Study paves the way for an active agent against hepatitis E

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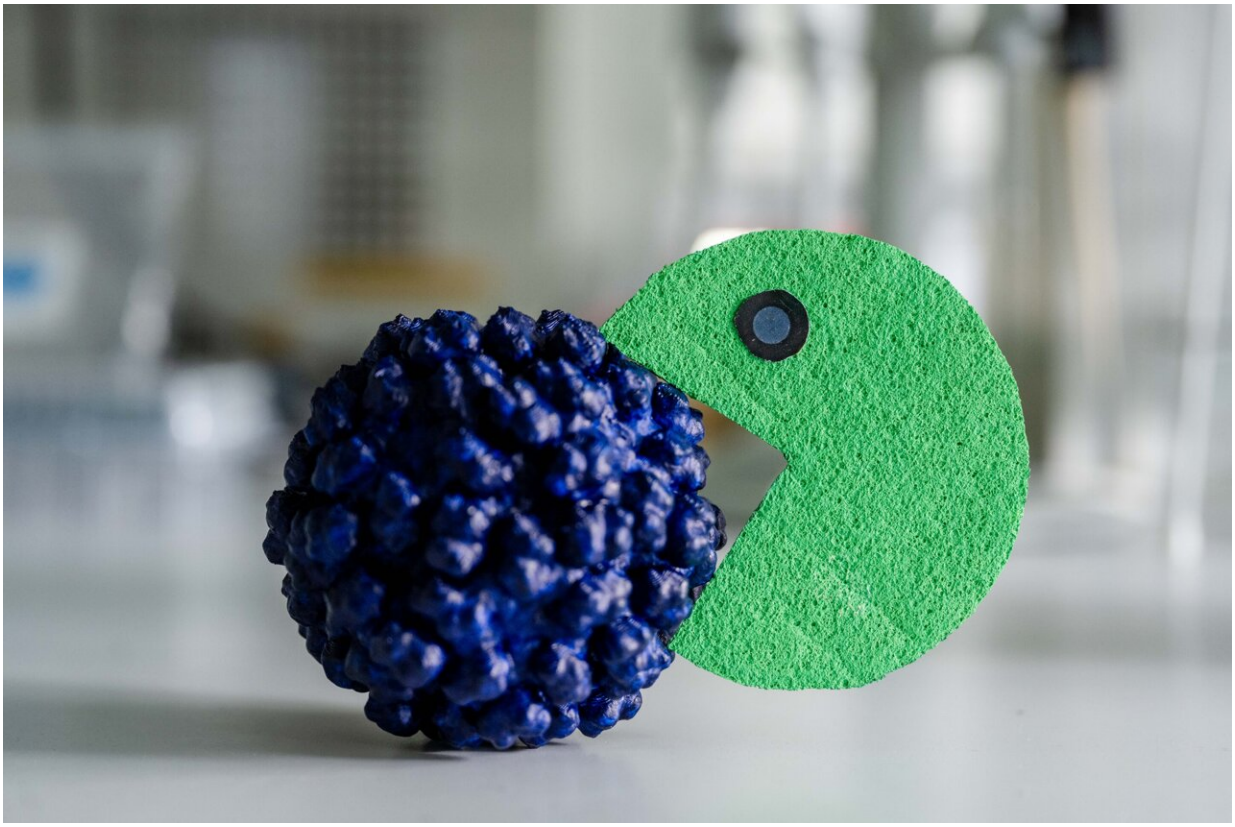

A compound called K11777 prevents body cells from splitting the viral capsid and thus helping the virus out of its capsid. This means that infection is no longer possible. Credit: Ruhr-Universitaet-Bochum

At present, there is no specific active substance against hepatitis E. As

the disease kills 70,000 people every year, researchers are actively searching for one. The team from the Department of Molecular and Medical Virology at Ruhr University Bochum, Germany, may have found what they're looking for.

The researchers showed that the compound K11777 prevents host cells from helping the virus out of its shell by cleaving the viral capsid. This means it can no longer infect cells. "The compound is already being tested in clinical trials against other viruses such as SARS-Cov-2," says lead author Mara Klöhn. "There's still a lot of work to be done to find out whether it can be used as an active substance against hepatitis E, but it's a first step."

The researchers published their findings on May, 10, 2024, in the journal *Hepatology*.

Help from the host cell

In order to infect an organ, viruses need the help of the host cells. "An effective approach is therefore to identify targets in the host that can be manipulated by drugs so that they no longer perform this helper function," explains Klöhn.

The researchers became aware of the compound K11777 in a roundabout way: During a control study conducted as part of cell culture studies on the hepatitis C virus with a known active ingredient, they discovered that this active ingredient was also effective against hepatitis E.

"However, the drug wasn't using the same pathway as with the hepatitis C virus, because the hepatitis E virus doesn't have the target structure that this active substance attacks," explains Klöhn. This suggested that the drug may have an effect on host cells instead.

The research team narrowed down the possible target structures and turned their attention to cathepsins, which can process proteins, i.e. cleave them. K11777 inhibits many cathepsin types, i.e., blocks their function. Tests in cell culture with human liver cells showed that the compound actually prevents infection with hepatitis E viruses.

"In follow-up experiments, we proved our hypothesis that the compound prevents cathepsin L from cleaving and opening up the viral capsid," says Klöhn. "This means that the virus can no longer infect host cells."

Hepatitis E

The hepatitis E virus (HEV) is the main cause of acute viral hepatitis. Approximately 70,000 people die from the disease every year. After the first documented epidemic outbreak between 1955 and 1956, more than 50 years passed before researchers began to address the issue in depth.

Acute infections usually clear up spontaneously in patients with an intact immune system. In patients with a reduced or suppressed immune system, such as organ transplant recipients or people infected with HIV, HEV can become chronic. HEV also poses a serious threat to pregnant women. There aren't any vaccines nor specific active substances against the virus.

More information: Mara Klöhn et al, Targeting cellular cathepsins inhibits hepatitis E virus entry, *Hepatology* (2024). DOI: 10.1097/HEP.0000000000000912

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