Press Release

May 8, 2020

研究成果

Research field: life science and medicine; **Keywords:** antiperspirant, heat stroke, hyperhidrosis, immortalized cell, long-term culture, myoepithelial cell, regenerative medicine, sweat gland

Applicable to the development of next-generation antiperspirants and to research on sweating dysfunction and sweat gland regeneration

Successful generation of immortalized human eccrine sweat gland myoepithelial cells

—Concluded a sales license agreement with Applied Biological Materials Inc. in Canada—

Gist of the research

- We successfully generated immortalized human eccrine sweat gland myoepithelial (iEM) cells that retain the characters of myoepithelial cells.
- The generated cell line will be sold globally through Applied Biological Materials Inc.
- This achievement will help advance research on sweat glands, which will lead to new approaches in the development of antiperspirants, development of methods to prevent and treat sweating dysfunctions such as hyperhidrosis and heat stroke, and regeneration of sweat gland tissue.

❖ Overview

Our research group, led by Guest Professor Fumihiro Okada of the Laboratory of Advanced Cosmetic Science※1, Graduate School and School of Pharmaceutical Science, Osaka University and Professor Kiyotoshi Sekiguchi of the Department of Contribution Research, Institute for Protein Research, Osaka University, has succeeded in generating immortalized※2 human eccrine sweat gland myoepithelial cells※3.

Myoepithelial cells are one of the several types of cell that make up human eccrine sweat glands. They are involved in the contraction of sweat glands and function as stem cells to maintain the function of sweat glands (Fig. 1). Identification of the components that regulate the function of human eccrine sweat gland myoepithelial cells will lead to new approaches in the development of antiperspirants and to methods of prevention and treatment of hyperhidrosis and heat stroke. To achieve these goals, we need many human eccrine sweat gland myoepithelial cells. However, up until now, no human eccrine sweat gland cell line have retained the characters of human eccrine sweat gland myoepithelial cells.

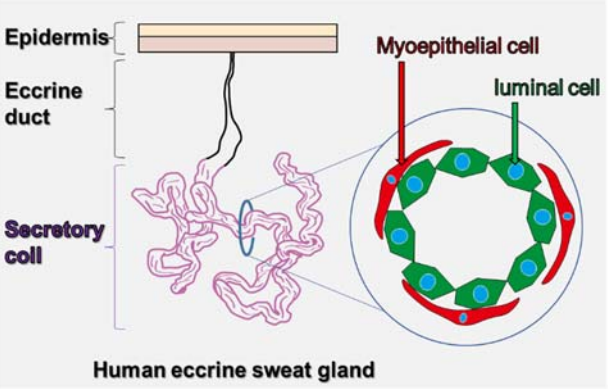


Figure 1.
Structure of the human eccrine sweat gland

Our research group had earlier established a method for culturing human eccrine sweat gland myoepithelial cells such that they retained their functional characters for a short period of time (refer to the News Release of October 27, 2016, https://www.mandom.co.jp/release/pdf/2016102701.pdf [in Japanese]). This time, by using this method

together with the introduction of an immortalizing gene, we have achieved a breakthrough in generating immortalized human eccrine sweat gland myoepithelial (iEM) cells that can be cultured for a long time.

This research achievement will accelerate research in this field, which will lead to the development of next-generation antiperspirants, the early establishment of methods for prevention and treatment of hyperhidrosis and heat stroke, and the establishment of techniques for regenerating sweat glands.

We have filed a patent application on the generation of iEM cells and we presented our research at the 49th Annual European Society for Dermatological Research Meeting in Bordeaux, France, 18–21 September 2019. The usefulness of iEM cells was accepted, and Mandom corporation (headquartered in Osaka city, Osaka, Japan. President: Motonobu Nishimura) concluded a license agreement with Applied Biological Materials Inc. (headquartered in Richmond, British Columbia, Canada)※4 for consignment sales of iEM cells. Additionally, Mandom corporation concluded a memorandum of understanding royalty with Osaka university (headquartered in Suita city, Osaka, Japan. President: Shojiro Nishio). This material transfer agreement (MTA) ※5 has made it possible to transfer iEM cells to many countries worldwide.

Product HP: https://www.abmgood.com/immortalized-sweat-gland-myoepithelial-cells.html#T0816

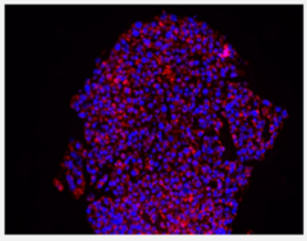
❖ Background of the research

Solving sweat-related concerns that occur in daily life, for example, hyperhidrosis and sweat smell, can improve people's quality of life. We thus focused on the regulation of sweating. To control sweating, we need to understand the characteristics of the cells that make up sweat glands and regulate the function of sweat glands. Myoepithelial cells, one of the various types of cell that make up human eccrine sweat glands, have two functions: they contract sweat glands to push sweat out of the body surface and they function as stem cells to maintain the homeostasis of the sweat glands (Fig. 1). Therefore, the activity of myoepithelial cells plays an important role in human sweating. Cultured cells are a useful means for elucidating the functions of human eccrine sweat gland myoepithelial cells; however, no method had been available for their long-term culture while retaining the characters of human eccrine sweat gland myoepithelial cells.

❖ Research content

To date, cultured human eccrine sweat gland cells have not retained the characters of myoepithelial cells. Our research group earlier established a method enabling human eccrine sweat gland cells to maintain the characters of myoepithelial cells for a short time by culturing human eccrine sweat gland myoepithelial cells under conditions similar to those *in vivo*. This time, we introduced an immortalizing gene into human eccrine sweat gland myoepithelial cells under culture, which resulted in the successful generation of iEM cells that can retain the characters of the human eccrine sweat gland myoepithelial cells for a long time. Although human eccrine sweat gland myoepithelial cells could previously be subcultured for only around 3 generations, iEM cells, which our research group has generated, can be subcultured for more than 10 generations. In addition, iEM cells express α-smooth muscle actin (α-SMA), a characteristic gene that supports the function of human myoepithelial cells and which helps maintain the characters of human myoepithelial cells (Fig. 2). Such characteristics are not found in conventional cultured human eccrine sweat gland cells.

Cell type	Proliferation rate (times)	Possible passage number (generation)
Human eccrine sweat gland myoepithelial cell	90	3
Immortalized human eccrine sweat gland myoepithelial cell	2.8×10^{25}	≧10



Red cells indicate human eccrine sweat gland myoepithelial cells expressing a characteristic gene (α-SMA).

Figure 2.
Viability of immortalized human eccrine sweat gland myoepithelial (iEM) cells established in this research, and expression of a characteristic gene

❖ Impact of the research achievements on society

(The significance of the research achievements)

Our research generated iEM cells that can be cultured for a long time. To control sweating, we need to elucidate the properties of the cells that make up sweat glands. Advancement of research on human eccrine sweat gland myoepithelial cells will lead to the development of next-generation antiperspirants that can inhibit sweating by regulating the activity of the cells that make up sweat glands, treatment methods that can restore normal sweating to improve sweating dysfunction, and techniques for regeneration of sweat glands.

❖ Special notes

Our research achievements, namely iEM cells and the process of their cultivation, are registered as a patent.

Title of Invention: IMMORTALIZED SWEAT GLAND MYOEPITHELIAL CELLS

Patent Number: 6563145

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❖ Glossary

※1. Laboratory of Advanced Cosmetic Science

The Laboratory of Advanced Cosmetic Science is a research laboratory established jointly by the Graduate School and School of Pharmaceutical Science, Osaka University and Mandom Corporation in June 2015. Joint research laboratories receive investments from private companies and other organizations. Researchers from the university and the investing company conduct research on the same theme on an equal footing, with the aim of achieving breakthrough research results. The Laboratory of Advanced Cosmetic Science is an independent research organization in Osaka University. The university and Mandom Corporation cooperate to conduct research flexibly and rapidly while exchanging information and creating knowledge.

※2. Immortalization

Immortalization is a technique that enables extension of the cellular proliferation limit by introducing exogenous genes that enhance cell proliferation.

※3. Sweat gland myoepithelial cells

The secreting part of sweat glands (the part that produces sweat) is made up of two types of cells: luminal cells and myoepithelial cells (Fig. 1). Myoepithelial cells contract the sweat glands to push sweat out onto the body surface. They also function as stem cells for sweat glands and therefore play a key role in terms of maintaining homeostasis of sweat glands.

※4. Applied Biological Materials Inc.

Applied Biological Materials Inc. is a company dealing with bio-related products, particularly recombinant products. The company sells recombinant cells and the equipment and products necessary for their production.

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Website: https://www.abmgood.com/about-us.html

※5.MTA (Material Transfer Agreement)

The contract between research institutes for the transfer of research materials (loan, transfer, etc.). It stipulates the handling and attribution of papers and intellectual property rights obtained as a result of research, in addition to the provisions on the handling of the substance itself.

❖ Contact us

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Message from the research representative (Hayakawa)

Cultured cells are widely used as a basic experiment method in biological research. However, with recent development of stem cell research, it has been pointed out that conventional cultured cells differ from those *in vivo* and are therefore problematic in terms of a test system. New test systems involving cultured cells that retain their *in vivo* characteristics by mimicking the natural biostructure have attracted attention as a solution to this problem. Sweat gland cells, unlike skin cells, originally did not have widely distributed cell lines, and alterations in myoepithelial cells of conventional sweat gland cell lines used by some researchers have been reported for the above reason. Our research group focused on the fact that human eccrine sweat gland myoepithelial cells cultured in an environment similar to that *in vivo* form a spherical structure covered with myoepithelial cells. Direct introduction of an immortalizing gene into the spherical structure enabled us to efficiently immortalize human eccrine sweat gland myoepithelial cells. The iEM cells generated by this method retain the characters of myoepithelial cells. Therefore, we expect that iEM cells, as a new test system for sweat glands, will help in the development of antiperspirants, treatment of sweat gland disorders, and regeneration of sweat glands.