



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Preface

MicroRNAs in viral gene regulation

The mechanism of RNA interference (RNAi) was discovered in the nematode worm *C. elegans* in 1998. This mechanism was soon linked to the potent and sequence-specific antiviral responses observed in plants, a phenomenon long known by other names such as co-suppression, post transcriptional gene silencing, or quelling. The RNAi pathway is also well conserved in many eukaryotes including animals and participates in controlling cell development by regulating gene activity.

Amongst others, two types of small double-stranded RNA molecules – microRNA (miRNA) and small interfering RNA (siRNA) – are central to the RNAi mechanism. These small RNAs can bind to specific mRNAs and either increase or decrease their activity, for example by preventing a mRNA from producing a protein. Of note, the RNAi mechanism involves more than just RNA molecules. Cellular proteins that are important to RNAi include the Drosha and Dicer endonucleases that process double-stranded mi-/si-RNA molecules and the Argonaut proteins in the RNA-induced silencing complex (RISC) and their cofactors that trigger the cleavage or silencing of targeted mRNAs. Some of these players are illustrated in the cartoon on the cover.

The principal idea behind this special issue is to provide a collection of expertly written articles that address the interface between RNA interference and viruses. In particular, we focus on events that are triggered by miRNAs of viral or cellular origin. A wide variety of molecular mechanisms at the virus–RNAi interface are presented, and these insights will also advance the understanding of cellular RNAi pathways. Many examples are illustrated for cellular miRNAs that control or enhance virus replication. On the other hand, there are also several descriptions of viruses that encode their own miRNAs, which are either involved in the control of viral gene expression or the preparation of the host cell for optimal virus replication. To accomplish our goal, this special issue travels along different kingdoms from plants to humans and focuses on a variety of viruses, including several important human pathogens.

RNAi research has led to the development of novel tools for the control of gene expression in biological investigations or drug discovery. The aim of this compendium is to address a range of important fundamental issues with potential implications for application at the virus–host interface. The articles provide up-to-date surveys of emerging and established concepts in the field of RNAi and how viruses modulate RNAi responses. As a powerful new technology, RNAi is emerging as an important modality that holds promise for the therapy of notoriously

challenging clinical pathogens such as hepatitis C virus (HCV) and human immunodeficiency virus (HIV). We envision that the articles in this collection will be useful to a wide range of readers – from basic science students, to seasoned virologists and RNAi researchers, and to molecular scientists and clinicians interested in developing novel antiviral strategies.



Ben Berkhout studied molecular biology at Leiden University and obtained his PhD in 1986 on a research project concerning the regulation of translation by means of RNA structure in RNA bacteriophages. He performed postdoctoral research at the Dana Farber Cancer Institute of the Harvard Medical School in the field of molecular immunology and initiated HIV-1 research at the National Institutes of Health in Bethesda.

Ben Berkhout initiated a molecular virology research line in 1991 upon his return to the Netherlands and he has been at the University of Amsterdam since then. He became Head of the Laboratory of Experimental Virology and was appointed as full professor in 2002. Ben Berkhout is editor for *Retrovirology*, *Journal of General Virology*, *RNA Biology*, *Journal of Biomedical Science*, and associate editor for several journals (*Nucleic Acids Research*, *Journal of Virology*, *Biotechnology*, *Current HIV Research*, *Journal of Biological Chemistry*, *Antiviral Research*, *Journal of RNAi and Gene Silencing* etc).

Ben Berkhout has published over 350 peer-reviewed manuscripts on diverse topics concerning HIV-1 replication (mechanism of transcription, reverse transcription, RNA-regulated functions), virus evolution (both as a research tool and the underlying molecular mechanisms of drug-resistance), virus discovery (human coronavirus NL63), new antiviral therapeutic strategies (RNA interference) and HIV-1 vaccine design.



Kuan-Teh Jeang is the Head of the Molecular Virology Section at the National Institute of Allergy and Infectious Diseases, the National Institutes of Health, USA. He attended undergraduate university at MIT (Boston, MA) and then medical school at the Johns Hopkins University School of Medicine (Baltimore, MD), graduating with MD and PhD degrees. Dr. Jeang's research interests are in the fundamental regulation of HIV-1 gene expression and in HTLV-1 transformation of human cells. He is the editor-in-chief of *Retrovirology*; (www.retrovirology.com), an Associate Editor of *Cancer Research*; and a member of the editorial boards for the *Journal of Biological Chemistry* and the *Journal of Virology*.

Dr. Jeang is an elected fellow of the American Society of Clinical Investigation (ASCI), the Association of American Physicians (AAP), the American Association for the Advancement of Science (AAAS), the American Academy of Microbiology (AAM), and an Academician of Academia Sinica. He is the president of the Society of Chinese Bioscientists in America (SCBA; www.scbasociety.org), the largest international society of bioscientists of Chinese extraction, and was previously a councilor of the American Society for Biochemistry and Molecular Biology (ASBMB) and the International Retrovirology Association (IRA).