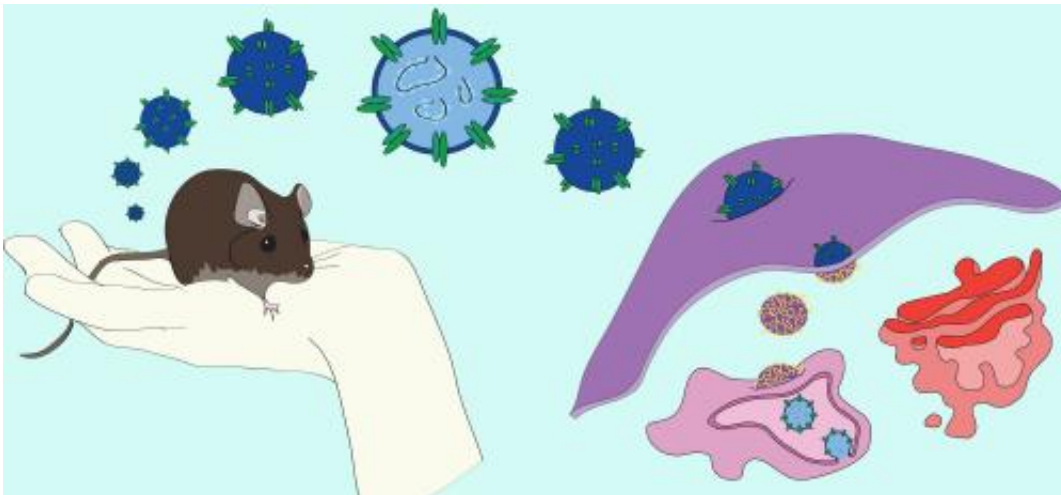


Cholesterol plays a critical role in hantavirus infection

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This graphic shows the rodent reservoir for hantaviruses, the aerosolized free virus, and the cellular entry pathway where the virus is taken up by endocytosis and enters within the endosomal compartment. Credit: Hannah J. Barbian

Viruses mutate fast, which means they can quickly become resistant to anti-viral drugs. But viruses also depend on proteins and nutrients provided by their hosts, and therefore one strategy to identify new anti-viral drugs is to identify and target such host-cell components. A paper published on February 6th in *PLOS Pathogens* reports that proteins involved in the regulation of cholesterol are essential for hantavirus entry into human host cells.

There are only about 30 known human cases of hantavirus infection in

the US per year (with the 2012 [cluster](#) in Yosemite National Park a recent example), but hanta is among the most deadly known human viruses: between 30 and 40% of people who are diagnosed die from hantavirus pulmonary fever. People who have hantavirus are not contagious, transmission only occurs when humans breath in small particles that carry excrements from infected rodents.

Together with colleagues, Paul Bates and Kenneth Briley, from the University of Pennsylvania, USA, set out to identify factors and pathways in human [cells](#) that were important for hantavirus infection. They focused on a member of the hantavirus group called Andes virus (ANDV). For their experiments they used mostly less dangerous viruses that were genetically engineered to share some characteristics with ANDV, and then used ANDV itself to confirm that the results were true for hantavirus as well.

In two independent genetic screens (systematic searches), they identified four proteins that were involved in hantavirus infection, and all of them were part of a [protein](#) complex that regulates [cholesterol](#) production in mammalian cells. The scientists next tested whether an experimental drug that targets one of the four proteins could prevent viral entry. They found that treating cells that originated from human airways with this drug before exposing them to virus resembling hanta made the cells less susceptible to virus infection.

Since one of the effects of this experimental drug is that it lowers cholesterol levels in cells, the researchers asked whether statins, a well-known group of cholesterol-lowering drugs that are taken daily by millions of people around the world, could also protect against hantavirus infection. Indeed, pre-treatment of human cells with mevastatin (a member of the statin group that lowers cholesterol by mechanisms that do not involve the proteins they had identified in their screen) made them less susceptible to ANDV infection.

The researchers say "The sensitivity of ANDV to safe, effective cholesterol-lowering drugs may suggest new treatments for ANDV infection and pathogenesis." Moreover, as cellular cholesterol balance has been found to be important for a number of other viruses as well, they hope that "targeting this process might lead to the development of broadly effective anti-virals".

More information: Petersen J, Drake MJ, Bruce EA, Riblett AM, Didigu CA, et al. (2014) The Major Cellular Sterol Regulatory Pathway Is Required for Andes Virus Infection. *PLoS Pathog* 10(2): e1003911. [DOI: 10.1371/journal.ppat.1003911](https://doi.org/10.1371/journal.ppat.1003911)

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