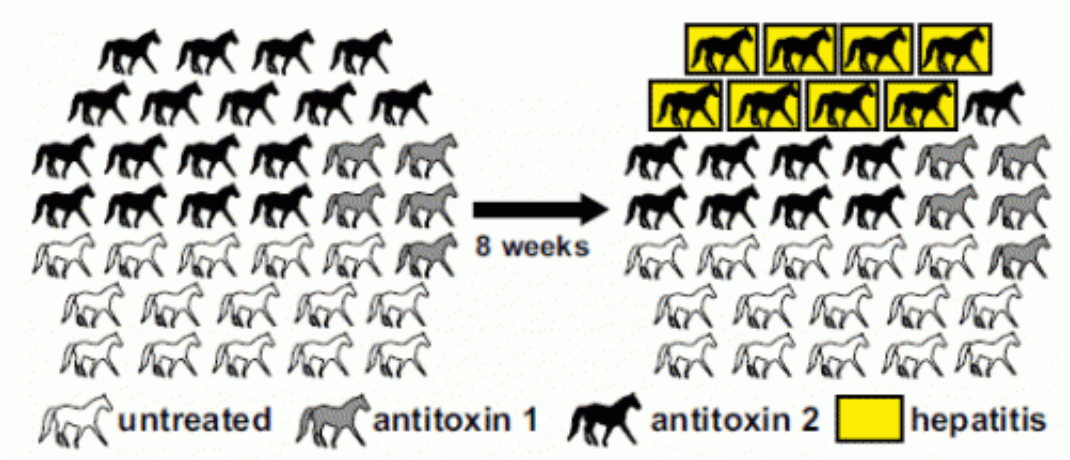
Researchers identify virus that causes horse hepatitis

March 19 2013, by Marcia Malory



Overview of a Theiler's disease outbreak. Credit: (c) *PNAS*, doi: 10.1073/pnas.1219217110

(Phys.org) —Theiler's Disease is one of the most common causes of equine hepatitis. Death rates in horses that develop symptoms range between 50 and 90 percent. Although veterinarians have known about Theiler's Disease for almost 100 years, until now, scientists have been unable to determine its cause. In a paper published in the *Proceedings of the National Academy of Sciences*, Donald Ganem and his colleagues at the Novartis Institute for Biomedical Research and Cornell University College of Veterinary Medicine report they have identified the virus that probably causes the disease.

First identified in 1919, Theiler's Disease is associated with the use of blood products. Many outbreaks have occurred in North America and Europe after horses received plasma or serum to protect them from contagious diseases, such as anthrax or encephalitis, or toxins, such as botulism or tetanus. Because of this, veterinary researchers have long believed that an infectious agent or toxin that contaminates the blood supply causes the disease. However, nobody had ever identified such a contaminant.

Ganem and his colleagues studied horses that contracted Theiler's Disease after receiving botulinum antitoxin. Out of 17 horses that received the same antitoxin after possible exposure to botulism, 8 developed Theiler's Disease.

To investigate the possibility that a virus in the antitoxin had caused the disease, the team extracted RNA from two of the horses that contracted it and from the antitoxin itself. They used next-generation sequencing to identify a previously unknown virus, which they designated "Theiler's Disease-associated virus" (TDAV). The researchers found TDAV in all eight horses that developed hepatitis and in the horse, from another farm, that provided the antitoxin.

TDAV is a member of the Flaviviridae family of viruses, which also includes the viruses that cause hepatitis C, yellow fever and dengue fever in humans. Amy Kistler, who participated in the research, believes that nobody identified TDAV before because it does not closely resemble any previously known viruses. It shares only 35.3% amino acid identity with its closest relative, a virus known as GB virus D.

Horses on the same farm that received a different antitoxin or no antitoxin at all never contracted the disease, indicating that horse-to-horse contact is not a means of transmission.

An epidemiological survey of horses on that farm and two other farms also revealed an association between exposure to TDAV-positive antitoxin and development of Theiler's Disease.

The team concedes that further research is required. They have not yet determined where TDAV originates. In addition, TDAV may not be the only cause of Theiler's Disease; five different viruses cause human hepatitis.

More information: Identification of a previously undescribed divergent virus from the Flaviviridae family in an outbreak of equine serum hepatitis, Published online before print March 18, 2013, doi: 10.1073/pnas.1219217110

Abstract
Theiler's disease is an acute hepatitis in horses that is associated with the administration of equine blood products; its etiologic agent has remained unknown for nearly a century. Here, we used massively parallel sequencing to explore samples from a recent Theiler's disease outbreak. Metatranscriptomic analysis of the short sequence reads identified a 10.5-kb sequence from a previously undescribed virus of the Flaviviridae family, which we designate "Theiler's disease-associated virus" (TDAV). Phylogenetic analysis clusters TDAV with GB viruses of the recently proposed Pegivirus genus, although it shares only 35.3% amino acid identity with its closest relative, GB virus D. An epidemiological survey of additional horses from three separate locations supports an association between TDAV infection and acute serum hepatitis. Experimental inoculation of horses with TDAV-positive plasma provides evidence that several weeks of viremia preceded liver injury and that liver disease may not be directly related to the level of viremia. Like hepatitis C virus, the best characterized Flaviviridae species known to cause hepatitis, we find TDAV is capable of efficient parenteral transmission, engendering acute and chronic infections

associated with a diversity of clinical presentations ranging from subclinical infection to clinical hepatitis.