News Release

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National Institutes of Biomedical Innovation, Health and Nutrition

Mandom and the National Institutes of Biomedical Innovation, Health and Nutrition confirmed for the first time in Japan that TRPM4, a cell sensor, controls inflammatory reactions in keratinocytes

～A TRPM4 activating effect was confirmed for potassium alum, which is a spa ingredient～

Mandom Corporation (headquarters: Osaka City, President Executive Officer & Director, Motonobu Nishimura, hereinafter referred to as “Mandom”) and the National Institutes of Biomedical Innovation, Health and Nutrition (Ibaraki City, Director General, Yoshihiro Yoneda, hereinafter referred to as "NIBIOHN") jointly worked on an investigation of the immune system in the skin and the development of control technology. The purposes of this joint research are to develop technologies that maintain the health and beauty of the skin for Mandom, and to use to the less painful vaccine technology for NIBIOHN.

For the first time in Japan, Mandom and the project leader of the Laboratory of Mockup Vaccines, Dr. Ken Ishii, professor in the Institute of Medical Science, the University of Tokyo, confirmed that TRPM4 controlled inflammatory reactions in keratinocytes. TRPM4 belongs to the TRP (*1) channel family of cell sensors. We

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further confirmed that potassium alum, which is known as a spa ingredient, activates TRPM4 and suppresses the production of inflammatory signals from keratinocytes. These results indicate that potassium alum tones the skin by controlling the inflammatory reactions in skin through TRPM4 activation.

The results of this research were presented at the 9th Joint Symposium of the Federation of Asian and Oceanian Physiological Societies Congress: FAOPS2019 and the 96th Annual Meeting of the Physiological Society of Japan, held between March 28 and 31, 2019. The results will also be presented at 25th Conference of International Federation of Societies of Cosmetic Chemists: IFSCC held between Sep. 30 to Oct. 2, in Milan, Italy.

1. The role of TRP channels in the immune system in the skin

Most of the problems in skin are related to its inflammation. The immune system is essential in protecting the human body against attacks by harmful viruses and bacteria and exposure to certain antigens. However, immune reactions in the skin lead to excessive inflammation and degrade its appearance, including problems such as dryness, decreasing elasticity, and conspicuousness of pores.

To prevent skin troubles, it is important to control immune reactions, especially in their early stages. Inflammatory signals (cytokines) produced by keratinocytes trigger immune reactions in the skin. Therefore, controlling the immune reactions in keratinocytes is necessary.

To date, Mandom has been studying TRP channels that are expressed in nerve fibers in the skin. These sensors determine whether cosmetics are comfortable to use. We hypothesized that TRP channels participate in immune reactions in the skin. Therefore, the expression of TRP channels in the keratinocytes was investigated.

2. TRPM4 channels expressed in keratinocytes were confirmed to control immune reactions in keratinocytes

We investigated the mRNA expression of TRP channels in keratinocytes and the expression of TRPM4 was detected. The function of TRPM4 in the skin was unknown, therefore we examined its effect on immune reactions. We used artificial conditions under which keratinocytes produce inflammatory cytokines. We found that the known TRPM4 agonist, BTP2, suppressed cytokine production (Fig.1). This result indicated that TRPM4 controls immune reactions in keratinocytes.

3. Potassium alum activates TRPM4

We screened TRPM4 activating agents, examining compounds that have similar structures to known TRPM4 agonists, aromatic chemicals and mineral compounds. Potassium alum, which is a spa ingredient, was found to have TRPM4-activating effects (Fig.2).

4. Potassium alum was confirmed to suppress the cytokine production from keratinocytes

Under conditions in which keratinocytes produce inflammatory cytokines after artificial induction, potassium alum suppressed cytokine production from keratinocytes (Fig. 3). This result indicated that potassium alum has immune-controlling effects in keratinocytes.

NIBIOHN continues research on the immune system in the skin and the relationship between TRP channels

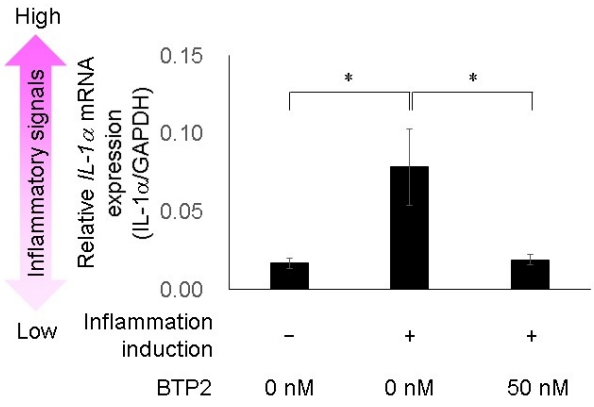
and inflammation, and is applying it to less painful and highly effective vaccine technology.

Mandom is using this research to develop immune-controlling technology in the skin, and is applying it to the development of new cosmetics that maintain the health and beauty of skin.

(*1) The family of cation channel proteins acts as sensory receptors. Sensor proteins detect various environmental signals such as chemicals, and temperature and converts them to electric signals.

【Reference materials】

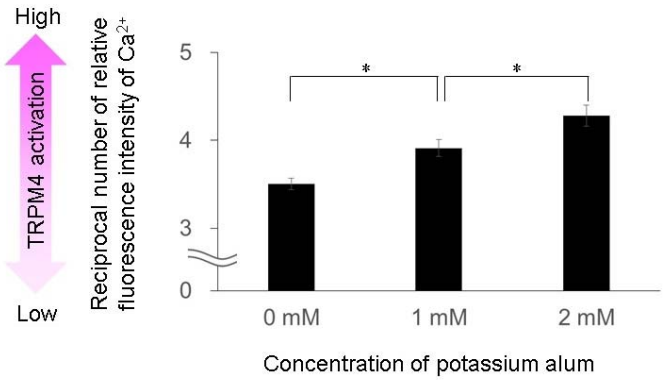
Fig.1. Effect of TRPM4 activation on an inflammatory signal (cytokine) produced by keratinocytes



*p<0.05, One-way ANOVA with Steel test
Inflammation was artificially induced by adding TNF-α (20 ng/mL)

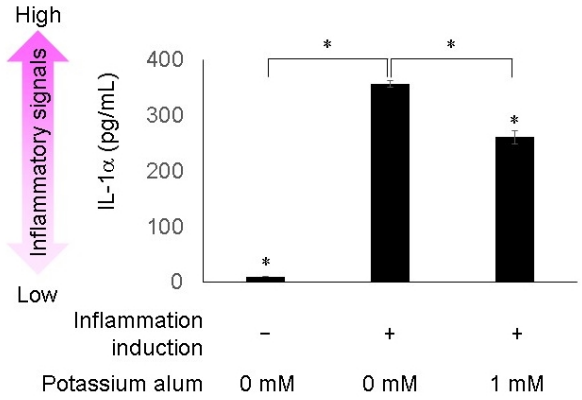
Cytokine production in keratinocytes induced by TNF-α was suppressed by the activation of TRPM4.

Fig.2. TRPM4 activating effect of potassium alum



* p<0.05, One-way ANOVA with Turkey test

Fig.3. Effect of potassium alum on the inflammatory signal (cytokine production) from keratinocytes



∗p<0.05, One-way ANOVA with Steel test
Inflammation was artificially induced by adding TNF-α (20 ng/mL)

Cytokine production by keratinocytes that was induced by TNF-α addition was suppressed by potassium alum

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