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CONTROL OF SCARRING IN ADULT WOUNDS USING ANTISENSE TRANSFORMING GROWTH FACTOR-β OLIGODEOXYNUCLEOTIDES

Byung-Min Choi[1], Su-Ung Kim[2], Seong-Yong Lee[2], and Hun-Taeg Chung[1]

[1]Department of Microbiology and Immunology, Wonkwang University School of Medicine, Iri 570-749, Korea and [2]Laboratory of Biotechnology, Central Research Institute, Il Yang Pharm. Co., Young-In, 449-900 Korea

Although synthetic antisense oligodeoxynucleotides (ODNs) have been used to dissect gene function *in vitro*, technical difficulties of targeted delivery prevented the use of this approach for investigating the effect of gene products *in vivo*. Here we report the use of local delivery of antisense transforming growth factor-β1 (TGF-β1) oligonucleotides to decrease the fibrosis in the skin wound. Adult wounds heal with scar-tissue formation, whereas fetal wounds heal without scarring and with a lesser inflammatory and cytokine response. We reasoned that strategy emplying antisense TGF-β1 ODNs complementary to TGF-β1 mRNA might decrease the scarring in dermal wound of mouse. To evaluate this concept, we tested the effects of antisense ODNs targeted to TGF-β1 mRNA by topical application of the chemical on the skin wound. Phosphorothioate antisense ODNs was employed to retard their degradation. When antisense TGF-β1 ODNs were applied into the wound site, there was a maked reduction of scar compared with control wound site. These effects of antisense TGF-β1 ODNs on the scar formation were associated with decreased expression of TGF-β1 gene. However sense TGF-β1 ODNs had no effect on expression of TGF-β1 gene. Also, control wounds healed with excessive fibrosis, whereas the antisense treated wounds healed with less fibrosis. In conclusion, our results indicate that antisense TGF-β1 ODNs could be used for amelioating scar formation during wound healing.