Chapter 2

Targeted cell replacement with bone marrow cells for airway epithelial regeneration


A link to the published paper can be found at

http://ajplung.physiology.org/cgi/content/full/293/3/L740
2.1 Rationale

Human and animal studies have shown that bone marrow-derived stem cells can engraft and develop into lung and airway epithelium. We explored the potential of using a targeted cell replacement approach with short-term cultured BMC in regenerating the airway epithelium as a novel therapeutic modality.

**Objective of Study:** We examined the phenotype and potential of bone marrow cells (BMC) to reconstitute airway epithelium in an acute injury model that selectively depletes Clara cells.

**Summary of Results:** Here, we show that the combination of mild airway injury (naphthalene-induced) as a conditioning regimen to direct the site of BMC localization and transtracheal delivery of short-term cultured BMC enhances airway localization and adoption of an epithelial-like phenotype. Confocal analysis of airway and alveolar localized BMC (fluorescently-labeled) with epithelial markers show expression of the pulmonary epithelial proteins, CCSP and surfactant protein-C (SP-C). To confirm epithelial gene expression by BMC, we generated transgenic mice expressing green fluorescent protein (GFP) driven by the epithelial-specific cytokeratin-18 promoter and injected BMC from these mice transtracheally into wild-type recipient after naphthalene-induced airway injury. BMC retention in the lung was observed to at least 120 days following cell delivery with increasing GFP transgene expression over time. Some BMC cultured in vitro over time also expressed GFP transgene suggesting epithelial transdifferentiation of the BMC.
Conclusion: The results indicate that targeted delivery of short-term cultured BMC can promote airway regeneration. Donor-derived BMC retained in the airway express the lung epithelial markers, CCSP, proSP-C and K18. The injured lung milieu appears to facilitate BMC engraftment and possibly, epithelial differentiation.

Please go to the journal’s website to read the contents of Chapter 2.

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