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ABSTRACTS

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Background Matrix metalloproteinases (MMPs) are enzymes that serve to degrade the extracellular matrix, giving them a central role in the inflammatory process. MMP activity has been shown to be up-regulated in various pathologic conditions, including hypertrophic scarring. The purpose of this study was to examine the effect of minocycline, a known MMP inhibitor, on hypertrophic scarring.
Methods Multiple standardized wounds, through the excision of skin and perichondrium, were created on the anterior ears of adult New Zealand white rabbits. A total of 64 identical wounds were created on eight rabbits. Four of the rabbits received daily injections of minocycline, while the other four rabbits received saline injections. After 4 weeks, the resulting scars were harvested and their thicknesses measured by using a micrometer.
Results All wounds healed with some degree of hypertrophic scarring. In the rabbits treated with minocycline, the scars averaged 0.43 + 0.04 mm in differential thickness (i.e., the elevation above the level of the surrounding, unwounded skin), compared to 0.57 + 0.04 mm in the rabbits treated with saline, a statistically significant difference (p = 0.008, by independent t-test). The relative hypertrophy (i.e., the thickness of the scar expressed as a percentage of the surrounding, "baseline" skin thickness) of the scars in the minocycline-treated rabbits averaged 131 + 11%, compared to 175 + 12% in the control rabbits, also a statistically significant difference (p = 0.003, by Mann–Whitney rank sum test).
Conclusion Systemically administered minocycline significantly reduces the severity of hypertrophic scarring in a rabbit model. Although not directly examined in this pilot study, MMP inhibition likely contributes to this effect. Determination of the effect of minocycline at different doses, as well as measurement of the expression and activity of MMPs and other components of the hypertrophic scar milieu, are the objectives of future investigations.

MMP14 Gene Polymorphism is Strongly Associated with Dupuytren's Disease

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Dupuytren's disease (DD) is a progressive and recurrent fibroproliferative disease of unknown etiology affecting human hands. It is a familial disorder and genetic studies have yet to identify the genes involved in its formation.

Matrix metalloproteinases (MMPs) are proteolytic enzymes and, via their function in protein degradation, have an important role in fibrogenesis. MMP3 (Stromelysin-1) and MMP14 (membrane-type MMP1) are members of the MMP family, produced by connective tissue cells that can synergistically degrade the major components of the extracellular matrix.

Previous studies have suggested that MMPs may be involved in the pathogenesis of DD; a decrease in the systemic MMP ratio to their natural inhibitors causes increased synthesis and deposition of collagen. Therefore, the aim of this study was to assess the association between single nucleotide polymorphisms (SNPs), in the MMP3 and MMP14 genes, with the risk of the development of DD. DNA isolated from 256 cases of Caucasian origin and 288 Caucasian control subjects from northwest of England were used for this study. SNPs were genotyped in all subjects by using the 5′ nuclease assay for allelic discrimination (TaqMan).

The frequency of a missense mutation in the 5′ UTR region of the MMP14 gene was found to be more common in cases vs. controls. The odds ratio is 2.75 (95% CI;2–3.7) in the DD group when compared to the controls. These results indicate a strong genetic link for an MMP14 gene polymorphism to the development of DD. This mutation may potentially affect mRNA stability with translational regulation.

Experimental Limb Transplantation: Induction of Immune Tolerance in a Mouse Limb Transplant Model Using Triple Therapy

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Introduction The application of clinical hand transplantation is limited by long-term use of toxic antirejection drugs. The purpose of this study was to determine whether a short course of monoclonal antibody against CD45RB (mAb), LF 15-0193 (LF) and rapamycin (Rap) would achieve long-term survival by inducing tolerance in a mouse limb transplant model.
Methods Twenty-one hind limb transplants were performed across MHC incompatible C57BL/6 and BALB/c mice. Four mice were treated with mAB (3 mg/kg) and LF (2 mg/kg) alone, and 14 mice were treated with mAB, LF, and Rap (2 mg/kg) for 14 days posttransplantation. Three C57BL/6 to BALB/c transplants receiving no drug therapy