Capturing the onset of stem cell differentiation in the skin

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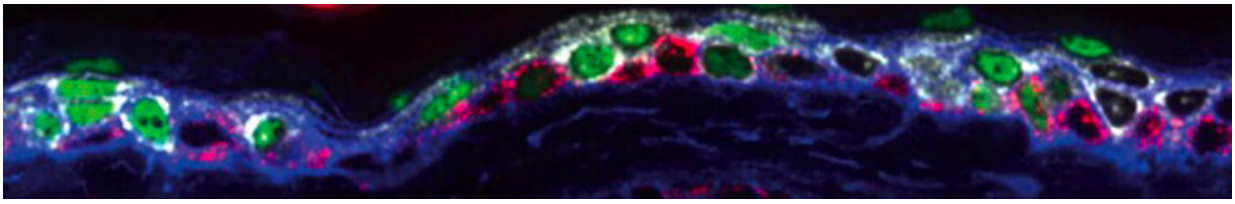


Microscopy images illustrating the heteterogeneity of the skin stem cell layer. Stem cells are in red and differentiating cells in white or green. Credit: Karl Annusver

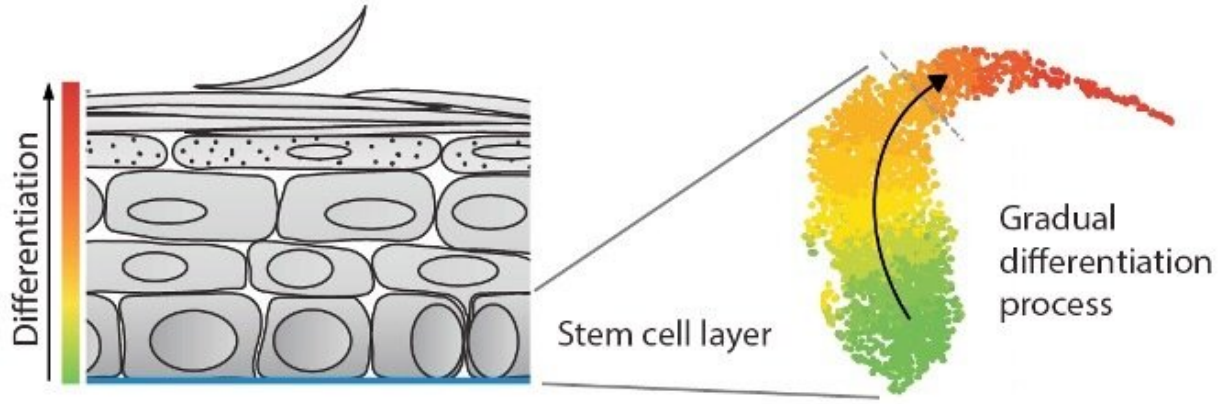
Researchers at Karolinska Institutet and at Yale University in U.S. have uncovered how stem cells behave in real-time while adapting their gene expression for differentiation. The study is published in the journal *Nature Cell Biology*.

Skin is essential for protecting our body from outside harm, such as injury, microbes, and radiation. This protective skin function is maintained by the tireless effort of resident stem cells to self-renew (remain stem cells) and differentiate (produce specialized cells) throughout our lifetime.

Skin stem cells residing in the epidermis give birth to daughter cells that eventually become specialized barrier cells, forming our protective,

watertight skin. This skin renewal process has been previously thought to depend on multiple types of stem cell populations with long- and short-term abilities to produce new daughter cells.

Instead, this new study revealed that these different populations are a snapshots of a gradual differentiation process, where a single stem cell population and their differentiating daughter cells flexibly adjust to local demands. That is, in response to different environments and needs, stem cells rapidly create more, or fewer, specialized daughter cells which surprisingly is not coupled with cell cycle exit as previously thought.



Graphic of skin epidermis and a single-cell transcriptomics representation of the stem cell layer. Credit: Karolinska Institutet

Importantly, changes in such cell behaviors underlie an extensive list of diseases such as cancer (increased stem cell self-renewal) or age-related impaired wound healing (reduced stem cell activity). Thus, it is significant to first understand "how" stem cells and their daughter cells behave, and "how quick" stem cell differentiation can occur.

To answer these questions, researchers from Karolinska Institutet and

Yale University teamed up to study stem cell behavior in real time with the corresponding gene expression changes at the same time. "With sequencing of individual skin cells, we were able to describe genes that get activated or deactivated at different stages during skin maturation, which was essential for uncovering skin renewal as a continuous differentiation process," says Karl Annusver, co-first author of the study in the lab of Maria Kasper, associate professor at the Department of Cell and Molecular Biology.

"Through live imaging we observed how skin stem cells create daughter cells on demand, with built-in flexibility to respond to different environments and needs," said co-first author Katie Cockburn, post-doctoral fellow in the lab of Valentina Greco, Carolyn Walch Slayman Professor of Genetics at Yale University.

More information: Albert Herms et al, Splitting up differentiation and cell cycle exit, *Nature Cell Biology* (2022). DOI: 10.1038/s41556-022-01022-7

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