

Arboviruses

Molecular Biology, Evolution and Control

Edited by

Nikos Vasilakis

Department of Pathology
Center for Biodefense and Emerging Infectious Diseases
Center of Tropical Diseases and Institute of Human Infections and Immunity
University of Texas Medical Branch
Galveston, TX
USA

and

Duane J. Gubler

Program on Emerging Infectious Diseases
Duke-NUS Graduate Medical School Singapore
Singapore

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Foreword

More than 100 years since the demonstration of *Aedes (Stegomyia) aegypti* transmission of yellow fever virus by Walter Reed and colleagues, arboviruses continue to be the causes of major public health challenges, the subjects of many new viral discoveries, and the etiologic agents of new and repeated disease emergence. Following peaks of arbovirus discovery during the 1930s, due to technological advances in virus isolation and identification, and the during 1950–1960s largely thanks to the efforts of the Rockefeller Foundation and their international virus discovery programmes, arbovirology underwent a dramatic transformation beginning in the 1980s with the advent of modern molecular virology. Although field ecology and epidemiology studies have in many cases declined during this molecular biology era, advances in the study of arboviral genetics and the molecular basis of arbovirus–host and –vector interactions have led to exciting new opportunities for vaccine development and promising new targets for antiviral development, offering hope for the control in the near future of some of the most important arboviral diseases. Increasingly efficient amplification and sequencing of viral genomes and the ability to manipulate RNA viral genomes via cDNA rescue systems has revolutionized the study of arbovirus evolution and pathogenesis. Mechanisms of emergence into new transmission cycles that either directly impact spillover from enzootic cycles or mediate the development of urban, human–human transmission mediated by anthropophilic vectors have begun to be elucidated. Improved understanding of the effects of anthropogenic change on arbovirus transmission cycles and exposure of humans and domesticated animals has also revealed the increasing challenges that human activities such as international travel and commerce, deforestation, and climate change will place on our ability to control arboviral diseases.

In this comprehensive book on arboviruses, the first in several decades, all of the major arbovirus groups are reviewed with emphasis on taxonomy and discovery, including recently identified and characterized ‘insect-specific’ viruses that are revolutionizing our understanding of the evolution of their related arbovirus taxa, and advances in the understanding of virus–host interactions from the organismal to molecular

levels. The advent of deep sequencing has revealed details of arbovirus population structure throughout the transmission cycle, which influences transmission and evolution, and the recent discovery of major effects of small RNAs on infection and replication in both arthropod vectors and vertebrate hosts is already having major impacts on the field. Molecular genetics is also beginning to impact directly our strategies for controlling arboviral diseases, with novel transgenic mosquito approaches and *Wolbachia* bacterial infections of mosquitoes already being tested in field settings for dengue control.

Despite the exciting advances in science and technology of the past three decades and their promise for applications aimed at controlling arboviruses, the challenges remain sobering: dengue viruses continue to expand and are now estimated to infect about 400 million persons annually, and chikungunya virus has recently spread to near pandemic proportions, affecting both tropical and temperate regions. Bluetongue virus is spreading northward into Europe as increasing temperatures permit northward expansion of the *Culicoides* spp. vectors, and West Nile virus has undergone a dramatic resurgence in the United States since 2012, without a clear explanation or any major improvement in our ability to predict outbreaks in time or space, let alone to mitigate them. Insecticide resistance continues to limit our ability to reduce exposure to arboviruses through vector control, and the anthropophilic behaviour of mosquito vectors like *A. aegypti* and *A. (Stegomyia) albopictus*, which continues its invasive spread on four continents, challenges control even when vectors remain susceptible. These and many other continuing challenges will require new, interdisciplinary approaches to better understand the determinants of enzootic and epidemic circulation, and both scientific and public policy advances to accelerate product development and clinical trials to bring antivirals and vaccines to the markets where they are desperately needed. This book, written by experts in their respective fields, provides a comprehensive treatment of the many topics that will need to be considered and included in these interdisciplinary efforts to improve in our ability to predict, prevent, and control arboviral diseases in the 21st century.

Preface

In the waning years of the 20th century, arboviruses (viruses transmitted to humans and other animals by arthropod vectors) re-emerged as major global public health problems. Today, this diverse array of viruses is among the most important cause of emerging epidemic infectious diseases worldwide. It has been almost 30 years since the last comprehensive coverage of the taxonomy, epidemiology, ecology, evolution and biology of the arboviruses. Since then, there has been a tremendous amount of new knowledge published on these viruses. This book revisits all of the above aspects of arbovirus research plus new information on the molecular biology, risk factors underlying the re-emergence of arboviral disease epidemics in human and animal populations. We are fortunate to have recruited the expertise of a diverse set of contributors, whose effort undoubtedly required sacrifices of both time and energy in the face of many other commitments.

The recent adoption of new detection technologies [next-generation sequencing (NGS)] has resulted in a cataclysm of discovery of newly recognized viruses with restricted host range in arthropods whose detection was not possible with the classic serology and isolation methods of the past. As result the question of how arboviruses should be defined has been brought to the forefront. An important question is should the definition be broadened to include arthropod-associated viruses that are in the same families as known arboviruses such as *Togaviridae*, *Flaviviridae*, *Bunyaviridae*, *Rhabdoviridae*, *Reoviridae*, etc.?

Our intention with this book is to provide a forum in which members of the arbovirus community could highlight new

approaches, concepts or concerns without any preconceptions, thus providing a stimulating baseline where new investigators from a wide variety of disciplines might consider joining in arbovirus research providing a set of 'fresh eyes' and perspectives. This book is divided into four sections that cover: (i) molecular biology, (ii) viral diversity and evolution, (iii) arbovirus diagnosis and control and (iv) future trends.

We owe a large amount of gratitude to the many people who made this book a reality. To the fellow contributors and authors of each of the chapters, whose dedication, patience and collaboration made this endeavour a delightful experience. We would like to acknowledge Shannan Rossi, Nicholas Bergren and Ashley Rhame for assistance with proofreading the chapters and preparing the index. We must also thank Annette Griffin, Acquisitions Editor at Horizon Press, and Melanie Woodward, Project Leader at Prepress Projects Ltd, for their invaluable help.

Finally, we dedicate this book to our spouses, whose patience, dedication, understanding and everlasting support for our scientific journeys made it all worth it.

It is with great sadness that the editors note the passing of one of our authors, Dr Kate Ryman, in November 2015 just before this book went to press. Dr Ryman was an outstanding virologist who made seminal contributions to our understanding of the pathogenesis of many arboviruses in the alphavirus and flavivirus genera, and she will be sorely missed by us and her many friends in the arbovirology community.

Nikos Vasilakis
Duane J. Gubler