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Future Respiratory Disease in Pharmacological Studies

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Introduction

Organ on a chip models have been constructed and studied extensively. They are microfluidic devices that imitate the cellular architecture and physiological milieu of an organ. The chips can be customised to accommodate illness situations in a variety of organs. When compared to traditional *in vitro* models, lung on a chip models produce a more realistic reflection. Lung on a chip is a micro-engineered cell culture system that mimics the 3D microarchitecture and microenvironment, breathing movements, and key physiological activities of the human lung, with applications in physiology, disease aetiology, toxicological investigations, and drug screening [1].

The first model was created utilising soft lithography based microfabrication techniques as a polymer Polydimethylsiloxane (PDMS) lung on a chip model [2]. A thin (10 mm) flexible, microporous, Extracellular Matrix (ECM) coated membrane separated the upper and bottom microchannels in this model. Micro milling and solvent bonding techniques were used to develop the thermoplastic process. The lung airway milieu, as well as interactions between Smooth Muscle Cells (SMCs), Epithelial Cells (ECs), and supporting ECM, was all replicated on the chip. 3D cell bioprinting was used to create an airway on a chip model with a vascular network. Poly Capro Lactone (PCL), Lung Fibroblasts (LFs) bioink, endothelial cells bioink, and PDMS were employed in the Vascular Platform (VP). The VP was 3D printed directly from a cell laden decellularized Extracellular Matrix (dECM) bioink, with a central reservoir and two lateral reservoirs for EC and LF bioinks.

For simulating physiological functions within chips, researchers have devised a range of models based on the experimental requirements [3]. This also increased the production of pulmonary surfactants, which are important for maintaining the alveolar capillary interface. In comparison to cells cultivated in liquid medium, this method resulted in higher electrical resistance across the distinct tissue layers, improved structural integrity, and normal barrier permeability. Organs on chip models are expected to be used in toxicity assessment in the near future, perhaps replacing or lowering the requirement for animal experiments. Researchers employed their micro device to conduct toxicological research on the effects of nanoparticle exposure on the lungs [4].

Description

The alveolar epithelium was exposed to silica nanoparticles, which activated the underlying endothelium and raised the amount of Intercellular Adhesion Molecule-1 (ICAM-1) expression. In the case of cystic fibrosis, germs infiltrate the lungs, producing inflammation and eventually respiratory failure. Detailed pathogenic mechanisms, on the other hand, are still unknown. As a result, Cystic Fibrosis (CF) has only been simulated on these chip models a few times. Lung on a chip models can help fill the gap between disease drug studies and accurate drug identification. *In vitro* studies of complex processes will be aided by these models. With the increasing societal and economic burden of lung diseases and drugs, lung on a chip might become a growing platform for identifying new and possibly optimal therapies for individuals, in addition to improving the patient's health state. It reduces pharmaceutical companies' and researchers' reliance on traditional *in vitro* and animal models, which are time consuming, expensive, and occasionally unreliable [5].

Within Three-Dimensional (3D) structures, cells of various origins and phenotypes interact with one another to form functioning tissues and organs in the human body. Most *in vitro* models, on the other hand, are Two-Dimensional (2D) and so do not accurately represent the fundamentally complex nature of tissues and organs. As a result, traditional 2D models fail to accurately represent the structural, mechanical, and functional features of human tissue. In most 2D cell culture models, for example, just one cell type is cultivated on petri dishes or well plates, which does not reproduce the *in vivo* cellular milieu where cells interact with one another. In these models, monoculture influences cell shape, cell division mode, gene expression, cellular secretions, and physiological functioning [6].

Despite the fact that Chronic Obstructive Pulmonary Disease (COPD) is a serious global health issue with escalating incidence and morbidity, little pharmacotherapeutic improvements have been made in recent decades. The challenges of developing such agents are multifaceted, including a lack of understanding of the biological genesis of human disease, insufficient *in vitro* and *in vivo* models, un-validated biomarkers, inefficient physiological and clinical endpoints, and inconsistent regulatory review across the globe. Blocking multiple inflammatory pathways and mediators is a viable therapeutic method for changing the natural course of COPD. There is significant variation in clinical presentation, physiology, imaging, response to medication, deterioration in lung function, and survival.

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Several endpoints have been proposed for clinical research in COPD, and novel techniques are being investigated [7].

Conclusion

MiRNAs have the potential to be a new class of medications for the treatment of numerous lung disorders in the near future, but there is currently no information of how these identified therapeutic moieties can be engineered into an effective, patient friendly, and targeted drug delivery system. Because of their short size and low molecular weight, miRNAs can be easily turned into an effective drug delivery method. In this study, we summarised the concept of miRNAs and several ways that can be used to transport miRNAs effectively and safely to target cells, as well as the problems associated with their development, with a focus on pulmonary disorders.

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