

## Topical Anti-TNF- $\alpha$ Antibody Enhances Wound Healing in Diabetic Mice

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Chronic wounds such as venous leg ulcers and diabetic foot ulcers represent a significant health problem for which current treatment options are limited and not highly effective. These wounds have major impacts on the quality of life for affected individuals, frequently lead to amputation, and cost many thousands of dollars per year to treat.

Assessment of wound fluid from such wounds indicates greatly elevated and persistently high levels of inflammatory cytokines, in particular Tumor Necrosis Factor-alpha (TNF- $\alpha$ ). As such, these wounds are not in a physiologic state conducive to healing. Our study in diabetic mice (db/db) suggests that topical application of antibodies capable of neutralizing TNF- $\alpha$  can enhance cutaneous wound healing.

Full-thickness wounds 8 mm in diameter were created on the backs of db/db diabetic mice and wild type mice. After 24 hours, the wounds were treated topically with vehicle alone, vehicle + control antibody or vehicle + anti-TNF- $\alpha$  antibody. Wound healing was followed for up to 21 days with reapplication of the appropriate treatments every 2-3 days. Compared to wild type mice, untreated db/db mice exhibited an approximate 4 day delay in wound healing. When wounds on diabetic mice were treated topically with a TNF- $\alpha$  neutralizing antibody, this delay was shortened by about 1 day or 25%. The improvement in healing was confirmed by histologic analysis of the wound areas after euthanasia of the mice.

This data suggests that topical treatment of diabetic wounds with antibodies that neutralize TNF- $\alpha$  may be a viable approach to promote healing of these difficult to heal wounds.