Advancement of Research on Allergic Rhinitis

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Antigen-specific immunotherapy is effective for changing the natural course of allergic rhinitis, preventing development of other allergic diseases, and reducing new sensitization to allergen. Subcutaneous immunotherapy SCIT has been conducted over the years, but it is associated with a risk of anaphylactic shock, albeit low, and the inconvenience of frequent visits to hospital. While, sublingual immunotherapy SLIT, according to recent reviews, is safe and effective as an alternative route of administration. So, SLIT is expected to be introduced in Japan.

To clarify the efficacy of SLIT for Japanese cedar pollinosis, we have conducted several clinical trials and therapeutic efficacy has been suggested. No major adverse effects were observed in all studies. SLIT is one of the most expected treatments, but includes some problems. Objective biomarkers that show the therapeutic efficacy have not been established. Therefore, it is necessary to identify relevant biomarkers for monitoring efficacy. Then, we tried to find the therapeutic biomarkers of SLIT. We focused on the antigen specific Th2 cells, and antigen specific induced regulatory T cells (iTreg cells) as the candidates from the mechanism. A significant increase in specific Th2 clone was observed only in the placebo group after the pollen season, but no significant change was observed in active SLIT group. Next, we examined the change of the proportion of cedar specific iTreg cells before and after the pollen season. A significant change was not observed in active SLIT group as well as placebo group after the pollen season. So, we divided the SLIT group into subgroups based on an increase or decrease in Cry j 1 specific iTreg levels. The subgroup with increased iTreg cells showed significant improvement of QOL-symptom score compared to the placebo group, while the another subgroup with decreased iTreg cells did not show significant improvement compared to placebo. Allergen specific Th2 cells and specific iTreg cells are suggested to be biomarkers for reflecting therapeutic efficacy of SLIT.

In order to develop a predictive method for the therapeutic efficacy of SLIT at the early point of the treatment, we tried to identify predictive biomarkers. Peripheral bloods were taken from the both SLIT group and Placebo group before and 2 months after starting of SLIT. Gene expression changes in the blood were analyzed. A number of gene expression changes were observed 2 months after the treatment. The best combination was calculated from the genes. Validation study of candidate genes will be done in a clinical trial of SLIT. We are now developing a simple method for predicting the efficacy of SLIT.

Recently, environmental challenge chamber (ECC) has been used to examine the efficacy of various treatments for allergic rhinitis. ECC can induce symptoms in patients with allergic rhinitis under well-controlled stable conditions and is expected to offer consistent results. ECC built at Chiba University, can accommodate up to 50 subjects. The pollen level is monitored during the exposure at each chair using automatic pollen counters to maintain the pollen at constant levels everywhere in the room. Each patient can record the frequencies of symptoms such as sneezing and nose-blowing, and subjective assessment of symptoms induced by pollen exposure using mobile communication devices for the precise evaluation.

After pollen exposure in ECC, many patients had late phase symptoms including rhinorrhea and sneezing as well as nasal congestion. It has not been clear the local response causing in rhinorrhea and sneezing in late phase. Therefore we focused on symptoms and local responses induced by cedar pollen dispersal in ECC. Volunteers with cedar pollinosis were exposed with cedar pollen for 3 hours in ECC. Nose-blowing and sneezing appeared during pollen exposure.
in the ECC and 3 hours after leaving ECC. But even 6 hours after leaving ECC, rhinorrhea and sneezing were observed continuously. It has been thought that rhinorrhea and sneezing are induced by histamine. Then histamine levels in nasal discharge were examined. Interestingly, a substantial amount of histamine was detected in nasal discharge from almost examinee even 6 hours after leaving ECC. Then we examined the cells in nasal discharge with confocal microscopy. Basophiles were increased in nasal discharge. So, it is assumed that an accumulation of basophile is involved in histamine release causing in sneezing and rhinorrhea in the late phase.