Complex relationships between bacteria and markers of lower airway infection and inflammation in cystic fibrosis

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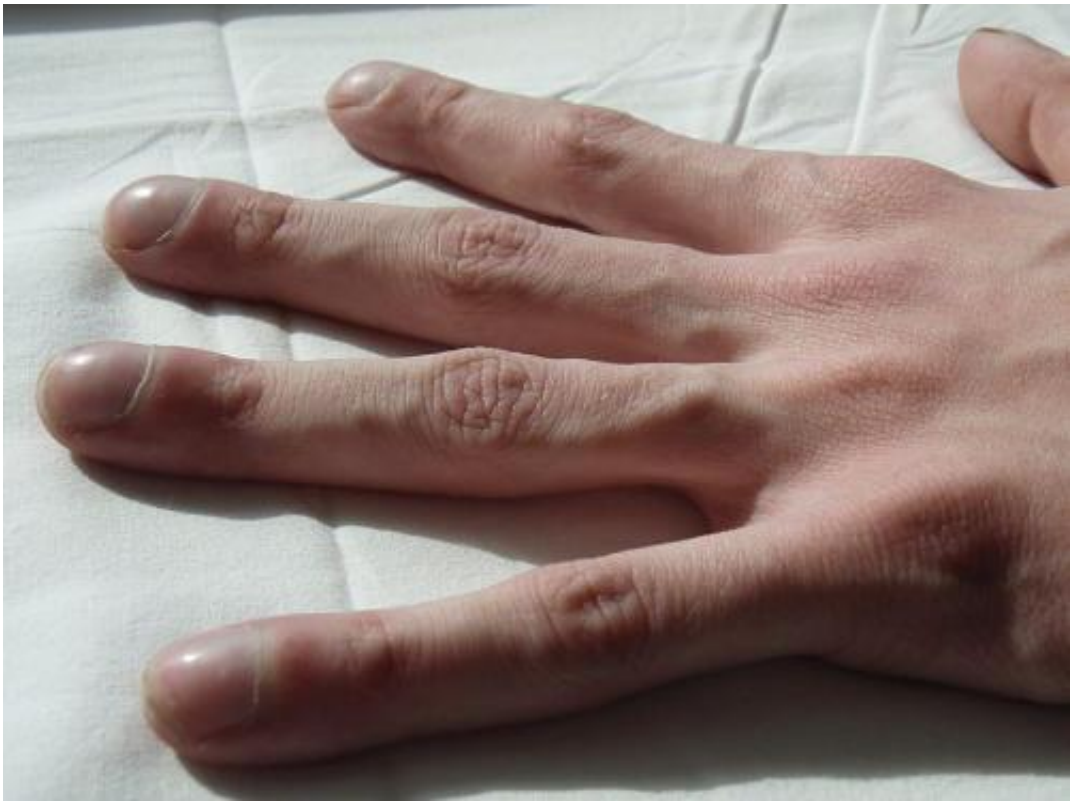

"Clubbing" of the fingers is a classic features of Cystic Fibrosis, although not present in many patients. Credit: Jerry Nick, M.D./ Wikipedia

The lower airways of patients with cystic fibrosis (CF) have unique biochemical features that correlate with the complex communities of

lung bacteria typical of this disease, according to a multicenter study led by researchers from Ann & Robert H. Lurie Children's Hospital of Chicago. These findings offer insights into the underlying biological mechanisms driving infection and inflammation in the CF lungs, and may help develop novel targeted therapies and more precise diagnostics to improve the care of children with CF. Results were published in the journal *Frontiers of Cellular and Infection Microbiology*.

Chronic airway infection and inflammation resulting in progressive, obstructive lung disease is the leading cause of illness and death in people with CF. To better understand the biological mechanisms of infection and inflammation, in a study conducted Lurie Children's in collaboration with researchers at Children's Hospital Colorado and the University of Minnesota, several metabolites were measured in 90 bronchoalveolar lavage fluid (BALF) samples acquired from bronchoscopy. These lower airway samples were collected from children with and without CF. Researchers also used genetic sequencing to characterize the bacterial communities present in these samples, which were then correlated to the metabolites in the lungs.

"Our study was the first to both examine these metabolites in lower airway samples and identify networks of relationships between metabolites and lower airway bacterial communities," said lead author Jack O'Connor from Lurie Children's. "We discovered metabolite biomarkers that could be related to biochemical processes associated with increased inflammation and bacterial burden in the CF lung. These features that are unique to CF lung biology could eventually aid the development of new treatments and diagnostics."

Two metabolomic characteristics—increased amino acids and decreased acylcarnitines—were found to be unique to CF and potentially could serve as biomarkers of the inflammation and infection. Additionally, a metabolite of interest, L-methionine-S-oxide, was positively corrected

with the abundance of Staphylococcus, a traditional CF pathogen, and negatively correlated with the abundance of anaerobic bacteria of interest in the development of chronic CF lung disease. The study provides some interesting clues about what may be happening biologically in the CF airway.

"Our findings are in the very early stages of research and are not yet ready for clinical applications," said senior author Theresa Laguna, MD, MSCS, Division Head of Pulmonary and Sleep Medicine at Lurie Children's and Associate Professor of Pediatrics at Northwestern University Feinberg School of Medicine. "Our results lay important groundwork for future studies that ultimately will advance clinical care for children with CF."

More information: John B. O'Connor et al, Network Analysis to Identify Multi-Omic Correlations in the Lower Airways of Children With Cystic Fibrosis, *Frontiers in Cellular and Infection Microbiology* (2022). DOI: 10.3389/fcimb.2022.805170

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