BIOLUMINESCENCE GENE EXPRESSION WITH A LENTIVIRAL VECTOR IN AIRWAYS OF CYSTIC FIBROSIS MICE

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Introduction

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

Methods

[illegible] received a nasal bolus of lysophosphatidylcholine (LPC) or control [illegible] received LPC one hour prior to an empty vector (LV-MT). Bioluminescence was measured at 1, 3, 6, 9, 12, 15, 18, 21 and 27 months after [illegible]. Circulating antibodies to the Luc transgene were analysed in sera by E[illegible] at all time points.

Results

Nasal 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 of circulating antibodies to the Luc transgene in those mice that received LPC prior to LV-Luc compared to both [illegible] to Luc persisted from 1 month to 21 months, peaking at 3 months, following a single gene therapy dose of LPC/LV-Luc.

There was no difference in lung luminescence between the LPC and PBS pre-treated mice.

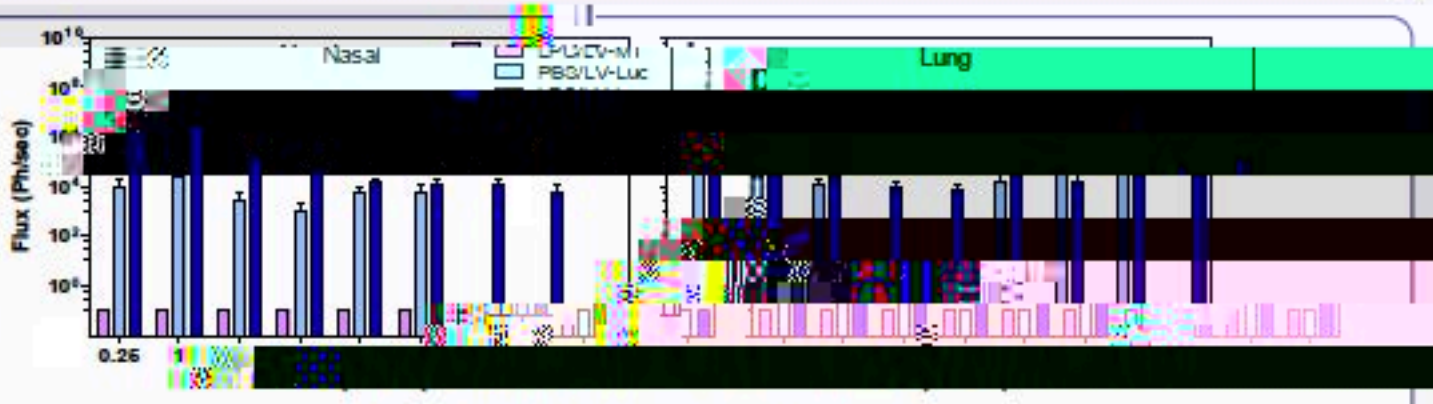

Fig. 1. a) Nasal and b) Lung LV-luciferase luminescence.
Mean +/- SEM,*p<0.05, RM ANOVA, n=3-12, # n too low for analysis.

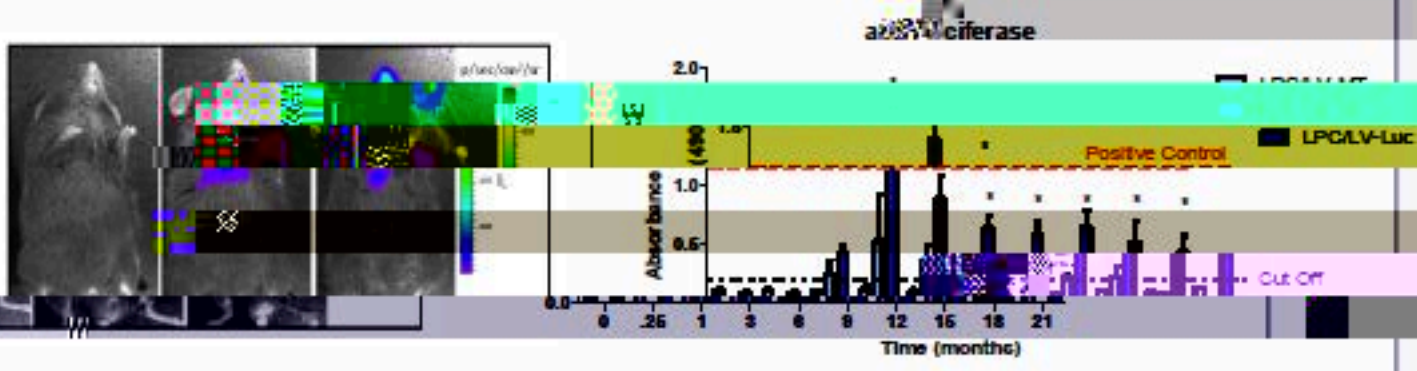

Fig. 2. LV-luciferase luminescence

Fig. 3. Circulating antibodies to the transgene Luciferase.

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 the 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 [illegible]

Ackno[illegible]

Dr Don Anson for LV vector [illegible]