CD103 integrin identifies a high IL-10-producing FoxP3+ regulatory T cell population suppressing allergic airway inflammation

Sofia Tagkareli[1], Maria Salagianni[1], Ioanna Galani[1], Maria Manioudaki[1], Eleftherios Pavlos[1], Kalliopi Thanopoulou[1], and Evangelos Andreakos[1]

[1]Biomedical Research Foundation, Academy of Athens

March 21, 2021

Abstract

Background: Although FoxP3+ regulatory T (Treg) cells constitute a highly heterogeneous population, with different regulatory potential depending on the context, distinct subsets or phenotypes remain poorly defined. This hampers the development of immunotherapy for allergic and autoimmune disorders. This study aimed at characterizing distinct FoxP3+ Treg subpopulations involved in the suppression of Th2-mediated allergic inflammation in the lung. Methods: We used an established mouse model of allergic airway disease based on ovalbumin sensitization and challenge to analyze FoxP3+ Tregs during the induction and resolution of inflammation, and identify markers that distinguish their most suppressive phenotypes. We also developed a new knock-in mouse model (Foxp3creCd103dtr) enabling the specific ablation of CD103+FoxP3+ Tregs for functional studies. Results: We found that during resolution of allergic airway inflammation in mice >50% of FoxP3+ Treg cells expressed the integrin CD103 which marks FoxP3+ Treg cells of high IL-10 production, increased expression of immunoregulatory molecules such as KLRG1, ICOS and CD127, and enhanced suppressive capacity for Th2-mediated inflammatory responses. CD103+FoxP3+ Tregs were essential for keeping allergic inflammation under control as their specific depletion in Foxp3creCd103dtr mice lead to severe alveocapillary damage and eosinophilic pneumonia, markedly reducing the lifespan of the experimental animals. Conversely, adoptive transfer of CD103+FoxP3+ Tregs effectively treated disease, attenuating Th2 responses and allergic inflammation in an IL-10-dependent manner. Conclusion: Our study identifies a novel regulatory T cell population, defined by CD103 expression, programmed to prevent exuberant type 2 inflammation and keep homeostasis in the respiratory tract under control. This has important therapeutic implications.

Hosted file

`Manuscript Combined FI.pdf` available at https://authorea.com/users/403029/articles/514703-cd103-integrin-identifies-a-high-il-10-producing-foxp3-regulatory-t-cell-population-suppressing-allergic-airway-inflammation