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The stem cell dynamics of wound healing

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Researchers at the Université libre de Bruxelles, ULB define for the first time the changes in the stem cell dynamics that contribute to wound healing.

One of the key questions in biology is to identify how tissues are repaired after trauma and understand how stem cells migrate, proliferate, and differentiate to repair tissue damage.

In a study published in *Nature Communications*, researchers lead by Pr. Cédric Blanpain, MD/PhD, WELBIO investigator, and Professor at the Université libre de Bruxelles, Belgium, defined the cellular and molecular mechanisms that regulate wound healing in the skin.

The skin is the first barrier protecting the animals against the external environment. When the skin barrier is disrupted, a cascade of cellular and molecular events is activated to repair the damage and restore skin integrity. Defects in these events can lead to improper repair causing acute and chronic wound disorders. In the skin, distinct stem cells populations contribute to wound healing. However, it remains unclear how these different stem cells populations balance proliferation, differentiation and migration during the healing process.

In this new study published in *Nature Communications*, Mariaceleste Aragona, Sophie Dekoninck and colleagues define the clonal dynamics and the molecular mechanisms that lead to tissue repair in the skin epidermis. They used state of the art genetic mouse models to study different stem cells populations. Specifically, they use a technique called

lineage tracing to mark stem cells and follow the fate of their progeny over time. Interestingly, they found that stem cells coming from different epidermal compartments present very similar response during wound repair, despite the fact that they are recruited from different regions of the epidermis. "It was particularly exciting to observe that the repair of the skin epidermis involves the activation of very different stem cells that react the same way to the emergency situation of the wound and have the power to completely restore the damaged tissue", comments Mariaceleste Aragona, the first author of the study. The authors defined the gene signature of the different regions surrounding the wound to uncover the gene expression signature of the cells that actively divide and those that migrate to repair the wound. "The molecular characterization of the migrating leading edge suggests that these cells are protecting the stem cells from the infection and mechanical stress allowing a harmonious healing process", comments Sophie Dekoninck, the co-first author of the study.

Altogether, this study provides important insights into the changes in the mechanisms that lead to tissue repair, and demonstrates that the capacity of the stem cells to regenerate a tissue does not depend on their cellular origin but rather on their proliferation capacity.

"This new study uncovers for the first time the dynamic of stem cells during wound healing and identifies new molecular players associated with skin regeneration. The deregulation of several of these genes in patients with chronic ulcers, suggest that defects in the formation and/or function of these two different structures may induce defect of wound-healing leading to chronic ulcer formation. Further functional studies will be needed to define the role of these genes and to identify new therapeutic targets to treat chronic wound disorders that cost each year billions of dollars", explains Cédric Blanpain, the senior and corresponding author of this new study.

More information: Defining stem cell dynamics and migration during wound healing in mouse skin epidermis. *Nature Communications*, 2017. DOI: 10.1038/NCOMMS14684