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## ENHANCED EXPRESSION OF CYTOKINES BY CD4<sup>+</sup> T CELLS IN AN ACUTE EXACERBATION OF CHRONIC ASTHMA

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T-lymphocyte-derived cytokines produced by CD4<sup>+</sup> Th2 cells are believed to play an important role in the pathogenesis of asthma. Cytokines secreted by Th1 and Th17 cells may also be involved. The contribution of such mediators to acute exacerbations of asthma, which are associated with exaggerated distal airway inflammation and airway hyperresponsiveness, is unclear. Therefore, we compared production of cytokines by pulmonary CD4<sup>+</sup> T-lymphocytes in mouse models of mild chronic asthma and an allergen-induced acute exacerbation.

**Methods** To induce chronic inflammation in the airways, BALB/c mice were systematically sensitized with ovalbumin and challenged with a low-mass concentration of aerosolized antigen for 30 minutes/day, 3 days/week for 4 weeks. Additional animals received a further 30 minute, moderate-level challenge (30 mg/m<sup>3</sup>) with ovalbumin aerosol to induce and acute exacerbation. Lung tissue was disaggregated with collagenase and CD4<sup>+</sup> cells isolated using Dynabead magnetic cell separation. Expression of cytokines was assessed by qRT-PCR and ELISpot assays.

**Results** Compared to naïve mice, CD4<sup>+</sup> T-lymphocytes from chronically challenged animals exhibited significantly increased expression of mRNA for cytokines characteristic of Th2 (IL-5, IL-13), Th1 (IFN- $\gamma$ ) and Th17 (IL-17A) cells. Compared to chronically challenged animals, an acute exacerbation was associated with significantly increased expression of mRNA for IL-4, IL-13, IFN- $\gamma$ , TNF- $\alpha$ , GM-CSF and MIP-1 $\alpha$ . The increased expression of IL-4 and IFN- $\gamma$  by CD4<sup>+</sup> T-lymphocytes was confirmed by ELISpot assays.

**Conclusions** Our findings strongly support a role for not only Th2 and Th1 but also Th17 cells in the pathogenesis of chronic asthmatic inflammation. Furthermore, enhanced expression of cytokines by CD4<sup>+</sup> lymphocytes is likely to contribute to the exaggerated inflammatory response seen in an acute exacerbation.

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**Conflict of Interest** No.