Cystic Fibrosis Research News

Title:

Pf bacteriophage is associated with decline in lung function in a longitudinal cohort of patients with cystic fibrosis and Pseudomonas airway infection

Lay Title:

Presence of bacteriophage is associated with lung function decline in people with cystic fibrosis and a pseudomonas infection

Authors:

Elizabeth B. Burgener[1, 2], Aditi Gupta[2], Kayo Nakano[2], Sophia L. Gibbs[2,3], Maya E. Sommers[4], Arya Khosravi[4], Michelle S. Bach[4], Colleen Dunn[2], Jacquelyn Spano[2], Patrick R. Secor[5], Lu Tian[6, 7], Paul L. Bollyky[4], Carlos E. Milla[2]

Affiliations:

1. Division of Pediatric Pulmonology and Sleep Medicine, Children's Hospital of Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA 90027
2. Center for Excellence in Pulmonary Biology, Department of Pediatrics, Stanford University, Stanford, CA 94305
3. Department of Epidemiology and Population Health, Stanford University, Stanford, C
4. Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University, Stanford, CA 94305
5. Division of Biological Sciences, University of Montana, Missoula, MT 59812
6. Biomedical Data Science Administration and Statistics, Stanford University, Stanford, CA 94305
7. Primary Care and Population Health, Stanford University, Stanford, CA 94305

What was your research question?

Is the Pf bacteriophage of Pseudomonas (Pf phage), a virus that infects but does not kill Pseudomonas, associated with poor outcomes over time in people with cystic fibrosis (CF)?

Why is this important?

Pf phage is found in high levels in the sputum of some people with CF with Pseudomonas infection. Most phages infect bacteria resulting in lysis or killing of the bacteria. However, Pf phage infects Pseudomonas and then uses the Psuedomonas to make many phage particles. Those particles are then pushed out of the Pseudomonas bacteria without killing the Pseudomonas, acting more like a parasite than a pathogen. The phage particles then

incorporate into the surrounding CF sputum. These Pf phage particles make sputum stickier and thicker. As a result, the sputum becomes more difficult to clear from the airways and it is harder for antibiotics to penetrate. Thus, we suspected these effects would promote chronic infection and would make people with Pf phage in their sputum more ill.

What did you do?

We followed a cohort of people with CF for 5 years. We collected sputum samples and clinical data, including lung function, at clinic visits and hospital admissions. We evaluated sputum for Pf phage presence and measured inflammatory cytokine levels. For the enrolled people who underwent lung transplantation we also evaluated the explanted lung tissue for evidence of Pf phage.

What did you find?

People with CF with Pf phage in their sputum were more likely to have chronic Pseudomonas infection (as opposed to a Pseudomonas infection that went away with antibiotic treatment). We found that people with high levels of Pf phage in their sputum lost lung function faster than those without Pf phage over the five-year observation period, even in those on highly effective CFTR modulator therapy. Those with Pf phage in their sputum also had increased markers of inflammation. We demonstrated evidence of Pf phage in the airways of explanted lungs from people with CF known to have Pseudomonas infection with Pf phage in their sputum.

What does this mean and reasons for caution?

Our results indicate that Pf phage may play a role in the lung disease caused by Pseudomonas infection in CF, perhaps leading to more severe disease in those infected with both Pseudomonas and Pf phage. Pf phage may be a biomarker used to predict who is at risk for faster progression of lung disease. These findings also suggest that targeting Pf phage could improve treatment of Pseudomonas infection and outcomes among individuals with CF.

What's next?

Larger and multi-center studies are needed to better understand the clinical implications of Pf phage. Additional laboratory studies are needed to understand how the Pf phage impacts sputum and antibiotic penetration, so that new drugs can be developed to target Pf phage for treating or preventing Pseudomonas infections.

Cystic Fibrosis Research News

Original manuscript citation in PubMed
https://pubmed.ncbi.nlm.nih.gov/39490215/