

## Shiseido Develops a New Lip Care Approach Based on Comprehensive Analysis of the Stratum Corneum Components of the Lips

- Hyaluronic acid enhances the barrier function of the lip stratum corneum -

Shiseido revealed the properties of the lips in detail by exhaustively analyzing proteins and the microbiome\*1 of the stratum corneum of the vermilion (hereinafter, lips). In the past, information on the lips from histological aspects has been obtained, such as the observation of the surface shape and cross-sectional structure of the lips. This time, by exhaustively analyzing the components and ratios of proteins in the stratum corneum of the lips, as well as the microbiome of the stratum corneum, Shiseido found that a care approach from the perspective of the mucosa – which exists continuously from the lips – is important for lip care, in addition to the dermatological and skin care perspectives (Figure 1). Moreover, hyaluronic acid was identified as a component that enhances the barrier function of the lips to maintain and improve the healthy state of the lip mucosa. It is expected that adding this component to the lips, which have the properties of the mucosa as well as the general skin properties, will enhance the barrier function of the lips, making the lips less susceptible to chapping and helping to retain moisture. A part of the results of this study was presented at the Annual Meeting of the Japan Society for Analytical Chemistry (2022/9/14-16).

This study is being conducted based on the Inside/Outside approach based on Shiseido's R&D philosophy, "DYNAMIC HARMONY." Going forward, Shiseido will continue the research to elucidate the properties of the lips in detail and create innovative values that can lead to the lips with healthy beauty.

\*1 A group of microorganisms living in a certain environment.

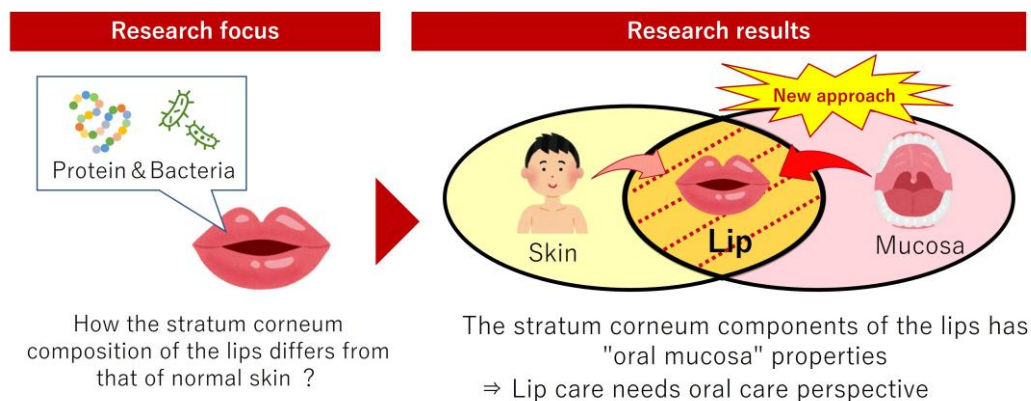


Figure 1. New lip care approach developed in the present study (image)

### Research background

The lips have a thinner stratum corneum and do not readily form sebum membranes, which differ from features that generally apply to the skin. Therefore, their barrier function is very weak, and consumers describe this body part as trouble-prone, with a "tendency to become dry easily" and "susceptibility to chapping." In order to address such troubles among consumers, it is important to develop correct lip care based on lip research. Meanwhile, studies on the lips in the cosmetic field have not progressed much as compared with skin studies, and particularly with regard to proteins and the microbiome of the stratum corneum of the lips, detailed information has not been revealed. Accordingly, at Shiseido, we set out a

study to elucidate the properties of the lips in further detail by employing exhaustive analysis methods, including proteome analysis<sup>\*2</sup> and microbiome analysis<sup>\*3</sup>, in addition to the conventional immunohistochemical staining method<sup>\*4</sup>.

\*2 A method to exhaustively analyze the type and composition ratio of proteins present in a sample

\*3 An exhaustive method for the determination of the type and composition ratio of microorganisms in the microbiome present in a sample

\*4 A method for detecting specific proteins in tissue using antibodies

### Comprehensive analysis of lip stratum corneum proteins and microbiome

We collected the stratum corneum from the cheeks and lower lips, and exhaustively analyzed proteins present in the stratum corneum by proteome analysis. A total of about 500 types of proteins were detected. Principal component analysis<sup>\*5</sup> of these proteins revealed that the composition and abundance of proteins in the stratum corneum of the cheeks and lower lips differ significantly (Figure 2). In particular, the proteins that are abundantly contained in the mucosa of the oral cavity (mucosal keratin) were present in a higher amount in the stratum corneum of the lips than in the stratum corneum of the cheeks (Figure 3).

\*5 An analysis method to summarize multiple indices present in the subject of the analysis to make it easier to visualize them.

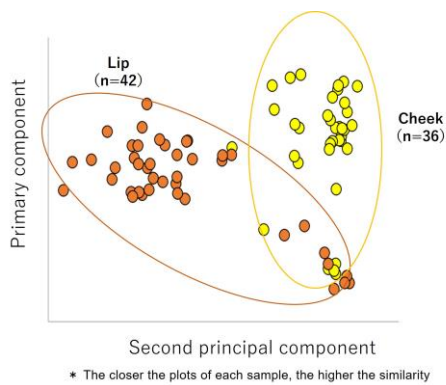


Figure 2. Differences in properties of stratum corneum proteins present in the lips and cheeks

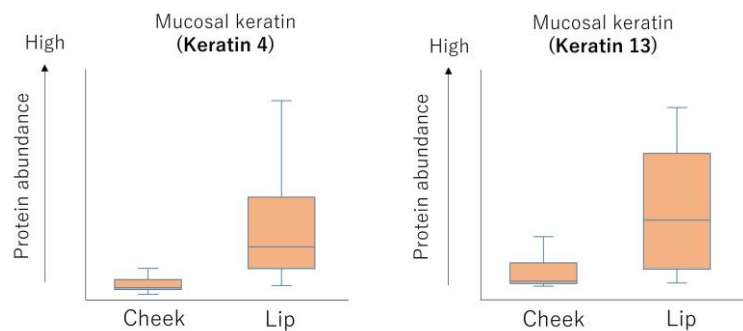


Figure 3. Mucosal keratin is present in a higher amount in the lip stratum corneum than in the cheek stratum corneum

Next, microbiome samples from the cheek, lower lip, and oral mucosa were collected, and bacteria present in each part were exhaustively analyzed by microbiome analysis. As a result, more than 4,000 types of bacteria-derived DNA were detected. Principal coordinate analysis<sup>\*6</sup> based on similarities among the microbiome samples revealed that the microbiome of the lower lip is more similar to that of the mucous membrane than to that of the cheek (Figure 4).

\*6 An analysis method to summarize multiple indices present in the subject of the analysis to make it easier to visualize them with two-dimensional plots, etc.

As described above, the results of proteome analysis and microbiome analysis revealed that the lower lip has the properties of the mucosa, which exists near the lips, from the perspectives of both lower lip proteins and microbiome. These findings suggest that, in order to keep the lips healthy, the perspective of maintaining the healthy state of the lip mucosa is important.

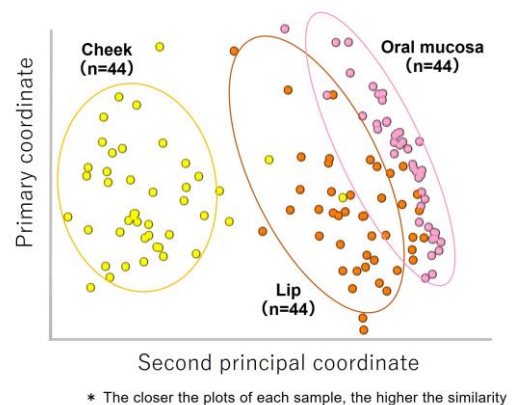


Figure 4. The microbiome of the lip resembles more to that of the oral cavity than that of the cheek

## Search for ingredients that enhance the barrier function of the lip mucosa

We explored raw materials that can be used to care for the lips, which have the properties of the mucosa. As a result, we newly discovered that hyaluronic acid, which is known as a component having a high skin moisture retaining effect, has an effect to enhance the barrier function of the mucosa (Figure 5). By administering this component to the lower lip, which also has the properties of the mucosa, it is expected that the barrier function of the lips is further enhanced, and the moist lips that are less susceptible to chapping can be maintained.

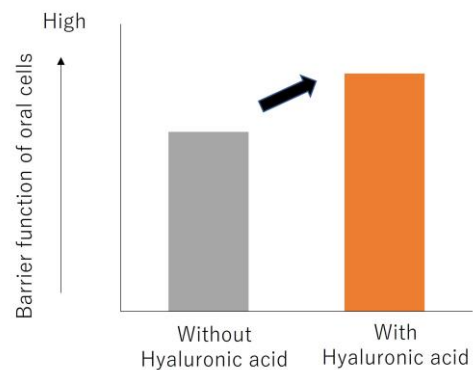


Figure 5. Effect of hyaluronic acid enhancing the barrier function of oral cavity cells

## Future prospects

In the present study, we have newly demonstrated that the lips have "mucosal" properties, which differ from those of the skin, in terms of proteins in the lip stratum corneum as well as its microbiome. With the aim of realizing our mission, "BEAUTY INNOVATIONS FOR A BETTER WORLD," we will advance our research to provide appropriate solutions for each part of the body, and create more values that are innovative on the basis of cutting-edge research knowledge.

### 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=0000000003252>

The DYNAMIC HARMONY special website:

<https://corp.shiseido.com/en/rd/dynamicharmony/>

## Researchers' challenges

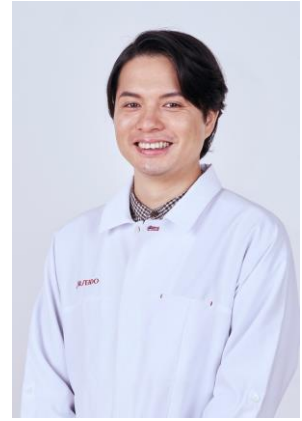
- The opportunity for this study arose thanks to the bottom-up proposal system for researchers

Shiseido's research institute values the curiosity and active challenge among researchers themselves, and there is a "system that allows proposal of research themes based on free thinking," in which all researchers can participate. The present findings are new findings obtained from a study that was initiated by young researchers,

including Mr. Murata who had just joined the company at the time, by making use of this system. "Why do lips look different from normal skin?" "Why are lips so susceptible to chapping?" – challenges to lip research from this new perspective started, driven by the curiosity of those researchers in the early period of their career.



Researcher, Katsuyuki Maeno, Ph.D.



Researcher, Daichi Murata

- Challenge to overcome the high hurdles of lip research

The lips are a unique tissue with features different from normal skin, e.g., a thin stratum corneum, abundant blood vessels, and the absence of pores. That is why there is a need to develop lip care based on lip research, which is not limited to the perspective of dermatology. On the other hand, there was also an issue, difficulty in collecting research materials, including lip cells and tissues. Therefore, as the subject of research, we focused on the "stratum corneum of the lips." Shiseido has been conducting stratum corneum research for many years, and so the present study was made possible by applying the knowledge we have acquired, as well as our cutting-edge stratum corneum measurement technologies, to lip research. As putting on a mask has become a routine practice these days, new troubles such as irritated lips due to mask wearing have also emerged. We believe that the new research knowledge will surely be useful in addressing these new troubles experienced by consumers.