

Abstract

Cystic Fibrosis (CF) is the most common lethal inherited disease in the Caucasian population with an incidence of approximately 1 in 2,500 live births. Pulmonary complications of CF, which are the most morbid aspects of the disease, are due to primary abnormalities in epithelial cells that lead to impaired mucociliary clearance. One potential therapeutic strategy is to reconstitute expression of the CF gene in airway epithelia by somatic gene transfer. To this end we have developed an animal model of the human airway using bronchial xenografts and have tested the efficiency of *in vivo* retroviral gene transfer. Using the LacZ reporter gene we find the efficiency of *in vivo* retroviral gene transfer to be dramatically dependent on the regenerative and mitotic state of the epithelium. Within an undifferentiated regenerating epithelium in which 40% of nuclei label with BrdU, 5-10% retroviral gene transfer was obtained. In contrast, no gene transfer was noted in a fully differentiated epithelium in which 1% of nuclei labeled with BrdU. These findings suggest that retroviral mediated gene transfer to the airway *in vivo* may be feasible if the proper regenerative state can be induced.

Key Words: Gene Therapy, Cystic Fibrosis, Recombinant Retroviruses, Airway Epithelial Cells, and Gene Transfer.