

Histamine modulates Th2 cell cytokine production

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Background

Induction of Th2 cell responses is well described as being dependent on IL-4. The initial source of IL-4 are believed to originate from basophils. Basophils are the rarest of the granulocyte, and readily produce inflammatory mediators such as IL-4 and histamine following cross-linking of IgE-bound Fc ϵ R1. The effect of histamine on Th2 cell differentiation is much less known. This study aimed to characterize expression of histamine receptors on in vitro primed Th2 cells as well as investigate histamines effect in in vitro differentiated Th2 cells.

Methods

PBMCs, CD4⁺ T cells and naïve CD4⁺ T cells were purified from buffy coats obtained from the blood bank. Naïve CD4⁺ T cells were polyclonal activated with anti-CD3 and anti-CD28 and stimulated with or without IL-4 and α -IFN- γ for either 4, 12, 16, 24 and 48 hours for mRNA analysis or 2, 3 and 4 days for analysis by flow cytometry. The cultures were restimulated with PMA and ionomycin for 6 hours and brefeldin A for 4 hours prior to flow cytometry for intracellular cytokines and harvest of supernatant for multiplex cytokine analysis.

Results

We were able to detect expression of histamine receptor 1 and 2 (HR1 and HR2) on mRNA level of CD4⁺ T cells stimulated in the presence or absence of IL-4 and α -IFN- γ . Interestingly, the expression of both HR1 and HR2 appears to drop within the first 4 hours of stimulation and peak after 12 hours, where after the expression stabilizes. The presence of HR1 was further established by flow cytometry, where expression was observed on the surface of CD4⁺CRTh2⁺CD45RO⁺ PBMCs. We observed that stimulation of CD4⁺ T cells with histamine had a tendency to potentiate the Th2 primed cells to produce more of the Th2 hallmark cytokine IL-13. Moreover, histamine had a tendency to dampen the production of the Th1 cell associated cytokine IFN- γ . Likewise, histamine appears to potentiate the secretion of IL-13 and also dampen the secretion of IFN- γ .

Conclusion

Taken together, we were able to detect HR1 and HR2 on mRNA level of CD4⁺ T cells and observe HR1 on the cell surface of CRTh2⁺ cells. Furthermore, histamine had a tendency of potentiating Th2 cell differentiation observed by a potentiated increase of IL-13 and dampening of IFN- γ production.