

Hepatitis A virus discovered to cloak itself in membranes hijacked from infected cells

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A pathogenic picornavirus acquires an envelope by hijacking cellular membranes. Credit: *Nature* (2013), Published online March 31, 2013.

Viruses have historically been classified into one of two types – those with an outer lipid-containing envelope and those without an envelope. For the first time, researchers at the University of North Carolina have discovered that hepatitis A virus, a common cause of enterically-transmitted hepatitis, takes on characteristics of both virus types depending on whether it is in a host or in the environment.

"The whole universe of virology is divided into two types of viruses – viruses that are enveloped and viruses that are not enveloped. If you look at any basic virology textbook, it will say that these are categories that distinguish all viruses," said lead researcher Stanley M. Lemon, MD, professor of medicine and a member of the UNC Lineberger Comprehensive Cancer Center and the Center for Translational [Immunology](#).

In a paper published online in *Nature* on March 31, Dr. Lemon's team discovered that [hepatitis A virus](#) does not have an envelope when found in the environment, but acquires one from the cells that it grows in within the [liver](#). It circulates in the blood completely cloaked in these membranes.

"What we have discovered is that a virus that has been classically considered to be 'non-enveloped', that is hepatitis A virus, actually hijacks membranes from the cells it grows in to wrap itself in an envelope. It steals membranes from the cell, as it leaves the cell, to [cloak](#) itself in this envelope that then protects it from [antibodies](#). And that's really novel. No one has shown that previously for a virus. It really blurs that classic distinction between these two types of viruses," said Dr. Lemon.

Being enveloped in host membranes helps the virus to evade host immune systems and spread within the liver. Enveloped viruses are generally quite fragile in the environment, while non-enveloped viruses

are hardier outside of a host and can survive for longer periods between hosts. Dr. Lemon believes the dual nature of hepatitis A virus allows it to use the advantages of both virus types to enhance its survivability.

"What hepatitis A virus has done, and we don't totally understand how it has accomplished this, is to have the advantage of existing as a virus with no envelope and being very stable in the environment so it can be transmitted efficiently between people, but to wrap itself in a membrane to evade neutralizing antibodies and facilitate its spread within the host once it has infected a person," said Lemon. While no other virus has been shown to exhibit this particular behavior, Dr. Lemon said that it is likely that hepatitis A virus is not unique in its dual nature.

Hepatitis A is endemic in developing nations that lack modern sanitation and clean water. The virus is transmitted orally and then passed back into the environment through feces. By not needing its envelope to survive outside the host, the virus gains the ability of non-enveloped viruses to survive longer and be transmitted efficiently.

One major question raised by the finding is why the hepatitis A vaccine works so well to contain the infection. The vaccine, one of the most effective in use, was thought to elicit neutralizing antibodies that attack the virus in the blood. Since it is now known that the envelope surrounding the virus in the blood prevents this, the vaccine cannot work as previously thought.

"It makes us rethink completely the mechanism underlying the well-documented efficacy of [hepatitis](#) A vaccine. I think this is one of the most important things to come out of the study," said Dr. Lemon.

The research at UNC was funded by the National Institute of Allergy and Infectious Diseases. Future studies will investigate the mechanisms behind the vaccine's effectiveness, Dr. Lemon said. While it was

previously thought that vaccine-induced antibodies attacked the [virus](#) outside of the cell, the new findings suggest antibodies may actually be able to restrict viral replication within a cell.

"Understanding how this really good vaccine works will help us in the future to develop better vaccines for other viruses that we are having difficulty developing vaccines for," said Dr. Lemon.

Provided by University of North Carolina Health Care

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