Endogenous lung epithelial stem/progenitor cell compartments differ in cystic fibrosis and normal mice

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Introduction:

We have recently described a ... epithelial stem/progenitor cells (EpiSPC) in the adult lung of normal mice ... EpiSPC self-renew and give rise to colonies of mixed, and lineage-restricted ... in a 3-dimensional organotypic ... this study to analyse the comparative incidence and proliferative potential of EpiSPC in the ... CF mice and ... wildtype littermates.

Methods:

We excised and disaggregated the lungs and conducting airways from CF (UNC) colony mice that were hete... (normal) or homozygous CF (-/-) and from CF(FABP) colony mice. The sorted CD45[neg] CD31[neg] EpCAM[pos] Sca-1[low] α6-integrin[pos] β4-integrin[pos] CD24[low] cells isolated from these three groups of mice were then cultured ... matrigel-based clonogenic assay to quantif...

Background and Results:

The lung epithelial colony-forming cell assay: CD45[neg]CD31[neg]EpCAM[hi]CD... colonies (CFU) comprising cells of both airway and alveolar epithelial lineages when co-cultured in matrigel with Sca-1[pos]EpCAM[neg] mesenchymal cells and mesenchym...

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

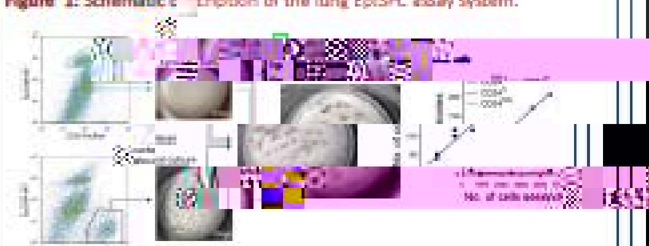
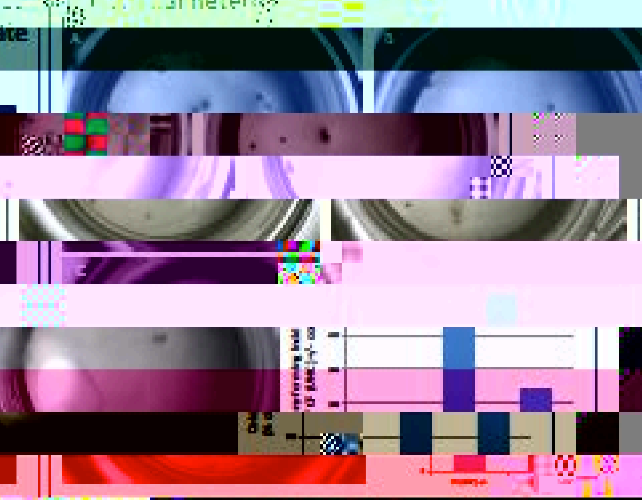


Figure 2: The clonal ... EpCAM[hi] CD24[low] EpiSPC reveals an obligatory ... mesenchymal support. There is a linear relationship between ... potential is regulated ... factors.

Multi-lineage p... expression profiling of epithelial ... reclonging experiments reveal the existence of distinct colonies with differing developmental potential. This ... stem/progenitor cell hierarchy in the lung in which multilineage stem cells give rise to lineage ... airway and alveolar progenitor cells that differentiate into all the ... epithelial cells in the adult lung (Fig 3).

... relative to 18s control ... Mixed colonies demonstrate multi-lineage potential.

... Using our assay we have observed an increase in airway ... cells in the trachea of cystic fib... mice. ... we detected a 3 fold and a 2.4 fold increase in epithelial ... in the incidence of EpiSPC ... CF(UNC) and CF(FABP) mice respectively compared to ... heterozygous ...



... increased compared ... heterozygous (UNC +/-) mice ...

Summary:

These preliminary findings are consistent with the notion that an expanded and dysregulated airway EpiSPC compartment of CF mice could contribute to airway remodel... help understand CF lung pathogenesis ... models more similar to humans and that are able to recapitulate CF airway disease development more closely than in ... Similarly, these techniques may also be applic...

References:

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