T helper 1 (T_H1), Th2, and Th17 cytokine-profiles during long-term sublingual immunotherapy for Japanese cedar pollinosis

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Introduction: Sublingual immunotherapy (SLIT) for Japanese cedar pollinosis (JCP) has also started to be covered under the national health insurance system in Japan. The mechanisms of action of SLIT also include early desensitization effects, modulation of T cell and B cell responses, and induction of blocking antibody, as well as decreased migration of eosinophils, basophils, and mast cells to tissues and the release of their mediators. Regulatory T cells have also been identified as key regulators of immunologic processes in peripheral tolerance to allergens. We performed long-term sublingual immunotherapy (SLIT) for patients with JCP, screened molecules as candidate biomarkers, and investigated the serum levels of T helper 1 (T_H1), Th2, and Th17 cytokines in order to evaluate whether these molecules show changes correlated to symptom scores.

Method: The patients received SLIT from a pre-seasonal period (October) through to the end of the high-pollen season (April) for four consecutive years. The symptom medication scores were evaluated in accordance with the Japanese guidelines for allergic rhinitis. Blood samples were obtained and the serum was stored at -80°C. We measured the levels of molecules including T_H1, Th2, and Th17 cytokines in the serum at

the peak of pollen dispersion using ELISA or multiple assay system using kits.

Results: The levels of IL-4 showed a significant decrease at year 4 compared with those at year 1. On the other hand, the levels of IL-5, IL-13, and IFN- γ at year 4 did not change significantly compared with those at year 1. The long-term SLIT reduced the serum levels of IL-17A and TSLP. Significant positive correlations were found between the symptom medication scores and the levels of IL-17A or TSLP during long-term SLIT. The scores in the group in which the IL-17A or TSLP levels decreased were significantly lower than those in the group in which these levels did not decrease.

Conclusion: IL-17A and TSLP might be involved in pathological features of JCP or mechanisms of SLIT efficacy, suggesting that it could be one of the suitable biological parameters for SLIT efficacy. Further studies are needed to evaluate the difference between responders and non-responders in SLIT. In addition, collaboration among scientists and pharmaceutical companies is necessary to produce new therapeutics for non-responders in whom serum IL-17A and TSLP levels are still higher at year 4 for JCP.