

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

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## Abstract

**Background:** Although FoxP3 + regulatory T (Treg) cells constitute a highly heterogeneous population, with different regulatory potential depending on the disease context, distinct subsets or phenotypes remain poorly defined. This hampers the development of immunotherapy for allergic and autoimmune disorders. **Objective:** 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 ( *Foxp3<sup>cre</sup> Cd103<sup>dtr</sup>* ) 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 *Foxp3<sup>cre</sup> Cd103<sup>dtr</sup>* mice lead to severe alveocapillary damage, eosinophilic pneumonia, and markedly reduced lifespan of the 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.

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