Researchers identify genetic factors for acute viral bronchiolitis in the first year of life

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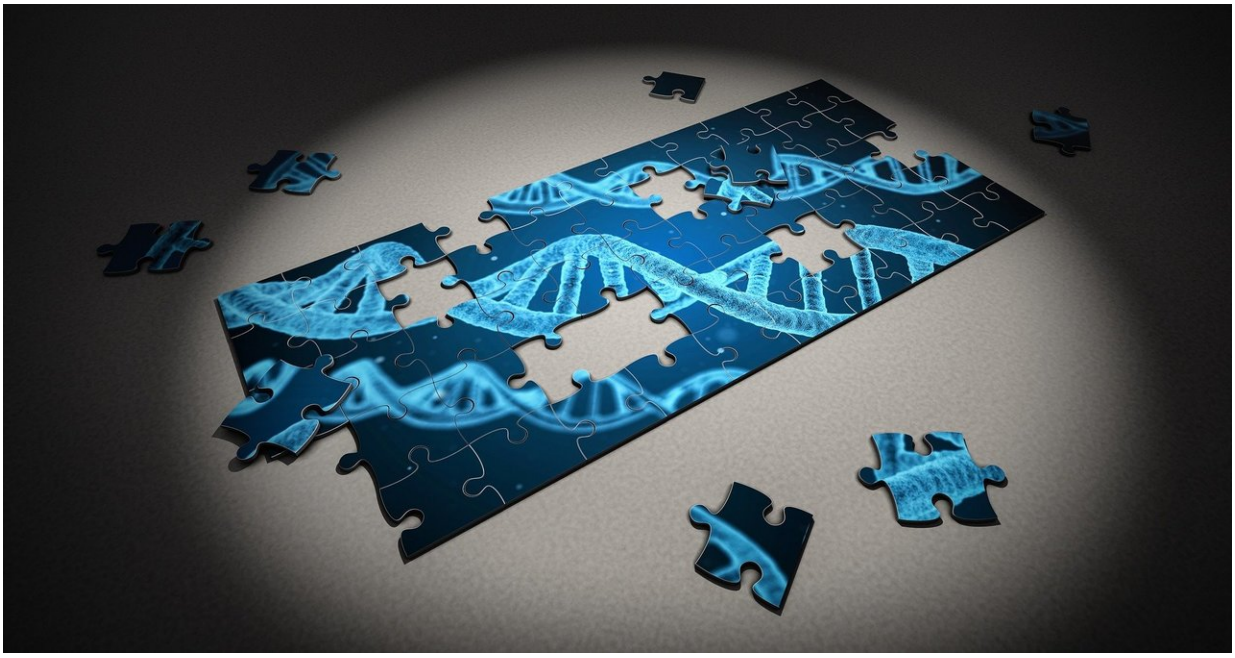

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A scientific study conducted at the State University of Campinas (UNICAMP) in São Paulo State, Brazil, has identified genetic factors associated with the severity of acute viral bronchiolitis. The study was supported by the Sao Paulo Research Foundation - FAPESP. The results were published in the journal *Gene*.

Principal investigator José Dirceu Ribeiro says that bronchiolitis is the most common disease during the first year of life, and also the leading cause of hospitalization during this period of infancy worldwide. Bronchiolitis, an infection of the respiratory tract that causes acute inflammatory damage to the bronchioles, is mostly a disease with minor consequences. However, 1 to 3 percent of patients require hospitalization, with some of them needing supplemental oxygen. A smaller proportion requires ICU treatment including mechanical ventilation.

"Detecting genetic associations in cases of acute viral bronchiolitis is the first step toward the development of tests to predict the possible clinical outcome for each patient diagnosed with the disease soon after arrival at the emergency room," said Fernando Augusto de Lima Marson, a researcher at FCM-UNICAMP and one of the authors of the article.

The new study set out to find correlations between genetic factors and the severest forms of acute viral bronchiolitis in patients that did not present any of the risk factors, such as prematurity, a history of lung disease, and passive smoking. "A very significant proportion of patients present with no risk factors, and the question arises in these cases of how to explain progression of the disease to its most severe form," Ribeiro said.

To investigate the existence of possible genetic factors that may influence the severity of the disease, the researchers studied 181 children admitted over a period of two years to three hospitals in the Campinas area. All were diagnosed with acute viral bronchiolitis and given oxygen therapy. Screening was conducted at UNICAMP's teaching hospital (Hospital das Clínicas), the Sumaré State Hospital, and Vera Cruz Hospital.

The researchers first took samples of the patients' nasal secretions to

determine the type of virus that had caused bronchiolitis in each case. As expected, in most cases, it was respiratory syncytial virus (RSV). More specifically, infection by RSV accounted for 69.9 percent of the cases, while rhinovirus accounted for 26.5 percent.

The researchers also evaluated all 181 children to find out if they fell within one or more risk groups for acute viral bronchiolitis. The result of this analysis was revealing in that 131, or 72 percent, were not part of any risk group.

Molecular biology and statistical techniques were used to study and compare the patients' DNA. Specific genetic markers were sought, especially single-nucleotide polymorphisms (SNPs), a type of DNA sequence variation that accounts for over 90 percent of genetic variation in the human genome.

In the statistical treatment of the data, patient outcomes were compared, and polymorphism frequency was compared between patients and a control group comprising 536 healthy individuals aged 19-25, randomly invited and with no personal or family history of lung disease.

Polymorphism frequencies were also analyzed for each type of virus, including RSV subtypes A and B, as well as rhinovirus, and possible cases of virus co-detection were identified.

"Our study focused on the genetic factors that might be associated with the severity of acute viral bronchiolitis," Marson said. "It provides evidence of a link between the patient's genetic predisposition and the severity of the disease. As far as we're aware, it's the first study worldwide to show this in such detail, including a large number of genetic variants."

Some genes are indeed associated with the presence of specific viruses

that can cause the disease. The researchers at UNICAMP found a link between the SNP rs2107538*CCL5 and bronchiolitis caused by RSV and RSV subtype A and a link between the SNP rs1060826*NOS2 and bronchiolitis caused by rhinovirus.

"The SNPs rs4986790*TLR4, rs1898830*TLR2 and rs2228570*VDR were associated with very severe cases of the disease, which progressed to a fatal outcome. The SNP rs7656411*TLR2 was associated with the need for oxygen supplementation, while rs352162*TLR9, rs187084*TLR9 and rs2280788*CCL5 were associated with cases in which ICU admission was required. Finally, rs1927911*TLR4, rs352162*TLR9 and rs2107538*CCL5 were associated with the need for mechanical ventilation," Marson said.

The authors of the study stress the importance of replication using other datasets. Nevertheless, they consider the results highly promising.

"Medicine is advancing toward the development of therapies tailored to the needs of each patient," Marson said. "In this context, the identification of SNPs associated with the disease in question could provide a target for genetic therapy, so that treatments and management strategies can be developed for precision medicine and preventive medicine, respectively."

More information: Alfonso Eduardo Alvarez et al, Association between single nucleotide polymorphisms in TLR4 , TLR2 , TLR9 , VDR , NOS2 and CCL5 genes with acute viral bronchiolitis, *Gene* (2017). DOI: 10.1016/j.gene.2017.12.022

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