Rhamnolipids: essential virulence factors for early invasion of primary human airway epithelium by Pseudomonas

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The opportunistic bacteria Pseudomonas aeruginosa (Pa) cause chronic respiratory infections in cystic fibrosis. However, the mechanism by which the pathogen interacts with the respiratory mucosa is not fully understood. The study provides direct evidence for a previously unknown mechanism whereby purified rhamnolipids, applied on the surface of the epithelia, are sufficient to promote the paracellular invasion of Pa, even of strains deficient in the quorum sensing systems; 3) at variance with previous reports, Pa remains exclusively in the paracellular space of the epithelia; 4) fluorescent rhamnolipids interact with the apical cell membrane, indicating a specific alteration of ciliated cells, between which pathogens infiltrate and 5) blockade of this interaction prevents early Pa infection. The study provides direct evidence for a hitherto unknown mechanism whereby the junction-dependent barrier of the respiratory mucosa is selectively altered by rhamnolipids, thereby accounting for its invasion by Pa.

Factors influencing adenovirus-mediated airway transduction in fetal mice


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Fetal gene therapy for the treatment of cystic fibrosis has several advantages over similar treatment in the adult. Treatment before birth may allow avoidance of in utero pathology and may allow permanent correction of the genetic defect by transduction of fetal stem cells. Intranasal injection of marker/vector allows access to the fetal airways following natural fetal breathing movements. This administration method is promising for use in gene therapy for cystic fibrosis where the main target for exogenous gene expression is the lung. Here, we have investigated factors that may affect the efficacy of gene transfer to the murine fetal lung. We examined marker compound distribution and transgene expression (from a first generation adenoviral vector) at different stages of fetal development. This demonstrated that fetal breathing movements at 15–16 days of gestation are of sufficient intensity to carry marker/vector into the fetal lung. These movements can be significantly stimulated by the combination of intra-amniotic theophylline administration and post-operative exposure of the dam to elevated CO2 levels. However, the most important factor for efficient and consistent pulmonary transgene delivery is the dose of adenoviral vector used, as both the degree of transduction and the percentage of lungs transduced increases with escalating viral dose.