EXTENDS THE LIFETIME OF CF MICE

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Introduction

Effective airway gene [illegible] functionally correct the CFTR gene defect in CF airways has been the primary goal of gene therapy development in the CF mouse animal model.

In [illegible] repeated-measure [illegible] examined the success and effect [illegible] partial CFTR gene correction [illegible]

Methods

PBS (control) or 0.3% lysophosphatidylcholine (LPC - a transduction facilit[illegible] treatment) 1 hour prior to delivery of a LV-CFTR gen[illegible] A th[illegible] received LPC fr[illegible] ed by an empty LV vector control [illegible] Nasal PD was assessed at 1 wk & 1, 3 and 3 monthly intervals until 21 months following LV delivery. Survival [illegible] was expressed as K[illegible] plots. Outcomes were also compared [illegible] historical data from [illegible] with the Luc gene instead of the CFTR gene.

Results

1) A continuous partial correction of the ch[illegible] re[illegible] LPC and LV-C[illegible] [illegible] and LPC/LV-MT (to 3 mo) control groups (Fig. 2) [illegible] months (Fig.1).

2) In the two control groups the mean ΔPD after PBS pre-treatment or LV-MT treatment was not different to th[illegible] [illegible] treated CF mice (n.s. RM ANOVA).

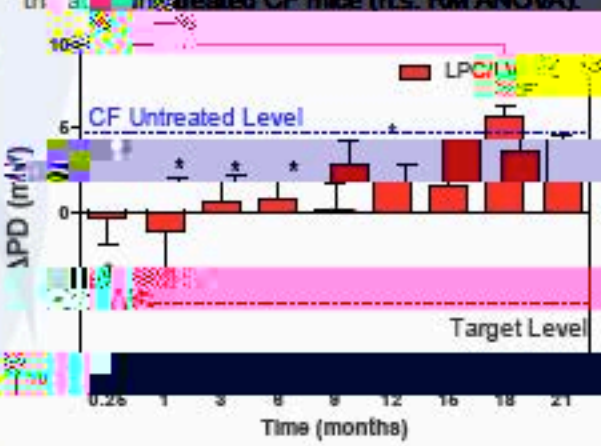

Fig. 1. Partial CFTR correction[illegible]

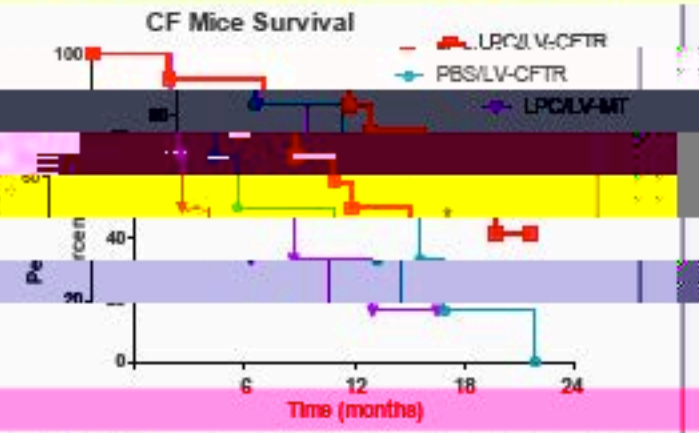

Fig. 2. Survival Curves of CF Mice (*p<0.05 Mantel-Cox log rank, n=6-12)

4) Survival in normal C57[illegible] [illegible] larly treated with the reporter gen[illegible]e Luc was no differen[illegible]e[illegible]en all groups with a median [illegible] survival greater than 23 mo[illegible]s (Fig. 3).

5) The survival of the LPC/LV-CFTR treated CF [illegible]se was not significantly different from normal untre[illegible] C57 mice.

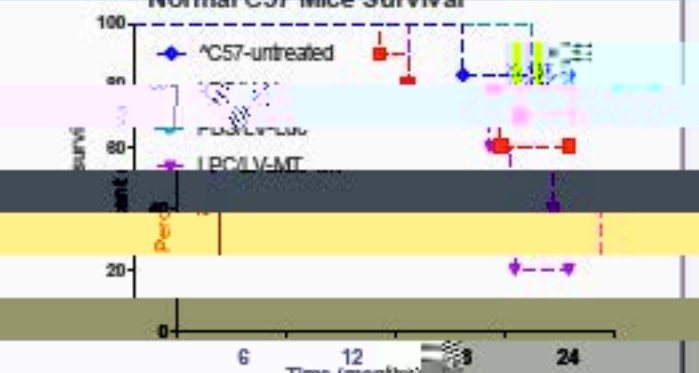

Fig. 3. Survival Curves C57 Mice (^C57 Historical data).

Conclusion

Successful nasal airway gene transfer in CF mice can significantly improve the lifetime of the treated animals. [illegible] body longevity was boosted to near that of normal C57 mice. This is the first report to our knowl[illegible] for a generalised and physiologically significant health improvement in CF animals due to partial [illegible] correction of airway CFTR dysfunction by vector gene transfer. The findings validate the therapeutic utility of LV CFTR gene transfer in a CF disease-specific animal model.

Acknowledgements

NH&MRC

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