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Differential role of T-helper 2 cells and group-2 innate lymphoid cells in allergic airway inflammation

Allergic asthma is a chronic inflammation of the airways mediated by an adaptive type-2 immune response. In house dust mite (HDM)-driven allergic airway inflammation both T helper-2 (Th2) cells and group-2 innate lymphoid cells (ILC2) are major producers of IL-5 and IL-13. We found that in HDM-challenged mice the induction of ILC2 required prior sensitization with HDM. ILC2 induction was dependent on T-cells, whereby activation of ILC2 and Th2 cells was concomitant. In this HDM-driven allergic asthma model, ILC2 are therefore not an early source of Th2 cytokines but rather contribute to type-2 inflammation in which Th2 cells play a key role. Next, we used GATA3-YFP knock-in mice for direct *in situ* visualization of GATA3+ Th2 cells and ILC2s. Confocal microscopy revealed that Th2 cells and ILC2 occupied distinct locations in lungs from mice with HDM-driven allergic airway inflammation: ILC2s were scattered underneath the mucosa and Th2 cells were present within clusters of lymphocytes. We produced epigenetic maps of FACS-sorted GATA3+ Th2 cells and ILC2s isolated from mediastinal lymph nodes and broncho-alveolar lavage of GATA3-YFP mice with an allergic airway inflammation. Chromatin immunoprecipitation and deep-sequencing (ChIP-Seq) experiments revealed a remarkably similar genome-wide histone-3 lysine-4 dimethylation (H3K4Me2) active chromatin signature in *in vivo* activated Th2 cells and ILC2s. However, particular loci showed significant differences between the two cell types, including loci associated with allergic inflammation, ILC2 plasticity and metabolic homeostasis. Taken together, these findings indicate novel biological roles for ILC2s in asthma distinct from Th2 cells.

Biography

Rudi W Hendriks is the Head of the Experimental Research Laboratory of the Department of Pulmonary Medicine of the Erasmus MC Rotterdam, Netherlands. His main line of research is the differentiation program of lymphocytes in health and disease, in particular the regulation of differentiation and function of T helper subsets and group-2 innate lymphoid cells in the context of type-II immunity and the role of aberrant B and T cell activation in autoimmunity and interstitial lung disease.

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