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Shiseido Company, Limited

Press Release

Shiseido Discovers Relationship of Macrophage Balance to Skin Aging for the First Time in the World

-New anti-aging skincare solution focus on “Inflammaging” caused by chronic inflammation-

Shiseido Company, Limited (“Shiseido”) has confirmed for the first time in the world that a skewing of balance between two types of macrophages*1 (M1 and M2) is involved in the occurrence of “inflammaging”, which is an aging accelerated by chronic inflammation. Furthermore, we have identified the possibility of a completely new anti-aging solution with a focus on inflammaging as a new approach to curb chronic skin inflammation and promote cell rejuvenation.

Going forward, Shiseido will continue research with the aim to create anti-aging solutions for various inflammatory skin problems.

Some of the research results were presented at the 45th Annual Meeting of the Japanese Society for Investigative Dermatology on December 13, 2020.

*1 A type of immune cell whose main function is to collect and process bacteria and waste products.

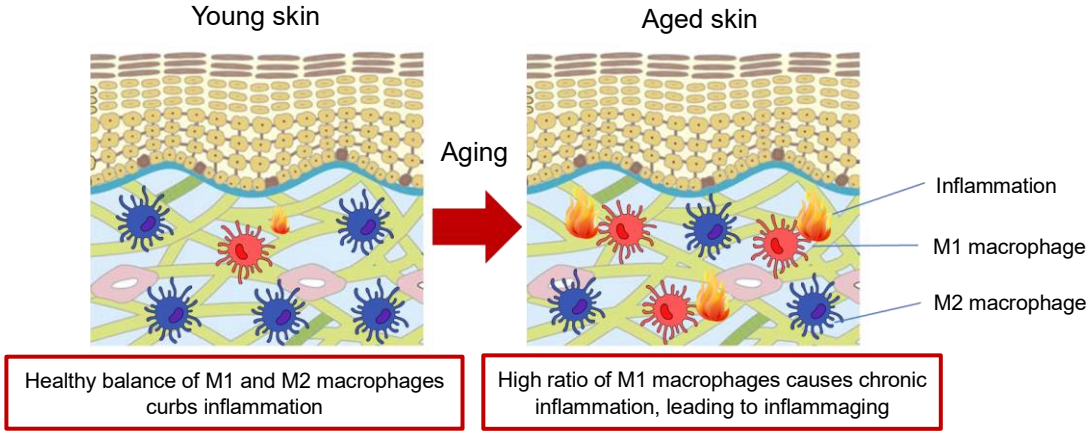

Figure 1. Overview of this research

Inflammaging and two types of macrophages

● What is inflammaging?

The inflammatory reaction is a necessary bodily defense reaction against external stimuli such as UV rays and dryness. However, it has been discovered that the inflammatory response does not disappear fully in the body, becoming more chronic, which has various adverse impacts on the body. The phenomenon of accelerated aging due to chronic inflammation is called inflammaging, and in recent years, there has become an urgent need to develop therapies for diseases caused by inflammaging. Although it has been suggested that a major cause of inflammaging may be failure to curb chronic inflammation in accordance with aging, the causes and mechanisms in the skin are not fully understood.

● Balance of M1 and M2 macrophages

In order to address chronic inflammation, the cause of inflammaging, it is considered important to remove the causes of inflammation such as waste products and normalize the function to stop inflammation. Shiseido has already accumulated various knowledge through research on lymphatic vessels that are responsible for removing waste products. This time, in pursuit of normalization of the function to stop inflammation, we conducted research to elucidate the mechanism of inflammaging by focusing on the balance between M1 and M2 macrophages*2.

*2 M1 macrophages are mainly responsible for inflammatory reaction and removing foreign materials, whereas M2 macrophages promote the anti-inflammatory reaction and repair of tissues damaged by inflammation.

Verification of relationship between M1 / M2 balance of macrophages and skin aging

It was well known that the balance between M1 and M2 macrophages (M1 / M2 balance) plays an important role in the process of healing wounds in the skin, however, little was known about its relationship with aging. Therefore, we visualized macrophages in terms of the relationship of M1 / M2 balance with regard to skin aging in sun-exposed areas via immunohistochemical staining, and found that the population of M1 macrophages increased and M2 macrophages decreased in the mature group (average age of 73.5 years) compared to the younger group (average age of 33.5 years) (Figure 2), and that the ratio of M1 macrophages was extremely high in the mature group (Figure 3).

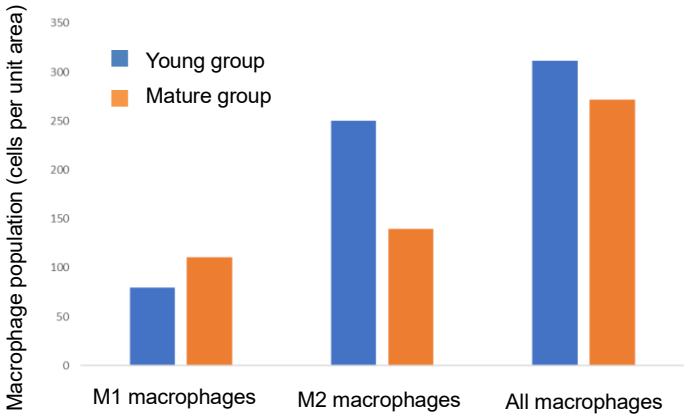

Figure 2. Population of M1 / M2 macrophages in young and mature groups

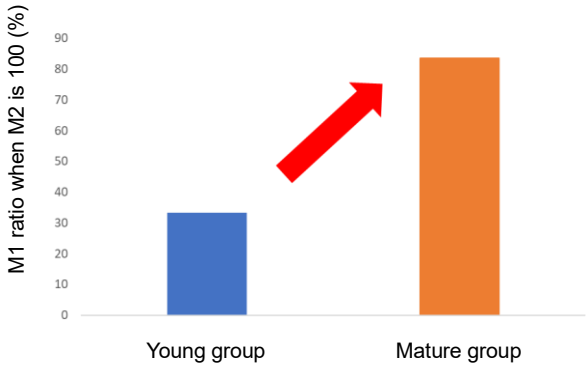

Figure 3. Comparison of M1 / M2 balance between young and mature groups

M1 macrophages age cells

Next, we evaluated the effects of M1 and M2 macrophages on cellular senescence through experiments using dermal fibroblast culture. As a result, we discovered for the first time that the proportion of senescent cells (p21-positive cells) in fibroblasts significantly increased when a culture supernatant of M1 macrophages was applied (Figure 4).

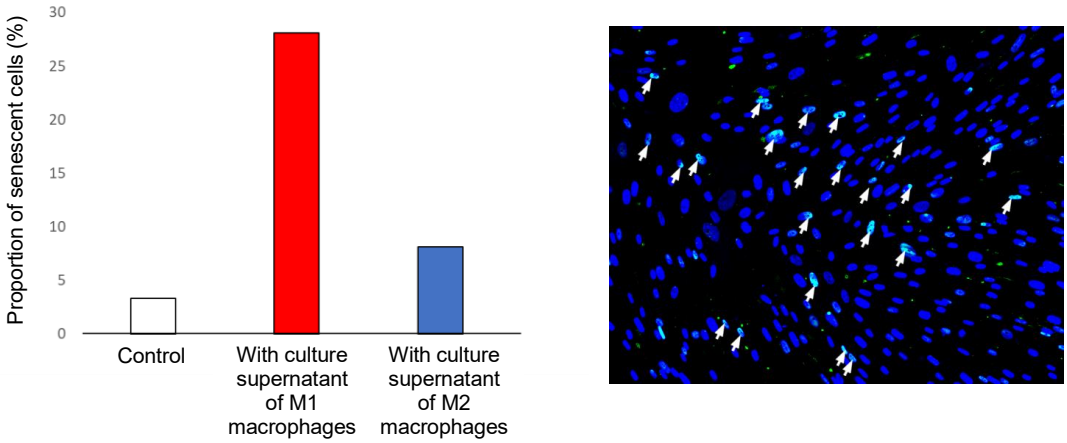

Figure 4. Effects of M1 / M2 macrophages on cellular senescence

Left (graph): Proportion of senescent cells after applying culture supernatant of M1 / M2 macrophages to fibroblasts

Right (image): When culture supernatant of M1 macrophages is applied, many senescence markers (green) accumulate (arrows) in fibroblast nucleus (blue)

New aging care solution focused on inflammaging

Until now, anti-inflammatory solutions, which suppress inflammation intensity against inflammatory reactions caused by external stimuli such as UV rays and dryness, have been the mainstream. However, for chronic inflammation that accelerates skin aging (inflammaging), it is necessary to create anti-inflammatory solutions that not only suppress inflammation intensity but also promote inflammation resolution (Figure 5).

In this study, we revealed for the first time in the world that the skewing of M1 / M2 balance in the skin results in failure to alleviate chronic inflammation and causes inflammaging. This discovery can be expected to help develop a brand-new approach to anti-aging skincare solutions focused on inflammaging. Going forward, Shiseido will continue to develop anti-aging skincare products that exceed consumer expectations for treatments of various skin problems.

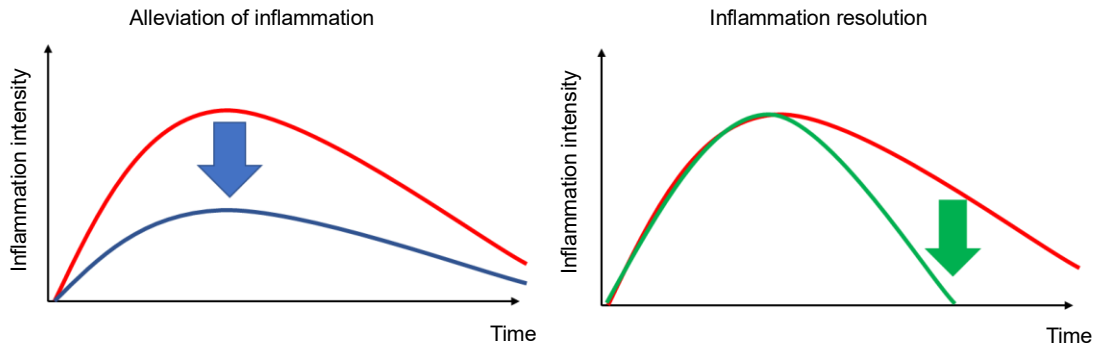

Figure 5. Difference between “alleviation of inflammation” and “Inflammation resolution” (image)