
Dysregulation of the microbial 'gut-lung' axis in bronchiectasis

J. Narayana (Singapore, Singapore), S. Aliberti (Milan, Italy), M. Mac Aogáin (Dublin, Ireland), T. Jaggi (Singapore, Singapore), N. Ali (Singapore, Singapore), I. Fransiskus Xaverius (Singapore, Singapore), F. Amati (Milan, Italy), A. Gramegna (Milan, Italy), K. Tsaneva-Atanasova (Exeter, United Kingdom), F. Blasi (Milan, Italy), S. Chotirmall (Singapore, Singapore)

Introduction: Emerging work supports the existence of a microbial 'gut-lung' axis which remains unexplored in bronchiectasis. **Methods:** Prospective and concurrent sampling of sputum (lung) and stool (gut) in a bronchiectasis cohort (n=57) was performed and subjected to bacteriome (16S rRNA) and mycobiome (18S ITS) assessment. Shotgun metagenomics was performed in a subset (n=15). Data from lung and gut compartments were integrated by weighted similarity network fusion (wSNF) followed by spectral clustering and co-occurrence analysis to assess clinically relevant 'gut-lung' networks. **Results:** We report the first description of a 'gut-lung' axis in bronchiectasis. Microbial communities demonstrate greater fungal overlap but reduced bacterial diversity between the lung and gut, respectively. Multi-biome integration followed by clustering reveals a 'high-risk' patient group characterised by severe clinical and radiological bronchiectasis including increased exacerbations. These patients exhibit enhanced 'gut-lung' microbial interactions and significant increases in airway *Pseudomonas* accompanied by gastrointestinal *Bacteroides* and *Saccharomyces*. Profiles of the 'low-risk' group were characterized by oral commensals. **Conclusion:** A dysregulated 'gut-lung' axis associates with poorer clinical outcome in bronchiectasis. Immunomodulation of the 'gut-lung' axis in bronchiectasis warrants further assessment. **Funding:** Singapore Ministry of Health's National Medical Research Council under its Clinician-Scientist Individual Research Grant (MOH-000141) (S.H.C) and Clinician Scientist Award (MOH-000710) (S.H.C).
