

TITLE: CAN THE DATA OF MICROBIOME BE USED TO PREDICT THE PRESENCE OF *BURKHOLDERIA* SPP IN PULMONARY MICROBIOTA OF CYSTIC FIBROSIS PATIENTS?

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ABSTRACT:

Burkholderia cepacia complex (Bcc) comprise the main pathogens related to clinical infections in patients with Cystic Fibrosis (CF). Infection/colonization by Bcc in the CF airway may lead to a necrotizing pneumonia. The detection of microbial pathogens in the CF airways is traditionally performed by bacteriological culture but this method may present low sensitivity and requires the presence of viable bacterial cells. Culture independent methods, such as metagenomic analysis by 16S rRNA sequencing, allows the identification of bacterial communities with no need of the conventional culture. The aim of this study was to compare the detection of the genus *Burkholderia* in the CF sputum by microbiome analysis and by the bacteriological culture. A total of 22 sputa collected for routine bacteriological culture of 9 patients from a CF reference center, were submitted to microbiome sequencing. DNA was extracted and the metagenomics was performed by 16S rRNA sequencing (V3V4 region) in an Illumina MiSeq (Illumina, San Diego, US). The bacteriological culture was performed according to standard protocol of the routine microbiology laboratory. *Burkholderia* genus was detected by microbiome analysis in 14 clinical specimens (63.6%) with at least one sputum specimen positive in all nine patients. Conversely, the bacteriological culture was capable to detect Bcc in only 4 sputa (18.2%) from 3 different patients. Analysis of historical data of bacteriological culture indicated that six of the nine CF patients presented Bcc in previous sputum. The time lapse between the results of the culture positive for Bcc and the detection of *Burkholderia* spp by microbiome varied from 2 months to more than 5 years. Noteworthy, three patients never had Bcc identified by bacteriological culture, although, it was possible to detect the *Burkholderia* genus by microbiome in their sputa. The identification of *Burkholderia* spp by microbiome analysis can predict the presence of Bcc in the airway of CF patients and can be used to anticipate the treatment with antibiotics to prevent the increase growth of viable cells of the bacteria in the respiratory tract. We consider that both methods, microbiome analysis and conventional bacteriological culture, are complementary and should be considered in conjunction to contribute to the best clinical management of CF airway infections.

Keywords: Microbiome; *Burkholderia* sp; Cystic Fibrosis; culture-independent technique.

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