Press Release

Research and Development

Shiseido Discovers "Maturation" of Thick and Dense Collagen by M2 Macrophages

- Rose Extract Promotes M2 Macrophage Differentiation -

Shiseido has been investigating the effects of the balance between two types of macrophages (M1/M2),* immune cells, on the collagen life cycle. In this study, the company introduced a new perspective of "maturation" to the series of collagen life cycle processes, which traditionally include "production," "degradation," and "digestion." As a result, it discovered that M2 macrophages have the ability to interact with fibroblasts to thicken and densify collagen fibers. Additionally, rose extract was found to be effective in promoting the differentiation of M2 macrophages. Due to skin aging caused by ultraviolet rays, the function of M2 macrophages declines. However, rose extract is expected to support their function, promote the formation of high-quality collagen, and enhance skin elasticity and firmness.

In the future, Shiseido will continue to deepen its research on collagen and enhance the understanding of its relationship with skin aging, aiming to provide innovative solutions for achieving healthy skin. Some of the research results were presented at the 56th Annual Meeting of the Japanese Society of Matrix Biology and Medicine (June 2024) and received the Young Investigator Award. The study was also presented at the 17th Asian Societies of Cosmetic Scientists (ASCS) Conference Manila 2025 (June 2025) and received the 1st Best Podium Presentation Award.

* A type of immune cell primarily responsible for taking in and processing bacteria and waste products. M1 macrophages mainly handle inflammatory responses, helping to eliminate pathogens, defend infection sites, and break down collagen in damaged tissues. M2 macrophages promote anti-inflammatory responses and assist in repairing tissues damaged by inflammation.

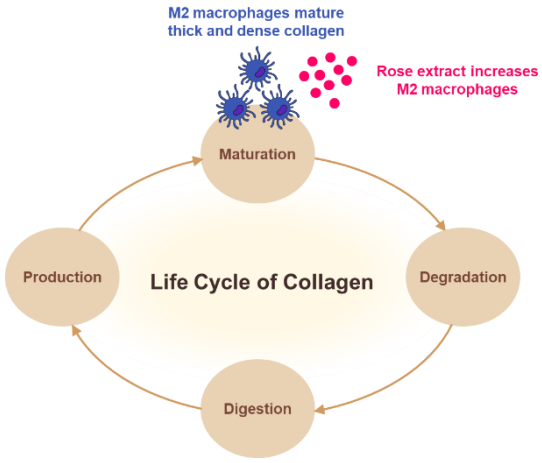

Figure 1 Overview of this research (image)

Research Background

While the importance of maintaining dermal collagen in a healthy state for achieving healthy skin is well known, many studies on collagen have focused on fibroblasts, the main producers of collagen. However, the influence of other cells present in the dermis and their interactions with fibroblasts remain largely unexplored.

Shiseido has been conducting collagen research for over 40 years, and since 2020, has been focusing on immune cells, "macrophages," which support the function of fibroblasts in producing collagen. So far, it has elucidated that the disruption of the balance between M1 and M2 macrophages can be caused by photoaging from ultraviolet rays, leading to the induction of fibroblast senescence** and negatively impacting the collagen life cycle.***

In this study, the company further deepened its collagen research to determine whether macrophages not only promote collagen production but also have the potential to mature thick and dense collagen fibers.

** Shiseido Discovers Relationship of Macrophage Balance to Skin Aging for the First Time in the World (2020)
https://corp.shiseido.com/en/news/detail.html?n=00000000003038
*** Shiseido Discovers That Age-Induced Macrophage Imbalance Affects Collagen Metabolism (2022)
https://corp.shiseido.com/en/news/detail.html?n=00000000003374

Role of M2 Macrophages and Mechanism of Collagen Maturation

In an experiment where the culture supernatant of either M1 or M2 macrophages was added to fibroblasts, it was found that the addition of M2 macrophage culture supernatant resulted in higher gene expression related to the maturation of collagen fibers compared to the addition of M1 culture supernatant. This includes "processing enzymes" (which trim both ends of procollagen, a collagen precursor, converting it into collagen molecules) and "cross-linking enzymes" (which orderly assemble collagen molecules, promoting fiber formation) (Figure 2). This suggests that M2 macrophages interact with fibroblasts to induce various enzymes, thereby promoting the formation of thicker and denser collagen fibers.

To further assess collagen fiber quality in detail, Shiseido created a three-dimensional (3D) dermis model by adding the culture supernatant of M1 or M2 macrophages, along with a collagen solution, to observe the formation of collagen fibers. The results showed that the collagen fibers in the M2 macrophage supernatant treated model were thicker and denser, exhibiting a cross-striated structure (striped pattern) compared to those in the M1 macrophage supernatants treated model, suggesting enhanced collagen maturation (Figure 3). This condition indicates that collagen molecules are arranged in an orderly manner, resulting in the formation of mature fibers.

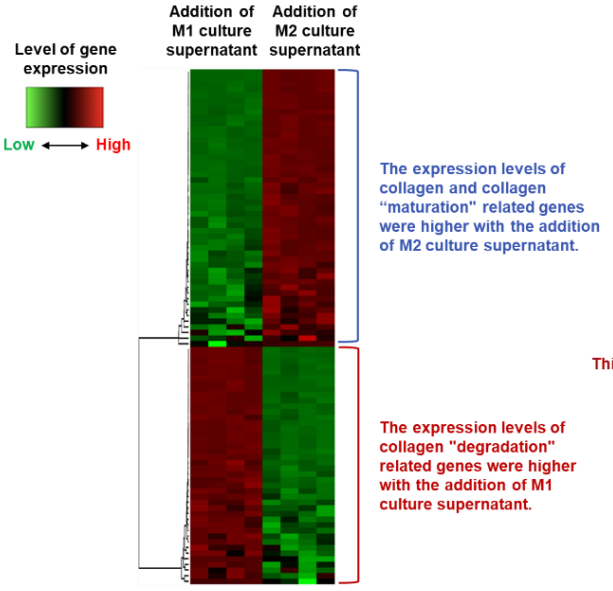

Figure 2 The addition of M2 macrophage culture supernatant resulted in higher expression of genes related to the maturation of collagen fibers

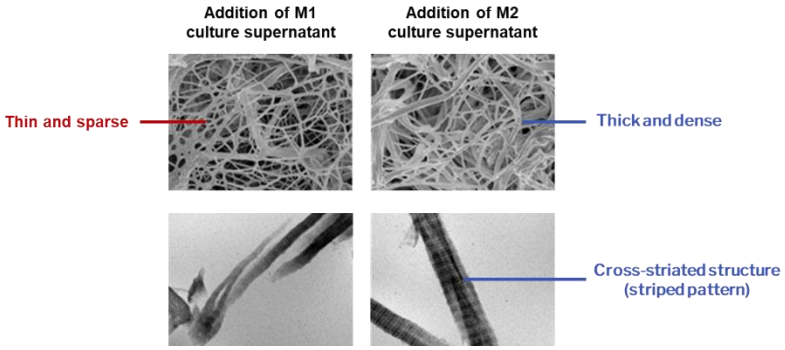

Figure 3 Collagen fibers in the 3D dermis model
Upper panel: Scanning electron microscope image
Lower panel: Transmission electron microscope image

The Effect of Rose Extract on Promoting M2 Macrophage Differentiation

Next, Shiseido explored various extracts for their potential to promote the differentiation of M2 macrophages, which contribute to collagen maturation, and found that rose extract is effective in promoting the differentiation of M2 macrophages.

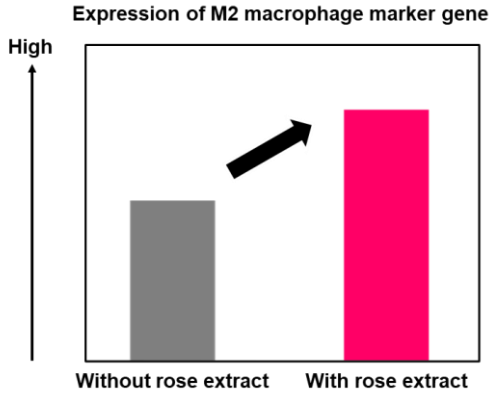

Figure 4 The effect of rose extract on promoting M2 macrophage differentiation

Future Prospects

Shiseido aims to further deepen its collagen research and enhance the understanding of its relationship with skin aging. The company will also explore new agents, such as rose extract, and examine synergistic effects with other agents, with the goal of developing innovative solutions that create value beyond consumer expectations.

Researcher

Ryozo Tobita
Researcher
MIRAI Technology Institute
Shiseido Company, Limited

R&D Strategy
Shiseido has established three pillars under its R&D philosophy "DYNAMIC HARMONY" to accelerate innovation: "Skin Beauty Innovation: Enhancing brand value," "Sustainability Innovation: Creating circular value," and "Future Beauty Innovation: Challenging new domains." Additionally, Shiseido promotes open innovation and advances new value creation through research alliances with various external organizations. The innovative research outcomes generated from the fusion of Shiseido's advanced science and the knowledge and technology of world-class research institutions are highly regarded academically on a global scale, including at the IFSCC Congress, the world's largest and most prestigious research conference on cosmetic technology.

About R&D Philosophy "DYNAMIC HARMONY"
https://corp.shiseido.com/en/rd/dynamicharmony