The ultimate viral stowaways: A Trojan Horse story

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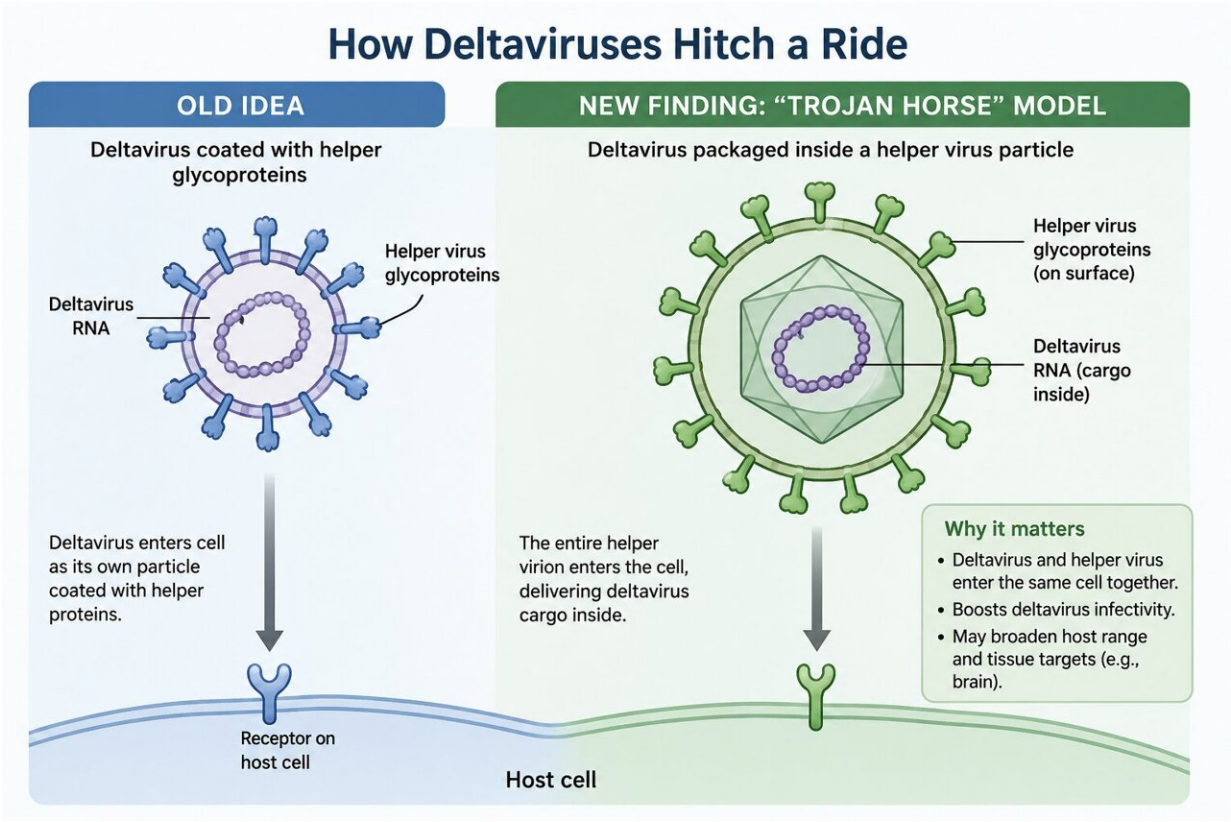


Simple schematic showing two models side-by-side: old idea (delta virus coated with helper glycoproteins) vs new "Trojan Horse" (delta virus cargo inside a helper virion). Credit: Generated using AI tools for illustrative purposes

Forget hitchhiking; some tiny viruses are playing viral "Trojan Horse,"

literally sneaking inside other viruses to invade new species and even our brains. It's a microscopic masterclass in stealth infection.

Scientists had believed they understood how viruses move around for decades. They recognized that some minuscule parasitic viruses—like the famous hepatitis D virus (HDV)—simply could not survive on their own. Their shells were only large enough for a bare handful of molecules to slip through. To invade cells, they depended on a larger "helper" virus to wrap them in a protective coat. It was a trick, and one of viral mimicry.

But what if the truth was far stranger, far more insidious?

What if these microscopic freeloaders weren't just mimicking their hosts, but literally hiding inside them?

This incredible scenario is no longer theoretical; it has been experimentally verified, unveiling an invisible realm of virus espionage. Scientists have discovered that these "satellite" viruses were not just riding along with their helper viruses but were actually embedded within them, serving as Trojan Horses at a micro level to invade cells.

The research is published in the journal *Cell*.

This paradigm shift in our knowledge is not only a new method of infection but an innovative way of transmission for these mysterious agents, which are typically associated with human liver diseases but could now be spreading silently across other species and even invading vital organs such as the human brain through unrelated viruses.

Hidden hitchhikers: Deltaviruses and their helpers

Deltaviruses are bare-bones RNA agents that, on their own, cannot

spread far. The classic example is HDV, which relies on the hepatitis B virus (HBV) for its outer proteins. Recently, scientists uncovered HDV-like deltaviruses in a wide range of animals—snakes, rodents, birds and more—often in organs beyond the liver. That raises the question: how do these tiny parasites travel so far without obvious helpers?

Prior work showed deltaviruses could "borrow" envelope proteins from various viruses (a process called pseudotyping), but it was assumed each virus formed its own particle. The new study reveals a surprising twist.

By co-infecting cells with deltaviruses and candidate helper viruses (for example, rabies-like VSV, herpesvirus HSV-1, or a snake arenavirus UGV-1), the team separated the viral particles and tested infectivity. Astoundingly, they found that the deltavirus genome was actually enclosed within the same virions as its helper virus.

As the authors put it, "Here, we challenge this paradigm and demonstrate that deltaviruses are packaged within helper virus particles, using them as viral Trojan Horses for cell entry." In other words, one virus was literally hidden inside another.

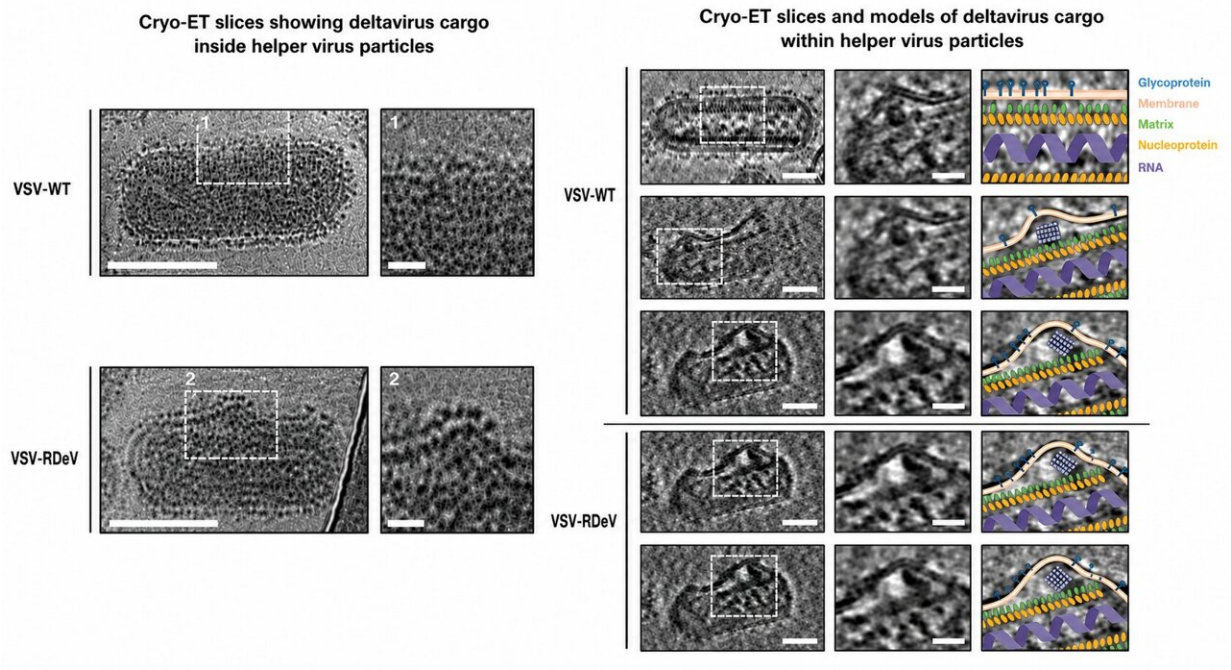
Inside the Trojan Horse: Catching viruses in the act

To catch this in action, the researchers used high-resolution imaging. Under cryo-electron microscopy and super-resolution fluorescence, they saw helper-virus envelopes enclosing tiny spheres of deltavirus RNA and proteins.

Critically, when they tested these particles on fresh cells, only the co-packed virions were infectious—free deltavirus pieces or helper-virus proteins alone did not initiate infection. This shows the Trojan-horse form was required for entry and spread. This strategy appeared across very different viruses.

The team observed deltaviruses lodged inside vesiculovirus (VSV), herpesvirus (HSV-1), and arenavirus particles. Packing the two together enhances spread: the helper virus provides the envelope (and cell entry), and both genomes ride through together.

"We show that this conserved hitchhiking mechanism ensures concomitant deltavirus-helper virus spread," the study notes, a method that "broadens [the deltaviruses'] host range and expands their tropism." In plain terms, hiding inside another virus gives the deltavirus access to new cell types and possibly new species it couldn't infect by itself.



(left) Representative cryo-EM micrographs of VSV-WT or VSV-RDeV virions. Inset 2 zooms on the local membrane elevation. A total of 44 of these events were seen over 137 fields. Scale bars, 100 nm; inset, 20 nm. (right) Averaged 100-Å-thick central slices from a representative tomogram of VSV-WT and from a tomogram of a VSV-RDeV particle. The VSV-RDeV example shown here contains 2 RDeV positioned between the matrix layer and membrane of the VSV virion, resulting in 2 local membrane elevations, one proximal to the basal

end and the other proximal to the apical end of the virion. The two slices correspond to regions centered 250-Å apart along the z axis. The insets show the boxed regions enlarged for clearer visual comparison between VSV-WT and VSV-RDeV. The right boxes show a schematic illustrating the different virion components as a cartoon. RDeV vRNP, light blue RDAg with gray RNA; membrane, light orange; VSV-G, blue; VSV gRNA, purple; VSV-M, green; and VSV-N, yellow. Scale bars, 50 nm; insets, 20 nm. This corresponds to Videos S3 and S5. A total of 15 of these events were seen over 62 tomograms. Credit: www.cell.com/cell/fulltext/S0092-8674(26)00165-0 DOI: 10.1016/j.cell.2026.01.037

Why it matters: Beyond the liver

This discovery opens fresh questions about deltavirus biology. Until now, deltaviruses have mainly been associated with liver disease via HBV. The new work "reveals a previously unrecognized mode of viral transmission," the authors emphasize.

It suggests scientists should look for hidden deltavirus infections outside the liver, in nervous tissue or other organs. For example, common human viruses like HSV-1 (which infects over half the population) might serve as helpers, meaning deltaviruses could lurk undetected in people.

As the authors themselves say, this serves "a framework for studying neglected deltavirus infections beyond the human liver."

The next steps involve looking at wildlife samples for such virus hitchhikers, discovering new helper viruses, and studying if the co-infection makes diseases either less or more severe.

In summary, viruses are more cunning than we knew. A deltavirus within another virus switches our understanding of viral infection, indicating

that these viral "hitchhikers" may be more common and important for health than we realize.

More information: Joe McKellar et al, Deltaviruses spread through a viral Trojan Horse, *Cell* (2026). DOI: 10.1016/j.cell.2026.01.037