



# Cystic Fibrosis Research News

## **Title:**

**CFTR-dependent defect in alternatively-activated macrophages in cystic fibrosis**

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## **What was your research question?**

Lung disease begins very early in life in children with CF, characterized by an excessively vigorous inflammation. We wondered why the normal control mechanisms do not turn this off in CF.

## **Why is this important?**

Despite improvements in treatment and in the general survival of patients with CF, most children are entering school with evidence of scarring, known as bronchiectasis, in their lungs due to excessively vigorous inflammation. This scarring is persistent and progresses despite treatment. The best way to stop this from happening is to understand why it happens and then design new treatments that can prevent the onset and progression of bronchiectasis in early life.

## **What did you do?**

We studied a type of white blood cell known as a macrophage. Macrophages are key cells for initiating inflammation but also for turning it off. They do this by adopting different forms, the classically-activated pro-inflammatory macrophage or the alternatively-activated inflammation-resolving macrophage. Macrophages can swap between types if provided with the right stimulus. We developed a method for studying macrophages obtained from blood samples collected from patients with CF or non-CF controls

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## **What did you find?**

We found that if cystic fibrosis transmembrane conductance regulator (CFTR), the key genetic abnormality in CF, function was deficient, either naturally occurring in patients with CF or if we blocked this using CFTR inhibitors, macrophages were unable to develop into the inflammation-resolving type. There was no defect with the pro-inflammatory macrophages leaving a potential imbalance; inflammation could be initiated but not switched off. We also provided some information about how this happens but more study is required.

## **What does this mean and reasons for caution?**

Our studies were undertaken in test tubes using white blood cells obtained from patients with CF and controls. There is a possibility that the situation may be different in the body. However, our findings go quite some way to providing an explanation for why inflammation in the lung seems to persist in early life in CF.

## **What's next?**

In the next phase of our research we want to uncover the reasons why CF macrophages are unresponsive to the stimuli that turn them into "inflammation fighters". We can then design and test new treatments to resolve inflammation in CF.

## **Original manuscript citation in PubMed**

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