CRTH2 Expression on Dysfunctional Treg Cells in Correlation with Asthma Control

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Background: CRTH2 is the new target for the treatment of allergic diseases and expression of various cell types. The rationale of CRTH2 expression on regulatory T cells (Treg, CD3+CD4+CD25+CD127-) in asthma patients remains unknown.

Objective: To assess CRTH2 expression level in Treg cells with correlation to asthma clinical outcomes.

Methods: The CRTH2 expression on Treg cells in whole blood was analyzed using flow cytometry. % predicted PEFR, asthma control test (ACT), and asthma quality of life questionnaire. Absolute eosinophil count was investigated to find the correlation with CRTH2 expression level.

Results: Forty-six asthma patients (11 eosinophilic asthma patients, 30 non-eosinophilic allergic asthma patients, 5 non-eosinophilic non-allergic patients) and 11 healthy control were enrolled in the study. Asthma patients had more circulating CRTH2+ Treg cells of total CD3+ cells than the control group (0.12% ± 0.09 and 0.04% ± 0.03, p = 0.001). In subgroup analysis, we found the frequency of CRTH2 expression on Treg cells in eosinophilic asthma patients (0.19% ± 0.14) was significantly higher than non-eosinophilic allergic (0.10% ± 0.06) and non-eosinophilic non-allergic asthma patients (0.06% ± 0.03). The frequency of CRTH2 expression on Treg cells among asthma patients revealed negative correlation with ACT scores (r = -0.29, p = 0.04) and positive correlation with absolute eosinophil count (r = 0.39, p = 0.007). The CRTH2+ Treg cells decreased their suppressive activity on the proliferation of T effector cells in in-vitro study. Decreased CCR7, CD27, TIGIT expression and increased CD69, ILT3, PD-L1 expression on CRTH2+ Treg cells compared with CRTH2- Treg cells were observed. CRTH2+ Treg cells decreased FOXP3 and Helios expression, but increased GATA3 expression. Decreasing of IL-10-production, vice versa IL-4, IL-5, and increasing of IL-13-production were revealed in CRTH2+ Treg cells. After PGD2 stimulation, CRTH2+ Treg cells showed more reduced Treg suppression. We also found CRTH2+ cells were elevated in asthma exacerbation patients more than asthma well-controlled patients, with a decrease during allergen-specific immunotherapy in those with asthma.

Conclusion: The new Treg cells subtype is found to reduce functional regulation. The elevated level of peripheral CRTH2 expressions on Treg cells is featured in asthma and associated with asthma control which could be a new targeted therapy for asthma.

Keywords: Asthma, CRTH2, Treg cell