A role for squamous metaplasia in COPD airway obstruction

Airway wall thickening has been established as an important factor in airway obstruction in patients with COPD, and squamous metaplasia of columnar epithelium correlates with the severity of airway obstruction. Here, through a number of experiments, the authors provide evidence for a mechanistic link between these two processes. An in vitro model of airway squamous metaplasia was created using human airway bronchial cells in serial culture which closely resembled metaplastic squamous epithelium in COPD in vivo. The levels of interleukin (IL)-1β and IL-1α were increased as cells underwent squamous metaplasia, with IL-1β and IL-1α genes among the most highly induced during epithelial cell passage. Levels of transforming growth factor β (TGF-β), a fibrogenic cytokine activated via the integrins αvβ6 and αvβ8, was also increased with increasing disease severity. The authors co-cultured squamous metaplastic cells and human airway fibroblasts and analysed the changes in COPD lungs in pneumonectomy samples. They then put forward a model whereby squamous metaplastic epithelial cells activated fibroblasts through IL-1β-dependent upregulation of integrin αvβ8 on small airway fibroblasts. This resulted in TGF-β activation, increased matrix production and contractility and, ultimately, airway wall thickening. This study did not evaluate the effect of the basement membrane on paracrine interactions between epithelial cells and fibroblasts, but highlights a potentially important role for squamous metaplastic cells in the pathogenesis of airway obstruction in COPD.

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