Lung Regeneration And Organoids

Abstract

In recent times there has been a great increase in the number of chronic lung diseases and lungs being one of the vital soft tissue organs of the body need transplantation or excision of the damaged tissue1,2. Though recent medical advances and transplantation procedures have saved numerous lives their efficiency to provide a better life outcome are suboptimal. Stem cells, induced pluripotent stem cells and tissue regenerative scaffolds have made huge strides to improve patient therapies for the same2–5 but in case of lungs a 3D tissue model mimicking the functioning of an actual organ is absolutely necessary because in disease modelling, developmental studies and regenerative medicine4,6–8, just cells cultures are not enough to understand the diseases in-vivo or regrow a fully functioning 3D tissue or organ1,8–10. This where organoids come into the picture, they are stem cell-derived 3D structures that are supported by an extracellular matrix and contain multiple cell types whose spatial arrangement and interactions mimic those of a native organ.7 Aim of this article is to explore the different and novel strategies3,4,9,11–13 used for lung regeneration and their use or interplay with lung organoids, hence ultimately determining their impact in regenerative medicine.

Introduction: -

Anatomy of human lung and lung diseases:

A brief outline on the structure and physiological function of the human lung. Focus on pointing of the most vulnerable and important parts or areas of the lung tissue1.

And leading to impairment of these parts either due to physiological deterioration, invasion of pathogens etc. leads to various chronic diseases like Pneumonia, lung collapse, COPD, lung cancer etc2–4.

Lung organoids

They are stem cell-derived 3D structures that are supported by an extracellular matrix and contain multiple cell types whose spatial arrangement and interactions mimic those of a native organ. Highlight on the different cellular population necessary for its proper formation4–9

Purpose is to define and understand what organoids are and their importance so as to be used in regenerative medicine.

Regeneration of lungs

Principles governing the natural process of regeneration in lungs and tissue turn-over. Tissue turn-over is obviously quite low in human adult lungs. There are complex signaling pathways working and communicating between many different cell types like facultative lung progenitor cells, basal cells, lung progenitor and stem cells, allowing them to become activated, get

recruited at the site of injury and ultimately repair the tissue1,3,10,11.

Current Therapeutics in Lung Regeneration and Repair

Medical strategies in lung repair

Many people suffer from chronic lung diseases where the possibility to heal or repair the damaged tissue is next to impossible job, hence in todays medicinal world doctors use procedures like lung grafting – to partially or completely replace the damaged tissue by a healthy one obtained from a donor12–14.

Therapeutic strategies in lung regeneration

Stem cell mediated therapies have long been looked up as the alternative for lung regeneration and repair8,10,11,15.

Problems like immune reactions to grafts, organ failures, unaccounted or uncontrollable cell growth and many more are often faced while implementing current therapeutic strategies8,11–13,16

Culture Systems for Organoids Development

Cell cultures where the cells are grown on a monolayer, either to observe their behavior or obtain a specific cell type lineage through directing cell specific differentiation and proliferation by providing different factors7,8,17–19

The air-liquid interface culture helps us derive a more lung like environment and drives airway epithelial cells to proliferate and differentiate in-vitro2,7,20,21.

New approaches allowing to attain more organ like in-vivo environment thereby helping to obtain organoids. Cells are grown in a three dimensional either natural or synthetically fabricated scaffold where the cells differentiation and proliferation is tightly regulated by the extrinsic factors5,7,8,21,22.

Different Approaches to form Lung Organoids

Lung organoids have known to be obtained from many different sources of cells, the most prominent and successful ones are discussed and enlisted below. Though trying to achieve the same result of a functional organoid, they do differ and, in the process, how they are obtaine

3D ALI organoids obtained from stem or different progenitor population were retaining their regenerative capabilities both in-vivo and in-vitro thereby providing great solutions as tissue/scaffold replacement so as to repair or regenerate lung tissue2,8,24,35–37

To treat human diseases, one must have a thorough understanding of the same and these studies give much more accurate results when they are carried in systems which mimic the actual tissue or organ as closely as possible, like an organoid. Thereby also reducing animal and human sacrifices too4,7,8,31,36,38:

Post understanding the ailment it is necessary to test and develop a cure for it, most of times in the form of drugs. That's why organoid systems allow to asses the real time and immediate affects of the drug in that specific tissue, seeing their effect on multiple cell lineages and also on the crosstalk between them8,16,39–45

Outlook

The new approach with stem and progenitor cells and their use in 3D cultures have enabled to researchers to produce reproducible and regenerative organoid systems which closely mimic the tissue of desire. Opening up endless possibilities and unique solutions to many of our recent problems.

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