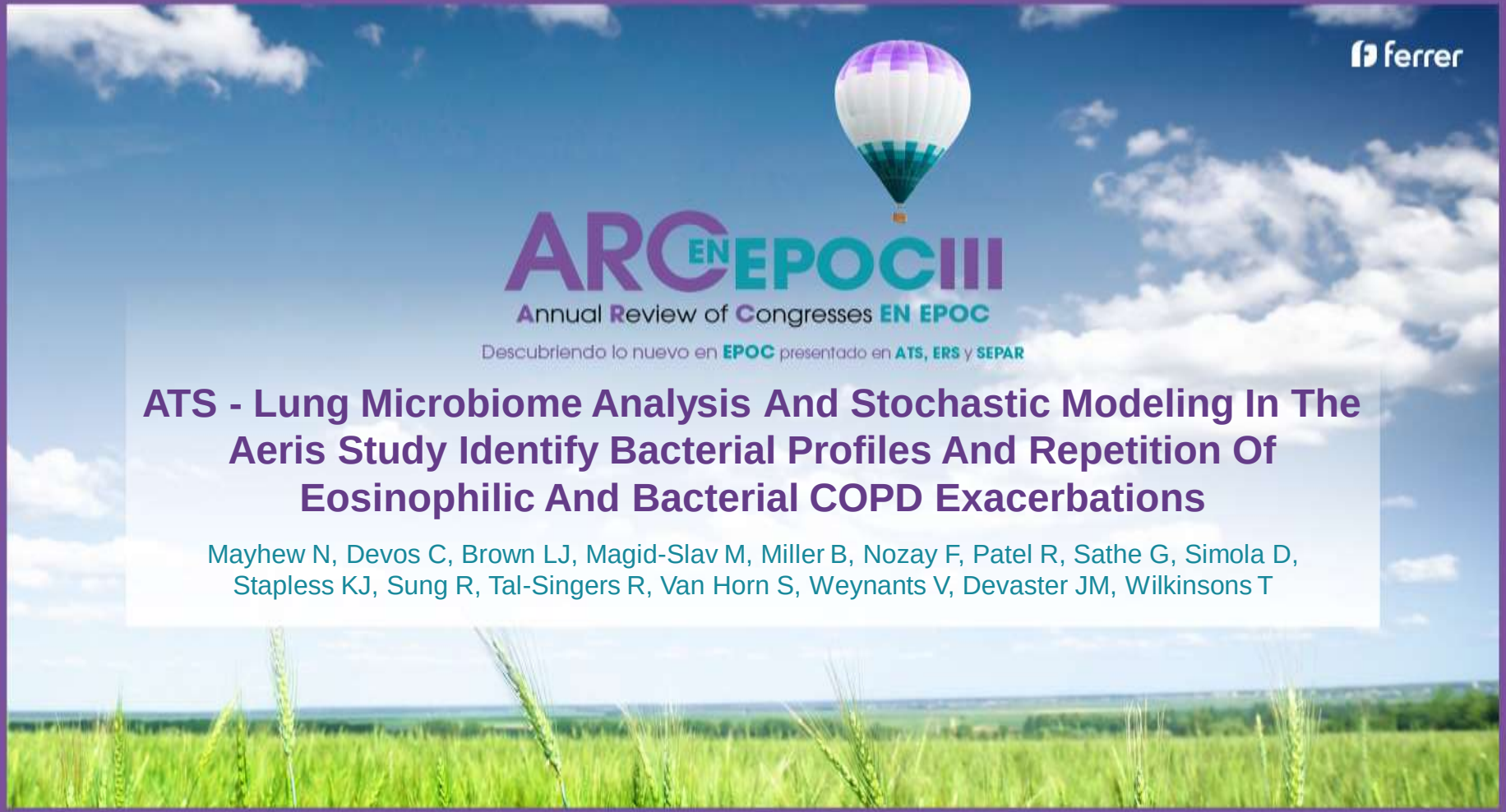

ATS - Lung Microbiome Analysis And Stochastic Modeling In The Aeris Study Identify Bacterial Profiles And Repetition Of Eosinophilic And Bacterial COPD Exacerbations

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Rationale (I)

– Healthy human lungs are not sterile and contain a variety of commensal microbiota. Alterations in the composition of the lung microbiome, known as **dysbiosis** have been associated with lung disease and in particular may play a functional role in disease severity and exacerbations obstructive pulmonary disease (COPD).

Rationale (I)

- The AERIS study (Acute Exacerbation and Respiratory Infections in COPD: GSK Study 114378; NCT01360398) provides a unique opportunity to **observe dynamic changes in the lung microbiome and associated biomarkers in a cohort of 127 COPD patients,** who were followed monthly and within 72h of exacerbation onset over two years.

Methods:

- We surveyed 584 sputum samples from 104 patients to analyze the lung microbiome at both stable and exacerbation time points in the first year of the study via 16S rRNA sequencing.

Results (I)

- We obtained a mean of 5.7 samples per subject, 2.1 of which were collected during an exacerbation event.
- **Ranking subjects by GOLD status showed a significant decrease in entropy of the microbiome** (Shannon diversity index) and an increase in the relative abundance of Proteobacteria, such as Haemopnius, with an increase in disease severity.
- **The genus with the most significant increase between stable and exacerbation events was Moraxella** (p= 0.0134).

Results (II):

- Exacerbations **with different phenotypes** (containing bacterial pathogens detected by culture compared to eosinophils in sputum) had significantly distinct ratios of Proteobacteria to Firmicutes.

- Moreover, using a Markov chain analysis of exacerbation phenotypes, we found that **bacterial and eosinophilic (p= 9.25E-11 and 1.42E-3 respectively) but not viral (p=0.141) exacerbations were more likely to be repeated in subsequent exacerbations within a subject.**

Results (III):

- Finally, we analyzed the temporal **stability of the lung microbiome within each subject and found that microbiome composition in both stable and exacerbation states became more variable in patients experiencing exacerbations during the year.**

- **Patients with bronchiectasis (n 10) showed notably more stability in microbiome composition,** which was characterized by a high proportion of Haemopnius relative to that in patients without bronchiectasis.

Conclusions:

– These findings improve our understanding of lung microbiome behavior over time in COPD, providing insight into our ability to use dysbiosis as a biomarker in COPD classification and establishing for the first time infective and inflammatory longitudinal phenotypes that may be used to guide future therapeutic strategies.


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