AIRWAY TRANSDUCTION WITH A BACULOVIRUS GP64 LENTIVIRAL VECTOR IS INEFFICIENT IN THE ABSENCE OF PRETREATMENT

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Lentivirus vectors are being investigated as gene delivery vehicles for cystic fibrosis airway gene therapy. Vesicular stomatitis virus G glycoprotein pseudotyped lentivirus infects airway epithelia *via* receptors located on the basolateral surface of the airway epithelium. Our group has previously shown that pre-treatment of airway with lysophosphatidylcholine (LPC) allows effective transduction of the airway epithelium *in vivo*. Here we ask whether transduction *via* the apical surface with a baculovirus GP64 pseudotyped virus allows efficient gene transfer in the absence of pre-treatment.
Methods: C57Bl/6 mice received either 4 µL of LPC pre-treatment (1% w/v in phosphate buffered saline (PBS)) or 4 µl of PBS only. 1 hr later each group received 20 µL of a GP64 pseudotyped vector carrying the LacZ gene. Mice were sacrificed at 1, 4 & 12 wks, & gene transfer assessed by histological analysis of LacZ gene expression.
Results: Analysis of gene transfer showed a dramatic decrease in the level of gene transfer achieved from 1 week (58.3 ± 6 cells) to 4 weeks (13.83 ± 8 cells) in mice pre-treated with LPC. Twelve weeks post treatment, levels of gene transfer had decreased to that of background (< 1 cell). With mice pre-treated with PBS, gene transfer was seen at only very low levels at all time points equal to that of background levels.
Conclusions: In the absence of LPC pre-treatment the GP64 pseudotyped lentivirus did not result in efficient gene transfer to the airway epithelium. Since LPC enhanced gene transfer with the apically targeted GP64 lentivirus, the mechanisms by which LPC enhances gene transfer appear not to be limited to disruption of tight junctions. The lack of persistence of gene expression seen with the GP64 pseudotyped virus suggests that it does not efficiently infect progenitor cells of the airway epithelium.
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