Role of regulatory T cells in the antigen specific induction of tolerance in murine asthma

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Introduction

Allergic asthma is a complex inflammatory syndrome. Its severity correlates with the presence of activated T lymphocytes and eosinophils in the bronchoalveolar lavage fluid (BALF).

Induction of tolerance via the nasal route results in reduced recruitment of eosinophils into bronchial fluid (BALF) upon challenge, inhibition of T2 pro-inflammatory cytokine secretion and T cell hyporesponsiveness.

Regulatory T cells (Tregs) are key players in controlling the development of asthmatic inflammation.

Here we showed that, in a mouse model of asthma, CD4+CD25+Foxp3+ natural regulatory T cells were generated early after induction of tolerance. We also demonstrated that CD25+ T cells depletion severely hampered tolerance induction. Transfer of CD4+CD25+ T cells in asthmatic mice was sufficient to induce tolerance whereas transfer of CD4+CD25+ T cells was not able to do so. However when CD4+CD25+ were purified from donor mice depleted of CD25+ T cells, they were no longer able to transfer tolerance. Taken together, our data suggest that both CD4+CD25+ and CD4+CD25- T cells are implicated in tolerance induction.

Conclusion

In our murine model of asthma intranasal treatment led to the generation of natural Tregs (CD4+CD25+Foxp3+ T cells) that were crucial for tolerance induction. However cell transfer experiments revealed that only CD4+CD25+ T cells were able to tolerate recipient asthmatic mice. These CD4+CD25+ T cells were however not suppressive if purified from a donor mice depleted of CD25+ T cells.

In conclusion, both CD4+CD25+ T cells and CD4+CD25- T cells appear to be essential in tolerance induction. The relationship both subsets will have to be investigated.