

Metagenomic Sequencing and Evaluation of the Host Response in the Pediatric Aerodigestive Population

Chelsea Gatcliffe¹, Aparna Rao¹, Matthew Brigger¹, David Dimmock², Christian Hansen², Jesse Montgomery³, Robert Schlager³, Nicole Coufal², and Lauge Farnaes²

¹University of California San Diego

²Rady Children's Hospital San Diego

³IDbyDNA Inc.

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Abstract

Objectives To assess the diagnostic utility of metagenomic sequencing in pediatric aerodigestive clinic patients being evaluated for chronic aspiration. Clinical metagenomics allows for evaluation of both the respiratory microbiota and the transcriptome of the host immune response. **Study Design and Methods** Twenty-four children referred to an aerodigestive clinic were enrolled in a prospective, single-site, cross-sectional cohort study. At the time of clinical evaluation under anesthesia, two additional samples were obtained: an upper airway sample and a sample from bronchoalveolar lavage (BAL). Samples were sent for routine culture and analyzed using Explify® Respiratory, a CLIA Laboratory Developed Test (LDT) which identifies respiratory commensals and pathogens through RNA and DNA sequencing. Incidentally obtained host transcriptomics were analyzed to evaluate the host immune response. The results of these studies were correlated with the clinical presentation of the research subjects. **Results** In ten patients, organisms primarily associated with oral flora were identified in the BAL. Standard culture was negative in three patients where clinical metagenomics led to a result with potential clinical significance. Transcriptomic data correlated with the presence or absence of dysphagia as identified on prior videofluoroscopic evaluation of swallowing. Differentially expressed genes included upregulation of genes involved in the immune response, such as CXCL8 (interleukin 8) and ITGB2 (CD18). **Conclusions** Clinical metagenomics allows for simultaneous analysis of the microbiota and the host immune response from BAL samples. As the technologies in this field continue to advance, such testing may improve the diagnostic evaluation of patients with suspected chronic aspiration.

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