Cystic Fibrosis Research News

Title:

In Vitro 3D culture lung model from expanded primary cystic fibrosis human airway cells

Authors:

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What was your research question?

Airway cells from people with cystic fibrosis (CF) are crucial for developing effective treatments for this disease. However, these cells are difficult to obtain and have a limited ability to survive and divide outside the body. We wanted to find optimal conditions that could be easily used by research laboratories to expand stocks of these cells.

Why is this important?

There are more than 2,000 genetic mutations that cause CF, making it difficult to treat and cure CF patients. By growing a "copy-cat" model of the cells lining the surface of the airways from CF patients, drugs or treatments can be tested in the laboratories to determine which would be more effective for humans, and better understand how these drugs or treatments work.

What did you do?

We grew and expanded stem cell-like cells from people with CF and homozygous for the F508del mutation. The CF cells were grown in a culture medium that does not require two common additions to other culture conditions in the laboratory. To resemble the human airway lining, cells were triggered to assemble into a multiple-layered structure with ciliated (hair-like) and goblet (mucus-producing) cells. We tested the ability of tezacaftor drug alone to improve the function of the mutated CF protein (F508del).

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What did you find?

The ideal culture condition enabled CF airway cells to be grown and expanded to ~25 population doublings (e.g. starting with 2 cells and end up with 33 million cells) in a relatively short time (~30 days). This was better than cells grown with other culture conditions. The cellscould be re-grown with ciliated and goblet cells, mimicking the cells lining the airways. Most importantly, both CFTR protein function and cilia beating function improved after being treated with the tezacaftor drug.

What does this mean and reasons for caution?

CF donor-derived airway cells can be expanded and grown into an airway epithelium that responds to tezacaftor drug. While this model can be used to predict responses of people with CF to CF drugs, other factors can influence the level of the response, such as infection, which is not present here.

What's next?

As new drugs are developed, screening for their effectiveness can be performed in the laboratory on grown CF airway cells. The study of rare CF mutations could benefit from cell expansion and could lead to the design of personalized medicine/treatments.

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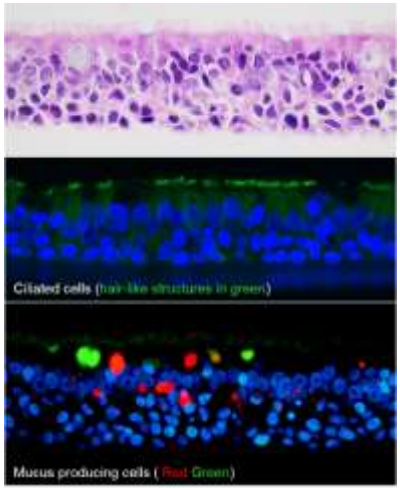

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