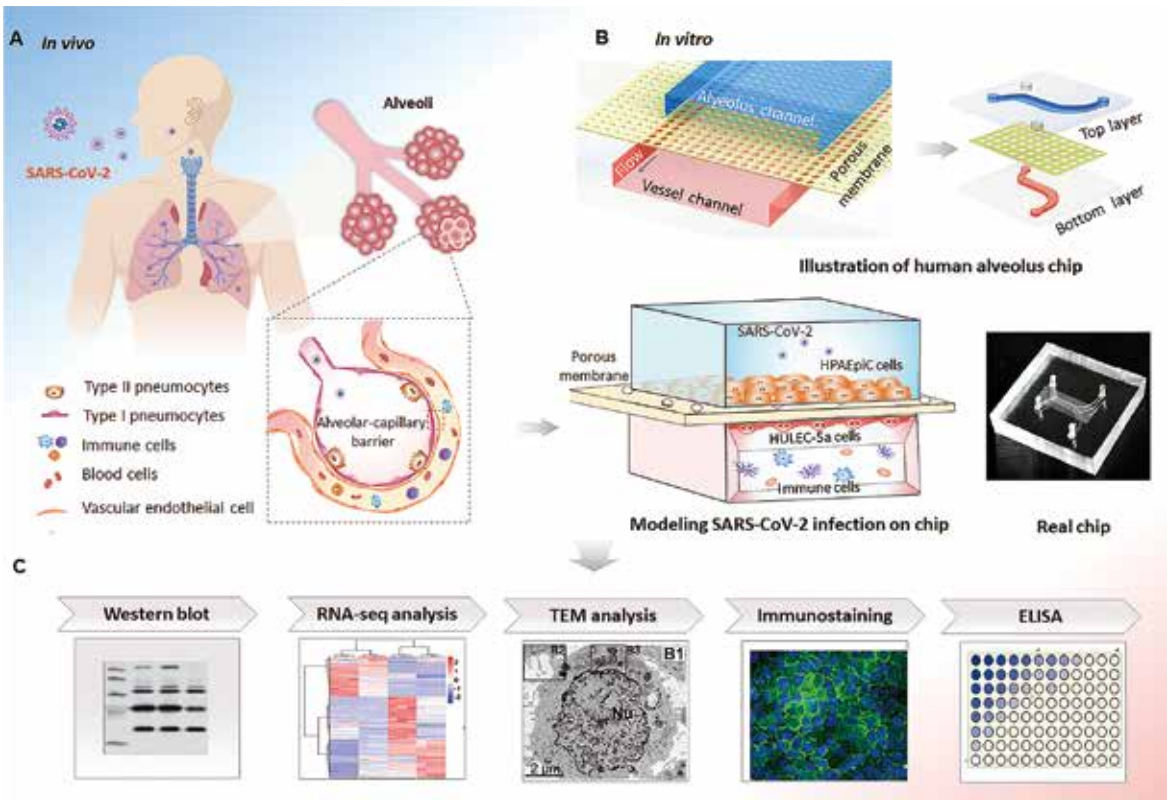
Life Sciences

Recapitulating the Lung Pathophysiology of COVID-19 in a Human Organ Chip

Coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), have posed a big threat to human life.

The human lung takes the primary hit, characterized by the process ranging from mild syndrome to severe lung injury, and then the damage usually expands to multi-organ failure. Till now, the in-depth mechanism of the pathogenesis of COVID-19 remains elusive. The model that can accurately resemble human-relevant responses to this novel viral infection are still lacking.

To this end, a research team led by Prof. QIN Jianhua from the Dalian Institute of Chemical Physics (DICP) of the Chinese Academy of Sciences (CAS) and Prof. ZHENG Yongtang from Kunming Institute of Zoology (KIZ) of CAS, developed a biomimetic human disease model that allows to recapitulate the SARS-CoV-2-induced lung injury and immune responses on organ chip system.



Researchers use a self-developed organ chip to recapitulate SARS-CoV-2-induced lung injury and immune response. (Image by DICP)

This study, entitled "Biomimetic Human Disease Model of SARS-CoV-2 Induced Lung Injury and Immune Responses on Organ Chip System," was published on *Advanced Science* on October 24, 2020,

Organ on chip is a bioengineered microfluidic cell culture device that enables to reflect the key function of human organs at physiologically relevant manner. In this study, the researchers created a biomimetic human disease model that allowed to resemble lung injury and immune responses induced by SARS-CoV-2 *in vitro* at organ level. This microengineered human lung chip reproduced the key features of alveolar-capillary barrier by co-culture of human alveolar epithelium, microvascular endothelium and circulating immune cells under fluidic flow in normal and diseased conditions.

Upon SARS-CoV-2 infection, the epithelium exhibited higher susceptibility to virus than endothelium. Transcriptional analyses showed activated innate immune responses (e.g., IFN-1 signaling) in epithelium and cytokine-dependent pathways (e.g., JAK-STAT signaling) in endothelium following viral infection, revealing the distinctive responses in different cell types.

Notably, viral infection caused the immune cell recruitment, endothelium detachment, and increased inflammatory cytokines release (IL-6, IL-8, IL-1B and TNF-a), suggesting the crucial role of immune cells involving in alveolar barrier injury and exacerbated inflammation. The established disease model system was also used to test the candidate anti-viral drugs, demonstrating the capability of this organ chip system for modeling the pathophysiology of COVID-19 and the screening of effective candidates against SARS-CoV-2.

This microengineered organ on chip system reflects the major patho-physiology of COVID-19 by closely mirroring human-relevant pathological lung injury, vascular disruptions and immune responses to SARS-CoV-2 infection at organ level, which is difficult to be achieved by existing *in vitro* models.

The advantages of this chip platform lie in its accessibility to simultaneously study responses of various cells to virus in real time, and to rapidly test candidate drugs with low cost and short time. It may provide unique and promising platform for accelerating SARS-CoV-2 research and the development of new therapeutics against COVID-19.

(DICP)

Reference

Min Zhang, Peng Wang, Ronghua Luo, Yaqing Wang, Zhongyu Li, Yaqiong Guo, . . . Jianhua Qin, (2021) Biomimetic human disease model of SARS-CoV-2-induced lung injury and immune responses on organ chip system. *Advanced Science* 8, 2002928. doi: 10.1002/advs.202002928.