Expert Review of Vaccines

ISSN: 1476-0584 (Print) 1744-8395 (Online) Journal homepage: informahealthcare.com/journals/ierv20

Influenza: Molecular Virology

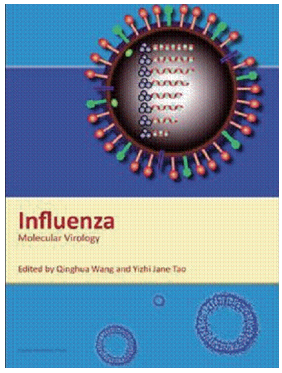
Iain Stephenson

To cite this article: Iain Stephenson (2010) Influenza: Molecular Virology, Expert Review of Vaccines, 9:7, 719-720, DOI: 10.1586/erv.10.71

To link to this article: https://doi.org/10.1586/erv.10.71

Influenza: Molecular Virology

Expert Rev. Vaccines 9(7), 719–720 (2010)



Editors: Qinghua Wang and Yizhi Jane Tao

Publisher: Caister Academic Press, UK

ISBN: 9781904455578

Iain Stephenson
Leicester Royal Infirmary, Leicester LE1 5WW, UK
Tel.: +44 116 258 6952
iain.stephenson@uhl-tr.nhs.uk

"*Influenza: Molecular Virology* provides an up-to-date review of the advancements in molecular influenza virology, with additional discussions regarding the use of molecular technology in diagnostic platforms, and statistical modeling to quantify antigenic differences between influenza viruses."

Current circulating seasonal influenza A/H1N1, A/H3N2 and B viruses infect up to 10% of the world's population every year and are responsible for an estimated 500,000 excess deaths annually. The potential public-health threat posed by pandemic influenza has been especially highlighted over the last decade by the prominence and spread throughout Eurasia of highly pathogenic avian influenza H5N1 viruses. Pandemics of influenza A occur infrequently when a novel influenza virus subtype with the capacity for efficient human-to-human transmission emerges to which there is limited or no background immunity in the population. Reasons for the decline and replacement of existing influenza subtypes are uncertain, but previous experience suggests that novel influenza A viruses of pandemic potential emerge from the animal reservoir following genetic reassortment between human and nonhuman strains. The emergence of swine-origin 2009 influenza A H1N1 as the first pandemic virus in over 40 years demonstrates the unpredictable nature of influenza. Although unexpected, the 2009 H1N1 pandemic was the most prepared for, and the first during which antiviral medications were available. Effective pandemic-specific vaccines, based on the 2009 H1N1 hemagglutinin, were produced and widely deployed within 6 months of the WHO pandemic declaration. Overall, the control strategies for the 2009 H1N1 pandemic worked reasonably well, but containment of pandemics in the future may be challenged by the emergence of a virus with greater virulence, the development of transmissible drug resistance during treatment and limitations in the availability of effective vaccines and their manufacturing capacity. In order to gain an advantage in the ongoing battle against seasonal and pandemic influenza control, the improvement of existing anti-influenza viral drugs and vaccines, and the design of new interventions and vaccine targets are continually needed. For this, it is essential to understand the structure, function and mechanisms of antigenic variation of influenza virus proteins at the molecular level.

The publication of the book, *'Influenza: Molecular Virology'*, edited by Qinghua Wang and Yizhi Jane Tao, is therefore timely. The book contains a series of excellent and high-powered articles on the molecular virology of influenza. The ten chapters are principally written by American or Chinese authors, and provide a detailed structural and functional review of the various internal influenza virus proteins, namely the nonstructural protein 1 (NS1), nucleoprotein, M2 channel and polymerase protein complex; as well as the hemagglutinin surface glycoprotein. For completeness, a future edition should consider the inclusion of a chapter on the neuraminidase surface glycoprotein, which was excluded in this edition. These chapters are comprehensive and unlikely to become outdated in the near future, although their highly technical nature may direct the readership of this book towards

 10.1586/ERV.10.71 ISSN 1476-0584

already knowledgeable post-doctoral research workers, rather than the general virologist or public health practitioners. As there was some discussion on antibody responses to hemagglutinin, the principal ingredient of current influenza vaccines, a future edition might also consider the inclusion of a chapter on immunological responses to internal influenza proteins being considered as novel vaccine targets to widen the appeal of the book.

The first two chapters, perhaps with some overlap, discuss the structure of the NS1 protein and its interactions with cellular ligands. The role of the NS1 protein in pathogenesis, viral synthesis and inhibition of host antiviral responses is reviewed.

In many reviews of influenza, influenza B viruses are neglected, so the third chapter covering the hemagglutinin B surface glycoprotein is notable. This chapter discusses the structure and antigenicity of the two major influenza B virus lineages, with receptor binding and membrane fusion functions of the hemagglutinin glycoprotein. Important differences between influenza A and B hemagglutinins can be understood after completion of chapter 5, which reviews the structure and function of influenza hemagglutinin A. In this chapter, there is a discussion of the basis of the antigenicity of various influenza A subtypes, the mechanisms of antibody-mediated neutralization and the role of hemagglutinin A in virus entry, membrane fusion and pathogenesis.

> "The emergence of swine-origin 2009 influenza A H1N1 as the first pandemic virus in over 40 years demonstrates the unpredictable nature of influenza."

As the cytotoxic T-lymphocyte responses to influenza are predominantly directed towards conserved epitopes within the nucleoprotein protein, it has been considered to be a potential vaccine target capable of inducing a broad spectrum of immunity to influenza A viruses. Chapter 4 focuses on the crystal structure and functional role and importance of the influenza A nucleoprotein during the virus replication cycle.

Chapter 6 reviews another specific anti-influenza virus drug target and potential conserved vaccine target: the M2 channel. The NMR and x-ray structure of both open and closed forms of the M2 channel are discussed and placed in the context of antiviral drug binding and the subsequent emergence of drug resistance.

The molecular correlates of pathogenesis are of particular interest when evaluating the potential threat posed by nonhuman virus subtypes, particularly the highly pathogenic avian influenza H5N1 and H7N1 viruses. Chapter 7 reviews the origins and pathogenesis of the 1918 pandemic H1N1 virus before a discussion of the particular molecular patterns in the NS1, HA, NA and PB1 gene segments that are associated with virulence of the reconstructed 1918 H1N1 virus in *in vitro* cell and animal models. A section on the molecular correlates of virus transmissibility would add value.

Chapter 8 is the last of the section discussing the molecular structure and function of each of the influenza virus proteins and focuses on the polymerase protein. This heterotrimeric complex comprises PA, PB1 and PB2 components, and is suggested as a target for novel antiviral compounds.

Chapter 9 describes the advancements in simple single-gene molecular subtyping and diagnostic techniques that could be utilized to improve the global surveillance of circulating influenza viruses necessary for the design of appropriately matched vaccines, and the early detection of emerging novel subtypes. The chapter focuses on the development and potential applications of a low-density MChip microassay based on a matrix gene segment developed by the authors.

Influenza A viruses are subject to continuous antigenic drift, and antigenic differences between drifted viruses are traditionally determined by means of ferret antisera hemagglutinin-inhibition assays. The final chapter in the book discusses alternative approaches to the selection of vaccine seed strains that match the predicted circulating virus strains, including the use of a statistical mechanics-based computer model, developed by the authors, to quantify the antigenic distance between dominant hemagglutinin epitopes on virus variants. Additional models of pandemic virus transmission and predictors of vaccine efficacy are discussed.

In summary, *Influenza: Molecular Virology* provides an up-to-date review of the advancements in molecular influenza virology, with additional discussions regarding the use of molecular technology in diagnostic platforms, and statistical modeling to quantify antigenic differences between influenza viruses. Therefore, the book would be of interest to a range of readers including post-graduate and basic science researchers, virologists and those involved with drug design and development.

Financial & competing interests disclosure

Iain Stephenson has received financial support for investigator-led research, travel and attendance at international meetings from Baxter, Hoffmann–La Roche, Novartis Vaccines and GSK, who manufacture influenza vaccines and antiviral drugs. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.