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Cystic Fibrosis Research News

Title:
Loss of ciliated cells and altered airway epithelial integrity in cystic fibrosis

Lay Title:
Damage in the cell lining of the airways in cystic fibrosis

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What was your research question?
The cell-lining (epithelium) is composed by cells that cover the large airways (bronchi) and form a barrier between the environment and inside the body. Is the epithelium of the bronchi composed by the same cell populations and is it able to play its role of barrier in cystic fibrosis (CF)?

Why is this important?
In people with CF (PwCF), the epithelial cells are genetically abnormal and also the target of further aggressions, notably by microbes. There are mainly three cell types at the surface of the bronchi: cells that discharge the mucus (goblet cells), cells with hairs (cilia) to remove the

mucus up to the throat (ciliated cells) and cells that generate the two previous ones (basal/stem cells). A detailed characterisation of this cellular barrier is however lacking in CF, as most previous studies focused on the upper airway (nose) – less affected by the disease – or cell lines harbouring the gene defect.

What did you do?

44 lung tissues from PwCF undergoing a lung transplant and from controls were studied for bronchial cell types. Bronchial cells isolated from PwCF or healthy donors lungs were grown (cultured) in the lab (*in vitro*) for 2, 4 or 6 weeks to evaluate whether the abnormalities persist upon *in vitro* culture.

What did you find?

Enhanced numbers of goblet cells and decreased numbers of ciliated cells were observed in CF bronchi, indicating a loss of normal structure of the epithelium. These features were recapitulated *in vitro* by culturing cells from PwCF, but were not caused by non-functioning CFTR (protein mutated in CF) nor by bacterial infection.

What does this mean and reasons for caution?

This study provides new insights into airway epithelium changes in PwCF, which are remembered by cells independently from the mutated CFTR. However, we only studied individuals with very severe disease and most of the controls were (ex)smokers – smoking having known to alter epithelium – since ethical issues preclude the access to early-diseased tissue or healthy participants.

In addition, cell cultures can reproduce some features observed in PwCF (and in other respiratory diseases) but do not represent the complexity of the airways.

What's next?

Since the complexity of the airways cannot be reproduced by culturing cells, an animal model of CF lung disease could help to further study the mechanisms of the changes acquired in the airway epithelium of PwCF.

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