Role of ICAM-2 in neutrophil transepithelial migration in the lung

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Body: Many inflammatory diseases of airways including COPD and cystic fibrosis are characterized by migration of neutrophils from the interstitium across the respiratory epithelium into the airspaces. Neutrophil transepithelial migration (egression) across the bronchial epithelial cell (BEC) barrier promotes resolution of inflammation, whereas movement across the alveolar epithelial cell (AEC) barrier, often required for pathogen control, may prove detrimental to the human and resulting lung injury. We have shown that intercellular adhesion molecule (ICAM)-2 is required for leukocyte migration across the bronchial epithelium. We have then used immunohistochemistry (IHC), to show that although ICAM-2 is expressed on the bronchial epithelium there is very little expression on the alveolar epithelium in normal human lung. Our hypothesis is that egression of neutrophils across the bronchial and alveolar epithelia are differentially regulated, and that understanding these processes is essential to develop effective ways to promote safe resolution of inflammation. Primary human (h)BECs and AECs are grown at air liquid interface on Transwell™ collagen coated polyester membranes. Then, the cells are stimulated with pro-inflammatory mediators (TNF-α, TGF-β, LPS) for 4h or 24h. IHC, qRT-PCR, western blot and flow cytometry assays of ICAM-2 are performed. The role of ICAM-2 in neutrophil migration across hBEC and hAEC monolayers in the physiological basal to apical direction is observed. Our results establish the role of ICAM-2 in regulating neutrophil-epithelial interactions in the lung and the central role of this molecule in the resolution of inflammation.