

Investigating the airway microbiome in cystic fibrosis patients with a severe decline in lung function: an opportunity for a personalized microbiome based therapy

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Background. Cystic fibrosis (CF) is characterized by chronic airway infections involving a complex and dynamic microbial lung community. Though several studies have investigated the taxonomic composition of the airway microbiota, little is still known about the overall functional capabilities of the resident microbial populations and their relation to patient's lung disease status.

Hypothesis and objectives. Previous studies found changes in CF airway microbiota associated with a severe decline in lung function. The overall goal of this project – which follows the FFC#10/2014 project – is to deeply investigate the airway microbiome of stable (S) and substantial decliners patients (SD) and single patients' dynamics over a 15-month period, to discover the functional traits harbored by microbial communities and new microbiome-based biomarkers, which may be predictive of decline in lung function.

Methods. The microbial metagenomic content of airways specimens of CF patients was investigated by Illumina HiSeq technology. Shotgun metagenomic sequencing data were compared with patients' status to assess the presence of gene functions related to a severe decline in lung function and define new potential biomarkers.

Results. Results indicated that the severity of CF lung disease is associated with an imbalanced presence of antibiotic resistance genes and with a differential abundance of genes involved in metabolic pathways putatively correlated with bacterial virulence. To deeply investigate single patients' dynamics of the sputum microbiome, a metagenomic longitudinal analysis was carried out. During the study period (15 months), sputum samples of twenty-one CF patients were collected

over the 15 months' longitudinal survey at different time points (4-5 samplings for each patient). DNA extraction and metagenomic sequencing were performed, and a bioinformatic pipeline for data analysis was defined. Bioinformatic analyses are currently at run time, and final results being expected in a short period.

Spin-off for research & clinical purposes. Data obtained highlighted that different pulmonary conditions in patients with CF co-occur with a different microbiome gene repertoire. The whole set of metagenomic data will permit to discover new microbiome-based biomarkers, which could be used as predictive markers of severe decline in lung function, allowing earlier intervention and improving health care treatment of patients with CF.

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