NEONATAL PULMONARY RESEARCH

Type 2 alveolar cells are stem cells in adult lung.

Background

Lung regeneration after an injury is a complex process involving numerous cell types, including alveolar and mesenchymal progenitor cells. Despite early identification of two different lung epithelial cell types by Freeman's group (Am J Pathol. 1973;70(2): 175-198),

the exact role and function of the cu- boidal SFTPC$^{pos.}$ type 2 alveolar epithelial cells (AEC2) remained subject of speculation.

Using a tamoxifen-inducable CreER in Sftpc-CreER$^{T\ 2}$;Rosa26R-tdTomato knocked-in mice, the group created a model to specifically label AEC2 in the adult murine lung. Follow-up of the labeled cells was performed after bleomycin induced lung injury or selective AEC2-depletion with diphthe- ria toxin in Sftpc-CreERT2;Rosa26R-loxp-GFP-stop-loxp-diphteria toxin A knocked-in animals. Furthermore, isolated AEC2 were cultured in an ex vivo organoid culture system together with PDGFRα$^{pos.}$ lung mesenchymal cells.

Summary of results

The group demonstrated for the first time that surfactant protein-C positive AEC2s exert stem-cell typical properties like consistent self-renewal and dif- ferentiation into AEC1 in vivo. Following targeted ablation by diphtheria to- xin A, a small proportion of surviving AEC2 undergo rapid clonal expansion and start repopulation of the injured lung. Ex vivo, the cells exert the potenti- al to form small lung-like alveolospheres when co-cultured with mesenchymal cells, indicating the crucial role of a proper mesenchymal-epithelial crosstalk in the developing and regenerating lung.

Practical conclusion

Brigid Hogan's group developed a very elegant mouse model for lineage tra- cing of AEC2 and selective AEC2-injury using a conditionally knocked-in diphtheria toxin A receptor. The paper highlights the crucial role of specific stem cell populations and their crosstalk with other resident cells in rege- neration on organs after injury and ends the speculations on the stem-cell identity of AEC2s in the fully developed, adult lung. However, the role of these cells as well as of the mesenchymal-epithelial crosstalk in the develo- ping lung was not within the scope of this study and needs to be addressed in order to understand lung development and lung repair in infants. Therefore, a different mouse model needs to be developed as Cre-LoxP mediated cell tracing leads to reduced expression of the target gene (Sftpc), which may affects development of the immature lung dramatically.

Barkauskas, et al. J Clin Invest. 2013;123(7):3025–3036. doi:10.1172/JCI68782

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