Complete skin regeneration system of fish unraveled

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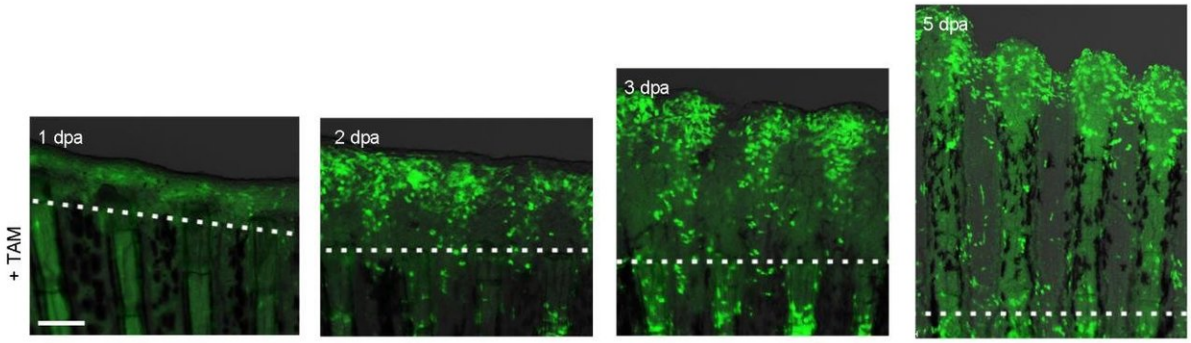

Cre-loxP was used as the cell-labeling technique. In this case, EGFP (enhanced green fluorescent protein) expression in the regenerative epidermis of zebrafish fins was switched on by using recombination enzyme Cre expressed under the regulation of the gene fibronectin 1b. Recombination can be induced by using a compound called tamoxifen (TAM). *dpa: the number of days since amputation. Credit: Tokyo Institute of Technology

Fish and amphibians such as newts can perfectly regenerate tissue without scar tissue in the event that they lose organs such as their limbs. Studying the mechanisms of regeneration and homeostasis of tissues has potential for application in human regenerative medicine. Not much has been known about the mechanism and the source of cells involved in the regeneration of tissue.

The research group led by Tokyo Tech's Associate Professor Atsushi Kawakami, graduate student Eri Shibata, and others used the regeneration of zebrafish fins as a model and labeled the cells of the regenerative tissue with fluorescence using a genetic cell-labeling technique (Cre-loxP site-specific recombination). The researchers tracked the cells over a period of weeks, and determined that epithelial cells near a wound follow heterogeneous cell fates.

The first group of epithelial cells recruited cover the wound but disappear within a few days via apoptosis. The second group of epithelial cells become the cells forming the regenerated skin. However, many of these regenerated skin cells are moved toward the end of the fin and disappear after about one to two weeks. In investigating the source of the replenishing skin cells, the researchers found that many new epithelial cells are supplied in the regeneration process by a large area of skin containing stem cells, and become active in cell proliferation. Intriguingly, the skin cells in the regeneration process do not undergo special processes such as de-differentiating into stem cells and regenerating, but existing stem cells in the basal layer and differentiated cells in the surface layer each proliferate with their own characteristics intact to regenerate the skin.

Based on this study, it is conceivable that regeneration of skin could be possible by controlling the autonomous proliferation of stem cells in the basal layer in other vertebrates as well, including humans. If the mechanism of skin regeneration discovered in this study proves to be the same in humans, it could be used in the future to determine the causes of various skin diseases, in regenerative medicine research, and for other purposes.

More information: Eri Shibata et al, Heterogeneous fates and dynamic rearrangement of regenerative epidermis-derived cells during zebrafish fin regeneration, *Development* (2018). DOI:

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