INCREASED *IN-VIVO* SENSITIVITY FOR TRANSGENE EXPRESSION IN MURINE NASAL AND LUNG AIRWAYS USING LUCIFERASE IMAGING

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Introduction

Non-invasive bioluminescence imaging has allowed for rapid and in vivo quantitation of long-lasting gene therapeutic transfer in experimental animals. We are testing the longevity of single nasal delivery of our lentiviral gene transfer system in mouse airways.

Methods

One nostril of C57Bl/6 mice was treated by a bolus instillation of a control (PBS) or the detergent lysophosphatidylcholine (LPC) one hour prior to delivery of LV containing the reporter-gene luciferase (Luc) at $1.8x10^{10}$tu/ml. Imaging to detect luminescence was performed using the IVIS system (Xenogen) 10-15 minutes after a 50µl intranasal bolus of the substrate D-luciferin (15mg/ml PBS stock), at 1 week (Fig. 1a) and 1, 3 and 6 months (Fig. 1b) post LV.

Results

LPC pre-treated LV gene transfer resulted in significantly greater nasal gene transfer compared to PBS pre-treatment at all time points (*p<0.05, ANOVA). A significant reduction in nasal luminescence was noted at 3 and 6 months compared to 1 week for LPC pretreated animals (# p<0.05, RM ANOVA, Fig. 2). Luciferase activity was also detected in the lung in [illegible] mice. By the 6 month time point an increase in lung luminescence was observed in mice pre-treated with PBS prior to LV (# p<0.05, RM ANOVA).

Results

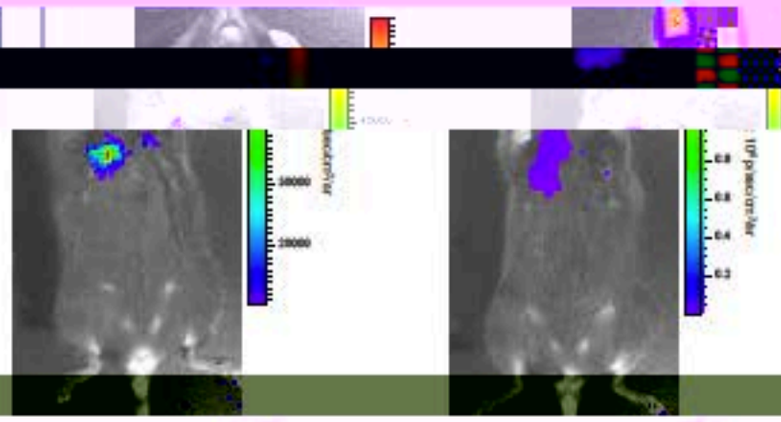

Fig. 1a. 1 week LV-luciferase luminescence PBS (left) vs LPC (right)

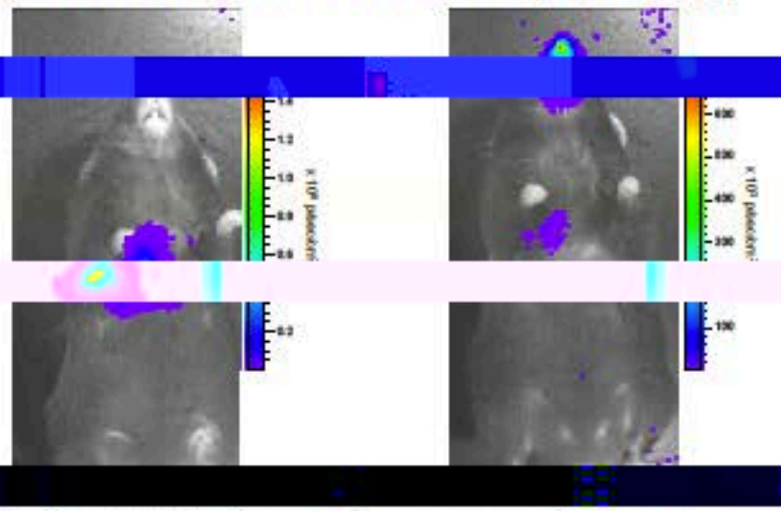

Fig. 1b. 6 months LV-luciferase luminescence; same animals as above

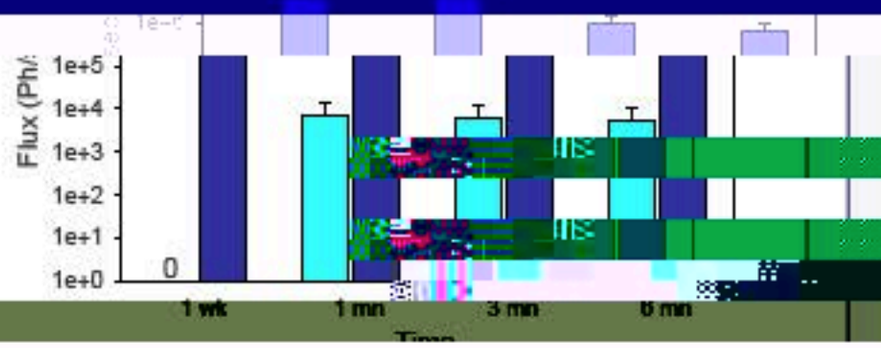

Fig. 2. Nasal LV-luciferase luminescence

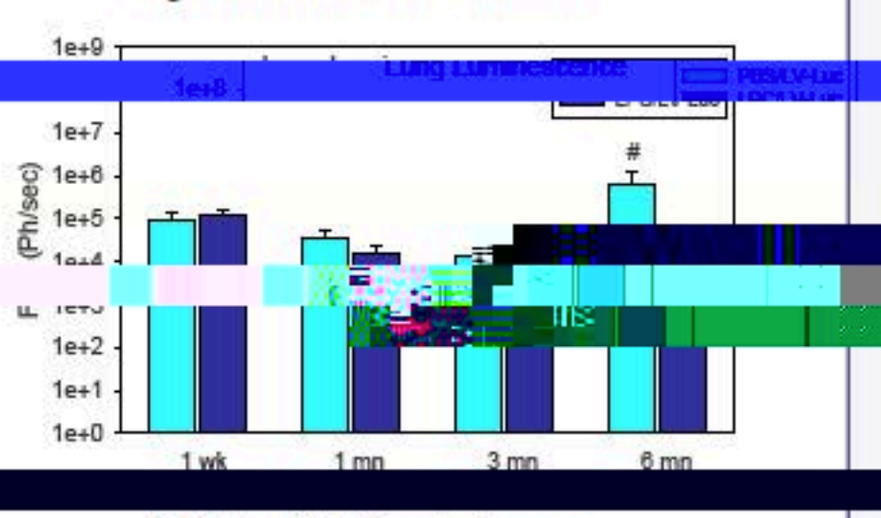

Fig. 3. Lung LV-luciferase luminescence

Conclusion

Nasal epithelial luciferase ge[illegible] and was enhanced with LP[illegible] pre-treatment. The luciferase gene expression could also be detected in the lung, with or without LPC pre-treat[illegible] is in contrast to LacZ reporter gene expression; after similar nasal administration LacZ was only detected in nasal airways. The luciferase re[illegible] reporter gene has greater sensitivity for in vivo gene transfer detection

Acknowledgement

[illegible] donors (www.[illegible]