

Mandom discovers that the sensitivity of cellular sensors, “TRP channels,” to acidity and alkalinity changes with environmental temperature

—The results of 20 years of research have a wide range of applications in hair care, body care, skin care, etc.—

Mandom Corporation (Head office: Osaka, President Executive Officer & Director: Ken Nishimura, hereinafter “Mandom”) pursues “creation of new value” as a human-oriented company to delight, excite, and bring joy to consumers, and it conducts research and development with the aim of achieving maximum safety, functionality, and comfort during use.

Based on this pursuit, Mandom has been conducting research into “TRP channels” (Figure 1), cellular sensors that are activated by temperature and chemical stimuli and are separate from the five senses. This research is being conducted in collaboration with Guest Professor Fumitaka Fujita of the Laboratory of Advanced Cosmetic Science of the Graduate School of Pharmaceutical Sciences, the University of Osaka; Specially Appointed Professor Makoto Tominaga of the Nagoya Advanced Research and Development Center of Nagoya City University; and Professor Ken Ishii of the Department of Microbiology and Immunology, the Institute of Medical Science, the University of Tokyo. We are conducting research into TRP channels in sweat glands in collaboration with a research group involving Professor Kiyotoshi Sekiguchi of the University of Osaka Institute for Protein Research, Associate Professor Atsushi Tanemura and Lecturer Yukinobu Nakagawa of the University of Osaka Graduate School of Medicine, and Professor Hiroyuki Murota of the Nagasaki University Graduate School of Biomedical Sciences.

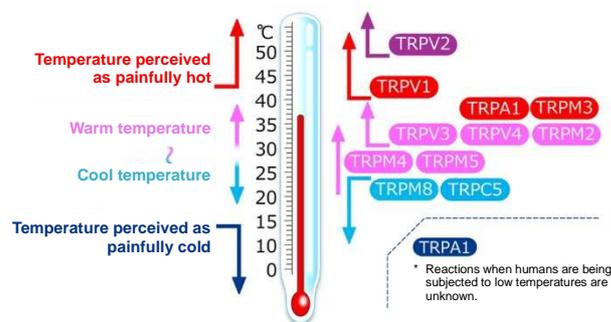


Figure 1. Cellular sensors, “TRP channels”

Mandom has been conducting research on TRP channels since 2005. The results of 20 years of research have been presented at numerous academic conferences, including the prestigious IFSCC (International Federation of Societies of Cosmetic Chemists), an international congress where cosmetic chemists present and discuss the latest research findings.

The new findings are as follows.

- TRP channels are polymodal receptors (receptors that respond to a variety of stimuli) and have diverse expression patterns in various cells present in the skin.
- Temperature and pH affect the activity of TRP channels.
- Potassium alum (aluminum potassium sulfate) exerts various inhibitory effects on all TRP channels except TRPM4 and has analgesic effects as well as sweat suppression effects.
- The cooling sensation is enhanced by alkaline pH.



We presented these findings at the 35th IFSCC Congress 2025, held in Cannes, France, from Monday, September 15 to Thursday, September 18, 2025.

■ Research background

TRP channels, which are cellular sensors, are polymodal receptors that detect not only temperature but also various environmental changes and transmit that information to cells, and they are known to play a variety of roles in many cells. Furthermore, it is known that they can be activated or inhibited by many chemical substances, and they have long been used in a variety of industries, as exemplified by menthol, the main component of mint, and capsaicin, the main component of chili peppers, which have been utilized by humans since ancient times. Following the discovery in 1997 of TRPV1, which can respond to capsaicin and heat, 11 thermoreceptors were discovered, furthering our understanding of the mechanisms by which cells sense temperature and chemicals. Although many of the functions of these TRP channels have been clarified since then, there has been little progress in understanding the expression of TRP channels in peripheral skin cells and the effects of simultaneous environmental changes caused by different factors, including the application of functional ingredients to the skin.

■ Research summary and results

1. Elucidating the expression patterns of TRP channels in each cell type of skin

This research group analyzed gene expressions in epidermal keratinocytes, immune cells isolated from blood (monocytes, macrophages, and dendritic cells), and constituent cells of human sweat glands (secretory luminal cells, secretory myoepithelial cells, ductal luminal cells, and ductal basal cells) and elucidated the expression pattern of TRP channels in each cell type. In particular, it elucidated the expression pattern of the constituent cells of sweat glands, which had previously been unknown (Figure 2, Table 1). TRPV4 is highly expressed in the luminal cells of the secretory coil that control sweat production, and TRPV3 is highly expressed in the luminal cells of the reabsorptive ducts that control sweat reabsorption. The fact that these TRP channels are important for regulating sweat secretion is important information when considering sweating.

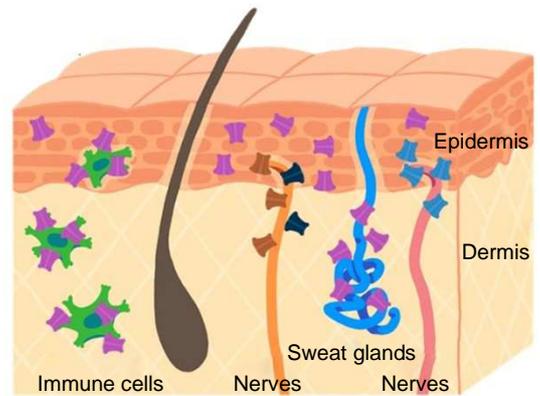


Figure 2. Various skin cells and TRP channels

V1 V3 V4 M8 A1 : TRP channels

Table 1. Diversity of TRP channel expression in peripheral skin cells

	Skin	Immune cells			Sweat gland cells				Nerves*	
	Epidermal keratinocytes	Monocytes	Macrophages	Dendritic cells	Secretory coil		Reabsorptive duct		Pain	Cold sensation
					Luminal cells	Myoepithelial cells	Luminal cells	Basal cells		
TRPV1	+	++	++	+	+	-	+	+	++	-
TRPV2	-	++	+	+					-	-
TRPV3	+	+	-	-	+	+	++	+	-	-
TRPV4	+	+	-	+	++	+	+	+	-	-
TRPM2	-	++	++	++					-	-
TRPM3	-	-	-	-					-	-
TRPM4	+	++	-	+	++	++	++	++	-	-
TRPM5	-	-	-	+					-	-
TRPM8	-	-	-	-					-	++
TRPA1	-	-	-	-					+	-

2. Comprehensive understanding of polymodal receptors in various cells

In the environment in which cosmetics are used, multiple factors such as temperature and pH act simultaneously on the skin. Understanding how the TRP channels present in sensory nerves, the epidermis, and sweat glands respond under these complex conditions is important for product

development. Therefore, in this study, we focused on the effects of pH and temperature changes on TRP channel activity and also analyzed how these environmental factors affected TRP activity induced by functional ingredients (potassium alum, menthol).

- (1) Focusing on TRPV1, A1, and M8, which have already been reported to play important roles in sensory neurons, and TRPV3 and V4, which are widely expressed in skin cells used for this analysis, we checked for changes in TRP channel activity in response to temperature changes from room temperature to high temperatures (25–39°C) and acidic to alkaline conditions (pH 5–9) by measuring changes in intracellular calcium concentration* (Figure 3). TRPV1 was less affected by pH at high temperatures, while TRPA1, V3, V4, and M8 tended to be more active in alkaline conditions regardless of temperature. This indicates that each TRP channel exhibits different tendencies in response to temperature and pH changes.

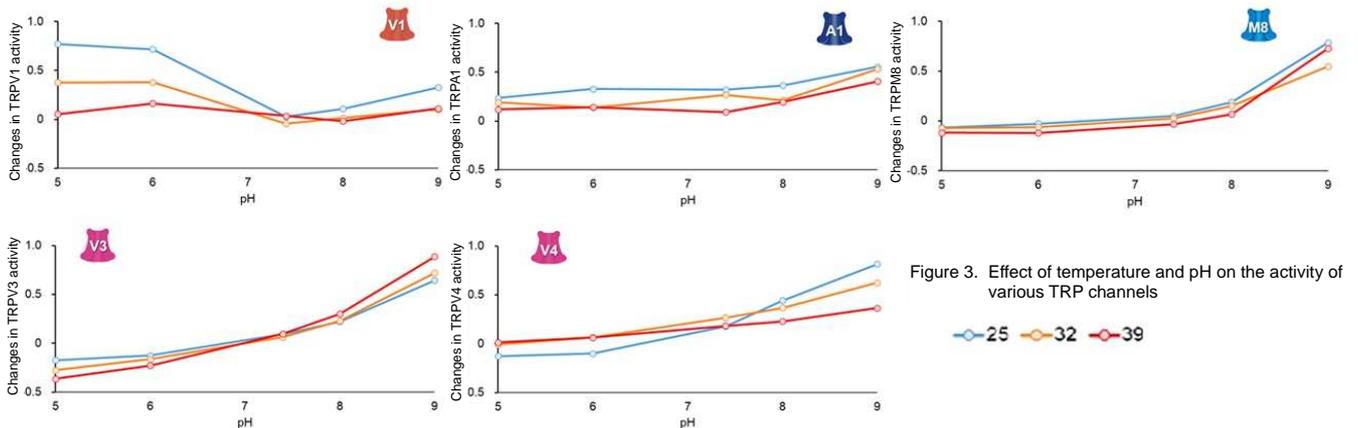


Figure 3. Effect of temperature and pH on the activity of various TRP channels

—●— 25 —■— 32 —●— 39

- (2) Next, we investigated whether these changes affected the effectiveness of the functional ingredients, focusing on potassium alum (aluminum potassium sulfate) and menthol.

- With regard to potassium alum, we found that its inhibitory effect on the activity of the pain sensors TRPV1 and A1, which had already been identified by our research group, became greater as the temperature increased (Figure 4). In addition, we found that potassium alum also has the effect of inhibiting the activity of TRPV4, which is present in sweat glands and is said to control sweating (Figure 5). This may be one of the reasons why aluminum has long been used as an antiperspirant.

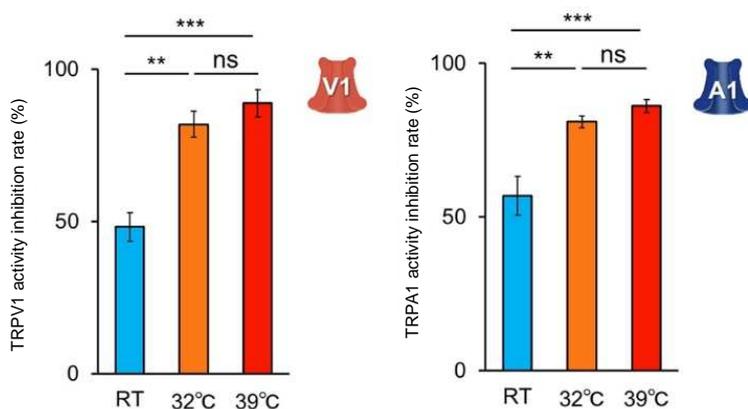


Figure 4. Temperature-dependent inhibitory effect of potassium alum on TRPV1 and A1 activity

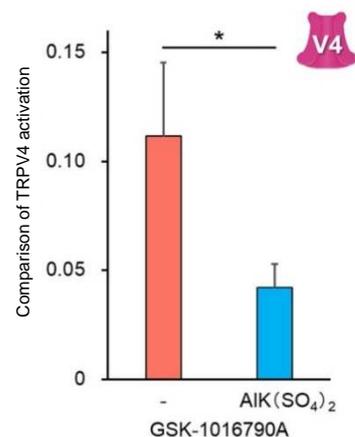


Figure 5. Inhibitory effect of potassium alum on TRPV4 activity
GSK-1016790A: TRPV4 activator

- Furthermore, measurements of the cold temperature threshold in human subjects revealed that human TRPM8, a cold temperature receptor, is directly activated under alkaline conditions, which revealed that the cooling sensation induced by menthol is enhanced under alkaline conditions (Figure 6).

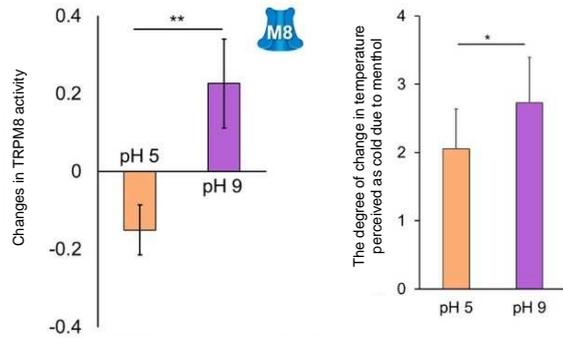


Figure 6. Effect of pH on TRPM8 activation (Left: Effect of pH on TRPM8 activity, Right: Effect of pH on cold sensation perceived by humans)

Future developments

In this study, we clarified the expression patterns of TRP channels in each cell type of skin and confirmed that changes in temperature and pH affect the activity of TRP channels and the state of TRP channel activities induced by functional ingredients.

When using cosmetics, the skin is simultaneously exposed to multiple environmental factors, so understanding the response of TRP channels under these complex conditions is believed to be extremely important in terms of product design and improving comfort during use.

Going forward, we will apply these findings to product development and will also work to elucidate the mechanisms by which skin responds to environmental factors by further exploring the characteristics of the way TRP channels respond to various combinations of environmental factors and by deepening functional analysis.

The results of our research into TRP channels have already been widely applied to hair care, body care, skin care, and other products.

Mandom pursues “creation of new value” for consumers and conducts research and development with the aim of achieving maximum safety, functionality, and comfort during use. As part of this pursuit, we will continue to engage in research and development, such as elucidating the various mechanisms of TRP channels and searching for components that control their activity.



* Some of the products related to this research are listed here.

◆: This is a “quasi-drug” mark.

[Related information]

A list of past news releases on Mandom research related to TRP channels can be found below.

https://www.mandom.co.jp/release/search/?kw=TRP&cat%5B%5D=release-develop&from_year=&from_month=&from_day=&to_year=&to_month=&to_day= (Japanese only)

Remarks

* Calcium imaging: A technique to indirectly measure TRP channel activity by making calcium, which enters cells when TRP channels open, emit fluorescence and then recording the intensity of the fluorescence in the cells as an image.