Bioengineering the Lung: Directed Differentiation of Human Pluripotent Stem Cells into Definitive Endoderm on a Lung Extracellular Matrix

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Lung disease, which includes asthma, emphysema, cancer and cystic fibrosis, is one of the leading causes of death in the world, with more than 3 million deaths annually. Transplantation is usually the only option for patients with irreversible structural lung damage; however, numerous complications and limitations arise with this process due to the paucity of organ donors and immune rejection responses. Regeneration of lung tissue from human-induced pluripotent stem cells (hiPSCs) derived from human skin cells is a novel alternative to transplantation. Hence, this research seeks to understand a possible method through which functional lung epithelial cells can be efficiently derived from hiPSCs using a lung extracellular matrix (ECM). To the best of the author's knowledge, the effects of the lung ECM alone on the growth and differentiation of stem cells have not yet been investigated. I hypothesized that the proteins from the lung ECM would facilitate the differentiation of the hiPSCs into definitive endoderm (DE) cells. In order to test this hypothesis, I synthesized a hydrogel derived from a decellularized lung ECM, defined the media conditions to grow the hiPSCs into DE using the hydrogel, identified marker genes for DE within the hydrogel-cultured cells, and finally, injected the cells into a mouse lung scaffold as an end-point assay to determine their regenerative potential. Data from the research indicate that the ECM has the potential to facilitate the differentiation of hiPSCs into DE and thus represents a significant step forward in the fields of personalized and regenerative medicine.

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