

Matrix therapy in regenerative medicine, a new approach to chronic wound healing.

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Abstract

Nonhealing wounds remain a major health problem whose treatment is challenging and costly. Treatments based on cells or growth factors are still not very effective. We developed an entirely novel strategy consisting in treatment of the wound-tissue matrix with biopolymers engineered to mimic heparan sulfates called OTR4120. This compound was dextran polymer with sulfated and carboxymethyl groupments. After binding to matrix proteins, the heparan-sulfate-mimicking polymer protects the microenvironment, maintaining the normal production of signals and growth factors needed for healing to occur. Here, we show that a specific biopolymer accelerates ulcer closure and improves re-epithelialization and dermal-matrix-component remodeling. OTR4120 treatment was associated with faster maturation of epidermal structures, most notably regarding the number of epithelial-cell layers, and with an appearance that more closely resembled normal skin. Treatment had also a main effect on collagen I and III expression. Necrotic skin ulcers induced in mice with doxorubicin recovered normal collagen levels and organization, with no evidence of fibrosis. Thus, appropriate polymer-based matrix therapy is a valid and simple alternative to regenerative medicine.