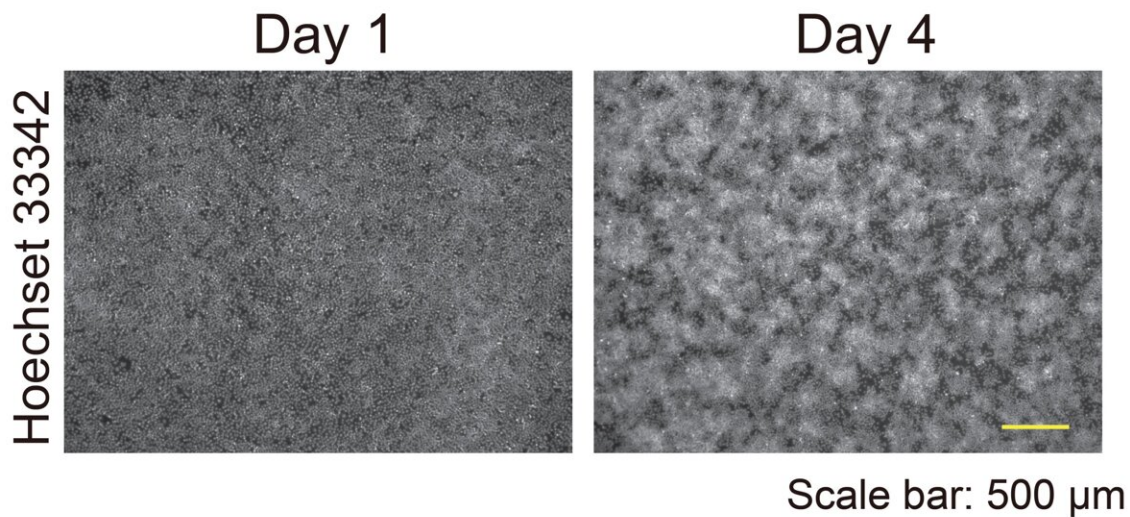


Starvation and adhesion drive formation of keratinocyte patterns in skin, research reveals

August 13 2024



Keratinocytes display a self-organized pattern after four days in cultures. Credit: Yosuke Mai, et al. Life Science Alliance. July 18, 2024

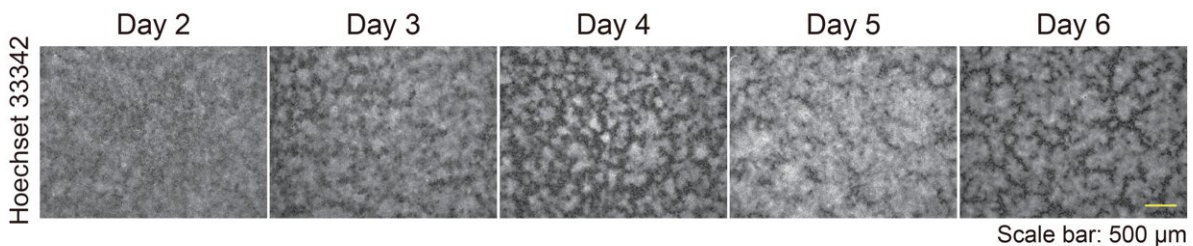
Fingerprints are one of the best-recognized examples of pattern formation by epithelial cells. The primary cells in the epithelium are the keratinocytes, and they are known to form patterns at the microscopic and macroscopic levels. While factors affecting this pattern formation have been reported, the exact mechanisms underlying the process are

still not fully understood.

A team of researchers, led by Associate Professor Ken Natsuga at the Faculty of Medicine, Hokkaido University, have revealed that cell-cell adhesion governs pattern formation in keratinocytes. Their findings were [published](#) in the journal *Life Science Alliance*.

"In this study, we used an immortalized keratinocyte cell line, called HaCaT, which retains all the properties of normal keratinocytes," Natsuga explained. "In order to ensure that our findings were accurate, we established single-cell cultures from this cell line."

The team observed pattern formation in both the original heterogeneous cell line, as well as in single-cell-derived cultures. During culturing, the keratinocytes moved randomly and spontaneously formed high- and low-density regions, leading to pattern formation.



Refreshing the culture medium led to a loss of patterning in keratinocyte cultures. This is particularly noticeable at Day 5, after fresh medium was added on Day 4. Credit: Yosuke Mai, et al. *Life Science Alliance*. July 18, 2024

The [pattern formation](#) was markedly influenced by starvation. When the culture medium was renewed, patterns were obscured, but reappeared as

the nutrients in the culture medium were consumed by the keratinocytes.

The team then examined the [gene expression](#) in the keratinocytes, which revealed that cell adhesion proteins and keratinocyte differentiation proteins were upregulated in high-density regions.

"As cell adhesion is necessary for the development of high-cell-density regions, we specifically investigated the expression of adherens junction (AJ) molecules such as E-cadherin and actin," Natsuga said. "We found that these molecules were localized at the intercellular junctions of high-density regions."



The Skin Stem Cell Research Team theme at the Department of Dermatology,

Faculty of Medicine and Graduate School of Medicine, Hokkaido University, including corresponding author Ken Natsuga (deep red jacket, furthest right) and first author Yosuke Mai (black jacket, back row, second from right). Credit: Ken Natsuga

The authors then used a [mathematical model](#) to confirm that, under spatially uniform density and stress, strong cell adhesion leads to the formation of density patterns. They were also able to demonstrate that the keratinocyte patterns influenced [cell proliferation](#) and differentiation, and that serum starvation influences epidermal stratification (a type of differentiation) in skin cells from mice.

"Our study presents a novel and robust model of cell–cell adhesion-induced patterning (CAIP)," concludes Natsuga.

"We have deepened our mechanistic insight into cellular organization and its consequences for cell fate decisions and epithelial stratification."

The team demonstrated that epithelial cell–[cell adhesion](#) is essential and sufficient for patterning. Future work will focus on adding more variables to the model to understand other processes that occur concurrently during development.

More information: Yosuke Mai et al, Patterning in stratified epithelia depends on cell–cell adhesion, *Life Science Alliance* (2024). [DOI: 10.26508/lsa.202402893](#)

Provided by Hokkaido University

Citation: Starvation and adhesion drive formation of keratinocyte patterns in skin, research reveals (2024, August 13) retrieved 14 August 2024 from <https://phys.org/news/2024-08-starvation-adhesion-formation-keratinocyte-patterns.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.