Paul Bieniasz, Ph.D.

INVESTIGATOR, HOWARD HUGHES MEDICAL INSTITUTE • PURNELL W. CHOPPIN PROFESSOR, LABORATORY OF RETROVIROLOGY

The biology and evolution of viruses and eukaryotes are closely linked. The Laboratory of Retrovirology seeks to define how host genes influence the replication of viruses, with an emphasis on human and primate immunodeficiency viruses. His lab seeks to characterize the host functions that viruses mimic, manipulate, and otherwise exploit, as well as the defenses cells have evolved against viral infection.

The laboratory, co-led by Bieniasz and Research Associate Professor Theodora Hatziioannou, studies multiple aspects of viral infection. In addition to determining the functions of viral genes and proteins, their research seeks to define how the replication of viruses is influenced by host genes and pathways. Some host functions are manipulated or exploited by viruses to enable their replication, while others have arisen specifically to curtail virus infection.

One aspect of the group's work is to define how virus components interact with host proteins to enable virus replication. This work, which employs biochemical, genetic, and imaging approaches, has revealed many details of HIV-1 replication, including the recruitment of host proteins that drive virus particle assembly and budding. The lab is also interested in defining how HIV-1 viral RNA synthesis, splicing, stability, transport, translation, and packaging into virions are regulated, as well as the role of viral components following the entry of HIV-1 particles into target cells. In new work, the team is extending these fundamental studies of virus replication to include the coronaviruses.

The group has also pioneered the field of "paleovirology," which explores how ancient viruses impacted the evolution of their hosts. Mammalian genomes contain a fossil record of viral DNA from extinct retroviruses that infected the germ cells of ancient mammalian ancestors, and the lab reconstituted functional viruses and proteins encoded by this ancient viral DNA. They also seek to understand how ancient retroviruses were extinguished, which may give clues about how to combat modern viral infections.

A major area of interest is the arsenal of host defenses against viruses. Selection pressures imposed by ancient viral infections have shaped an array of intrinsic host defense mechanisms that influence susceptibility to modern viruses such as HIV-1 and SARS-CoV-2. The lab works on several types of intrinsic defenses, some of which are induced by interferons to understand the mechanistic details by which they work. Two such inhibitors, discovered by the lab, include tetherin, which inhibits the release of a wide range of enveloped viruses from the surface of infected cells, and Mx2, which targets the capsid of HIV-1 to inhibit viral entry into the nucleus. Bieniasz and Hatziioannou have shown that species-dependent differences in antiviral proteins are critical determinants of HIV-1 host range, and they have used this information to engineer improved animal models of AIDS virus infection in monkeys. These models are providing testing grounds for new forms of therapy and prevention. The lab is discovering and investigating new types of intrinsic defenses against HIV-1 and coronaviruses and the mechanisms by which they work. For example, the lab recently found that mammalian cells can deplete viral RNA molecules that are recognized as foreign based on their nucleotide composition. They are also conducting a variety of investigations into the nature of antibody immunity to HIV-1 and SARS-CoV-2, including the development of protective vaccines, antibodies, and nanobody therapeutics.

EDUCATION

B.Sc. in biochemistry, 1990
University of Bath

Ph.D. in virology, 1996
University of London

POSTDOC

Duke University, 1996–1999

POSITIONS

Staff Investigator, 1999–2016
Aaron Diamond AIDS Research Center

Assistant Professor, 1999–2003
Associate Professor, 2003–2010
Professor, 2010–
The Rockefeller University

Investigator, 2008–
Howard Hughes Medical Institute

AWARDS

Elizabeth Glaser Award, 2003

Eli Lilly and Company Research Award, 2010

KT Jeang Retrovirology Prize, 2015

The Rockefeller University Distinguished Teaching Award, 2017

Biochemical Society Award, 2019

Chica and Heinz Schaller Foundation Award for Distinguished Achievements in Virology, 2024

HONORARY SOCIETIES

National Academy of Sciences

SELECTED PUBLICATIONS

Gonçalves-Carneiro, D. et al. Rational attenuation of RNA viruses with zinc finger antiviral protein. *Nat. Microbiol.* 7, 1558–1567 (2022).

Schmidt, F. et al. High genetic barrier to SARS-CoV-2 polyclonal neutralizing antibody escape. *Nature* 600, 512–516 (2021).

Weisblum, Y. et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. *Elife* 9, e61312 (2020).

Takata, M.A. et al. CG dinucleotide suppression enables antiviral defence targeting non-self RNA. *Nature* 550, 124–127 (2017).

Hatziioannou, T. et al. HIV-1–induced AIDS in monkeys. *Science* 344, 1401–1405 (2014).