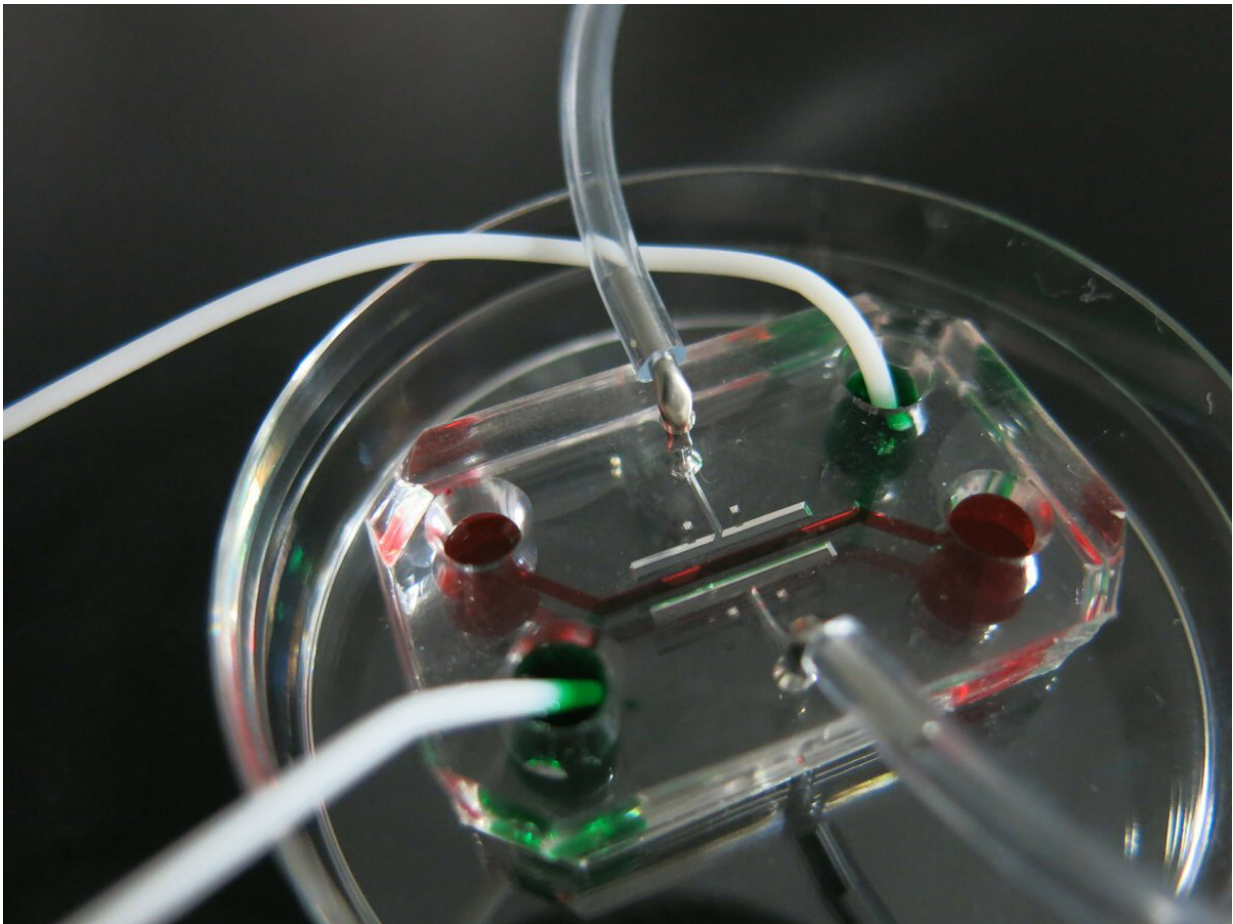


Organ-on-a-chip study reveals mechanism of SARS-CoV-2 invasion into blood vessels

September 28 2022



Credit: Kyoto University

A research group led by CiRA Junior Associate Professor Kazuo

Takayama and Associate Professor Yoshiaki Okada of Osaka University has revealed that SARS-CoV-2 disrupts the vascular endothelial barrier by suppressing the expression of Claudin-5 (CLDN5) to invade the blood vessels.

SARS-CoV-2 infects respiratory epithelial cells and then spreads to other organs via blood vessels. In this case, SARS-CoV-2 crosses the walls of blood vessels (the barrier of vascular endothelial cells) from respiratory organs and enters the [blood vessels](#). However, the mechanism was unknown. The research group created an airway-on-a-chip that mimics respiratory organs consisting of airway [epithelial cells](#) and vascular endothelial cells. Using the device, they found that SARS-CoV-2 disrupts the vascular endothelial barrier by suppressing the expression of CLDN5, a protein involved in adhesive junctions between vascular endothelial cells, and by subsequently weakening the vascular endothelial cadherin-mediated junctions.

The team confirmed that CLDN5 gene and protein expression levels were decreased in the lungs of a patient with COVID-19. They also demonstrated that increasing CLDN5 expression in [vascular endothelial cells](#) by gene transfer or small molecule drugs (fluvastatin) suppressed SARS-CoV-2-induced vascular endothelial barrier disruption.

These results indicate that suppression of CLDN5 expression is an essential mechanism for SARS-CoV-2-induced vascular endothelial barrier disruption, which increases the severity of COVID-19. The findings also indicate that up-regulation of CLDN5 expression is a new therapeutic strategy against COVID-19.

The airway-on-a-[chip technology](#), which can be used to reproduce the respiratory pathology of COVID-19 and search for therapeutic agents, is expected to become an excellent tool for elucidating the pathogenesis of severe respiratory tract infections, including COVID-19, and developing

therapeutic drugs in the future.

The results of this study were published online in *Science Advances* on September 22, 2022.

More information: Rina Hashimoto et al, SARS-CoV-2 disrupts respiratory vascular barriers by suppressing Claudin-5 expression, *Science Advances* (2022). [DOI: 10.1126/sciadv.abo6783](https://doi.org/10.1126/sciadv.abo6783)

Provided by Kyoto University

Citation: Organ-on-a-chip study reveals mechanism of SARS-CoV-2 invasion into blood vessels (2022, September 28) retrieved 19 November 2023 from <https://medicalxpress.com/news/2022-09-organ-on-a-chip-reveals-mechanism-sars-cov-invasion.html>

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