

Research field: life science and medicine; Keywords: sweat glands, anatomy, three-dimensional structure, heat stroke, hyperhidrosis, antiperspirant, regenerative medicine

Successfully visualized in joint research by Mandom Corporation and

Graduate School of Pharmaceutical Sciences, Osaka University

Newly revealed three-dimensional structures of human sweat glands shown in Gray' s Anatomy, **the gold standard anatomy textbook**

—Expectations on the development of better diagnostic measures and treatments for heat stroke and hyperhidrosis and application to sweat gland tissue regeneration —

Gist of the research

- ◆ The newly uncovered human sweat gland structures—spatial cell shapes and arrangements of sweat gland and blood vessels facilitating sweat secretion—successfully visualized by our joint research team and published in June 2017 are included in the latest edition of Gray' s Anatomy.
- ◆ Gray' s Anatomy is considered globally to be the gold standard textbook on anatomy.
- ◆ Our research findings shared through this textbook may contribute to a better understanding of sweat gland functions and therefore to the development of more effective diagnostic measures and treatments for sweating disorders, such as hyperhidrosis (excessive sweating) and heat stroke, and regeneration of sweat gland tissues.

❖ Overview

Three-dimensional (3D) structures of human sweat glands have been successfully visualized by a joint research team of Guest Professor Fumihiro Okada at Laboratory of Advanced Cosmetic Science ※ 1, Graduate School and School of Pharmaceutical Science, Osaka University; Professor Kiyotoshi Sekiguchi at Division of Matrixome Research and Application, Institute for Protein Research, Osaka University; and Assistant Professor Atsushi Tanemura, Associate Professor Hiroyuki Murota (currently professor at Nagasaki University Graduate School of Biomedical Sciences), and Professor Emeritus Ichiro Katayama at Graduate School of Medicine, Osaka University. Please visit the portal site for research at Osaka University, ResOU, for more details (as of June 22, 2017; https://resou.osaka-u.ac.jp/en/research/2017/20170622_3). **The fruit of the research is included in**

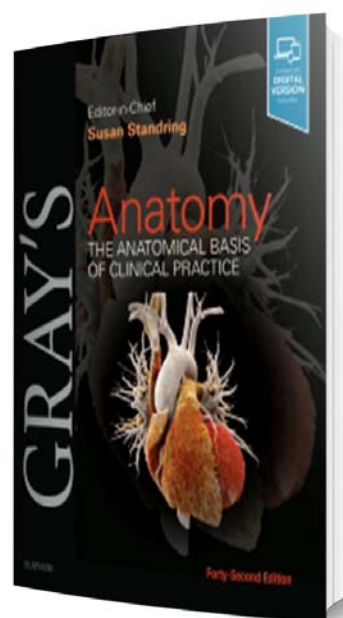


Figure 1
Gray's Anatomy(42nd edition)

the latest 42nd edition of Gray' s Anatomy^{※2},
the global gold standard textbook on anatomy.

During the 13th century, human anatomy was acknowledged as essential in medical education to promote the understanding of the body function and structure, and this area of science has since greatly contributed to advancement in modern medicine, including diagnosis and surgical treatment. The first 1858 edition of Gray' s Anatomy is said to be published to help medical students study human anatomy in dissection training. Over more than 160 years since its first publication, this book remains to be regarded by many as the most prestigious anatomy book and a great textbook for learners and thus read by many people in the medical field and students aspiring to become doctors or anatomists.

The newly visualized detailed structures of human sweat glands and spatial arrangement of blood vessels that facilitate the sweat secretion of the glands are contained in the 'skin' part in Section 1 of the latest edition of Gray' s Anatomy (consisting of seven sections; October 2020) at the request of its publisher.

The fruit of this research may help us deepen our understanding of sweat gland structures and thereby may be useful for the development of next-generation antiperspirants and also for further clarification of mechanisms of and advancement in treatment for heat stroke and hyperhidrosis.

We filed for a patent application for these research outcomes and have reported on their utility at Gordon Research Conference^{※3} and other occasions.

❖ Background of the research

With advancing global warming, despite our increasing efforts to prevent occurrence of heat stroke, many heat stroke patients are taken by ambulance to hospitals every summer in Japan, which is one of our social issues. Sufficient knowledge of the structures of sweat glands, which contract in sweating, is essential to improve impaired sweating function. Conventional analysis methods, however, were not good enough to clarify the complicated structures of the sweat glands. Our research group then succeeded, using whole-mount staining, in visualizing the 3D structures of human sweat glands and uncovering their characteristic structural features, which indicated that human sweat glands had unique secretory mechanisms for sweat excretion.

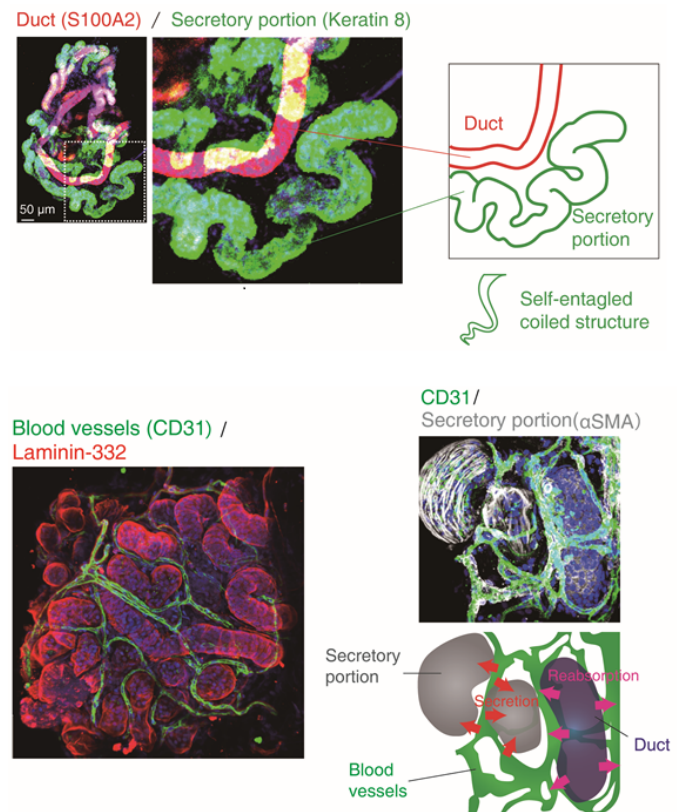


Figure 2
Three-dimensional structure of human sweat glands
with blood vessels

❖ Research content

Gray's Anatomy shows the three-dimensional structure of the human sweat glands that were visualized by our research group.

Sweat gland is tubular exocrine gland consisting of the secretory portion and the duct. The gland forms the complex coiled structure that compose secretory portion and part of the duct in deep dermis. The secretory portion in the coiled region generates sweat that is released to the skin surface through the duct. Several lines proposed that contraction of the secretory portion induce the sweating. To better understand the anatomical structure of sweat gland, the details of the three-dimensional (3D) coiled structures of sweat glands were visualized using a whole-mount staining method. 3D coiled gland structures demonstrated that the ducts and secretory portions were comprised of distinct tubular structures. Ductal tubules were occasionally bent, while secretory tubules were frequently bent and formed a self-entangled coiled structure like a towel being squeezed. 3D visualization of the glands also revealed the spatial arrangement of blood vessels facilitating sweat secretion. The blood vessels were situated adjacent to not only the ducts, but also the secretory portions of sweat glands, suggesting that blood vessels running along sweat gland tubules are involved in the supply and reabsorption of sweat.

❖ Social impact of the inclusion of our research results in Gray's Anatomy

Our joint research findings introduced in the gold standard anatomy textbook Gray's Anatomy may serve as the basis of new ideas for elucidating sweat gland disorders, leading to better understanding of basic mechanisms of sweat gland contraction and homeostasis maintenance, which may then result in clarification of and novel treatments for sweating related disorders (such as heat stroke and hyperhidrosis), and potentially development of next-generation antiperspirants that directly inhibit sweat gland contraction to suppress sweating and sweat gland regenerative technologies.

❖ Special notes

The images shown in Gray's Anatomy are those analyzed using the methods described in our report that appeared in the US scientific journal PLOS ONE (online).

Title: "Three-dimensional Cell Shapes and Arrangements in Human Sweat Glands as Revealed by Whole-mount Immunostaining"

Author: Ryuichiro Kurata^{1, 2, 3*}, Sugiko Futaki³, Itsuko Nakano³, Fumitaka Fujita^{1, 2}, Atsushi Tanemura⁴, Hiroyuki Murota⁴, Ichiro Katayama⁴, Fumihiro Okada^{1, 2}, and Kiyotoshi Sekiguchi^{3, **}

Our research achievements, visualization method of the three-dimensional structure of the sweat gland, is registered as a patent.

Title of Invention: THE CONFIRMATION METHOD OF THE SWEAT GLANDS

Patent Number: 6555973

Inventors: Ryuichiro Kurata^{1, 2, 3}, Fumitaka Fujita^{1, 2}, Sugiko Futaki³, Kiyotoshi Sekiguchi³, Atsushi Tanemura⁴, Hiroyuki Murota⁴, Ichiro Katayama⁴

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❖ Glossaries

※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 Gray's Anatomy (42nd edition)

Gray's Anatomy (42nd edition)- Anatomical Basis of Clinical Practice

Author: S. Standring

Publisher: ELSEVIER, LONDON

ISBN: 978-0-7020-7705-0

Total Pages: 1588pp.

Published Date: October 2020

※3 Gordon research conference

2019 Gordon research conference (Epithelial Differentiation and Keratinization)

Date: July 7 - 12, 2019

Venue: Jordan Hotel at Sunday River (Maine, USA)

Title: Isolation and characterization of sweat gland stem cells from human skin

Gordon research conference...One of the historic and prestigious scientific conferences

❖ Inquiries

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<About this news release>

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Message from the research representative (Ryuichiro Kurata)

Environmental changes forced our early ancestors to travel long distance in search of food and water, requiring them to opt to lose their fur and have hairless bodies to control body temperature by sweating through sweat glands. Humans are the only animal with this thermoregulatory mechanism. On the other hand, because our sweat gland system has not evolved enough to counter changes in our life styles or aging, these factors tend to affect our sweating, making sweating related disorders (heat stroke, hyperhidrosis) social issues, while data on human sweat glands, which are important in the treatment of sweating disorders, have been available only in a limited amount. We believe that continuing accumulation of outcomes of basic research on human sweat glands will lead to further new findings and advancement in relevant technologies, and then practical applications in some years' time.

We started our joint research in 2009, including an isolation method for human sweat gland cells and identification of human sweat gland stem cells, regeneration of an artificial human sweat gland organ, 3D structural analysis of sweat glands, monitoring of contracting motility of sweat glands, and establishment of immortalized sweat gland cells. It is our intention to continue to pursue our research to enable our under-evolved sweat glands to play their roles in the present social environment.