DELIVERY OF HUMAN AMNIOTIC STEM CELLS CORRECTS CFTR FUNCTION IN CF MOUSE NASAL AIRWAYS *IN VIVO*

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Background

- Many mutation ...
- Human amnion epithelial cells (hAEC) are immune-privileged epithelial cells that can be readily harvested from placenta after birth.
- Our *in vitro* studies (Kicic et al, unpublished) suggest that when CF airway epithelium is co-cultured with hAEC, hAEC can improve CFTR-associated defects such as increasing a low airway surface liquid (ASL) depth ... renewing defective epithelial chloride-ion transport.
- This study tested if delivery of hAEC to the (CFTR-defective) nasal airways of CF mice could improve the standard functional indicator of CFTR protein expression in CF airways - the nasal airway potential difference (PD) under low chloride perfusion.

Methods

- We employed a repeated-measures study design to measure the change in the bioele... defect in nasal airways in CF mice using ... (total n=24 CF mice, 12 ...
- ... solutions with or without chloride, infused into the nasal airway at a rate of 1µl/min (Figure 1).
- Nasal PD ... (baseline).
- Mice received either: a) 30 µl of condi... alone (media derived from hAEC cultures), or b) 0.5 -1.1 x10⁶ cells/ml in 30µl of hAEC in conditioned-media.
- Treatment was instilled into the ... aliquots, delivered a... minute intervals.
- PD was again measured at 1 at 7 days after delivery.

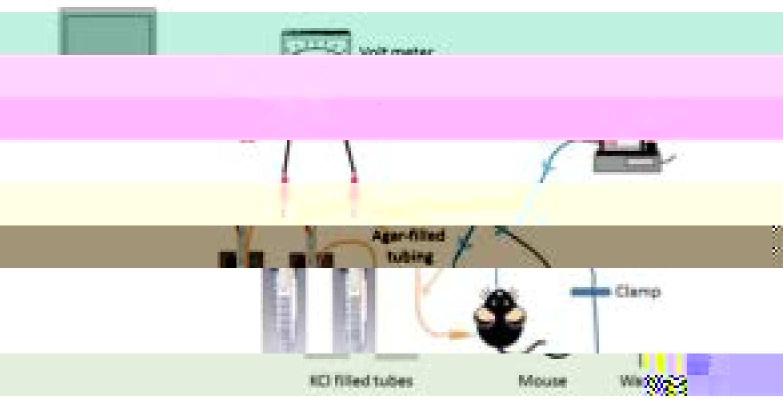

Figure 1: Diagrammatic representation of nasal PD setup

Results

- For the mice that r... *p<0.05 vs baseline, ... 2.83 ± 1.79) was not significantly different to baseline (Figure 2a).
- Nasal PD tested in the same animals following hAEC delivery (Figure 2b) retained a significantly-improved level of airway PD at both 1 day (ΔPD 0.68 ± 2.05, **p<0.01) and 7 days (ΔPD -0.45± 2.38, ***p<0.001) compared to baseline.

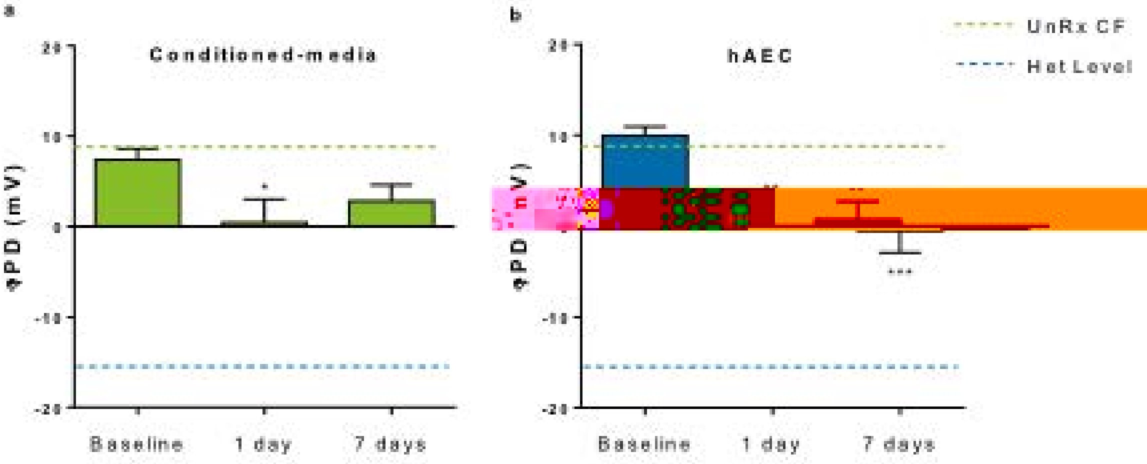

*Figure 2: The change in nasal PD in mice that received either a) conditioned-media or b) hAEC compared to pre-treatment (baseline). *p<0.05, **p<0.01, ***p<0.001, RM ANOVA vs baseline, n=12.*

Conclusion

- Improvement in CFTR functional e... airway as measured by airway PD, together with *in vitro* data (Kicic et al, unpublished) suggests that hAEC c... airway CFTR function.
- Interestingly, conditioned-media derived from hAEC culture ... improve airway PD ... therapeutic approaches for CF airway disease treatment (short and longer term) will further examine airway epithelial ion channel ... *in vivo* to help determine the mechanisms of action.

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