Stem Cell Biology and Regenerative Medicine

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Stem Cells in the Respiratory System

Humana Press

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Preface

Lungs are one of the most complex organs; mature lung is composed of at least 40 morphologically differentiated cell lineages with distinct functions. The proximal airways contain mucous, ciliated, basal, Clara, and pulmonary neuroendocrine cells, whereas the distal airways contain mainly ciliated cells and nonciliated Clara cells. Alveolar units are almost entirely composed of distinct type I and type II alveolar epithelial cells, directly exposed to the exterior and with the entire blood passing through to be oxygenated. These particular factors make the lung a susceptible organ, a target for multiple types of internal and/or external injury. The mechanisms of lung repair are complex and, depending on the type of cell affected, the repair process might have different characteristics.

Because of their multipotentiality, stem cells are considered as a novel and important alternative cell-based therapy in lung injury. To name a cell as a stem cell, it must meet two strict criteria: extended self-renewal capacity and multilineage differentiation. Progenitor cells have some but not limitless self-renewal capacity and restricted lineage differentiation potential. The most completely characterized adult stem cell is the hematopoietic stem cell, which can differentiate into all blood cells, including lymphoid, myeloid, platelet, and red blood cell lineages.

Today, the concept of plasticity and transdifferentiation of stem cells and, in particular, adult mesenchymal stem cells has engendered significant controversy regarding their use as a therapeutic agent. The benefit of stem cell therapy has been undoubtedly observed, however apparently independently of a lasting cell engraftment and differentiation. The protective effect with bone marrow cell therapy has been explained more recently by a paracrine secretion of anti-inflammatory factors that enhances the recovery from diverse acute and chronic injuries.

Lately, there has been increasing interest in local or endogenous stem cells in the lung. There is experimental evidence that the airway epithelium likely turns over every 30–50 days. Thus, resident local cells can mediate reestablishment of the airway epithelium with normal structure and function unless an injury is too severe, extensive, or chronic. Although there may be some contribution from circulating stem/progenitor cells, most evidence supports the concept that local stem/progenitor cells are the main source of new cells with the potential to differentiate into all cell types in the normal epithelium.

Taken together, these observations suggest that the process of lung repair is a very dynamic and well-coordinated set of events. In this process, external cells, preferentially bone-marrow-derived mesenchymal stem cells, are recruited into the lung after injury to downmodulate inflammatory responses. This phase of the repair will mediate a diminution of the severity of the wound, and will create an appropriate milieu for local progenitor cells and potentially some recruited bone-marrow-derived stem/progenitor cells, to regenerate the normal lung epithelium and parenchyma and restore the lung function.

In this book, the authors discuss the potential role of different types of stem cells, in the context of physiological stress and lung injury. In Chap. 1, Susan Reynolds reviews the lung structure and function and their correlation with endogenous lung stem cells. Daniel Weiss reviews in Chap. 2 the different sources of adult mesenchymal stem cells, as well as the controversial issue of cell differentiation into alveolar epithelial cells and the implications for future cell therapies in the lung. Recruitment of nonhematopoietic cells into the injured lung has not been well documented. In Chap. 3, Ellen Burnham explores the implications of mobilization and recruitment of progenitor cells, endothelial cells, and epithelial cells. In Chap. 4, Robert Strieter explains the role of another type of bone-marrow-derived progenitor cell, the fibrocytes. These cells have been implicated in pulmonary fibrosis, but as discussed by Strieter, these cells have unique properties that make them an indispensable element in the process of lung repair. An additional important factor that can determine the magnitude of cell recruitment and can have implications on the fate of the recruited cells is the type of extracellular matrix to which stem cells are exposed. In Chap. 5, Jesse Roman presents an extended review of the different proteins that form the extracellular matrix and how each of them can induce the differentiation of stem cells into fibroblasts and myofibroblasts. A novel concept for the mobilization of stem/progenitor cells is the effect of physical activity. In Chap. 6, Partick Wahl describes in detail the effect that exercise can have on the recruitment and homing of these cells into the different organs. Finally, we dedicate two chapters to discuss some clinical applications of mesenchymal stem cells. First, in Chap. 7, Micheal Matthay discusses the role of stem cells in acute lung injury and repair, and, finally, in Chap. 8, we present a complete review of the use of mesenchymal stem cells in animal models of lung diseases. These studies support the translation of mesenchymal-stem-cell-based therapy for acute lung injury, pulmonary hypertension, cystic fibrosis, and lung transplant.

The objective of this book is to review the most relevant and recent concepts for the use of local, endogenous, or exogenous progenitor/stem cells in the prevention and repair of the lung after injury. This is a very dynamic field, currently in constant evolution. The authors presenting their work here are indisputable leaders in their field, making this book an exciting collection of reviews by an outstanding group of investigators.

Atlanta, GA, USA Mauricio Rojas

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