

Genetic signature identified for RSV, the leading cause of infant hospitalizations worldwide

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(Medical Xpress)—Scientists have identified the genetic signature of respiratory syncytial virus (RSV), the leading cause of infant hospitalizations around the world. The work is a key step toward a better understanding of the immune response to RSV, which will aid the development of a vaccine and a tool that could allow physicians to determine the severity of the infection when symptoms first develop. The study, from a team at The Research Institute at Nationwide Children's Hospital, was published this week in *PLOS Medicine*.

The World Health Organization estimates that as many as 64 million children worldwide are infected with RSV at any given time. Although most infections result in mild, cold- or flu-like symptoms, RSV can lead to pneumonia or bronchiolitis, landing more than 144,000 infants and children in the hospital each year in the U.S. alone.

"Despite the disease burden, there is no approved vaccine and it is impossible to predict which patients will go on to develop more serious symptoms and require hospitalization," says Asuncion Mejias, MD, PhD, principal investigator in the Center for Vaccines and Immunity at Nationwide Children's and a co-lead author of the new study. "The ability to identify which patients are at risk for severe RSV disease when they first present for treatment would enable physicians to better triage patients, providing early and more targeted interventions."

One of the chief obstacles of managing infants with RSV infection is the lack of a diagnostic tool to predict which patients will develop a more severe illness that requires more aggressive interventions. For this study, Dr. Mejias and colleagues compared the RNA profiles—also called biosignatures—from 220 children under 2 years of age who were either healthy or hospitalized with

RSV or other respiratory viruses such as influenza or human rhinovirus, which causes the common cold but can also cause bronchiolitis.

They found that in patients with RSV, genes involved in the function of interferon and neutrophils—key components of the innate immune system—were activated, while genes that regulate T and B cells in the adaptive immune system were suppressed. The researchers plugged this biosignature into an algorithm used to compare the expression of specific genes between patients and healthy controls. The formula yields a score called "molecular distance to health." In the end, Dr. Mejias and her team were able to link specific scores to disease severity. The scores were so precise, in fact, that researchers could tell from the scores how many days RSV-infected infants had required hospitalization or supplemental oxygen.

"We showed that screening RNA profiles is a useful tool from the diagnostic point of view, as it allowed differentiation from influenza and rhinovirus infections with great accuracy," Dr. Mejias says. "It also helps us better understand the pathogenesis of this infection and, more important, to objectively assess disease severity in these patients."

Knowing the molecular distance to health score for RSV patients could soon have a direct application in the clinical setting, Dr. Mejias adds. Tools designed to calculate such scores in emergency rooms—the first stop for many patients with RSV—and even in pediatricians' offices are currently under development.

"These novel and affordable tools will have a much faster turn-around time that could facilitate the application of RNA profiles in 'real time' in the clinical setting," says Dr. Mejias, who also is an assistant professor of pediatrics at The Ohio State

University College of Medicine. "It may help triage patients when they first present to the emergency room or pediatric office, but it could also be useful for monitoring clinical changes during the course of the disease, with the ultimate goal of predicting clinical outcomes."

The findings also give researchers a better picture of just how the immune system responds to RSV, information vital to the development of a vaccine, says Octavio Ramilo, MD, a co-lead author of the study and chief of the Section of Infectious Diseases at Nationwide Children's.

"We urgently need better treatments for this disease and eventually a vaccine that can prevent RSV infection," says Dr. Ramilo, who also is a professor of pediatrics at The Ohio State University College of Medicine.

Dr. Ramilo is one of many scientists in the Center for Vaccines and Immunity who have spent decades trying to unravel the biological underpinnings of RSV, a virus that remains largely unknown to the general public. Despite its anonymity, RSV leads to one-quarter of all hospitalizations for pneumonia and 70 percent of hospitalizations for bronchiolitis in young children. RSV also causes severe pneumonia in immunocompromised patients and the elderly.

"We need to do a better job educating our [patients](#) and their families about RSV and the huge morbidity associated with these infections," he says.

Provided by Nationwide Children's Hospital

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