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COVID-19 studies bolstered by lung cells made from induced pluripotent stem cells

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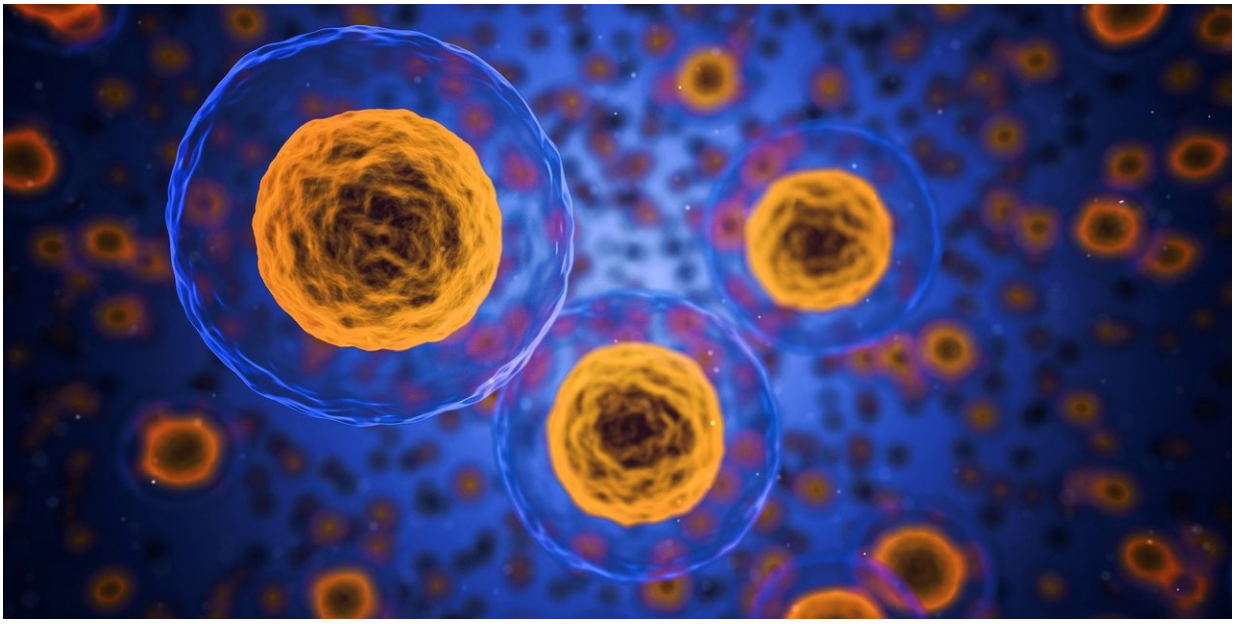

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A team led by researchers at Newcastle University, UK has successfully created a model of the cells found in the lungs that can be used to replicate how COVID-19 infects the airways. This information, reported today in the *STEM CELLS* journal, paves the way for broader studies of viral lung infections using a cost-effective system that can easily be manufactured on a large scale.

COVID-19, which to date has resulted in more than 3.5 million deaths worldwide, has brought on an urgent need for airway models that can be used to develop effective therapies. While the use of in vitro (outside the body) models generated from primary pulmonary epithelial cells that mimic the human airways has increased in popularity over recent years, their availability is limited to primary samples that can differ significantly depending on the various donors' genetic backgrounds.

Induced pluripotent stem cells (iPSCs) offer a potential way around this drawback. Generated from adult stem cells found in fat, skin, blood and elsewhere, they can be reprogrammed to become every other cell type in the body, including those making up the airways. Additionally, iPSCs can propagate indefinitely and, thus, provide a large supply of cells with the genetic background of a single donor, rather than the varied backgrounds of the multiple donors hindering primary pulmonary epithelial cell models.

In the study reported in *STEM CELLS*, airway epithelial cells were generated from iPSCs (using a mixed population of lung progenitors) by culturing them on a polyester membrane to allow formation of a confluent monolayer, then exposing them to an air liquid interface to induce differentiation into a pseudostratified epithelial model.

The researchers then went on to demonstrate that their model is composed of the cell types found in the human upper airway epithelium—including functional ciliated cells—and that the cells are capable of secreting mucus and of being readily infected by SARS-CoV-2, the virus that causes COVID-19.

"The infected model cells also secreted cytokines at levels corresponding to the behavior of the airway epithelium in the body following SARS-CoV-2 infection," said Lyle Armstrong, Ph.D., professor of stem cell sciences at Newcastle University, UK and corresponding author on the

study. (Cytokines are proteins that signal the immune system to take action during an infection.)

"Our protocol not only simplifies the manufacture of cellular models of the human upper airways," he added, "but it has a distinct advantage in that we have eliminated the need for primary samples that differ in genetic backgrounds. Our next step will be to expand on this model by including immune cell components."

"The development of this reproducible and highly scalable protocol to manufacture upper airway models is very important for the study of respiratory viral infections such as SARS-CoV-2 and others," said Dr. Jan Nolta, Editor-in-Chief of *STEM CELLS*. "Having such models available will greatly enhance the development of future therapies and will allow the field to be better prepared to study new viruses and viral variants."

More information: Ivo Djidrovksi et al, SARS-CoV-2 infects an upper airway model derived from induced pluripotent stem cells, *STEM CELLS* (2021). DOI: 10.1002/stem.3422

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