European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

Dissociation of Systemic and Mucosal Autoimmunity in Cystic Fibrosis

Authors:

Theprungsirikul, J[a], Skopelja-Gardner, S[a], Meagher, R. E[a], Clancy, J. P[b], Zemanick, E.T[c], Ashare, A[a,e], Rigby, W. F. C[a, d]

Affiliations:

[a]Department of Microbiology and Immunology, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA
[b]Division of Pulmonary Medicine, Department of Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA
[c]Department of Pediatrics, University of Colorado Anschutz Medical Campus, Children's Hospital Colorado, Aurora, Colorado, USA
[d]Division of Rheumatology, Department of Medicine, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA
[e]Division of Pulmonology, Department of Medicine, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA

What was your research question?

Pseudomonas aeruginosa infection in cystic fibrosis (CF) is accompanied by the immune system also producing antibodies that are directed against an anti-microbial protein found in the body called bactericidal/permeability-increasing protein (BPI). These antibodies are referred to as autoantibodies. Our goal was to understand this relationship between *P. aeruginosa* infection and the generation of BPI autoantibodies.

Why is this important?

No one understands the preference for *P. aeruginosa* to colonize the lungs of people with CF and mediate lung damage. We believe that the development of autoantibodies to BPI may be a tantalizing clue in this process. Understanding these issues is an essential step in identifying the role of these autoantibodies in disease progression, as well as contributing to the improvement of symptoms management in CF patients, since these autoantibodies may reduce the ability to eliminate *P. aeruginosa* from the lung.

Cystic Fibrosis Research News

What did you do?

We assessed the presence and level of antibodies to BPI and *P. aeruginosa* in blood and bronchoalveolar lavage (BAL) samples of 131 adults and paediatrics with CF. The same samples from healthy individuals were used as the control group. In our study, CF patient samples were obtained from Dartmouth Hitchcock Medical Center (DHMC), Cystic Fibrosis Foundation (CFF), Cincinnati Children's Hospital, and Children's Hospital Colorado.

What did you find?

BPI autoantibodies were common (~43%) in adults while rare (<5%) in paediatrics (≤18yrs) with CF. Several findings suggested that BPI autoantibodies arose independently of the *P. aeruginosa* antibody development. We found a strong correlation between the presence of antibodies to BPI and *P. aeruginosa* in the blood samples, but not in BAL fluid in CF. Curiously, BPI breakdown by enzymes produced by *P. aeruginosa* in the BAL fluid predicted the development of airway antibody responses against BPI in the lungs.

What does this mean and reasons for caution?

These results suggest that BPI, when being cleaved by enzymes produced by *P. aeruginosa*, induces autoantibody production in the lungs of people with CF regardless of age. Our data suggest that these autoantibodies to BPI may have been generated from *P. aeruginosa*-infected airways of CF patients, and later induced in blood through a separate pathway. However, our study poses some limitations, as we are unable to test the sequence of antibody generation and their interaction in the lungs, so the results and interpretation must be viewed with caution.

What's next?

Future research will focus on an animal model mimicking the infection in CF. This would be beneficial in determining the origin of antibody generation which could direct us to better symptoms management in people with CF.

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=Dissociation+of+Systemic+and+Mucosal+Autoimmunity+in+Cystic+Fibrosis

cfresearchnews@gmail.com