

Researchers map pathway of infection for a common, potentially life-threatening respiratory virus

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Researchers at the University of Toronto, The Hospital for Sick Children (SickKids), St. Paul's Hospital and the University of British Columbia have identified a new treatment target for a virus that causes severe lung infections and an estimated 10% of common colds.

The virus, called human <u>respiratory syncytial virus</u> or RSV, is the most common reason for hospitalization of infants and children under two years of age; currently there is no <u>effective therapy</u> or vaccine for it.

"This discovery provides an understanding of the mechanism through which RSV causes infection and offers a <u>target molecule</u> for development of new cell-based therapies," said the study's principal investigator Prof. Richard Hegele, Chair and Professor in U of T's Department of Laboratory Medicine and <u>Pathobiology</u> who is also Chief of Paediatric Laboratory Medicine at SickKids.

The research is published in the current edition of the journal *Nature Medicine*.

The researchers found that RSV interacts with healthy cells by binding with a molecule located on the surface of those cells called nucleolin. By manipulating the function of nucleolin in cell culture, they were able to decrease RSV infection or increase susceptibility to it.



In mice, the researchers showed that disruption of lung nucleolin was associated with significantly reduced RSV infection, confirming that the molecule is a viable <u>therapeutic target</u>.

"While other factors may influence the frequency and severity of RSV infections, our results indicate that the presence of nucleolin on the cell surface is sufficient for RSV to successfully infect cells," said Hegele. "We can now pursue strategies designed to block the interaction of RSV with cell surface nucleolin, the idea being to find approaches that will safely and effectively halt infection by preventing RSV from entering the cell in the first place."

Researchers have been searching for a receptor for RSV for over five decades.

"This is a long-awaited and much-needed discovery that will help researchers develop new therapies for this disease, which has a large global burden, primarily affecting young children and other vulnerable populations," said Dr. David Marchant, a research associate at UBC's James Hogg iCAPTURE Centre at St. Paul's Hospital, and co-lead on the study. "What is especially encouraging is that there is already a lot of ground work done in terms of understanding the biology of nucleolin to treat other ailments like cancer. The discovery of the RSV receptor combined with this knowledge could help deliver a potential therapeutic much faster."

Increasingly, RSV is being recognized as a serious pathogen of the elderly for causing lung infections such as pneumonia. It is also a common cause of middle ear infections and can infect other organ systems, and has been implicated in the onset of asthma and allergy in children. Organ transplant recipients or other individuals whose immune systems are compromised are also at increased risk for serious RSV <u>lung infections</u>.



According to the World Health Organization, the global RSV disease burden is estimated at 64 million cases and 160,000 deaths each year. It is considered the single most important cause of severe respiratory illness in infants and young children.1

Provided by University of Toronto

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