Cystic Fibrosis Research News

Title:
Bronchial epithelial cell lines and primary nasal epithelial cells from cystic fibrosis respond differently to cigarette smoke exposure

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What was your research question?
How does cigarette smoke affect inflammation of cells taken from the airways of people with cystic fibrosis (CF) as well as healthy individuals? Furthermore, does a particular mechanism e.g. epidermal growth factor receptor pathway (EGFR), control the release of inflammatory substances from these airway cells in response to cigarette smoke.

Why is this important?
Inflammation of the airways in people with CF and chronic obstructive pulmonary disease (COPD) is mainly caused by cigarette smoking in this part of the world. This inflammation causes severe damage to the lungs, which reduces lung function and ultimately leads to death. We don't understand how the mechanisms controlling inflammatory responses in these conditions work. A better understanding of how these responses are triggered will lead to the development of new drugs for the treatment of CF and COPD.

What did you do?
Airway cells taken from people with CF with different genetic mutations, and also from healthy individuals, were exposed to cigarette smoke and then further exposed to bugs which persistently infect people with CF, along with a mixture of other substances present in the airways of people with CF and COPD which can cause inflammation and damage, e.g. IL-8. We measured the release of IL-8. We then blocked the EGFR pathway and assessed the effect of this blockade on normal IL-8 release and IL-8 release induced by cigarette smoke from the

airway cells.

What did you find?

When we exposed airway cells to cigarette smoke before we to exposed them to bugs and inflammatory substances, more IL-8 was released from the cells taken from people with CF compared to those taken from healthy individuals. Importantly, by blocking the activation of EGFR in airway cells (taken from people with CF as well as healthy individuals) we also showed that normal IL-8 release, and IL-8 release in response to cigarette smoke, is partly controlled via the EGFR pathway.

What does this mean and reasons for caution?

Our findings suggest that the EGFR pathway is particularly important in controlling airway inflammation in people with CF or COPD. This means that the EGFR pathway may be a potential target for new drugs used to treat airway inflammation in people with CF or COPD. However, caution should be exercised, as blocking the EGFR was shown to substantially suppress normal (potentially protective) IL-8 release from airway cells taken from both people with CF and healthy individuals.

What's next?

We used 2D flat airway cell cultures in our investigations, as these have been the main culture method used by investigators. However, these cultures do not model the airways very accurately. Consequently, future studies will focus on the effect of cigarette smoke on inflammation of 3D models of airway cells taken from people with CF and healthy individuals.

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