

Unraveling the mechanism of skin barrier formation

April 14 2017

Scientists have identified the gene responsible for generating acylceramide, the key lipid in forming the skin barrier that protects us from pathogens, allergens and other harmful substances. This finding could prove crucial in developing medicines for treating atopic dermatitis and ichthyosis.

Defects of the [skin barrier](#) can trigger skin diseases such as atopic dermatitis, which is said to afflict about 10 percent of the population in some developed countries. Acylceramide, a lipid only found in skin, plays a pivotal role in forming this barrier. Although most of the genes needed to generate this special lipid have been recently identified, the gene responsible in the final step to produce acylceramide has been missing. Finding the last piece in the puzzle, therefore, was essential for elucidating the skin barrier's molecular mechanism.

The team led by Professor Akio Kihara at Hokkaido University established a cell system that produces the acylceramide precursor ω -hydroxyceramide and used it to evaluate the activity of several candidate genes to produce acylceramide. The research methodology addressed a long-standing hurdle in experiments using epidermal keratinocytes which caused the inefficiency of gene delivery to the cells. By using other type of cultured cells transfected with the [genes](#) required for other steps of acylceramide synthesis, the team has overcome the issue and tested the function of the [candidate genes](#).

As a result, the team succeeded in finally identifying the key gene as

PNPLA1. The researchers also found evidence that suggests the lipid triglyceride acts as a linoleic acid donor. Furthermore, they discovered that mutant PNPLA1 proteins found in patients with ichthyosis, a serious genetic skin disorder characterized by dry and scaly skin, show reduced or no enzyme activity.

As there is no curative treatment for [atopic dermatitis](#), patients are currently given only symptomatic therapies. No treatment has been established for ichthyosis. "To better treat such patients, it is essential to restore the functions of the skin barrier," says Akio Kihara. "Having unraveled the [molecular mechanism](#) of acylceramide synthesis, our study should enable the search for compounds that boost acylceramide synthesis and therefore restore the skin barrier."

This study was conducted as a part of a project under the Advanced Research and Development Programs for Medical Innovation (AMED-CREST) of the Japan Agency for Medical Research and Development.

More information: Yusuke Ohno et al. PNPLA1 is a transacylase essential for the generation of the skin barrier lipid ω -O-acylceramide, *Nature Communications* (2017). [DOI: 10.1038/NCOMMS14610](https://doi.org/10.1038/NCOMMS14610)

Provided by Hokkaido University

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