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# Cystic Fibrosis Research News

## Title:

Pseudomonas aeruginosa infection, but not mono or dual-combination CFTR modulator therapy affects circulating regulatory T cells in an adult population with cystic fibrosis

## Lay Title:

Pseudomonas aeruginosa infection, but not CFTR modulator therapy affects circulating regulatory T cells in an adult population with cystic fibrosis

## Authors:

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## What was your research question?

Several parts of the immune system are not functioning well in people with CF (PWCF). CFTR modulator therapy might influence immune cell abnormalities in PWCF.

## Why is this important?

CF lung disease is the major cause of death and reduced quality of life in PWCF. Lung infections, but also an exaggerated inflammation independent of infection are key drivers of CF lung disease. CFTR modulator therapy may or may not influence parts of the immune system that are involved in inflammatory processes. Therefore, characterizing immune cells in the era of CFTR modulator therapy may identify additional potential treatment options.

## What did you do?

In this study we analyzed subsets of certain defense cells (lymphocytes) and lymphocyte-associated signaling proteins in blood from PWCF and people with non-CF bronchiectasis. We collected blood from 108 PWCF (of which 55 participants received mono or dual-combination CFTR modulator therapies) and 40 participants with non-CF bronchiectasis. Blood samples were then analyzed by a technique called flow cytometry.

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## What did you find?

There were no differences in subsets of analyzed lymphocytes and lymphocyte-associated signalling proteins between PWCF who were versus were not receiving CFTR modulator therapy. However, regulatory T cells, a subpopulation of lymphocytes that limit the activation of the immune system, were reduced in PWCF and chronic pulmonary *Pseudomonas (P.) aeruginosa* infection. This difference was also present in PWCF treated with CFTR modulators. Regulatory T cells were not reduced in people with non-CF bronchiectasis and chronic pulmonary *P. aeruginosa* infection.

## What does this mean and reasons for caution?

We found reduced regulatory T cells among PWCF and chronic *P. aeruginosa* infection. Anti-inflammatory therapies that enhance regulatory T cells might be a therapeutic option for these individuals. However, we found no differences in lymphocyte subsets between PWCF who were versus were not receiving CFTR modulator therapy in this cross-sectional study design. Our study is limited by missing stored blood samples from PWCF before initiation of therapy for a longitudinal analysis. In our study we focused on lymphocyte subsets while other components of the immune system were not analysed.

## What's next?

Our results need to be confirmed in a longitudinal study (following the same individuals over a length of time) including samples from PWCF before and after starting treatment. PWCF receiving highly effective triple-combination CFTR modulator elexacaftor/ ivacaftor/tezacaftor were not analysed yet.

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