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Breakthrough research identifies new targets for wound healing

(Thursday, 26 September 2024) Novel research, presented today at the European Academy of Dermatology and Venereology (EADV) Congress 2024, has identified key molecular targets that could significantly enhance the healing of both acute and chronic wounds.[1]

These findings represent a crucial advancement in wound care, paving the way for more effective treatment options and improved patient outcomes.

Globally, acute and chronic wounds affect nearly one billion people.[2] In particular, chronic wounds pose a substantial economic burden on healthcare systems and severely impact the quality of life for those affected.[3] Despite this, current treatment strategies are often limited, highlighting an urgent need for a deeper understanding of the mechanisms underlying impaired wound healing.[4]

To address this, researchers conducted a study using healthy full-thickness human skin punches, creating central, partial wounds. These samples were then cultured under either physiological or pathological conditions, including hyperglycaemia, oxidative stress and hypoxia, to mimic acute and chronic wounds, respectively. Using advanced comparative transcriptomic profiling with bulk RNA sequencing, the team monitored gene expression changes over a five-day period.

The results revealed several critical differences in gene activity between acute and chronic wounds. Key wound repair-associated genes such as KRT6A-C, PTX3, KRT1, KRT10, COL1A1, along with pathways including Wnt signalling and actin cytoskeleton organisation, were differentially regulated between acute and chronic wounds.

Additionally, overall gene expression was downregulated in chronic wounds compared to acute wounds, suggesting that essential genes required for effective wound healing are inadequately transcribed in these conditions.

Notably, FGF7, a key promoter of epithelial cell proliferation and tissue repair was significantly downregulated in chronic wounds by Day 5. In contrast, MMP10, a tissue-degrading enzyme, was elevated throughout the study period in chronic wounds.

To counteract these imbalances, the researchers tested the effects of recombinant FGF7 protein and an MMP10-neutralising antibody (α-MMP10) on acute and chronic wounds in the ex vivo wound models. Topical administration of α-MMP10 led to a significant increase in wound tongue length, indicating improved healing in acute wounds. In contrast, FGF7 did not show a significant effect on its own.

The combined application of FGF7 and α-MMP10, however, significantly enhanced re-epithelisation in both types of wounds.

“While we must be cautious when discussing synergistic effects, our preliminary data reveal that combinatorial therapy may be a valid option for treating chronic wounds”, explains Dr Marta Bertolini, lead author of the study and Managing Director of QIMA Monasterium GmbH. “We believe that administering excessive FGF7 promotes epidermal keratinocyte proliferation and mobilisation, which are crucial for wound healing. At the same time, neutralising MMP10 removes a barrier to keratinocyte movement, potentially accelerating re-epithelisation.”

The study also identified osteopontin (SPP1) as a gene significantly upregulated on Days 3 and 5 in acute wounds compared to chronic wounds. To leverage this finding, the researchers administered FOL005, an osteopontin-derived peptide, to experimentally induced wounds ex vivo.

Treatment with FOL005 significantly enhanced skin re-epithelisation under both physiological and pathological conditions, highlighting its potential as an effective therapeutic option for acute and chronic wound management.

“We believe these findings mark a significant step forward in understanding the complex biology of wound healing,” concludes Dr Bertolini. “Our transcriptomic data will soon be accessible, and we hope this will inspire other researchers and industry to identify additional promising targets that could offer much-needed relief to patients affected by these challenging and often debilitating wounds.”

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Note to editors:

A reference to the EADV Congress 2024 must be included in all coverage and/or articles associated with this study.

For more information or to arrange an expert interview, please contact press@eadv.org.

Key terms defined:

An acute wound is defined as a recent wound, of any aetiology, that is expected to progress through the normal sequential phases of wound healing.[5]

Chronic wounds are commonly defined as wounds that have not reduced in size by more than 40% to 50% or healed within 1 month. Chronic wounds may have different aetiologies and are commonly classified in the categories of diabetic foot ulcers, wounds related to peripheral arterial disease, venous leg ulcers, pressure injuries and atypical hard-to-heal wounds.[3]

About the study author:

Marta Bertolini, PhD, is the Managing Director of QIMA Monasterium GmbH, Münster, Germany, belonging to the QIMA Life Sciences group. She graduated in Pharmaceutical Biotechnologies in Italy, and obtained her PhD in Germany, with

a thesis on hair follicle immunology. Her scientific contribution focuses on skin and hair translational research.

About EADV:

Founded in 1987, EADV is a non-profit organisation with a vision to form a premier European Dermatology-Venereology Society. The Academy counts over 11,000 members from all around the globe, providing a valuable service for every type of dermatologist-venereologist professional. The EADV is dedicated to advancing patient care, education and research by providing a unique platform to bring people together and share ideas.

This year, the EADV Congress will take place in Amsterdam, The Netherlands, and online from 25-28 September 2024. Find out more: https://eadv.org/congress/

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