

KOSÉ and Niigata University Develop a Three-dimensional Epithelial Model that Reproduces the Human Lip Area

To be Used for Evaluating the Efficacy and Safety of Cosmetic Ingredients and Products

KOSÉ Corporation (Headquarters: Chuo-ku, Tokyo; President: Kazutoshi Kobayashi) has developed in collaborative research with Professor Kenji Izumi and his colleagues at Niigata University Graduate School of Medical and Dental Sciences (Faculty of Dentistry) a three-dimensional epithelial model that reproduces the human lip area from the oral mucosa to the lips and surrounding skin, using cell culture. This will make it possible to verify efficacy and safety evaluations of cosmetic ingredients and products on a structure more similar to the actual lip area, which has been limited until now to verification using standard skin and oral mucosa *in vitro* models. The results of this research have been published online in the scientific journal *Histochemistry and Cell Biology* in June 2023.

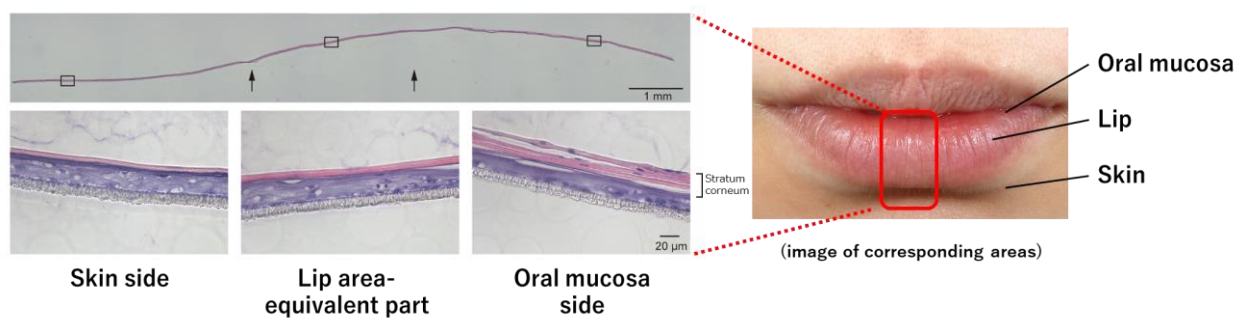


Fig. 1: Tissue staining images of the three-dimensional lip area model developed

Background

The lips are one of the most important elements that determine the impressions of the face, and they are also an area where many people suffer from problems, such as chapped lips in winter. The lip area is the transition area between the facial skin and the oral mucosa, and has a unique structure and properties that differ from both of them, such as the stratum corneum being thinner and more delicate than in skin. However, until now, there has been no evaluation system using lip area models, and it has been necessary to use skin and oral mucosa *in vitro* models to evaluate the usefulness and safety of new ingredients. Therefore, the development of lip area models that reproduce its unique structure, and their use for functional analysis of the lip area and evaluation of formulations and ingredients, is a useful tool to promote better formulation development.

The research group developed a lip area model with the aim of enabling it to be used in cosmetics research. They used only cells derived from the epidermis and oral mucosal epithelium to develop a three-dimensional model with characteristics similar to those of the human lip area.

Development of a three-dimensional epithelial model reproducing the lips part

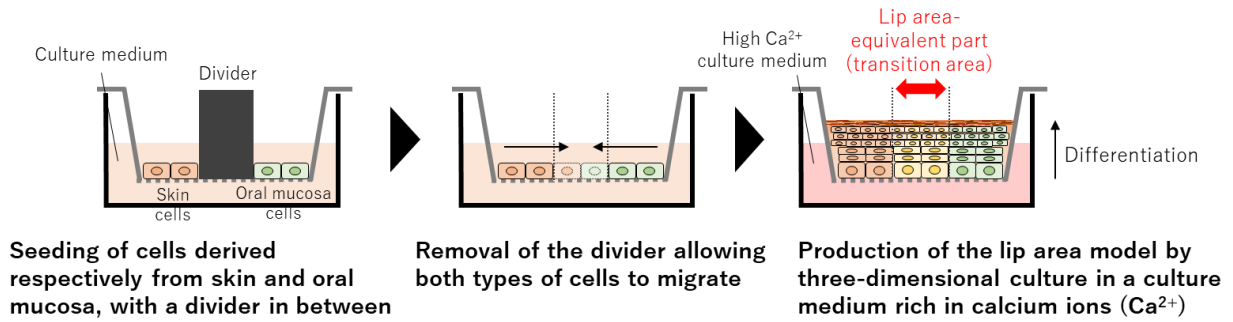


Fig. 2: Outline of method for creating the three-dimensional lip area model

To reproduce the lips part, a technique was used in which cells derived from skin and oral mucosa coexist. First, cells derived from skin and oral mucosa were seeded on both sides of a divider, and the divider was then removed to allow spontaneous migration (movement to another position) of the cells from both sides to the area where the divider was. Subsequently, the lip area-equivalent part was prepared by culturing the cells in air (Fig. 2). Tissue staining of the constructed lip area model revealed that the cells have structures and features similar to actual skin, lip areas, and oral mucosa, respectively (Fig. 1).

Confirmation that the model has a mode of differentiation similar to that of human lip area tissue

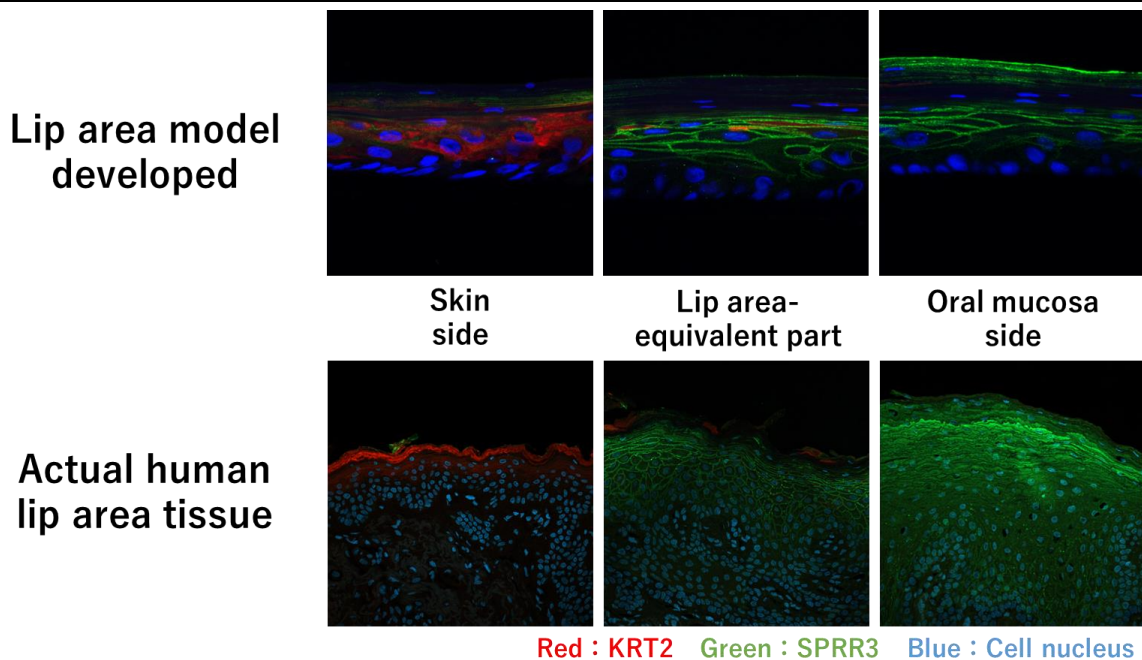


Fig. 3: Comparison of differentiation modes of the developed lip area model and human lip area tissue

Since it is known that the mechanism of cell differentiation (mode of differentiation), which is the process of cell maturation, differs between the skin, lips, and oral mucosa, the mode of differentiation was confirmed in the lip area model created. The lip area model was stained for keratin 2e (KRT2) and small proline-rich protein 3 (SPRR3), proteins representing differing modes of differentiation in cells derived from skin and oral mucosa, respectively. The results were that KRT2 was more abundant on the skin side, decreased in the lip area-equivalent part, and disappeared on the oral mucosa side (Fig. 3, red). On the other hand, SPRR3 was found to be more abundant on the oral mucosa side, and

decreased toward the lip area-equivalent part and skin side (Fig. 3, green). This differentiation mode is similar to that of actual human lip area tissue, confirming that the lip area model developed has a similar differentiation mode to that of the human lip area.

From the above, it is concluded that the lip area model developed in this research has a similar structure and differentiation mode to that of actual human lip area tissue, and it is expected to be used for evaluation of the effects of cosmetic ingredients on the lip area and other purposes.

Future outlook

The lip area model developed in this research will be used for basic research on the lips, which has only been possible until now with alternative methods using skin and oral mucosa, and for future development of lip care products and ingredients. We will continue our research and development to enable us to provide evidence-based solutions to customers' lip area problems, such as clarifying the mechanisms of chapped lips and developing useful ingredients.