Specific CD8 T cells in IgE-mediated allergy correlate with allergen dose and allergic phenotype.

Abstract: RATIONALE: Studies in humans and rodents have indicated a causative role for CD8(+) T cells in IgE-mediated allergic inflammation, but their function is still controversial. OBJECTIVES: To analyze the role of allergen-specific CD8(+) T cells during the development of allergic airway inflammation in two parallel but diverging outcome models. METHODS: We used H2-Kb SIINFEKL (OVA(257-264)) multimers to analyze induction, natural distribution, and phenotype of allergen-specific CD8(+) T cells in a murine C57BL/6 model of ovalbumin (OVA)-induced allergic airway inflammation using low-dose or high-dose OVA sensitization. MEASUREMENTS AND MAIN RESULTS: The low-dose protocol was characterized by a significant induction of total and OVA-specific IgE, eosinophilic airway inflammation, IL-4 levels in bronchoalveolar lavage fluid. And significant alterations in lung function. The high dose protocol was characterized by a significant reduction of the allergic phenotype. Using OVA(257-264) H2-Kb multimers, we observed lung and airway infiltrating OVA-specific CD8(+) T cells showing an effector/effector-memory phenotype. The high-dose protocol caused significantly higher infiltration of allergen-specific CD8(+) cells to the airways and enhanced their cytotoxicity. Adoptive transfer with CD8(+) T cells from transgenic OT-I
mice to TAP1(-/-) or wild-type mice showed their migration to the lungs and TAP1-dependent proliferation after OVA-aerosol exposure. TAP1(-/-) mice defective in CD8(+) T cells showed exacerbated symptoms in the low-dose sensitization model. CONCLUSIONS: Allergen-specific CD8(+) T cells seem to protect from allergic inflammation in the lungs. Their number, which is dependent on the sensitization dose, appears to be a critical predictor for the severity of the allergic phenotype.