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Wound healing rate is not impaired in mice with deficiency of liver-derived insulin-like growth factor-I (IGF-I)

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IGF-I has growth promoting effects and it is expressed in virtually all tissues. Liver-derived IGF-I constitutes the major part of circulating IGF-I. Mice with deficiency of liver-derived IGF-I (LI-IGF-I-/- mice) have 75% lower serum levels of IGF-I, but approximately unaffected postnatal body growth. However, liver-derived IGF-I exerts several important effects in adult life such as regulation of cortical bone mass. IGF-I has a positive effect on wound healing and is decreased in wounds with depressed regenerative potential as diabetic wounds. However, the importance of circulating IGF-I on wound healing is unknown. Here, we investigate the role of systemic IGF-I on the wound healing rate in LI-IGF-I-/- mice during normoglycemic and diabetic conditions.
Methods: LI-IGF-I-/- mice with complete inactivation of the IGF-I gene in the hepatocytes were generated by using the Cre/loxP recombinantion system. Mice homozygous for LoxP but lacking Mx-Cre were used as controls. Inactivation of the IGF-I gene in hepatocytes was performed at 1 month of age. Diabetes was induced with streptozotocin (50 mg/kg, i.p, five consecutive days) in LI-IGF-I-/- mice and in the controls. Wounds were made on the dorsum of animals, and evaluated by photos taken every second day. At the end of the experiment, wound biopsies were taken for being analyzed regarding granulation, dermal regeneration (hematoxilin eosin), angiogenesis (isolectin staining), markers for inflammation (CD45) and recruitment of endothelial precursor cells (EPC) (qRT-PCR). The IGF system (GH, IGF-II, IGF-R and IGFBP3) is analyzed in the skin biopsies at the mRNA (qRT-PCR) and /or protein level (immunohistochemistry, western blot). **Results:** The wound healing rate was similar in the LI-IGF-I-/- mice compared with the controls (50% wound closure at 4 +/- 0.5 days versus 4 +/- 0.3 days, p=ns).Diabetes significantly delayed the wound healing rate both in the LI-IGF-I-/- and control mice ($p < 0.05$). However, no significant difference was observed between diabetic animals, with normal or reduced hepatic IGF production (50% wound closure 6 +/- 0.2 days – diabetic controls versus 6 +/- 0.1 days diabetic LI-IGF-I-/- mice). **Conclusion:** Liver-derived IGF-I does not affect wound healing in mice, neither in normoglycemic conditions nor in diabetes.