Congress
EAACI 2016 – Vienna, Austria

EPIT-induced Tregs suppress T cell proliferation in specific and bystander conditions in a model of food allergen sensitized

Pelletier B. [1], Mondoulet L. [1], Puteaux E. [1], Ligouis M. [1], Dhelft V. [1], Plaquet C. [1], Prof. Dupont C. [1], Benhamou P.-H [1], H.A. Sampson[2]

1. DBV Technologies, Montrouge, France
2. DBV Technologies, New York, United States

Background: Epicutaneous immunotherapy (EPIT) on intact skin induces sustained desensitization in mouse models of food allergy. Mechanistic analyses show that EPIT significantly increases the Foxp3+ Tregs population. Adoptive transfer of EPIT-induced Tregs protects sensitized mice from anaphylaxis and prevents further sensitization to other allergens (bystander effect). This study investigates the suppressive properties of EPIT-induced Tregs with a focus on specific/bystander effects.

Method: Milk-sensitized BALB/c mice were treated with milk EPIT or not (Sham). Tregs (CD4+CD25+ T cells) from milk EPIT, Sham or non-sensitized groups were sorted, as well as effector T cells (CD4+CD25-) from milk or peanut sensitized mice, and co-cultured for 4 days at different ratios with allergen-pulsed CD11c+ antigen-presenting cells using either anti-CD3 or allergen stimulation. Anti-CTLA-4 and anti-TGF-β antibodies were used to determine whether EPIT-induced Tregs act via cytokines or cell-contact dependent mediation. Suppression was analyzed by tracking divided CD4+CD25- with CFSE by flow cytometry. Supernatants were also collected to quantify cytokine secretion.

Results: With anti-CD3 stimulation, Tregs were able to suppress effector T cell (from milk or peanut sensitized mice) proliferation whatever the experimental groups (up to 90%-98% of proliferation inhibition in EPIT and Sham groups). In contrast, with allergenic stimulation, only EPIT-induced Tregs significantly inhibited effector T cells proliferation in specific or bystander conditions (i.e. 20%-25% proliferation inhibition) compared to Sham or non-sensitized Tregs. Interestingly, blocking CTLA-4 and TGF-β abrogated the suppressive capacity of EPIT-induced Tregs in both conditions. IL-2 was barely detectable in supernatants of EPIT Tregs compared to Sham Tregs, suggesting that EPIT-Tregs highly consume this cytokine.

Conclusion: With allergenic stimulation, EPIT-induced Tregs inhibited effector T cell proliferation with the same potency in specific and bystander conditions. Suppression induced by EPIT-induced Tregs might use 3 complementary pathways: (i) a high consumption of IL2 reducing its availability for effector T cells, (ii) TGF-β secretion and (iii) CTLA-4 cell contact mediation.