Letter

Idiopathic pulmonary fibrosis: an epithelial/fibroblastic cross-talk disorder

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The recent review by Selman and Pardo in this journal [1] correctly points out that in idiopathic pulmonary fibrosis (IPF) there is insufficient evidence to suggest that chronic inflammation plays a primary role in pathogenesis and that animal experimental models of pulmonary fibrosis therefore do not model IPF particularly accurately. However, the suggestion in the accompanying commentary by Gauldie and colleagues [2] that this "suggests a new hypothesis for the aetiology of this progressive and usually fatal disease" seems to be stretching the point.

In a review published in 1995, Kumar and Lykke [3] discussed lymphocyte-macrophage-fibroblast as well as epithelial cell-fibroblast and reciprocal interactions in pulmonary fibrosis. We stated that " [i]njury to alveolar epithelial cells, especially type 2 pneumocytes, appears to be an important event in the genesis of pulmonary fibrosis. Both in vitro and in vivo studies suggest that failure to replace damaged type 1 epithelium by proliferation and differentiation of type 2 pneumocytes may be a determinant of whether or not progression to fibrosis ensues." The references cited at this point included not only the studies by Adamson and colleagues [4] to which Selman and Pardo refer, but also data from an animal model of resolving *vs.* non-resolving pneumonia [5].

Furthermore, we discussed the alveolar epithelial changes in pulmonary fibrosis and pointed out that " [b]oth in animal experimental models and in the human disease, these cuboidal epithelial cells develop cytoplasmic extensions ('spikes') which protrude through the epithelial basement membrane. The spikes may become intimately associated with interstitial fibroblastic cells, a finding that is especially noticeable in 'usual interstitial pneumonitis' associated with epithelial hyperplasia. These observations strongly suggest that 'handshakes' between type 2 pneumocyte-like epithelial cells and fibroblasts might take place during the development of pulmonary fibrosis." This part of the review included references to numerous descriptions of such spikes in the 1980s literature, electron micrographs demonstrating the spikes both in IPF and in murine bleomycin-induced pulmonary fibrosis, and discussion of the potential role of epithelial cell-derived transforming growth factor-β (and other growth factors) in the induction of fibrosis.

Although this review was not published in a respiratory sciences journal, it has been cited in standard textbooks [6,7], so one could reasonably argue that the concept of IPF as a disorder involving perturbed epithelial/fibroblastic cross-talk is not altogether novel.

Abbreviations

IPF = Idiopathic Pulmonary Fibrosis

References

1. Selman M, Pardo A **Idiopathic pulmonary fibrosis: an epithelial/fibroblastic cross-talk disorder.** *Respir Res* 2002, **3**:3
2. Gauldie J, Kolb M, Sime PJ **A new direction in the pathogenesis of idiopathic pulmonary fibrosis?** *Respir Res* 2002, **3**:1
3. Kumar RK, Lykke AWJ **Messages and handshakes: cellular interactions in pulmonary fibrosis.** *Pathology* 1995, **27**:18-26
4. Adamson IYR, Young L, Bowden DH **Relationship of alveolar epithelial injury and repair to the induction of pulmonary fibrosis.** *Am J Pathol* 1988, **130**:377-83
5. Rhodes GC, Lykke AWJ, Tapsall JW, Smith LW **Abnormal alveolar epithelial repair associated with failure of resolution in experimental streptococcal pneumonia.** *J Pathol* 1989, **159**:245-53
6. Kumar V, Cotran RS, Robbins SL **Basic Pathology, edn 6, ch 13.** *Philadelphia: WB Saunders* 1997,
7. Cotran RS, Kumar V, Collins T **Robbins Pathologic Basis of Disease, edn 6, ch 16.** *Philadelphia: WB Saunders* 1999,