

Inhibition of asthma relevant innate and adaptive human immune cells by epithelial cells

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Introduction: Mast cells and type 2 T cells are present in an abnormally activated state in the airway mucosa in patients with asthma. Most pathogenic models have focused on mechanisms of abnormal activation of these cells. It is also possible that failure of natural inhibitory mechanisms is relevant. We have tested this hypothesis that healthy airway epithelial cells exerts an inhibitory effect on mediator release by these cells.

Methods. Epithelial cells were cultured in plates overnight then mast cells were added to the epithelial cells, culture media or conditioned epithelial cell supernatant. After direct contact culture or culture through transwells, release of histamine in the culture supernatant was measured by ELISA and the expression of ckit by mast cells was measured by flow cytometry. For T cell co-cultures CRTH2+ CD4 cells or PBMC derived IL-4 driven T cell lines were added to epithelial cells or media as above with the addition of IL-2 to stimulate IL-13 release by these T cells.

Results. Epithelial cells were able to inhibit the constitutive release of histamine by mast cells both directly and via transwells. In addition to the reduction of histamine the level of ckit was also reduced on the mast cells. In T cell co-cultures the level of IL-13 release by T cells was reduced in the presence of epithelial cells. When histamine or IL-13 was added to epithelial cells the concentration of these mediators was not reduced after overnight culture.

Conclusions. Epithelial cells have the potential to reduce the constitutive release of histamine by mast cells and IL-13 production by type 2 cells and could reduce mast cell activation indicated by ckit expression. This process could contribute to damping down of type 2 responses and may have an important role in asthma pathogenesis.
