



Cystic Fibrosis Research News

Title:

Microbial interaction: *Prevotella* spp. reduce *P. aeruginosa* induced inflammation in Cystic Fibrosis bronchial epithelial cells

Lay Title:

What do different bacteria together do to the lung epithelium in Cystic Fibrosis

Authors: Anne

Bertelsen, J Stuart Elborn, Bettina C Schock

Affiliations:

Wellcome-Wolfson Institute for Experimental Medicine, Queens University Belfast, UK, Department of Medicine, University of Cambridge, UK, Imperial College London, UK

What was your research question?

The lungs of people with Cystic Fibrosis (CF) contain different types of bacteria, some need oxygen to grow (called aerobic), others do not (called anaerobic). Our study addresses the question how two of these bacteria, both aerobic and anaerobic *Pseudomonas* and anaerobic *Prevotella*, affect each other and the inflammation in the cells lining the airways.

Why is this important?

Inflammation of the airways in people with CF has been studied using one bacteria species at the time. However, in people with CF the presence of a variety of anaerobic bacteria in the airways is linked to better lung function and lower levels of markers of inflammation. This may suggest a relationship between *Pseudomonas aeruginosa* and anaerobic *Prevotella* species. Knowledge about how these two species affect inflammatory signals in the walls (epithelium) of the lung could be used to develop new anti-inflammatory drugs.

What did you do?

We exposed cells similar to those in the airways of people with the common CFTR mutation F508del/F508del to a clinical strain of *Pseudomonas aeruginosa* for 2 hours followed by exposure to *Prevotella* (clinical strains of *P. histicola*, *P. nigrescens*) for another 2 hours. We called this a mixed infection. The cells were incubated under anaerobic conditions for the duration of the experiments. We then determined bacterial growth, inflammatory signalling and secreted substances (mediators) from these cultures.

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cfresearchnews@gmail.com



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What did you find?

Our study showed that *Prevotella* species can reduce the growth of *Pseudomonas aeruginosa*. Furthermore, the inflammatory response of the lungs' epithelial cells was reduced when cells were exposed to *Pseudomonas* and a *Prevotella* strain. Subsequently we also found lower release of proteins (cytokines) that normally cause inflammation (Interleukin (IL)-6, IL-8).

What does this mean and reasons for caution?

The signalling pathways affected in the mixed cultures are particularly important in the control of local defense (immune) responses. Our work, for the first time, shows some mechanisms of how the presence of anaerobic bacteria in the airways is linked to better lung function and lower levels of inflammation.

However, there are many more aerobic and anaerobic bacteria in the lungs of people with CF. Investigating the interactions of so many species will be a challenge, but we will use gene expression and protein analyses to study this complex biological interaction.

What's next?

The next question is how can we support the survival of anaerobic bacteria in the lungs? We want to identify the molecular mechanism underlying this beneficial effect seen in our co-cultures and harvest this as a novel therapeutic approach to combat chronic *P. aeruginosa* infection in people with CF.

Original manuscript citation in PubMed

<https://pubmed.ncbi.nlm.nih.gov/34112603/>

The figure shows how infection with *P. aeruginosa* or anaerobic *Prevotella* spp. alone cause inflammation in CF lungs. In mixed infections, inflammation is reduced due to soluble factors secreted by *Prevotella* spp.

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