TRUE-SCALE BIOMIMETIC MULTI-GENERATION AIRWAY PLATFORMS OF THE HUMAN BRONCHIAL EPITHELIUM FOR *IN VITRO* CYTOTOXICITY SCREENING

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Lung exposure to inhaled particulate matter may injure the epithelial tissue and lead to a loss of function in affected regions via inflammation for example. Screening for the critical contaminate concentrations may provide essential information towards damage assessment and epithelial healing. To date, most approaches have typically relied on traditional *in vitro* well plate assays or alternatively *in vivo* animal experiments. Yet, such methods manifest some outstanding disadvantages such as the inability to capture physiological flow and aerosol deposition characteristics as well as significant differences in anatomy, immune system and inflammatory responses compared to humans. The advent of organ-on-chip platforms has shown promising results to reconcile many such drawbacks. In an attempt to provide an attractive *in vitro* gateway to monitor airway health, we discuss here a novel biomimetic platform which emulates the bronchial epithelium of a human upper airway, allowing to study organ-level characteristics in a homeostatic cellular microenvironment. This device reconstitutes a multi-generation pulmonary epithelial airway environment, capturing realistic respiratory transport phenomena and critical cellular barrier functions at an air-liquid interface (ALI), in analogy to the bronchial lumen. As a proof of concept, we demonstrate its feasibility for *in vitro* based assays by exposing the device to cytotoxic aerosolized particles under respiratory flow conditions. Subsequently, we investigate the cytotoxic effects of these particles including cellular viability, cytokine and mucus secretion as a function of local particle deposition patterns. Ultimately, our bronchial airway models are intended to provide off-the-shelf *in vitro* kits geared for the end-user interested in a wide range of broader biological assays that may be attractive for cytotoxicity and drug screening.

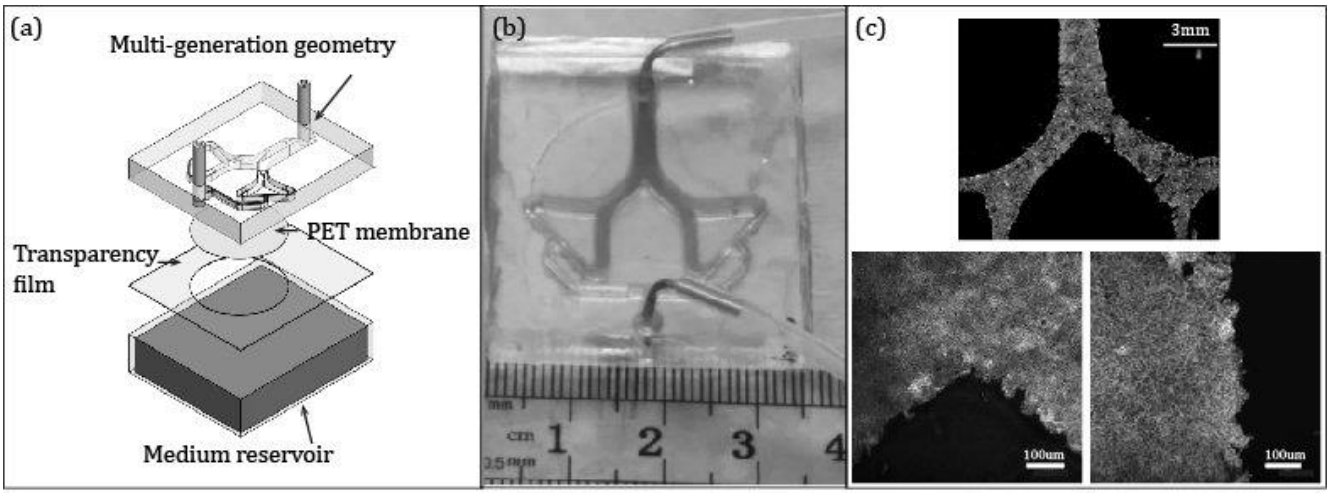

Figure 1: (a) Computer-aided drawing (CAD) of our model depicting a multi-generation airway tree, a PET membrane bonded with a transparency film that sits on a medium reservoir. (b) View of the whole device. (c) Calu-3 cells cultured at an ALI within the device: view of the entire tree (upper), the first bifurcation (bottom left) and the third branch (bottom right) of the structure (cells stained green for F-actin and blue for cell nuclei).