European Cystic Fibrosis Society

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Cystic Fibrosis Research News

Title:

Cystic Fibrosis Epithelial Cells are Primed for Apoptosis as a Result of Increased Fas (CD95)

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What was your research question?

To determine if alterations (increased or decreased) in programmed cell death (apoptosis) occur in lung (epithelial) cells expressing the mutated form of the cystic fibrosis transmembrane conductance regulator (CFTR) gene compared to normal cells with functional CFTR.

Why is this important?

Programmed cell death or apoptosis is an important physiological process that regulates cell number within organs and organ systems including the lung. However, altered levels of apoptosis (increased or decreased) are associated with disease and may impact on the integrity and function of the affected organ system.

What did you do?

In this study, apoptosis was measured in CF and non-CF epithelial cell lines by focusing on increased DNA breakage (breakage) and caspase enzyme activation, which are signs of programmed cell death. We also looked for mechanisms of increased apoptosis in CF cells by measuring how much a particular gene known as the 'Fas receptor' was turned 'on' in epithelial cells and lung bronchial tissue sampling from patients with CF.

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What did you find?

We found that levels of DNA breakage, as well as caspase-3 and caspase-8 enzyme activities, were significantly increased in CF cells compared to non-CF cells. In addition, we demonstrated an increase in the amount of the Fas receptor gene, which is involved in inducing apoptosis in CF cells

What does this mean and reasons for caution?

The findings from this study indicate that the CFTR mutation may predispose cells expressing the mutant CFTR gene to elevated levels of cell death compared to cells expressing normal CFTR. Unusual lung epithelial cell death by apoptosis may render these cells less effective at mounting a robust defence against bacterial infection, which is typical in CF sufferers. However, further studies need to be carried out to understand more fully the impact of infection on airway epithelial cell apoptosis.

What's next?

Future studies will focus on the use of primary CF and non-CF lung epithelial cells and the impact of infection on apoptotic rates. The impact of CFTR mutation on the immune response to infection, and its relationship to apoptosis in these cells, will also be assessed.

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