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Titel des Beitrags:
Improved efficacy of allergen-specific immunotherapy by JAK inhibition in a murine model of allergic asthma.

Abstract:
Allergen-specific immunotherapy (AIT) is the only curative treatment for type-1 allergies, but sometimes shows limited therapeutic response as well as local and systemic side effects. Limited control of local inflammation and patient symptoms hampers its widespread use in severe allergic asthma. Our aim was to evaluate whether AIT is more effective in suppression of local inflammation if performed under the umbrella of short-term non-specific immunomodulation using a small molecule inhibitor of JAK pathways. In C57BL/6J mice, a model of ovalbumin (OVA)-induced allergic airway inflammation and allergen-specific immunotherapy was combined with the administration of Tofacitinib (TOFA, a FDA-approved JAK inhibitor) from 48 hours prior to 48 hours after therapeutic OVA-injection. The effect of TOFA on human FOXP3+CD4+ T cells was studied in vitro. AIT combined with short-term TOFA administration was significantly more effective in suppressing total cell and eosinophil infiltration into the lung, local cytokine production including IL-1? and CXCL1 and showed a trend for the reduction of IL-4, IL-13, TNF-? and IL-6 compared to AIT alone. Furthermore, TOFA co-administration significantly reduced systemic IL-6, IL-1? and OVA-specific IgE levels and
induced IgG1 to the same extent as AIT alone. Additionally, TOFA enhanced the induction of human FOXP3+CD4+ T cells. This proof of concept study shows that JAK inhibition did not inhibit tolerance induction, but improved experimental AIT at the level of local inflammation. The improved control of local inflammation might extend the use of AIT in more severe conditions such as polyallergy, asthma and high-risk patients suffering from mastocytosis or anaphylaxis.