

Lung epithelial cell inhibition of cytokine production by peripheral blood mononuclear cells and lung lymphocytes

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Introduction: Type 2 cytokines such as IL-5, IL-13 and IL-4 produced by primed type 2 T cells have been shown to be important in the pathogenesis of eosinophilic airway inflammation. They . Factors regulating the state of activation of these cells are incompletely understood. We and others have shown that release of IL-13 by stimulated T cells can be inhibited by epithelial cells. In this study we used a PBMC based bulk culture system to: 1) determine whether production of other type-2 cytokines is inhibited by co-culture with epithelial cells; 2) compare inhibition of activated PBMC and human lung lymphocytes; and 3) investigate whether specific soluble mediators modified inhibition of IL-13 release. PBMC isolated from blood and lymphocytes isolated from lung tissue were cultured with IL-2 for five days in the absence and presence of A549 and BEAS2B epithelial cells. The cytokines IL-13, IL-5, IL-9 and TNF α were measured in the supernatant of these cells. We also did similar co-culture experiments in the presence of different inhibitors or blocking cytokine antibodies.

Results: We found that production of all cytokines were reduced in the presence of epithelial cells. PBMC and lung cells were inhibited to a similar degree although, importantly, lung cells produced more IL-9 and less TNF α than a comparable number of PBMC. We found that adding inhibitors to IL-10, TGF- β , Aryl Hydrocarbon Receptor (AHR blocked with CH-223191), prostaglandins (indomethacin) and nitric oxide (NMMA) did not alter the A549 mediated regulation of IL-13 release by the PBMC or lung cells.

Conclusions: Mononuclear cells from lung or blood secrete different types of cytokines which may reflect different activation status or cellular location and this could have implications about whether cytokines can be measured in the serum or localised lung sampling is required. We also found that blocking of IL-10, TGF- β , AHR, prostaglandins and nitric oxide were not able to change the regulation of the cytokine release but more specific inhibitors may be required. These results will help in the elucidation of potential inhibitory factors produced by epithelial cells that could have a role in asthma pathogenesis.