Alveoleye – an alveoli-on-a-chip model to recapitulate lung microarchitecture

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Introduction

Alveolar tissue exhibits a highly complex multiscale morphology, consisting of a thin epithelial layer arranged in a three-dimensional architecture and surrounded by a branched capillary network. Most current lung-on-chip platforms rely on flat membranes that inadequately reproduce native alveolar geometry, limiting structural biomimicry and physiological relevance.
Aim. The aim of this work was to develop a biomimetic alveoli-on-a-chip integrating a patterned scaffold and a cell-laden hydrogel to better recapitulate alveolar packing within a controlled microfluidic environment.

Materials and Methods

A Voronoi-based scaffold reproducing the spatial organization of alveolar sacs was fabricated via digital light processing (DLP) using a flexible biocompatible resin. The scaffold was designed to generate physiologically relevant pore dimensions within a defined circular area for epithelial cell seeding.
The scaffold was positioned onto a fibrin hydrogel intended for co-encapsulation of human umbilical vein endothelial cells (HUVECs) and lung fibroblasts (MRC-5). The hydrogel was laterally confined within a DLP-fabricated bottomless microfluidic chip (Figure 1, center-right) featuring micropillars to ensure mechanical retention. Adjacent microchannels enabled medium perfusion. The device was sealed to a glass substrate to allow optical monitoring during culture, and a removable lid enabled controlled air exposure.

Results

The Voronoi design yielded a reproducible alveolus-like architecture with controlled pore size and high printing fidelity (Figure 1, left). Integration between scaffold, hydrogel, and microfluidic chip was successfully achieved, with stable positioning of the hydrogel ensured by the micropillar array.
Perfusion tests confirmed the proper functionality of the microfluidic channels and demonstrated hydraulic sealing of the gel compartment without leakage or gel displacement under flow conditions. The overall device showed structural integrity and compatibility with optical inspection.
Biological validation of the vascularized compartment is currently ongoing.

Conclusion

The proposed alveoli-on-a-chip combines additive manufacturing and hydrogel-based tissue engineering strategies to recreate key structural features of the alveolar niche within a perfusable microfluidic platform. This system represents a promising foundation for future studies on lung physiology and pollutant-induced pulmonary fibrosis in a controlled in vitro setting.

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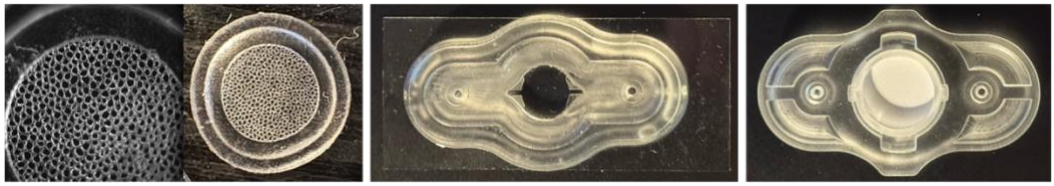


Figure 1 Voronoi-based alveolar scaffolds (left), Base of the microfluidic chip (center) and lid of the microfluidic chip (right)