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Title: Epithelial cell regulation of immunity in cystic fibrosis

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Body: Introduction: Despite clinical importance, the adaptive immune system in cystic fibrosis (CF) lung disease has been sparsely studied. Methods: We isolated CF primary human bronchial epithelial cells (PBEC) and assessed their modulation of monocyte-derived dendritic cell (moDC) function and downstream T cell activation, hypothesising that epithelial cells skew immunity to favour chronic infection and lung damage in CF. Healthy monocytes were cultured with conditioned medium from 6 steady-state CF patient PBEC during moDC differentiation with IL-4 and GM-CSF. Results: Compared to control moDC, epithelial cell conditioned moDC were tolerogenic and macrophage-like (↓CD1a, ↓ CD86, ↑CD14 and ↑ IL-10), inducing low T cell proliferation and interferon-γ production in an allogeneic mixed lymphocyte reaction (MLR). Stimulation of PBEC or direct stimulation of moDC with clinically isolated Burkholderia cenocepacia whole cell lysate gave a mature, highly stimulatory moDC phenotype while Pseudomonas aeruginosa induced poor maturation and a less potent T cell response. Figure 1. Steady state moDC phenotype and function altered by PBEC derived soluble factors. (MFI - median fluorescence intensity, CPM - counts per minute).

Conclusion: CF epithelial cells secrete factors which contribute to immune tolerance. CF pathogens may have a variable ability to overcome this regulation and induce an immune response which may favour chronic infection by Pseudomonas aeruginosa.