SUSTAINED REPORTER AIRWAY GENE EXPRESSION WITH A LENTIVIRAL VECTOR IN CYSTIC FIBROSIS MICE

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Introduction

Non-invasive bioluminescence imaging has allowed for rapid *in-vivo* quantification of long-lasting gene transfer in experimental animals. We studied the sustainability of lentiviral (LV) reporter gene transfer over the lifetimes of cystic fibrosis (CF) mice.

Methods

CF^{tm1unc} mice received a nasal bolus of lysophosphatidylcholine (LPC) or control (PBS) pre-treatment one hour prior to delivery of a LV vector containing the reporter gene luciferase (LV-Luc). Another control group received LPC one hour prior to an empty vector (LV-MT). Bioluminescence was measured at 1 wk & 1, 3, 6, 9, 12, 15 [illegible] dosing. Circulating antibodies to the Luc transgene were analysed in ser[illegible] by ELISA at all time points.

Results

Nasal bioluminescence was significantly increased with LPC/LV-Luc compared to controls for 12 months (Fig. 1a, $p<0.05$, ANOVA). There was no difference in lung luminescence between the LPC and PBS pre-treated mice that received LV-Luc (Fig. 1b). No bioluminescence was detected in the airways of mice treated with LPC/LV-MT (Fig. 2). At later time points, the low sample size due to animal attrition influenced mean expression levels. There was a significant increase in the presence circulating antibodies to the Luc transgene in those mice that received LPC prior to LV-Luc compared to both cont[illegible] (Fig. 3, $p<0.05$, ANOVA). Antibodies to Luc persisted from 1 month to 21 months, peaking at 3 months, following [illegible]

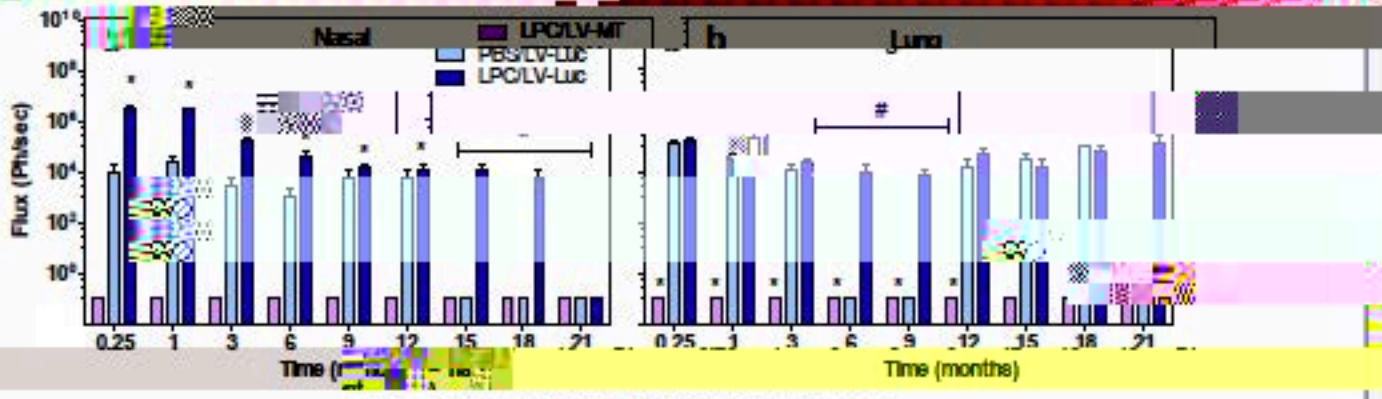

Fig. 1. a) Nasal and b) Lung LV-luciferase luminescence.
Mean +/- SEM, *p<0.05, RM ANOVA, n=3-12, # n [illegible]

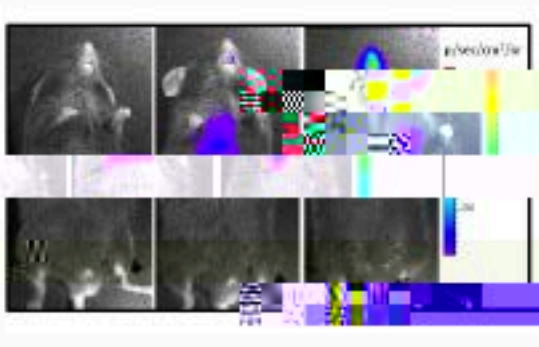

Fig. 2. LV-luciferase luminescence
LV-MT (left), PBS (middle) vs LPC (right)

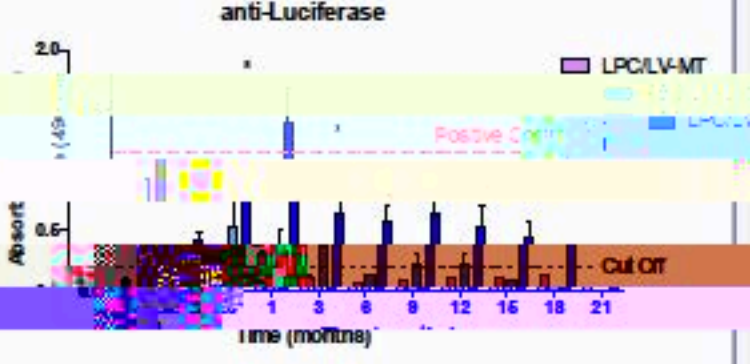

Fig. 3. Circulating antibodies to the transgene Luciferase.
Mean +/- SEM, *p<0.05, RM ANOVA, n=3-12.

Conclusions

Lentiviral luciferase gene expression was significantly improved in mouse nasal airways using LPC pre-treatment. However, pre-treatment made no difference to luciferase expression in lungs of CF mice. The presence of circulating antibodies to luciferase for longer than 18 months suggests an immune response to a sustained long term transgene expression.

Acknowledgements

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Cure4CF.org)