Advanced lung-on-a-chip: a tissue engineered microphysiological model to investigate flavored e-cigarette-induced airway disease

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Abstract

Nicotine vape exposure from active or passive smoking can cause a wide range of respiratory health problems and represents a major public health concern. Inhalation toxicology of ecigarettes is an area of active research that focuses on investigating the deleterious effects of ecigarette aerosols on the human respiratory system. While traditional cell culture models have gained widespread use as a simple and convenient research tool for in vitro investigation of ecigarette aerosol toxicity, they have limited capacity to recapitulate the complexity of native human lung tissues. In this proposal, we present a novel microengineered biomimetic model that reconstructs the airway region of the human lung for experimental studies of the respiratory toxicity of e-cigarette aerosol in the distal lung, which remains an outstanding question in the inhalation toxicology of flavored e-cigarettes. The microengineered airway model is composed of two microfabricated 3D chambers separated by a semipermeable membrane. The design of this microdevice makes it possible to mimic tissue compartmentalization in native airways by permitting long-term co-culture of stem cell-derived airway epithelial cells, primary human pulmonary microvascular endothelial cells, and lung fibroblasts in a physiological 3D microenvironment to engineer fully differentiated airway epithelium directly exposed to air and supported by vascularized, perfusable 3D stromal tissues. Notably, our preliminary data revealed the potential of the underlying pulmonary vasculature to accelerate and promote differentiation and maturation of lung epithelial cells during air-liquid interface culture. Using the lung-on-a-chip systems in conjunction with the cigarette smoking machines, we will accurately predict the deleterious potential of flavored e-cigarettes to induce acute injury of airway tissue in a dose-dependent manner. We believe that the microengineered systems developed here represent an important advance in our ability to model acute respiratory responses to environmental toxins, including e-cigarette aerosol, and may provide a powerful in vitro platform to study biochemical threats and develop medical countermeasures against them.