



# Cystic Fibrosis Research News

## Title:

Defective immunometabolism pathways in cystic fibrosis macrophages

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## What was your research question?

Macrophages are immune system cells that typically engulf and kill bacteria, but these cells do not function well in people with cystic fibrosis (CF). The goal of our study was to identify how mitochondria contribute to CF macrophage dysfunction. Mitochondria are well-known as the powerhouse of the cell, producing energy that cells use to do work. However, mitochondria also play a key role in the immune system by regulating the activity of macrophages.

## Why is this important?

Macrophages that do not function well have difficulty killing bacteria. This contributes to chronic bacterial infections in CF. It is known that mitochondria are dysfunctional in other types of cells in CF, such as epithelial cells that line the airway. However, there is not much known about mitochondria in CF macrophages. By studying mitochondria in CF macrophages, we are increasing our understanding of the factors that prevent the immune system from functioning well in CF. This may lead to the development of new CF therapies that can treat the mitochondria in order to improve the ability of CF macrophages to kill bacteria.

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## What did you do?

We isolated macrophages from healthy mice and CF mice. We then performed several functional tests to investigate how well the mitochondria in the CF macrophages can work compared to the mitochondria in the healthy macrophages. We also investigated how infection impacts mitochondrial function by infecting the macrophages with *Burkholderia cenocepacia*. This is a multi-drug resistant bacterium that causes serious lung infections in people with CF.

## What did you find?

We found that mitochondria in CF macrophages cannot work as hard as mitochondria in healthy macrophages both before and after infection. CF mitochondria appeared more fragmented following infection, which indicates that the mitochondria are damaged and not functioning well. During an infection, mitochondria produce mitochondrial reactive oxygen species (mROS), which is used to directly attack and kill bacteria. We observed that mitochondria in infected CF macrophages produced less mROS than mitochondria in infected healthy macrophages.

## What does this mean and reasons for caution?

Healthy mitochondria are critical for macrophages to function properly, especially when the macrophages are fighting a bacterial infection. Our findings provide an explanation as to why CF macrophages do not kill bacteria as well as healthy macrophages.

## What's next?

We have identified several mitochondrial defects that may prevent macrophages from functioning well in CF. The next steps include finding ways to correct these defects in order to help CF macrophages improve their ability to kill bacteria.

## Original manuscript citation in PubMed

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