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Roles of Matrix Metalloproteinases in Cutaneous Wound Healing

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Abstract

Wound healing is a complex process that consists of hemostasis and inflammation, angiogenesis, re-epithelialization, and tissue remodeling. Matrix metalloproteinases (MMPs) play important roles in wound healing, and their dysregulation leads to prolonged inflammation and delayed wound healing. There are 24 MMPs in humans, and each MMP exists in three forms, of which only the active MMPs play a role in the pathology or repair of wounds. The current methodology does not distinguish between the three forms of MMPs, making it challenging to investigate the roles of MMPs in pathology and wound repair. We used a novel MMP-inhibitor-tethered affinity resin that binds only the active form of MMPs, from which we identified and quantified active MMP-8 and active MMP-9 in a murine diabetic model with delayed wound healing. We showed that up-regulation of active MMP-9 plays a detrimental role whereas active MMP-8 is involved in repairing the wound in diabetic mice. These studies identified MMP-9 as a novel target for therapeutic intervention in the treatment of chronic wounds. A selective inhibitor of MMP-9 that leaves MMP-8 unaffected would provide the most effective therapy and represents a promising strategy for therapeutic intervention in the treatment of diabetic foot ulcers.

Keywords: MMPs, chronic wounds, wound healing, selective MMP-9 inhibitor, MMP profiling

1. Introduction

Skin is one of the largest organs in humans. Its three main functions are protection against environmental damage, regulation of body temperature, and perception of environmental


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