Okayama University Medical Research Updates （OU-MRU） 2022.10 Vol.105

Source: Okayama University (JAPAN), Public Relations Division

For immediate release: 6 October 2022

Okayama University research: The dynamics of skin regeneration revealed

(Okayama, 6 October) **In a study recently published in the journal *iScience*, researchers from Okayama University use the axolotl, an amphibian species, to understand the real-time regeneration process of the inner skin.**

While the outermost layer of our skin is attuned to wear and tear, the layer below—known as the dermis—is more sensitive to damage. Although the dermis is the thickest layer of the skin, it is difficult to visualize properly due to the skin's hairy surface and opacity. Now, a research group led by Associate Professor SATOH Akira and KASHIMOTO Rena (graduate students) from Okayama University, used the amphibian axolotl to illuminate the structure of the dermis and understand its regeneration process.

The axolotl was selected for this study due to the biological similarities of its skin layers to that of mammals. Plus, axolotls have transparent skin that is easy to see through the dermal structures under a microscope. Amphibians also have heightened regenerative properties which make them ideal organisms to study such processes. The investigation began by examining the structure of axolotl dermal tissue.

Collagen, which confers the skin its elasticity and suppleness, is the primary protein found within the dermis and is released by dermal cells (known as fibroblasts). The dermal tissue revealed a grid-like "lattice" pattern comprising fibers of collagen. When individual fibroblasts were analyzed deeper using a high-resolution microscope, the images unveiled a dual-lattice arrangement; the fibroblasts had protrusions arranged in a mesh-like network which released collagen molecules that followed the same pattern.

After visualizing healthy tissue, the team sought to analyze the repercussions of damage to the dermis. First, wounded dermal tissue was isolated and analyzed up to 120 days after injury. The wounded tissue no longer showed an organized lattice structure. In fact, the fibroblasts now had protrusions in disarray resulting in haphazard patterns of collagen release. Next, the axolotl limb was amputated and the ensuing limb regeneration process was followed closely. In this case, an organized lattice arrangement of fibroblasts and collagen was restored within 50 days. A full recovery of dermal tissue was seen.

The researchers then probed the collagen fibers to understand what was different in both these conditions. They observed that the collagen fibers in regenerated dermal tissue showed bidirectional growth. On the contrary, wounded tissue had collagen fibers growing on one side only. What's more, it was the presence of nerves that facilitated this growth in regenerated tissue. The wounded tissue lacked nerve intervention.

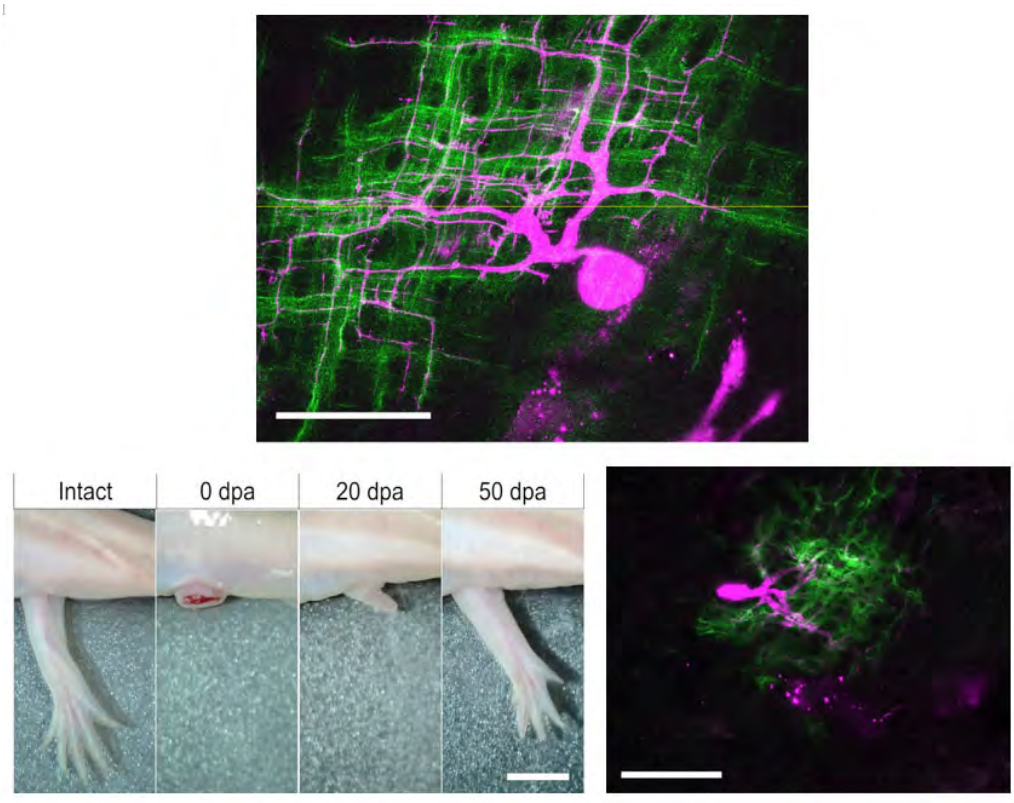
OKAYAMA University
1-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530 Japan

This study elucidated the structure of collagen within dermal tissue and highlighted its role in regeneration. “In the present study, we also demonstrated that nerve deviation improves the collagen reconstitution in skin wound healing,” concludes the group. Therapies directed at restoring nerve function might aid with skin regeneration. This information is vital given the dangers our largest organ is constantly exposed to.

Background

Collagen: Collagen is a protein released by cells known as fibroblasts and is usually found in the space surrounding these cells (known as the extracellular matrix). It provides strength to the skin, bones, and other skeletal tissues. Besides strength and support, collagen is also responsible for ensuring that neighboring cells stick together and it provides elasticity to the skin. Thus, as people age they often turn to collagen supplements to replenish declining endogenous levels.

While collagen is said to be involved in wound healing and skin regeneration, its exact role is unknown. Hence, this investigation was aimed at unraveling the structure and mechanics of collagen fibers in healthy and healing skin.



Figure

Top. Collagen fibers (green) surrounding the fibroblast protrusions (purple) and forming a lattice in healthy skin tissue.

Bottom. Axolotl limb regeneration 50 days after amputation (left) and the corresponding restoration of its collagen lattice structure (right).

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Reference
Kashimoto R., Furukawa S., Yamamoto S., Kamei Y., Samamoto J., Nonaka S., Watanabe TM., Samamoto T., Sakamoto H., Satoh A. Lattice-patterned collagen fibers and their dynamics in axolotl skin regeneration. *iScience*, 25, 104524. July 15, 2022.
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Correspondence to
Associate Professor SATOH Akira, Ph.D.
Regeneration Laboratory, Research Core for Interdisciplinary Sciences(RCIS), Okayama University, 3-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530, Japan
E-mail: satoha@cc.okayama-u.ac.jp
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Associate Professor SATOH Akira

Further information
Okayama University
1-1-1 Tsushima-naka , Kita-ku , Okayama 700-8530, Japan
Public Relations Division
E-mail: www-adm@adm.okayama-u.ac.jp
Website: http://www.okayama-u.ac.jp/index_e.html
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OKAYAMA University
1-1-1 Tsushima-naka, Kita-ku, Okayama 700-8530 Japan

「Pergola」 Kazuyo Sejima + Ryue Nishizawa / SANAA
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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

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Hirofumi Makino, M.D., Ph.D.
President , Okayama University

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