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 and B viruses (HCV, HBV), which cause liver cancer and liver failure. RNA viruses like Zika, yellow fever, dengue, chikungunya, and SARS-CoV-2 also cause significant morbidity and mortality. Rice's lab works to understand virus replication mechanisms and innate immune responses that limit infection. His group is also developing new in vitro culture systems and animal models to facilitate this work.

Many viruses, including the hepacivirus HCV, are challenging to culture and new approaches are required to study them. Rice's group identified critical sequences in the HCV genome required for infectivity, demonstrated it was a causative agent of hepatitis, and pioneered novel cell culture methods for growing and studying it. This and other work was seminal in developing the antiviral drugs now used to cure HCV. Despite this success, a vaccine is still sorely needed. To this end, Rice's group has established the first immunocompetent mouse model for hepacivirus infection using the Norway rat hepacivirus, which replicates key aspects of liver disease observed in HCV-infected humans, including cancer. The lab also uses human liver chimeric mice to study the roles of diet and human genetics in fatty liver disease, yellow fever vaccine attenuation mechanisms, and the human genetic causes of rare but serious post-vaccine disease. Trained immunity, or how exposure to one pathogen can result in resistance to an unrelated pathogen, is another area of active interest.

The Rice lab also studies virus-host interactions to learn how factors limit or facilitate virus replication. Responses to viral pathogens include an innate, rapidly activated expression of proteins called interferons. Rice's group has developed high-throughput screens to identify interferon-stimulated genes (ISGs) that limit or, in some cases, enhance virus infection, focusing on viruses of global health concern such as HCV, HBV, influenza A, dengue, yellow fever, Zika, chikungunya, and coronaviruses. The group has also used CRISPR technology to systematically knock out human genes to identify those whose loss affects viral infection. Ultimately, a better understanding of virus-host biology may reveal novel therapeutic targets and improve disease prevention and treatment.

Research Associate Professor Margaret R. MacDonald leads studies using cellular and animal models to investigate Powassan virus (POWV), a tick-borne flavivirus causing severe encephalitis in the United States. In collaborative efforts, she explores human antibody responses to flaviviruses to develop therapeutic antibody reagents and gain insights for vaccine development. She also collaborates to develop nanobodies against POWV and the Lyme disease spirochete for potential diagnostics or therapeutics.

Research Assistant Professor Hans-Heinrich Hoffmann leads investigations on how mosquito-borne and tick-borne viruses navigate infection in both vertebrate and invertebrate cells. His work includes conducting genome-wide CRISPR knockout screens to identify host factors critical for these viruses, followed by targeted knockdown screens in vector cells to further characterize viral mechanisms and explore potential antiviral targets. He also develops new tools to study virus-vector cell interactions, with a particular emphasis on ticks.

Research Assistant Professor William M. Schneider leads efforts to investigate replication mechanisms of HBV, a small DNA virus that causes cirrhosis and liver cancer, and LINE-1, an endogenous retroelement active in the human genome. In recent and ongoing work, the team developed new cell culture methods to study HBV and has employed CRISPR and deep mutational scanning technologies to research HBV and LINE-1 replication and identify critical host interactions.

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

Yu, Y. and Kass, M.A. et al. Deep mutational scanning of hepatitis B virus reveals a mechanism for cis preferential reverse transcription. *Cell* 187, 2735–2745 (2024).

Lercher, A. et al. Antiviral innate immune memory in alveolar macrophages following SARS-CoV-2 infection ameliorates secondary influenza A virus disease. *Immunity* 57, 2530–2546 (2024).

Le Pen, J. and Paniccia, G. et al. A genome-wide arrayed CRISPR screen identifies PLSCR1 as an intrinsic barrier to SARS-CoV-2 entry that recent virus variants have evolved to resist. *PLoS Biol.* 22, e3002767 (2024).

Hoffmann, H.H. and Schneider, W.M. et al. TMEM41B is a pan-flavivirus host factor. *Cell* 184, 133–148 (2021).

Billerbeck, E. et al. Mouse models of acute and chronic hepacivirus infection. *Science* 357, 204–208 (2017).