|  |
| --- |
| **Localised *pseudomonas aeruginosa* lung infection in cystic fibrosis rat models** |
| Nicole Reyne1-3, Bernadette Boog1-3, Patricia Cmielewski1-3, Alexandra McCarron1-3, Ronan Smith1-3, Nina Eikelis4, Kris Nilsen4, John Finnie2, Jennie Louise5, David Parsons1-3 and Martin Donnelley1-3. |
| *1 Robinson Research Institute, University of Adelaide, Adelaide, South Australia, Australia*  *2 Adelaide Medical School, University of Adelaide, Adelaide, South Australia, Australia*  *3 Respiratory and Sleep Medicine, Women's and Children's Hospital, Adelaide, South Australia, Australia*  *4 4DMedical, Melbourne, Victoria, Australia*  *5 Biostatistics Unit, South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia* |
| **Introduction/Aim:**  Recurrent *Pseudomonas aeruginosa* infections cause chronic airway inflammation, lung damage and eventual respiratory failure, leading to high morbidity and mortality in people with CF. While CF animal models reflect different aspects of CF pathophysiology, few fully replicate lung disease. Introducing bacteria that are embedded in agar beads into wildtype and CF animal lungs can stimulate persisting lung infections that mimic the chronic nature of clinical CF infections. This study evaluated a localised CF-like lung infection model in WT and two CF rat models.  **Methods:**  A miniature bronchoscope was used to deliver 50 μl of *P. aeruginosa* embedded agar beads to the right main bronchus of wildtype, knockout, CF and *Phe508del* rats. The effects of the infection were measured at 7, 14 or 21 days using flexiVent and X-ray Velocimetry assessments to quantify lung function. Rats were then humanely killed with bacterial counts, bronchoalveolar lavage, and histology performed. **Results:**  Lung infections were produced in all rat genotypes and persisted for at least 21 days. Knockout rats showed a higher inflammatory response than wildtype after 7 days, which remained elevated from baseline level at 21 days. Histological analysis in knockout rats exhibited widespread alveolar thickening, while wildtype and *Phe508del* rats demonstrated focal inflammation surrounding agar beads. Delivering bacteria to a single lobe produced a localised infection without compromising the health of the whole lung, thus reducing associated mortality, and improving rat welfare.  **Conclusion:**  We have successfully developed a practical method to induce a localised, chronic *P. aeruginosa* infection in CF rats, providing a valuable tool for CF lung research. Using a miniature bronchoscope, bacterial-laden beads could be precisely delivered, creating a controlled infection lasting at least three weeks, with minimal health impact. This model should have value in studying targeted treatments for *P. aeruginosa* infection.    **Grant Support:** |