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BOOK REVIEW

Günter Witzany (ed): Viruses: essential agents of life

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Frank Ryan

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Many biologists still see viruses as non-living entities whose contribution to life is exclusively that of genetic parasitism. This book sets out to explain why this perspective, while still largely pertinent in relation to disease, is inadequate if we wish to understand their wider biological role. It is a compilation of 19 chapters, each written by one or more experts, and each comprising an overview, or opinion or essay on a different facet of the general theme. They include chapters on the evolutionary origins of viruses, the contribution of viruses to the evolution of life per se, to biodiversity, ecology and to host genomic evolution.

The opening chapter explores viruses as a source of neogenes, looks at the possible role of viruses as symbionts–this is unfortunately reduced to mutualism–and generally explores the nature of the virus-host interaction. The second chapter explores the concept and dynamics of RNA viruses as a quasispecies. Chapter three posits a modern overview of the three main hypotheses for the origins of virions and virocells, revisiting the virus first hypothesis, regressive evolution from protocells, and escape as fragments of cellular genomes. Interestingly they conclude that whatever the mechanism, or mechanisms, of evolutionary origins, viruses almost certainly date to before the Last Universal Common Ancestor of modern cells (LUCA).

Chapter 4 is an essay on the theme of viruses as "the dark matter of the biological universe", being the most populous biological entities in the biosphere as well as being the least characterized in terms of their genetic, taxonomic, and functional diversity–an ignorance that amounts to an unexplored viral universe. The fact that these same viruses exchange genes with one another as well as with their hosts on a major scale makes this viral contribution to the biosphere worthy of further exploration. Chapter 5 is devoted to factors that limit viral structural architecture, portraying commonalities across host domains. Chapter 6 explains and extrapolates two important viral strategies, the so-called "addiction module" and the "quasispecies concept" mentioned above, showing how these concepts are capable of explaining a wide variety of phenomena seen in the virus host interaction, such as cooperation, network formation, symbiosis, host immunity and group identity. It also includes a powerful defence of why viruses should be redefined as living organisms. When viruses infect a host, they tend to hijack multiple cellular functions in order to promote their own replication. Infection with a surprising number of different viruses, including DNA-based examples such as the herpes viruses, Epstein-Barr virus, and hepatitis-B, in addition to the well-known RNA-based retroviruses, will sometimes involve viral insertions into the host germ line. Chapter 7 considers the implications, whether potentially deleterious or evolutionarily beneficial, for the host when viruses insert themselves into the host genome. Many plants harbour persistent viruses within the cytoplasm of their cells. These viruses have curious transmission characteristics and some may be functionally beneficial to the plants. This chapter also poses an intriguing question with regard to the dynamics of genomic integration of retroviruses. Do retroviruses insert anywhere in the chromosomes of their hosts, when they invade the germ cells, or do they favour particular locations? It would appear that retroviruses may not insert as randomly as was previously believed. Chapter 8 looks at the differences between persistent and acute viruses of plants before focusing on the origins and possible beneficial role of persisting plant viruses.

The next three chapters are devoted to the fascinating questions provoked by the discovery of the Megaviruses,

F. Ryan (✉)
Academic Unit of Medical Education, Faculty of Medicine,
The University of Sheffield, Sheffield, UK
e-mail: F.Ryan@sheffield.ac.uk

the most familiar of which is the Mimivirus, which have larger genomes than some of the smallest of the bacteria. Thus one chapter extrapolates from these "giant" viruses to question the traditional concept, and definition, of viruses per se; another looks at what is known of their evolution and then explores their ecological importance; and the third proposes that they be considered a fourth domain of life. It is noteworthy that two of these three chapters also challenge the old idea that viruses should be considered non-living, a conclusion also drawn by the editor in the final resume.

Emerging viruses have global implications for health and research. Colleagues might be surprised to discover that a significant number of viruses result in cross-species infections between bats and humans. This is the theme of chapter 12, including rabies, Ebola in Africa, Hendra virus infection in Australia, Nipah virus in Malaysia and Bangladesh and SARS in China. The following chapter deals with a topic close to my own field of interest–the viral contribution of functional proteins to host evolution. Symbiologists will be familiar with a similar dynamic involving bacterial genetic symbioses with hosts. Virologists, who, by and large, are not so familiar with symbiogenetic thinking, and terminology, refer to this as "molecular domestication". Chapter 13 describes examples of the contribution of retroviruses, and "transposable elements" linked to retroviruses, to the emergence and diversification of the vertebrate lineage. This is a rapidly expanding field, with considerable importance to human evolution, development and physiology. Although still in the early stages of investigation, it is also a field likely to prove important to medicine.

The evolutionary dynamics of retroviruses, and how this applies to their potential to invade and change host germ lines, is the theme of the following chapter, which looks at the currently on-going invasion of the koala genome in Australia by the koala retrovirus. This affords an opportunity to study viral endogenization as it actually happens. The emerging koala retrovirus may have jumped species from a rodent. It is currently inserting into the koala genome in observable fashion, opening up the potential for original observation into the evolutionary dynamics of host germ line colonisation. One of the most extensively studied examples of such endogenization is exemplified by the following chapter, chapter 15, which looks at the evolutionary interplay between the exogenous Jaagsiekte Sheep retrovirus and its endogenous variant in sheep, which has more universal implications for the retrovirus-host interplay.

Chapters 16 and 17 continue the in-depth appraisal of retroviruses and their contribution to host genomic evolution. The first of these describes how the epigenetic regulation of endogenous retroviruses can also exert substantial regulatory effects on host genes. These effects can be deleterious or functionally beneficial, resulting for example in ERV-derived promoter and enhancer sequences in the human genome that are epigenetically modified in a cell-type specific manner to help drive differential expression of host genes. The following chapter looks specifically at the effects for good and for disease of the "multiple captures" by animal genomes of envelope genes originating from infectious retroviruses, and in particular the resultant expression of viral proteins, known as syncytins, in host reproduction. Syncytins donate the potential for cell fusion and immune-suppression to the host genetic and physiological repertoire. But we should not forget that these are virus-derived proteins, deriving from so-called viral loci–in other words the selection-transformed former viral genomes embedded in the chromosomes–often promoted by the viruses' own regulatory regions, known as long terminal repeats (LTRs). Although virologists have derived their own terminology for such evolution, symbiologists will see a close parallel with the dynamics of the genetic symbioses involving bacteria and protists that gave rise to mitochondria and plastids. This chapter discusses the difficulty in classification and nomenclature of endogenous retroviruses as well as touching upon the re-activation of a prototype HERV-K virus and the multiple sclerosis-associated virus, MSRV, which is now recognised as belonging to the HERV-W group.

The final two chapters are devoted to medical virology. Chapter 18 is a review of the potential of hepatitis G virus (GBV-C) in slowing the progression of AIDS, caused by HIV-1. It poses a question that might be extrapolated more widely to therapeutics of virus-induced serious diseases: can infection by a pathological virus be ameliorated or even truncated by infection with a rival virus? GBV-C is parenterally transmitted, replicates in hemopoietic cells and T-lymphocytes (like HIV-1) but appears to cause no observable disease pathology. It would appear that the GBV-C virus may have the potential to interfere with HIV-1 replication and the subsequent progressive T-cell depletion and immune deficiency that characterises AIDS. In the minds of the public, and perhaps some biologists, viruses are seen exclusively as the harbingers of disease. The final chapter, 19, eschews such a blinkered outlook to look more universally at the "salutary contributions" of viruses to medicine and public health. The use of vaccines might immediately spring to mind, not least the pioneering discovery by Jenner that the cowpox virus, Vaccinia, could prevent the dreadful scourge of smallpox. This chapter looks in detail at the extraordinary diversity of uses made of a very different group of viruses, the bacteriophages, which, as the name suggests, parasitize bacteria. In particular it explores the phage ubiquity in nature–they are thought to be the most numerous viruses on Earth, estimated at 10^{31} or more–and are being increasingly recognised as major players in the ecology of the oceans. They have the extraordinary ability to move host DNA from one bacterium to

another, with obvious implications for bacterial evolution, and medical implications for the acquisition of resistance to antibacterial drugs. The chapter also looks at the potential of this same property of phages as delivery vehicles in genetic engineering of bacteria, and even non-bacterial cells.

The book concludes with a chapter by the editor, a philosopher of science, on infection-derived viral consortia as natural genetic engineers, including an excellent contribution to the growing perspective of virus-first, as opposed to cell-first, in the origins of life on Earth.

Criticisms:

Overall this book offers a topically relevant compendium for biologists, evolutionary biologists, geneticists and molecular biologists interested in how viruses have contributed to host evolution and, perhaps, even to the origins of life on Earth. While viral symbiosis is mentioned on the cover outline as well as in several chapters, there is no chapter on viral symbiosis per se, or on the contribution of viruses to symbiotic relationships in general. Some readers might be disappointed in the lack of a chapter or detailed discussion of the growing field of the role of viruses in oceanic and other ecologies.