## **Supporting Information**

## Biswas et al. 10.1073/pnas.1001653107

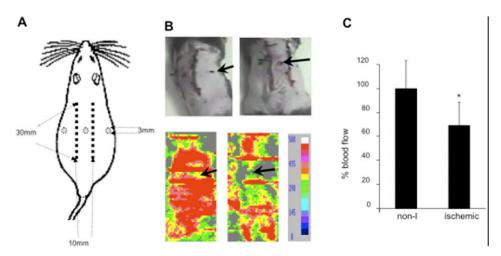


Fig. S1. The murine ischemic wound model. (A) A bipedicle flap (30 mm  $\times$  10 mm) was developed on the back of 8-week-old C57/Bl6 mice as described in Materials and Methods. A full-thickness (3 mm) excisional wound was developed in the middle of each flap. Two additional wounds were developed similarly in normoxic skin at the same cranio-caudal location compared to the wound on the flap. (B) Digital (Upper) and corresponding laser Doppler image (Lower) of the ischemic and corresponding nonischemic wounds showing compromised blood flow in the ischemic flap. Arrows indicate wound location. (C) Comparison of blood flow between normal and ischemic wounds as measured by laser Doppler flowmetry. Data are mean  $\pm$  SD; n = 8; \*, P < 0.05.

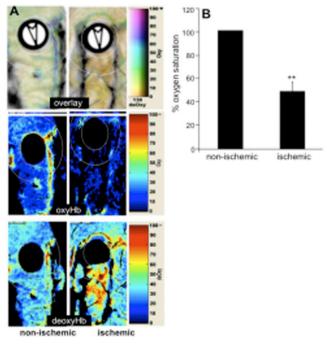


Fig. 52. Hyperspectral imaging of wound tissue oxygen saturation. (A) (Top) Overlay image demonstrating digital image (arrow-marked sticker at center on wounds required as landmark for the hyperspectral camera) in combination with OxyHb as well as deoxyHb images. (Middle) Oxy-hemoglobin image showing more OxyHb in nonischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound. (Bottom) Deoxy-hemoglobin image showing more deoxy-Hb in ischemic wound.

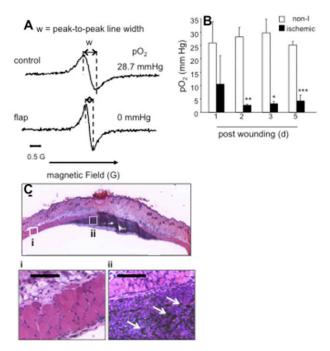


Fig. S3. Quantitative analysis of tissue oxygen using EPR. (A) In vivo EPR spectra obtained from LiNcBuO probe implanted in mouse skin. The peak-to-peak line widths were used to calculate  $pO_2$  using a calibration curve. (B)  $pO_2$  measurements of normal skin (non-I, open bars) and ischemic flap (solid bars). Data shown are mean  $\pm$  SD; n=3; \*,P<0.05; \*\*,P<0.05; \*\*,P<0.01; and \*\*\*,P<0.001. (C) Histology of mouse skin showing embedded EPR particles. Mosaic image of H&E-stained section of EPR particle embedded ischemic flap (*Upper*). The zoomed views of a no particle area (*Lower Left*, corresponding to box i in *Upper*) and an area with embedded particles (*Lower Right*, corresponding to box ii in *Upper*). White arrows show embedded particles. (Scale bar, 100  $\mu$ m.)

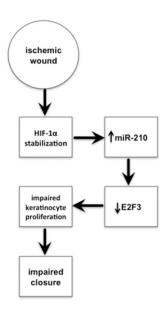


Fig. S4. Ischemic wounds result in impaired wound healing. An ischemic wound results in the wound environment becoming hypoxic; this in turn promotes the stabilization of HIF-1 $\alpha$ . One of the consequences of HIF-1 $\alpha$  stabilization is the up-regulation of miR-210, which in turn represses the expression of E2F3. Keratinocyte proliferation, which is dependent on E2F3, is thus impaired, resulting in an open or nonhealing wound.