

## Press Release

Research and development

## Shiseido makes the world's first discovery of the effect of Fermented Camellia Seed Extract to promote the expression of a factor that recruits senescent cell-eliminating immune cells

### Focusing on CD4 CTL (Memory T cells) involved in the prevention of skin aging and the underlying mechanism

Shiseido discovered for the first time in the world<sup>\*1</sup> that Fermented Camellia Seed Extract can increase the expression of CXCL9<sup>\*2</sup>, which potentially recruits the immune cells CD4 CTL<sup>\*3</sup> (Memory T cells<sup>\*4</sup>) having the function to eliminate senescent fibroblasts in the skin. In other words, Fermented Camellia Seed Extract is expected to enhance the effect of skin immune cells to eliminate senescent cells (Figure 1).

Thus far, Shiseido has collaborated with the Cutaneous Biology Research Center (CBRC)<sup>\*5</sup> at Massachusetts General Hospital to support research conducted at CBRC, which has discovered that CD4 CTL (Memory T cells) selectively eliminate senescent cells in the skin, and that CXCL9, a protein produced by epidermal keratinocytes, is a factor that recruits CD4 CTL (Memory T cells) around senescent cells.

Going forward, Shiseido aims to further advance its skin immunity research to create values that lead to the innate beauty of the skin beyond the boundaries of age with the care for immune cells.

<sup>\*1</sup> The world's first technology to promote the expression of CXCL9, an epidermal factor important for maintaining the healthy skin (a factor that attracts the immune cells CD4 CTL), by Fermented Camellia Seed Extract (according to Shiseido using a prior technological survey (2024/3))

<sup>\*2</sup> Proteins that promote migration of immune cells and other cells

<sup>\*3</sup> Cytotoxic CD4<sup>+</sup> T cell (CD4 CTL): A type of T cell, it is also known to be an immune cell that is abundant in very long-lived people, who are considered models of ideal health and longevity.

<sup>\*4</sup> Memory T cells: After T cells encounter foreign substances such as pathogens and fulfill their roles, many of them die except for some that remain in the body and retain memory in preparation for reinfection and recurrence. In this way, Memory T cells respond quickly and fiercely against the same foreign substances.

<sup>\*5</sup> Cutaneous Biology Research Center (CBRC): A comprehensive center for advanced research and development in dermatology. Established in 1989 by Harvard Medical University and Massachusetts General Hospital with the support of Shiseido. Shiseido dispatches personnel to conduct joint research with world-class researchers.

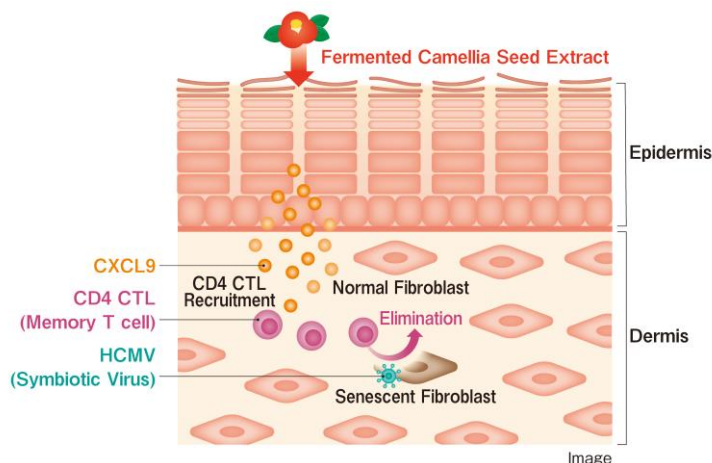


Figure 1. Fermented Camellia Seed Extract promotes the production of CXCL9 in the epidermis, recruiting CD4 CTL (Memory T cells) that are expected to eliminate senescent cells

## Research data

Shiseido evaluated the expression of the protein CXCL9, a factor that attracts CD4 CTL (Memory T cells) and found that Fermented Camellia Seed Extract promotes the expression of CXCL9 in epidermal keratinocytes (Figure 2).

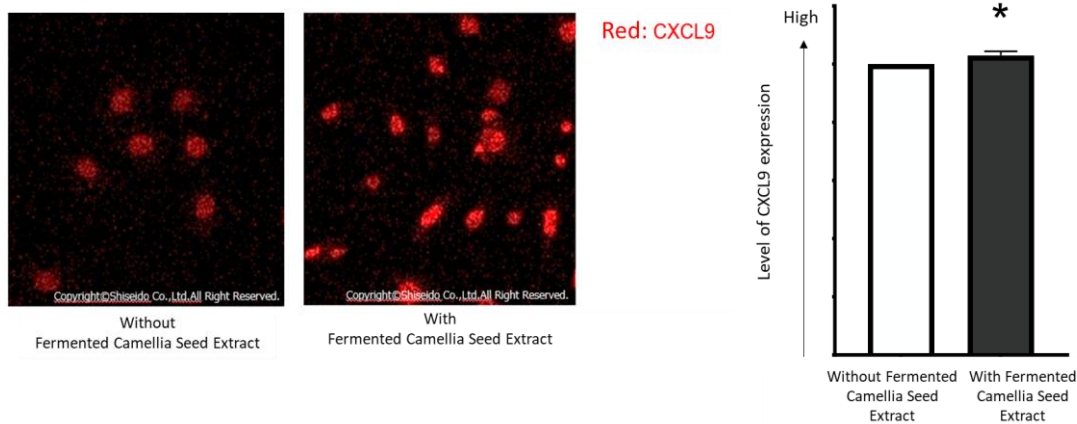


Figure 2. Fermented Camellia Seed Extract increases the level of CXCL9 expression

## Fermented Camellia Seed Extract helps the effect of skin immune cells to remove senescent cells

Fermented Camellia Seed Extract was developed in collaboration with Yaegaki Sake & Spirits, Inc., a long-established Japanese sake brewing company, for the purpose of making effective use of Japanese camellia resources growing wild in the Goto Islands, Nagasaki Prefecture, since ancient times. For many years, Shiseido has found value in various parts of Japanese Camellia, including its seeds, flowers, and leaves. In addition, we have created an extract by combining Japanese fermentation technology and the upcycled camellia seed pomace from the production process of camellia oil, which mostly ends up as wastes in typical cases. The present discovery suggests this extract to promote the expression of CXCL9. Among a number of koji Fungi used in the fermentation of Japanese sake, Shiseido selected Ki-koji (*Aspergillus Oryzae*), which contains in abundance proteases that break down proteins into amino acids, and examined the optimal fermentation conditions for the camellia seed cake. This successfully led to a marked increase in the amounts of amino acids, i.e., the sources of beauty ingredients.

About our R&D strategy:

This study was conducted under "Skin Beauty INNOVATION," one of the three pillars of Shiseido's R&D strategy, to clarify the relationship between the skin and its internal condition such as blood vessels, lymph vessels, immunity, and nerves.

- Integrated Report 2023 (Beauty Innovation)

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

- Keywords

Skin Beauty INNOVATION, skin immunity

## References: News Release/Literature

(1) Research supported by Shiseido reveals the mechanism by which skin's immune cells eliminate senescent cells (2024)

<https://corp.shiseido.com/en/news/detail.html?n=00000000003896>

(2) Cytotoxic CD4+ T cells eliminate senescent cells by targeting cytomegalovirus antigen (2023)

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