ENDOGENOUS STEM/PROGENITOR CELL COMPARTMENTS OF CONDUCTING AIRWAYS DIFFER IN CYSTIC FIBROSIS AND NORMAL MICE

Nigel Farrow[1,2], Jonathan L McQualter[3], David Parsons[1,2] Ivan Bertoncello[3].

[1]Department of Respiratory and Si

Introduction:

Recently McQualter *et al* (PNAS 107:1414) prospectively isolated and characterized rare EpCAM^{pos}α6-integrin^{pos}β4-integrin^{pos}CD24^{low} multipotent adult lung epitheli and alveolar progenitor cells when co-cultured with lung stromal cells and cytokines. We have used this assay to compare the incidence and proliferative potential or epi in the proliferative activity of tracheal epithelium.

Methods:

The conducting airways from heterozygous (no quantify EpiSPC. Parallel studies analysed site-s

The lung epithelial colony-form g cell assay:

CD45^{neg}CD31^{neg}EpCAM^{hi} CD24^{low} lung cells generate colonies (CFU) containing cells of both airway and alveolar epithelial lineages when co-cultured in matrigel with Sca-1^{pos}EpCAM^{neg} mesenchymal cells and mesenchyme-derived growth factors (Fig 1 & 2).

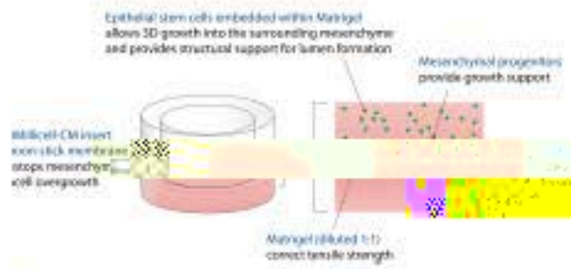

Figure 1: Schematic description of the lung EpiSPC assay system.

Figure 2: The clonal growth of CD45^{neg}CD31^{neg}EpCAM^{hi} CD24^{low} EpiSPC reveals an obligatory requirement for mesenc [illegible] potential is regulated by mesenchyme-derived stimulatory and inhibitory

Upper airway epithelial stem/progenitor cells in mouse models of cystic fibrosis:

Using our assay we have assessed tracheal airway progenitor cells in the trachea of cystic fibrosis mice. We detected a 5.2-fold and a 2.4-fold i the incidence of EpiSPC in the tracheal epithelia of CF (UNC) and CF (FABP) mice respe y, compared to normal heterozygous mice (Fig

compared to C) heterozygous (UNC WT) mice (Fig 4D).

Upper airway epithelial stem/progenitor cell proliferation index:

Sections containing excised tracheae were evaluated for stem/progenitor cell proliferation via immunohistochemistry for a nuclear proliferation antigen, Ki-67. A compared to heterozygous CF (UNC) mice. (Fig 4)

Figure 4: : Histology and immunohistochemistry for KI-67 in control and cystic fibrosis (CF) upper [illegible] (bottom graph)

Summary:

[illegible] progression of proliferation in CF lungs and may airway EpiSPC to sustain gene expression in a gene therapy setting.

Acknowledgements :

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References:

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