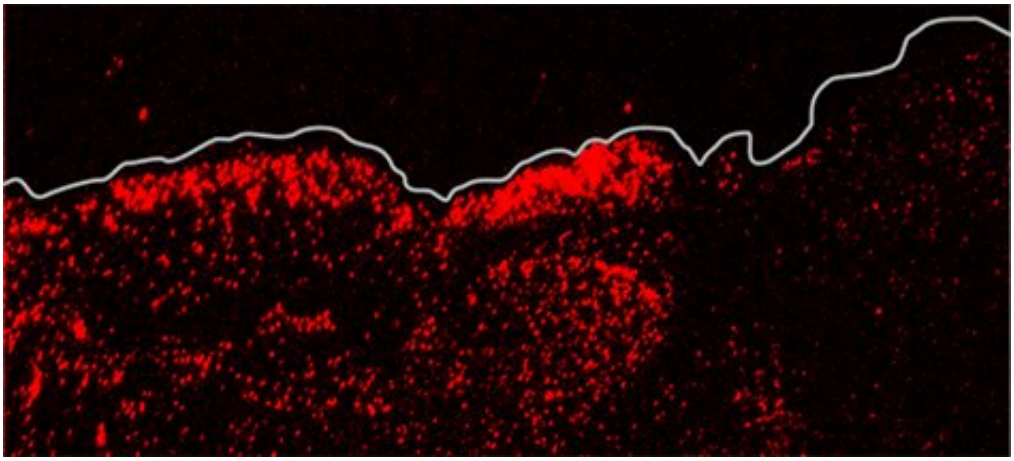
Researchers reveal critical role of mechanosensor in skin wound healing

November 9 2021



PIEZO1 accumulates at the wound edge to slow wound healing. Credit: UCI School of Medicine

PIEZO1, an ion channel mechanosensor found within cells, has been revealed to play a key role in regulating the speed of skin wound healing by researchers at the University of California, Irvine (UCI).

Published today in *eLife*, the study, titled, "Spatiotemporal dynamics of PIEZO1 localization controls keratinocyte migration during wound healing," found that in mice lacking the ion channel protein PIEZO1 in keratinocytes, skin wounds heal faster than in mice with increased PIEZO1 function in keratinocytes.

"Our collaborators from Ardem Patapoutian's lab at The Scripps Research Institute, observed that in mice with reduced PIEZO1, wound healing is faster. We wanted to determine the 'how', 'when' and 'where' of PIEZO1's involvement, in order to find potential treatments that might speed healing," said Medha Pathak, Ph.D., assistant professor at the UCI School of Medicine Department of Physiology & Biophysics. "For this, my lab developed new approaches to visualize PIEZO1 while wound healing is taking place in vitro."

PIEZO1 is among a number of other proteins that are able to sense mechanical cues and provide instructions on the actions the cell should take. Previous research suggested that mechanosensors are instrumental in wound closure; however the specific mechanosensor involved was unknown. This was the first study in which the role of PIEZO1 in wound healing was investigated.

The skin, the largest organ of the body, protects against external insults while also enabling touch sensation. Wounding of the skin interferes with these functions and exposes the body to an increased risk of infection, disease and scar formation. During wound healing, keratinocytes, the most abundant cell type in the topmost layer of the skin, move inward from the edges of the wound to close the wound gap. This helps to restore the skin barrier, reestablishing the skin's protective function.

"Earlier studies in the field showed that mechanical cues regulate keratinocyte migration during wound healing. Here, we show that in keratinocytes, PIEZO1 is in fact acting as the mechanosensor that processes such cues to regulate the speed of wound healing. To our surprise, we found that PIEZO1 accumulates at the wound edge and inhibits healing," said first author Jesse Holt, a graduate student in the Pathak Lab.

The findings from this study provide an understanding of how skin wound healing occurs and have the potential to guide research into new wound healing treatments. However, more research needs to be performed to confirm that reducing the activity of PIEZO1 does not cause unwanted effects, such as reduced touch sensation, and human testing will be required.

PIEZO1 has been identified as a key ion channel with various important physiological roles. Co-author on this study and the 2021 Nobel Prize laureate Ardem Patapoutian, Ph.D., a neuroscience professor and Howard Hughes Medical Institute investigator at Scripps Research, is well known for his work in characterizing the PIEZO1, PIEZO2 and TRPM8 ion channels. PIEZO1 is emerging as an area of active research at UCI: Michael Cahalan, Ph.D., chair of the UCI School of Medicine Department of Physiology & Biophysics, and Wendy Liu, professor of biomedical engineering also study PIEZO1, in the immune system. In May 2021, the Liu, Cahalan and Pathak labs together reported on the role of the protein in macrophages and the foreign body response; and in July 2021, the Cahalan and Pathak labs published a study identifying PIEZO1 as having an important role in T cell function related to autoimmune neuroinflammatory disorders.

More information: Jesse R. Holt et al, Spatiotemporal dynamics of PIEZO1 localization controls keratinocyte migration during wound healing, *eLife* (2021). DOI: 10.7554/eLife.65415

Provided by University of California, Irvine