European Cystic Fibrosis Society

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

Cystic Fibrosis Research News

Title:
Interleukin-1 beta is a potential mediator of airway nitric oxide deficiency in cystic fibrosis

Lay Title:
Reduced levels of nitric oxide in cystic fibrosis airways may be caused by interleukin-1 beta

Authors:
Gyde Nissen[1,2,3]*, gyde.nissen@uksh.de
Elad Ben-Meir[1]*, elad.ben-meir@sickkids.ca
Matthias Kopp[2,3,4], matthias.kopp@insel.ch
Michelle Shaw[1,5], michelle.shaw@sickkids.ca
Felix Ratjen[1,5], felix.ratjen@sickkids.ca
Hartmut Grasemann[1,5], hartmut.grasemann@sickkids.ca
* These authors have contributed equally

Affiliations:
1. Division of Respiratory Medicine, Department of Paediatrics, The Hospital for Sick Children, Toronto, Canada
2. Department of Pediatric Pneumology and Allergology, University of Lübeck, University Medical Center Schleswig-Holstein, Lübeck, Germany
3. Airway Research Center North (ARCN), Member of the German Center of Lung Research (DZL), Lübeck, Germany
4. Division of Pediatric Respiratory Medicine, Department of Pediatrics, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
5. Translational Medicine, Research Institute, The Hospital for Sick Children and University of Toronto, Toronto, Canada

What was your research question?
Cystic fibrosis (CF) airways are deficient for nitric oxide (NO) and concentrations of interleukin-1 beta (IL-1β) are increased. Both, NO and IL-1β, are mediators of inflammation but it is not clear whether the NO-deficiency is regulated by IL-1β. We therefore asked the question of whether the lack of NO production in the airways of people with CF is linked to the increase in IL-1 β.

Why is this important?

Cystic Fibrosis Research News

Reduced airway NO production is a hallmark of CF and is thought to contribute to a narrowing of the airways and to risk of lung infection. If we better understand what causes low NO production, we may be able to develop treatment to correct the deficiency. Furthermore, ivacaftor (CFTR modulator) therapy improves salt transport in the CF airway surface and, among other beneficial effects, has been shown to increase NO in the airways.

What did you do?

We measured different mediators of inflammation including IL-1β in sputum samples from 15 people treated with ivacaftor over a period of two years. A total of 54 sputum samples were used, and exhaled NO and lung function were also measured over the study period.

What did you find?

Ivacaftor therapy significantly reduces the concentration of IL-1β in sputum, but not any of the other mediators that we measured. IL-1β levels were closely linked to an improvement in lung function, measures of NO metabolism in sputum and exhaled NO.

What does this mean and reasons for caution?

The results of this study suggest a potential interaction between chloride transport in CF airway epithelium, IL-1β and airway NO production. The increase in airway NO in people living with CF and treated with ivacaftor may be mediated by IL-1β.

There are several limitations to this study which include the low numbers of participants and the fact that the links that we saw are not proof of cause. However, as far as we know, this is the first study to report a potential link between CFTR function, IL-1β and airway NO in people living with CF.

What's next?

We hope that our observations can be repeated in future studies of people living with CF and treated with elexacaftor/tezacaftor/ivacaftor (Trikafta or Kaftrio).

Original manuscript citation in PubMed

https://pubmed.ncbi.nlm.nih.gov/35260353/

cfresearchnews@gmail.com