New finding may help accelerate diabetic wound healing

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University of Notre Dame researchers have, for the first time, identified the enzymes that are detrimental to diabetic wound healing and those that are beneficial to repair the wound.

There are currently no therapeutics for diabetic wound healing. The current standard of care is palliative to keep the wound clean and free of infection. In the United States, 66,000 diabetic individuals each year undergo lower-limb amputations due to wounds that failed to heal.

A team of researchers from Notre Dame's Department of Chemistry and Biochemistry, led by Mark Suckow, Shahriar Mobashery and Mayland Chang, searched for metalloproteinases (MMPs) in the wounds of healthy and diabetic mice.

Gelatinases, a class of enzymes, have been implicated in a host of human diseases from cancer to cardiovascular conditions. Chang has been researching activation of MMPs, particularly gelatinase B or MMP-9.

The MMPs remodel the extracellular matrix in tissue during wound healing.

"We show that MMP-9 is detrimental to wound healing, while MMP-8 is beneficial," Chang said. "Our studies provide a strategy for diabetic wound healing by using selective MMP-9 inhibitors."

The team treated diabetic mice with an inhibitor of MMP-9 and discovered that wounds were healed 92 percent after 14 days, as compared to 74 percent healing in untreated mice.

The identification of the enzyme that interferes with diabetic wound healing and that which repairs the wound opens the door to new, novel treatment strategies.

"Currently, advanced wound dressings containing collagen are used for diabetic wound healing," Chang said. "The collagen provides a substrate so that the unregulated MMP-9 chews on the collagen in the dressing, rather than on the wound. It would be better to treat the diabetic wounds with a selective MMP-9 inhibitor to inhibit the culprit enzyme that is impeding wound healing while leaving the beneficial MMP-8 uninhibited to help repair the wound."

The study appeared in the American Chemical Society's journal *ACS Chemical Biology*.

Provided by University of Notre Dame