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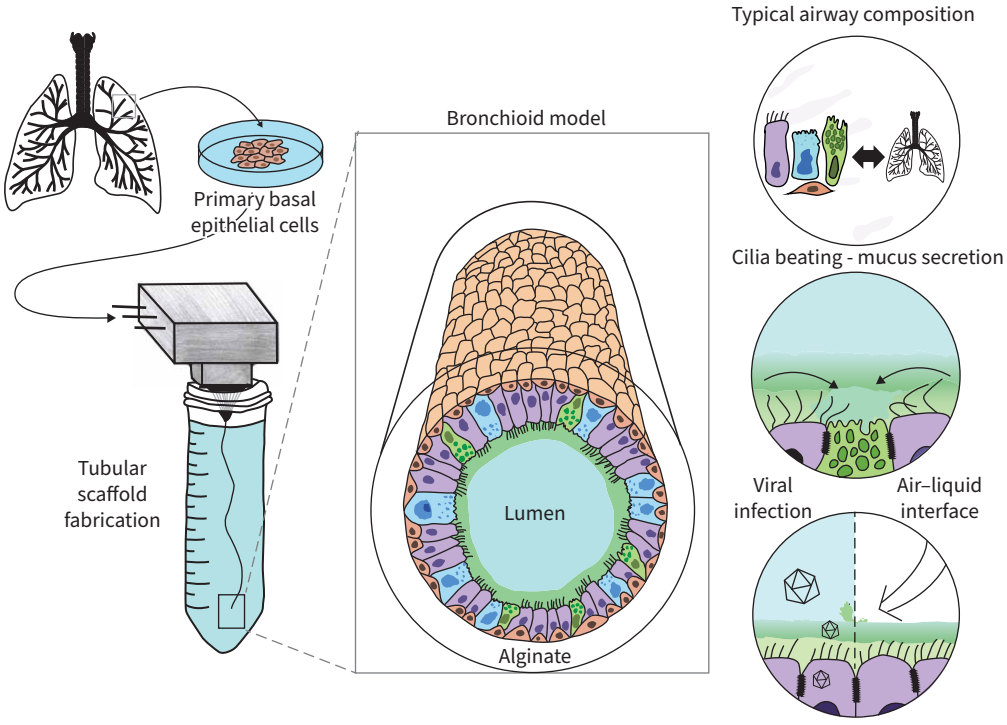

GRAPHICAL ABSTRACT Overview of the study: the bronchioid model.

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A novel tubular engineered lung model called a "bronchioid" exhibits mucociliary function and is compatible with the establishment of an air–liquid interface https://bit.ly/3LMdnkx

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Abstract

Background Airflow limitation is the hallmark of obstructive pulmonary diseases, with the distal airways representing a major site of obstruction. Although numerous *in vitro* models of bronchi already exist, there is currently no culture system for obstructive diseases that reproduces the architecture and function of small airways. Here, we aimed to engineer a model of distal airways to overcome the limitations of current culture systems.

Methods We developed a so-called bronchioid model by encapsulating human bronchial adult stem cells derived from clinical samples in a tubular scaffold made of alginate gel.

Results This template drives the spontaneous self-organisation of epithelial cells into a tubular structure. Fine control of the level of contraction is required to establish a model of the bronchiole, which has a physiologically relevant shape and size. Three-dimensional imaging, gene expression and single-cell RNA-sequencing analysis of bronchioids made of bronchial epithelial cells revealed tubular organisation, epithelial junction formation and differentiation into ciliated and goblet cells. Ciliary beating was observed, at a decreased frequency in bronchioids made of cells from COPD patients. The bronchioid could be infected by rhinovirus. An air–liquid interface was introduced that modulated gene expression.

Conclusion Here, we provide a proof of concept of a perfusable bronchioid with proper mucociliary and contractile functions. The key advantages of our approach, such as the air–liquid interface, lumen accessibility, recapitulation of pathological features and possible assessment of clinically relevant end-points, will make our pulmonary organoid-like model a powerful tool for preclinical studies.