Allergen immunotherapy (AIT)-induced increases of regulatory T (Treg) cells and regulatory B (Breg) cells in Japanese cedar pollinosis patients

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[Background] AIT is the only causative treatment for allergic diseases, whereas the mechanisms are not fully understood. Purpose of this study was to know (1) whether levels of antigen (Ag)-specific IgE and IgG4 antibodies (Abs) in serum are affected by AIT, (2) whether Treg and Breg cells are increased in peripheral blood mononuclear cells (PBMCs) by AIT, (3) whether mRNAs of four IL-10-related transcription factors, E4BP4, c-maf, Egr-2 and Foxp3 are increased in PBMCs by AIT, and (4) these molecules and cells are correlated with allergic rhinitis symptoms.

[Methods] Just after the pollen season (May, 2017), the pollen extract-induced allergic rhinitis symptoms (sneezing, aqueous nasal discharge and nasal mucosal edema) were scored in the pollinosis patients and patients treated with subcutaneous immunotherapy (SCIT). Levels of antibodies in sera were measured by ELISA. Collected PBMCs were stimulated with the specific antigen, Cry j 1, followed by staining molecules for analyzing by FACS. mRNA levels of the transcription factors in PBMCs were determined by real time RT-PCR.

[Results] In SCIT-treated patients, allergic rhinitis symptoms were significantly mild compared to patients without SCIT treatment. (1) Although Cry j 1-specific IgE level of SCIT-treated patients was markedly lower than that of pollinosis patients, Cry j 1-specific IgG4 level was considerably high in the SCIT-treated patients. (2) Effector Treg (CD45RA⁺ Foxp3^{high} CD4⁺ T) cells in SCIT-treated patients were much higher than those in patients without SCIT treatment. Cry j 1-specific IL-10⁺ Foxp3⁺ CD4⁺ T cells in SCIT-treated patients were also statistically higher than those in patients without treatment. Additionally, Cry j 1-specific IL-10⁺ B cells in SCIT-treated patients were statistically higher than those in patients without treatment. (3) Among four transcription factors, only E4BP4 mRNA level of SCIT-treated patients was significantly higher than that of patients without treatment. (4) IgG4, effector Treg cells, IL-10⁺ Foxp3⁺ CD4⁺ T cells and IL-10⁺ B cells showed weak correlations with the allergic rhinitis symptom score.

[Conclusions] Cry j 1-specific IgG4, effector Treg cells, Cry j 1-specific IL-10⁺ Foxp3⁺ CD4⁺ T cells, and Cry j 1-specific IL-10⁺ B cells may be involved in the efficacy of SCIT.