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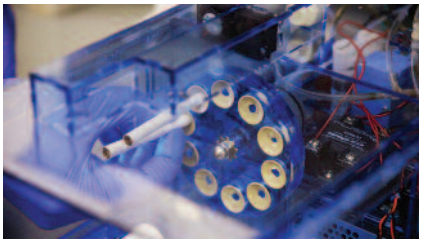
Mimicking cigarette smoke exposure and patient-specific responses



Standard cigarettes, in a rotating unit of the smoking machine, are lit and burned in intervals that mimic smokers' breathing patterns and smoking. Photo credit: Wyss Institute at Harvard University.

BOSTON, MA—Cigarette smoking is a major cause of lung disease and a key exacerbating factor for patients with chronic obstructive pulmonary disease (COPD). However, researchers have been challenged in modeling the effects of smoking on human lungs under normal breathing conditions. Classical systems containing human small airway cells are unable to reproduce the breathing motions of the lung. Commonly used laboratory animals cannot reflect human smoking because they are obligate nose breathers and their inflammatory responses differ from those of humans. In addition, clinical studies have shown great variability in the physiological and biochemical responses between patients and usually do not allow direct comparisons of smoke exposure versus no exposure in the same individual.

Integrated system mimics smoking behavior

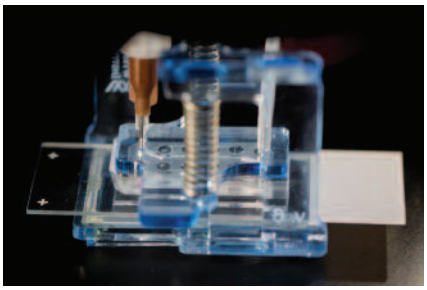
Now a team from the Wyss Institute for Biologically Inspired Engineering at Harvard University, led by founding director Donald Ingber, MD, PhD, has combined their previously developed small airway-on-a-chip with a smoking machine that burns cigarettes and a microrespirator that inhales and exhales small volumes of cigarette smoke and fresh air in and out of the airway-on-a-chip's epithelium-lined channel, at programmable intervals. Using cells derived from healthy subjects or patients with COPD, the system faithfully mimics smoking behavior.

Better understanding of pathological changes

The researchers have found the integrated system provides a better understanding of smoke-related pathological changes in individual smokers. In their study published in Cell Systems, when exposed to cigarette smoke, the airway-on-a-chip experienced changes in oxidation-reduction pathways and gene expression profiles that matched those found in human smokers. In addition, cilia in some areas beat normally but in other areas beat at much reduced rates. When testing e-cigarettes, the researchers found less evidence of changes in oxidation-reduction pathways but similar changes in cilia beat patterns.

Future research plans

The authors intend to develop more elaborate chips that would include other types of airway cells, including immune cells, to more closely imitate human-level responses. They also plan pre-clinical studies to identify potential therapeutic targets for COPD.



In the airway-on-a-chip, a hollow channel lined by living, human bronchiolar epithelium from COPD patients or healthy subjects is exposed to air delivered by the smoking instrument. Cell culture medium is continually flowed through a parallel channel to support the epithelium up to four weeks and create an air/liquid interface similar to that in a lung airway. Photo credit: Wyss Institute at Harvard University.

Adapted from: "Mimicking life-like cigarette smoke exposure and patient-specific responses in human lung airway chips," Wyss Institute, October 27, 2016 and "Airway-on-a-chip could lead to new treatments for cigarette smoke-induced lung injury," Science Daily (Source: Cell Press), October 27, 2016. Journal reference: Benam KH, et al., Matched-comparative modeling of normal and diseased human airway responses using a microengineered breathing lung chip, Cell Systems, 2016; DOI: 10.1016/j.cels.2016.10.003.