



Charles M. Rice, Ph.D.

MAURICE R. AND CORINNE P. GREENBERG PROFESSOR IN VIROLOGY, LABORATORY IN VIROLOGY AND INFECTIOUS DISEASE

Millions of people are infected with hepatitis C or hepatitis B viruses, which cause liver cancer and liver failure. Meanwhile, other RNA viruses such as Zika, yellow fever, dengue, chikungunya, and SARS-CoV-2 coronavirus cause significant morbidity and mortality. Rice's lab works to understand virus replication and innate immune responses that limit infection. His group is also developing new in vitro culture and animal models to facilitate this work.

Many viruses resist conventional virus culture methods, and creative new approaches have been required to study them. Rice pioneered novel methods for growing and studying the hepatitis C virus (HCV), including a mouse with a human liver that allowed the first studies of HCV replication and tests of candidate drugs in a small animal model. This and other work was seminal to the development of antiviral drugs that are now used to cure HCV. Despite this success, a vaccine is still sorely needed. Rice's group has established the first immunocompetent mouse model of hepatitis C infection, paving the way toward vaccine development and studies of hepatitis C-associated liver cancer that can be applied to HCV.

Hepatitis B virus (HBV) also causes cirrhosis and liver cancer, and Rice's group is now applying the human liver mice, as well as new in vitro culture methods, to study HBV, which is often refractory to curative treatment due to the virus's highly stable covalently closed circular DNA genome (cccDNA). The work is revealing new strategies to target cccDNA and other critical HBV lifecycle steps. Rice's group continues to develop new technologies, such as 3D and induced pluripotent stem cell-derived cultures, to study HCV, HBV, and other viruses. They are also using the human liver mice to study the roles of diet and human genetics on the development of non-infectious causes of liver disease.

The host immune response to pathogens includes an innate, rapidly activated component involving a molecule called interferon. Rice's group has developed high-throughput screens to identify interferon-stimulated genes (ISGs) that limit or, in some cases, enhance virus infection. Understanding how ISGs work may lead to improvements in prevention and treatment of infectious diseases. In that context, the Rice lab has focused on viruses of global health concern, such as HCV, HBV, influenza A, dengue, yellow fever, Zika, chikungunya, and coronaviruses. The lab also investigates the mechanisms of attenuation of the yellow fever vaccine, and the human genetic causes of serious liver disease that can occur after vaccination.

Besides understanding host antiviral responses to these pathogens, the lab seeks a broad knowledge of how host factors facilitate virus replication. They use CRISPR technology to systematically knock out human genes to identify those whose loss prevents viral infection. These studies may reveal novel therapeutic targets for the viruses, including SARS-CoV-2. Rice is also using methods his lab developed to study HCV replication in order to screen a large collection of registered drugs from around the world for those that may inhibit SARS-CoV-2.

Studies led by research associate professor Margaret R. MacDonald are investigating cellular interactions of the tick-borne Powassan virus, a flavivirus causing severe encephalitis here in the US. She, in collaboration with others, also studies human antibody responses to Zika and other flaviviruses with the goals of developing antibody reagents for therapeutic use, while gaining insight into successful immune responses that will guide vaccine development. With collaborators, she is also developing nanobodies targeting Powassan virus and the Lyme disease spirochete that can potentially be used for diagnosis or treatment.

EDUCATION

B.S. in zoology, 1974
University of California, Davis
Ph.D. in biochemistry, 1981
California Institute of Technology

POSTDOC

California Institute of Technology, 1981–1985

POSITIONS

Assistant Professor, 1986–1990
Associate Professor, 1991–1995
Professor, 1995–2000
Washington University School of Medicine
Professor, 2001–
Scientific and Executive Director, Center for the Study of
Hepatitis C, 2001–2018
Director, Stavros Niarchos Foundation Institute for Global
Infectious Disease Research, 2023–
The Rockefeller University

AWARDS

Pew Biomedical Scholar, 1986
M.W. Beijerinck Virology Prize, 2007
The Rockefeller University Distinguished Teaching Award, 2010
Robert Koch Award, 2015
InBev Baillet Latour Health Prize, 2016
Lasker-DeBakey Clinical Medical Research Award, 2016
C. Chester Stock Award, Memorial Sloan Kettering Cancer Center, 2017
Nobel Prize in Physiology or Medicine, 2020

HONORARY SOCIETIES

National Academy of Sciences
American Academy of Arts and Sciences
Fellow, American Association for the Advancement of Science

SELECTED PUBLICATIONS

Ricardo-Lax, I. et al. Replication and single cycle delivery of SARS-CoV-2 replicons. *Science* 374, 1099–1106 (2021).
Hoffmann, H.H. et al. TMEM41B is a pan-flavivirus host factor. *Cell* 184, 133–148 (2021).
Chung, H. et al. Human ADAR1 prevents endogenous RNA from triggering translational shutdown. *Cell* 172, 811–824 (2018).
Wu, X. et al. Intrinsic immunity shapes viral resistance of stem cells. *Cell* 172, 423–438 (2018).
Billerbeck, E. et al. Mouse models of acute and chronic hepatitis C infection. *Science* 357, 204–208 (2017).