blasts correlated directly with mortality in our small series of patients. Interstitial cells immunoreactive for ASMA were seen in all 3 disorders, and their presence did not correlate with survival. Patchy fibrosis with vascular prominence was noted primarily in IFP and the presence of this lesion correlated negatively with survival. Finally, a peculiar smooth muscle proliferation was identified around terminal airways in HP, in association with inflammation and foreign body reactions to inhaled material.

We conclude that the development of air space fibroblasts immunoreactive for ASMA may be a more common event in noninfectious lung disease than previously realized. Based on our findings we would speculate that contractile air space fibroplasia may be a precursor lesion to interstitial fibrosis in inflammatory lung diseases.

REFERENCES


Tropoelastin Pre-mRNA Is Alternately Spliced at Different Frequencies During Rat Lung Development

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Elastin, a major component of lung connective tissue, is important for alveolar development and maintenance of normal lung structure. The elastin precursor, tropoelastin, is encoded by a single multi-exon gene and its pre-mRNA is alternatively spliced in several species. We found that the rat tropoelastin pre-mRNA is subject to alternative splicing in 2 regions: 1 corresponding either to exons 13-15 or to exons 14-15 (by analogy to the bovine gene), and the other mapping to sequences beginning at the equivalent of bovine exon 33. The objective of this study was to examine potential developmental or tissue-specific regulation of splice site usage.

Total RNA was extracted from pooled aorta, lung, or skin tissues obtained from neonatal (10-d) and adult (6-wk) rats. An overlapping set of rat tropoelastin cDNA clones was used as probes in S1 nuclelease protection assays. Autoradiographs were scanned by densitometry to determine the frequency of alternative splice site usage. Messenger RNAs lacking exons 14 + 15 were observed at low frequency in all tissues. Within a given tissue in neonatal or adult rats, the 3 sites of alternative splicing were used at different frequencies. In general, the frequency of alternative splicing, and particularly the frequency of alternative splicing at exon 33, decreased in adult tissues. Some differences in use of alternative splice sites were also observed between tissues at each developmental stage, with the greatest differences observed in skin vs aorta and lung at 10 d and 6 wk.

We conclude that the frequency of alternative splicing is developmentally regulated and tissue specific. The regulation of tropoelastin pre-mRNA by alternative splicing during the neonatal period could have significant implications for the role of elastin in lung development and in resynthesis of elastin after lung injury.

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