

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



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Introduction

Non-invasive bioluminescence imaging has allowed for rapid *in-vivo* quantification of long-term gene transfer in experimental animals. We studied the sustained expression of a lentiviral (LV) reporter gene in mice with cystic fibrosis (CF) after a single gene therapy dose of LPC/LV-Luc.

Methods

CF mice were treated with a single dose of LPC/LV-Luc or LPC/LV-MT (empty vector) one hour prior to an empty vector (LV-MT). Bioluminescence was measured at 1 week and 1, 3, 6, 9, 12, 15, 18 and 21 months after LV dose. Circulating antibodies to the Luc transgene were analysed in sera by ELISA at all time points.

Results

There was no difference in lung luminescence between the LPC and FBS pre-treated mice. 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 no significant increase in the presence of circulating antibodies to the Luc transgene in those mice that received LPC prior to LV compared to both FBS and empty vector. The presence of antibodies to Luc persisted from 1 month to 21 months, peaking at 3 months, following a single gene therapy dose of LPC/LV-Luc.

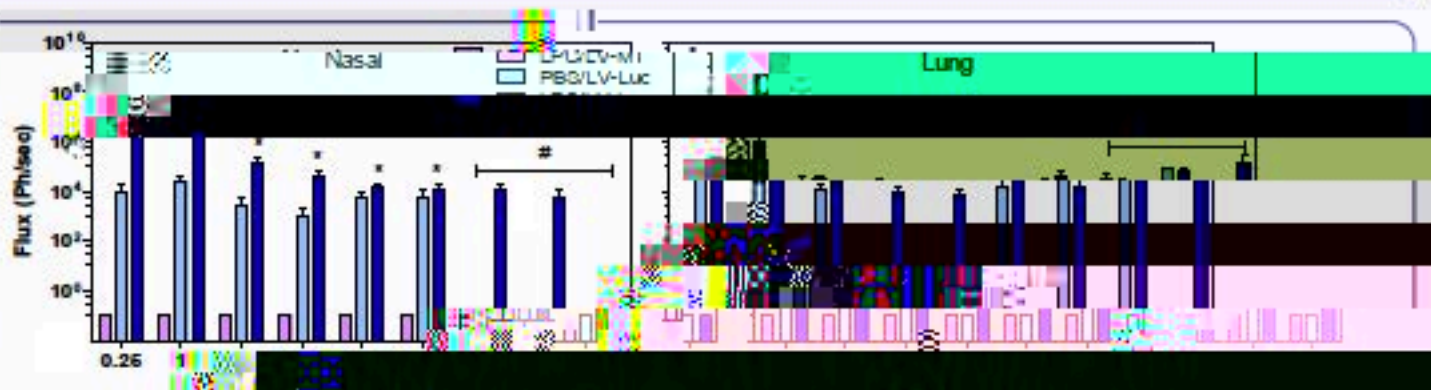


Fig. 1. a) Nasal and b) Lung LV-luciferase luminescence. Mean +/- SEM, *p<0.05, RM ANOVA, n=3-12, # n too low for analysis.

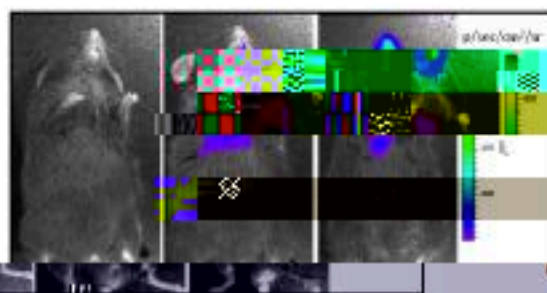


Fig. 2. LV-luciferase luminescence

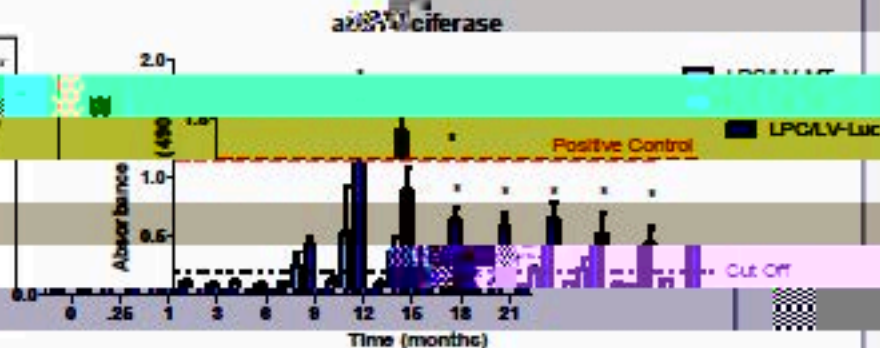


Fig. 3. Circulating antibodies to the transgene Luciferase.

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

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