Press Release

Research and development

Shiseido discovers new features in Alternative Autophagy through joint research with The Institute of Science Tokyo

Elucidation of its function to suppress skin photoaging and discovery of the Lamiaceae extract

Shiseido revealed that "alternative autophagy"[*1] works to suppress photoaging of the skin caused by ultraviolet (UV) rays through joint research with Distinguished Professor at The Institute of Science Tokyo, Dr. Shigeomi Shimizu. Among autophagic pathways known as mechanisms that break down unwanted intracellular materials and restructure cells, alternative autophagy comes into play particularly when cells are damaged to a marked degree (Figure 1). In addition, Shiseido identified the Lamiaceae plant extract that activates alternative autophagy.

Alternative autophagy, a second type of autophagy discovered in 2009 by Professor Shimizu at The Institute of Science Tokyo (formerly, Tokyo Medical and Dental University), Advanced Research Initiative, Pathological Cell Biology comes into play when cells are subjected to excessive damage due to UV rays and other factors. It is distinct from regular autophagy in that it serves as a mechanism to restructure cells by destroying unwanted intracellular materials such as damaged mitochondria.[*2] Alternative autophagy has been known to be involved in the maintenance of skin health, but the joint research with Shiseido led to the elucidation of its new feature, namely, the suppression of UV-induced photoaging of the skin.

Dark spots, wrinkles, and skin sagging caused by photoaging represent timeless skin problems that many people experience. Solutions developed from the findings of this joint research have enabled a revolutionary approach to prevent such skin problems from the inside of the skin, in addition to conventional approaches from the outside, such as UV protection agents and anti-inflammatory agents. The results of this research have been published in the international scientific journals *Journal of Biological Chemistry* (dated March 16, 2024) and *Autophagy Reports* (dated September 5, 2024).

*1 Another name: Golgi membrane-associated degradation = GOMED

*2 Subcellular organelles that play an important role critical to our survival, such as energy production. More than 100 mitochondria exist in one cell.

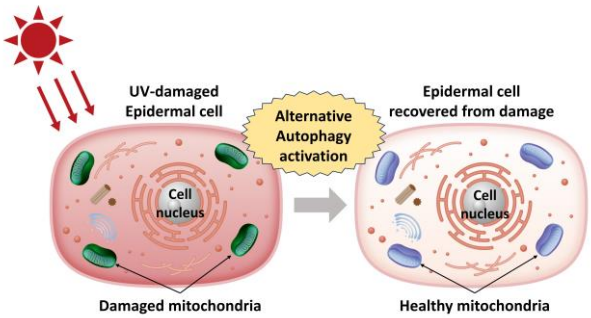

Figure 1. Alternative autophagy, which comes into play when cells are subjected to excessive damage

Research background

Shiseido started UV protection research more than 100 years ago, when photoaging of the skin had not yet widely been known. Since then, the company has been developing technologies to meet the needs of consumers whose desire is to protect the skin from the adverse effects of UV rays in all environments. In addressing the growing demand in recent years for daytime cosmetics that combine UV protection and high skin care functions, Shiseido has been pondering how such an expectation could be met. Against this backdrop, the company launched a study based on the idea that learning the specifics of relationship between UV rays and alternative autophagy, a mechanism that cells themselves have in place to maintain skin health, would be key to meeting consumer expectations.

Discovery 1: Alternative autophagy suppresses UV-induced inflammation of epidermal cells

First, it was found that when epidermal cells are exposed to ultraviolet B (UVB) radiation, mitochondria in epidermal cells become damaged. We also confirmed that, nearby UV-damaged mitochondria, the inflammasome, a group of protein complexes that command inflammation, are activated, giving rise to inflammatory factors (Figure 2-(1)). Next, it was found that, by activating alternative autophagy, the inflammatory factors can be suppressed (Figure 2-(2)). This may be due to alternative autophagy, which, when activated, results in the degradation of damaged mitochondria, thereby reducing cellular inflammatory responses.

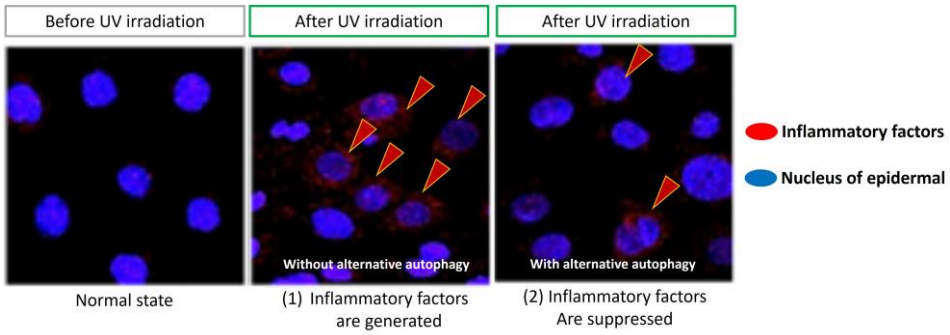

Figure 2. Alternative autophagy suppresses UV-induced inflammation of epidermal cells caused by UV rays

Discovery 2: Collagen-degrading enzymes are produced when inflammation reaches the dermis

It was found that when alternative autophagy does not work and inflammatory factors are released outside the epidermal cells, the expression of collagen-degrading enzymes (MMPs) increases as the effects of the released inflammatory factors reach the dermal cells (Figure 3). In other words, decomposition of dermal collagen advances in the skin with a defect in the function of alternative autophagy, possibly leading to photoaging. Moreover, findings revealed that alternative autophagy may also exhibit an aging-related decline in function (Figure 4).

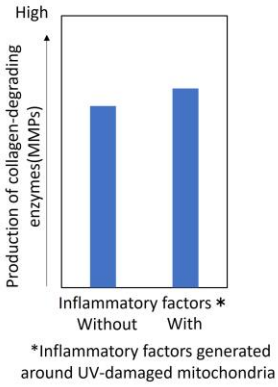

Figure 3: Increase in collagen-degrading enzymes (MMPs) due to inflammatory factors

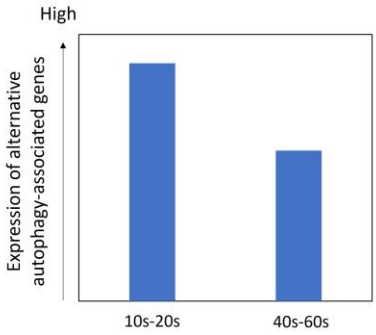

Figure 4: Decrease in the expression of alternative autophagy-associated factors due to aging

Discovery 3: Alternative autophagy function is activated by the Lamiaceae plant extract

The Lamiaceae plant extract that activates alternative autophagy (Figure 5) was then identified. Due to this discovery, the active functioning of the alternative autophagy can be maintained regardless of age, and because a healthy environment inside the cell will be maintained even under exposure to UV rays, it is expected to lead to the suppression of dermal collagen degradation and photoaging of the skin.

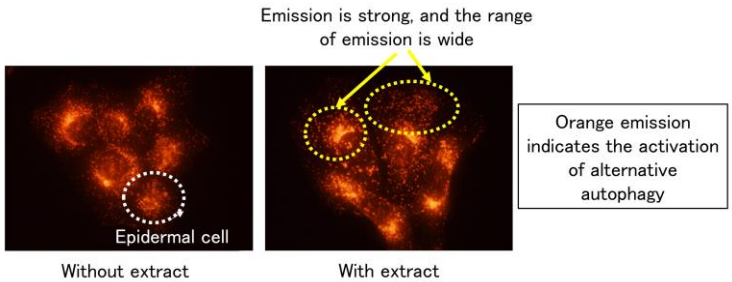

Figure 5. Alternative autophagy is activated by the Lamiaceae plant extract

About our R&D strategy:

This research, conducted under "Skin Beauty INNOVATION," one of the three pillars of Shiseido's R&D strategy, was advanced as a study to clarify the sequence of processes in the development of and recovery from UV-induced inflammation with the aim of realizing skin that is less susceptible to damage by UV rays by taking care of the skin from within its cells.

- Integrated Report 2023 (Beauty Innovation)

https://corp.shiseido.com/report/en/2023/message/cmio/

- Keywords

Skin Beauty INNOVATION, UV rays, alternative autophagy

<Reference>

News Release

(1) Shiseido achieves the world's first application of "alternative autophagy" to the cosmetics field (2020)
https://corp.shiseido.com/jp/news/detail.html?n=00000000002961 (Japanese)

Dr. Tatsuya Hasegawa, Researcher

Researchers' challenges

■ R&D Philosophy "DYNAMIC HARMONY" approach

This research has been carried out with the Inside/Outside approach of Shiseido's unique R&D philosophy, "DYNAMIC HARMONY." By elucidating and strengthening the new mechanism of the relationship between the skin and the environment, Shiseido aims to realize healthy and beautiful skin, even in today's rapidly changing environment.

■ The challenge to solving the mystery of skin that has evolved with the sun and UV rays

UV rays are not visible. We humans, like other organisms, have lived and evolved side by side with the invisible wavelengths of light. These rays of UV light, however, also cause great damage to our skin. How do UV rays cause inflammation in the skin, and how do we recover from it? The present research originated as an attempt to answer such questions.

■ One of the answers was "alternative autophagy"

As was investigated, it became clear that, although there are several known factors that cause UV-induced inflammation, not much was known about how inflammation was restored to a normal state, leading to recovery. That being the case, what drove the research forward was the anticipation of coming to understand the series of mechanisms from the beginning of UV-induced inflammation to restoration to a normal state and finding the clues for UV or photoaging protection that have never been available. After more than 10 years, one of the answers was found to be "alternative autophagy." This discovery is the result of the company's joint research with Distinguished Professor at The Institute of Science Tokyo, Dr. Shigeomi Shimizu—who discovered and named "alternative autophagy"—and his lab members.

■ To a society liberated from UV damage

Shiseido will continue to work on research and development to realize a society where we, who will continue to live under the sun, can lead healthy lives, increasingly free from the damage and anxiety of invisible UV rays.

What is research and development (R&D) philosophy "DYNAMIC HARMONY"

・Shiseido formulates its unique R&D philosophy "DYNAMIC HARMONY" (2021)
https://corp.shiseido.com/en/news/detail.html?n=00000000003252

・The DYNAMIC HARMONY special website
https://corp.shiseido.com/en/rd/dynamicharmony