O453
1-hour Oral Session
New insights into host-pathogen interactions

Nasopharyngeal microbiota, host transcriptome and disease severity in children with respiratory syncytial virus infection.

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Background: Respiratory syncytial virus (RSV) is the leading cause of acute lower respiratory tract infections and hospitalizations in infants and young children worldwide. Currently known risk factors incompletely explain the variability in RSV disease severity between individuals. We postulate that RSV disease severity can be influenced by specific nasopharyngeal microbiota that modulate the host immune response to RSV infection.

Material/methods: We studied the nasopharyngeal bacterial community profiles of 106 RSV patients, who were enrolled in the outpatient care clinic or admitted to the hospital, and 26 healthy children using 16S-rRNA sequencing. In parallel, we performed a whole blood gene expression analysis to characterize the systemic host immune response in 104 of these infants. Using both supervised and unsupervised data-analysis techniques we conjunctively studied the associations between nasopharyngeal microbiota, host transcriptome and RSV infection.

Results: We identified five nasopharyngeal microbiota profiles characterized by enrichment of *H. influenzae*, *Streptococcus (pneumoniae)*, *Corynebacterium*, *Moraxella* and *S. aureus.* RSV infection alone, as well as RSV hospitalization, were positively associated with *H. influenzae* and *Streptococcus* abundance, and negatively associated with *S. aureus* abundance, independently of age. The host immune response to RSV, regardless of nasopharyngeal microbiota profiles, was defined by increased expression of interferon-related genes and pathways. However, patients included in the *H. influenzae*, and to a lesser extent in the *Streptococcus* clusters, showed differential expression of genes related to pro-inflammatory innate immunity pathways, including neutrophil recruitment and toll-like receptor-signalling, suggesting an additive or synergistic effect of *H. influenzae and Streptococcus* colonization on the RSV-induced inflammatory immune response.

Conclusions: Nasopharyngeal microbiota typified by *H. influenzae* and *Streptococcus* predominance were associated with RSV hospitalization and specific host transcriptional profiles, suggesting viral-bacterial co-signalling. Future studies are warranted to unravel the directionality and mechanism of these interactions, which could have implications for the prevention and treatment of RSV disease.