Emulate’s Lung-Chip Demonstrates New Capabilities to Predict Human Lung Inflammation and Drug Responses in Asthma and COPD

Results published in *Nature Methods* with pharmaceutical collaborators use Organs-on-Chips to model diseases of the human Lung Small Airway-on-Chip

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CAMBRIDGE, Mass. – Emulate Inc. announced today that it has developed a new living human Lung-Chip system that accurately recreates the unique structure and function of the human lung small airways within microengineered chips—as reported today in the journal *Nature Methods*. The results demonstrate that the Small Airway Lung-Chip can model complex tissue functions of the lung within the microengineered chips to enable a human model of lung inflammatory disorders, specifically asthma and chronic pulmonary obstructive disease (COPD), and more effectively predict human response to anti-inflammatory drugs, compared to existing animal models.

The publication in *Nature Methods*, entitled "A microfluidic lung small airway-on-a-chip enables analysis of human lung inflammation and therapeutic responses in vitro," includes collaborative research by Emulate, Inc., the Wyss Institute for Biologically Inspired Engineering at Harvard University, and pharmaceutical collaborators at Merck, known as MSD outside the United States and Canada, and Pfizer, Inc. This collaborative research with the Small Airway Lung-Chip has enabled greater mechanistic insight into the physiology and disease states of the lung and created a model to better understand human respiratory diseases, identify potential new therapeutic targets, and test the safety and efficacy of new drugs. In addition, these studies showed the ability to either develop a disease phenotype in the chips from normal cells or maintain a phenotype of disease in cells acquired from diseased patients. The data also demonstrated that pharmacological interventions with a glucocorticosteroid in the Small Airway Lung-Chip mirrored the clinical experiences with this class of drugs.

“In advancing the capabilities of the Lung-Chip technology, we addressed the distinct biology of the small airway in order to more accurately model and predict human response for airway inflammation and respiratory diseases,” said Remi Villenave, Ph.D., a lead author of the *Nature Methods* publication and Principal Investigator at Emulate. “We have now demonstrated that our Small Airway Lung-Chip recreates human lung inflammation and can predict responses to drugs targeting small airway diseases. This opens up new opportunities for answering questions earlier and more accurately in the drug development process and furthering our understanding of human pulmonary diseases.”
The Small Airway Lung-Chip offers a new and potentially superior model system for research into asthma and COPD by recreating, in vitro, the physiology and key functions of human airways in two respiratory diseases that represent major public health challenges,” said Michael Salmon, Ph.D., principal scientist, Immunology at Merck. “The potential for Organs-on-Chips technology to provide more relevant and predictive human models of disease supports industry-wide efforts to refine new drug development in ways that increase the probability of success for new drug candidates and reduce the need for animal-based research models.”

Respiratory diseases frequently involve obstruction and inflammation of the small airways in the lung specifically in diseases such as asthma and COPD1. Current animal models are limited in their relevance to humans in that their physiology is distinctively different from the human, and the mechanisms driving key disease process such as inflammation show marked species differences.2 The study published in Nature Methods, provides evidence that the Small Airway Lung-Chip recreated the complexity of function required to accurately model the human lung and recreated key aspects of the pathophysiology of asthma and COPD, including inflammatory cellular infiltration, goblet cell hyperplasia, and cytokine hypersecretion. Emulate's new Small Airway Lung-Chip provides an authentic and more predictive approach to understanding human pulmonary biology and to designing therapeutics for the treatment chronic respiratory diseases.

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“It has been a remarkable process for us to work with collaborators across the pharmaceutical industry to advance the Lung-Chip product portfolio so that it can be a robust system for transforming the R&D paradigm in drug development and to better predict humans response,” said Geraldine A. Hamilton, Ph.D., President and Chief Scientific Officer of Emulate. “Our new capabilities with the Small Airway Lung-Chip provide a novel path to improve the ability to develop new drugs for asthma and COPD, as we help to accelerate the discovery and development of better and safer drug products for patients.”

The new capabilities of the Small Airway Lung-Chip expand Emulate’s industry-leading work in developing Organ-Chips that recreate the complexity of human organs within microengineereed environments and build on Emulate's previous work with the Alveolar Lung-Chip. The addition of the Small Airway Lung-Chip represents a different functional unit of the lung that is critically involved in many pulmonary diseases. This new capability allows Emulate to expand the applications of the Organ-Chips in drug discovery and development and expands capabilities to elucidate additional aspects of lung function and disease.

The Lung-Chip was first described in 2010 by Emulate's team in a landmark publication.
in Science. The human Alveolar Lung-Chip modeled the alveolar air sacs in the lung and demonstrated the ability to model lung absorption and nanoparticle toxicity. It further demonstrated the critical requirements for mechanical forces in order to recreate normal biological function and drug response. In collaboration with industry partners, Emulate has since continued to develop the original Alveolar Lung-Chip and demonstrated the ability to model disease states at the alveolar tissue level such as pulmonary edema, in collaborative research with GlaxoSmithKline, Inc. (work published in 2012 in Science and Translational Medicine). Emulate has on-going research on developing a pulmonary thrombosis model in collaborative research with Janssen Biotech, Inc. and Johnson & Johnson Innovation.

About The Lung-Chip
Emulate has developed specialized Lung-Chip products that recreate true-to-life functions of the human lung. Due to the distinct structure and biology of different parts of the lung and their differentiated role in disease processes, Emulate has developed a range of Lung-Chip products to enable human-relevant research related to lung diseases and various aspects of lung biology. The Alveolar Lung-Chip emulates the fundamental lung functions such as oxygen-exchange and absorption in the breathing human lung and has been used in a range of applications, including evaluation of nanoparticle absorption and toxicity, study of disease development and assessment of adverse drug effects, such as pulmonary edema and pulmonary thrombosis. The Small Airway Lung-Chip models a different aspect of lung biology, distinct from the alveolar air sacs. It recapitulates the physiology and function of the small airways that conduct inhaled air to the alveolar air sacs, and Emulate has demonstrated that the Small Airway Lung-Chip models inflammation and therapeutic responses in human small airway diseases, such as asthma and chronic obstructive pulmonary disease (COPD).

Organ-Chips for Emulating Human Biology
Based on the Organ-on-Chip technology, Emulate has created a new living Human Emulation System that provides a real-time window into the inner-workings of human biology, offering researchers ways to predict human response with greater precision and detail than today’s cell culture or animal-based testing. An Organ-Chip—such as the lung, liver, brain or kidney—contains tiny hollow channels lined with tens of thousands of living human cells and tissues, and is approximately the size of a USB memory stick. Each chip is a living, micro-engineered environment that recreates the natural physiology and mechanical forces that cells experience within the human body. The Human Emulation System can link multiple Organ-Chips together to model interactions between different organs and predict whole body or systemic-level responses.

About Emulate, Inc.
Emulate Inc. is a private company that creates living products for understanding how diseases, medicines, chemicals, and foods affect human health. Our Human Emulation System sets a new standard for recreating true-to-life human biology and is being used to advance product innovation, design, and safety across a range of applications including drug development, agriculture, cosmetics, chemical-based consumer products,
and personalized health. Emulate continues to develop a wide range of Organ-Chips and disease models through collaborations with industry partners and internal R&D programs. Emulate is also working with clinical partners to produce Organ-Chips personalized with an individual patient’s stem cells for applications in precision medicine and personalized health. Our founding team pioneered the Organs-on-Chips technology at the Wyss Institute for Biologically Inspired Engineering at Harvard University. Emulate holds the worldwide exclusive license from Harvard University to a robust and broad intellectual property portfolio for the Organ-Chips technology and related systems.

For more information, visit emulatebio.com.

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