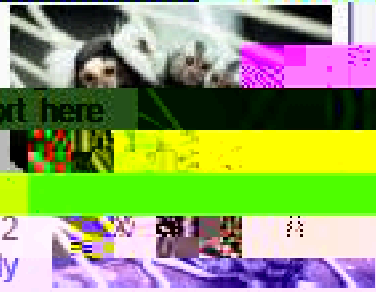
AIRWAY LENTIVIRAL GENE TRANSFER IN MARMOSETS

David Parsons[1,3,4,5]

1. Respiratory and Sleep Medicine, Women's and Children's Hospital, Adelaide, South Australia
2. Gene Technology Unit, SA Pathology, Adelaide, South Australia
3. Department of Paediatrics, University of Adelaide, Adelaide, South Australia
4. Centre for Stem Cell Research, University of Adelaide, Adelaide, South Australia
5. Women's and Children's Health Research Institute, Adelaide, South Australia

BACKGROUND: Preclinical studies in non-human primates (NHP) are important for developing clinically-appropriate gene transfer protocols to treat CF airway disea... initial findings from the first studies of LV lung gene transfer ... *jacchus* (Fig 1). Marmosets typically have a lifespan of ~12 years, a body weight of ~250-350g and are ... increasingly used animal model for gene manipulation studies.



MATERIALS AND METHODS: LPC pre-treatment (0.1%, 200-350 µl) was followed 1 hour later ... samples were collected to examination the presence of vector particles. It is plann... the remaining two animals will be examined by the end of 2012.

RESULTS: A rapid but transient O_2 desaturation was present in some animals after LPC administration, however all behavioural and physiological indices were normal post-procedure.

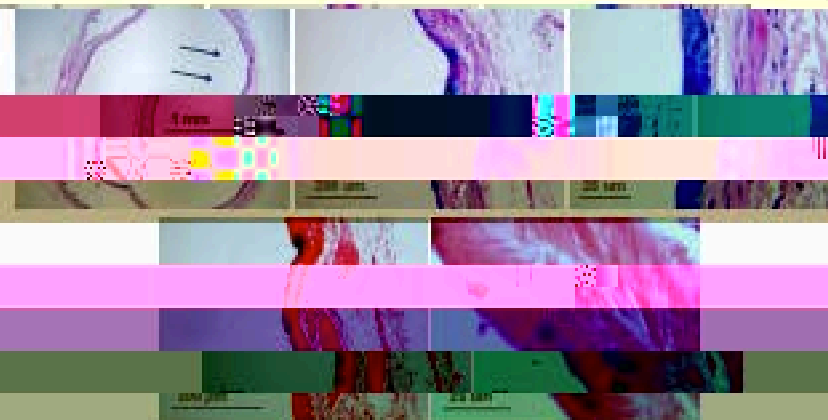
Body weights followed usual post-anaesthesia trajectories. Patchy epithelial cell LacZ gene expression was evident en face (Fig 2) and in cross-sections (Fig 3, 4), primarily in conducting airways.

No evidence of LacZ gene expression was detected in any other organ tissue.

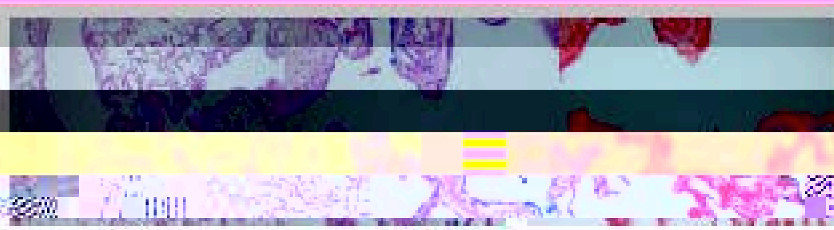
LV vector capsid protein levels (p24) were present in serum at Day 1 but absent from Day 2 onwards (Fig 5).

Histological, immunological and RT-PCR analyses await completion for the 2 remaining animals (Fig 6).

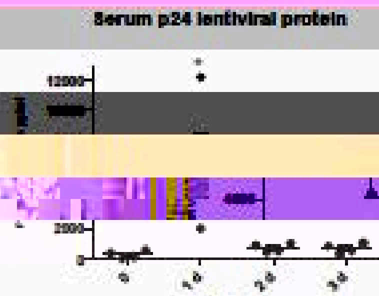
(2) En face examples of lung LacZ gene expression.



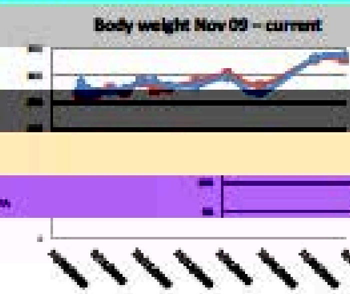
...on in cross sections. H/E and Saf-O staining. Ciliated ...



(4) LacZ transduction in distal airways.



(5) Lenti... protein was briefly present in serum.



(6) ... weights of long term animals are ... normal trajectory.

CONCLUSION: These initial st... LPC/LV dosing procedures are well-tolerated and can produce transgene expression in this non-human primate lung. Two ad... animals are being maintained for longer-term assessment of single-dose lung gene transfer. Gene vector components can reach the vascular space after airway dosing, indicating attention to host immunity and vector distribution is warranted. The marmoset appears a suitable animal model for testing airway gene transfer procedures prior to consideration of human clinical trials.

ACKNOWLEDGEMENTS: Studies supported by NH&MRC and philanthropic donors via www.CURE4CF.org