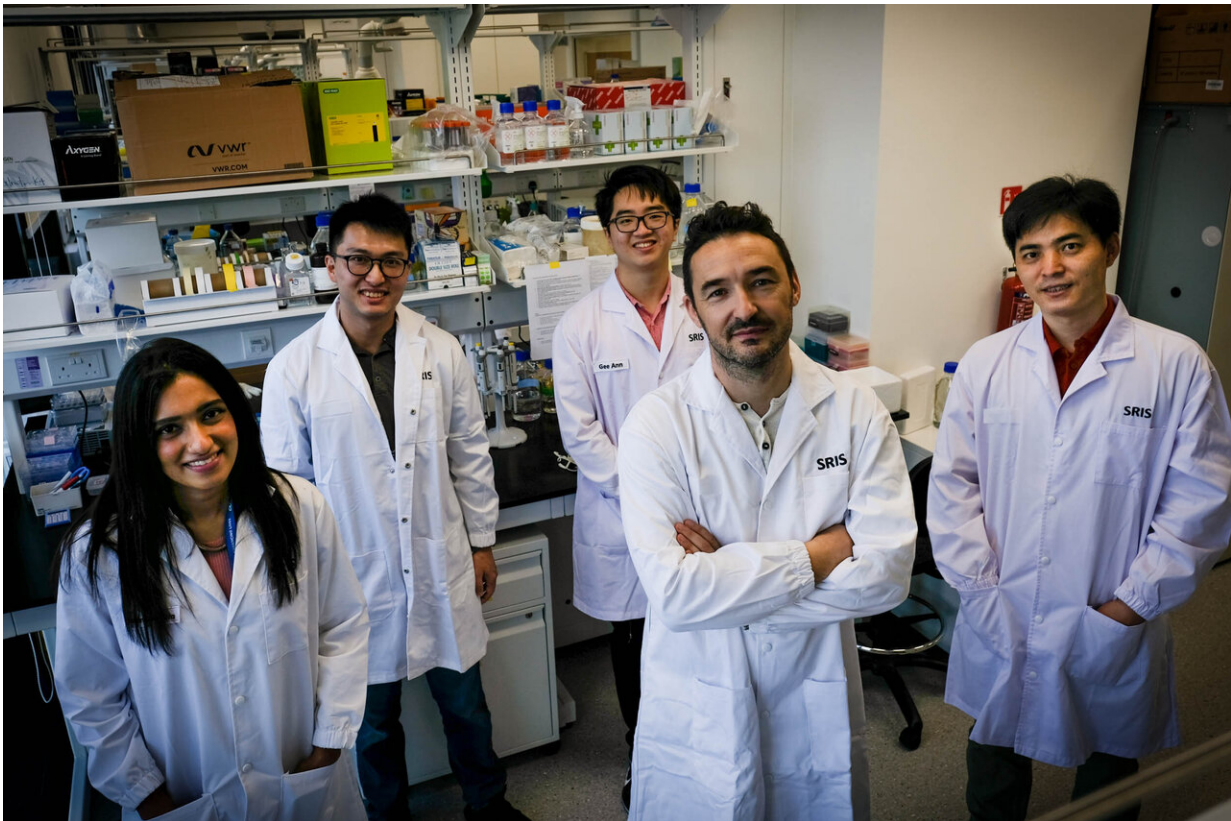# Scientists discover role of protein in detecting the common cold virus

December 1 2020

(Left to right) Dr Kim S. Robinson, from SRIS and Institute of Medical Biology (IMB), Asst Prof Franklin Zhong from NTU's Lee Kong Chian School of Medicine (LKCMedicine) and A*STAR's Skin Research Institute of Singapore (SRIS), Mr Toh Gee Ann, Research Assistant at LKCMedicine, Prof Bruno Reversade from A*STAR's Genome Institute of Singapore and Institute of Molecular and Cellular Biology, and Dr Sun Zijin, Senior Research Fellow at LKCMedicine. Credit: Nanyang Technological University

The role of a protein in detecting the common cold virus and kickstarting an immune response to fight infection has been uncovered by a team of scientists from Nanyang Technological University, Singapore (NTU Singapore), the Agency for Science, Technology and Research (A*STAR) and the National University of Singapore.

In a study published in one of the world's leading scientific journals *Science* on 22 October 2020, they showed that the protein NLRP1, found on the skin and in the airways, is a sensor that detects the human rhinovirus (HRV). When NLRP1 breaches the respiratory tract, it triggers an immune response leading to inflammation in the lungs and causes symptoms of the common cold.

HRV is a major cause of the common cold and acute respiratory disease in children and adults, which in severe cases, leads to bronchiolitis and pneumonia.

The research team said that discovering NLRP1's purpose could lead to new treatments for the symptoms of the common cold, which affects millions of people annually. They plan to work with clinicians to develop drugs that 'turn off' or block NLRP1, to lessen the severity of symptoms for HRV-related diseases. However, the team noted that blocking the protein in human lung cells did not increase the viral load, which refers to the amount of virus in an infected person's blood.

"Now that we know that NLRP1 is the 'on switch' for inflammation after it detects the common cold virus, the next step is to figure out how to block its activation and to minimize the inflammatory response it triggers," said Assistant Professor Franklin Zhong from NTU's Lee Kong Chian School of Medicine and A*STAR's Skin Research Institute of Singapore (SRIS).

Asst Prof Zhong is the corresponding author of the study, along with

Professor Bruno Reversade from A*STAR's Genome Institute of Singapore and Institute of Molecular and Cellular Biology and first author, Dr. Kim S Robinson, Research Fellow at SRIS, A*STAR.

Asst Prof Zhong said that their new insights into immune system functions could help scientists to develop more effective treatments for other inflammatory diseases of the human airway.

"This work represents a significant advance in our understanding of how our immune system uses special proteins to sense and defend against viral pathogens. This knowledge will be useful in the design of treatments for viral diseases including influenza and COVID-19," he said.

NLRP1 has been known to scientists for years but its exact purpose was unknown. It is a member of a class called 'Nod-like Receptor' proteins that are sensors in the immune system that trigger the human body's response against invading pathogens.

When the team began their study in 2017, they hypothesized that NLRP1 serves as a sensor for viruses, because it is highly abundant in the human skin and lungs—surfaces that are commonly exposed to viral pathogens.

The team screened NLRP1 against several viruses to see if any would trigger the protein. After months of trials, they observed that an enzyme made by HRV called 3Cpro activated NLRP1 in human airway cells.

They saw that the 3Cpro enzyme cut into NLRP1 at a specific point, triggering a form of inflammatory 'cell death', which is an important process in rapidly clearing pathogens like HRV during an infection.

Prof Reversade, who is also Professor of Genetics at Koç University in

Istanbul, Turkey, said that pinpointing NLRP1's purpose marked a key step in understanding how our bodies react to HRV infections.

"There is immediate value from this finding, as we can better understand why an HRV infection could lead to complications in individuals with weaker immune systems, such as young children, the elderly, and those with asthma," said Prof Reversade.

He added that the value from this research could extend to other diseases caused by viruses of the same family.

"Targeting NLRP1 in patients is likely to provide therapeutic benefits in a number of human diseases. Our findings on the immune response to this class of viruses also bear relevance to Coxsackieviruses which are responsible for hand, foot, and mouth disease (HFMD) in young children."

Provided by Nanyang Technological University