Identification by Mandom of the mechanism by which hypo-osmotic solutions such as water cause irritation in the nasal cavity and eyes

-Adopting TRP channels to develop cosmetics that do not cause eye irritation-

Mandom Corporation (Head Office: Osaka, President Executive Officer: Motonobu Nishimura, hereafter "Mandom"), through joint research with Professor Makoto Tominaga of the Okazaki Institute for Integrative Bioscience, has developed an evaluation method for cosmetics focusing on TRP (Transient Receptor Potential) channels as sensors of skin sensations, and applied it in product evaluations.

Here, we report the discovery of TRPA1 (an irritation sensor), one of TRP channels, that is activated by cells responding to low osmotic pressure, and the identification of a functional sensory irritation mechanism for water or other low osmotic solvents as they enter the nasal cavity or eyes.

We have presented these results at "The 76th Workshop of the Society of Cosmetic Chemists of Japan (SCCJ)" held on July 9, 2015.

1. Hypo-osmotic solutions like water cause pain when they enter the nasal cavity and eyes

People experience pain when rinsing their eyes with water or aspirating water up their nose. This pain is caused because water has low osmotic pressure compared to cellular or bodily fluids; such that the concentration of the dissolved ingredients becomes diluted.

The pain is partly due to the semipermeable nature of the cell membranes (membranes encompassing cells). A semipermeable membrane allows the transfer of water and hypo-osmotic solutions, but does not easily allow the passage of salts. When cells encompassed by semipermeable cell membranes are placed in water (or hypo-osmotic solution), the large concentration difference between the "fluid in the cells" and "water", allows movement of water content from the low concentration to the inside. This results in expansion of cells, and if extreme, results in rupturing. To avoid this, the human body is protected by defense such as the skin. However, in areas with less protection such as the nasal cavity and eye mucosa, ass the cells come in contact with a hypo-osmotic solution, signal is transmitted from such cells to the brain, and "pain" is experienced.

2. Identifying the mechanism of pain in hypo-osmotic conditions

TRPA1 receptor reacts to various pains, and this receptor's role has been reported by Mandom in various cases. On one hand, TRPA1 is said to receive physical (hitting or pulling) stimulation, but despite the many previous reports, the validity of this is unclear. We concluded that TRPA1 activation is amplified under hypo-osmotic conditions, and discovered that hypo-osmotic solutions play a direct role in the activation of TRPA1 (Fig. 1). In addition, we observed consistent correlation between the magnitude of cell expansion in hypo-osmotic solution and TRPA1 activation. We discovered that physical irritation in the form of cell expansion contributes to TRPA1 activation under hypo-osmotic conditions (Fig. 2). This discovery clarifies the unknown fact that TRPA1 functions as a mechano-sensitive receptor.

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3. TRPA1 as an alternative to evaluating eye irritation in human and animal subjects

Based on the results of this research, we concluded that TRPA1 is involved in pain due to hypo-osmotic solutions occurring in the nasal cavity and eyes. We thereby, enabled the evaluation of eye irritation using TRPA1 for the purpose of cosmetics development.

We confirmed that the pain occurring in case of hypo-osmotic model lotions enters the eyes and loses pressure necessitating osmotic pressure adjustment (Fig. 3).

This evaluation for eye irritation using TRPA1 is gradually being applied to the development of safe and reliable cosmetics. In addition, at Mandom we are already applying TRP channels for raw material screen and at development stages to evaluate skin irritability.

Furthermore, Mandom is keen to explore this area to develop newer products for customers to use them reliably and safely.

<Reference material>

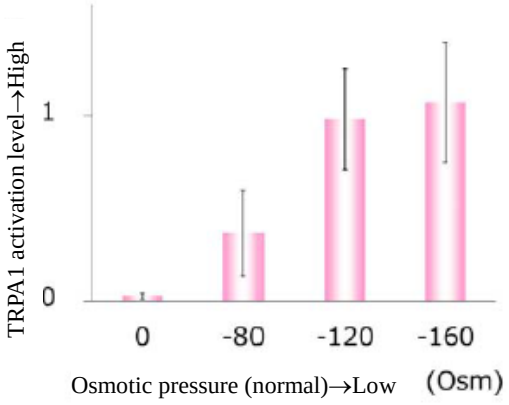

Fig. 1 Activation level of TRPA1 due to low osmotic pressure

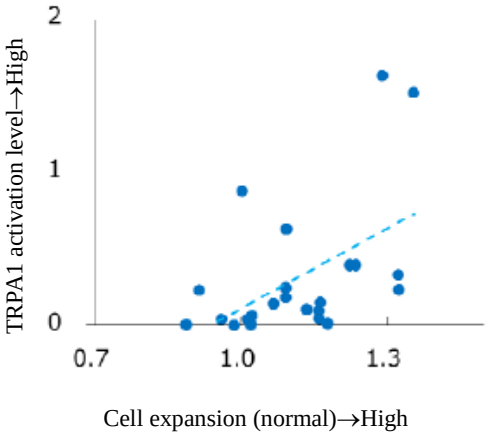

Fig. 2 Relationship of cell expansion and TRPA1 activation

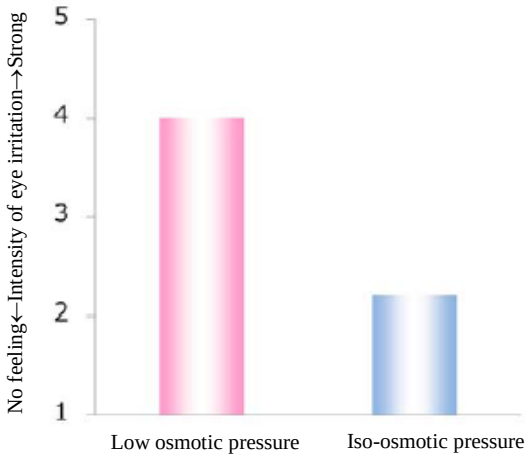

Fig. 3 Differences in eye irritation from lotion based on osmotic pressure