

# Scientists create first genetically humanized mouse model for hepatitis C

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Scientists at Rockefeller University and The Scripps Research Institute have developed the first genetically humanized mouse model for hepatitis C, an achievement that will enable researchers to test molecules that block entry of the hepatitis C virus into cells as well as potential vaccine candidates. The finding is reported in the June 9 issue of the journal *Nature*.

While the [hepatitis C virus](#) can infect chimpanzees and humans, scientists have been unable to study the progression of the virus' life cycle or possible treatments in small animal models. The new [mouse model](#) is the first to be developed with a fully functioning immune system.

"Our genetically humanized mouse model for hepatitis C will allow us to gain deeper insights in the biology of this important pathogen," says senior author Alexander Ploss, a research assistant professor at Rockefeller. "This robust small [animal model](#) also has the potential to serve a critical role in testing and prioritizing drug and [vaccine candidates](#). Results from these tests can potentially guide more expensive pre-clinical and clinical studies in higher order organisms, including humans."

The development of this mouse model is the culmination of several years of research by scientists in the laboratory of Charles M. Rice and other research groups. In 2006, Rice and his colleagues were the first to successfully create a strain of hepatitis C in the laboratory, which can

efficiently be grown in the laboratory, and is also infectious in animals. More recently, Rice, Ploss and their colleagues discovered that hepatitis C [virus infection](#) requires previously identified CD81 and scavenger receptor type B class I, as well as two tight junction molecules, claudin 1 and occludin. The Rockefeller researchers showed that human CD81 and occludin were required for hepatitis C virus to enter [mouse cells](#).

In the new study, the Rockefeller researchers and colleagues at The Scripps Research Institute tested whether introducing some of these previously identified human genes into mice would allow them to infect the animals with the hepatitis C virus. The researchers compared two groups of mice: one group expressed two genes, CD81 and occludin, while mice in the second group were normal. They found that expression of human CD81 and human occludin in the mouse liver rendered the animals susceptible to HCV infection. Ploss and his colleagues also developed a novel reporter system, which allowed them to sensitively detect HCV infection in living animals.

"We have established a precedent for applying mouse genetics to dissect viral entry and validate the role of scavenger receptor type B class 1, a molecule that is being considered as a novel antiviral drug target, for HCV uptake in a living animal," says Charles M. Rice, Maurice R. and Corinne P. Greenberg Professor and head of the Laboratory of Virology and Infectious Disease at Rockefeller. Rice also is executive and scientific director of the Center for the Study of Hepatitis C, an interdisciplinary center established jointly by The Rockefeller University, New York-Presbyterian Hospital and Weill Cornell Medical College.

Worldwide at least 130 million people are chronically infected with HCV, which poses a risk of severe liver injury and liver cancer. Current treatments are only partially effective and have considerable side effects, and a vaccine against [hepatitis C](#) does not exist.

"The global HCV epidemic mandates the development of more effective therapeutics including a vaccine," says Ploss. "This mouse model is a first step toward a platform that effectively serves this purpose."

Provided by Rockefeller University

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