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Successful infection of the respiratory tract occurred with detection of the 40-kd core protein of biglycan or decorin by Western blot analysis in the BAL at 3 and 7 days. Histologic findings from the lungs of animals infected with the AdBGN showed a fibroblastic response in the interstitium and a fibrotic thickening of the pleura, with evidence of increased collagen but not elastin deposits at both sites using specific histochemical staining (elastin van Gieson [Miller stain]). These interstitial and pleural changes were evident at day 7 and 14 but had largely resolved by day 21. No such fibroblastic responses were seen in the AdDEC- or the AdE1 delete-treated animals.

In conclusion, we have demonstrated a successful system for transiently overexpressing the core proteins of the small proteoglycan biglycan or decorin and suggest that biglycan may play a novel role in the process of fibrogenesis aside from its structural function.

Adenovirus-Mediated Gene Transfer of the Proteoglycan Biglycan Induces Fibroblastic Responses in the Lung*

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Biglycan and decorin are small chondroitin-dermatan sulfate proteoglycans which form part of the extracellular matrix. In addition to their structural roles, they may have other important effects on cell behavior by binding via their core proteins to the potentially fibrogenic cytokine transforming growth factor-β1, and indeed their expression is altered in fibrotic tissues from lung, kidney, and liver. Previous studies on the role of these proteoglycans have been difficult due to the problems of purifying them from tissues in sufficient quantities. We have therefore engineered replication-deficient recombinant adenovirus 5 vectors expressing the cDNAs of the human biglycan [AdBGN] and decorin [AdDEC] core proteins and used these to transiently overexpress biglycan and decorin in the rat respiratory tract.

Sprague-Dawley rats were injected intratracheally with 10⁶ plaque-forming units of AdBGN, AdDEC, or control [E1 delete] virus, and the BAL fluid and lung tissues were examined at time points from 3 to 21 days.

Surfactant Protein and CC-10 Expression in Acute Lung Injury and in Response to Keratinocyte Growth Factor*

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The alveolar epithelium is a critical element in response to acute lung injury. Recently, the surfactant proteins SP-A and SP-D have been found to be elevated in the serum of patients with pulmonary fibrosis and diffuse type II cell hyperplasia. It is possible that the expression of these two proteins is regulated in part by inflammatory cytokines.

We recently demonstrated that keratinocyte growth factor (KGF) was a potent mitogen for type II cells, could alter surfactant protein gene expression in vitro, and could protect against lung injury due to acid instillation, bleomycin, or oxygen toxicity. The current study was designed to measure surfactant protein gene expression during injury due to acid instillation, and during the protection afforded by pretreatment due to KGF. As a control, we measured the effect of KGF on the mRNA for surfactant proteins in the normal lung. Because of alterations in small airways, we also measured CC-10 which is a differentiation marker for nonciliated bronchiolar cells.

Adult Fischer 344 rats were intubated and 0.5 mL of 0.1N hydrochloric acid (HCl) was instilled into the left lung on day 0. Saline (0.5 mL) or KGF (5 mg/kg/0.5 mL) was given by unilateral instillation 3 days before HCl

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