# COMPARING THE TRANSDUCTION EFFICIENCY OF A LIQUID BOLUS AND AEROSOL DELIVERED LENTIVIRAL VECTOR FOR CYSTIC FIBROSIS LUNG GENE THERAPY

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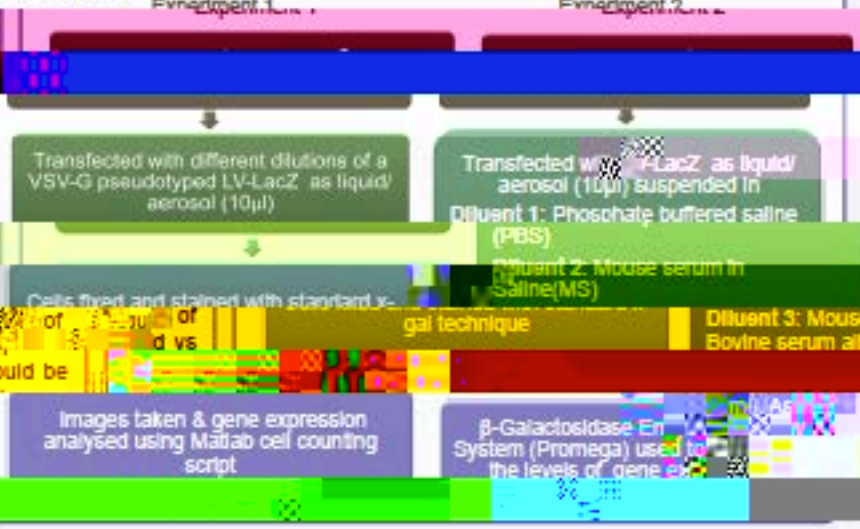
## BACKGROUND:

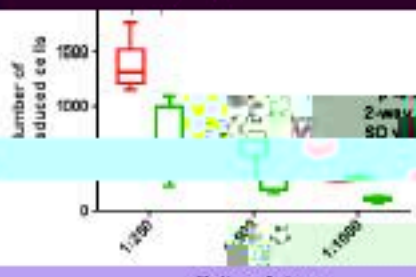
Gene therapy is a potential treatment for cystic fibrosis (CF) lung disease whereby the therapeutic gene is delivered to a gene vector to the lung is an ideal treatment approach because it is non-invasive, easy to administer and less cumbersome compared to liquid delivery. In this study we have carried out *in-vitro* experiments to test the effectiveness of aerosolising our lentiviral (LV) vector carrying the reporter gene LacZ, using a vibrating mesh nebuliser (Aeroneb®Pro). It has been speculated that the virus particles on the surface of aerosols are subjected to surface tension or stress [illegible] this study was to [illegible] effectiveness vs aerosol delivery of LV-La[illegible] if efficacy could be improved by suspending the virus in a range of diluents.

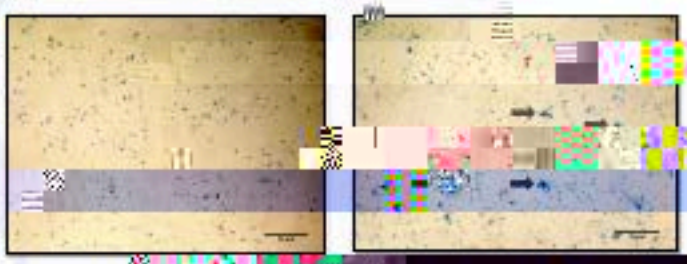
## METHODS:




## RESULTS:

- [illegible] was generally homogenous across the culture (Figure 2a) compared to the clusters observed (arrows on Figure 2b) when using the liquid bolus delivery.
- The transduction obtained via aerosol was 33% to 51% of the number of cells [illegible] dilutions of the virus (Figure 3).
- Levels of transduction were lower with aerosol delivery compared to liquid delivery when virus was suspended in different diluents (Figure 4).
- Virus suspended in MS+BSA showed significantly higher levels of transduction when compared to virus suspended in PBS (Figure 4).



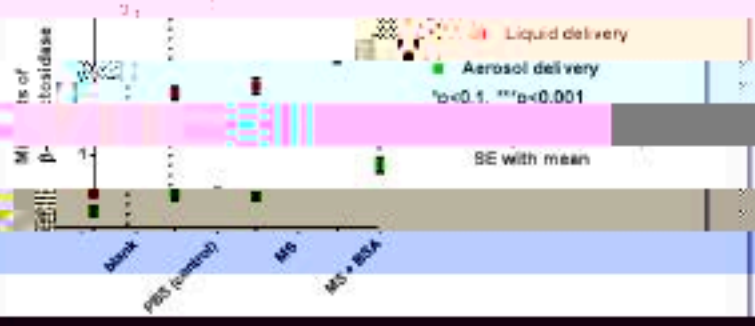



Figure 2: (a) Aerosol [illegible] (b) [illegible] delivery

## CONCLUSION:

- Cells can be transduced by an LV aerosol delivered using a vibrating mesh nebuliser (Aeroneb®Pro).
- Although the levels of transduction were lower in the aerosol group than in the liquid bolus group, the dispersion produced by the Aeroneb®Pro may be advantageous in improving transduction of [illegible]
- We speculate that the [illegible] protecting [illegible] from shear [illegible]
- To improve the levels of gene transduction we plan to test other potentially protective agents and different nebulization platforms.
- These findings assist in our understanding of LV aerosolisation and provide practical information for further testing in the lungs of animal models and ultimately for CF airway disease.

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1. Yang W, Marr LC. Mechanisms by Which Ambient Humidity May Affect Viruses in Aerosols. Appl Environ Microbiol