UNIVERSITÀ di VERONA | Department of Biotechnology

SEMINAR

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Scuola di Medicina e Chirurgia, Università degli Studi di Verona
Lente Didattica - Aula Roberto Vecchioni

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New approaches in lung bioengineering

Abstract
End-stage lung disease is the third leading cause of death worldwide, accounting for 400,000 deaths per year in the United States alone. To reduce the morbidity and mortality associated with lung disease, new therapeutic strategies aimed at promoting lung repair and increasing the number of donor lungs available for transplantation are being explored. Because of the extreme complexity of this organ, prior attempts at bioengineering functional lungs from fully decellularized or synthetic scaffolds lacking functional vasculature have been largely unsuccessful. An intact vascular network is not only critical for maintaining the blood-gas barrier and allowing for proper graft function, but also for supporting the regenerative cells. We therefore developed an airway-specific approach to remove the pulmonary epithelium, while maintaining the viability and function of the vascular endothelium, using a rat model. The resulting vascularized lung grafts supported the attachment and growth of human adult pulmonary cells and stem cell-derived alveolar progenitor cells. This has provided the methodological basis for even more specific approach: selective removal of *only* injured alveolar type II (ATII) cells and replacement with healthy ones. ATII cells are central to the pathogenesis of multiple acute and chronic lung diseases, such as severe and progressive neonatal respiratory distress, surfactant protein deficiencies, childhood interstitial lung disease (ChILD) and adult interstitial lung disease (ILD). Our team has engineered a novel fusion protein that links a normal ligand of ATII cells to a toxin to specifically target and remove *only* ATII cells in lung disease secondary to injury of those cells. This innovative approach will allow us for the first time to treat ATII cell–dependent lung diseases with a specific molecule targeting defective ATII cells and to replace them with therapeutic cells, re-establishing alveolar homeostasis, with a significant impact on patients who suffer from lung injury and disease related to ATII cells.

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