# Cystic Fibrosis Research News

**Title:**
Modeling Pulmonary Cystic Fibrosis in a Human Lung Airway-on-a-chip

**Lay Title**
A microengineered laboratory model of human CF lung

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## What was your research question?
Can we successfully mimic the effects of cystic fibrosis (CF) on human lungs by growing human lung cells from CF patients in an organ-on-a-chip (Organ Chip) as a way to possibly replace animal testing and advance personalized medicine? An Organ Chip model of the lung is a microdevice the size of a USB memory stick made of a clear, flexible rubber that has one tiny hollow channel lined by living human cells from the lung airway that are separated by a porous membrane from a parallel channel lined with lung capillary blood vessel cells. The airway cells are exposed to air and the vessel cells experience dynamic fluid flow of a blood substitute medium just like in our lungs inside our bodies. By doing this, this simple device is able to mimic many complex functions of the living lung organ, such as mucus secretion and inflammation caused by a lung infection.

## Why is this important?
CF is a debilitating genetic disease that causes severe damage to the lungs, and although there are promising new drugs for treating CF, many patients sadly do not survive past middle age due to lung infections and inflammation linked to these infections. Animal models do not

accurately predict how a person will respond to treatment. So, if we can create a simplified human, model of lung infection and inflammation using cells from people with CF, we can more reliably study these processes of infection and inflammation and speed up the development of new treatments. We might also be able to create chips with cells from individuals with CF to develop more effective personalized treatments.

## What did you do?

We grew lung airway cells from both people with CF and healthy individuals along with lung capillary cells in the Organ Chip, and then studied whether this microengineered models of CF lung exhibited similar changes seen in living lung in people with CF compared to healthy lung. Some of the key changes seen in lung in people with CF is a thickened mucus layer, increased numbers of immune cells due to increased inflammation, and sometimes overgrowth of a bacterium called Pseudomonas aeroginas, which is a common cause of infection in CF patients.

## What did you find?

The Lung Chip made from cells of people with CF, reproduced key features of CF in people, including a thicker mucus layer and more growth of the *Pseudomonas* bacteria compared to Lung Chips made with cells from healthy people. We also observed an increased response to bacterial infection similar that which happens in the airways of someone with CF as well as movement of more white blood cells into the lung airspace, which is also a hallmark of CF in people.

## What does this mean and reasons for caution?

This work opens entirely new avenues to study CF and test potential drugs in a setting that better resembles humans than using animals. As the Lung Chip is built using cells taken from patients, it also provides an entirely new approach to personalize therapies for people with CF. One limitation is that while the lung cells were taken from people with CF so they contained the genetic mutation that causes CF, the blood vessel cells and immune cells were from healthy people. This means that the current version of the model might not provide a complete picture of what happens in a person with CF.

## What's next?

We hope to measure the activity of the abnormal CFTR channel on-chip and to build chips where all the cells are from the same person with CF. Other human cell types, such as macrophages and fibroblasts, also could be added in future studies.

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