Functional lower airways genomic profiling of the microbiome to capture active microbial metabolism

Imran Sulaiman[1], Benjamin G. Wu[1], Yonghua Li[1], Jun-Chieh Tsay[1], Maya Sauthoff[1], Adrienne S. Scott[1], Kun Ji[1], Sergei B. Koralov[2], Michael Weiden[1], Jose C. Clemente[3,4], Drew Jones[5], Yvonne J. Huang[6], Kathleen A. Stringer[7], Lingdi Zhang[8], Adam Geber[8], Stephanie Banakis[8], Laura Tipton[8], Elodie Ghedin[8,9] and Leopoldo N. Segal[1]

[1]Division of Pulmonary, Critical Care, and Sleep Medicine, Dept of Medicine, New York University School of Medicine, New York, NY, USA. [2]Dept of Pathology, New York University School of Medicine, New York, NY, USA. [3]Dept of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [4]Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [5]Dept of Biochemistry and Molecular Pharmacology and Dept of Radiation Oncology, New York University School of Medicine, New York, NY, USA. [6]Division of Pulmonary and Critical Care Medicine, Dept of Medicine, University of Michigan Medical School, Ann Arbor, MI, USA. [7]Dept of Clinical Pharmacy, College of Pharmacy, and Division of Pulmonary and Critical Care Medicine, Dept of Medicine, School of Medicine, University of Michigan, Ann Arbor, MI, USA. [8]Center for Genomics and Systems Biology, Dept of Biology, New York University, New York, NY, USA. [9]Dept of Epidemiology, School of Global Public Health, New York University, New York, NY, USA.

Corresponding author: Leopoldo N. Segal (Leopoldo.Segal@nyumc.org)

Shareable abstract (@ERSpublications)
This study shows that both whole-genome shotgun and RNA metatranscriptome sequencing can be done on lower airway samples and can provide valuable information on bacterial function
https://bit.ly/3hNmZfi

Cite this article as: Sulaiman I, Wu BG, Li Y, *et al*. Functional lower airways genomic profiling of the microbiome to capture active microbial metabolism. *Eur Respir J* 2021; 58: 2003434 [DOI: 10.1183/13993003.03434-2020].

This article has supplementary material available from erj.ersjournals.com

This article has an editorial commentary: https://doi.org/10.1183/13993003.00321-2021

Received: 16 Oct 2020
Accepted: 19 Dec 2020

Abstract

Background Microbiome studies of the lower airways based on bacterial 16S rRNA gene sequencing assess microbial community structure but can only infer functional characteristics. Microbial products, such as short-chain fatty acids (SCFAs), in the lower airways have significant impact on the host's immune tone. Thus, functional approaches to the analyses of the microbiome are necessary.

Methods Here we used upper and lower airway samples from a research bronchoscopy smoker cohort. In addition, we validated our results in an experimental mouse model. We extended our microbiota characterisation beyond 16S rRNA gene sequencing with the use of whole-genome shotgun (WGS) and RNA metatranscriptome sequencing. SCFAs were also measured in lower airway samples and correlated with each of the sequencing datasets. In the mouse model, 16S rRNA gene and RNA metatranscriptome sequencing were performed.

Results Functional evaluations of the lower airway microbiota using inferred metagenome, WGS and metatranscriptome data were dissimilar. Comparison with measured levels of SCFAs shows that the inferred metagenome from the 16S rRNA gene sequencing data was poorly correlated, while better correlations were noted when SCFA levels were compared with WGS and metatranscriptome data. Modelling lower airway aspiration with oral commensals in a mouse model showed that the metatranscriptome most efficiently captures transient active microbial metabolism, which was overestimated by 16S rRNA gene sequencing.

Conclusions Functional characterisation of the lower airway microbiota through metatranscriptome data identifies metabolically active organisms capable of producing metabolites with immunomodulatory capacity, such as SCFAs.