



# Respiratory Virome Dysbiosis in Children with Asthma

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## DESCRIPTION

Respiratory virome play an important role in asthma exacerbation and persistence. Virus presence is typically examined using targeted methodologies during periods of disease activity and infections, leaving viral recurrence during steady states unaccounted for, using metagenomics, we look at the virome in the upper respiratory tracts of healthy and asthmatic preschool children during asymptomatic/non-infection periods. The dysbiosis virome of children with asthma is linked to illness severity and control. Bacteriophage insufficiency is the most common cause of dysbiosis, whereas eukaryotic virus prevalence is on the rise. Differential viral species co-occurrence patterns at the meta community level show a decline in asthmatic microbiota community resilience. As a result, viral dysbiosis is a crucial feature of asthma pathogenesis.

According to the microbial immigration and elimination concept, the respiratory tract harbours heterogeneous microbiota that decreases in biomass and richness from the 'source' Upper Respiratory Tract (URT) to the lower airway. Bacterial communities have been shown to be disrupted in disease or infectious circumstances, and the bacterial component of the respiratory microbiome is rapidly being recognized as playing a key role in the susceptibility and severity of acute respiratory illness and asthma. Early infancy microbial colonization of the nasal cavity and nasopharynx has been associated to wheeze episodes and asthma progression, which could be mediated by resistance or susceptibility to acute respiratory infections.

Acute respiratory viruses, in particular, have historically been studied in isolation from the respiratory microbial environment. Most notably, despite being the most direct link between viruses and bacteria in the respiratory system, our knowledge of prokaryotic viruses that infect bacteria (bacteriophages or phages) is exceedingly poor. Only a few researches have looked at the respiratory prokaryotic virome, and none have looked into

asthma. Despite the well-established effects of individual viral infections on asthma exacerbation, aggravation, and persistence, the association between viral ecology of the airways and asthma remains poorly known, with prokaryotic viruses receiving less attention in particular. Preschool children with asthma exhibit a notably dysbiosis virome during asymptomatic/infection-free times, which correlates with disease severity and control.

Bacteriophage insufficiency is the most common cause of dysbiosis, but the prevalence of eukaryotic viruses, primarily Anelloviruses and Picornaviruses, is on the rise. The networks of viral-viral and viral-bacterial co-occurrence were dramatically loosening, implying that microbial communities in asthma may be less robust. As a result, viral dysbiosis appears to be not only a critical feature of asthma pathogenesis, but also one that may be treatable. Increased incidence, richness, and diversity of eukaryotic viruses were found in the asthmatic virome. Since there is no reason to believe that children with asthma are exposed to viruses differently than healthy children, this could indicate differences in viral control through immunological competence. Asthmatics may not be able to eliminate eukaryotic viruses as effectively as healthy children, allowing viruses to persist in the airways at low levels during asymptomatic periods. This may also explain a differential threshold for susceptibility to viral infection in asthma.

In this study, a number of choices had to be made regarding the design, analysis, and interpretation of metagenomic data. To begin, metagenomics sequencing can identify viral and microbial genomes, or genome 'traces,' without concluding the presence of infectious diseases. Because technique relies on prior knowledge of the physical properties of the virions or virus-like particles, viral enrichment via gradient ultra-centrifugation can skew the sequencing results. To address the aforementioned, we used a sample-processing method that filtered away 'bare' nucleic acids while maintaining encapsulated viral sequences of DNA and RNA genomes, allowing us to get as near to identifying virus-like particles or viruses as feasible.

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