

P001 Human Pulmonary Artery Endothelial Cells (HPAEC) Secrete A Novel Protein That Inhibits Eosinophil Apoptosis
N. Farahi, P. Upton, J. Deighton, N.W. Morrell, E.R. Chilvers and A.S. Cowburn
Respiratory Medicine Division, Department of Medicine, University of Cambridge, Addenbrooke's and Papworth Hospitals, Cambridge CB2 2QQ, UK.

Tissue eosinophilia plays a major role in asthma pathogenesis. The recognition that eosinophil apoptosis can be inhibited by IL-5 and GM-CSF suggests that enhanced eosinophil survival is a mechanism promoting eosinophil-mediated tissue damage. While the influence of certain cytokines on eosinophil apoptosis has been characterised, less is known about the effects of transendothelial migration across the vascular wall in this process. We examined the effects of HPAEC-CM on eosinophil apoptosis *in vitro*. HPAEC-CM inhibited morphological apoptosis from $28 \pm 6\%$ (DMEM) to $11 \pm 5\%$ at 24h. This was comparable to GM-CSF and IL-5 (each 10ng/ml) and confirmed by Annexin-V. The HPAEC-CM survival effect was heat-labile, trypsin-sensitive, and did not affect neutrophil apoptosis. HUVEC, smooth-muscle and fibroblast-CM did not influence eosinophil apoptosis. ELISA, antibody neutralisation and multiplexed flow cytometry excluded a role for GM-CSF and IL-5 in HPAEC-CM. Gel filtration of the HPAEC-CM revealed a peak of eosinophil survival activity at approx. 9kDa. These data suggest that HPAECs secrete a novel survival factor that inhibits eosinophil apoptosis; this factor may explain the paucity of eosinophil apoptosis observed in asthmatic airways.