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313 Viral Infections and Their Impact on the Respiratory Microbiome in Pediatric Patients with Cystic Fibrosis



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RATIONALE: Viruses are known to impact clinical status in patients with cystic fibrosis (CF); however their effects on the respiratory microbiome are unclear. The goal of our study is to assess changes in the lung microbiome of pediatric patients with CF during periods of wellness and exacerbation, with a focus on the impact of viral infection, using culture-dependent and independent techniques. **Our hypothesis is that viruses impact the respiratory microbiome leading to worse clinical sequelae during exacerbation.**

METHODS: In this **prospective, longitudinal** study we recruited 101 pediatric patients with CF, ages 0-22 years. We collected oropharyngeal swab, sputum, and BAL samples from subjects during their clinical baseline and exacerbation states. We used Illumina sequencing and standard culture for bacterial detection and quantitative RT-PCR techniques for viral detection.

RESULTS: We collected 380 samples from 102 subjects between March, 2013 and June, 2014. Seventy-three samples are virus positive and 307 are virus negative. The most prevalent viruses in our cohort are rhinovirus/enterovirus and coronavirus. **Virus (+) samples are associated with a greater prevalence of traditional CF pathogens ($p = 0.0018$).** We found no clear relationship between viral infections and clinical status or lung function. Using deep-sequencing, we defined 1,772 OTUs rarified to 10,000 reads and found some changes in relative abundances of organisms in virus (+) compared to virus (-) samples, particularly prevotella species.

CONCLUSIONS: Detection of viruses in pediatric patients with CF may predict subsequent infection with traditional CF pathogens. Viruses may also be associated with subtle changes in the microbiome but further analysis is needed.

314 A Prospective Microbiome-Wide Association Study of Childhood Food Sensitization and Allergy



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RATIONALE: Alterations in the intestinal microbiome are prospectively associated with the development of asthma; it is unknown whether these differences occur in food allergy.

METHODS: Child intestinal microbiome samples were collected at age 3-6 months in children participating in the follow-up phase of an interventional trial of high dose Vitamin D given during pregnancy. At age 3, sensitization to foods (milk, egg, peanut, soy, wheat, walnut) was assessed. Food allergy was defined as caretaker report of healthcare provider-diagnosed allergy to the above foods prior to age 3 years with evidence of IgE sensitization. Analysis was performed using phyloseq and DESeq2; p-values are adjusted for multiple comparisons.

RESULTS: Complete data were available on 225 children; there were 87 cases of food sensitization and 14 cases of food allergy. Microbial diversity measures did not differ between food sensitization and food allergy cases and controls. The genera *Haemophilus* (\log_2 fold change -2.10, $p=0.003$), *Clostridium* (\log_2 fold change -1.57, $p=0.007$), and *Dorea* (\log_2 fold change -1.57, $p=0.03$) were underrepresented among subjects with food sensitization. The genera *Oscillospira* (\log_2 fold change -2.85, $p=0.02$), *Citrobacter* (\log_2 fold change -3.40, $p=0.02$), *Lactococcus* (\log_2 fold change -3.33, $p=0.03$), *Dorea* (\log_2 fold change -3.05, $p=0.03$), and

Clostridium (\log_2 fold change -2.55, $p=0.04$) were underrepresented among subjects with food allergy.

CONCLUSIONS: The temporal association between bacterial taxa and food sensitization and allergy suggest that the microbiome may have a causal role in the development of food allergy. Our findings have therapeutic implications for the prevention and treatment of food allergy.

315 Features of the Bronchial Bacterial Microbiome Associated with Allergy and Mild Allergic Asthma.



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RATIONALE: While the composition of lower airway microbiota has been reported to differ in subjects with asthma compared to healthy controls, it is unclear whether these differences are a function of asthma or are related to allergy. Here we dissect the specific bacterial taxa associated with mild allergic asthma and those associated with allergy alone, in an attempt to identify potential bacterial contributors to asthma pathogenesis.

METHODS: Bacterial composition in protected bronchial brushings, from 28 mild corticosteroid-naïve allergic asthmatics (AA), 15 allergic non-asthmatics (AN) and 13 non-allergic non-asthmatics healthy controls (HC), was profiled using 16S rRNA sequencing on the Illumina MiSeq platform.

RESULTS: Compared to AN and HC, AA exhibited a loss of bacterial taxa, such as *Lactobacillus*, and *Methylobacterium*, which were predicted to encode putatively protective functions, and increased relative abundance of *Haemophilus*, *Neisseria*, *Porphyromonas* and *Sphingomonadaceae*. A number of these taxa were significantly correlated with systemic eosinophilia and elevated serum IgE, implicating these organisms as potential contributors of eosinophilic inflammation in allergic asthma. A number of taxa, including *Fusobacterium*, *Actinomyces* and *Treponema*, which were enriched in AA compared to HC airways were also enriched in AN compared to HC, and were considered as allergy-associated.

CONCLUSIONS: This study distinguishes taxa associated with allergy from those which are potential contributors to asthma pathogenesis. Understanding which specific members of the airway microbial community associated with allergy and which are associated with asthma may prove crucial for development of targeted therapeutics to control, or ideally, to prevent the development of disease.