

Press Release

Research and Development

Shiseido discovers that aging increases the risk of hyperpigmentation under UV light exposure during daytime hours, leading to the development of suppression methods

Addressing both UV radiation and aging in the elucidation of the true nature of chronic inflammation specific to areas of hyperpigmentation

Shiseido discovered that, in the skin with dark spots, the expression of "interleukin 6 receptor (IL-6R),"^{*1} an inflammatory factor receptor that is known to be involved in chronic inflammation in age-related diseases, increases more with advancing age in conjunction with UV irradiation during the day. The study revealed that, even when the amount of exposure to UV light is the same, the risk of dark spot formation (hyperpigmentation) and/or worsening may increase because of aging factors, given that the higher the expression of IL-6R in epidermal cells, the higher the activity of melanocytes.^{*2} In addition, Shikuwasa (Hirami lemon) extract was found to be useful as an agent to suppress inflammatory reactions caused by UV radiation and aging, and its effect to inhibit the activity of melanocytes was confirmed.

Until now, the details have remained unclear regarding the mixed effects of UV radiation and aging in the hyperpigmentation process. The present discovery will make it possible to approach dark spot prevention from the two aspects, i.e., UV radiation as an external factor and aging as an internal factor, demonstrating, once again, the importance of dark spot risk care in the daytime. This knowledge will be applied to future product development. The results of this study were partly presented at the 25th International Pigment Cell Conference (23/5/30–6/2) and the 1st Annual Congress of the Society of Cosmetic Chemists of Japan (SCCJ) (23/12/5–7).

*1 The receptor that receives IL-6, an Inflammatory factor, and transmits the signal in response to inflammation in the cell.

*2 A condition in which the length and number of dendrites of melanocytes increase, and melanin delivery is promoted.

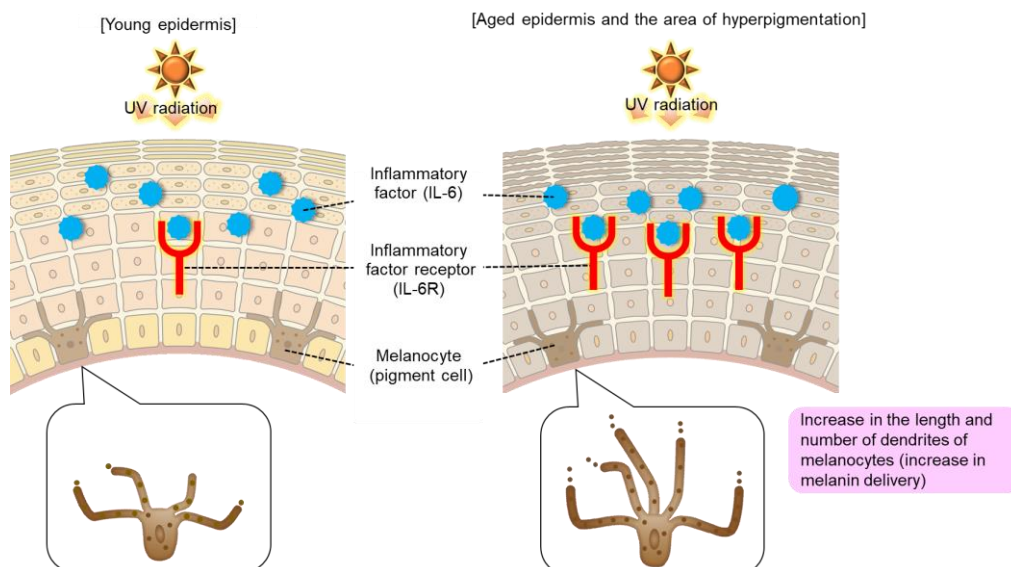


Figure 1. The receptor IL-6R, which triggers inflammatory response, is highly expressed due to aging, and increases melanocyte activity (conceptual diagram)

Research background

From early on, Shiseido has pursued studies in the field of dark spot research focused not only on "melanin production," which is a localized phenomenon, but also on the "dark spot-prone skin environment" that increases the risk of hyperpigmentation by promoting melanin production, advocating the company's unique research findings pertaining to dark spots that explain how the skin environment prone to dark spots is created under the condition of inflammation—"chronic micro-inflammation."³ Meanwhile, regarding the two major factors of inflammation that lead to the creation of dark spot-prone skin environment, namely, the external factor of UV radiation and the internal factor of aging, their mixed effects have only partly been elucidated. Against this backdrop, the present study was undertaken with the aim to clarify the mechanism of hyperpigmentation from both aspects.

*3 A condition in which weak inflammation continues to occur chronically in the epidermis and dermis

The skin with dark spots shows increased expression of the inflammatory factor receptor IL-6R in epidermal cells

We discovered that, when the inflammatory condition in human skin tissue was compared between areas with hyperpigmentation and without (non-hyperpigmented area), the level of expression of the inflammatory factor receptor IL-6R was higher in the hyperpigmented area (Figure 2). It was speculated that the hyperpigmented area of the skin is in a state prone to "worsening" dark spots, as inflammation is chronically activated due to an excessive increase in IL-6R, the receptor for the inflammatory factor IL-6.

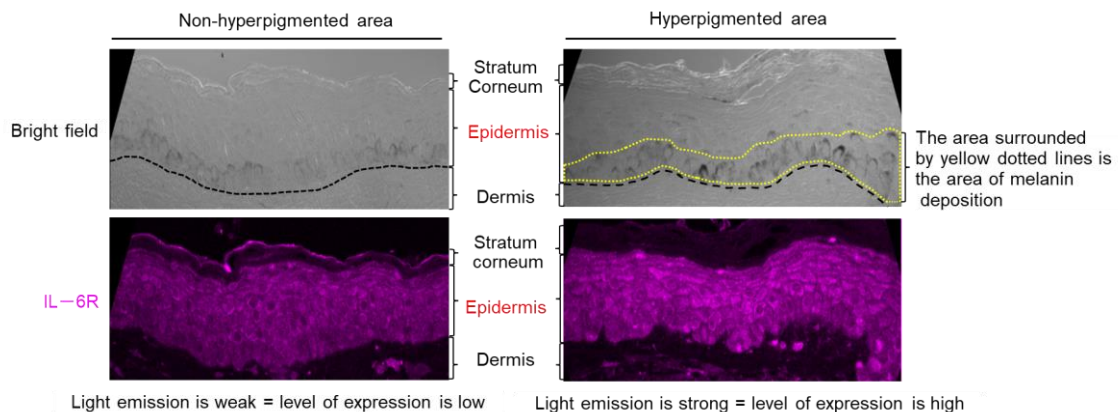


Figure 2. IL-6R, a receptor for the inflammation-inducing factor, was overexpressed in the hyperpigmented area

The increase in IL-6R in epidermal cells due to aging and UV radiation leads to activation of melanocytes

Next, we investigated "aging" as a factor that influences the expression of IL-6R, which was increased in the hyperpigmented area. Experiments using young or aged human-derived epidermal cells revealed a higher increase in the expression of IL-6R in the cells due to UV light exposure, assuming daytime sunlight, in aged cells (Figure 3). Moreover, when we observed the condition of melanocytes co-cultured with aged epidermal cells in order to investigate whether IL-6R actually affects the activation of melanocytes, the number and length of dendrites, which are indicators of melanocyte activation, increased and elongated compared with those of melanocytes co-cultured with young epidermal cells (Figure 4).

An increase in IL-6R in epidermal cells triggers the activation of melanocytes, and this is potentially prompted by "aging."

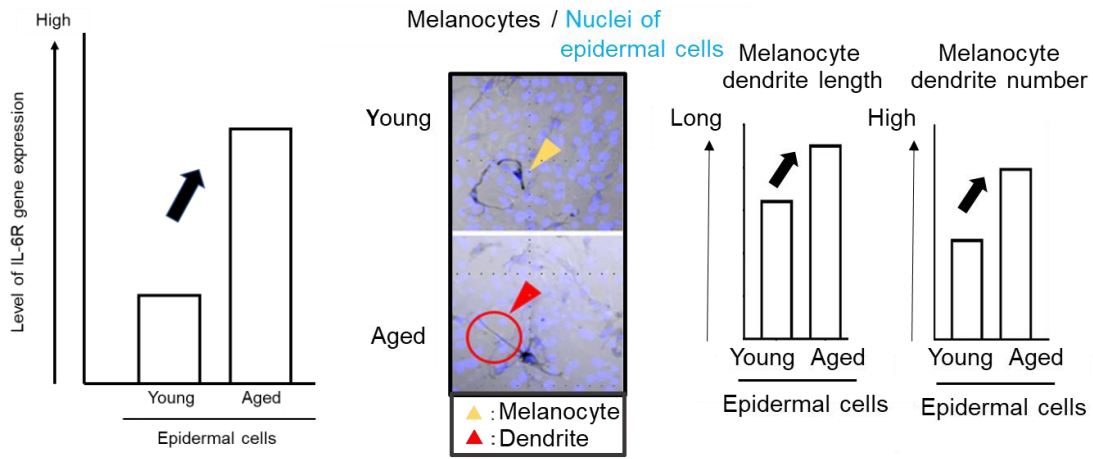


Figure 3. Increased IL-6R gene expression due to UV radiation and aging

Figure 4. UV light exposure induces melanocyte activation in aged epidermal cells

Discovery of an extract effective for suppressing IL-6R expression

This time, upon finding that the risk of developing or worsening hyperpigmentation due to UV radiation is increased via promotion of IL-6R expression due to aging, we searched for an agent that could suppress the expression of IL-6R. As a result, we discovered that the extract of Shikuwasa extract has an effect to suppress the expression of IL-6R in epidermal cells (Figure 5). Moreover, we found that Shikuwasa extract has an effect to suppress an increase or extension of the number and length of dendrites of melanocytes co-cultured with aged epidermal cells (Figure 6). We believe that, by suppressing IL-6R expression, it will be possible to realize a new approach to prevent dark spots, i.e., to prevent an increase in the risk of developing or worsening hyperpigmentation even in aged skin.

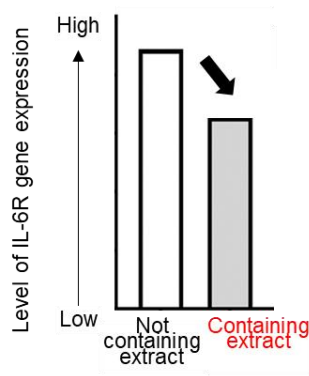


Figure 5. Shikuwasa extract suppresses IL-6R gene expression

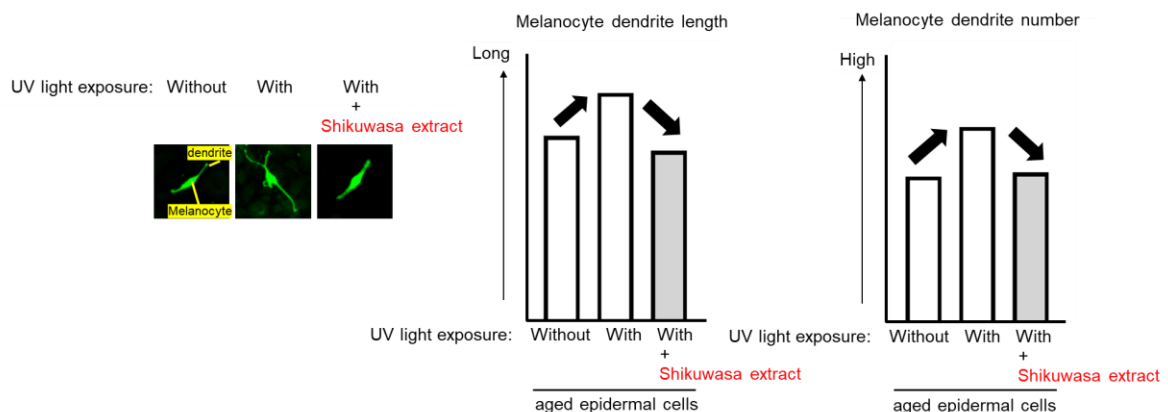


Figure 6. Shikuwasa extract suppresses the activation of melanocytes after UV light exposure

Under the company vision "PERSONAL BEAUTY WELLNESS COMPANY" toward 2030, Shiseido has been striving to become a company that people in realizing unique beauty and wellness throughout their lives. In order to provide proactive care for worrisome dark spots and dullness and support one's own unique beauty and wellness , we will continue to carry out studies with the aim of promoting dark spot and dullness prevention and improvement in a fundamental way.

About our R&D strategy:

This study was conducted with the aim of elucidating the causes of "eternal skin concerns" that our customers have been expressing for many years, including dark spots/dullness, wrinkles, sagging, and pores, and developing solutions under "Skin Beauty INNOVATION," one of the three pillars of Shiseido's R&D strategy.

- Integrated Report 2022 (Beauty Innovation Part)

https://corp.shiseido.com/report/en/2022/value_creation/innovation/

- Keywords

Skin Beauty INNOVATION, eternal skin concerns, dark spots

<Reference>

Researchers' challenges

■R&D Philosophy DYNAMIC HARMONY approach

This research was carried out under the Inside/Outside approach of Shiseido's R&D philosophy, DYNAMIC HARMONY. To address dark spots, which are externally visible skin concerns manifesting as differences in skin tone, we are approaching the nature of fundamental causes occurring inside dark spots and underlying mechanisms, with the aim of radically preventing or improving dark spots and dullness.



Researcher Daigo Inoue

■Familiar causes of dark spots, which seem obvious but have yet to be unraveled:

Inflammation led by UV radiation and aging

It is normally a common belief that UV radiation and aging are causes of dark spots. However, in reality, there are many things that are too familiar to be seen in the form of their original representations. Chronic inflammation in the setting of hyperpigmentation has been the topic of interest in Shiseido's skin brightening research over 100 years or more, but its true nature in a concrete sense and how it is connected to "pigments" in dark spots have remained unknown. This time, our researchers took a hint from the phenomenon that inflammatory symptoms, such as stiff shoulders and muscle pain, which they are bothered by on a daily basis, become more persistent as they age. The task of exploring and analyzing the true identity of inflammation related to dark spots, which had not been elucidated as a research topic anywhere in the world, was a challenge to the unknown, and we were groping in the dark. So, it really was the Aha! moment when we got the results with the discovery that aged keratinocytes promote change in the shape of melanocytes induced by UV radiation. This discovery then led us to identify the effect of Shikwasa extract to inhibit IL-6R, the actual entity of chronic inflammation specific to dark spots and control the activation of melanocytes appropriately. By approaching the phenomenon, where inflammatory conditions tend to remain and lead to pigmentation because of aging factors even when cells are similarly exposed to UV light, we believe that both the inhibition of melanin production and the inhibition of melanin delivery via suppression of inflammatory conditions could be addressed, leading to the prevention and improvement of dark spots.

Shiseido's 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>

DYNAMIC HARMONY website:

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