

Targeted Delivery of Natural TGF- β antagonist Suppresses Scar Formation during Wound Healing

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We have used a phage library (CX₇C) to identify peptides that bind to angiogenic vasculature in regenerating wound tissue. We identified a nona- and hexapeptides that selectively target phage to skin and tendon wounds. Peptide 1 shows preference for the early stages of the wound healing. Its sequence is homologous to a sequence in the heparin-binding site of the bone morphogenetic protein 4 (BMP4). Peptide 2 (CRK) is homologous to a part of thrombospondin type 1 repeat (TSR1) and binds preferentially to wounds at the later stages of wound healing. We constructed fusion proteins in which the peptides serve as

a homing element and decorin as a therapeutic protein. Decorin is a natural antagonist to transforming growth factor- β (TGF- β), which is thought to be responsible for scar formation. The wound-targeted decorin fusion proteins were vastly more effective than non-targeted decorin in suppressing scar formation in skin wounds upon systemic administration. These results identify new therapy option for surgical wounds as well as for various kinds of internal trauma that goes beyond approaches based on the direct, topical application of therapeutic molecules at the wound site.