

Shiseido Reveals That Age-Related Inflammatory Factors Damage Epidermal Stem Cells

-A new skincare approach focusing on the lymphatic function of the skin-

Shiseido Company, Limited (“Shiseido”) has discovered that age-related inflammatory factors (IL-8) damage epidermal stem cells and accelerate cell aging. IL-8 is a type of waste product collected by lymphatic vessels in the skin.

Although it has been known that the age-related decrease of lymphatic vessels causes deterioration in the collection of waste product, resulting in the accumulation of inflammatory factors in the skin, it was unclear that how such accumulated inflammatory factors affect epidermal stem cells. This time, we have revealed that one inflammatory factor (IL-8), a type of skin waste product, causes damage to epidermal stem cells and affects the barrier function of the skin.

These research findings will lead to the development of a new skincare approach that focuses on the functions of lymphatic vessels to care for epidermal stem cells, which play an important role in the rejuvenation of skin cells.

Some of the research results will be presented at the 45th Annual Meeting of The Japanese Society for Investigative Dermatology (December 11-13, 2020).

Research background

The cutaneous lymphatic vessels are characterized by the collection of skin waste products as a starting point for lymphatic routes. Our previous studies have revealed that lymphatic vessels are abundant right beneath the epidermis. In addition, various studies have confirmed that waste products accumulate in the skin as the density of lymphatic vessels decreases with age.

However, although it was known that epidermal stem cells, which are the source of healthy epidermal cells, decrease in number with aging, the mechanism by which the accumulation of waste products in the skin causes damage to epidermal stem cells has not been proven.

Thus, we elucidated the cause of the age-related decrease of epidermal stem cells and examined how inflammatory factors, which are one of the waste products collected by lymphatic vessels, have an adverse impact on epidermal stem cells, while pursuing the development of a new skincare approach.

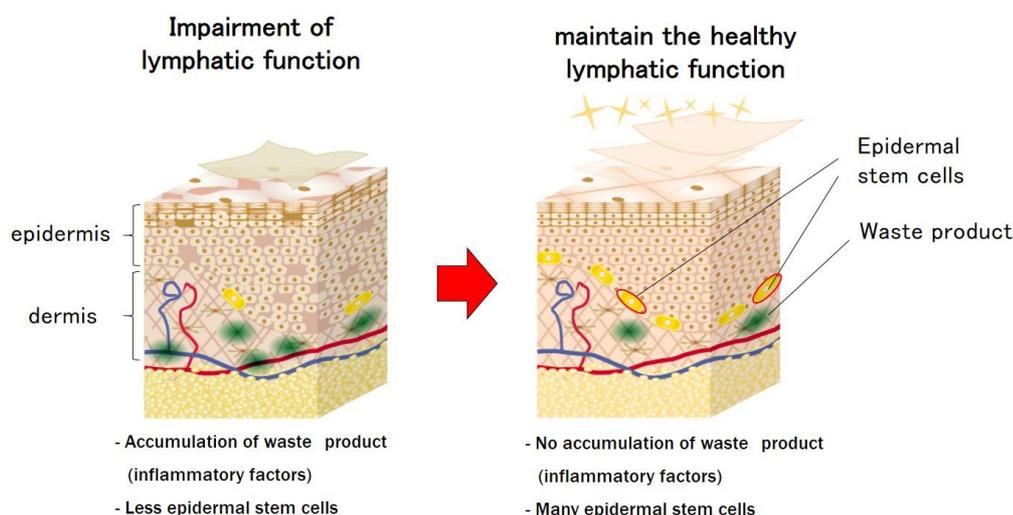


Figure 1. Overview of this research (illustration image)

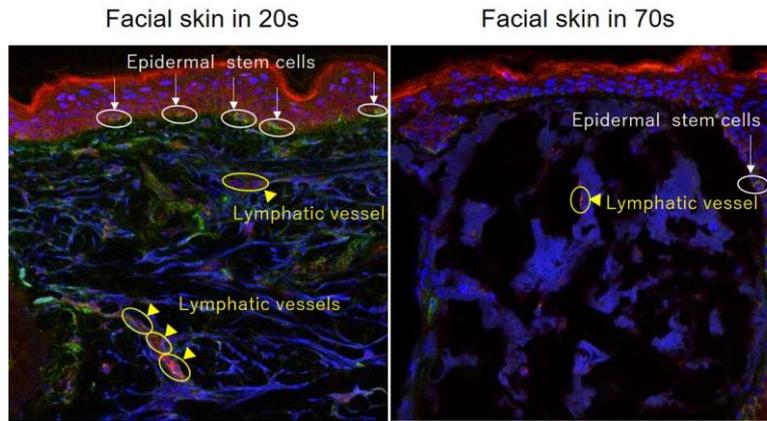


Figure 2. Age-related changings of Epidermal stem cells and Lymphatic vessels

Inflammatory factors inhibit the rejuvenating ability of epidermal stem cells

First, we examined the colony-forming ability, which is an index of the self-replication of epidermal stem cells. We cultured IL-8 in the culture medium and compared the number of colonies formed. As a result, it was found that colony-forming (cell rejuvenation ability) deteriorates significantly in the group with IL-8 (Figure 3).

Then, we examined the expression level of the Lrig1 gene, which is a marker for epidermal stem cells, and found that the gene expression level was significantly reduced when IL-8 was added, suggesting a loss in the stem characteristics of epidermal stem cells (Figure 4).

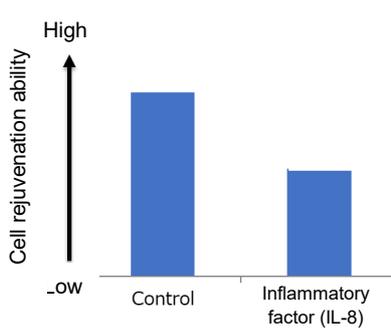


Figure 3. Inhibition of cell rejuvenation ability by inflammatory factor IL-8

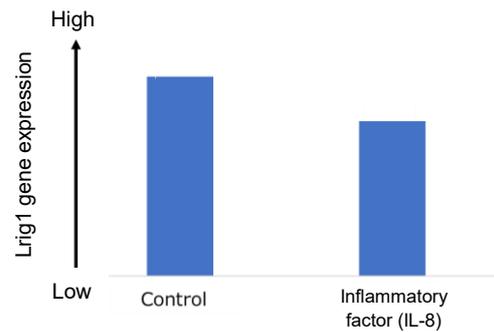


Figure 4. Expression of Lrig1 gene in epidermal stem cells

Inflammatory factors accelerate epidermal cell aging

We conducted an experiment to selectively stain senescent cells (β -galactosidase staining) in order to verify the effect of IL-8 on cellular senescence (Figure 5). As a result, it was found that the addition of inflammatory factors to epidermal cells increases senescent cells* (Figure 6).

* Senescent cells; β -galactosidase-stained positive cells.

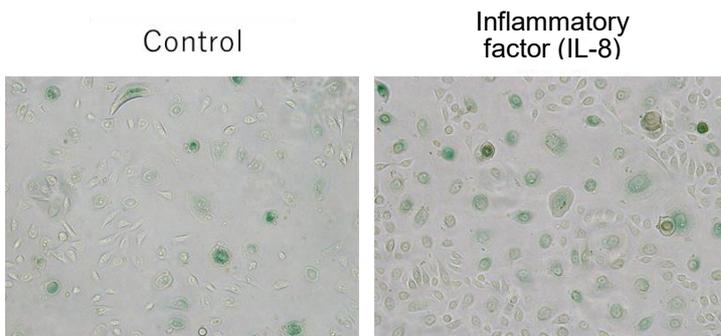


Figure 5. Increase in senescent cells (green) due to inflammatory factors

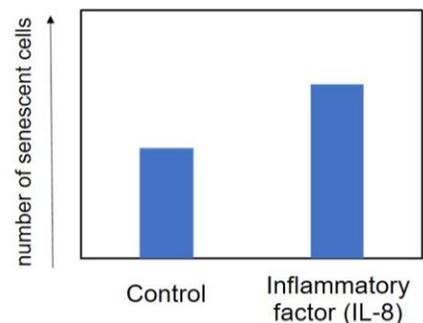


Figure 6. Increase in number of senescent cells due to inflammatory factors

Inflammatory factors reduce skin barrier function

After adding an inflammatory factor (IL-8) to the skin model and culturing it for five days, we confirmed that there was a decrease in the expression of bleomycin hydrolase (NMF-producing enzyme), which maintains the skin barrier function, suggesting that IL-8 deteriorates the barrier function of the skin (Figure 7).

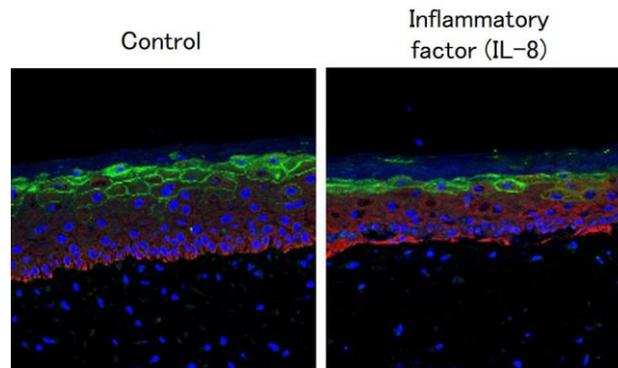


Figure 7. Impact of inflammatory factor IL-8 on skin barrier function
(Bleomycin hydrolase reduces after adding IL-8 (green))

Summary and future outlook

From this study, it has become clear that the accumulation of inflammatory factors, which are one of the skin waste products, ages epidermal cells and reduces their barrier function.

This suggests that skincare to enhance the collection of waste products may prevent the accumulation of waste products and maintain the healthy function of epidermal stem cells and epidermal cells.

Shiseido believes these research results will lead to the development of skincare technology with a new approach to improve skin aging by maintaining normal functions of epidermal stem cells, which play an important role in skin cell rejuvenation.

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- Shiseido Establishes Lymphatic Vessel Visualization Technology (2020)

<https://corp.shiseido.com/en/news/detail.html?n=00000000002997>

- Shiseido Reaches World’s First Elucidation of Aging Mechanism of Lymphatic Vessels in the Skin (2020)

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