Generation of new cystic fibrosis rat models in Australia using CRISPR/Cas9 genome editing

Chantelle McIntyre1,3, Martin Donnelly1,3, Patricia Cmielewski1,3 and David Parsons1,3
1. Robinson Research Institute, 2. Adelaide Medical School, University of Adelaide, South Australia
3. Respiratory and Sleep Medicine, Women’s and Children’s Hospital, South Australia

Background: Cystic fibrosis (CF) mice do not develop spontaneous CF-like lung disease, and so they are unsuited to understanding CF lung pathogenesis and testing therapies. The first CF rats produced in the USA (Birke 2015, Tuggle 2014) have shown an excessive mucus production in the lung, abnormal submucosal gland formation and impaired bacterial clearance

**Aim:** To establish and characterise a CF rat model on a Sprague Dawley background for use in Australia in studies of CF airway gene correction.

**Results:** The Adelaide CF rat colony has generated more than 70 CF individuals to date and characterisation is underway. Light microscopic observations of lung and trachea from a limited number of CF rats has not revealed clear respiratory differences compared with normal rats at 8 weeks of age (data not shown). However, differences in weight, mortality, tooth development and gut histology are observed by 8 weeks of age and earlier.

**Conclusion:** Similar to the USA-developed CF rats, the Australian CF rat has not shown clear respiratory abnormalities by 8 weeks of age, although we anticipate changes to occur at later time points. Characterisation of the rats is ongoing and will utilise nasal and tracheal potential difference measurements, immunohistochemistry, and computed tomographic x-ray velocimetry, among other methods, for the assessment of CF abnormalities in animals at more advanced ages than those currently reported.

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