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**EMBARGOED FOR RELEASE:**  
November 21, 2018 - 1:00 PM Eastern  
*Fort Detrick, MD*

CONTACT: Caree Vander Linden  
(301) 619-2285  
teresa.l.vanderlinden.civ@mail.mil

### **USAMRIID Scientists Help Identify Key Hantavirus Receptor**

A global team of investigators has identified a key protein involved in Hantavirus Pulmonary Syndrome (HPS), a serious and sometimes fatal respiratory disease, according to research published today in the journal *Nature*.

Specifically, a cell-surface receptor protein called protocadherin-1 (PCDH1), commonly associated with human asthma, is responsible for facilitating lung cell infection and triggering HPS.

For decades, scientists have been attempting to identify the host molecules that mediate hantavirus infection and lead to HPS, which has a case fatality rate of 35-40 percent. Currently there are no licensed vaccines, prophylactics, or therapeutics to prevent or treat this highly pathogenic disease, which is transmitted to humans by infected rodents.

The study was co-led by John M. Dye, Ph.D, U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID); Kartik Chandran, Ph.D, Albert Einstein College of Medicine (AECM); Thijn R. Brummelkamp, Ph.D., Netherlands Cancer Institute; and Zhongde Wang, Ph.D., Utah State University.

Through a genetic screen, the research team discovered that new world hantaviruses found in North and South America (Sin Nombre virus and Andes virus, respectively) were unable to infect cells when PCDH1 was “knocked out.” Furthermore, when hamsters were depleted of PCDH1, then challenged with Andes virus, they were largely resistant to infection and lung injury.

“Our animal studies established that PCDH1 is essential for lung infection with new world hantaviruses, providing us with a viable target for blocking the disease,” said co-first author and USAMRIID senior staff scientist Andrew S. Herbert, Ph.D.

Pathogenic hantaviruses first emerged in the United States in 1993, and USAMRIID played a key role in that discovery. In the midst of an unexplained outbreak of severe respiratory distress in several western states, USAMRIID and the Centers for Disease Control and Prevention worked jointly to confirm that the disease was caused by a hantavirus that had not previously been reported.

Notably, USAMRIID scientists went on to demonstrate that Syrian hamsters exposed to very low doses of Andes virus developed a disease that closely mimicked human HPS. This hamster model laid the groundwork for further research, including the study published today.

“The discovery of the cellular receptor for hantaviruses allows for rational and logical drug and antibody design,” said Dye. “Stopping the virus from infecting lung tissue provides a route to eliminating HPS.”

He also noted that the team’s work showcases the importance of international collaboration, and further demonstrates how basic science research discoveries are critical to the development of medical countermeasures around the world.

“While hantavirus infections are rare, they’re expected to increase in the coming decades as temperatures across the globe rise due to climate change,” commented AECM’s Chandran. “And we need to be better prepared for that possibility.”

USAMRIID’s mission is to provide leading edge medical capabilities to deter and defend against current and emerging biological threat agents. Research conducted at USAMRIID leads to medical solutions—vaccines, drugs, diagnostics, and information—that benefit both military personnel and civilians. The Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency’s Joint Science and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command. For more information, visit [www.usamriid.army.mil](http://www.usamriid.army.mil)

#### *Funding:*

The work was supported by funds from U.S. Joint Science and Technology Office/Defense Threat Reduction Agency; the National Institutes of Health; Netherlands Organisation for Scientific Research, Cancer Genomics Center (Netherlands); Ammodo KNAW Award for Biomedical Sciences (Netherlands); Integrative Biology of Emerging Infectious Diseases Labex project (France); Investissements d’Avenir program (France); Canadian Institutes of Health Research; Comisión Nacional de Investigación Científica y Tecnológica (Chile); and the Irma T. Hirschl/Monique Weill-Caulier Trust.

#### *Reference:*

Protocadherin-1 is essential for cell entry by New World hantaviruses.

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<https://doi.org/10.1038/s41586-018-0702-1>