News Release

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Pigeon Corporation

Artificial Infant Epidermal Model Using Human Pluripotent Stem Cells (iPSC-Derived RHE) Created, Shown Effective as Method for Evaluating Safety in Infant Cosmetics Development

Research Paper Published in SCI-Indexed Journals

Pigeon Corporation (Headquarters: Tokyo; President and CEO: Ryo Yano) Group company PIGEON MANUFACTURING (SHANGHAI) CO., LTD (Local Chinese subsidiary: QingPu District, Shanghai; Chairman: Ken Kaku), which operates the Pigeon Skincare Research Center where it conducts research on infant skin, has successfully used human induced pluripotent stem cells (iPSC) to construct an iPSC-derived reconstructed human epidermal model (RHE), mimicking the human epidermal structure with the unique characteristics of infant skin.

The paper describing the results of this research was published in *Cosmetics* 2025, 12(2), an international academic journal included in the Science Citation Index.

This epidermal model shows higher expression of barrier-related genes than previous models using adult epidermal cells, functions as a highly reliable replacement for testing skin irritation from cosmetics, and resolves the challenges of reducing reliance on animal testing and overcoming the limitations of existing epidermal models. It is expected to be useful as a tool for evaluating the safety and effectiveness of skincare products for infants

Overview of the Research Paper

Background

In cosmetics, medicine, and other fields, skin irritation testing is essential to confirm that products under development are safe to use on the skin. Furthermore, because infant skin differs from adult skin, the approach adopted when developing products for infants must differ from that used for products meant for adults.

However, existing skin irritation testing methods, including animal testing, raised ethical concerns and faced limitations related to biological differences between human and animal skin. A reconstructed human epidermal (RHE) model based on normal human epidermal keratinocyte (NHEK) cultivated from human skin cells (NHEK-derived RHE) has previously been developed, but the limited availability and short usable lifespan of NHEK made securing stable supply and uniformity difficult. To resolve these issues, this research focused on induced pluripotent stem cells (iPS cells or iPSC), which have recently attracted scholarly attention, and sought to develop an artificial epidermis for infants that would combine safety, efficacy, and ethicality. This has made it possible to test and evaluate products safely and effectively in an environment very close to that of infant skin.

Method

We created iPSC from human fibroblasts (skin cells) and then, in stages, optimized a method for differentiating them into keratinocytes. Using these iPSC-derived keratinocytes, an artificial infant epidermal model (iPSC-derived RHE) was constructed. This RHE, cultivated in the laboratory, was tested for the ability to predict skin irritation, using several known irritants according to standard guidelines. The performance of the iPSC-derived RHE was compared to the commercially available NHEK-derived RHE.

Results

The completed iPSC-derived RHE clearly showed multiple keratin layers, similar to real human skin. Compared to the existing commercially available NHEK-derived RHE, expression of genes like Filaggrin, which retains skin moisture, and Aquaporin 3, which transports moisture, was found to be much higher. Furthermore, in skin irritation tests, the iPSC-derived RHE showed functionality equivalent in level to the standard international model (SkinEthic™), and accurately determined the irritation levels of the chemical substances tested, which included sodium lauryl sulfate (SLS), triton X-100 (TX-100), and benzalkonium chloride (BC).

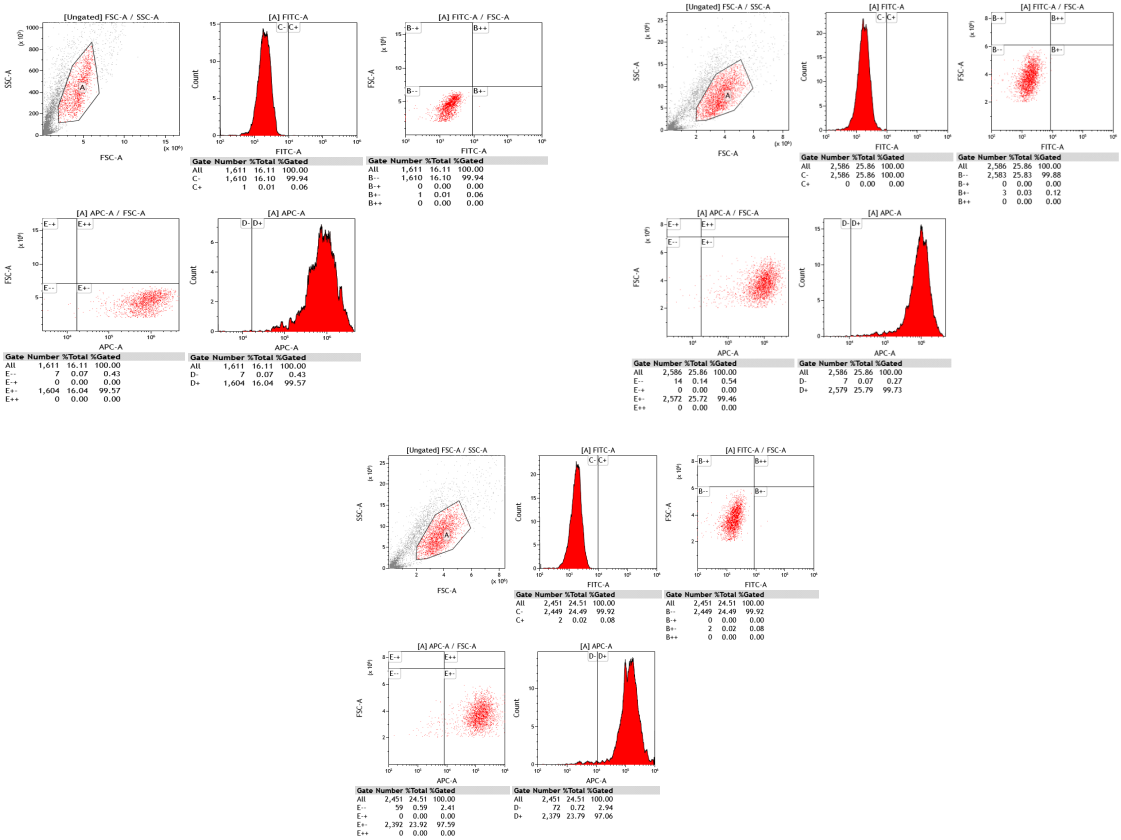
Discussion

The iPSC-derived RHE established by this research resolves known problems such as a lack of cell providers, variation among individuals, and limits on supply, making possible an unlimited and stable supply of a genetically uniform RHE. It is also simpler and faster to construct than existing RHEs. These findings indicate that this iPSC-derived RHE is a reliable tool for evaluating skin irritation capable of reducing the need for animal testing while contributing to the development of safe cosmetics and medical products better suited to infants.

Comment from Pigeon

This was the first research applying iPS artificial pluripotent stem cell differentiation technology to construct an RHE. The stratum corneum is thinner in infants than in adults, and the skin barrier function is undeveloped. The skin contains a great deal of moisture, but it dries easily. Cell regeneration is also rapid. The iPSC-derived RHE that we constructed simulates these characteristics of infant skin extremely well. We hope to see the results of this research used in the development of baby skincare products and to contribute to further research on infant skin.

Figure 1. Above: Expression of iPSCs in SSEA-4, TRA-1-60, and TRA-1-81 in flow cytometry; Below: Immunofluorescence staining results of SSEA-4, TRA-1-60, and TRA-1-81 protein expression



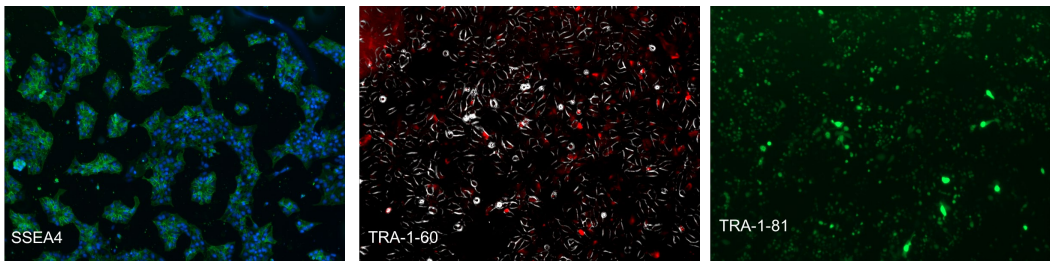


Figure 2. Differentiation steps of iPSC-KC (A), differentiation process of iPSC-KC (B), and expression of signature genes at different stages of iPSC-KC differentiation (C)

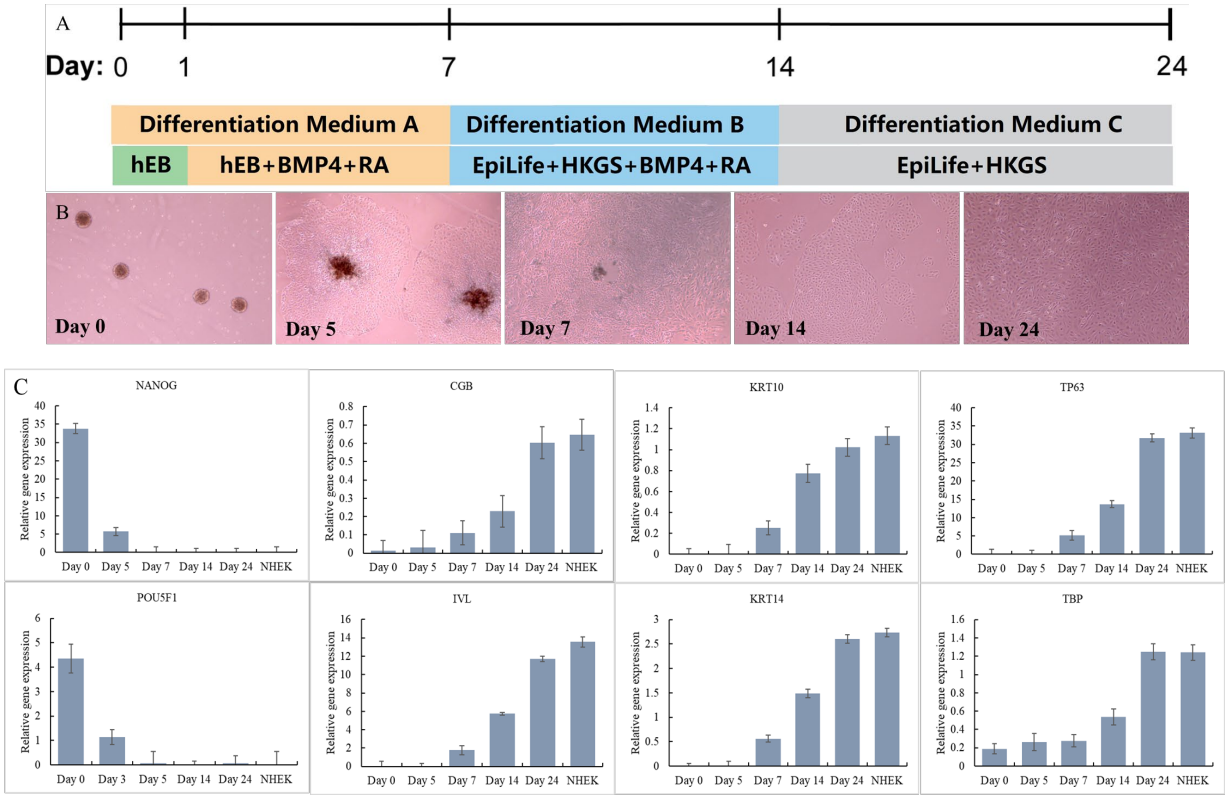


Figure 3. Expression of NHEK and iPSC-KC on Keratin 14 and AQP3

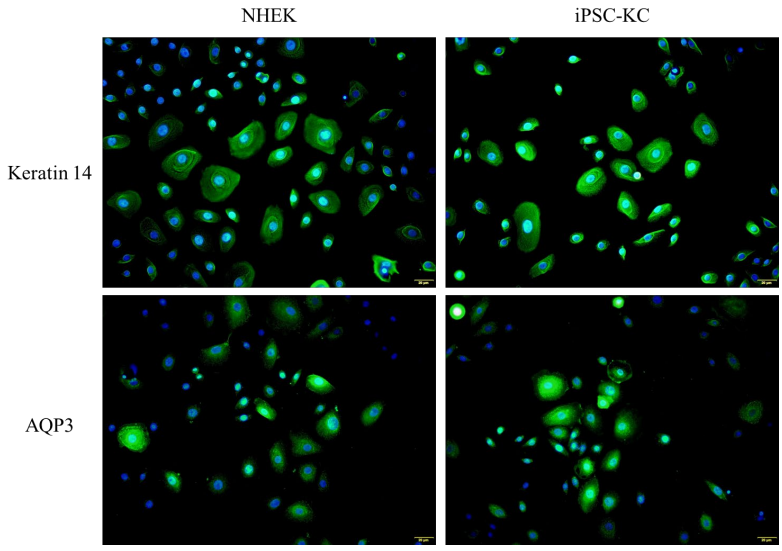
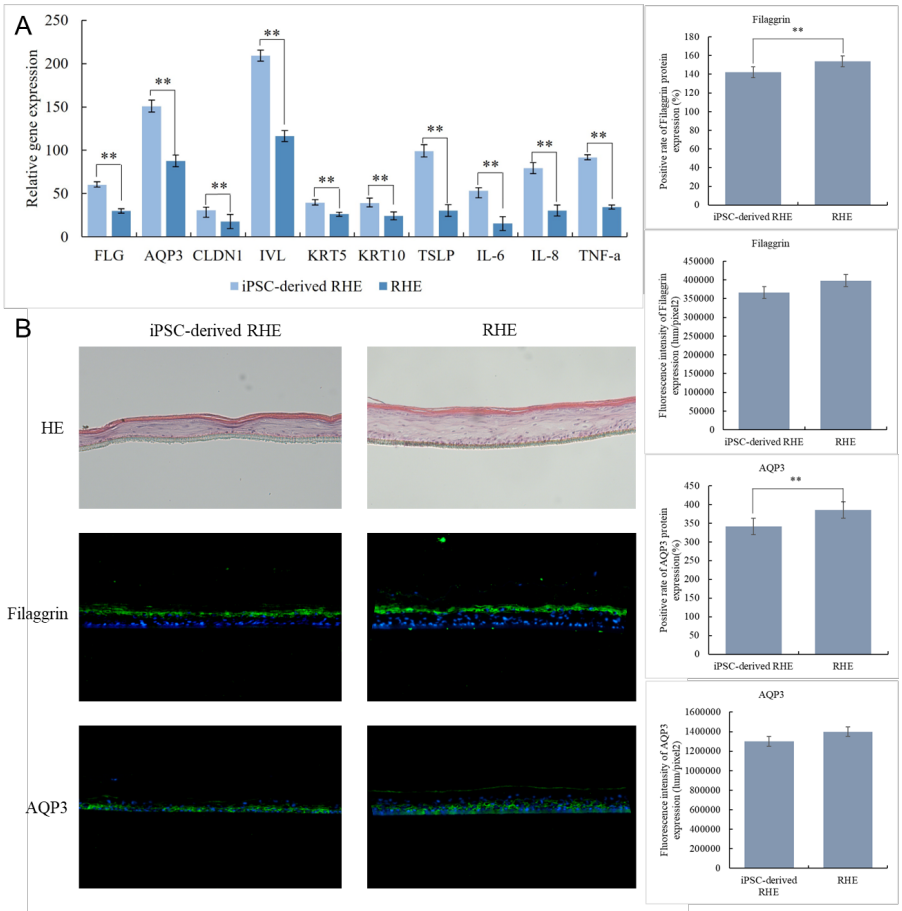


Figure 4. iPSC-derived gene expression of RHE and RHE (A), HE staining results and expression on Filaggrin and AQP3 of iPSC-derived RHE and RHE (B), and immunofluorescence staining results of iPSC-derived RHE and RHE (C)



Bibliographical Information

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