

## 'Silent' Viral Infections Promote Profound Biological Response

New technique offers insight into back and forth of viral infection and immune defense

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DENVER — Despite an absence of clinical illness, respiratory virus infection can cause significant changes in the biology of their airways, according to researchers at National Jewish Health. Many of those changes may contribute to asthma exacerbations in susceptible children. The researchers used a novel RNA-sequencing technique that provides insight into the human response to respiratory viral infections, the most common cause of asthma exacerbations.

“Despite lack of overt clinical illness these children exhibited profoundly altered molecular and cellular profiles in their airways,” said senior author Max Seibold, associate professor in the Center for Genes, Environment and Health at National Jewish Health. “These findings offer insight that could help us learn why and how viral infections are such a potent cause of asthma attacks.”

The researchers screened 92 asthmatic and 69 healthy children without apparent illness for respiratory virus infections evident in brushings taken from the children’s nasal passages. They used traditional quantitative polymerase chain reaction techniques to detect viral infections in 21 children and suspected infection in two more children.

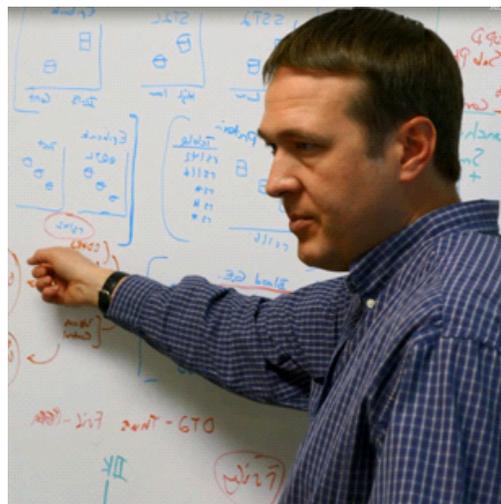
They also used a novel technique, called dual RNA-seq, to detect both viral infections and the genomic response in the children’s airways with the same biological sample. The novel technique detected 18 of the 21 virus-positive samples for an 86 percent sensitivity. They also found viral infections in 2 of 25 samples judged virus-free by traditional techniques. Overall, the two techniques combined to detect 25 viral infections among 161 children.

“The cutting-edge molecular and analytical techniques we used allow us to detect minute amounts of any virus and simultaneously track the host response in one experiment with one sample,” said Dr. Seibold.

Viral infections were associated with altered expression of 8,126 genes, notably those associated with asthma, infiltration of the airways by immune cells, down regulation of airway cilia genes, and cellular remodeling. Virally infected subjects exhibited striking down-regulation of ciliary genes, which could have dramatic consequences clearance of inhaled insults. Dr. Seibold also observed significant down-regulation in ribosomal subunit genes, even among the most lowly infected subjects, a cellular response to control infection.

“This is a profound airway genomic response among children who do not appear to have respiratory illness,” said Dr. Seibold. “Dual RNA-seq offers an exciting view of viral infections and human host responses.”

**National Jewish Health** is the leading respiratory hospital in the nation. Founded 121 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the media resources page.



Our team is available to arrange interviews, discuss events and story ideas.

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