

Distinctive virus behind mystery horse disease

Origin of Theiler's hepatitis was a century-old puzzle.

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For almost 100 years, veterinarians have puzzled over the cause of Theiler's disease, a mysterious type of equine hepatitis that is linked to blood products and causes liver failure in up to 90% of afflicted animals.

A team of US scientists has now discovered that the disease is caused by a virus that shares just 35% of its amino acid sequences with its closest-known relative. The team named it Theiler's disease-associated virus (TDAV), and published the discovery in the *Proceedings of the National Academy of Sciences*¹.

Led by Amy Kistler at the Novartis Institutes for BioMedical Research in Emeryville, California, the team responded to an outbreak of Theiler's disease at a farm in which eight horses had suddenly developed hepatitis after being injected with an antitoxin to prevent them from developing botulism. The researchers used next-generation sequencing to analyse RNA samples from the antitoxin and from two of the horses, and assembled the complete genome of the new virus. The virus was found in every one of the eight horses, as well as in the animal (from a different farm) that was the source of the contaminated antitoxin.

"In the span of a few months, we were able to sequence and validate a virus that had gone undetected for almost a century," says Kistler. She thinks that traditional virus-hunting techniques failed to find TDAV because they rely on strong similarities to known viruses, or on the ability to culture the mystery culprit. By contrast, her team sequenced everything in their samples — an approach "that meant we didn't have to know what we were looking for", she says.

Progress check

To better understand the role of the virus, the team inoculated four healthy horses with the contaminated antitoxin. Within ten weeks, all of them carried TDAV in their bloodstream, and one later showed rising levels of liver enzymes that suggested liver disease.

Although the researchers did not purify the virus before injecting it into the horses, Pablo Murcia, a virologist from the University of Glasgow, UK, says that "they have a strong case: I will be very surprised if TDAV turns out not to be the cause of equine serum hepatitis". "Now, a new question arises," he says, "where does this virus come from?".

It is also possible that there is another unknown virus behind Theiler's disease. After all, human hepatitis can be caused by at least five viruses.

TDAV belongs to the family Flaviviridae, which includes the viruses behind yellow fever, dengue fever and hepatitis C. It is most closely associated with a genus of newly discovered viruses called *Pegivirus*, and is the first of these to be convincingly linked to disease.

"The challenges in culturing [pegiviruses] mean that we're only now getting an understanding of how widely distributed and significant they are," says James Wood, who studies animal infections at the University of Cambridge, UK. He hints that some studies on new pegiviruses may be published in the future.

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References

1. Chandriani, S. *et al.* *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1219217110> (2013).



Philectric Arts Photography/Getty

A mysterious hepatitis that causes liver failure in most horses has now been linked to an unusual virus.