## Topical application of metallic soap on the skin induces Th2-type immune responses in a model for human atopic dermatitis, NC/Tnd mice

Akane Tanaka<sup>1)</sup>, Akira Matsuda<sup>1)</sup>, Kyunsook Jung<sup>1)</sup>, Masaki Takai<sup>2)</sup>, Yuka Makita<sup>2)</sup>, Keitaro Ohmori<sup>1)</sup>, and Hiroshi Matsuda<sup>1)</sup>

- **A) Background:** Hardness in water is consisted with mineral salts, including calcium (Ca<sup>++</sup>) and magnesium (Mg<sup>++</sup>). Reaction of the mineral salts with soap eventually forms an insoluble precipitate known as metallic soap (soap scum). Since metallic soap remains tightly on the skin and is hard to rinse off, it may become one of irritants that exacerbate dermatitis. In this study, we first demonstrated that metallic soap had antigenic activity when it was topically applied on to the barrier-disrupted skin of NC/Tnd mice, a model for human atopic dermatitis.
- **B) Methods:** We generated Ca<sup>++</sup>- or Mg<sup>++</sup>-based metallic soap for the study. Twice a week, stratum corneum was gently removed by repeated tape-stripping from the dorsal skin of specific pathogen free NC/Tnd mice without dermatitis, followed by topical application of metallic soap. Every 2 weeks, scratching analysis and pathological examination were performed. Cytokine expression in the treated skin was evaluated by a real time RT-PCR. Plasma total IgE was measured by an ELISA.
- **C) Results:** Scratching behavior of mice applied with metallic soap was significantly increased, whereas that of diluent-applied control mice was unchanged. Hyperplasia of epidermal keratinocytes and infiltration of inflammatory cells were obvious in the skin of metallic soap-applied mice. Levels of plasma total IgE were elevated in mice treated with metallic soap. Expression levels of pro-inflammatory (thymic stromal lymphopoietin, TSLP) and Th2 cytokines (IL-4 and IL-10) were increased in the skin of metallic soap-treated mice. On the other hand, IFN-γ levels were unchanged.
- **D) Conclusions:** We first demonstrated that topical application of metallic soap onto the skin with mild disruption of epidermal barrier induces allergic inflammation and itch sensation to mice with predisposition of atopic dermatitis. Our results revealed that daily use of water with high concentrations of Ca<sup>++</sup> and Mg<sup>++</sup> for bathing might rise a risk of susceptibility to atopic dermatitis.

<sup>&</sup>lt;sup>1)</sup>Tokyo University of Agriculture and Technology, <sup>2)</sup>MIURA CO., Ltd.