Description of the Lung Microbiome in Chronic Obstructive Pulmonary Disease

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Abstract

Background. Chronic obstructive pulmonary disease (COPD) is an inflammatory disorder characterized by persistent airflow obstruction. While bacterial lung infections contribute to approximately 50% of COPD exacerbations, macro- and microorganisms of the lung harbor a bacterial community, termed the microbiome. This microbiome may initiate a chronic inflammatory state that drives COPD pathogenesis. This study describes the lung microbiome in a group of stable Moderate and Severe COPD patients without recent COPD exacerbation.

Methods. Frozen bronchoalveolar lavage fluid (BALF) samples from 14 patients with Moderate COPD, 8 patients with Severe COPD, and 10 healthy controls were obtained from previous studies. At the time of bronchoscopy, all COPD patients were non-smokers for at least 6 months and had not received oral steroids or antibiotics at least 2 months. Total DNA was extracted from control lungs BALF and used as a PCR template with primers specific for the hypervariable 3 region of bacterial 16S rRNA. 454 pyrosequencing was performed on all PCR amplicons. Skin analysis and taxonomic identification were performed using mothur, Ribosomal Database Project, Fast taxonomic classification.

Results. Over 942,888 sequences were obtained from 32 samples. After quality control filtering, each sample averaged 14,451 sequences. The Shannon and Simpson (1-1) microbial diversity indices demonstrated a significant increase in diversity with the development of COPD (p<0.005 and 0.0167, respectively) with age associated with increased diversity. The main phyla in all samples were Actinobacteria, Firmicutes, and Proteobacteria. Principal coordinate analyses demonstrated separate clustering of control and COPD samples, but COPD samples did not separate based on disease severity. COPD samples clustered based on the use of inhaled corticosteroids (ICS) and related bronchodilators (ICS). Metastats analysis demonstrated an increased abundance of specific oral bacteria in COPD samples, consistent with microaspiration.

Conclusions. The COPD lung microbiome reflects microaspiration of oral flora, while microbial diversity increases with development of COPD and greater age. The use of ICS or BID may alter the lung microbiome.

Methods

- Frozen bronchoalveolar lavage fluid (BALF) was obtained from:
  - 10 healthy controls
  - 14 patients with Moderate COPD
  - 8 patients with Severe COPD

- All COPD patients had not
  - Smoked for at least 6 months
  - Received systemic steroids or antibiotics for at least 2 months

- Data analysis was performed using mothur, Ribosomal Database Project, Fast UniFrac, and Metastats

Conclusions

- Microaspiration of oral flora is likely the source of the lung microbiome
- In COPD, the microbial diversity is increased, and age is associated with diversity.
- The microbiome may be altered by inhaled corticosteroids or inhaled bronchodilators