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BITS AND BYTES

Fixing a hole: CCN2 closes chronic wounds

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Chronic wounds, especially on the feet, are a clinical feature resulting from diabetes and often result in limb amputation. Identification of strategies that promote closure of chronic wounds are essential. In a study authored by Henshaw et al. (J Diabetes Res. 2015;2015:236238), CCN2/CTGF was able to accelerated closure of wounds in diabetic rats. Moreover, in humans, the ability of wounds in diabetic patients to heal correlated with CCN2 expression. Thus CCN2 might, in the future, be used to promote healing of chronic wounds.

Diabetic foot ulcers are a significant cause of morbidity and are a substantial financial burden. Approximately 25 % of diabetics have foot ulcers, and these account for up to 70 % of non traumatic lower limb amputations (Most and Sinnock 1983). About 6.5 million people in the USA suffer from chronic wounds, costing~$25 billion dollars (Sen et al. 2009). Developing novel methods of promoting closure of chronic diabetic wounds is therefore of paramount importance.

CCN2 is a member of the CCN family of matricellular proteins that is induced by TGFβ and in response to wounding (Klaassen et al. 2015; Cicha and Goppelt-Struebe 2009). Although CCN2 is dispensible for normal cutaneous tissue repair kinetics, CCN2 is responsible for the recruitment and differentiation of progenitor cells into myofibroblasts (Liu et al. 2014; Tsang and Leask 2014). CCN2 is overexpressed in fibrotic disease including diabetes, and is believed to contribute to the kidney and eye fibrosis observed in this disorder (Mason 2009; Klaassen et al. 2015). However, the role of CCN2 in diabetic wounds is unknown.

In a recent study from the Twigg laboratory (Henshaw et al. 2015), Sprague–Dawley rats were made diabetic using streptozotocin and subjected to dermal wounding. Wounds in diabetic rats closed more slowly than those in control rats. Wounds in diabetic rats treated with recombinant CCN2 showed enhanced closure; CCN2 had no effect on control wounds. Diabetic wounds showed reduced levels of type IV collagen (which assists in repithelialization) and a-smooth muscle actin and CCN2 treatment somewhat alleviated this phenotype. CCN2 treatment of diabetic mice trended higher α-SMA staining score in fibroblasts and endothelial cells compared with scores in untreated diabetic rats although this did not reach statistical significance. Macrophage number was increased in CCN2-treated wounds, but this result did not achieve statistical significance, Young's modulus was increased by in animals that were treated with CCN2 compared to untreated control and diabetic mice.

Thus, although CCN2 promoted closure of diabetic wounds, only a few parameters were affected in a statistically significant fashion. Perhaps CCN2 might work with other matricellular proteins to promote closure of diabetic wounds.

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