Inhibition of asthma-related immunological responses in mast cells and Th2 cell lines by cultured epithelial cell lines

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Previous studies have shown that constitutive and IgE-mediated histamine production by human lung mast cells is inhibited by a transferable factor produced by the airway epithelium. We investigated the effect of co-culture of epithelial cells with mast cell lines. We also measured the effect of co-culture of epithelial cell lines and T_H2 cells on interleukin (IL)-13 production. A549 or BEAS-2B cells were grown to confluence overnight and LAD2, HMC1.2 or human ex-vivo T-cells added. For transwell experiments epithelial cells were added to a 24w plate for 16h and mast cells added to the insert. Wells and transwell insert supernatants were harvested and mediator release quantified by histamine or IL-13 ELISA. Mast cell surface expression of ckit was measured by flow cytometry. Constitutive histamine production by HMC1.2 was reduced from 191 ± 13 ng/ 10^6 cells by 60.9% (95% CI 54.1, 67.8; $p < 0.0001$) when co-cultured with A549 and 21% (95% CI 14.2, 28.1; $p < 0.0001$) with BEAS-2B cells. Similar findings were seen with the LAD2 mast cell line. Constitutive IL-13 production by T_H2 cells was reduced from 18000 ± 1800 pg/ 10^6 cells by 68.6% (95% CI 62.0, 75.1; $P < 0.0001$) by A549 and 59.9% (95% CI 53.3, 66.5; $p < 0.0001$) by BEAS-2B. Epithelial inhibition was similar when cells were separated by a transwell suggesting involvement of a soluble factor. Surface expression of ckit measured by flow cytometry was also reduced in the presence of epithelial cells. Epithelial cell lines inhibit a range of asthma-related mediators and reduce the cell surface expression of ckit. Deficiency in this process may be important in the pathogenesis of the abnormal airway responses seen in asthma.