Press Release

Shiseido Discovers Nerve Involvement in Skin Elasticity

- Confirmed that Labiatae plant-derived ingredient Phytoconnect activates sensory neurons and enhances collagen production in the skin cells -

Shiseido Company, Limited ("Shiseido") has established a unique technology (patent applied) that visualizes nerve fibers in the skin in three dimensions to a depth of about 2 millimeters including the deep dermis layer*1, and revealed for the first time that peripheral nerve fibers*2 decrease with age, and the components released from sensory neurons stimulate the production of collagen in fibroblasts, which are involved in skin elasticity. The research team also found that the Labiatae plant-derived component Phytoconnect has the effect of activating sensory neurons and increasing collagen production.

This study suggests the possibility of a new skincare regimen that can create firm skin by caring for the nerves and going forward, Shiseido will apply this finding to the development of skincare products.

These research results were presented at "Neuroscience 2019 (Society for Neuroscience)" (October 19-23, 2019) and the "44th Annual Meeting of the Japanese Society of Investigative Dermatology" (November 8-10, 2019).

*1 Human skin is composed of the epidermis, dermis, and subcutaneous tissue in order of skin surface layer. The thickness of the epidermis is generally about 0.2 mm and of the dermis is about 2 mm although there are differences depending on age and skin regions.

*2 The human nervous system is classified into the "central nervous system" such as the brain and spinal cord that control commands and judgments, and the "peripheral nervous system" that spreads throughout the body. Sensory nerves that play a role in transmitting external stimuli to the brain such as sense of touch through contact with an object are a type of "peripheral nervous system".

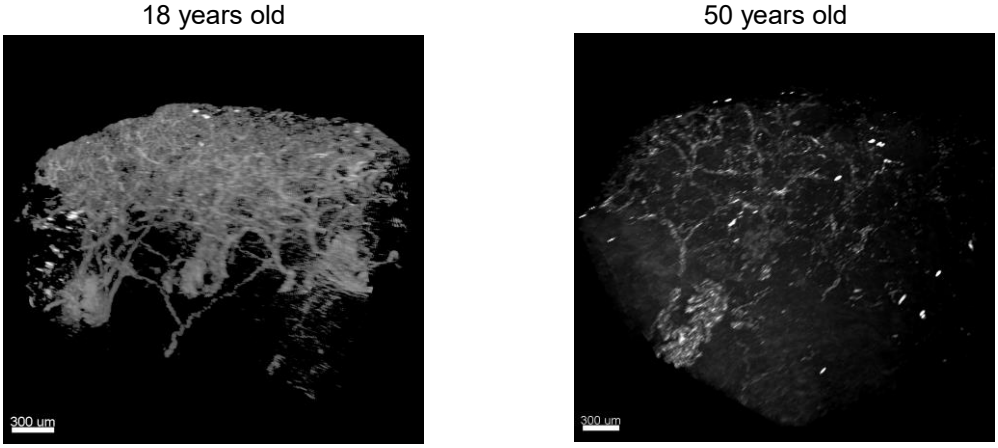

Figure 1. 3D visualization of nerve fibers deep inside the skin;
nerve fibers decrease with age and density decreases significantly

3D visualization of nerve fibers

Shiseido has been engaged in research focusing on the relationship between nerves and skin especially the epidermis. However, the conventional methods were limited in terms of observable area and accuracy, and it was not possible to fully understand the complex network structure of nerves deep inside the skin. Therefore, the team applied a unique technology that visualizes capillaries in the skin in three dimensions with a wide field of view using the method developed by Shiseido in 2018 that makes skin tissue

transparent, and successfully achieved 3D visualization of nerve fibers deep inside the skin including the deep dermis layer for the first time (patent applied). Using this technology, the team clearly observed a wider area up to a depth of about 2 millimeters, and found that peripheral nerve fibers in the skin decrease with age and density decreases significantly. Based on these results, the team carried out research assuming that there was a relationship between nerves and skin elasticity.

Relationship between sensory neurons and skin collagen production

Shiseido conducted research using human iPS-derived sensory neurons*3 to elucidate the role of nerves in human skin. As a result of the study on the involvement of various cells in human skin, it was found that components released from human iPS-derived sensory neurons stimulate collagen production in fibroblasts, which are one of the cells that make up the dermis.

*3 Since nerve cells do not proliferate, there was a limit to research using cells. However, by adopting cutting-edge research methods using human iPS-derived sensory neurons, it has become possible to more accurately verify phenomena occurring in the human body.

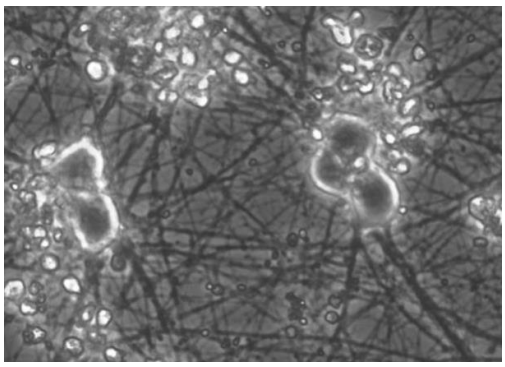

Figure 2. Human iPS-derived sensory neurons

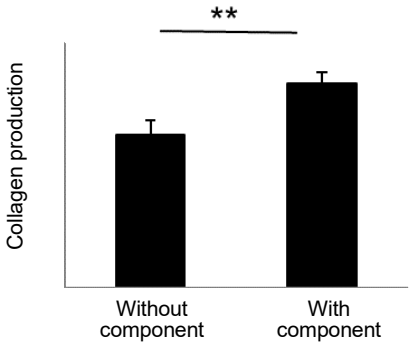

Figure 3. Stimulation of collagen production by components released from human iPS-derived sensory neurons

Exploration of ingredients that activate sensory neurons

The team explored ingredients that activate sensory neurons with a focus on the phenomenon that when sensory neurons are activated, the amount of released components increases. As a result, it was found that the Labiatae plant-derived ingredient Phytoconnect activates sensory neurons by simultaneously acting on three types of TRP channels*4 (TRPA1, TRPM8, TRPV1) expressed in sensory nerves, and revealed that the collagen production in fibroblasts is further increased by the components released from these activated human iPS-derived sensory neurons.

*4 TRP (Transient Receptor Potential) channels: Known as biosensors that sense temperature. They have recently been found to sense not only temperature but many other chemical and physical stimuli.

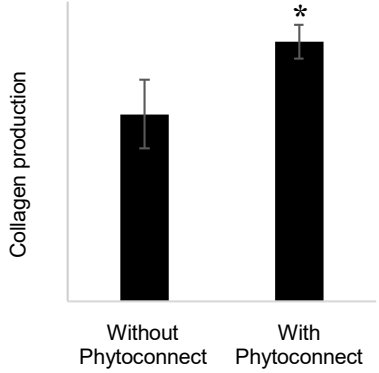

Figure 4. Stimulation of collagen production with Labiatae plant-derived ingredient Phytoconnect