An in vitro lung biomimetic model

An *in vitro* lung biomimetic model

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Abstract

The design and fabrication of a system to both mimic the multicellular composition of the lung and its vascular network, as well as the composition and structure of extracellular matrix (ECM) was developed.

Introduction

The lung cancer, also known as lung carcinoma, is a malignant tumour characterized by uncontrolled cell growth in the specific tissue of respiratory system.[1] The lack of new therapies to treat lung carcinoma requires experimental models that can reproduce the behaviour of healthy and pathological tissues.[2] To overcome ethical, experimental and technological limitations of the traditional *in vivo* and *in vitro* models, we describe the implementation of a lung biomimetic model to resemble the behaviour of the alveolar wall.

Materials and Methods

The alveolar basement membrane was reproduced through gelatin/polycaprolactone (GL/PCL) electrospun membranes. The mechanical, physical and chemical properties of the mats were investigated. The GL/PCL electrospun membrane was housed into a commercial bioreactor (IvTech S.r.l) where HULEC-5a cells (human lung microvascular endothelium cells) and A549 cells (human alveolar basal epithelial cells) were co-cultured on each side of the GL/PCL membrane to recreate the physiological alveolar wall composed by an epithelial layer and an endothelial layer separated by the basal membrane. The bottom layer of the PCL/GL membrane, seed using A549 cells, was cultured in air-liquid interface condition thanks to the ALI module (IvTech S.r.l) while for the bottom layer a constant flow of 400 µl min^{-1} was applied.

Results

Scanning Electron Microscopy (SEM) images showed randomly-oriented nanofibers. *In vitro* stability tests were performed to evaluate the degradation rate of the electrospun nanofibers both in static and dynamic conditions. Cyclical traction tests were performed to evaluate the effect of the physiological breathing motion (10% of strain at 0.2 Hz) on membranes mechanical properties demonstrating good fatigue resistance during the 100 tested cycles. The nuclei and cytoskeleton of A549 and HULEC-5a cells were stained with DAPI and phalloidin, respectively (Figure 1b, c) confirming the adhesion of cells on the two sides of the electrospun membrane.

Discussion and Conclusions

A lung biomimetic model was implemented to mimic the architecture of the basement membrane of the alveolar wall. The obtained results suggest that the proposed model could be used to reproduce the microenvironment of both healthy and pathological tissues thanks to the implementation of dynamic cell culture conditions.

References

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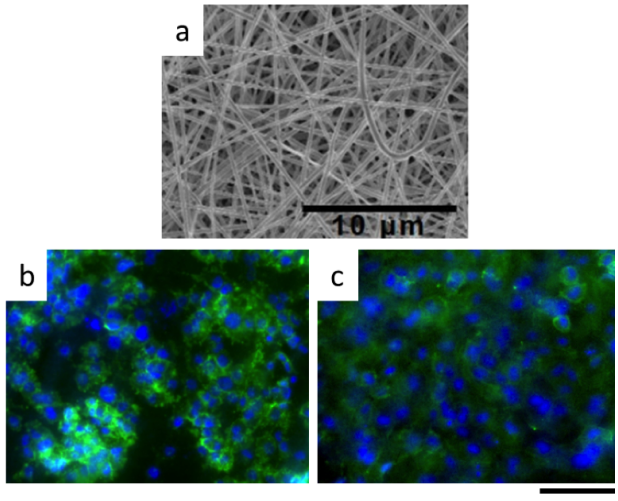

Figure 1. (a) A SEM image of GL/PCL electrospun nanofibers. Fluorescent microscopy images of (b) A549 cells and (c) HULEC-5a cells stained with DAPI (blue) and phalloidin (green) (bar scale = 100 µm).