DIFFERENCES IN LONGEVITY OF LENTIVIRAL LUCIFERASE EXPRESSION IN AIRWAYS OF NORMAL AND 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 are testing the longevity of a single nasal delivery of our lentiviral (LV) gene transfer system in normal and cystic fibrosis (CF) mouse airways.

Methods

Normal (C57Bl/6) and cystic fibrosis (CF) mice received a nasal bolus of lysophosphatidylcholine (LPC) or a 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 week (Fig. 1a, b) & 1, 3 months and 3 monthly intervals until 21 or 24 months after LV dosing to assess the level and longevity of gene transfer.

Results

Normal mice: Mice that received LPC/LV-Luc treatment had significantly greater gene transfer compared to the two control groups at all time points ($p<0.05$, RM ANOVA, Fig 2a). No luminescence was detected in mice treated with LPC/LV-MT. Unexpectedly luciferase activity was also detected in the lung. There was no difference in lung luminescence between the LPC and PBS pre-treated mice that received LV-Luc (Fig 2b). **CF mice**: A statistically significant increase in nasal luminescence persisted for up to 6 months following LPC/LV-Luc ($p<0.05$, RM ANOVA, Fig 2a). Similar to normal mice, there was no statistical difference in lung luminescence between mice that received LPC and PBS LV-Luc (Fig 2b).

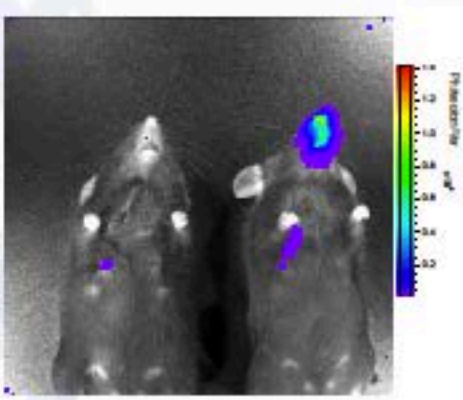

Fig. 1a. LV-luciferase luminescence
Normal mice: PBS (left) vs LPC (right)

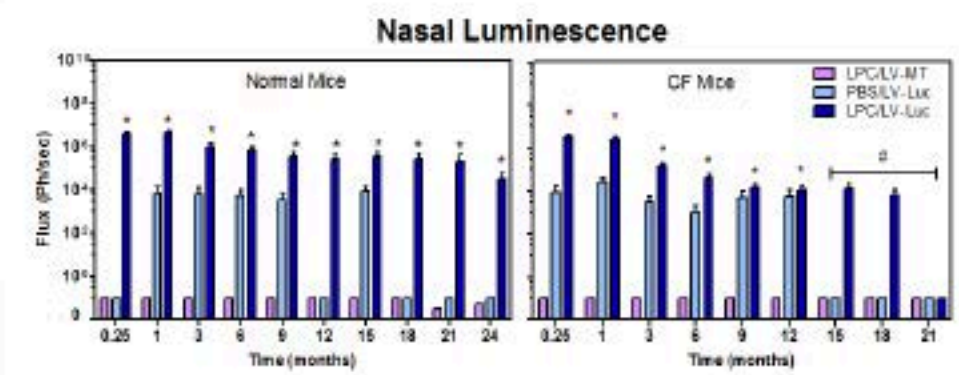

Fig. 2a. Nasal LV-luciferase luminescence. Normal (left) vs CF mice (right), Mean +/- SEM,*p<0.05, RM ANOVA, n=3-12, # n too low for analysis.

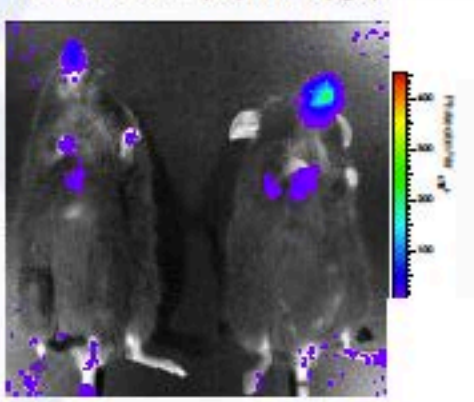

Fig. 1b. LV-luciferase luminescence
CF mice: PBS (left) vs LPC (right)

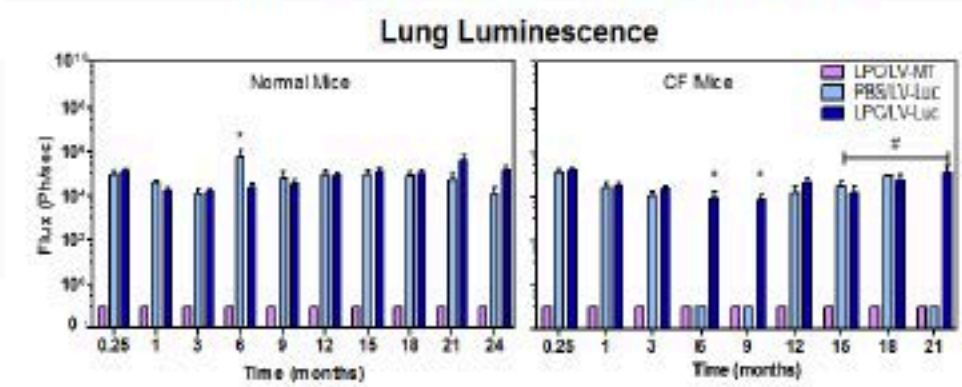

Fig. 2b. Lung LV-luciferase luminescence. Normal (left) vs CF mice (right), Mean +/- SEM, *p<0.05, RM ANOVA, n=3-12, # n too low for analysis

Conclusions

Lentiviral luciferase gene expression was significantly improved in mouse nasal airways using LPC pre-treatment in both strains. However the longevity of transduction was reduced in CF mice, which may, in part, be due to reduced animal numbers affecting statistical analyses at the later time points tested.

Acknowledgements

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