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Researchers identify stem cells responsible for tissue repair

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The skin, which is an essential barrier that protects our body against the external environment, undergoes constant turnover throughout life to replace dead cells that are constantly sloughed off from the skin surface. During adult life, the number of cells produced must exactly compensate for the number of cells lost. Different theories have been proposed to explain how this delicate balance is achieved.

In a new study published in *Nature,* researchers lead by Pr. Cédric Blanpain, MD/PhD, FNRS/FRS researcher and WELBIO investigator at the IRIBHM, Université libre de Bruxelles, Belgium, in collaboration with Pr. Benjamin Simons, University of Cambridge, UK, demonstrate the existence of a new population of stem cells that give rise to progenitor cells that ensure the daily maintenance of the epidermis and demonstrate the major contribution of epidermal stem cells during wound healing.

In this new study, Guilhem Mascré and colleagues used novel genetic lineage tracing experiments to fluorescently mark two distinct epidermal cell populations, and follow their survival and contribution to the maintenance of the epidermis overtime. Interestingly, in doing so, they uncover the existence of two types of dividing cells. One population of proliferative cells presented a very long term survival potential while the other population is progessively lost overtime. In collaboration with Pr. Benjamin D. Simons, the authors developed a mathematical model of their lineage tracing analysis. The authors proposed that the skin epidermis is hierarchically organized with slow cycling stem cells

residing on the top of the cellular hierarchy that give rise to more rapidly cycling progenitor cells that ensure the daily maintenance of the skin epidermis. Analysis of cell proliferation confirms the existence of slow cycling stem cells and gene profiling experiments demonstrate that the stem and the progenitors cells are characterized by distinct gene expression.

Importantly, by assessing the contribution these two populations of cells during wound healing, they found that only stem cells are capable of extensive tissue regeneration and undergo major expansion during this repair process, while the progenitors did not expand significantly, and only provide a short-lived contribution to the wound healing response. As well as resolving the cellular hierarchy of epidermis, this is the first demonstration of a critical role of epidermal SC during wound healing. "It was amazing to see these long trails of cells coming from a single stem cell located at a very long distance from the wound to repair the epidermis" comments Cédric Blanpain, the senior author of this study.

This work demonstrates the existence of slow-cycling stem cells that promote tissue repair and more rapidly cycling progenitors that ensure the daily maintenance of the epidermis. A similar population of slow cycling stem cells that can be rapidly mobilized in case of sudden need has been observed in other tissues, such as the blood, muscle and hair follicle, and the partition between rapidly cycling progenitors and slow cycling stem cells could be relatively conserved across the different tissues. This study may have important implications in regenerative medicine in particular for skin repair in severely burnt patients or in chronic wounds.

More information: Guilhem Mascré, Sophie Dekoninck, Benjamin Drogat, Khalil Kass Youssef, Sylvain Brohée, Panogiata A. Sotiropoulou, Benjamin D. Simons and Cédric Blanpain. Distinct contribution of Stem and progenitor cells to epidermal maintenance.

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