n = 5) and miR-223<sup>Y/-</sup> (day 3; n = 6, day 7; n = 4) mice.
- C Measurements of MIP-1 $\alpha$  at wound sites using ELISA (n = 6).

Data information: All values represent the mean  $\pm$  SD. Unpaired *t*-tests were used to generate *P*-values indicated in the Figure. \**P* < 0.05, \*\**P* < 0.01.



# Figure EV3. miR-223<sup>Y/-</sup> mice show accelerated Staphylococcus aureus-infected skin wound healing.

- A H&E staining of re-epithelialization at day 7 after injury (wound margin (arrowheads) and the leading edge of epithelia (arrows)). Dotted line indicates pathological necrotic lesion. Scale bars: 500 µm (top) and 100 µm (bottom).
- B Schematic indicating the measurements derived from histological sections.
- C Measurement of the epithelial tongue at day 3 and day 7 after injury in WT (day 3; n = 4, day 7; n = 8) and miR-223<sup>Y/-</sup> (day 3; n = 5, day 7; n = 6) mice.
- D Measurement of the total wound area, necrotic lesion area, and granulation tissue area at day 7 after injury in WT neutrophil-transplanted and  $miR-223^{\gamma/-}$  neutrophil-transplanted wounds (n = 6).
- E Quantification of the expression of  $\alpha$ SMA at day 7 in S. aureus-infected wound sites from WT (n = 6) and miR-223<sup>YI-</sup> mice (n = 7).
- F Measurements of the granulation tissue area at day 14 in WT (n = 7) or miR-223<sup>Y/-</sup> wound sites (n = 5).

Data information: All values represent the mean  $\pm$  SD. Unpaired t-tests were used to generate P-values indicated in the Figure. \*P < 0.05.



Figure EV4. miR-223 AS ODN in PB gel-treated Staphylococcus aureus-infected skin wound sites are improved compared with Pluronic gel.

- A The proportion of the wound remaining open relative to the initial *S. aureus*-infected wound area at each time point after the injury in control ODN in Pluronic gel versus *miR-223* AS ODN in Pluronic gel-treated wounds (*n* = 8).
- B The proportion of the wound remaining open relative to the initial S. aureus-infected wound area at each time point after injury in PB gel (n = 7) versus Pluronic gel (n = 8).
- C Measurement of the epithelial tongue at day 7 after injury in control ODN in PB gel and miR-223 AS ODN in PB gel-treated wounds (n = 6).

Data information: All values represent the mean  $\pm$  SD. Two-way ANOVA followed by Sidak multiple comparison test was used to generate the *P*-values indicated in the Figure. \*\**P* < 0.01. \*\*\**P* < 0.001.



# Figure EV5. Expression of CEBPA, RINX1, and PU.1.

- A Gene expression of CEBPA, RINX1, and PU.1 in dHL-60 after stimulation with PGN for 6 h measured by qPCR relative to beta-2-microglobulin (B2m) (n = 3).
- B Schematic representation of the genomic composition of the pre-*miR-223* locus and C/EBPα binding sites. ChIP-PCR was performed with PCR primers #1 and #2. The location of primers (-1,030/-810 with respect to the 5' end of the pre-*miR-223*) is shown in the lower panel together with sequence for the C/EBPα binding sites.
  C Representative image of ChIP-PCR production amplified by primers (220 bp) on 2% agarose gel. Anti-C/EBPα Ab-ChIP amplification in non-stimulated dHL-60 cells was markedly increased compared with 6-h PGN-stimulated dHL-60 cells. Control amplification was carried out using anti-IgG isotype control Ab-ChIP (negative control), anti-H3 histone Ab-ChIP (procedure positive control), and input chromatin.

Data information: All values represent the mean  $\pm$  SD. Unpaired *t*-tests were used to generate *P*-values indicated in the Figure. \*\*P < 0.01.