Retroviruses: Molecular Biology, Genomics and Pathogenesis
Edited by Reinhard Kurth and Norbert Bannert

Since the discovery of human immunodeficiency virus (HIV), the world of retrovirology has gained a degree of prominence that is the envy of most other fields of virology. The Retroviridae family is truly enormous, both in the scope of host range and in its molecular and genomic diversity. The editors have gathered together an extensive array of experts that present their respective topics clearly, with a plentiful supportive data. Each chapter concludes with an extensive and up-to-date bibliography.

Retrovirology consists of 16 chapters whose primary aim is to inform experienced readers, but the book also includes sufficient entry-level information that it would entice novices to delve more deeply than they otherwise might. The book contains an array of acronyms, requiring continuous reference to the list of abbreviations at the beginning.

The first 2 chapters cover retrotransposons and endogeneous retroviruses. These chapters are replete with very detailed information on how these elements are classified and the biofunctional consequences of their presence. We learn that several distinctive and overlapping genome defense mechanisms have evolved over time to protect host organisms from these mobile “retro” elements. The lack of clarity with regard to the function of these elements has resulted in an eclectic mixture of descriptive terms, such as “junk DNA,” “controlling elements,” “genomic parasites,” and “evolutionary rubbish.” The section on genome biology of retrotransposons provides a nice backdrop to the battlefront of host-mediated defense against these elements, including cytosine methylation, small RNAs, and APOBECs. The authors of this chapter pose the very interesting thought that retroviruses may be useful in host defense against other infectious (retro)viruses.

The next 5 chapters, chapter 2–7, review the life cycle of retroviruses, from particles, to reverse transcription, to integration, assembly, and release of the daughter virions. After reviewing these chapters and perhaps delving into the bibliographies, readers will have a thorough understanding of the biology of retroviral replication and completion of the life cycle. Chapter 8 finishes this section, with a review of transmission and epidemiology. Reading this chapter, one learns that interspecies transmission occurs; retroviruses as a family have a preferred host but many are somewhat promiscuous with respect to species restriction. Transmission is usually restricted to direct contact, and vaccines have helped decrease the prevalence of infections with such viruses as feline leukemia virus.

Chapter 9, “Pathogenesis and Oncogenic Infections,” is probably the most interesting chapter in the book, and it will appeal to a wide variety of audiences. Pedersen and Sorensen provide a fascinating merger between the worlds of virology and oncology. The approach is very scientific, but one can immediately see that oncovirolgy helps reveal the inner workings of oncology, and translational research opportunities may provide new avenues for antiviral therapy. The 2 tables in this chapter nicely summarize examples of oncogenic retroviruses and oncogenes captured in transducing retroviruses.

Chapter 10, “Pathogenesis of Immunodeficiency Virus Infections,” provides an excellent description of the genome organization of HIV, the function of the proteins produced from the viral genome, and how lentiviruses are often nonpathogenic. The nonpathogenic infection in native hosts reflects a likely adaption to the virus and may provide the infected host with protection for other lentivirus infections. The description of the innate and adaptive immune system will give the reader a good understanding of the immune processes involved in the response to HIV and the immunopathogenesis and neuropathogenesis of HIV and simian immunodeficiency virus (SIV) infections. The authors also review the much-debated “chicken-egg” conundrum of whether long-term nonprogressors (also known as elite controllers) are protected as a result of a potent CD8+ T cell response or because of infection with a weakened virus. Poli and Erflé conclude that the HIV pandemic has taught us that pathogenic retroviruses are not easily eliminated by the innate and adaptive immune systems, that infected cells can be long lived, and that there is a pressing need for ongoing research into all potentially pathogenic microbes, even if they first appear irrelevant. This latter point links with the translational research potential of retrovirology, covered in chapter 9.

“Retroviral Restriction Factors,” chapter 11, nicely complements the information outlined in chapter 10. The review and discussion of the functional significance of the apolipoprotein B mRNA editing enzyme, catalytic polypeptide family (APOBEC), linked with the activities of tripartite motif-containing 5 (TRIM5), etc, are very detailed.
Chapter 12 focuses on the holy grail of vaccinology, which has been the development of vaccines to retroviruses such as HIV. Several noted trials have not yielded the expected immune protection. Norley and Kurth provide a very good explanation of why the classic approach to the development of vaccines is not optimal for HIV. Preexisting immunity to many of the viral vectors used to deliver the encoding DNA is a considerable challenge for the development of pan-isolate anti-HIV vaccines. The single-cycle or single-round immunodeficiency virus strategy has shown promise in stimulating cellular and humoral immunity, but these have failed to yield protective immunity to subsequent challenges with pathogenic SIVmac. The viral quasispecies or heterogeneity phenomenon exhibited by viruses such as HIV is an obvious reason why many vaccines are at best weakly efficacious, despite their ability to generate target specific antibodies. However, the authors rightly point out that protein heterogeneity is not solely responsible for the failure of classic and molecular vaccine strategies. They speculate that the risk benefit of vaccine induced protection may outweigh the disease-causing potential of replication-competent vectors as vaccine agents. This caveat may apply only in those areas of the world where the endemicity of HIV is high and access to antiretroviral therapy is limited. This chapter is essential reading for anyone interested in understanding the history of vaccinology and retrovirology. Chapter 13 covers gene therapy as an adjunct to vaccines in the control of retroviral infections.

Chapters 14 and 15 provide a good amount of detail on nonprimate, primate, and fish retroviruses. These chapters conclude with statements that investigation of these retroviral elements will add to our understanding of disease pathogenesis and that nonhuman retroviral infection represents a clear and present danger.

Chapter 16 provides an in-depth review of the history of the discovery of human T lymphototropic virus and HIV, the work that preceded the discovery of these viruses, and the impact their discovery had on our understanding of the natural history of these infections. This chapter nicely complements the information in chapters 10 and 11.

Finally, the authors provide a helpful perspective on the future of chapter 16 HIV therapies.

Overall, the book is very well written and provides a detailed reference source for scientists; students of virology, immunology, and oncology; those clinically trained in infectious disease; and researchers interested in the current scope of understanding in the field and opportunities for exploration. Given the pressing need for new and evolving therapies as antiretroviral agents, the chapters on oncovirology and vaccine development should be required reading for individuals involved in guiding research priorities.

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