Enzyme involved in glucose metabolism promotes wound healing, study finds

March 10 2016

An enzyme involved in glucose metabolism in cells plays a major role in the early steps of wound healing, a finding that could lead to new therapeutic approaches for wound care, according to researchers at

Georgia State University.

When immune cells called neutrophils release pyruvate kinase M2 (PKM2), an enzyme that acts in the last step of the glycolysis pathway, PKM2 aids wound healing by promoting the development of new blood vessels at the wound site. The findings are published in the journal *Wound Repair and Regeneration*.

The discovery could pave the way for new treatments that promote wound healing, tissue regeneration and tissue transplantation, said Zhi-Ren Liu, lead author of the study and professor in the Department of Biology at Georgia State.

"We could easily imagine PKM2 being used for wound dressing," Liu said. "It could also likely be used for binding wounds. For example, when you've transplanted skin from a donor, sometimes this new skin doesn't attach well because of immune rejection, so therefore, it's easy to fail, especially if it's a large transplant."

PKM2 could also help heal internal surgical incisions, he said.

Wound repair is a complex process. When an organ or skin is first wounded, immune cells go to the site to clean the wound and remove any bacteria and debris. Next, immune cells send a signal they've completed their job, which triggers the proliferation phase that involves forming connective tissue fibers and capillary blood vessels. Then, the wound is sealed and covered with epithelial tissue, which forms the covering or lining of internal and external body surfaces. The fibers under the epithelial tissue will slowly remodel into normal tissue, but this process can take months or years.

The researchers treated wounds in mice with different agents, including PKM2, mixed with a pharmacy cream, and found topical application of

PKM2 aided early wound closure and promoted higher levels of vessel growth. The results suggest PKM2 plays a functional role in the wound healing process.

In tissue samples, PKM2 was detected in the extracellular space of wound tissues, suggesting secretion during the wound repair process. PKM2 released at the wound site was found in close proximity to neutrophils. The enzyme reached its peak at the wound site on the third day after wound formation and then decreased in the mouse model of wound healing. This is the first time the function of PKM2 in the extracellular space of cells has been investigated, Liu said.

"We don't know exactly how PKM2 is released, but we know it is released by neutrophils," Liu said. "Once it's released outside the cell, it does a totally different thing. It has nothing to do with metabolism anymore."

The role of neutrophils, the first immune cells at the wound site, in the wound repair process has not been well understood. The researchers studied isolated neutrophils in cell culture and found PKM2 was released into the culture medium of activated neutrophils.

"PKM2 probably plays a more important role than many other factors for signaling to the next step in wound repair," Liu said. "PKM2 connects the immune response to the next phase, which is proliferation. PKM2 tells the cells to come in to fill the wound. Our studies reveal a new and important molecular link between the early inflammation response and the proliferation phase in the tissue repair process."

More information: Yinwei Zhang et al. PKM2 Released by Neutrophils at Wound Site Facilitates Early Wound Healing by Promoting Angiogenesis, *Wound Repair and Regeneration* (2016). DOI: 10.1111/wrr.12411

Provided by Georgia State University