Regulatory T cell secificity directs tolerance versus allergy against aeroantigens in Humans.

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Abstract

FOXP3+ regulatory T cells (Tregs) maintain tolerance against self-antigens and innocuous environmental antigens. However, it is still unknown whether Treg-mediated tolerance is antigen specific and how Treg specificity contributes to the selective loss of tolerance, as observed in human immunopathologies such as allergies. Here, we used antigen-reactive T cell enrichment to identify antigen-specific human Tregs. We demonstrate dominant Treg-mediated tolerance against particulate aeroallergens, such as pollen, house dust mites, and fungal spores. Surprisingly, we found no evidence of functional impairment of Treg responses in allergic donors. Rather, major allergenic proteins, known to rapidly dissociate from inhaled allergenic particles, have a generally reduced capability to generate Treg responses. Most strikingly, in individual allergic donors, Th2 cells and Tregs always target disparate proteins. Thus, our data highlight the importance of Treg antigen-specificity for tolerance in humans and identify antigen-specific escape from Treg control

as an important mechanism enabling antigen-specific loss of tolerance in human allergy.

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