Cystic Fibrosis Research News

Title:

Infection with *Prevotella nigrescens* induces Toll-like Receptor 2 signalling and low levels of p65 mediated inflammation in Cystic Fibrosis bronchial epithelial cells

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What was your research question?

We wanted to understand if anaerobic bacteria (bacteria that do not require oxygen) were contributing to infection and inflammation in people with cystic fibrosis (PWCF). Understanding the complex environment in the lungs of PWCF will help us to develop therapies to reduce the burden of chronic infection in PWCF.

Why is this important?

Bacteria such as *P. aeruginosa* and *S. aureus* are known to cause severe infections and inflammation in the lungs of PWCF. Our lungs also contain anaerobic bacteria and in PWCF high numbers of these bacteria in the lung are linked to fewer *P. aeruginosa* infections, but the role of anaerobes in the lung is not well understood.
Therefore, we wanted to understand if anaerobe *Prevotella* (*P. nigrescens*) contributes to infection and inflammation in the CF lung.

What did you do?

In the laboratory we grew CF lining the inner surface of the lungs, called epithelial cells, and infected them with equal numbers of either *P. aeruginosa* or *P. nigrescens* bacteria that were taken from a person with CF. We then assessed how these surface cells responded to the infection by analysing mediators (cytokine Interleukine-6 gene expression and how many cells died. We compared the responses of the two bacteria and found that there were big differences in the responses from the cells. Based on this we then looked closer into the inflammation caused by the Prevotella strain and how this would differ from the way *P. aeruginosa* causes inflammation in CF lung.

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What did you find?

The strain of *Prevotella* we used (*P. nigrescens* B021S) did cause an inflammatory response in CF lung cells, but this response was much lower than to *P. aeruginosa*. *P. aeruginosa* is recognised by the cells of the lungs through a receptor on the cell surface called Toll-like Receptor 4' (TLR4) and this engagement with TLR4 causes a rapid and strong inflammation reaction of a protein called transcription factor NF-kB(p65). *P. nigrescens*, however, caused inflammation through TLR2 and through a different route, which led to a later and lower activation of NF-kB and their cytokines.

What does this mean and reasons for caution?

Our results indicate that *Prevotella* may be less inflammatory to the surface cells than other bacteria found in the CF lung. However, as we only used one strain of *Prevotella* for this study we cannot say for sure all *Prevotella* species activate these pathways. We also cannot say whether these bacteria are beneficial to the lungs or if they actively trigger the inflammatory cascades that are a feature of CF.

What's next?

Our next experiments will look at the responses of CF lung cells to a range of *Prevotella* strains to see if all *Prevotella* stains activate similar pathways in CF lung cells. We will also investigate co-infections of *Prevotella* with *P. aeruginosa* to see if *Prevotella* can modify the *P. aeruginosa*-induced inflammatory responses.

Original manuscript in PubMed

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