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Title: Blocking costimulatory signal for treating steroid-resistant asthma model

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Body: Background: We have constructed steroid sensitive (SS) and resistant (SR) murine asthma models by transferring SS and SR helper T (Th) clones into unprimed mice, respectively. Effect of CTLA4-Ig was analyzed both in vitro and in vivo. Method: For in vitro experiments, ovalbumin (OVA) reactive Th clones were cultured with antigen presenting cells, OVA, and various concentrations of dexamethasone (DEX). The proliferative response of each Th clone was measured by ^{3}H-thymidine uptake. For in vivo experiments, unprimed BALB/c mice were transferred with Th clones, challenged with OVA, and administered with DEX subcutaneously. CTLA4-Ig was administered through nasal inhalation or venous injection. The number of infiltrating cells in bronchoalveolar lavage fluid (BALF) was measured. Results: SS and SR clones were selected in terms of the in vitro effect of DEX on the proliferative responses of antigen-stimulated clones. Airway infiltration of eosinophils and lymphocytes of mice transferred with SS clones were effectively inhibited by the administration of DEX. In contrast, those of mice transferred with SR clones were not significantly inhibited by DEX. Administration of CTLA4-Ig significantly suppressed in vitro proliferation of DEX-treated SR clones, and in vivo eosinophil infiltration of SR asthma model transferred with SR clones. Conclusion: Steroid sensitivity of Th clones measured in vitro were consistent with that of adoptively transferred asthma model measured in vivo. Steroid resistant asthma models can be treated by blocking costimulatory signal mediated through CD28-CD80 and 86.